

SIX-MEMBERED MESOIONIC HETEROCYCLES OF THE m-QUINODIMETHANE DIANION TYPE

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Dedicated to Prof. Dr. Erich Ziegler on the occasion of his 70th birthday

ABSTRACT: In this review is brought together the chemistry of six-membered mesoionic heterocycles which can be derived formally from the m-quinodimethane dianion.

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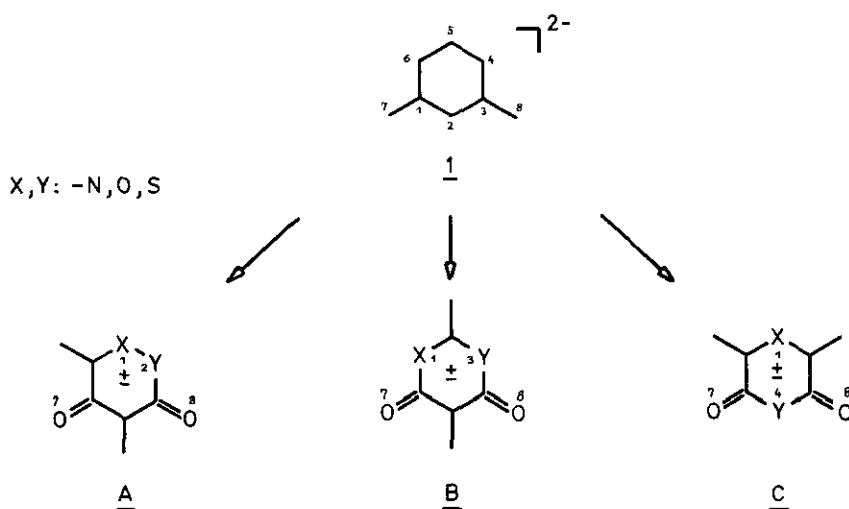
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1. INTRODUCTION

In a recent proposal, the term "meso-ionic" has been confined to five-membered heterocycles "which cannot be represented satisfactorily by any one covalent or polar structure and possess a sextet of electrons in association with the five atoms comprising the ring"¹. We^{2,3} and others^{4,5} prefer a broader definition of this term - i.e. one which covers six-membered heterocycles^{6a} as well, and it seems appropriate to include mesomeric betaine derivatives of heteropentalenes^{6b} and even squaraines⁷. In this review, only those six-membered mesoionic heterocycles will be dealt with which can be derived formally from the m-quinodimethane dianion (Chap. 2.).

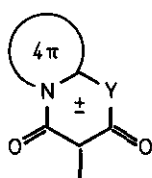
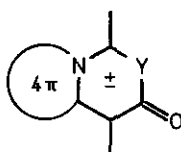
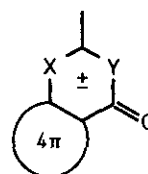
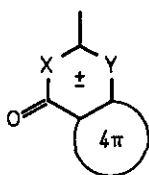
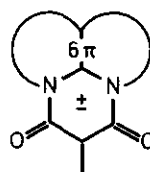
2. DEVELOPMENT OF POSSIBLE SYSTEMS; NOMENCLATURE

If the atoms 4,5, 4,6 or 2,5, and⁸ 7,8 in the m-quinodimethane dianion (1, Scheme 1)

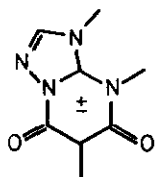
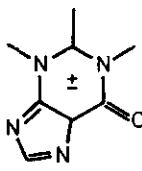
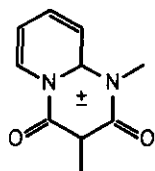
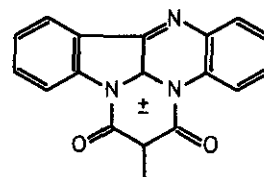


SCHEME 1

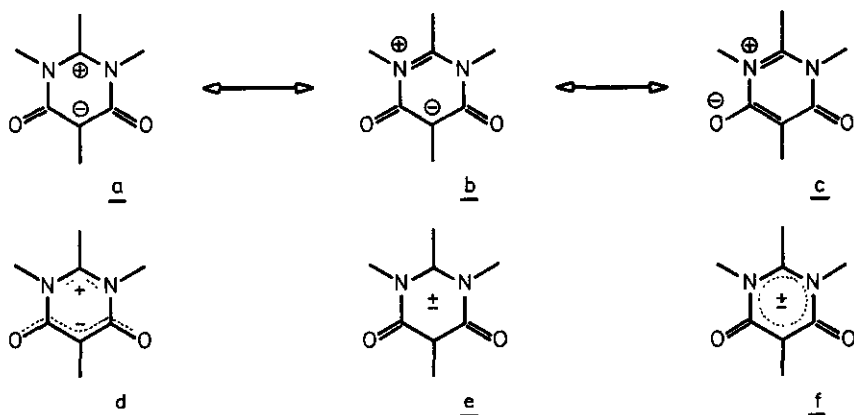
are substituted by N-, O, or S, respectively, three types of monocyclic mesoionic six-membered heterocycles will be obtained (A, B, C) which can be considered as 1,3- (A,C) or 1,4-dipolar (B) systems. Further introduction of appropriate heteroatoms (e.g. -N in position 4 of A, in position 2 and/or 5 of B) enlarges the number of possible heterocycles considerably; the extension of these general types, including selenium¹⁰, provides the possibility of even more systems (Chap. 4.1.4). The connection of atoms C2 and N1, N1 and O7, O7 and C5, or C5 and O8, respectively, with homo- and/or heterocyclic 4π -rings leads to bi- and polycyclic systems (Scheme 2). The extension of this development is straightforward (B5 in Scheme 2), but since examples of these types of compounds are rare, this matter will not be further dealt with.


B 1

B 2

B 3

B 4

B 5

Examples : (Type B2 unknown)


 Type B1

 Type B3

 Type B5
SCHEME 2

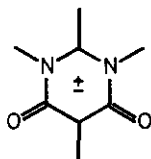
As in the case of five-membered mesoionic heterocycles, their six-membered analogues can be described only by several formulas involving positive and negative charges at various positions (Scheme 3, e.g. a-c); there may be arguments favouring one of these symbols, but it should be recognized that the electron distribution differs



SCHEME 3

from one system to the other and that a "neutral" formulation (d,e) is to be preferred at the moment. Formula d implies a partial double bond character of the C=O-bonds; however, X-ray data do not substantiate this view (Chap. 3). With regard to these results, we advocate a description in which the carbonyl groups (or their equivalents) are explicitly written and which does not anticipate an experimentally unexplored charge distribution. In the opinion of one of these authors (W.F.), formula e serves quite well for this purpose, differing only marginally from a description (f) given by Coburn¹¹ and Glennon¹².

The systematic naming of mesoionic compounds is not standardized. In Chemical Abstracts



- (1) : 5,6-Dihydro-4,6-dioxo-4H-1,3-diazinium hydroxide, inner salt.
- (2) : Anhydro-4-hydroxy-6H-6-oxo-1,3-diazinium hydroxide.
- (3) : 6H-6-Oxo-1,3-diazin-1-ium-4-olate.
- (4) : Mesoionic 4,6-Dioxo-1,3-diazine.

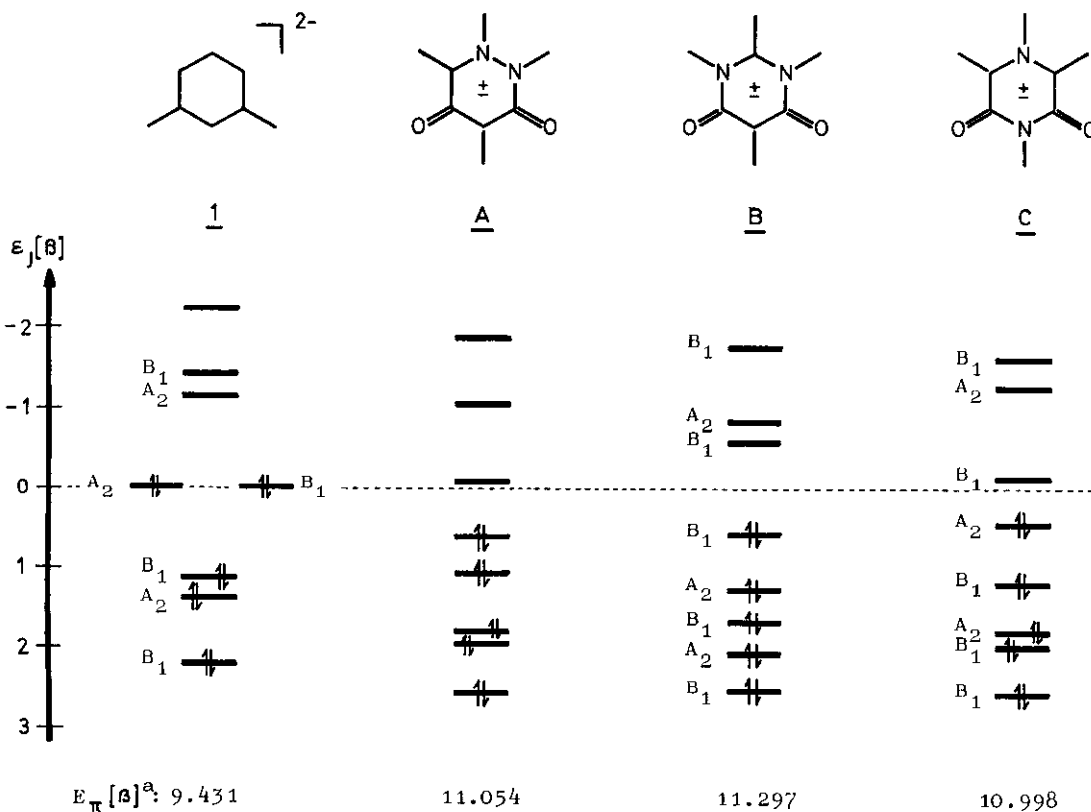
Naming of Mesoionic Six-Membered Heterocycles

SCHEME 4

nomenclature (1), (Scheme 4) is used. Still another systematic description is in use, especially in the German literature ((5)): the mesoionic compound is treated as an intramolecular salt of an alcohol ("olat") with a cationic system ("ium" as suffix). However, these designations are somewhat cumbersome; therefore as a short-hand notation it seems convenient to refer to the mesoionic systems in terms of the parent heterocycle together with the adjective "mesoionic" (Chap. 4).

3. THEORETICAL AND STRUCTURAL INVESTIGATIONS

Even simple HMO calculations reveal that there is a remarkable stabilisation to be found in going from the *m*-quinodimethane dianion (1) to mesoionic heterocycles of type A, B, and C (Scheme 5). HMO-, together with CNDO/2¹⁴-data¹⁵ of the mesoionic



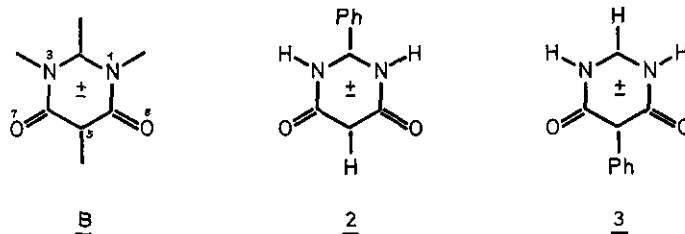
a: Net π -bonding energy¹³.

HMO eigenvalues; heteroatom parameters :

$$\delta\alpha_N = 1.5\beta, \delta\alpha_O = 1.0\beta; \delta\beta_{C-N} = 0.8\beta, \delta\beta_{C-O} = 1.0\beta, \delta\beta_{N-N} = 0.6\beta.$$

SCHEME 5

4,6-dioxo-1,3-diazines B, 2, and 3, show - as expected - a reduced π -electron density at C2 and an enhanced π -electron density at C5. Interestingly, in 2 the heterocyclic ring acts as an electron acceptor, whereas in 3 it acts as an electron donor. These results are also obtained within the Hückel scheme. Both the Hückel and the CNDO/2 method predict a 2-phenyl-substituted 1,3-diazine (2) slightly more stable than the 5-substituted derivative (3). An important conclusion concerning the structures of compound B, as well as mesoionic 4,6-dioxo-1,3-oxazines, can be drawn from these



method q_i, p_{ij}	HMO; <u>B</u> ^a	HMO; <u>2</u>	CNDO/2; <u>2</u> ^b	CNDO/2; <u>3</u> ^b
q_1 ^c	1.6766	1.7048	1.6204	1.5694
q_2	0.4741	0.5918	0.7435	0.7544
q_4	0.7659	0.7650	0.8143	0.8365
q_5	1.2093	1.2161	1.4300	1.3412
q_7	1.7158	1.7161	1.5292	1.4973
p_{12} ^d	0.5751	0.4994	0.6007	0.6642
p_{34}	0.3653	0.3689	0.2920	0.2972
p_{45}	0.6255	0.6233	0.5450	0.5059
p_{47}	0.5811	0.5812	0.7396	0.7545

a: Heteroatom parameters employed as in Scheme 5.

b: Standard geometry¹⁶.

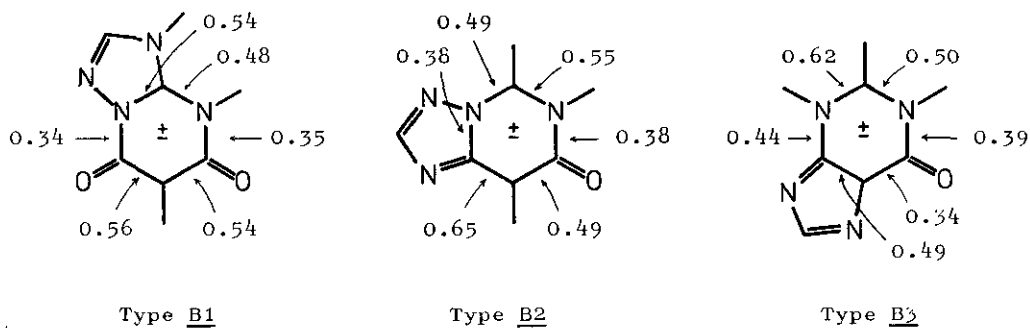
c: π -Electron densities.

d: π -Bond orders.

TABLE 1

calculations. As shown in Table 1, the bond order between N3 and C4 is very small - even lower than the corresponding value in the m-quinodimethane dianion.

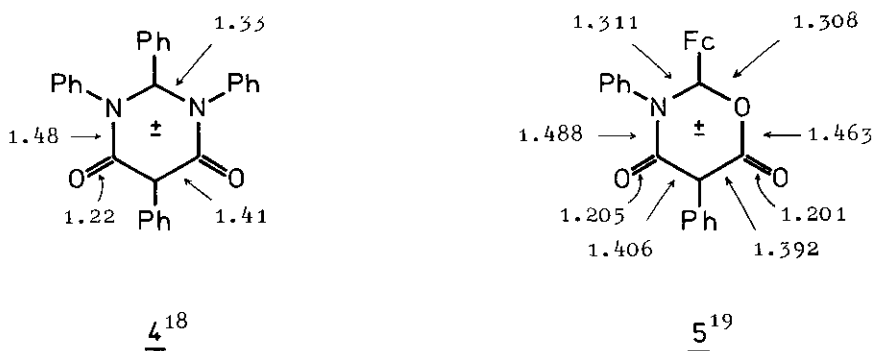
Similar values are obtained for the bicyclic derivatives B1, B2, and B3 with the variable-electronegativity PPP-SCF procedure (VESCOF-MO)^{17a} (Scheme 6). One would expect an unusual long bond length between these atoms; these results have been confirmed recently by X-ray structure determinations. Up to now only two structure de-



Bond Orders in Bicyclic Mesoionic 4,6-Dioxo-1,5-diazines¹⁷.

SCHEME 6

terminations of compounds of type B have been described. Both the mesoionic 1,2,3,5-tetraphenyl-4,6-dioxo-1,5-diazine (4) and the 2-ferrocenyl-1,4-diphenyl-4,6-dioxo-1,3-oxazine (5) show extraordinarily long C-N- and C-O-distances (Scheme 7). These



X-ray Data of 4 and 5; bond lengths given in Å.

SCHEME 7

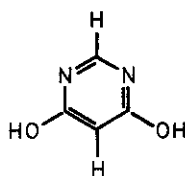
findings have also been discussed¹⁸ in terms of Dähne's concept of two coupled polymethines²⁰. It may be remarked that compounds 4 and 5 show C=O-bond lengths, which are in the range of the values for normal carbonyl groups; a partial double bond character which is suggested by a mesomeric form d (Scheme 3) could not be substantiated.

4. SYNTHESSES AND SPECTROSCOPIC PROPERTIES

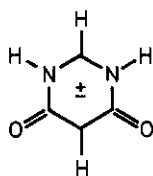
4.1 1,4 - DIPOLAR SYSTEMS

4.1.1 Mesomeric 4,6-Dioxo-1,3-diazines Monocyclic Compounds. Syntheses

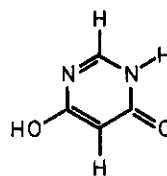
The parent compound of mesomeric 4,6-dioxo-1,3-diazine is the 4,6-dihydropyrimidine (6). Katritzky and coworkers^{21,22} have demonstrated by UV, IR, ¹H-NMR, and pK_a measure-



6

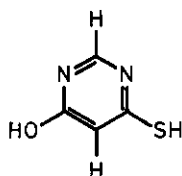


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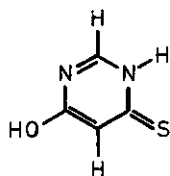


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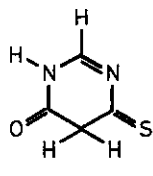
ments that 6 exists in water predominantly as mesomeric 7²³, together with a substantial amount of 6-hydroxypyrimidine-4(3H)-one (8)²⁴. 4-Hydroxy-6-mercaptopyrimidine (9) may exist also in various tautomeric forms. Brown and Tatei²⁵ have advanced arguments



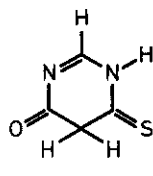
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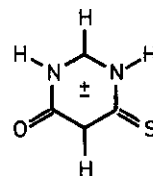
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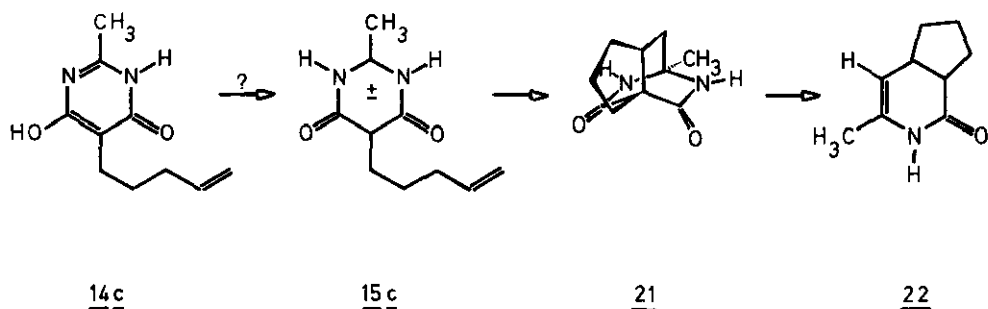
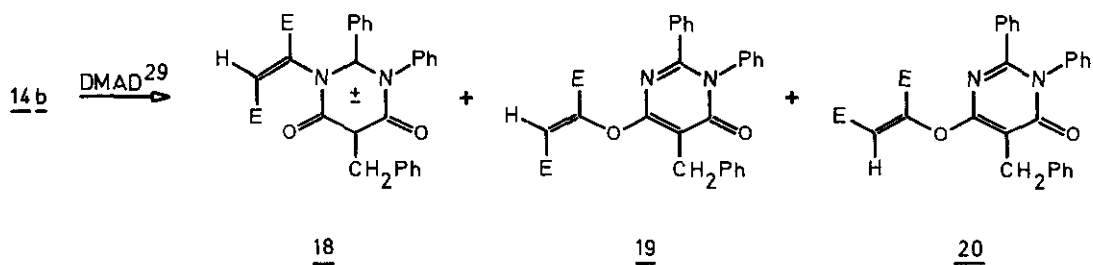
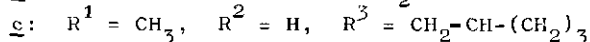
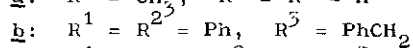
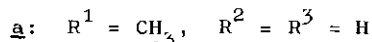
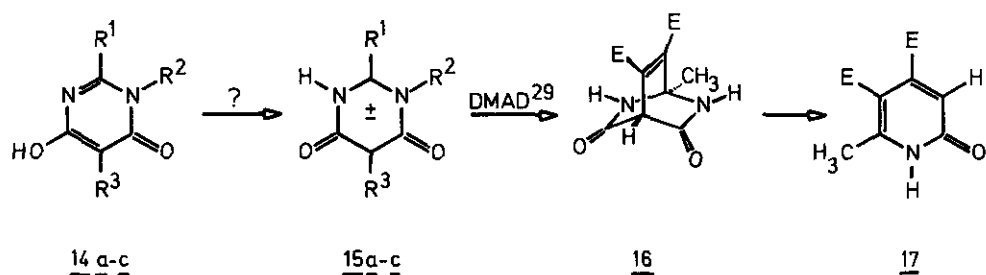
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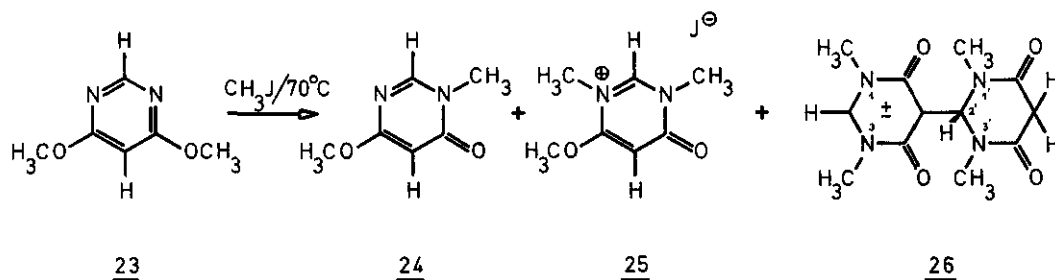
for the oxo-thiono form (11) in water and ethanol, possibly with small amounts of 10 and 12; however, the mesoionic tautomer 13 which has not been taken in account by these authors has recently been considered as the most likely structure²⁶.

It is noteworthy that 6-hydroxy-4-pyrimidones may undergo inter- and intramolecular $[\pi 4+\pi 2]$ -cycloaddition reactions²⁷, possibly via the 1,4-dipolar form (15). In some instances the primary adducts (16,21) have been detected. However, with bulky sub-



stituents in position 2, 3, and 5 of the hydroxypyrimidone (14b) no cycloaddition with DMAD²⁹ could be observed and the addition products 18, 19, and 20 are obtained²⁸.

True monocyclic derivatives of 7 have been described for the first time by M. Prystas^{30,31}. The already reported³³ treatment of 4,6-dimethoxypyrimidine (23) with



SPECTRAL DATA OF COMPOUND 26^{30,34}:

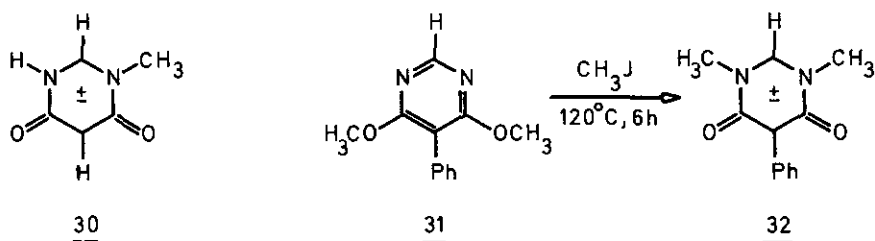
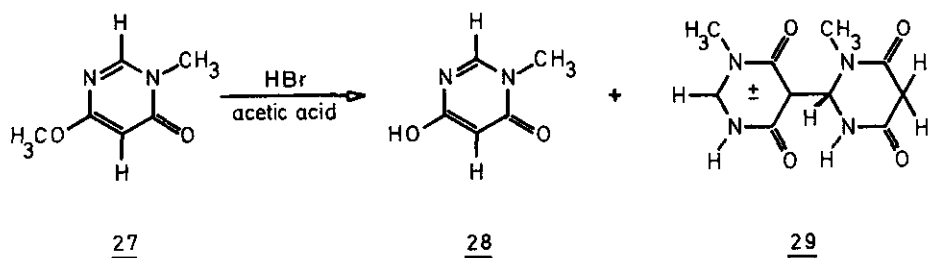
UV ($p_{\text{H}} = 1 - 10$)³⁰ : 214 (4.17), 253 (3.31), 270-295 nm (plateau, 3.09);
UV (neutral medium)³⁴ : 253 (3.34), 258 nm (3.06).

¹ H-NMR	(N1'-CH ₃ , N3'-CH ₃)	(CH ₂)	(N1-CH ₃ , N3-CH ₃)	(C2'-H)	(C2-H)
(DMSO-d ₆) ³⁰ : δ =	2.70	2.93	3.35	5.75	9.28 ppm
(D ₂ O) ³⁴ : δ =	2.68		3.40	5.90	9.05 ppm

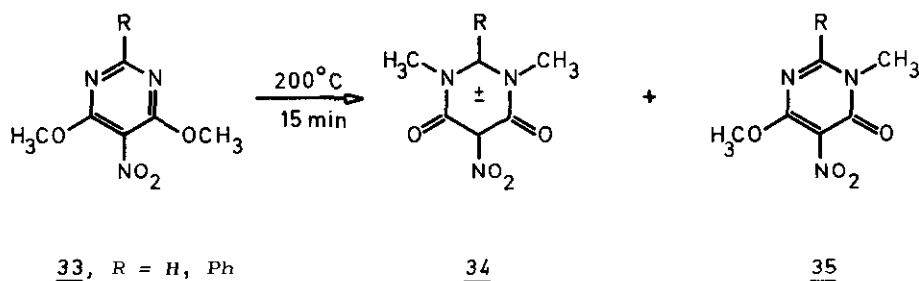
SCHEME 8

methyl iodide yields the known compound 24 accompanied by its methiodide (25) and the high melting (mp 276-278°C (nitromethane)) dimeric mesoionic 4,6-dioxo-1,3-diazine 26. By heating the reaction mixture in a sealed vessel at temperatures exceeding 70°C, an almost quantitative yield of 26 is obtained. Fission of 25 with hydrogen bromide in acetic acid, which has been reported by Soviet authors³⁴ to give the monomeric form of 26, also leads to 26 (90% yield); a short heating of 25 (220°C, 5 min.) produces 26 in 77% yield.

The action of hydrogen bromide in acetic acid on 27 yields 28 (which may exist in solution as 30) and 29³⁰. In the same paper, the reaction of 4,6-dimethoxy-5-phenylpyrimidine (31) with methyl iodide is described to give 32. Later on³⁵, the thermal

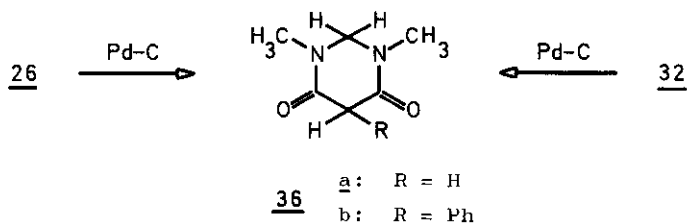


$\delta(\text{N-CH}_3) = 3.31 \text{ ppm}$,
 $\delta(\text{C2-H}) = 9.16 \text{ ppm}$,
 (in DMSO-d_6).
 $\bar{\nu}_{\text{C=O}} = 1688 \text{ cm}^{-1}$.



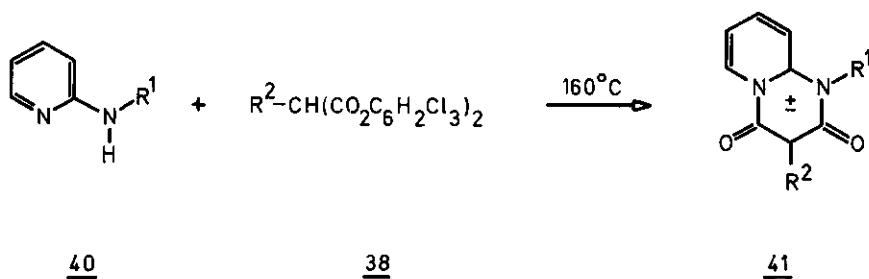
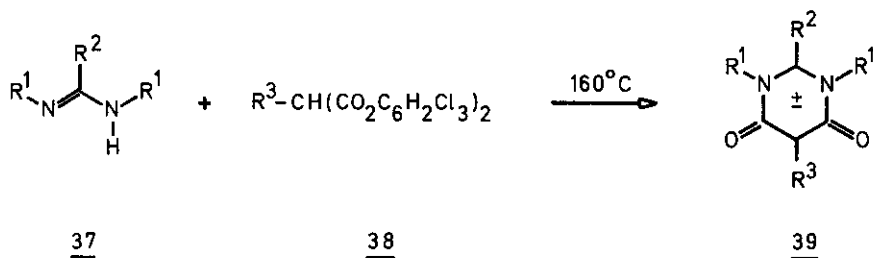
rearrangements of 4,6-dimethoxy-5-nitropyrimidines (33) are reported to yield 34 and 35. Obviously, compounds 35 are intermediates; on heating to 200°C they give the final products (34). The mechanism of these reactions is not yet clear; a double 1,3-dialkyl $\text{O} \rightarrow \text{N}$ migration via a radical mechanism is suggested.

The proposed structures 26 and 32 rest on spectral data (Scheme 8) and chemical reactions. Compound 26 is very readily cleaved by alkali under the formation of malonic acid $\text{N,N}'$ -dimethylamide. Furthermore 26 and 32 are hydrogenated (Pd/C) to give 36a,b; the hydrogenation of 26 proceeds sluggishly because of a very slow attainment of



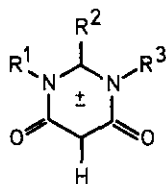
an equilibrium of 26 and its mesoionic monomer. Only this monomer then undergoes the hydrogenation³⁰.

The first general syntheses of mono- and bicyclic mesoionic 4,6-dioxo-1,3-diazines were published almost simultaneously by two research groups^{36,37}. The reaction of N,N'-disubstituted amidines³⁸ (37) with reactive malonic esters as malonic acid bis-(2,4,6-trichlorophenyl)esters³⁹ at 160°C gives 39 in good to excellent yields (trichlorophenyl malonate procedure)³⁷. Bicyclic derivatives (41b-g) are obtained in the same way from N-substituted 2-aminopyridines. Refluxing anisole (bp. 154°C) has proved to be a suitable solvent for this reaction⁴⁰. Longer reaction times and enhanced temperatures should be avoided since liberated trichlorophenol specifically catalyzes a rearrangement of the mesoions 39⁴¹ (See Chap. 5.5). Both compounds 41a and 41h were



<u>39</u>	R ¹	R ²	R ³	<u>41</u>	R ¹	R ²
<u>a</u>	Ph	Ph	Ph	<u>a</u>	Ph	H
<u>b</u>	Ph	Ph	PhCH ₂	<u>b</u>	Ph	Ph
<u>c</u>	Ph	Ph	(CH ₃) ₂ CH	<u>c</u>	Ph	PhCH ₂
<u>d</u>	Ph	CH ₃	Ph	<u>d</u>	Ph	Et
<u>e</u>	Ph	CH ₃	PhCH ₂	<u>e</u>	Ph	(CH ₃) ₂ CH
<u>f</u>	Ph	H	PhCH ₂	<u>f</u>	PhCH ₂	PhCH ₂
<u>g</u>	Ph	Ph	Et	<u>g</u>	2-pyridyl	Et
<u>h</u>	(4-OCH ₃)C ₆ H ₄	Ph	Et	<u>h</u>	CH ₃	H
<u>i</u>	(4-NO ₂)C ₆ H ₄	Ph	Et			
<u>j</u>	(4-OCH ₃)C ₆ H ₄	Ph	PhCH ₂			
<u>k</u>	(4-NO ₂)C ₆ H ₄	Ph	PhCH ₂			

prepared from the corresponding N-substituted 2-aminopyridine with carbon suboxide^{42,43} at room temperature in the absence (41a)³⁷ or presence (41h)³⁶ of a catalytic amount of AlCl₃. (For further details on bi- and polycyclic derivatives, see below.) This reaction has also been used for the preparation of monocyclic mesoions

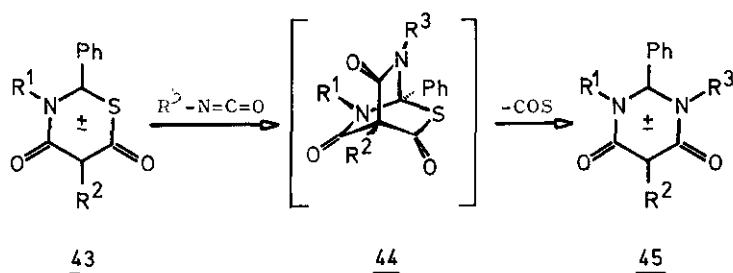
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<u>42</u>	R ¹	R ²	R ³
<u>a</u>	Ph	Ph	Ph
<u>b</u>	CH ₃	Ph	Ph
<u>c</u>	Ph	H	Ph
<u>d</u>	Ph	CH ₃	Ph
<u>e</u>	PhCH ₂ O	Ph	Ph
<u>f</u>	Ph	CH ₃ S	Ph
<u>g</u>	Ph	EtS	Ph
<u>h</u>	(4-CH ₃)C ₆ H ₄	CH ₃ S	(4-CH ₃)C ₆ H ₄
<u>i</u>	(4-CH ₃)C ₆ H ₄	EtS	(4-CH ₃)C ₆ H ₄
<u>j</u>	(2-CH ₃)C ₆ H ₄	CH ₃ S	(2-CH ₃)C ₆ H ₄
<u>k</u>	(2-CH ₃)C ₆ H ₄	EtS	(2-CH ₃)C ₆ H ₄
<u>l</u>	C ₆ H ₁₁	CH ₃ O	C ₆ H ₁₁
<u>m</u>	C ₆ H ₁₁	EtO	C ₆ H ₁₁
<u>n</u>	Ph	EtO	Ph
<u>o</u>	(4-CH ₃)C ₆ H ₄	EtO	(4-CH ₃)C ₆ H ₄

bearing no substituent at C5 (42a-d^{44a}, 42e (from an oxime ether)^{44b}, 42f-k (from isothioureas)^{44b}, 42l-o (from isoureas)^{44b}).

The reactivity of the bielectrophilic malonic acid derivative can be enhanced by the use of bis(pentachlorophenyl)esters. Thus 39a is prepared from *N,N'*-diphenylbenzenecarboximidamide and malonic acid bis(pentachlorophenyl)ester in acetone with two equivalents of triethylamine at room temperature^{45a}. However, the yields obtained by this procedure amount to about 50% of the thermal condensation reaction only^{48b}. The extension to bicyclic "malonyl- α -aminopyridines" has been reported^{45a}.

In a further synthesis of monocyclic compounds of type 39 mesoionic 4,6-dioxo-1,3-thiazines (43) are used as starting materials⁴⁶, which in turn are available from *N*-monosubstituted thioamides and reactive malonic acid derivatives (malonic acid dichlorides, substituted chlorocarbonylketenes; see Chap. 4.1.2). When the compounds 43 are heated together with aryl isocyanates, the mesoionic 4,6-dioxo-1,3-diazines 45 are obtained in 35-83% yield; an intermediate of type 44 is possibly involved which on loss of COS gives the final products. This synthetic sequence may be pre-

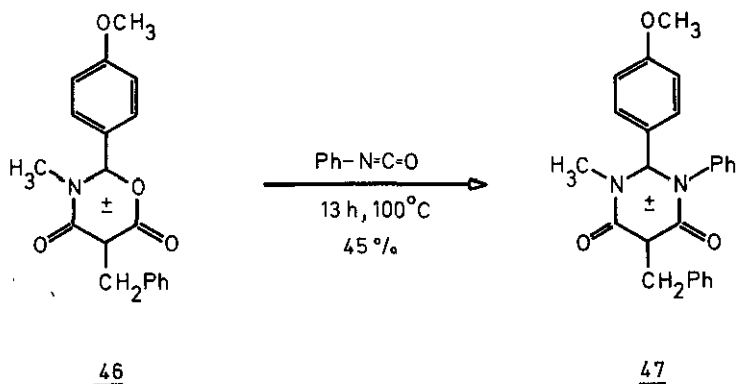


<u>45</u>	R ¹	R ²	R ³
<u>a</u> ^a	Ph	Ph	Ph
<u>b</u> ^b	Ph	PhCH ₂	Ph
<u>c</u>	PhCH ₂	Ph	Ph
<u>d</u>	PhCH ₂	Ph	(4-Cl)C ₆ H ₄

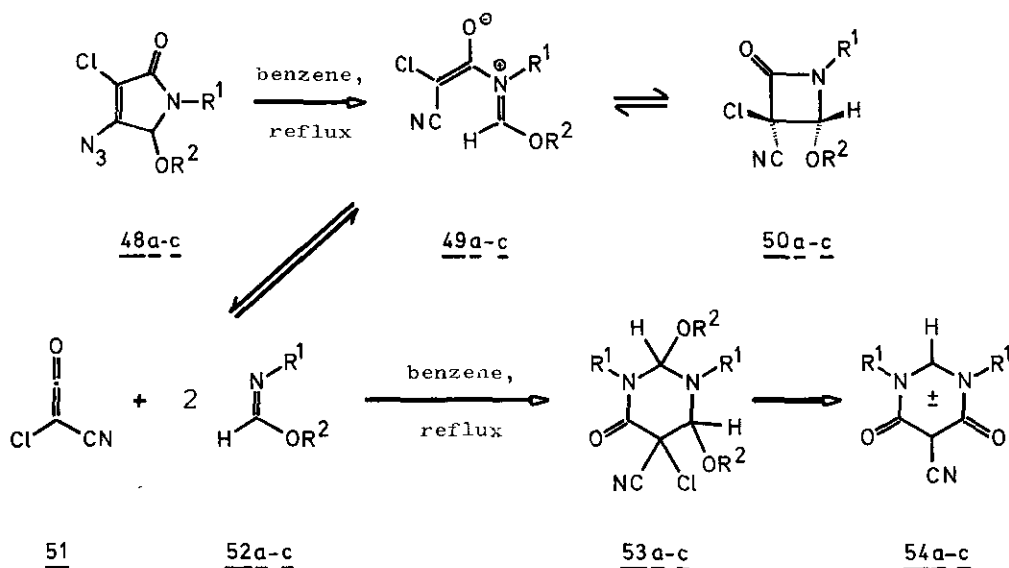
a: \equiv 39a; b: \equiv 39b

ferred over the trichlorophenyl malonate procedure described above in those cases where *N*-monosubstituted thioamides are readily available.

In the same way, mesoionic 4,6-dioxo-1,3-oxazines^{3,47-50} (Chap. 4.1.2) (e.g. 46) may react with aryl isocyanates to produce 4,6-dioxo-1,3-diazines (e.g. 47)⁵¹.



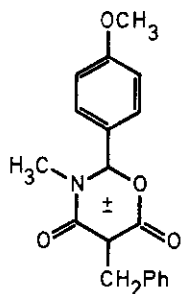
An unusual route to mesoionic 4,6-dioxo-1,3-diazines was described by H.W. Moore and coworkers⁵². When 4-azido-2-pyrrolinones (48) were thermolyzed in refluxing benzene or when one equivalent each of chlorocyanoketene (51)⁵³ and the formimidates 52 were subjected to the same reaction conditions, in addition to the major β -lactams (50)



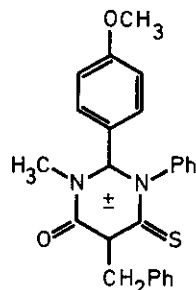
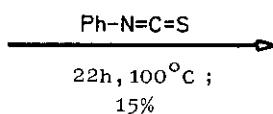
<u>48-50, 52-54</u>	R ¹	R ²
<u>a</u>	CH ₃	CH ₃
<u>b</u>	CH ₃	Et
<u>c</u>	C ₆ H ₁₁	Et

SCHEME 9

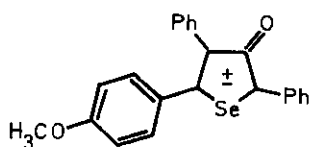
the 4,6-dioxo-1,3-diazines 54 were isolated (5-20%). Yields, however can be improved by carrying out the thermolysis in the presence of an excess of the formimidates 52. A mechanism which accommodates to the observed products is given in Scheme 9. Mesoionic 4-oxo-6-thiono-1,3-diazine (13) is the parent compound for unsymmetrical systems of this type. Only a few monocyclic - and polycyclic (see below) - derivatives have been described hitherto. On heating with phenyl isothiocyanate, the meso-



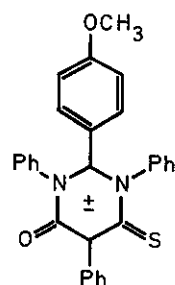
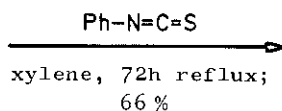
46



55



56



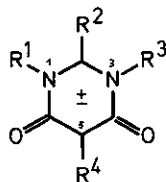
57

ionic oxazine 46 yields 55⁵¹ with loss of CO₂. In a comparable reaction, 56 reacts with the same heterocumulene to yield 57⁵⁴. This seems to be the first example of the conversion of a five-membered mesoionic ring system into a six-membered mesoionic ring system.

Monocyclic Compounds. Spectral Data

Monocyclic mesoionic 4,6-dioxo-1,3-diazines are colorless (Table 2, compounds a-d) or slightly yellow to yellow-orange (compound e, 42f-o) well-crystallized high melting solids. In their IR spectra, they exhibit a very strong carbonyl band at 1650 to 1670 cm⁻¹ normally associated with a shoulder or a second absorption at slightly higher wave numbers. The UV spectra show a long wavelength absorption at approximately 350 nm ($\epsilon: 10^4$) with a second maximum near 260 nm⁵⁵. The ¹H-NMR spectra show

TABLE 2: Spectral Data of Monocyclic Mesoionic 4,6-Dioxo-1,3-diazines
(Selected examples and data)



	R ¹	R ²	R ³	R ⁴	IR (KBr); (in cm ⁻¹)	UV; λ (lg ε) (in nm)	¹ H-NMR; (δ in ppm)	Ref.
<u>a</u>	Ph	Ph	Ph	H	1700, 1665	215 (4.62), 235 (4.25) ^a , 255 (3.96) ^a , 270-350(plateau) ^c	4.99 (C5-H) ^b	44
<u>b</u>	CH ₃	Ph	Ph	H	1695, 1670	217 (4.27), 255 (3.39), 275-350(plateau) ^c	3.05 (N1-CH ₃), 4.87 (C5-H) ^b	44
<u>c</u>	Ph	H	Ph	H	1680, 1670	243 (4.36), 280 (3.65) ^a , 315-360(plateau) ^d	4.75 (C5-H), 9.32 (C2-H) ^b	44
<u>d</u>	Ph	CH ₃	Ph	H	1699, 1655	208 (4.66), 252 (3.82), 345-370(plateau) ^c	1.90 (C2-CH ₃), 4.79 (C5-H) ^b	44
<u>e</u>	Ph	Ph	Ph	Ph	1680 ^a , 1660- 1630; 1695, 1652	224 (4.558), 357 (3.982) ^e		37, 40
<u>f</u>	Ph	Ph	Ph	PhCH ₂	1680 ^a , 1655- 1630; 1651, 1693	220 (4.565), 260 (4.238), 345 (3.774) ^e	3.88 (CH ₂) ^f	37, 40

TABLE 2 (Continued)

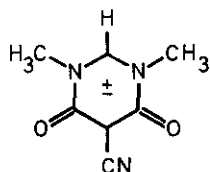
	R ¹	R ²	R ³	R ⁴	IR (KBr); (in cm ⁻¹)	UV; λ (lg ε) (in nm)	¹ H-NMR; (δ in ppm)	Ref.
<u>g</u>	Ph	CH ₃	Ph	Ph	1670 ^a , 1655-1630		1.92 (C2-CH ₃) ^b	37
<u>h</u>	Ph	CH ₃	Ph	PhCH ₂	1680, 1655-1630		1.88 (C2-CH ₃) ^b , 3.65 (CH ₂) ^b	37
<u>i</u>	Ph	H	Ph	PhCH ₂	1685 ^a , 1675-1650		3.68 (CH ₂), 9.40 (C2-H) ^b	37
<u>j</u>	Ph	Ph	Ph	Et	1652, 1690	222 (4.599), 260 (4.435) ^a , 345 (4.148) ^e	1.20 (t, J=7.2 Hz, CH ₃) 2.62 (q, CH ₂) ^f	40
<u>k</u>	Ph	(4-OCH ₃)C ₆ H ₄	Ph	Et	1648, 1694	210 (4.651) ^a , 224 (4.649), 260 (4.495) ^a , 345 (4.141) ^e	1.20 (CH ₃), 2.60 (CH ₂), 3.60 (OCH ₃) ^f	40
<u>l</u>	Ph	(4-NO ₂)C ₆ H ₄	Ph	Et	1650, 1687	213 (4.664), 260 (4.540) ^a , 290 (4.492) ^a , 345-350 (4.042) ^e	1.20 (CH ₃), 2.60 (CH ₂) ^f	40
<u>m</u>	CH ₃	H	CH ₃	CN	1693		3.24 (CH ₃), 9.68 (C2-H)	52

a : Shoulder ; b : DMSO-d₆ ; c : CH₃OH ; d : CH₂Cl₂ ; e : CH₃CN ; f : CDCl₃ .

the C2-proton at very low field (comp. 26,32) in the pyrimidine region⁵⁶. The N-CH₃ group appears in the amide area with a small downfield shift (32: δ (CH₃)=3.16 ppm)^{30,3}. H5 suffers from a remarkable downfield shift compared with CH₂-groups flanked by two carbonyl moieties; whether these values are the result of two opposite effects -a ring current effect and a highfield shift induced by a partial negative charge at C5- is open to question. In trifluoroacetic acid there occurs protonation on the exocyclic oxygen atom; this is accompanied by a considerable downfield shift of C5-H and C2-CH₃ (δ = 1.5 and 0.5 ppm, respectively, for compounds a-d of Table 2)⁴⁴. Only a few ¹³C-NMR data have been reported. Two representative examples are shown

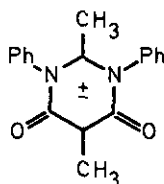
¹³C-NMR (DMSO-d₆);
 δ in ppm; ref.52.

34.7,
 73.9,
 116.5,
 154.5,
 159.0.



¹³C-NMR (DMSO-d₆);
 δ in ppm; ref.57.

88.0 (C₅),
 156.0 (C₂),
 157.0 (C=O).



¹³C-NMR Data of Mesoionic 4,6-Dioxo-1,3-diazines.

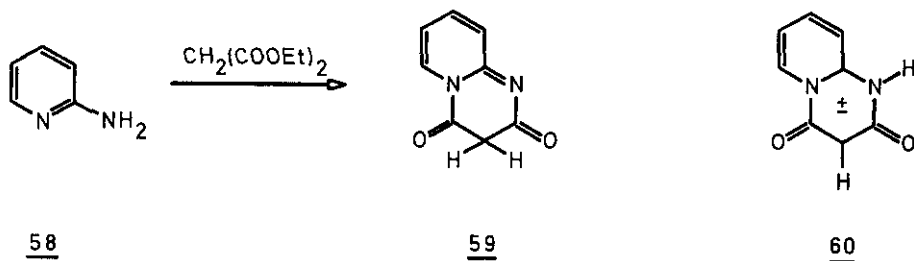
SCHEME 10

in Scheme 10. Attempts have been made to relate charge densities (calculated by a MINDO method) and ¹³C-NMR chemical shifts⁵⁷. It is interesting to note that there seems to be no significant delocalisation, neither of a positive or of a negative charge, into phenyl-substituted derivatives⁵⁷.

The charge distribution in monocyclic and bicyclic mesoionic 4,6-dioxo-1,3-diazines (and a bicyclic 4,6-dioxo-1,3,5-triazine; see Chap. 4.1.6) has been investigated by ESCA spectroscopy⁵⁸. In the former two types of compounds the positive charge is distributed among both nitrogen atoms; the N-1s bond energies are found to be in the region of 401.1-401.5 eV⁵⁹.

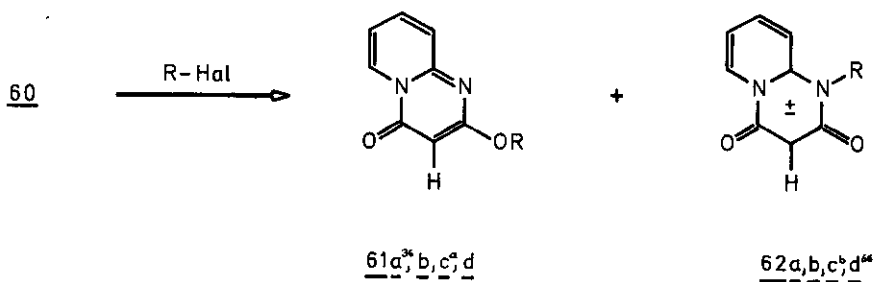
B1- and Polycyclic Compounds. Syntheses

2-Aminopyridine (58) reacts with diethyl malonate to give a compound named "malonyl- α -aminopyridine"^{60,61} which has been formulated by Tschitschibabin in the dioxo-form (59). As Snyder and Robinson have pointed out, the physical properties (e.g. high mp 301-302°C⁶², low solubility in non-polar solvents) were in contrast to this for-



mula; these authors favored hydroxy-oxo-structures. Katritzky and Waring⁶² have indicated that only the mesoionic formulation (60) is in accordance with the physical properties of "malonyl- α -aminopyridine"²².

Alkylation of "malonyl- α -aminopyridine" with alkyl halogenides yields - in contrast with previous investigations⁶³ - O- and N-alkylated products^{64,65}. C-Alkylation seems



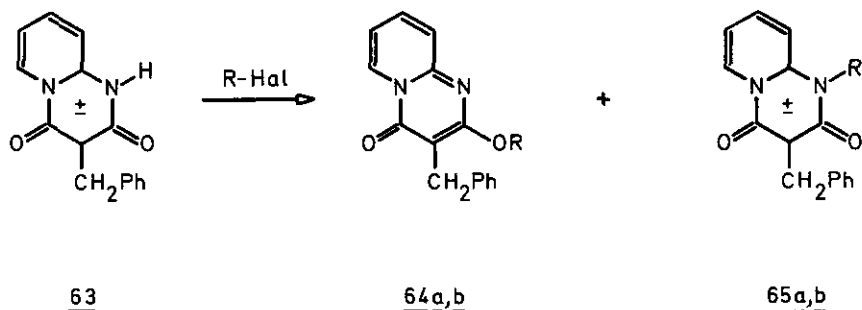
<u>61,62</u>	R
<u>a</u>	CH ₃
<u>b</u>	CH≡C-CH ₂
<u>c</u>	CH ₃ -CH ₂ -CH ₂
<u>d</u>	PhCH ₂

a: Obtained by direct alkylation.

b: By reduction of 62b (Pd/CaCO₃).

SCHEME 11

to have been observed in only one case, i.e. where the reaction of 60 with benzyl bromide (DMF/K₂CO₃) yields - besides 61d/62d (40% and 20%, resp.) - 5% of a mixture



<u>64,65</u>	R
<u>a</u>	CH ₃
<u>b</u>	PhCH ₂ (≡ <u>41f</u>)

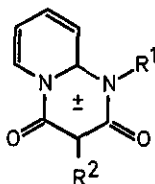
SCHEME 12

which consists of 64b and 65b (Scheme 12). These compounds result from a primary C-alkylation⁶⁵. The methylation with methyl iodide which has been reported⁶² to give 62a yields 61a also⁶⁵. A mixture of 61a (20%) and 62a (50%) is also obtained from 60 and diazomethane (in dioxane/methanol)⁶⁵. The alkylation of 63 yields O- and N-products also (64,65)⁶⁵.

IR, UV, and ¹H-NMR spectra of mesoionic pyrido[1,2-a]pyrimidine-2,4-diones have been investigated extensively^{36,45,62,65,68b}. Some representative examples are collected in Table 3. The IR spectra show at least two bands in the C=O-region. The UV spectra exhibit an absorption at longer wavelengths with an extinction coefficient of approx. 4 · 10³, depending somewhat on the substitution at N1 and C3. (For details with figures of IR and UV spectra, see loc.cit.68b) The ¹H-NMR spectra are similar with those of the monocyclic compounds (see Table 2) in respect of the C3-proton and the N-alkyl groups.

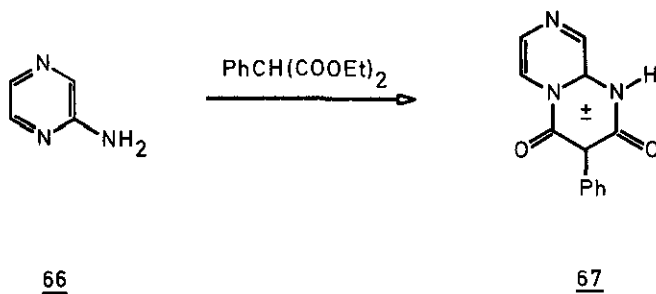
The alkylation reactions have been extended to various substituted mesoionic pyrido[1,2-a]pyrimidine-2,4-diones⁶⁸ and to 67, which is obtained by condensing aminopyrazine (66) with ethyl phenyl malonate⁶⁹. Physical properties of 67 indicate that it exists predominantly as mesoion. It differs chemically from "malonyl- α -aminopyridine" in such a way as to fail to produce a chloride when treated with POCl₃; base-catalyzed alkylation resulted only in O-alkylated products.

TABLE 3: Spectral Data of Mesolonic Pyrido[1,2-a]pyrimidine-2,4-diones
(Selected examples and data)

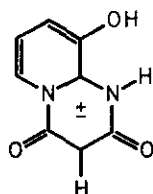
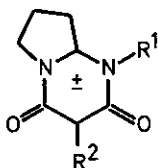


	R ¹	R ²	IR (cm ⁻¹)	UV; λ (lg ε) (nm)	¹ H-NMR; δ in ppm	Ref.
a	H	H	1651, 1690, 2700 ^a ; 1640, 1660, 1710, 2700 ^b	230(4.48), 252(4.10), 312(3.63) ^c	4.98 (C3-H) ^d	62, 68b
b	H	n-C ₄ H ₉	1630, 1670, 2400- 2900	330, 345 ^e		45
c	CH ₃	H	1665, 1720	230(4.51), 257(4.08), 322(3.67) ^{f, g}	3.53 (CH ₃), 4.88 (C3-H) ^d	36, 62
d	Ph	H	1640-1685, 1700, 1710		4.95 (C3-H) ^d	65
e	Ph	PhCH ₂	1600-1630, 1690, 1700		3.86 (CH ₂) ^d	65
f	Ph	Ph	1620-1645, 1680			65

a: Nujol⁶²; b: KBr^{68b}; c: 0.01N H₂SO₄⁶²; d: DMSO-d₆; e: Details (p_H and solvent dependence) see loc.cit.45; f: In phosphate buffer (p_H=6.99), identical values in methanol; g: Fig.of the UV spectrum (EtOH) see loc.cit. 68b.



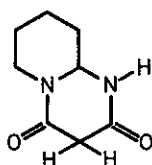
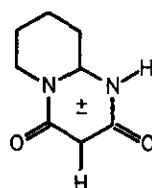
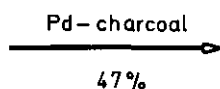
Spectral evidence has been given for the mesoionic structures 68⁷⁰, 69⁷¹, and 71²¹;

6869

<u>69</u>	R ¹	R ²	Ref.
<u>a</u>	H	H	a
<u>b</u>	H	CH ₃	a
<u>c</u>	H	Et	a
<u>d</u>	H	C ₄ H ₉	a
<u>e</u>	H	Ph	a
<u>f</u>	CH ₃	H	a, b
<u>g</u>	CH ₃	Ph	a, b

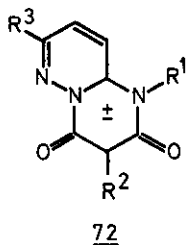
a: From 2-aminopyrrolidine and malonic ester.

b: By alkylation with (CH₃)₂SO₄.

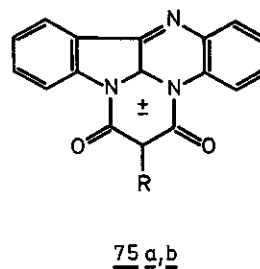
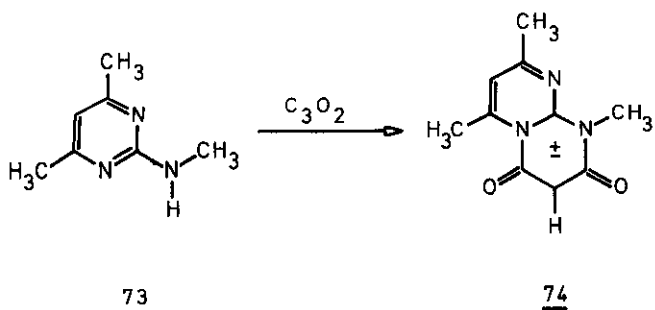
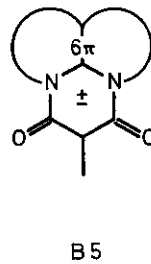
7071

this latter compound was obtained by dehydrogenation of perhydropyrido[1,2-a]pyrimidine-2,4-dione (70).

As already mentioned in the subsection "Monocyclic Compounds", mesoionic systems of type 62 (and 65) can be conveniently prepared from the corresponding N-substituted aminopyridine with a bielectrophilic malonic acid derivative (C₃O₂, substituted malonyl dichlorides, substituted chlorocarbonylketenes, alkyl malonates, bis(2,4,6-trichlorophenyl) malonic esters). This procedure has been extended to various bi- and polycyclic systems which contain an amidine moiety. Mesoionic pyrimido[1,2-b]-pyridazine-2,4-diones (72) were prepared by the condensation of 3-(N-substituted amino)pyridazines with bis(2,4,6-trichlorophenyl) methylmalonate at 160°C under a slow stream of nitrogen until a clear melt was obtained (7-10 min.); purification was conveniently achieved by recrystallization from acetonitrile⁷². The chloro group could be displaced to give 72 with substituents such as methoxy, anilino, morpholino,



R¹=Alkyl, Aryl; R²=CH₃; R³=Cl ^{72a}
 R¹=R²=Alkyl, Aryl; R³=Cl, OAlkyl ^{72b}

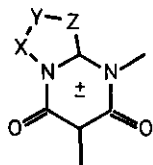


a: R=Ph; b: R=CH₂Ph

N-methylpiperazyl, and hydrogen. Some of these compounds exhibited evidence of antimicrobial activity^{72a}. The mesoionic 2,4-dioxopyrimido[1,2-a]pyrimidine (74) was prepared from 4,6-dimethyl-2-methylaminopyrimidine (73) and carbon suboxide⁷³.

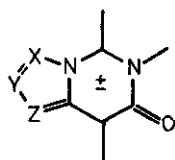
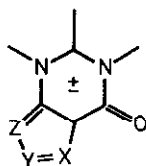
A very interesting system (75) has been described which can formally be considered as a dibenzo analogue of a 12π-system (B5, Scheme 2)³⁷. These compounds can be prepared in the usual manner from indophenazine using the trichlorophenyl malonate procedure; they form deep green (75a) or deep red (75b) high melting solids which seem to show a pronounced solvatochromic behavior. Further compounds of this type have not been described as yet.

The connection of mesoionic 4,6-dioxo-1,3-diazines with a five-membered heterocyclic ring leads to a class of compounds which have been called "mesoionic purinone analogues" (B1: mesoionic xanthenes; B2: mesoionic purin-2-ones; B3: mesoionic hypoxanthenes)¹⁷. In this review, these bicyclic systems (the extension to polycyclic analogues is straightforward) will be treated as members of mesoionic six-membered heterocycles of type B (Scheme 1). Only a few examples have been described up until now.


B1

	a*	b	c	d	e	f	g	h	i	J	k	l
X	CH	CH	CH	CH	CH	CH	S	N-	O	N	N	N
Y	CH	CH	CH	N	N	N	CH	CH	CH	CH	CH	CH
Z	S	N-	O	S	N-	O	CH	CH	CH	S	N-	O

+: Selected examples

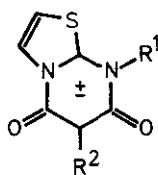

B2

B3

	a*	b	c	d	e	f	g
X	CH	CH	N	CH	N	N	N
Y	CH	N	CH	N	CH	N	N
Z	N	CH	CH	N	N	CH	CH

+: Selected examples

 Mesoionic Purinone Analogues ¹⁷
SCHEME 13

Mesoionic thiazolo[3,2-a]pyrimidine-5,7-diones (76) have been prepared from N-substituted 2-amino-1,3-thiazoles via the trichlorophenyl malonate route ^{11,12} or with (chlorocarbonyl)phenylketene ⁷⁴. They form colorless to slightly yellow high melting


76 a-g

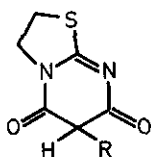
<u>76</u>	R ¹	R ²	Ref. ^a
<u>a</u>	Et	H	11 ^b
<u>b</u>	Et	CH ₃	11
<u>c</u>	Et	PhCH ₂	11
<u>d</u>	PhCH ₂	H	11
<u>e</u>	PhCH ₂	CH ₃	11
<u>f</u>	PhCH ₂	PhCH ₂	11
<u>g</u>	CH ₃	Ph	74

a: Selected examples.

 b: Also obtained with C₃O₂.

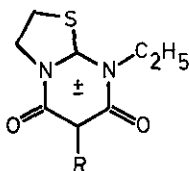
solids which can be purified by recrystallization from toluene, benzene, ethanol, DMF etc. The UV spectrum of 76a shows bands at 242 (4.46), 248 (4.44), and 280 nm (3.58) (in H_2O)⁷⁵. The IR spectra show two C=O-bands which are generally in the region of 1630-1655 and 1680-1690 cm^{-1} ; the average integrated intensities are in the same range as those determined for sydnones and isosydnones and are much higher than those observed for covalent carbonyl groups, indicating a highly polar nature of these pseudocarbonyl-groups. On the other hand, the carbonyl stretching frequencies suggest bond orders similar to covalent models. These findings support the charge distribution and bond order calculations¹⁷. The 1H -NMR spectra show the proton at C5 ($R^2=H$) at $\delta = 4.5$ to 5.5 ppm; in CF_3COOH this signal is shifted downfield (ca. 1.5-1.8 ppm) with an appreciable broadening (comp. 44a). In CD_3OD/CF_3COOH this proton is exchanged immediately. The CH_2 -group in 76a appears at a remarkably low field position ($\delta = 4.2$ ppm in $CDCl_3$).

Saturated analogues of 76 (78) also have been prepared by the trichlorophenyl malonate procedure⁷⁶. These compounds could not be prepared by alkylation of 77; only

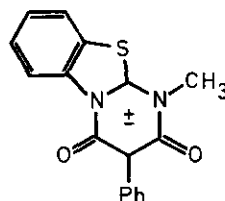


77

R = H, Et



78

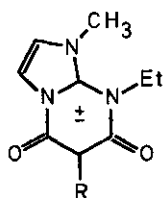
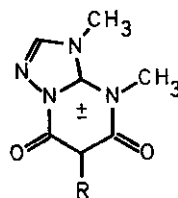


79

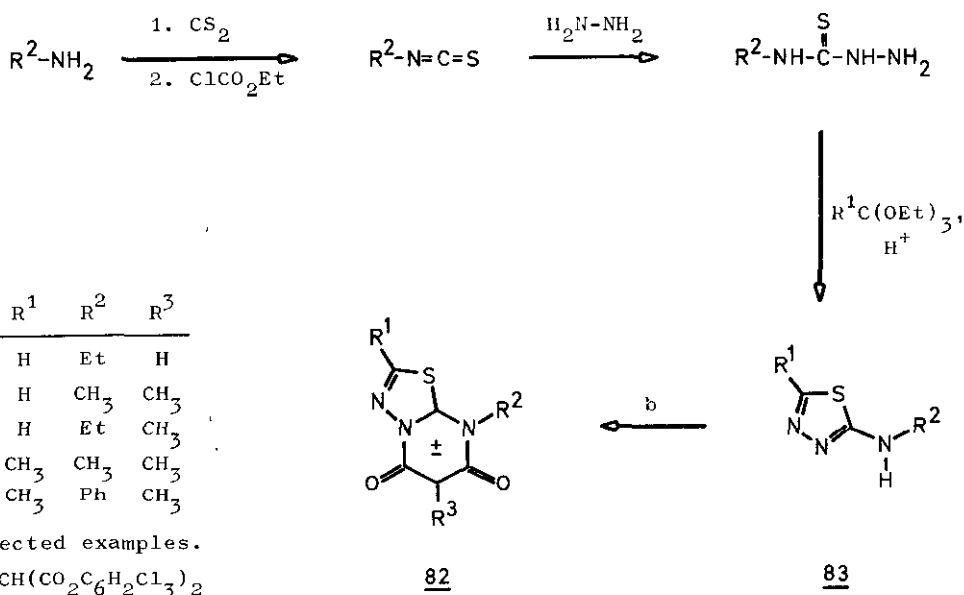
O-alkylation occurred⁷⁶. A benzo analogue of 76 (79) is obtained in bright yellow prisms from the corresponding 2-(N-methylamino)-1,3-benzothiazole and (chlorocarbonyl)phenylketene in dry THF⁷³. The N- CH_3 group appeared at $\delta = 3.68$ ppm ($CDCl_3$) in the 1H -NMR spectrum (76g: $\delta = 3.66$ ppm).

A number of mesoionic thiazolo[3,2-a]pyrimidine-5,7-diones (76) were found to exhibit antibacterial activity against both Gram-negative and Gram-positive organisms⁷⁷. These compounds also have been evaluated as inhibitors of cyclic AMP phosphodiesterase; some substances show theophylline-like activity¹².

Mesoionic imidazo[1,2-a]pyrimidines (80) and 1,2,4-triazolo[1,5-a]pyrimidines (81) were prepared from the corresponding N-substituted aminoheterocycles via the trichlorophenyl malonate procedure⁷⁸ (colorless or slightly colored products). In the carbonyl region, their IR spectra resemble quite closely those of the corresponding mesoionic 4,6-dioxo-1,3-diazines.


 $R = \text{H}, \text{CH}_3$
80a,b

 $R = \text{H}, \text{CH}_3, \text{Et}, n\text{-C}_3\text{H}_7$
81a-d

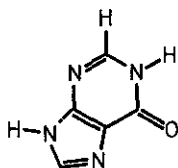
Mesoionic 1,3,4-thiadiazolo[3,2-a]pyrimidine-5,7-diones (82) were obtained from 2-sec-amino-1,3,4-thiadiazoles (83) via the trichlorophenyl malonate route^{77,79}. The



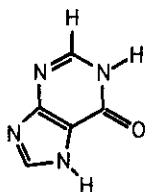
SCHEME 14

required thiadiazoles were prepared from the corresponding alkylamines by conversion to alkyl isothiocyanates (Kaluza reaction)⁸⁰ which were then treated with hydrazine to give N-alkylthiosemicarbazides; treatment of these compounds with triethyl orthoformate under acid catalysis gave the desired thiadiazoles 83 in high yields⁸¹.

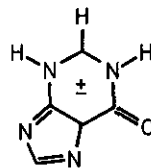
Whereas compounds of type B2 (mesoionic purin-2-one analogues, Scheme 13) are unknown, derivatives of type B3 (mesoionic hypoxanthines) have been described. The parent system can exist in various tautomeric forms (e.g. 84,85); 6-oxopurine (hypo-



84



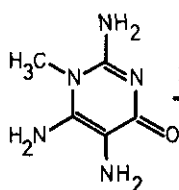
85



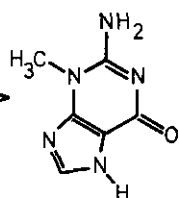
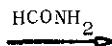
86

xanthine) exists predominantly in the oxo form (84,85)⁸² with no indication of 86. Pullman and Pullman⁸³ used quantum chemical methods for the study of this annular tautomerism; CNDO/2 calculations revealed an almost equal energy for 84 and 85. In the crystal state, the N9-H tautomer is present⁸⁴; UV comparisons (in H₂O) on the contrary indicate the N7-H form for hypoxanthine⁸⁵.

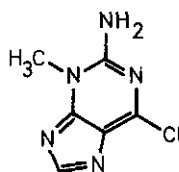
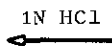
3-Methylguanine (88), which is available by ring closure of 2,4,5-triamino-3-methyl-6-pyrimidone 87 (as sulfate) with boiling formamide or by hydrolysis of 2-amino-6-chloro-3-methyl-purine (89) with 1N hydrochloric acid^{86,87}, seemed to be a likely



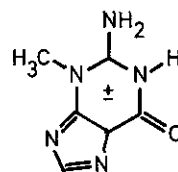
87



88



89



88a

candidate to exist in a mesoionic form (88a)⁸⁶. Pullman⁸⁸ concluded via molecular orbital calculations that 3-methylguanine probably exists as N7-H tautomer; these calculations predicted the mesoionic form to be about 50 kcal/mol less stable than any of the usual tautomers. The results of a recent crystal structure determination have clearly shown that 3-methylguanine exists as the N7-H tautomer (2-amino-3,7-dihydro-3-methyl-6H-purine-6-one, 88) proposed by Pullman⁸⁹.

True mesoionic hypoxanthines have been obtained by Coburn and Carapellotti⁹⁰. Treatment of the previously reported 1,3-dibenzylhypoxanthinium bromide (90a)⁹¹ and 1,3-dimethyl-8-phenylhypoxanthinium iodide (90b)⁹², respectively, as a suspension of the

salt in dry acetonitrile with an excess of a strong base ion-exchange resin at room temperature, yields 91a,b. 1,3-Diethyl-8-phenylhypoxanthinium iodide (90c) - prepared from 8-phenylhypoxanthine and ethyl iodide - results on treatment with an aqueous solution of 5% sodium bicarbonate (to p_{H} 7), in the precipitation of 91c. The mesoionic compounds 91a-c are obtained as white crystals stable to heat and light in air. Some spectroscopic properties are summarized in Table 4.

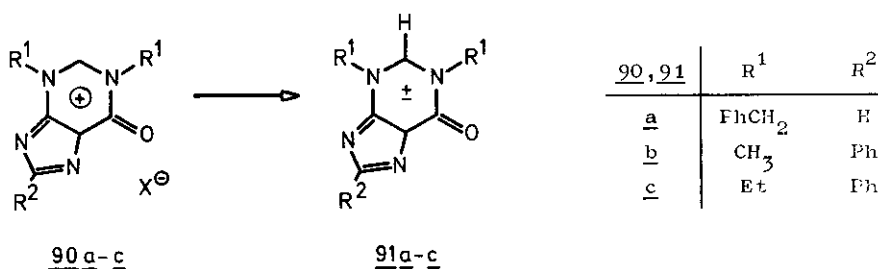
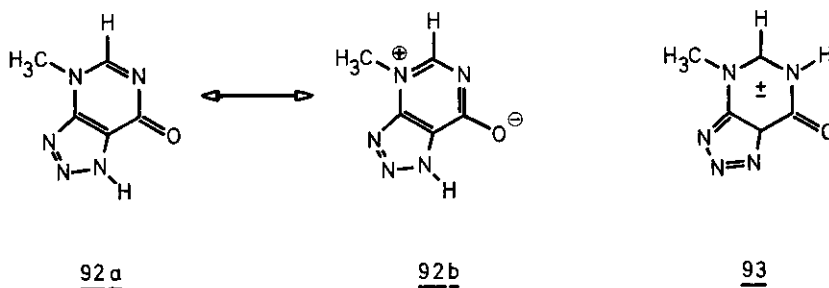


TABLE 4 : Spectroscopic Properties of Mesoionic 1,3-Dialkylhypoxanthines (91a-c).

<u>91</u>	IR (KBr) cm^{-1}	UV (EtOH); λ (lg ϵ) ^a	S_1 (calc.) ^b	¹ H-NMR (DMSO-d ₆); δ in ppm
<u>a</u>	1700	303 (3.73)	303 ^c (3.58)	7.70 (H8), 9.88 (H2)
<u>b</u>	1690	319 (4.14)	317 (4.14)	9.56 (H2)
<u>c</u>	1690	318 (4.08)	317 (4.14)	9.33 (H2)

a: Solvent shifts in acetonitrile: +6,+6,and +7 nm,resp.; b: Variable electronegativity PPP-SCF-CI^{17b} (10 singly excited configurations); c: Adjusted.

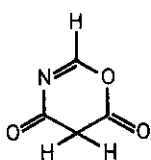
Recent investigations in the 8-azapurine series have shown⁹³ that the 3-alkyl derivatives exist in the neutral form (e.g. 92); the IR spectrum suggests a strong dipolar



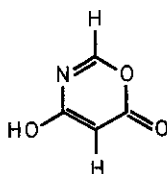
contribution (92b) to the resonance hybrid. As in the case of 3-methylguanine a mesoionic tautomer (93) does not seem to be present.

4.1.2 Mesoionic 4,6-Dioxo-1,3-oxazines

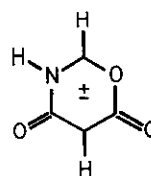
Derivatives of the parent system of this class of compounds (94, 4H-1,3-oxazine-4,6(5H)-dione) have hardly been described up until now⁹⁴; even quantum chemical calculations are still lacking. It would be of interest to investigate whether 94 (which exists probably as the hydroxy tautomer 95) or simple 2,5-disubstituted derivatives might prefer the mesoionic structure; theoretical work ought to be promising in this respect (compare the 3-methylguanine problem)⁸⁹.



94

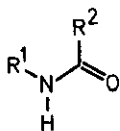


95

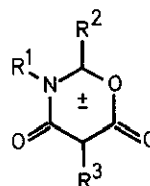
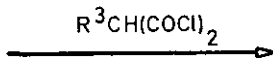


96

In strict analogy with the synthesis of 4,6-dioxo-1,3-diazines, mesoionic 4,6-dioxo-1,3-oxazines (98) have been prepared^{3,47,49} by the reaction of N-monosubstituted amides (97) with malonyl dichlorides (chlorocarbonylketenes⁹⁵); the trichlorophenyl malonate procedure had been unsuccessful in these cases. The stability of these compounds depends on the substituents, especially at C2 and C5, e.g. 98a suffers from hydrolysis in moist air. Recrystallization should be carried out with proton free



97



98

<u>98</u>	R ¹	R ²	R ³	IR (KBr); (cm ⁻¹)	UV (CH ₃ CN); λ (lg ε) (nm)	¹ H-NMR (CDCl ₃); (δ in ppm)
<u>a</u>	CH ₃	CH ₃	PhCH ₂	1660, 1758	209(4.14), 254(3.84), 308(3.13)	2.47(CH ₃), 3.40(CH ₃), 3.63(CH ₂)
<u>b</u>	CH ₃	CH ₃	Ph	1640, 1712, 1732	255(3.92), 323(3.53)	2.57(CH ₃), 3.48(CH ₃)
<u>c</u>	CH ₃	(4-OCH ₃)C ₆ H ₄	CH ₃	1655, 1745, 1760 ^a	217(3.95), 260(4.19), 282(4.04), 353(3.12)	1.93(CH ₃), 3.72(CH ₃), 3.97(OCH ₃)
<u>d</u>	CH ₃	Ph	Ph	1645, 1729	252(4.25), 365(3.64)	3.57(CH ₃)
<u>e</u>	CH ₃	(4-NO ₂)C ₆ H ₄	Ph	1660, 1769	255(4.63), 295(4.05) ^a , 390(3.74)	
<u>f</u>	Ph	CH ₃	Ph	1655, 1749	255(3.98), 265(3.92) ^a , 323(3.51) ^a	2.21(CH ₃)
<u>g</u>	Ph	Ph	Ph	1660, 1750	255(4.27), 374(3.47)	
<u>h</u>	Ph	(4-OCH ₃)C ₆ H ₄	Ph	1675, 1770	224(4.24), 262(4.27) ^a , 303(4.15), 375(3.78)	3.82(OCH ₃)

a: Shoulder

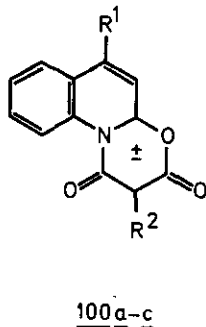
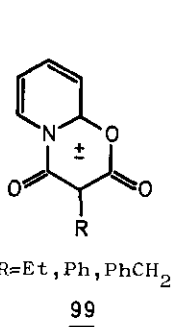
Spectroscopic Data of Mesoionic 4,6-Dioxo-1,3-oxazines
(Selected examples and data)³

SCHEME 15

solvents. The spectra support the formulation as mesoionic compounds. In the IR spectra there are two carbonyl absorptions at approx. 1660 cm⁻¹ ("amide") and 1725-1770 cm⁻¹ ("lactonic" carbonyl); the UV spectra show a long wavelength absorption between 300 and 400 nm which depends considerably on the substituents. In the ¹H-NMR spectra, the signals of C2-CH₃, N-CH₃, and OCH₃ (for R²=(4-OCH₃)C₆H₄) are shifted to lower fields compared with 4,6-dioxo-1,3-diazines (Chap. 4.1.1).

Bi- and tricyclic 4,6-dioxo-1,3-oxazines (mesoionic 2,4-dioxo-pyrido[2,1-b]-1,3-oxazines (99)^{3,47,49} and mesoionic 1,3-dioxo-pyrano[3,2-a]quinolines (100)⁴⁸) have been prepared in the same way; these compounds are considerably more stable against hydrolysis than the monocyclic heterocycles 98.

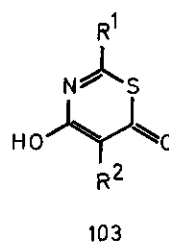
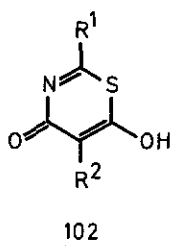
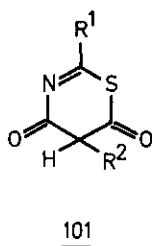
The IR spectra of 99 differ somewhat from the monocyclic compounds; both the "lactone" carbonyl and the "amide" absorption occur at lower frequencies (1730-1740, 1630-1635 cm⁻¹)³. The UV spectra show maxima in the region of 360 nm³.



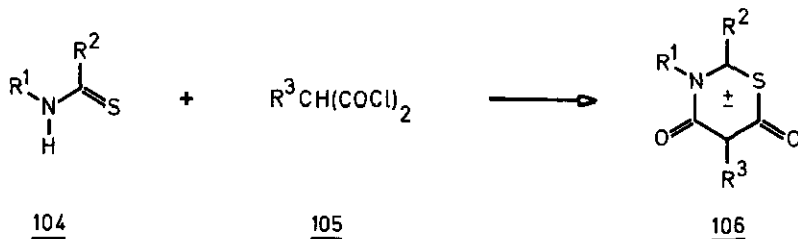
<u>100</u>	R ¹	R ²
<u>a</u>	H	PhCH ₂
<u>b</u>	PhCH ₂ O	Ph
<u>c</u>	PhCH ₂ O	PhCH ₂

4.1.3 Mesoionic 4,6-Dioxo-1,3-thiazines

It is well known that N-unsubstituted thioamides may react with malonic acid derivatives (or malonic acid together with dehydrating agents like POCl₃, PCl₅, and acetic acid anhydride) to give 1,3-thiazinediones (4H-1,3-thiazine-4,6(5H)-diones, 101)⁹⁷⁻¹⁰¹.



Little has been known about tautomeric equilibria¹⁰², but recent investigations (IR, ¹H-NMR, ¹³C-NMR, PPP-MO) show the oxo-hydroxy forms (102 and/or 103)^{103,104} to be present. As in the case of amidines (Chap. 4.1.1) and amides (Chap. 4.1.2), N-monosubstituted thioamides^{105,106} and trisubstituted ureas¹⁰⁶ with carbon suboxide, malonyl dichlorides (chlorocarbonylketenes⁹⁵) and - in certain cases¹⁰⁵ - bis(trichlorophenyl) malonates, yield the expected mesoionic 4,6-dioxo-1,3-thiazines (106).



These compounds are less stable than the corresponding mesoionic 4,6-dioxo-1,3-diazines (Chap. 4.1.1) in the presence of water or alcohol. In some cases they are sol-

<u>106</u>	R ¹	R ²	R ³	IR (cm ⁻¹)	UV (CHCl ₃); λ (lg ε) (nm)	¹ H-NMR (CDCl ₃); (δ in ppm)	Ref.
<u>a</u>	Ph	Ph	H	1630, 1675 ^a			105
<u>b</u>	Ph	Ph	Ph	1660, 1690, 1720 ^a			105
<u>c</u>	CH ₃	(4-Cl)C ₆ H ₄	Ph	1610, 1660	252(4.32), 460(3.32)	3.64(CH ₃)	106
<u>d</u>	Ph	(4-OCH ₃)C ₆ H ₄	Ph	1605, 1680		4.05(OCH ₃)	106
<u>e</u>	CH ₃	N(CH ₃) ₂	Ph	1590	243(3.78), 281(3.96)	3.06(CH ₃), 3.14 (CH ₃), 3.46(CH ₃)	106

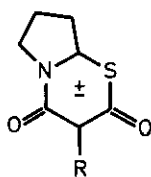
a: KBr

Spectroscopic Data of Mesoionic 4,6-Dioxo-1,3-thiazines (106)
(Selected examples and data)

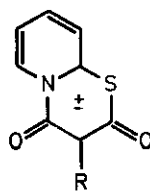
SCHEME 16

volytically cleaved to give the starting materials. The substituent in position 2 plays an important role both in stabilizing the nucleus and in increasing its basicity¹⁰⁶. Normally the IR spectra show two carbonyl bands. It is of interest that compounds 106 which are derived from trisubstituted thioureas (106, R²=NR₂) exhibit only a single carbonyl absorption at 1590-1600 cm⁻¹; the UV spectra are considerably different also (Scheme 16).

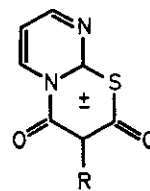
Applying the previous mentioned synthesis to cyclic thioamides yields the mesoionic heterocycles (107-109, 111, 114, 116-121). Compound 111 has also been obtained by



107¹⁰⁵

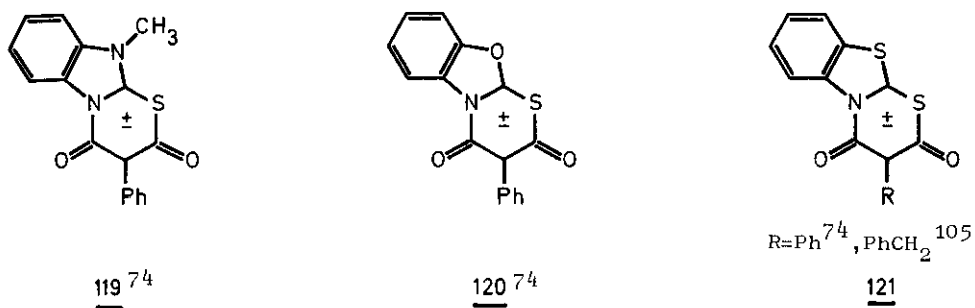
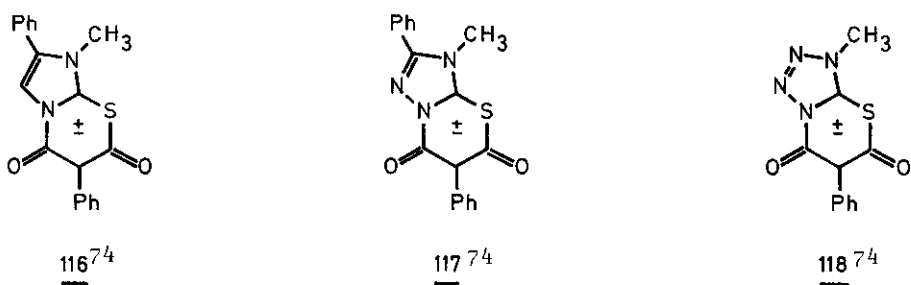
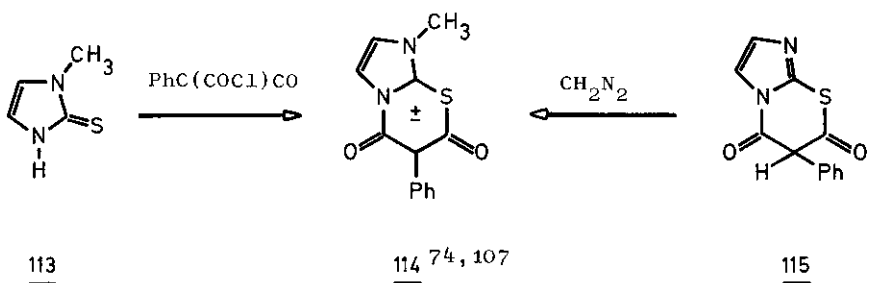
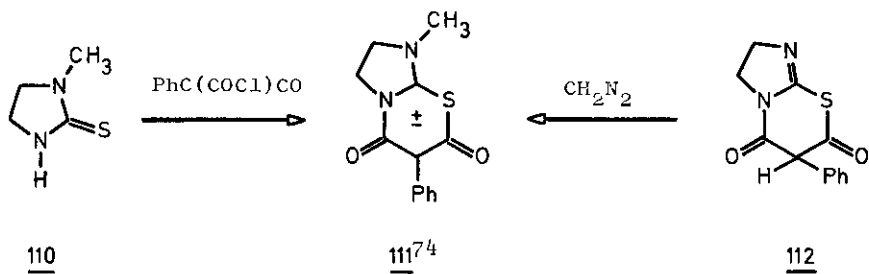


108¹⁰⁵



109¹⁰⁵

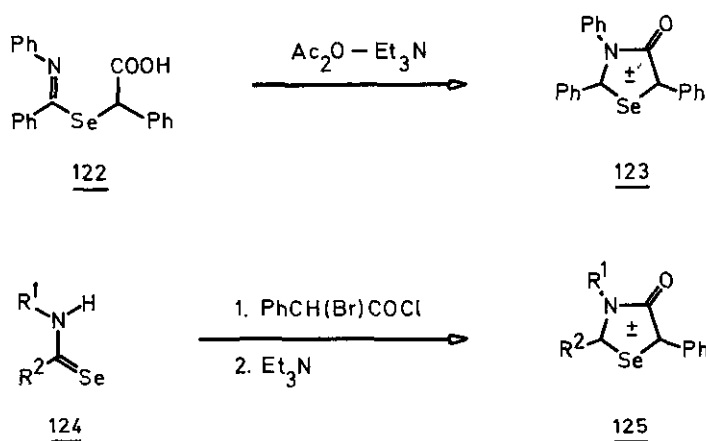
R=H, Ph, PhCH₂



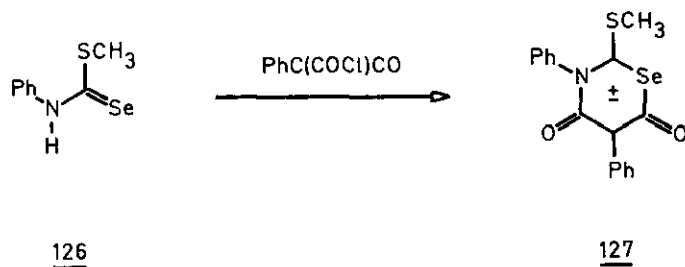
N-alkylation of 112 with diazomethane. It is interesting to note that in this case only the N-isomer (111) was obtained, whereas 115 reacted with diazomethane to give 114 and an O-methylated isomer. 119 could not be obtained by N-alkylation⁷⁴.

4.1.4 Mesoionic 4,6-Dioxo-1,3-selenazines

Selenium containing mesoionic heterocycles have been described only recently. The α -seleno acid 122 with acetic anhydride/triethylamine has given the mesoionic 1,3-selenazole-4-one (123) as magenta needles in 80% yield^{1,10}. Reaction of a variety of monoprotonic selenoamide derivatives (124) with 1,2-bielectrophiles as α -bromophenylacetic acid chloride also yields this system (125)⁵⁴. As a logical extension, replacement of the 1,2-bielectrophile in the reaction with selenoamide derivatives



with a 1,3-bielectrophile such as (chlorocarbonyl)phenylketene should provide a synthesis for mesoionic 4,6-dioxo-1,3-selenazines. Indeed, when selenothiocarbamate 126 is mixed with the ketene in anhydrous ether at room temperature, 127 is ob-

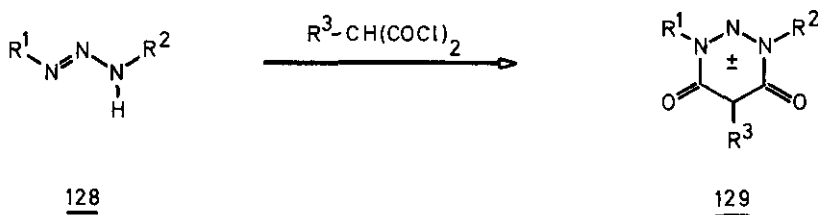


tained as orange prisms in 53% yield. The IR spectrum shows bands at 1615 and 1675 cm^{-1} . The compound displays a strong UV absorption at 325 nm ($\lg \epsilon = 4.02$)⁵⁴. The corresponding S-ethyl product was similarly formed. Both products decomposed on attempted recrystallization. They were considerably less stable than their appropriate sulfur analogues. The chemistry of these compounds has apparently not been investigated.

4.1.5 Mesoionic 4,6-Dioxo-1,2,3-triazines

Triazenes carrying a free hydrogen condense as the corresponding alkali salts with alkyl iodide and acyl chlorides to give N-alkyl and N-acyl derivatives¹⁰⁸. N,N'-Di-substituted triazenes (128) with malonyl dichlorides (chlorocarbonylketenes)⁹⁵ in ether yield mesoionic 4,6-dioxo-1,2,3-triazines (129)¹¹⁰ as yellow to orange (129a-d) or red (129e)¹¹¹ crystals.

Whereas generalizations concerning the stability cannot be made at the moment, mesoionic 4,6-dioxo-1,2,3-triazines seem to be less stable than mesoionic 4,6-dioxo-1,3-diazines (Chap. 4.1.1); 129a,c could not be recrystallized and 129b suffers from



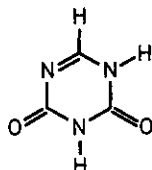
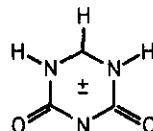
<u>129</u>	R ¹	R ²	R ³
<u>a</u>	Ph	Ph	Ph
<u>b</u>	Ph	PhCH ₂	Ph
<u>c</u>	Ph	Ph	PhCH ₂
<u>d</u>	Ph	PhCH ₂	PhCH ₂
<u>e</u>	(4-OCH ₃)C ₆ H ₄	(4-OCH ₃)C ₆ H ₄	Ph

solvolysis when heated for prolonged times in methanol. (For details on the reactivities, see Chap. 5.)

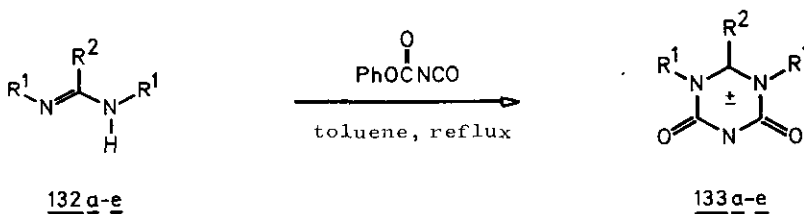
The IR spectra show a broad, intensive CO-absorption in the region of 1630-1680 cm^{-1} with a shoulder at slightly higher wave numbers; UV spectra of these compounds have not as yet been published.

4.1.6 Mesoionic 4,6-Dioxo-1,3,5-triazines

5-Azauracil (130) is the parent system of the mesoionic heterocycles to be discussed in this subsection. IR spectra in dioxane and ethanol indicate the dioxo form; the UV spectrum in water is similar to both the N-alkyl and O-alkyl models and on this account difficult to interpret^{112,113}. There is no indication of a mesoionic form (131)¹¹⁴.

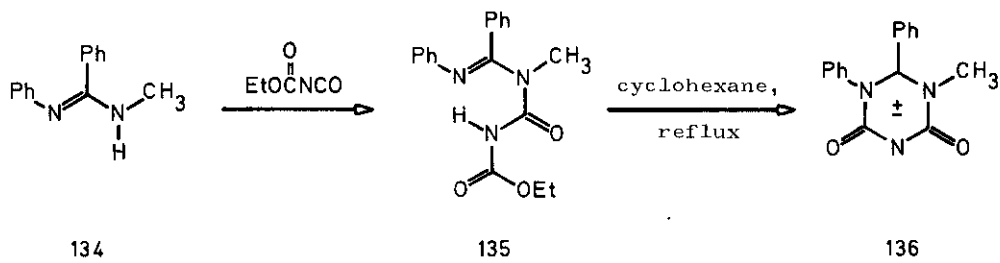
130131

Nevertheless monocyclic mesoionic 4,6-dioxo-1,3,5-triazines (133) are easily prepared by the reaction of N,N'-disubstituted amidines (132) with phoxycarbonyl isocyanate¹¹⁵ as white crystals with a pronounced susceptibility for hydrolysis. The synthesis obviously proceeds through an intermediate product. As has been reported by

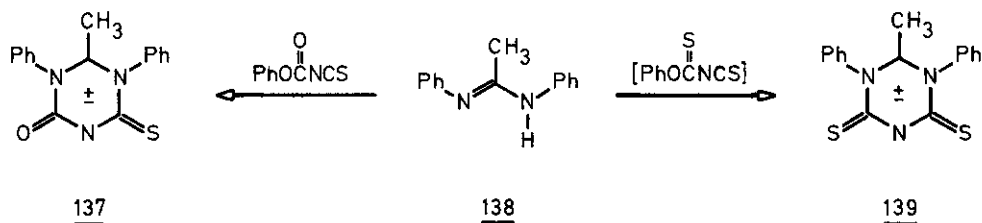


<u>132, 133</u>	R ¹	R ²
<u>a</u>	Ph	CH ₃
<u>b</u>	PhCH ₂	CH ₃
<u>c</u>	Ph	CH ₃
<u>d</u>	Ph	Ph
<u>e</u>	(4-OCH ₃)C ₆ H ₄	CH ₃

Kappe and coworkers¹¹⁶, the amidine 134 reacts with ethoxycarbonyl isocyanate at room temperature to produce the allophanic ester 135, which on heating in cyclohexane

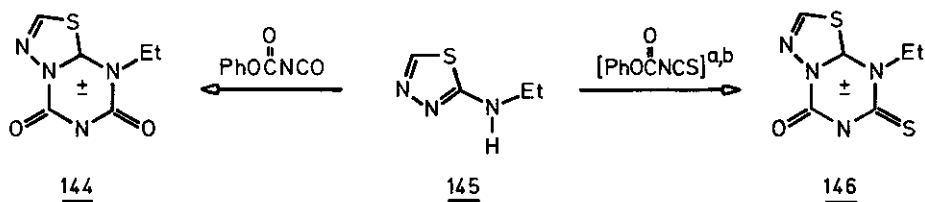
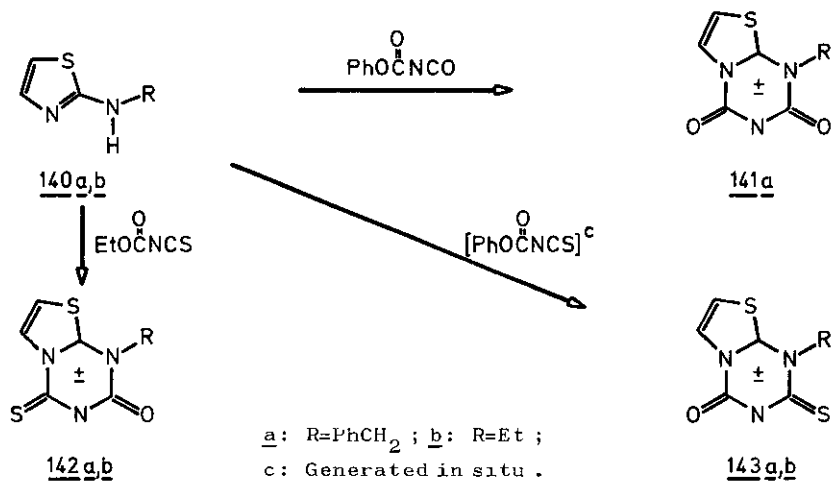


yields 136. The monocyclic mesoionic 4,6-dioxo-1,3,5-triazines show two C=O bands in their IR spectra (1680-1690 and 1725-1730 cm^{-1}); the UV spectrum of 133a exhibits a short wavelength absorption at 230 nm ($\lg \epsilon = 3.993$ in THF). In a strictly comparable reaction of N,N'-diphenylacetamidine (138) with phenoxy carbonyl isothiocyanate and phenoxythiocarbonyl isothiocyanate (generated in situ from phenoxythiocarbonyl chloride and lead thiocyanate) in refluxing toluene, the monothiono (137) and

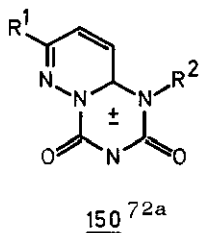
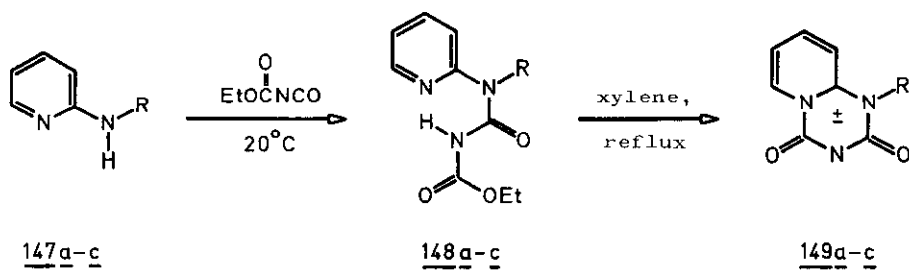


dithiono compound (139) are respectively yielded¹¹⁵.

In general compounds of type 133, (136) appear to be somewhat less stable than their 5-deaza analogues (Chap. 4.1.1); quantitative experiments, however, are still lacking. Bicyclic derivatives of the mesoionic 4,6-dioxo-1,3,5-triazine system are known also. 2-Amino-substituted 1,3-thiazoles (140) react with phenoxy carbonyl isocyanate to produce 141a; with ethoxycarbonyl isocyanate, only acylation of the aminothiazoles is observed¹¹⁷. Ethoxycarbonyl isothiocyanate and phenoxy carbonyl isothiocyanate exhibit a remarkable difference in their reactivity towards 140a,b: whereas the former¹¹⁸ yields 142a,b, the latter (generated in situ from phenylchloro formate and potassium thiocyanate in anhydrous ethyl acetate) leads to 143a,b¹¹⁷. In a similar fashion, 144 and 146 are obtained from 2-ethylamino-1,3,4-thiadiazole (145)¹¹⁷. As in the case of amidines (see above), N-substituted 2-aminopyridines (147) react with ethoxycarbonyl isocyanate in the first step to give allophanic esters (148); the mesoionic 2,4-dioxo-pyrido[1,2-a]-s-triazines (149) are obtained by refluxing



a: Generated in situ ; b: No reaction with ethoxycarbonylthiocyanate.



<u>147-149</u>	R
<u>a</u>	Ph
<u>b</u>	(4-CH ₃)C ₆ H ₄
<u>c</u>	PhCH ₂

R¹=Cl, OCH₃, Morpholino, N-Methylpiperazyl

R²=Alkyl, Aryl

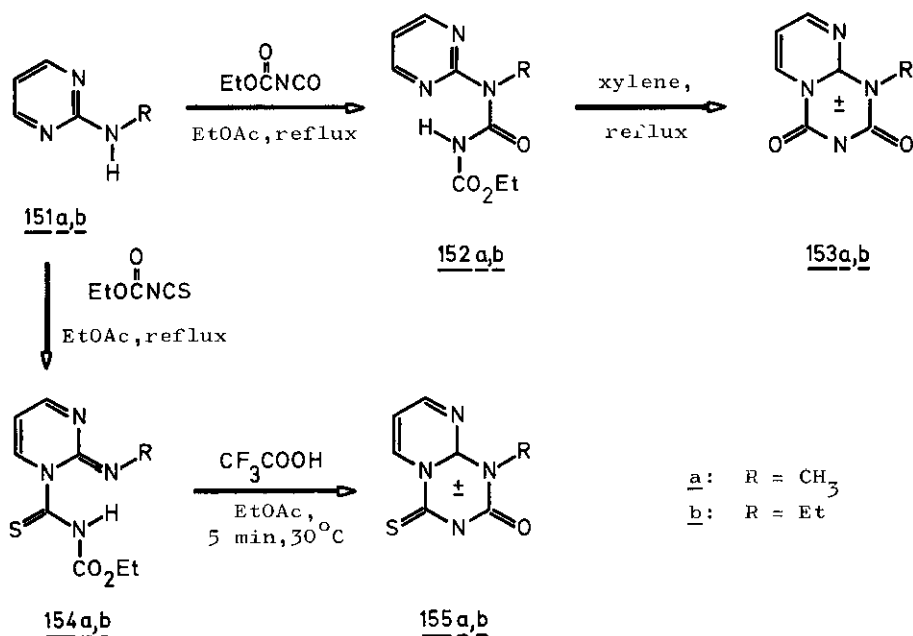
Comp.	IR(KBr) cm^{-1}	UV; λ ($\lg \epsilon$) nm	$^1\text{H-NMR}$; δ in ppm	Ref.
<u>141a</u>	1669, 1720	215(4.326), 272(3.749) ^a	5.53(CH_2), 7.68(d, 1H), 8.30(d, 1H) ^b	117
<u>142a</u>	1730	229(4.054), 275(3.964), 320(4.099) ^a	5.96(CH_2), 7.70(d, 1H), 7.26 ^c (d, 1H) ^b	117
<u>143a</u>	1669	217(4.567), 256(3.929), 302(3.628) ^a	5.53(CH_2), 7.66(d, 1H), 8.36(d, 1H) ^b	117
<u>144</u>	1667, 1734	221(3.958), 267(4.461) ^a	1.61(t, CH_3), 4.45(q, CH_2), 9.80(1H) ^b	117
<u>146</u>	1706	217(4.016), 277(4.449) ^a	1.60(t, CH_3), 4.43(q, CH_2), 9.70(1H) ^d	117
<u>149c</u>	1610-1670, 1730	220(3.92) ^e , 235(3.97), 285(3.39) ^e , 315(3.65) ^g	5.4(CH_2) ^f	116

a: H_2O ; b: CF_3COOH ; c: Should probably be 8.26 (W.F.);
d: CDCl_3 ; e: Shoulder; f: DMSO-d_6 ; g: CH_3OH .

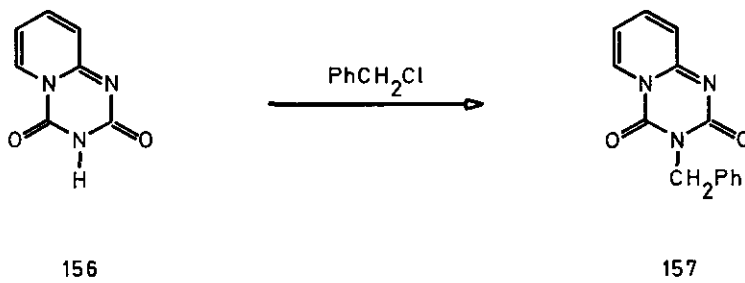
Spectral Data of C2-N3-Annelated Mesoionic 4,6-Dioxo-1,3,5-triazines
(Selected examples and data)

SCHEME 17

these intermediates in xylene¹¹⁶. Compounds of type 150 have been prepared from appropriate N-substituted aminopyridazines and phenoxycarbonyl isocyanate in dry acetonitrile^{72a}. Their in vitro antimicrobial activity has been tested.



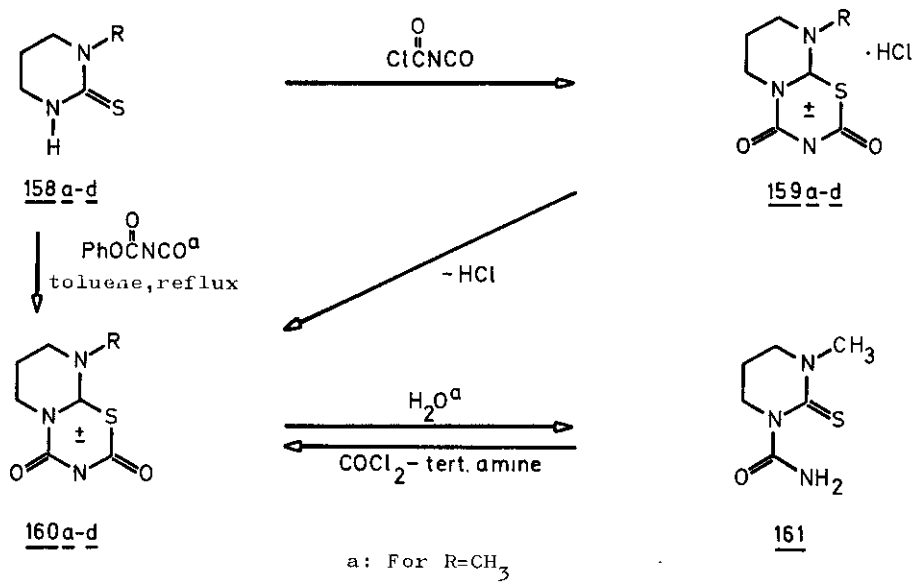
In a recent publication, the preparation of 153a,b and 155a,b as depicted above has been described¹¹⁹. Whereas the ring closure of 152a to 153a proceeds as usual, the transformation 154 → 155 is effected by a catalytic amount of trifluoroacetic acid. In contrast to the alkylation of "malonyl- α -aminopyridine" and related compounds (Chap. 4.1.1), 156 with benzyl chloride affords only a N3-substituted derivative (157)¹¹⁶.



The mesoionic bicyclic dioxo-1,3,5-triazines show two carbonyl bands in their IR spectra. The assignment is made possible by comparison with the oxo-thiono compounds 142, 143, and 146. As can be seen from the data of 141a, 142a, and 143a in Scheme 17, both the position and the intensity of the long-wave UV band depends greatly on the substitution of an oxo- by a thiono group; this seems not to be the case for 144 and 146.

4.1.7 Mesoionic 4,6-Dioxo-1,3,5-thiadiazines

As early as 1972⁴, the reaction of cyclic thioureas (158) with chlorocarbonyl isocyanate has been described. In the first step of this reaction, salt-like adducts (159) are obtained which on deprotonation yield the mesoionic compounds 160; 160a could also be obtained directly from 158a with phenoxycarbonyl isocyanate in refluxing toluene. The introduction of one carbon unit in 161 in the presence of an amine also yields this new mesoionic system. The photoelectron spectra of 160 show two signals in an intensity ratio of 2:1. Other spectral data have not been given.

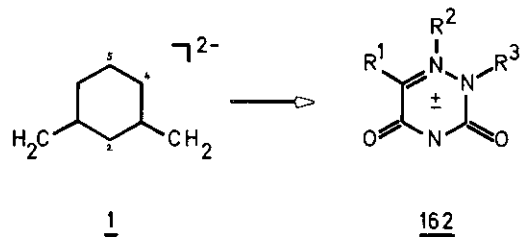


<u>158-160</u>	R
<u>a</u>	CH ₃
<u>b</u>	1-C ₃ H ₇
<u>c</u>	n-C ₄ H ₉
<u>d</u>	cyclohexyl

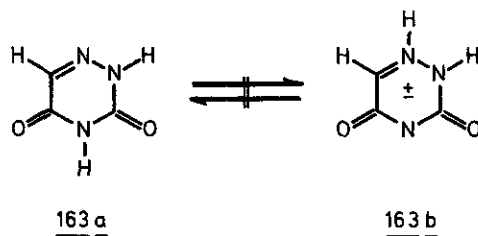
4.2 1,3 - DIPOLAR SYSTEMS

4.2.1 Mesoionic 3,5-Dioxo-1,2,4-triazines

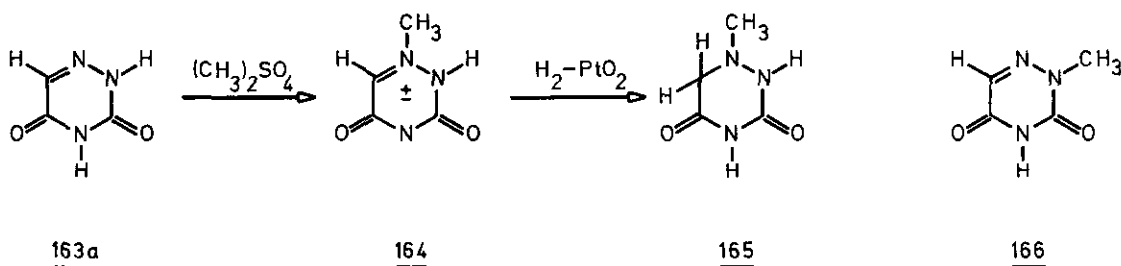
The introduction of heteroatoms (N, O, S) in the positions 4 and 5, as well as 7 and 8, of the m-quinodimethane dianion (1) leads to a new mesoionic 1,3-dipolar system



(A, Chap. 2) of which examples seem to be unknown. Further introduction of a nitrogen atom in position 2 creates a class of compounds (e.g. 162) which have recently come to light. The basis system, 6-azauracil (163), exists in the dioxo form (163a)^{120, 121}



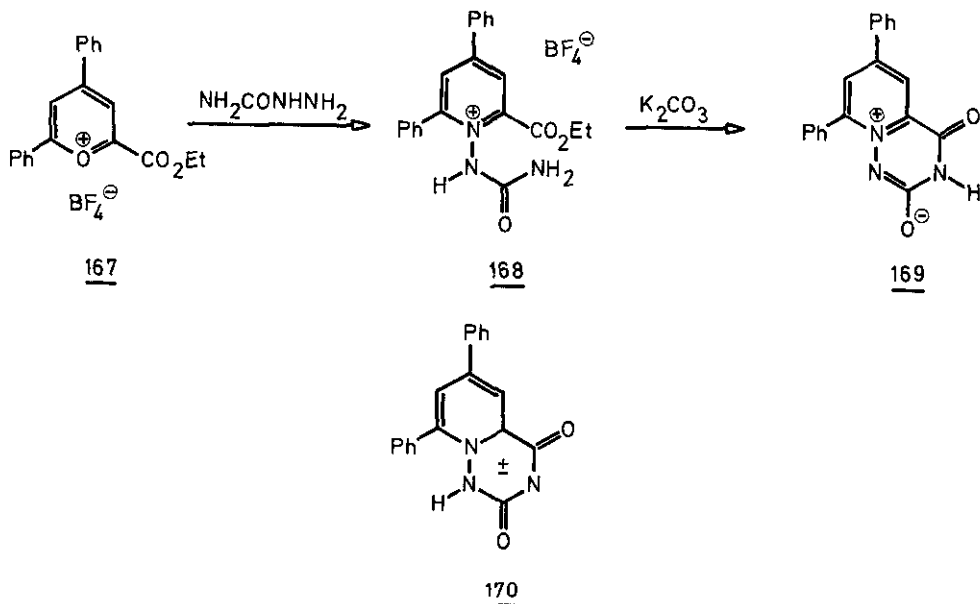
with no indication of the mesoionic tautomer (163b)^{122, 123}. Alkylations of 6-azauracil with alkyl iodides, dialkyl sulfates or benzyl chloride in aqueous alkali afford the 2- and 4-monoalkyl or 2,4-dialkyl derivatives, depending on the reaction conditions. The course of the reaction between 163 and dimethyl sulfate is different when alkali is absent; in this case, the mesoionic six-membered heterocycle 164 is



obtained in about 40% yield¹²⁷. The structure was confirmed by ¹H-NMR ($\delta(\text{CH}_3) = 3.92$, $\delta(\text{H6}) = 8.03$ ppm (166: $\delta(\text{CH}_3) = 3.45$, $\delta(\text{H6}) = 7.36$ ppm) (in DMSO-d₆) and IR. The compound 164 is hydrogenated over Adams catalyst to afford 165 in 83% yield.

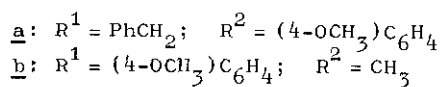
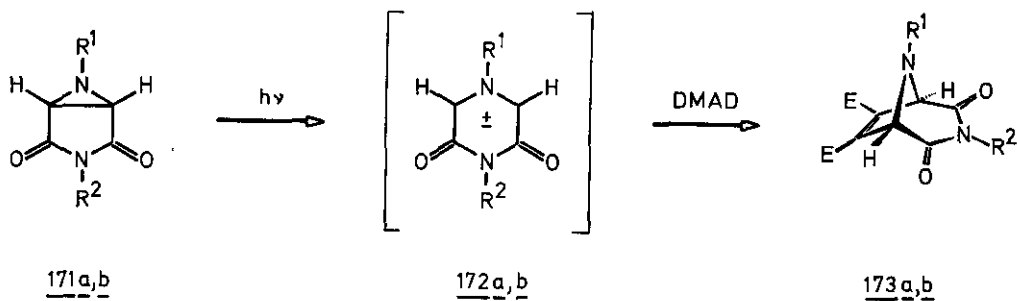
Quite recently a compound has been described which may be a benzanalogue of 162. The pyrylium tetrafluoroborate 167 reacts smoothly with semicarbazide to form the ureido-derivative 168 which on treatment with potassium carbonate in dimethoxyethane cyclized to 169 (mp. > 325°C (EtOH); $\nu_{\text{max}}(\text{CHBr}_3)$: 1710, 1630, 1610 cm⁻¹). Whether this product should be formulated as 169 or as a benzanalogue of 162 (170) is open to question¹²⁸.

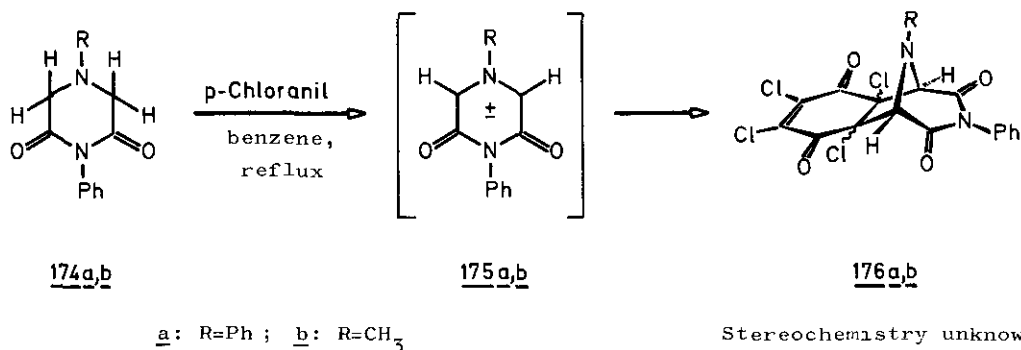
No further compounds of type A (Chap. 2) have apparently been described.



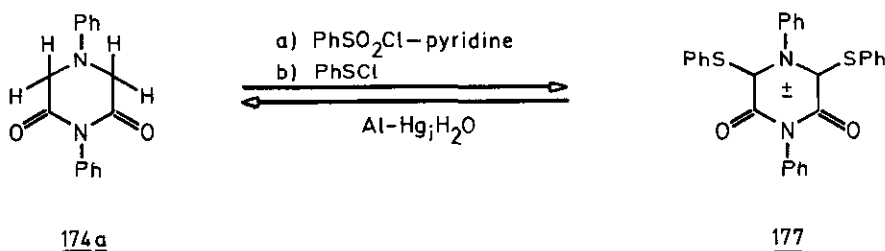
4.2.2 Mesoionic 3,5-Dioxo-1,4-diazines

Aziridines may undergo thermally or photochemically induced ring opening reactions to azomethine ylides¹²⁹, controlled stereospecifically as predicted by the Woodward-Hoffmann rules. In an extension of this work, photolyses of 171a¹³⁰ and 171b¹³¹ in the presence of DMAD²⁹ yield adducts (173a,b)¹³² which probably result from a 1,3-

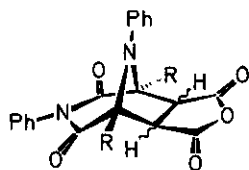




dipolar reaction of DMAD with 172a,b. The dehydrogenation of 1,4-disubstituted piperazinediones (174a,b) with an excess of p-chloranil yields products (176a,b) which have been suggested¹³⁵ to result from mesoionic 3,5-dioxo-1,4-diazines (175a,b) as intermediates. Both 172 and 175 can be considered as azomethine ylides^{130,131} or ¹³³ - in this context - as a mesoionic six-membered heterocycle of type C (Chap. 2). Whereas 172 and 175 have neither been proved nor isolated, M.Sorm and coworkers¹³⁴ have succeeded in preparing stable compounds of this type. In a peculiar reaction, 174a on treatment with either benzenesulfonyl chloride/pyridine or benzenesulfonyl chloride, affords the mesoionic compound 177 as yellow needles which yields of 28% and 9%, respectively¹³⁵. Activated Al reverts 177 back to 174a. The IR spectrum of

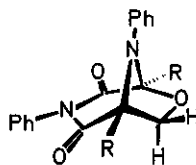


177 exhibits two bands in the carbonyl region ($1640, 1690 \text{ cm}^{-1}$); the UV spectrum shows an absorption at 438 nm of medium intensity ($\lg \epsilon = 3.17$). With maleic anhydride (benzene, reflux) and formaldehyde (THF, room temperature), cycloadducts (178, 179) are obtained; these reactions confirm the structure of 177. Nevertheless an X-ray structure determination is urgently desired.



178

R = SPh



179

Stereochemistry unknown

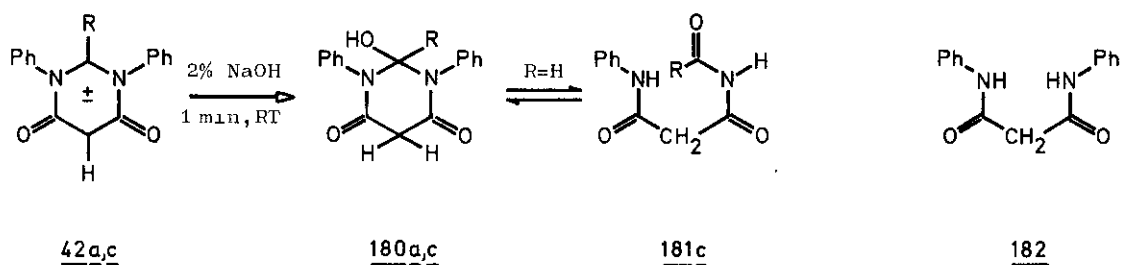
5. REACTIONS

In this chapter, only reactions of mesoionic six-membered heterocycles of type B (Chap. 2) will be dealt with.

5.1 REACTIONS WITH NUCLEOPHILES

Both mono- and polycyclic mesoionic six-membered heterocycles are more or less susceptible to solvolysis whereby the latter compounds are generally more stable than the former. These reactions are strongly accelerated by acids⁴⁹. A few examples of this reaction type will be given in this subsection.

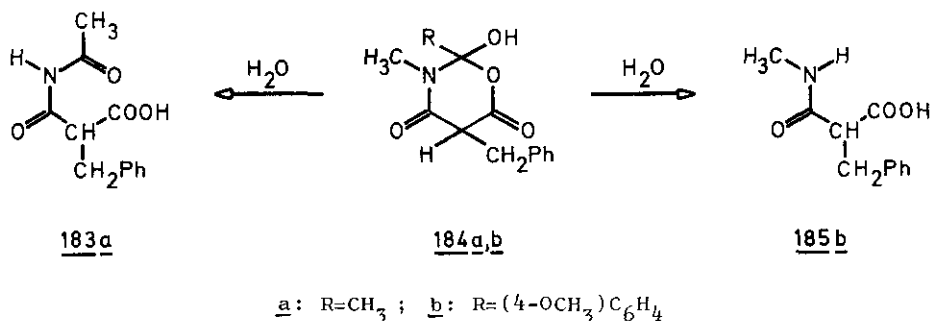
Mesoionic 4,6-dioxo-1,3-diazines may add water to give a hydrate (180a,c^{44a}; further example⁵²) which may exist in the carbinolamine form (R=Ph) or in the open chain form (R=H). Further hydrolysis leads to a malondiamide (182)³⁵. In this case, replacement of the 2-phenyl substituent in 42 with a hydrogen atom greatly increases the



a: R=Ph ; c: R=H

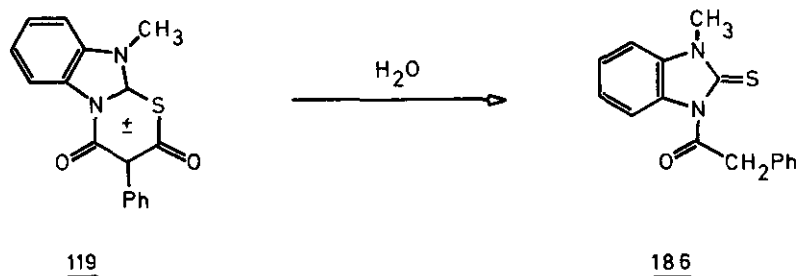
susceptibility of the ring system to hydrolysis.

Analogous reaction products have been observed with 4,6-dioxo-1,3-oxazines (98); reaction with water or sodium hydroxide leads to 183 and 185, possibly with 184 as



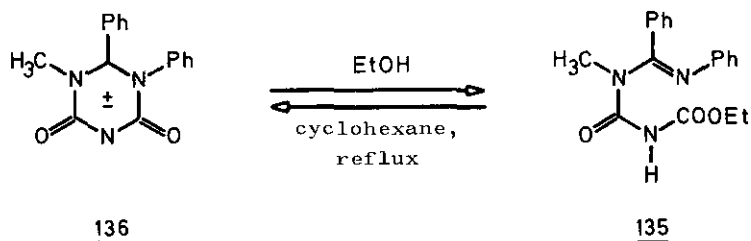
an intermediate³.

4,6-Dioxo-1,3-thiazines (Chap. 4.1.3) are less stable than 4,6-dioxo-1,3-diazines (Chap. 4.1.1); on hydrolysis usually thioamides and malonic acids are obtained¹⁰⁵. Compound 119 differs somewhat in this respect; hydrolysis in DMSO yields 186⁷⁴. This

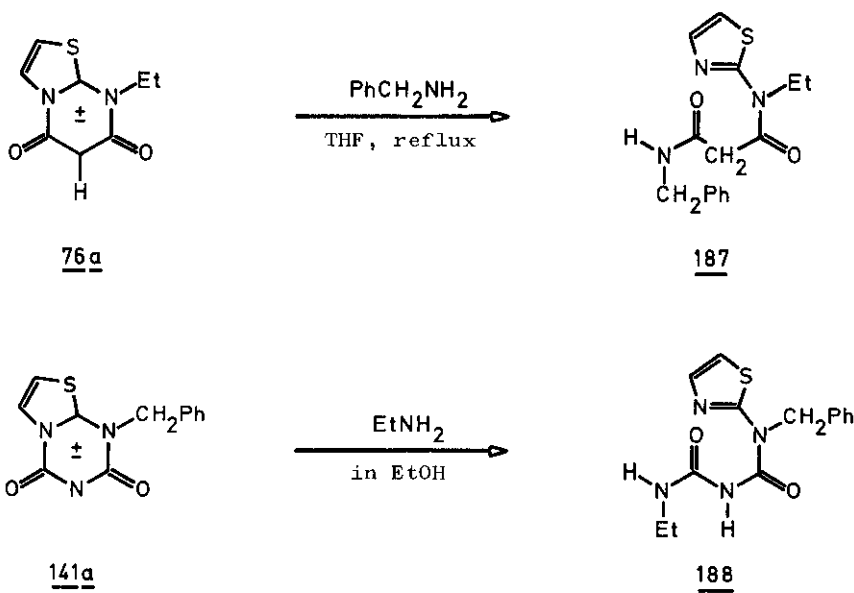


mode of ring opening is similar to that reported for 160a (to 161: Chap. 4.1.7)⁴. As already mentioned, 4,6-dioxo-1,2,3-triazines (129) may suffer from solvolysis when heated with methanol¹¹⁰; 129d on treatment with 2N HCl (reflux) yields benzylmalonic acid.

In alcoholic solution 4,6-dioxo-1,3,5-triazines are slowly cleaved (e.g. 136) to give



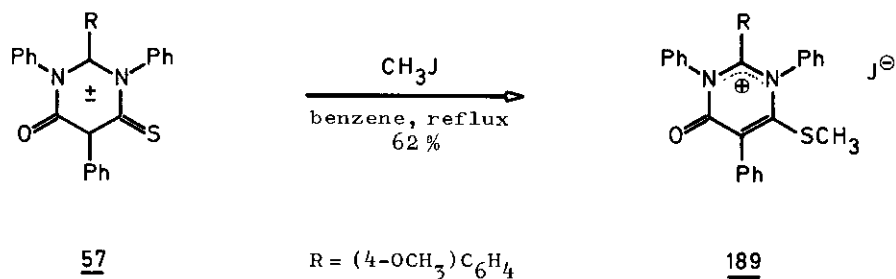
allophanic esters (135); this reaction is accelerated by hydrogen chloride. The cleavage proceeds further to give amidine and iminodicarbonic esters¹¹⁶. Cleavage of 76a¹¹ and 141a¹¹⁷ with amines affords 187 and 188, respectively, with regeneration of the 1,3-thiazole moiety. It has been reported that a 1,3,4-thiadia-



zole analogue of 76a (82a) reacts 10³ times faster with amines⁷⁹. Compound 141a is decomposed readily when heated in aqueous or alcoholic solution¹¹⁷ (compare the separate reactions of 144 with ethylamine and water)¹¹⁷.

5.2 ALKYLATIONS AT THE EXOCYCLIC HETEROATOMS

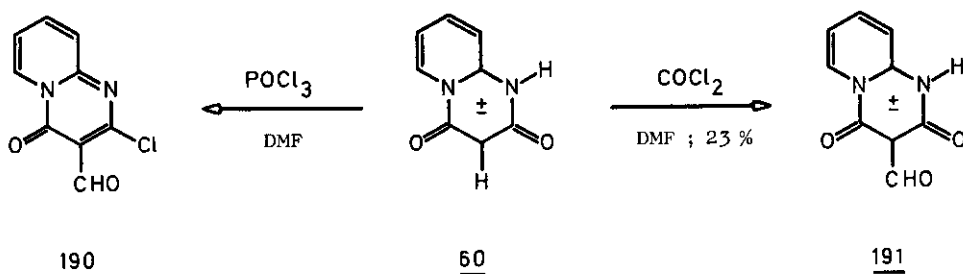
There seems to be only one report concerning the alkylation of mesoionic six-membered heterocycles of type B (Chap. 2) at the heteroatoms 7 or 8⁵⁴. Compound 57 on



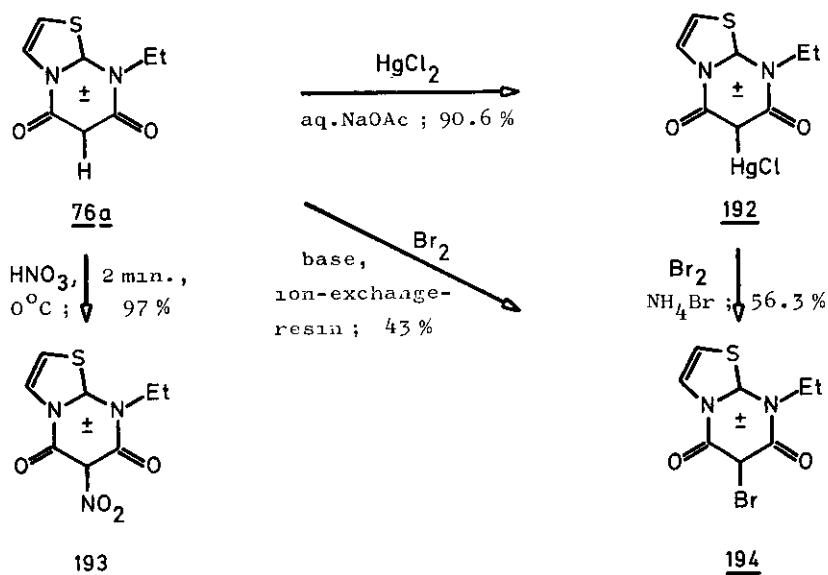
treatment with methyl iodide was found to yield 189. This type of reaction has been investigated extensively in the series of five-membered mesoionic heterocycles; it offers an advantage for introducing carbanionic stabilizing groups other than oxygen or sulfur^{1,136}.

5.3 REACTIONS WITH ELECTROPHILES

Mesoionic six-membered heterocycles of type B (Chap. 2) are amenable to electrophilic substitution reactions provided that they carry a methine group between the carbonyl groups. So far only reactions of bicyclic mesoionic 4,6-dioxo-1,3-diazines have been reported^{68a}. "Malonyl- α -aminopyridine" (60) reacts with DMF/COCl₂ to produce 23%

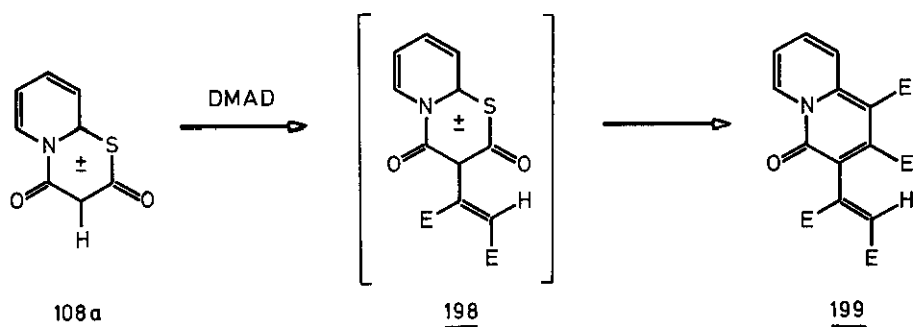
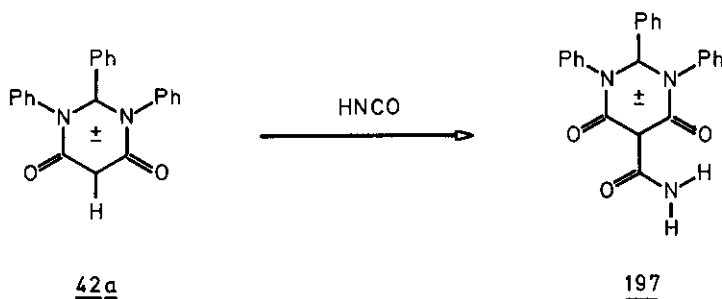
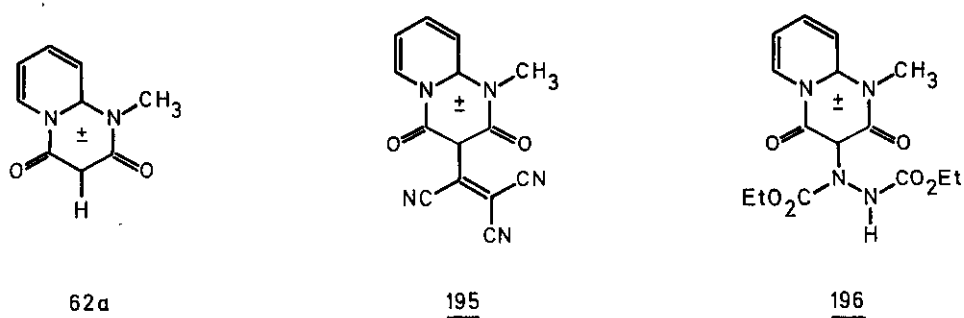


C-formylated product (191, besides 8.3% 190), whereas with DMF/POCl₃, only 190 is obtained. Compound 76a serves as starting material for C-substituted derivatives



(192, 193, 194)¹¹ which would be difficult to obtain on other routes. The versatility of these transformations is promising with respect to the preparation of other meso-ionic six-membered heterocycles.

In an attempt to cycloadd (Chap. 5.4) TCNE and ethyl azodicarboxylate to 62a "ene-type" reaction products, (195, 196) have been isolated³⁶. Isocyanic acid adds 42a yielding 197 (however, compare the reaction of the 5-substituted 39b with the same reagent, Chap. 5.4.1)^{37b}. In a similar manner, 108a reacts with DMAD²⁹ under forced conditions to give 199, probably via 198 followed by a 1,4-dipolar cycloaddition (Chap. 5.4) with subsequent loss of COS⁴⁶. A similar reaction type has been encountered in heating a 4,6-dioxo-1,3,5-triazene with DMAD¹¹⁵.



5.4 CYCLOADDITION REACTIONS

 5.4.1 With 2π - Components

Mesoionic six-membered heterocycles of type B (Chap. 2) - whether they are mono- or polycyclic - may be envisaged as 1,4-dipolar systems (Scheme 3). As expected for these compounds, the symmetry of the highest occupied molecular orbital (HOMO) and



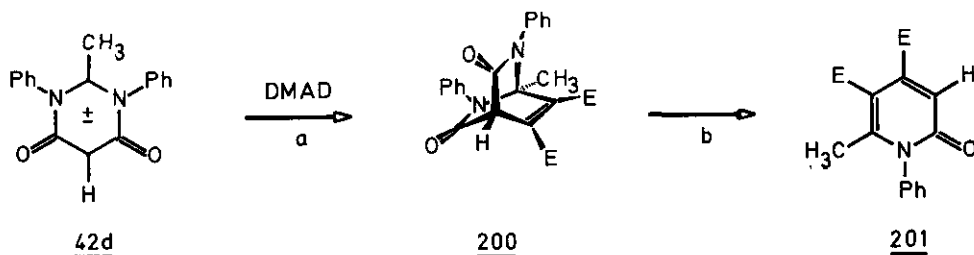
Symmetry of HOMO and LUMO of Mesoionic Six-Membered Heterocycles of Type B (Chap. 2).

Mesoionic 4,6-dioxo-1,3-diazine as representative example
(HMO data, parameters: Chap. 3).

SCHEME 18

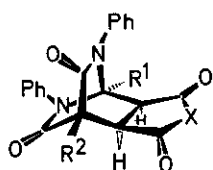
lowest unoccupied molecular orbital (LUMO) (Scheme 18) predicts them to be suitable candidates for cycloaddition reactions with 2π -components. This presumption has been verified in a great number of cases. Representative examples will be given in this chapter.

Mesoionic 4,6-dioxo-1,3-diazines have been shown^{137a} to react with DMAD producing 2-pyridones (201); the primary [2+4]cycloadduct (200) has been isolated as intermediate^{44a}. Whereas diethylamino-1-propine^{37b}, N,N-dimethylamino-phenylacetylene, ethyl propiolate as well as methyl malonate failed to give well defined products^{44a},



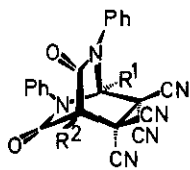
a: benzene, 24 h reflux; 94 %
b: 20 min. above mp. (188-189°C)

maleic anhydride^{137a,b} and maleic imides^{45b} add to mesoionic 1,3-diazines yielding 202. The reaction with TCNE gives the cycloadducts 203^{45b}.



X = O, N-Ar

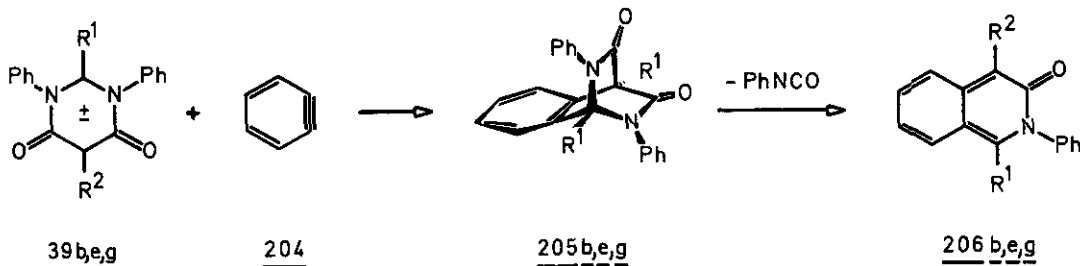
202



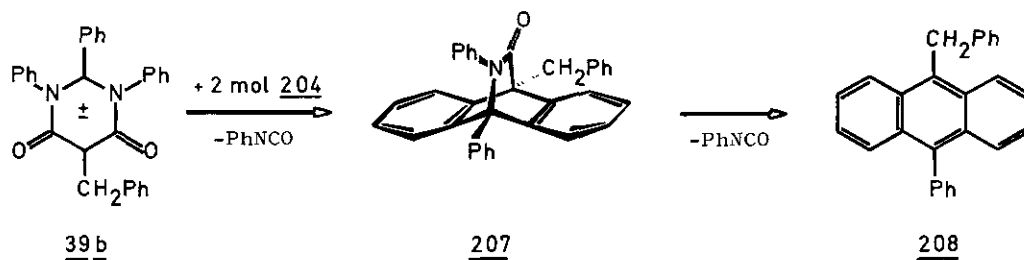
203

<u>203</u>	R ¹	R ²
<u>a</u>	H	H
<u>b</u>	CH ₃	CH ₃
<u>c</u>	Ph	C ₂ H ₅
<u>d</u>	Ph	PhCH ₂

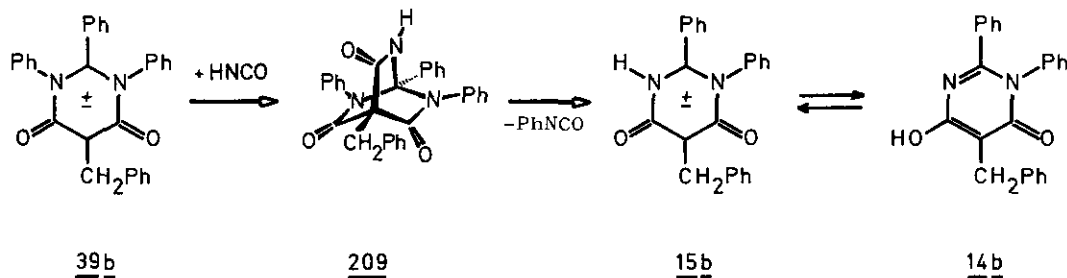
Mesoionic 4,6-dioxo-1,3-diazines such as 39b,e,g (and others) react with benzyne (204), prepared from benzenediazonium-2-carboxylate, yielding below 40°C the primary cycloadducts 205, which can be isolated. At higher temperature the isoquinoline-3-ones (206) are formed under the loss of phenyl isocyanate^{137c}. Compound 39b gives with an excess of 204 the adduct 207, which is converted upon heating into the anthracene derivative 208.



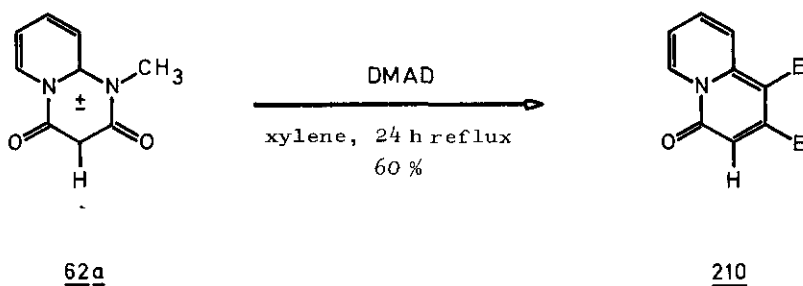
<u>39,</u> <u>205, 206</u>	R ¹	R ²
<u>b</u>	Ph	PhCH ₂
<u>e</u>	CH ₃	PhCH ₂
<u>g</u>	Ph	Et

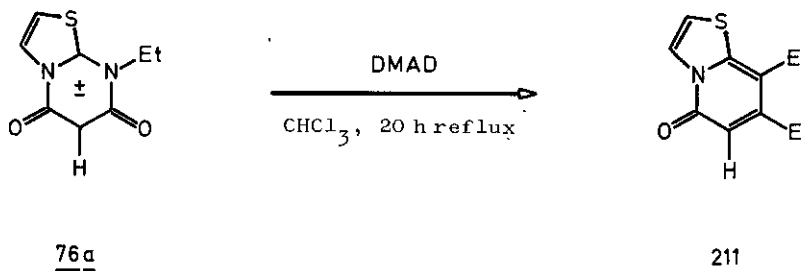


The addition of isocyanic acid, prepared by the thermolysis of isocyanuric acid or azodicarboxamide, to 39b yields, possibly via the bridged adduct 209 and subsequent loss of phenyl isocyanate, the 6-hydroxy-4-pyrimidone 14b^{37b}.

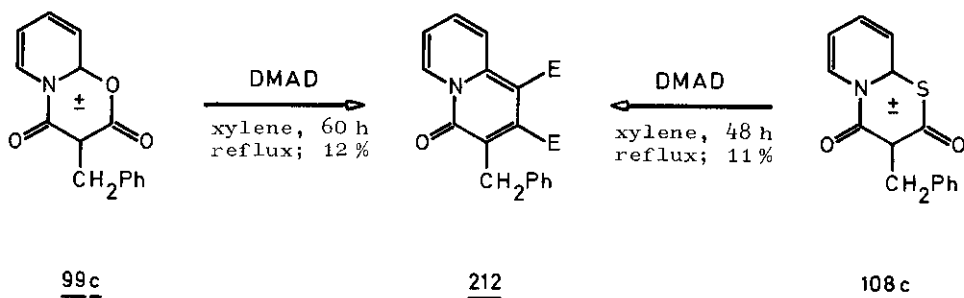


Bicyclic mesoionic compounds (e.g. 62a^{44a}, 76a¹¹) add DMAD to produce fused pyridines (210, 211) which might otherwise be difficult to obtain.

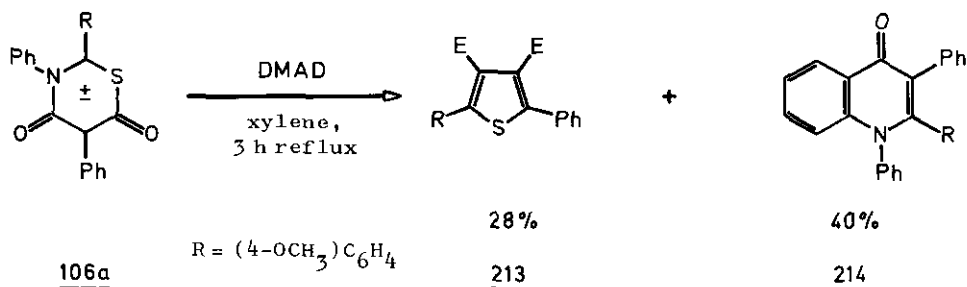




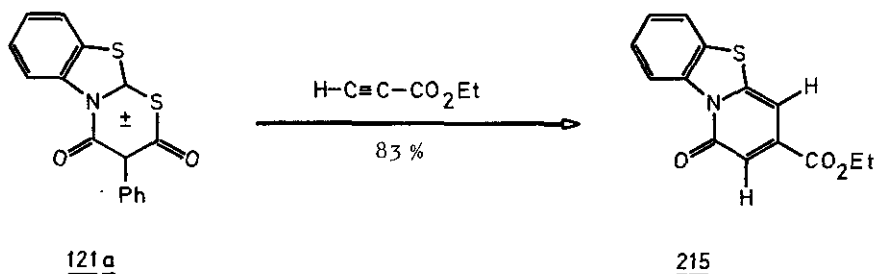
As has been mentioned above (Chap. 4.1.1) both mono- and bicyclic 4,6-dioxo-1,3-oxazines may react with heterocumulenes (aryl isocyanates, aryl isothiocyanates) to yield the corresponding 4,6-dioxo-1,3-diazines (or the oxo-thiono analogues)^{3,47-49}. Compound 99c as well as 108c add DMAD to give the fused α -pyridone 212, albeit in low yield^{46,49}.



Mesoionic 4,6-dioxo-1,3-thiazines react with aryl isocyanates with the elimination of COS to produce the corresponding mesoionic 4,6-dioxo-1,3-diazines (Chap. 4.1.1)⁴⁶; this transformation has been proven to be a convenient way of synthesizing these compounds, especially in cases where thioamides and aryl isocyanates are readily available. No cycloadducts have been obtained with a variety of acetylenic and olefinic dipolarophiles; conversion into 4-quinolones has been the preferred pathway (Chap. 5.5)¹⁰⁶. The mesoionic 4,6-dioxo-1,3-thiazine 106a, however seems to be an



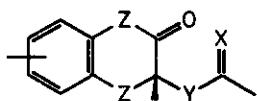
exception¹⁰⁶. The main product (214) results from a rearrangement of 106a (Chap. 5.5), whereas thiophene 213 is probably formed via an [2+4]-intermediate. An interesting case of regioselectivity is encountered in the reaction of 121a and ethyl propiolate⁷⁴. Only one isomer (215) has been isolated from the reaction mixture.



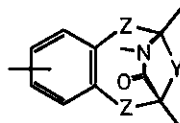
Both 4,6-dioxo-1,2,3-triazines and 4,6-dioxo-1,3,5-triazines (Chap. 4.1.5, 4.1.6) do not seem to undergo cycloaddition reactions^{110,115}.

5.4.2 With o-Quinonoid Compounds

Certain classes of five-membered mesoionic heterocycles of type A¹ react remarkably smoothly with o-quinonoid compounds (o-quinones, o-benzoquinone-dilimnes¹³⁸) yielding mainly 1:1 adducts of type 216 (formally derived from a valence tautomeric ketene form of the mesoion) and 217¹³⁹⁻¹⁴¹. In an obvious extension of this program, the reactions of both mesoionic 4,6-dioxo-1,3-diazines (Chap. 4.1.1) and 4,6-dioxo-1,3-oxazines (Chap. 4.1.2) with o-quinones have been investigated.



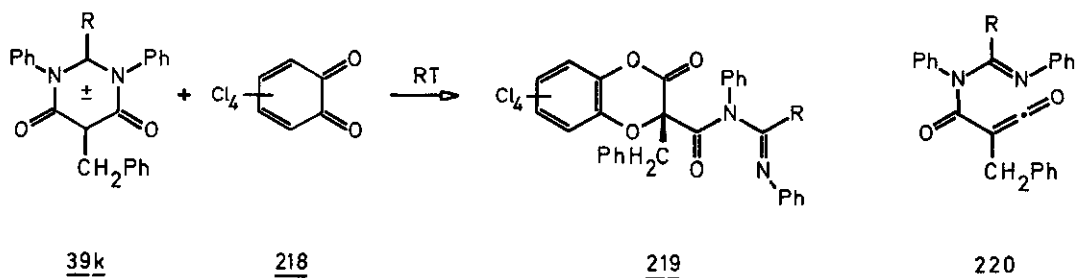
216



217

X: O,S ; Y: -N,O,S ; Z: O,N-Aroyl

Mesoionic 4,6-dioxo-1,3-diazines (e.g. 39k) react with tetrachloro-o-benzoquinone (218) to give a compound (219)¹⁴² which can be considered as an adduct of 218 with



39k

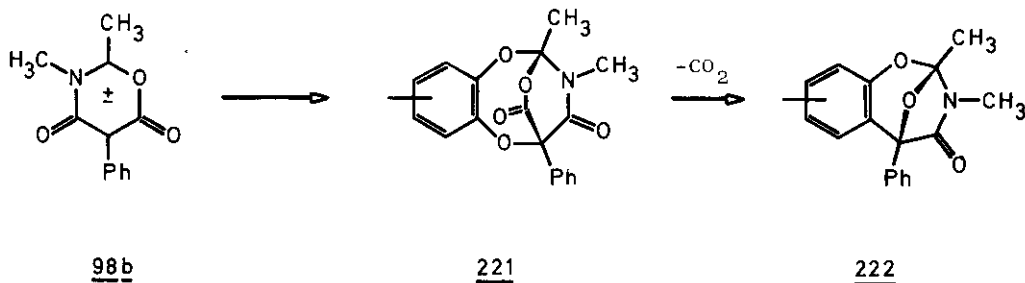
218

219

220

R = (4-OCH₃)C₆H₄

an open chain ketene tautomer of 39k (220)⁴⁰. These tautomers are not involved in this cycloaddition, however, but may be important intermediates in rearrangement reactions (Chap. 5.5). Mesoionic 4,6-dioxo-1,3-oxazines (e.g. 98b) react quite differently. CO₂ is evolved with both with o-quinones and with 9,10-phenanthrenequinone; this occurs even at room temperature. The products obtained (e.g. 222)^{50,51,142} can be rationalized by a primary [$\pi 4 + \pi 4$] cycloaddition (to 221) with subsequent ring



98b

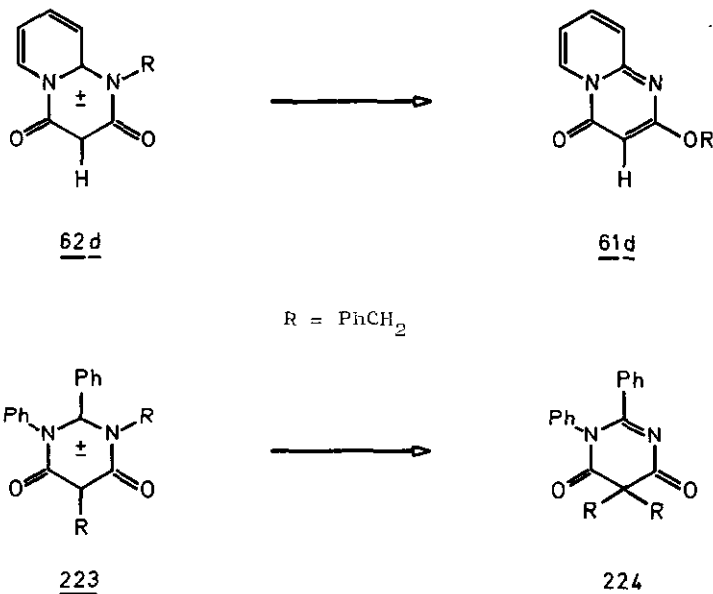
221

222

opening, loss of CO_2 , and rearrangement. This sequence can also be formulated as a concerted reaction. The extension of these investigations to o-benzoquinone-diamines is under way¹⁴³.

5.5 REARRANGEMENTS

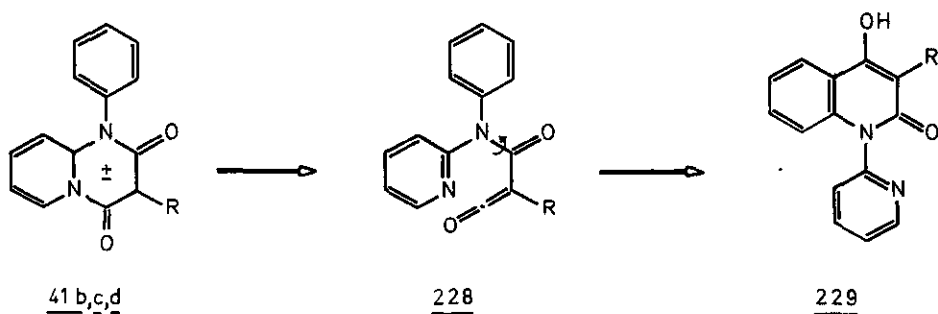
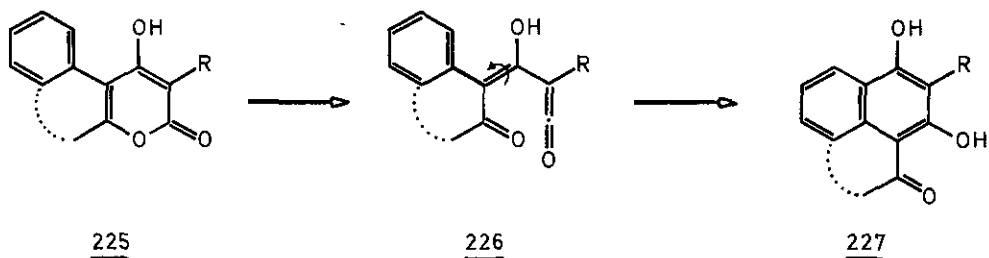
Heating of the bicyclic mesoionic 1,3-diazine 62d to about 250°C leads to the neutral benzyl ether 61d in poor yield. (This reaction is in contrast to the conversion of methyl ethers to mesoions; compare 31→32³⁰, or 35→34³⁵, Chap. 4.1) On the other hand, heating of the monocyclic mesoionic 4,6-dioxo-1,3-diazine 223 gives a N→C



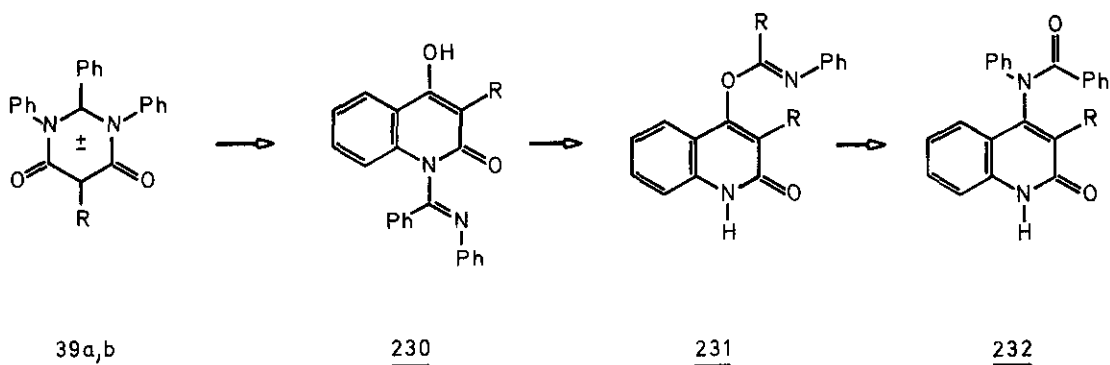
migration of the benzyl group yielding the 5,5-dibenzyl-4,6-dioxo-tetrahydropyrimidine 224⁶⁷. A radical mechanism is suggested for both cases, because dibenzyl and "tribenzyl" are isolated as side products¹⁴⁴.

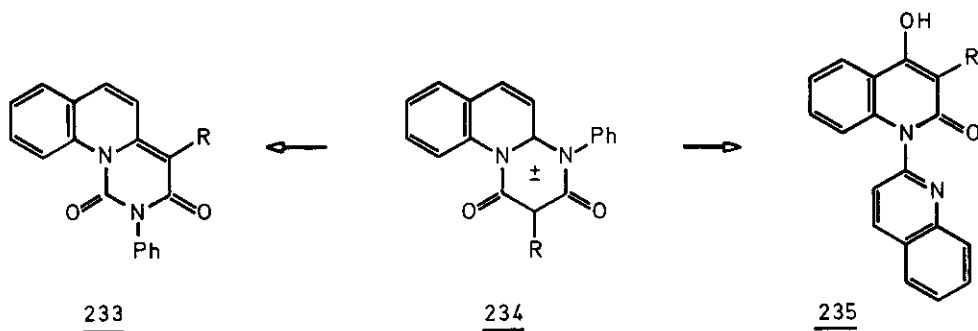
Malonyl heterocycles, such as 5-aryl-4-hydroxy-2-pyrones and benzocoumarins 225 react at higher temperatures via ketenes (226) to thermodynamically more stable carbocyclic compounds 227¹⁴⁵.

It is therefore not surprising that mesoionic N-aryl-2,4-dioxo-1,3-diazines rearrange to 2-quinolones¹⁴⁶. Thus the bicyclic mesoions 41 react at $260\text{--}300^\circ\text{C}$ via the ketene

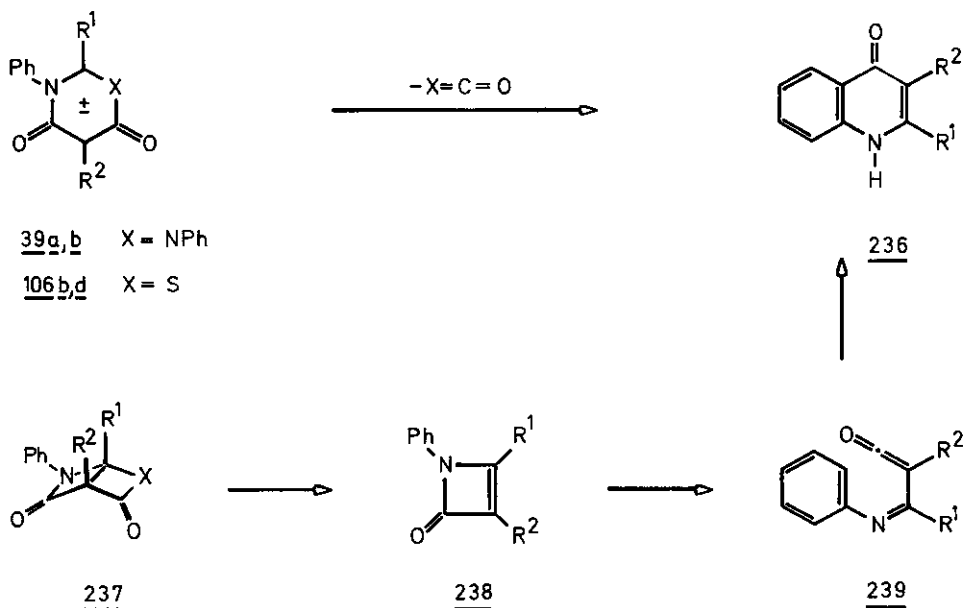


intermediate 228 to give the quinolones 229 in good yields. The monocyclic mesoions 39 react in an analogous way (with ketenes, however, the primary products (230) are stabilized by two consecutive reactions leading via 231 to the formation of 232). The mesoions 234 (obtained from 2-arylaminoquinolines and bis(2,4,6-trichlorophenyl) malonates or 100 and aryl isocyanates) react in 2,4,6-trichlorophenol to yield compound 233; on the other hand, if heated in a high boiling solvent, such as diphenyl ether, the 4-hydroxy-quinolones 235 are formed¹⁴⁸.



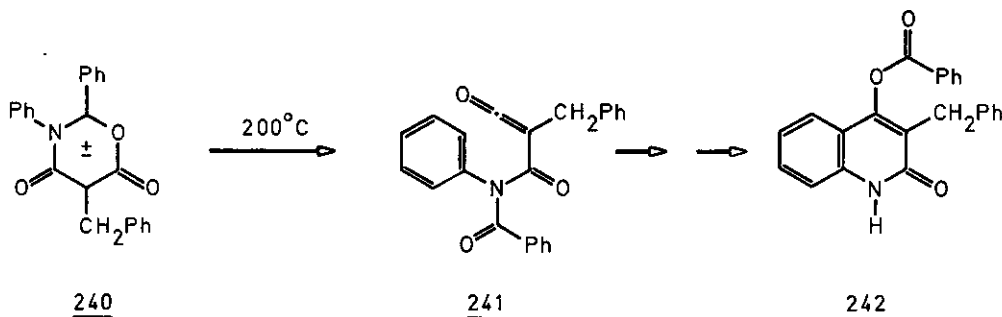


Another type of rearrangement for N-aryl-4,6-dioxo-1,3-diazines (39a,b)⁴¹ and 1,3-thiazines 106¹⁰⁶, leading in both cases to the same 4-quinolones, was published independently by two research groups in 1975. Thus the pyrimidines 39 react in 2,4,6-trichlorophenol at 200°C under loss of phenyl isocyanate to yield the 4-quinolones 236, whereas the 1,3-thiazines 106 are losing carbon oxysulfide in boiling benzene without catalysts. The mechanism of both reactions can be rationalized by bond formation between C2 and C5 (237), (simultaneous?) loss of X=C=O (238), with subsequent

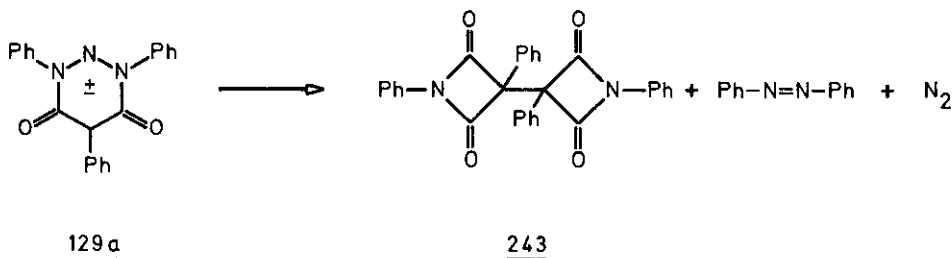


ring opening to the ketene 239 and ring closure to 236. The role of the solvent (tri-chlorophenol) in the reaction of the 1,3-diazine 39 is not yet clearly understood (compare the rearrangement of 39 to 232 without solvent above 260°C).

The thermolysis of the mesoionic 2,4-dioxo-1,3-oxazine 240 in trichlorophenol at 200°C yields the 2-quinolone 242^{49,149}, obviously by a similar pathway as described for the conversion of 39b to 231. The expected 4-quinolone (236) is formed in a low yield (1.6%) only, and at the present time there is no explanation for this different behavior of the oxazine 240 from the reaction of the thiazines 106.



An unexpected reaction occurs if the mesoionic 2,6-dioxo-1,2,3-triazine 129a is heated in boiling xylene, yielding the bisazetidone 243, azobenzene and nitrogen¹¹⁰. Most probably the reaction is initiated by a dimerisation step¹⁵⁰.



6. CONCLUSIONS

Meta-quinodimethane dianion (1) may be considered as a basis system for three types of mesoionic six-membered heterocycles (A, B, C, Scheme 1). Following the ingenious interpretation of Katritzky and Waring⁶² concerning the structure of "malonyl- α -aminopyridine", a great number of compounds of type B have come to light. Besides being interesting in their own right, they may serve as source of new heterocyclic systems, both mesoionic and covalent. Mesoions also remain a challenge for crystallographers and theoreticians in exploring the sometimes peculiar bond and electronic properties of these compounds.

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