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CONJUGATED SYSTEMS OBTAINED BY REACTION OF CYCLIC AMIDES WITH DEHYDROGENATION AND DEHYDRATION AGENTS—III*

MESOIONIC COMPOUNDS; ANHYDRO DIHYDROXIDES OF 1,4-DISUBSTITUTED-3,5-BIS(ARYLTHIO)-2,6-DIHYDROXY-PYRAZINIUM†

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Abstract—Derivatives of anhydro-3,5-bis(phenylthio)2,6-dihydroxy-1,4-diphenyl pyrazinium dihydroxide (IIa) with H atoms at the *para* positions of the phenyl rings systematically substituted with a NO_2 group, Br and a OMe group (IIb–j), and derivatives of the same compound with phenyl groups systematically substituted with Me groups at positions 1 and 4 (IVk–m) have been prepared. The IR, NMR and electronic spectra of these compounds are in agreement with the assumed prevailing participation of the canonic structure of the aromatic type VIII α in their real structure.

IN CONNECTION with the preparation of cyclic conjugated systems from dioxopiperazines[1] we have investigated the reaction of 1,4-diphenyl-2,6-dioxopiperazine (Ia) with benzenesulphonyl or benzenesulphenyl chloride in pyridine,[2] yielding a new type of mesoionic compound, anhydro-3,5-bis(phenylthio)2,6-dihydroxy-1,4-diphenylpyrazinium dihydroxide (IIa). The structure of this compound, which is in agreement with the IR and electronic spectra, was also proved by transformation into compounds having the 2,6-dioxo and 2,3,6-trioxopiperazine skeletons, as well as by cyclic dipolar addition which occurs at positions 3 and 5.

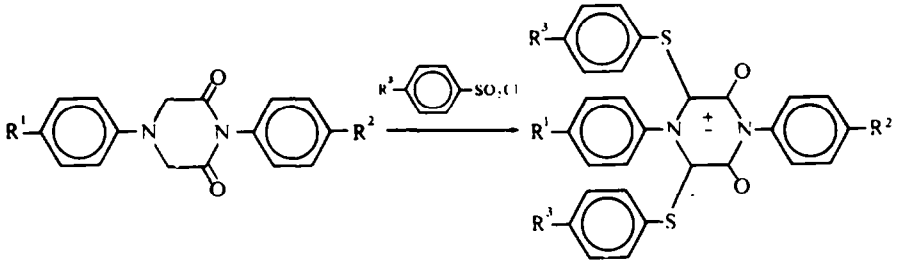
So far, the mechanism of formation of compound IIa has not been fully explained: in the case of reaction with benzenesulphenyl chloride, a radical or electrophilic substitution of methylene groups with the phenylthiol residues and 1,3-dehydrogenation of the dioxopiperazine ring are likely to take place. In the group of mesoionic compounds IIa is interesting as a compound having a 6-membered ring and a symmetric molecule which conforms with Baker–Ollis'[3–5] definition of the mesoionic structure and at the same time undergoes the 1,3-dipolar cyclic addition, typical of mesoionic compounds.[6,7]

An investigation of the electronic structure of the new bond system seemed therefore to be of interest as a contribution to the theory of mesoionic compounds. One of routes for obtaining information about the nature of this bond system consists of the investigation of the effect of substitution of the mesoionic ring on spectral and chemical properties of the system. For this purpose, two series of derivatives have been prepared. In the first series, the H atom at the *para* positions of various Ph rings in compound IIa was systematically replaced by a NO_2 group, Br and OMe group;

* Papers[1,2] should be regarded as the first two communications of this series.

† Preliminary communication: *Tetrahedron Letters* 3339 (1969).

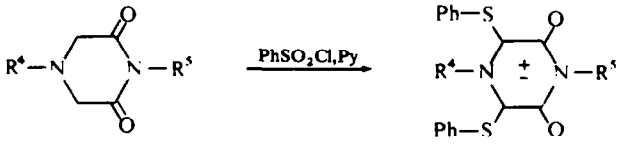
in the second series, Ph groups at positions 1 and 4 were replaced by Me groups. Reactions of dioxopiperazines Ia–g, or IIIk–m with benzenesulphonyl chloride or its *para* substituted derivatives in pyridine yielded mesoionic compounds IIb–j and IVk–m.



Ia–g IIa–j

	R^1	R^2	R^3
a	—	—	—
b	NO_2	—	—
c	Br	—	—
d	OCH_3	—	—
e	—	NO_2	—
f	—	Br	—
g	—	OCH_3	—
h	—	—	NO_2
i	—	—	Br
j	—	—	OCH_3

Substituents R^1, R^2, R^3 are the functional groups given in the Table or hydrogen.



IIIk–m IVk–m

IIIk–IVk $R^4 = CH_3$ $R^5 = C_6H_5$
IIIl–IVl $R^4 = C_6H_5$ $R^5 = CH_3$
IIIm–IVm $R^4 = R^5 = CH_3$

The starting dioxopiperazines, which with the exception of compounds Ia and IIIk[8] have not been described in the literature, were prepared from the corresponding N-substituted iminodiacetic acids Vb–d, via their cyclic anhydrides VIb–d and monoanilides VIIb–g (*cf* scheme 1). An analogous procedure was used to prepare 2,6-dioxo-1-methyl-4-phenylpiperazine (IIIl); 1,4-dimethyl-2,6-dioxopiperazine (IIIm) was obtained by methylation of the known[9] 4-Me derivative.

A comparison of the NMR, IR and electron spectra of the newly prepared mesoionic compounds allows to draw some conclusions on their electronic structure.

The chemical shifts of Me groups of dioxopiperazines of type III and mesoionic

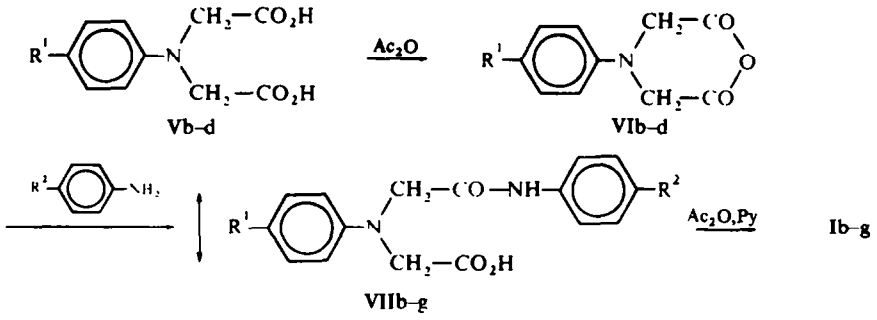


TABLE 1. NMR PEAKS OF PROTONS OF METHYLS AT POSITION 1 AND 4 OF COMPOUNDS IIIk–m AND IVk–m

Compound	τ(CDCl3) III		IV		Δ(III–IV)	
	1	4	1	4	1	4
k	—	7·6	—	5·6	—	2·0
l	6·9	—	6·5	—	0·4	—
m	6·9	7·7	6·7	5·8	0·2	1·9

TABLE 2. SPECTRA OF COMPOUNDS I–IV

Compound	IR spectrum ν C=O (cm⁻¹)		Compound	IR spectrum ν C=O, C=C, C=N mesoionic ring (cm⁻¹)		UV spectrum λmax mμ(log ε)
Ia	1705	1753	IIa	1640	1690	438 (3·17)
Ib	1697	1747	IIb	1635	1680	449 (4·00)
Ic	1700	1753	IIc	1635	1683	444 (4·12)
Id	1698	1752	IId	1636	1685	444 (4·05)
Ie	1704	1757	IIe	1640	1685	442 *
If	1700	1750	IIf	1637	1683	441 *
Ig	1700	1748	IIg	1636	1683	448 (3·76)
			IIh	1637	1686	442 (4·25)
			IIi	1632	1683	448 (4·64)
			IIj	1634	1685	445 (4·14)
IIIk	1695	1745	IVk	1635	1680	437 (3·53)
IIIl	1683b	1736	IVl	1620	1673	438 (4·16)
IIIm	1693	1745	IVm	1608	1653	428 (4·16)

* Extinction could not be ascertained because of high insolubility of the compound.

compounds of type IV prepared therefrom are given in Table 1. If we use compounds IIIk–l and IVk–l as models, we can, in the case of dioxopiperazine IIIm, assign the band having a higher τ to the Me group in position 4, while in the case of the mesoionic compound IVm it is a band of a lower value that corresponds to the Me group in the same position.

The transformation of the dioxopiperazine ring to the mesoionic ring is connected

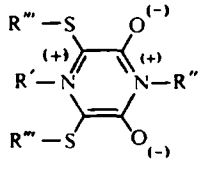
in all cases with a decrease in the τ value of the Me group protons on nitrogen, the decrease at position 1 being 0·4–0·2 τ, while a similar decrease at position 4 is 2·0–1·9 τ.

The difference in shielding of the Me group protons at both positions in the case of dioxopiperazines can be explained by a decrease in the electron density on the N atom 1 due to the effect of the CO groups being in conjugation with its free electron pair. The transformation to the mesoionic structure leads to a partial aromatization of the ring, and consequently to a decrease in the shielding of protons situated in the proximity of the nodal plane, of the π-electron system of the ring, i.e. Me groups in both positions considered. Moreover, the transformation to the mesoionic structure leads to a pronounced change in the electron density of the N atom 4 due to its participation in conjugation. Owing to this, the decrease in the τ value of the Me group protons in position 4 is much more marked than an analogous decrease in position 1. This interpretation requires taking into account the long range effect of the ring currents in the phenylthiol groups. A shift caused by this effect, however, can amount to 0·5 ppm at most, which is less than the shift observed in our case.

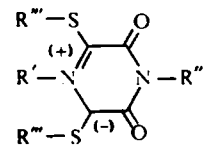
TABLE 3. ARYLIMINODIACETIC ACIDS MONOARYLAMIDES (VIIb–g)

Compound	Formula m.w.	M.p. solvent	Yield %	Analysis calculated/found %C	%H	%N	IR bands in the region 1500–1800 cm^{-1}
VIIb	$C_{16}H_{15}N_3O_5$ 329·3	193–6 water	80	58·40 58·31	4·59 4·71	12·77 13·04	1515, 1553, 1604, 1680, 1733
VIIc	$C_{16}H_{15}BrN_2O_3$ 363·2	110–114 ethanol	59	52·95 52·77	4·16 4·90	7·72 7·36	1507, 1558, 1604, 1656, 1723
VIId	$C_{17}H_{18}N_2O_4$ 314·3	85–86 ethanol	58	64·99 65·22	5·77 5·98	8·91 9·07	1525, 1573, 1615sh, 1640, 1735
VIIe	$C_{16}H_{15}N_3O_5$ 329·3	195·5–198 methanol	75	58·40 58·44	4·59 4·63	12·77 12·93	1517, 1567, 1608, 1663, 1706
VIIf	$C_{16}H_{15}BrN_2O_3$ 363·2	192–194 ethanol	89	52·95 52·84	4·16 4·24	7·72 7·98	1513, 1547, 1607, 1644, 1705
VIIg	$C_{17}H_{18}N_2O_4$ 314·3	207·5–208·5 ethanol	70	64·99 64·88	5·77 6·06	8·91 9·06	1518, 1557, 1620b, 1707

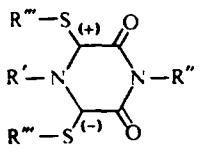
In comparison with the spectra of the initial dioxopiperazines, the IR spectra of all the mesoionic compounds prepared by us exhibit such a large decrease in the frequency of the CO bands (55–95 cm^{-1}) that these bands cannot any more be regarded as bands of the diacylamine grouping (*cf* Table 2).



VIIIα



VIIIβ



VIIIγ

TABLE 4. 1.4-DIARYL-2,6-DIOXOPIPERAZINES (Ib–g)

Compound	Formula m.w.	M.p. solvent	Yield %	Analysis calculated/found %C	%H	%N	IR bands in the region 1500–1800 cm^{-1}
Ib	$C_{16}H_{13}N_3O_4$ 311·3	233–236 acetone	56	61·73 61·63	4·21 4·30	13·52 13·98	1521, 1603, 1697, 1747
Ic*	$C_{16}H_{13}BrN_2O_2$ 345·2	171–174·5 ethanol	66	55·67 55·86	3·79 3·86	8·12 8·05	1505, 1598, 1700, 1753
Id	$C_{17}H_{16}N_2O_3$ 296·3	134–136 ethanol	49	68·91 68·84	5·44 5·42	9·45 9·62	1525, 1698, 1752
Ie	$C_{16}H_{13}N_3O_4$ 311·3	190–191 ethanol	55	61·73 61·67	4·21 4·31	13·52 13·72	1503, 1527, 1602, 1704, 1757
If†	$C_{16}H_{13}BrN_2O_2$ 345·2	189–192 ethanol	61	55·67 56·00	3·79 3·82	8·12 8·20	1607, 1700, 1750
Ig	$C_{17}H_{16}N_2O_3$ 296·3	177–179·5 ethanol	77	68·99 69·16	5·44 5·68	9·45 9·53	1516, 1607, 1700, 1748

* Analysis %Br: calculated 23·18: found 22·72.
† Analysis %Br: calculated 23·18: found 23·40.

Both the IR and NMR spectra of compounds type II and IV are in accordance with the assumed prevailing participation of the aromatic limit structure of VIIIα in the real structure of these compounds. This does not mean, of course, that these compounds could not react also according to other canonic structures: e.g., when interpreting the 1,3 dipolar cyclic addition it is necessary to assume the structure of the azomethinylide type VIIIβ, γ.

The position of bands of the IR spectrum belonging to the double bonds of the mesoionic ring remains essentially unchanged in the case of a systematic *para* substitution of the end phenyl rings with electron attracting or repulsing groups (compounds IIa–j): also λ_{max} of the electron spectrum of these compounds does not show any large changes.

The lack of effect of the substitution of *para* positions in the Ph groups upon the wave number of IR bands corresponding to the double bonds of the mesoionic ring indicates a large deviation of the phenyl rings from the plane of the mesoionic ring and a low degree of conjugation between these rings.

On the contrary, the substitution of Ph groups with Me groups at positions 1 and 4 of the mesoionic ring leads to a significant decrease in the band frequency of the IR spectrum (compounds IVl–m). The effects of conjugation and hyperconjugation, the induction effect and the steric effects can all be responsible for these changes. The substitution of the Ph group with the Me group is connected with a change in all the above effects: this is why it cannot as a rule be interpreted unambiguously. In our case the likeliest interpretation of the decrease in the frequency of bands of the IR spectrum is based on the steric effect: a replacement of the Ph group with a less bulky Me group allows to attain a normal arrangement of the π clouds of the mesoionic ring, which is reflected in an increase in the polar character of the C—O bonds.

TABLE 5. MESOIONIC COMPOUNDS IIb–i AND IVk–m

Compound	Formula m.w.	M.p. solvent	Yield %	Analysis calculated/found %C	%H	%N	%S	IR bands in the region 1500–1800 cm^{-1}
IIb	$C_{28}H_{19}N_3O_4S_2$ 525·6	223–226 benzene	14	64·01 63·79	3·64 3·75	8·00 8·34	12·20 12·08	1535, 1578, 1635, 1680
IIc	$C_{28}H_{19}BrN_2O_2S_2$ 559·5	243·5–246 benzene	37	60·11 60·02	3·42 3·43	5·00 5·15	11·46 11·43	1577, 1635, 1683
IId	$C_{29}H_{22}N_2O_3S_2$ 510·6	246·5–248 benzene	26	68·25 68·26	4·34 4·32	5·49 5·78	12·56 12·39	1517, 1600sh, 1636, 1685
IIe	$C_{28}H_{19}N_3O_4S_2$ 525·6	245–246·5 benzene	26*	64·01 64·07	3·64 3·65	8·00 8·16	12·20 12·06	1535, 1594, 1640, 1685
IIf	$C_{28}H_{19}BrN_2O_2S_2$ 559·0	254–256·5 benzene	25	60·11 60·45	3·42 3·46	5·00 5·31	11·46 11·52	1600sh, 1637, 1683
IIg	$C_{29}H_{22}N_2O_3S_2$ 510·6	242·5–245·5 benzene acetone	42	68·25 68·52	4·34 4·42	5·49 5·73	12·56 12·60	1510, 1600sh, 1636, 1683
IIh	$C_{28}H_{18}N_4O_6S_2$ 570·6	259·5–262·5 benzene	16	58·95 58·97	3·18 3·23	9·82 9·74	11·26 11·33	1523, 1587, 1637, 1686
IIi	$C_{28}H_{18}Br_2N_2O_2S_2$ 638·4	239–242 benzene	22	52·68 52·95	2·84 3·01	4·39 4·46	10·05 10·20	1568sh, 1600sh, 1632, 1683
IIj	$C_{30}H_{24}N_2O_4S_2$ 540·6	222·5–225·5 benzene* heptane	6	66·65 66·51	4·50 4·53	5·19 5·40	11·86 11·27	1598, 1634, 1685
IVk	$C_{23}H_{18}N_2O_2S_2$ 418·5	190–193 cyclohexane* benzene	10	66·03 65·96	4·34 4·49	6·70 6·92	15·32 15·24	1600sh, 1635, 1680
IVl	$C_{23}H_{18}N_2O_2S_2$ 418·5	245–248 benzene* acetonitrile	12	66·03 66·43	4·34 4·59	6·70 7·02	15·32 15·21	1600sh, 1620, 1673
IVm	$C_{18}H_{16}N_2O_2S_2$ 356·5	173–175 benzene acetonitrile	13	60·65 60·75	4·52 4·62	7·85 8·13	17·95 17·95	1608, 1653

* The yield was related to the starting amount of the crude product used in the reaction: in the other cases the yield was related to the amount of the crude product reacted in the reaction.

EXPERIMENTAL

The m.ps were determined with Kofler's block and were not corrected. In the column chromatography, a hundredfold excess of silicagel was employed. The samples for the analysis, IR spectra and UV spectra were dried *in vacuo* of an oil pump at 100° for 6 hr, if not specified otherwise. The IR spectra were measured with a UR-10 spectrometer in the KBr pellets: the UV spectra were recorded in an EtOH soln using a CF 4 (Optica Milano) registration spectrometer, and the NMR spectra were measured with a JEOL-JNM-3-60 (60 M cps) spectrometer in $CDCl_3$.

Compounds used. *p*-Nitrobenzenesulphonyl chloride and *p*-bromobenzenesulphonyl chloride were

prepared according to modified Sandmayer's method by reaction of diazonium salts with a soln of SO_2 and $CuCl_2$ in AcOH.[10] *p*-Anisidinosulphonyl chloride was obtained by reaction of *p*-anisidine with chlorosulphonic acid.[11] The *p*-methoxyphenyliminodiacetic acid and *p*-nitrophenyliminodiacetic acid were obtained according to the literature.[12, 13]

p-*Bromophenyliminodiacetic acid* (Vc). *p*-Bromophenyliminodiacetic acid was prepared by alcalic hydrolysis of the dimethylesther[13] in yield 95%, m.p. 175–176° (EtOH). (Found: C, 41·68; H, 3·61; N, 4·64; Br, 28·25. Calc. for $C_{10}H_{10}NO_4Br$ (288·1): C, 41·69; H, 3·50; N, 4·86; Br, 27·74%), IR spectrum: 1510, 1600, 1698 cm^{-1}.

Anhydrides of aryliminodiacetic acids (VIb–d). *p*-Nitrophenyliminodiacetic acid (1 mole) and Ac_2O (3 moles) was refluxed for 20 min with exclusion of moisture. The mixture was then left to crystallize, the crystals were filtered off, washed with ether and dried under reduced pressure. After recrystallization from acetonitrile, IVb was obtained, m.p. 199–202° in a yield 87%. (Found: C, 50·72; H, 3·40; N, 12·19. Calc. for $C_{10}H_8N_2O_5$ (236·2): C, 50·85; H, 3·41; N, 11·86%), IR spectrum: 1514, 1605, 1780, 1828 cm^{-1}. Compound, VIc was obtained in the same way, m.p. 164–167° (benzene), yield 78%. (Found: C, 44·94; H, 3·09; N, 5·24. Calc. for $C_{10}H_8BrNO_3$ (270·1): C, 44·47; H, 2·98; N, 5·19%), IR spectrum: 1507, 1595, 1770, 1832 cm^{-1}. Compound VId was obtained as in the preceding cases with the only difference that Ac_2O and AcOH were distilled off from the mixture *in vacuo*, and the crude product was used in further reaction without isolation.

Monoaryl amides of aryliminodiacetic acid (VIIb–g). A soln of aryliminodiacetic acid anhydride (1 mole) in THF was mixed with a soln of arylamine (1 mole) in the same solvent, and the mixture was left to stand 2 hr at room temp with exclusion of moisture. (In the preparation of VIIe the mixture was refluxed for 2 hr. During this time, a solid substance precipitated from the soln. In the case of VIIb and VIId, the product precipitated only after concentrating of the mixture). The crude product was filtered off, washed with a small amount of THF and crystallized from the respective solvent. The samples for analysis were recrystallized 3 times. The results of the experiments are given in Table 3.

In the same manner phenyliminodiacetic acid monomethylamide was prepared after crystallization from EtOH in a yield 72%, m.p. 193–194°. (Found: C, 59·41; H, 6·59; N, 13·25. Calc. for $C_{11}H_{14}N_2O_3$ (222·2): C, 59·45; H, 6·35; N, 12·60%), IR spectrum: 1513, 1615b, 1703 cm^{-1}.

1,4-*Diaryl*-2,6-*dioxopiperazines* (Ib–g). Aryliminodiacetic acid monoanilide (0·0591 mole), Ac_2O (0·255 mole) and pyridine (40 ml) was refluxed for 3 hr with exclusion of moisture. The monoanilide dissolved during the reaction. On cooling, the mixture was poured into a mixture of water and ice. The product which separated from the soln was filtered off, washed with water and twice crystallized in the respective solvent. The results are given in Table 4.

In the same manner IIIl was prepared from phenyliminodiacetic acid monomethylamide in a yield 61%, m.p. 108–110° (EtOH). (Found: C, 65·01; H, 6·28; N, 13·53. Calc. for $C_{11}H_{12}N_2O_2$ (204·3): C, 64·75; H, 5·93; N, 13·70%), IR spectrum: 1517, 1608, 1683, 1736 cm^{-1}.

1,4-*Dimethyl*-2,6-*dioxopiperazine* (IIIm). To a soln of NaOMe (14·8 g) in 1,2-dimethoxyethane (450 ml), a soln of 4-methyl-2,6-dioxopiperazine (32 g) in the same solvent was added, and the mixture was heated to 60° with exclusion of moisture. The Na salt of dioxopiperazine separated in the form of a suspension, to which a soln of MeI (42·5 g) in 1,2-dimethoxyethane (90 ml) was added dropwise during 5 min, and the mixture was stirred at 60° for 15 min. On cooling, the insoluble part was filtered off and the filtrate was evaporated under reduced pressure and the residue was twice extracted with chloroform. The extract after evaporation of chloroform was distilled off *in vacuo* of an oil pump at bath temp 100°, yield 11 g (32%). (Found: C, 50·62; H, 7·24; N, 19·23. Calc. for $C_6H_{10}N_2O_2$ (142·2): C, 50·65, H, 7·08; N, 19·70%), IR spectrum: 1693, 1745 cm^{-1}.

Mesoionic compounds IIb–j, IVk–m. To a soln of 1,4-disubstituted 2,6-dioxopiperazine (0·0452 mole) in pyridine (140 ml) arylsulphochloride (0·094 mole) was added, and the mixture was refluxed for 7 hr with exclusion of moisture. In the case of compound IIb, the reaction time was reduced to 1·5 hr, in the case of IIh to 3 hr. The reaction times needed for the preparations of compounds IVk and IVm were 3 hr and 45 min, respectively, and the mixtures were in both cases evaporated to half the volume *in vacuo* prior to treatment.

On cooling, the mixture was added dropwise into a mixture of water and ice while stirring. A brown-yellow ppt which separated was filtered off, washed with water and dried *in vacuo* over KOH. The crude product—a mixture of diarylsulfide, of unreacted 1,4-diaryl-2,6-dioxopiperazine, a mesoionic compound and deep-coloured impurities—was fractionated by column chromatography on silicagel (solvent system benzene, ether 85:15). The individual compounds were isolated in an order in which they are given in the characterization of the crude product. The mesoionic compounds were twice crystallized from the respective

solvent, and the samples for analysis were dried *in vacuo* of a diffusion pump at b.p. of toluene for 12 hr. The results are summarized in Table 5.

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