CHAPTER 4

Oxocarbons and their reactions

ROBERT WEST

The University of Wisconsin, Madison, Wisconsin, U.S.A.

and

JOSEPH NIU

Wyandotte Chemical Corporation, Wyandotte, Michigan, U.S.A.

I. INTRODUCTION

The term 'oxocarbon' designates compounds in which all, or nearly all, of the carbon atoms bear ketonic oxygen functions or their hydrated equivalents[1]. The most important oxocarbons are cyclic compounds, and this review will be limited to the chemistry of the monocyclic oxocarbons.

A few years ago we pointed out that monocyclic oxocarbon anions, $C_nO_n^{m-}$, are aromatic substances, stabilized by electron delocalization of π electrons in the ring[1,2]. At present four such species are known, the squarate (1), croconate (2) and rhodizonate (3) dianions, and the tetraanion of tetrahydroxy-p-benzoquinone (4). Much of the current
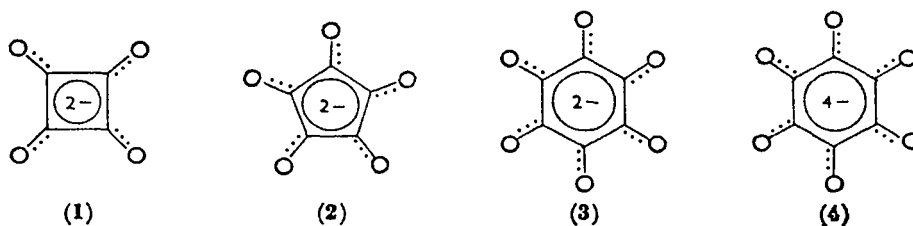
interest in the oxocarbons relates to physical studies of the chemical bonding in these species. However, in this review, in keeping with the purposes of this volume, the chemical reactions of the oxocarbons will be emphasized.

Although the oxocarbon anions have only recently been shown to form a previously unrecognized aromatic series, croconate and rhodizonate ions were actually among the first aromatic species ever synthesized. In 1823 Berzelius, Wöhler and Kindt observed the formation of a powdery black residue in the preparation of potassium by reduction of potassium hydroxide with carbon[3,4]. Dipotassium croconate and croconic acid (named from the Greek krokos = yellow, the colour of the acid and its salts) were isolated from this residue in 1825 by Gmelin[4]. A few years later, in 1837, Heller obtained rhodizonic acid (from the Greek rhodizein = rose red, the colour of the insoluble alkaline-earth derivatives) and dipotassium rhodizonate from the same material[5].

There is a further point of interest concerning these very early experiments. Both croconic acid and rhodizonic acid are now known to be products of microbiological oxidation of myoinositol (hexahydroxycyclohexane), a compound which is widely distributed in

plants[6,7]. Therefore Gmelin's preparation of croconic acid[4] in 1825 represents one of the very first preparations of an 'organic' compound from 'inorganic' starting materials. The classic synthesis of urea by Wöhler did not take place until three years later[8].

II. SYNTHESIS OF OXOCARBONS

A. The Reactions of Carbon Monoxide with Alkali Metals

The earliest preparations of oxocarbons were from potassium hydroxide and carbon[3], but it was soon found by Liebig that the same products could be obtained more conveniently from carbon monoxide and hot potassium metal[9]. The reductive cyclopolymerization of carbon monoxide thus provides a route to both five and six-membered oxocarbons. Although this interesting reaction has been known for more than a century, and the products have been studied repeatedly[10-14], only within the last few years has a clear picture of the nature of the reaction begun to emerge. Because the history of this classical reaction is intimately connected with that of the oxocarbons themselves, it is of interest to trace its development briefly.

I. $K_6C_6O_6$, rhodizonic acid and croconic acid

As early as 1834, it was discovered that hot potassium metal reacts with carbon monoxide[9]. The reaction is exothermic, and heat was usually allowed to develop freely, so that the temperature rose above 150°. Under these conditions, the first product which can be isolated is a grey solid, $K_6C_6O_6$[9]. This compound is very easily oxidized, and upon aqueous work-up in air, dipotassium rhodizonate or dipotassium croconate is obtained.

$K_6C_6O_6$ is now recognized to be the hexapotassium salt of hexahydroxybenzene[12-14]. Formally, it can be regarded as an oxocarbon salt with a 6 − charge on the anion. It is reasonable that air oxidation could transform $K_6C_6O_6$ into dipotassium rhodizonate:

$$C_6(OH)_6 \xleftarrow{\text{H}^+} K_6C_6O_6 \xrightarrow[\text{H}_2\text{O}]{\text{[O]}} K_2C_6O_6 + 4\,\text{KOH}$$
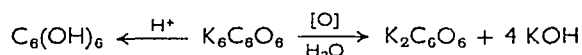
However, the production of croconate ion from the same reaction, providing an entry into the five-membered ring oxocarbons, is quite

surprising. Yet, as early as 1837, in work of amazingly high quality for the time, Heller correctly deduced that rhodizonate is the precursor of croconate ion[5].

The rhodizonate–croconate transformation was first investigated by Nietzki and Benckiser[12,15] and has been studied by several other investigators[6,16,17]. If air or oxygen is bubbled through an alkaline aqueous solution of rhodizonate, complete transformation to croconate takes place:

$$C_6O_6^{2-} \xrightarrow{[O]} C_5O_5^{2-} + CO_3^{2-}$$
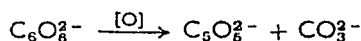
This remarkable reaction, involving contraction from a six to a five-membered ring, provides a most convenient method for the synthesis of croconates. The nature of the transformation has been in doubt, but it now seems clear that the reaction pathway is as follows:
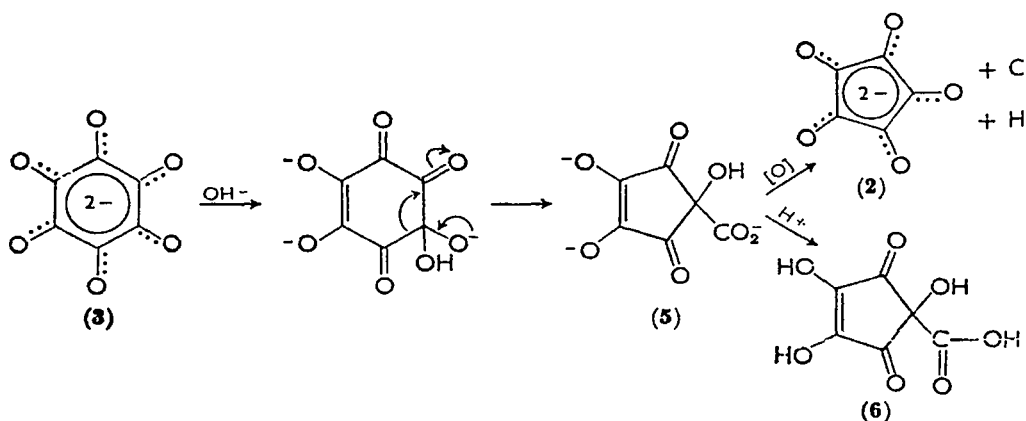

The intermediate anion **5** can be isolated from the solution in the form of the carboxylic acid **6**[15,17]. The ring contraction can be recognized as an example of an α-oxoalcohol rearrangement[18], related to the well-known benzil–benzylic acid rearrangement.

Sodium metal has been reported to react with carbon monoxide at 280–340° to produce the hexasodium salt of hexahydroxybenzene, $Na_6C_6O_6$[19]. This compound is oxidizable to disodium rhodizonate or croconate, just like the potassium compound. A careful recent study shows however that the reaction of sodium with carbon monoxide at temperatures from 200–500°C is complex, leading to a mixture containing sodium acetylide, sodium carbonate, and sodium rhodizonate as well as $Na_6C_6O_6$[19a].

2. The alkali metal salts of dihydroxyacetylene

If care is taken so that the reaction temperature of carbon monoxide with potassium never rises much above the melting point of potassium (63°), an intermediate black solid is formed[13,14,20-22], which is convertible to gray $K_6C_6O_6$ upon heating. In addition, carbon monoxide reacts with all of the alkali metals when they are dissolved in liquid ammonia to give yellowish 'alkali metal carbonyls', with the empirical formula MCO[23-25]. Recent investigations have begun to shed some light on these complex reactions.

In 1963 Sager and coworkers[13] published a study of the reaction between potassium and CO at low temperatures. They present evidence for two intermediates, $(K_3C_2O_2)_x$ and $(KCO)_x$, the latter undergoing conversion to $K_6C_6O_6$ upon heating:

$$K + CO \longrightarrow (K_3C_2O_2)_x \xrightarrow{CO} (KCO)_x \xrightarrow{\Delta > 100°} K_6C_6O_6$$
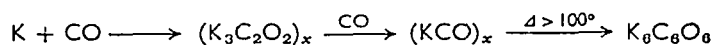
These investigators alkylated $(KCO)_x$ with methyl iodide and obtained a product with empirical formula $C_4O_4(CH_3)_4$, from which they
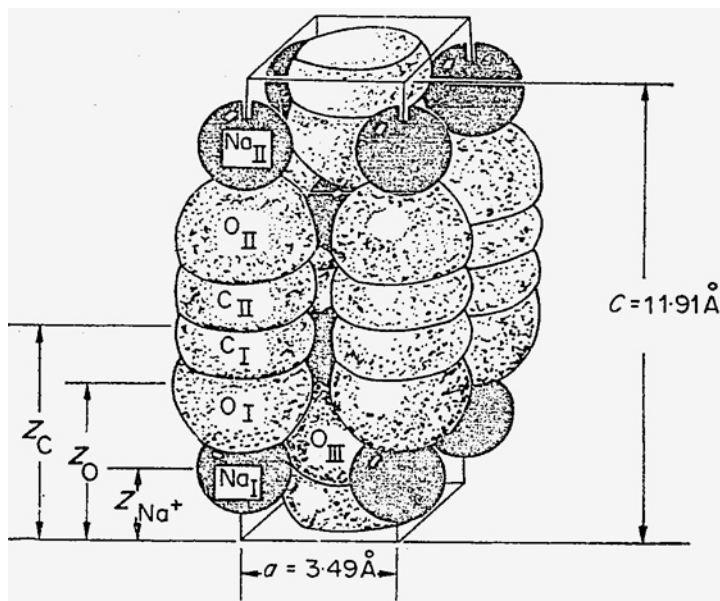

FIGURE 1. Arrangement of Na$^+$ and $^-$O—C≡C—O$^-$ ions in the crystal structure of the disodium salt of dihydroxyacetylene, $Na_2C_2O_2$, as determined by Weiss and Büchner[28].

deduced the formula $K_4C_4O_4$ for the black $(KCO)_x$, and inferred that the precursor was $K_6C_4O_4$.

The nature of the yellow 'alkali metal carbonyls' obtained in liquid ammonia has been clarified by Weiss and Büchner[26-28]. All of these substances appear to be principally salts of the dihydroxy-acetylene dianion, $M_2^+[OC\equiv CO]^{2-}$. The structures of the caesium, rubidium, potassium and sodium salts have been determined by x-ray crystal structure studies (Figure 1). Moreover, the black $(KCO)_x$ obtained by Sager and coworkers, despite its different appearance, is *crystallographically identical with* $K_2C_2O_2$[26]. The black colour must be the result of radical impurities or lattice imperfections.

The alkali metal dihydroxyacetylene salts can be regarded as linear oxocarbons; the anion is formally the first member of the series $C_nO_n^{2-}$. However, the bond lengths in the anion, about 1·20 Å for C—C and 1·27 Å for C—O[26,27], are consistent with the formula ^-O—$C\equiv C$—O^-, and suggest that electron delocalization in the system is slight.

The dianion of dihydroxyacetylene is a surprisingly weak base. Protolysis does not take place in acetonitrile solution with water or weak organic acids, but requires HCl, producing a mixture of *aci-*reductones, hexahydroxybenzene, and diglycolide (7), all thought to arise from HO—$C\equiv C$—OH[29]. On the other hand, Büchner[28] has found that the $M_2C_2O_2$ salts give a positive test for organometallic


(7)
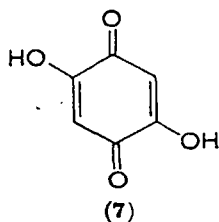
species and react with *n*-butyl bromide to give small amounts of α-hydroxy acid. He suggests that the 'alkali metal carbonyls' are really mixtures of M^+O^-—$C\equiv C$—O^-M^+ and an organometallic salt 8[28]:

(8)
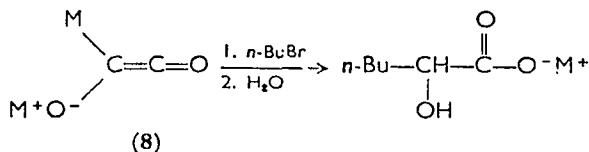
## B. *Other Syntheses of Rhodizonic and Croconic Acid and Their Salts*

Although the cyclopolymerization of carbon monoxide can be used to synthesize oxocarbons, other methods are often more convenient for laboratory preparations. One of the most useful is the oxidation of the readily available natural product, myoinositol, an isomer of hexahydroxycyclohexane[16,30].

If inositol is oxidized with warm concentrated nitric acid and the solution is then treated with potassium carbonate, the dipotassium salt of tetrahydroxy-*p*-benzoquinone is produced as green crystals[30]. If the oxidized solution is instead treated with potassium acetate and aerated, dipotassium rhodizonate is the product
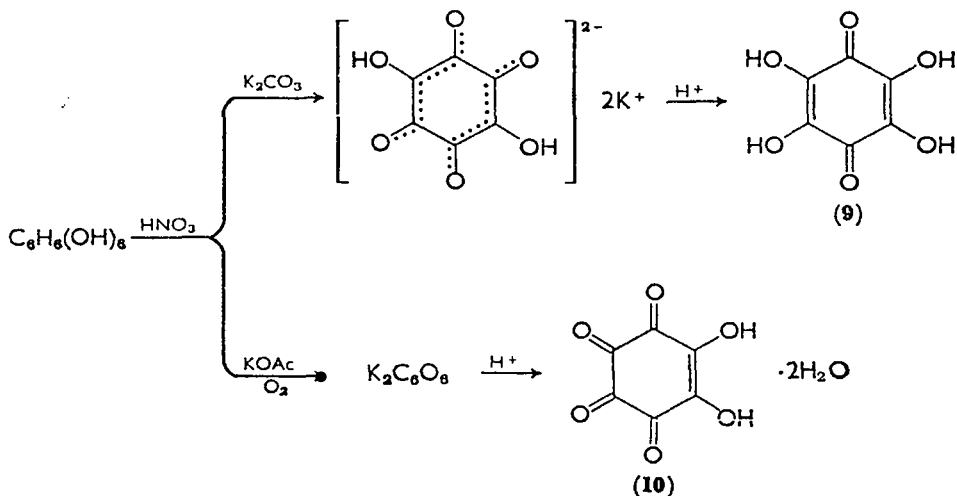
Free tetrahydroxyquinone (9) is stable and insoluble in water, so it is easily isolated as purple crystals by acidification of aqueous solutions of the dianion. Rhodizonic acid (10), however, is both sensitive to oxidation and quite soluble in water, so it is difficult to obtain from its salts. Small amounts of 10 can be obtained from basic aqueous solution by ion exchange using a H^+-form cation exchange resin[6], followed by low-temperature evaporation[31]; or the aqueous solution can be neutralized, evaporated, and 10 extracted with dioxane and precipitated with pentane[6]. Rhodizonic acid obtained by either of these methods is isolated as the colourless dihydrate, $H_2C_6O_6 \cdot 2H_2O$[32]. Sublimation in vacuum gives the dark orange anhydrous acid, first isolated only in 1958 by Bock and Eistert[32].

Another convenient route to **9** or **10** is the oxidative trimerization of glyoxal[33-35] discovered by Homolka[33]. The reaction is usually carried out in aqueous solution containing sodium sulphite and sodium hydrogen carbonate:

$$HCCH \xrightarrow[H_2O, O_2]{Na_2SO_3, NaHCO_3,} Na_2C_6O_4(OH)_2, 5-10\% \xrightarrow[170°]{[O]} Na_2C_6O_6$$
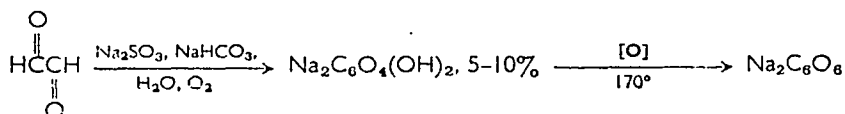
The yield in this synthesis is low, but according to recent patents considerable improvements in yield result when potassium cyanide is used as a catalyst[35,35a], or when ozone is used in place of oxygen[26]. The disodium salt of tetrahydroxyquinone which is the initial product can be converted to disodium rhodizonate simply by heating in air to 170°[33]. A relatively recent paper by Fatiadi and coworkers gives clear directions for the preparation of rhodizonic acid, croconic acid and their derivatives by this route[6].

Rhodizonic acid has also been prepared by reduction with SO_2 of its oxidation product, triquinoyl octahydrate[12,32] (see section V.A.), and by oxidation of 1,4-diamino-2,3,5,6-tetrahydroxybenzene with potassium persulphate[36a].

Croconic acid (**11**) and the croconates could presumably be made by oxidation of cyclopentane derivatives, but this has apparently never been done. The convenient ring-contraction from rhodizonate has invariably been used. A wide variety of six-membered ring precursors such as hexahydroxybenzene, rhodizonic acid, tetrahydroxyquinone, tetraaminohydroquinone, etc. can be converted to sodium or potassium croconate by oxidation in alkaline solution with air or with manganese dioxide[6,12,15].


(11)
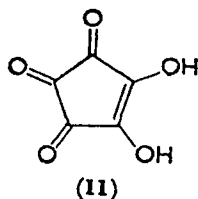
The alkali metal croconates are bright yellow salts, soluble in water to give stable solutions. Free croconic acid can be obtained by ion-exchange on aqueous solutions of the croconate salts, employing H^+-form cation exchange resins, followed by freeze drying of the solution[31]. Alternatively, the insoluble barium salt can be treated

with the equivalent amount of sulphuric acid to give an aqueous solution of croconic acid, which can be evaporated[6]. These syntheses give croconic acid as the trihydrate, which can then be recrystallized from ethanol–dioxan by addition of benzene. Drying under vacuum removes the water of crystallization[6].

C. Squaric Acid

Dihydroxycyclobutenedione, or squaric acid (12), was first isolated by Cohen, Lacher and Park by the acid hydrolysis of the halogenated cyclobutene derivatives 14 and 16[37]. Dimerization of 1,1-dichloro-2,2-difluoroethylene followed by dechlorination gives 1,2-dichloro-3,3,4,4-tetrafluorocyclobutene (13)[38]. Ethoxide ion converts the latter to the triether 14[39] which is converted to squaric acid by acid hydrolysis[40,41].
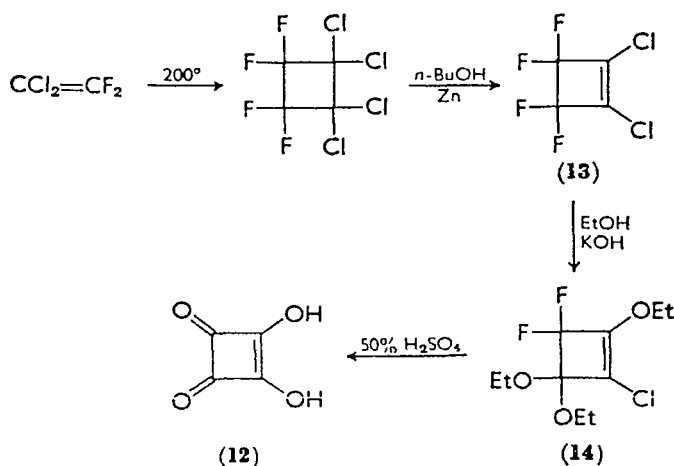
The commercially available hexafluorocyclobutene (15) made by cycloaddition of chlorotrifluoroethylene and dechlorination[38], also serves as a precursor for squaric acid by a similar reaction sequence[41].
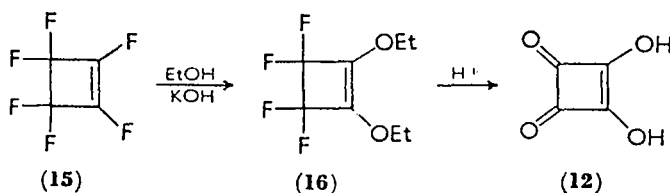

Recently, several useful preparations of squaric acid from hexa-chlorobutadiene have been discovered by Maahs[42-44]. Hexachloro-butadiene reacts with excess morpholine to form a trichlorotrimor-

9*

pholinobutadiene of unknown structure. When this is treated with water at pH 5–7 at 55°, it forms 3-morpholinotrichlorocyclobutene (**17**). This can be further hydrolysed to squaric acid.

$$CCl_2{=}CCl{-}CCl{=}CCl_2 \xrightarrow{C_4H_8ONH} (C_4H_8ON)_3C_4Cl_3 \xrightarrow{H_2O}$$

(**17**)

$\downarrow H_2O$
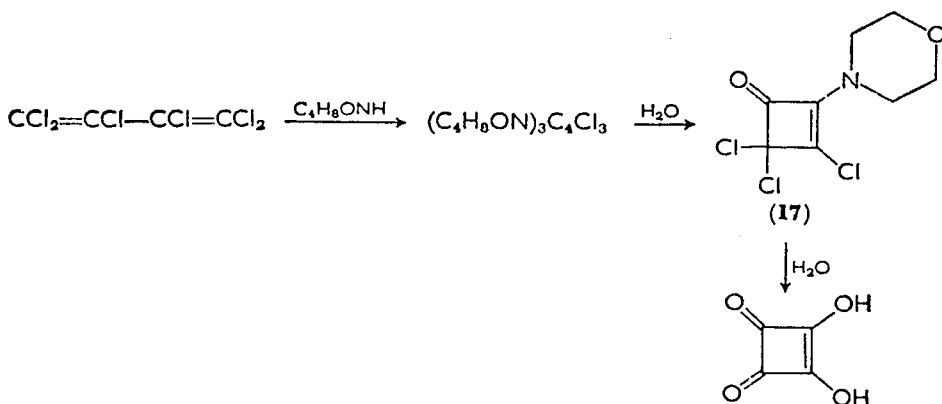
An even more convenient synthesis begins with the nucleophilic substitution on hexachlorobutadiene by ethoxide ion to give 1-ethoxy-pentachlorobutane-1,3-diene (**18**), described by Roedig and Bernemann[45]. Compound **18** condenses thermally or catalytically to tetrachlorocyclobutenone (**21**) with elimination of ethyl chloride. Maahs suggests that the reaction proceeds through **20** as an intermediate, but an equally likely pathway appears to be through 1,3 cycloaddition to **19** followed by loss of ethyl chloride. With sulphuric acid, **21** undergoes hydrolysis to squaric acid. The entire reaction sequence can be carried out in a single reaction vessel without isolating intermediates, and it therefore provides a 'one-step' synthesis of squaric

$$CCl_2{=}CCl{-}CCl{=}CCl_2 \xrightarrow{OEt^-}$$

(**18**)   (**19**)   or   (**20**)

$\downarrow$

(**12**) $\xleftarrow{H_2SO_4}$ (**21**)
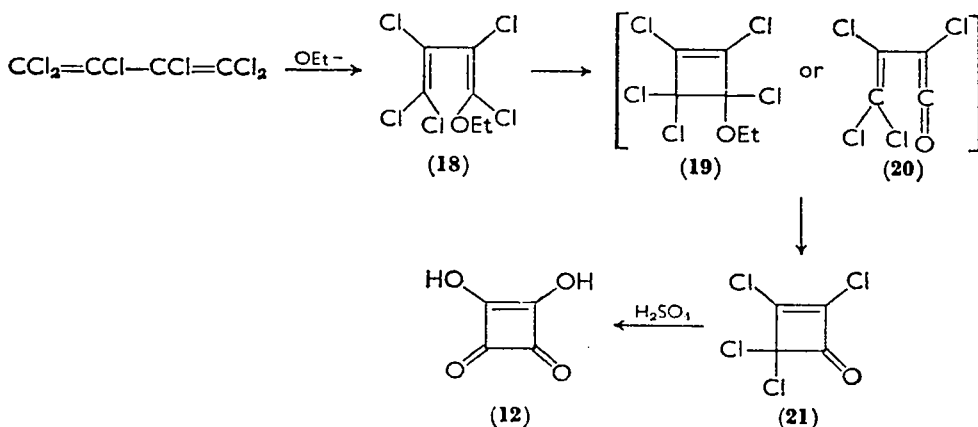
acid from cheap, readily-available starting materials. Squaric acid forms colourless crystals, decomposing only above 293°, and it is now available commercially.

III. STRUCTURES AND PROPERTIES OF THE OXOCARBON ACIDS

Structures of types **22** and **23** for rhodizonic acid (**10**)[46,47], and **24** and **25** for croconic acid (**11**)[12,48] have been proposed in the past, but the α-enediol structures shown for **10** and **11** now seem well established, though x-ray studies have not been done. Neither **10** nor **11** show C—H absorption in their infrared spectra, such as would be present in **22** and **24**. The easy conversion of **10** to **9** argues against structure **23**, as does the normal C=O infrared frequency of 1700 cm^{-1}[31]. Absorption at higher frequency would be expected for the cyclobutanedione structure present in **23**. The same argument applies
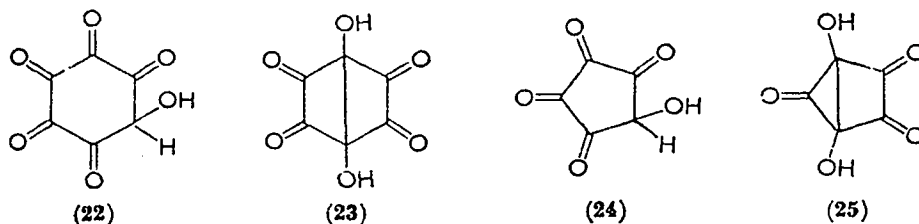
to **11**, which shows $\nu_{C=O}$ at 1755 cm^{-1}, consistent with the assigned structure[49]. Croconic acid has a very high dipole moment in dioxan (9–10 D), as expected for structure **11**[50]. Finally, the crystal structures of rubidium hydrogen croconate and ammonium hydrogen croconate show that these salts are correctly formulated as α-enediolates[51] (**26**). It is difficult to rule out completely the participation of tautomers such as **22** and **24** in solution[52], but there is no firm evidence for their existence.
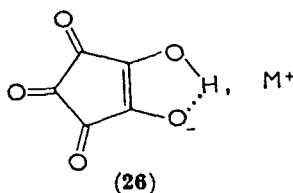
The mass spectra of the oxocarbon acids and of their oxidation products (section V. A) have recently been studied[52a]. The acids all show parent ion peaks in their mass spectra. A characteristic feature of the fragmentation is loss of CO and ring contraction.

The oxocarbon acids are all quite strong. pK values for these substances are given in Table I, which includes only reliable recent data. Croconic acid is decidedly stronger than squaric acid. Rhodizonic acid appears weaker than 11 or 12, but the species present in water is the dihydrate, $C_6O_4(OH)_2 \cdot 2H_2O$, in which two of the carbonyl groups of 10 are probably hydrated to $>C(OH)_2$ groups. Unhydrated 10 would be a much stronger acid than the dihydrate[56].

TABLE 1. pK values for oxocarbon acids

Acid	pK_1	pK_2	Reference
$C_4O_2(OH)_2$ (12)	1·7, 1·2	3·2, 3·48	53, 53a
$C_5O_3(OH)_2$ (11)	0·5	1·5–2·0	54, 55
$C_6O_4(OH)_2 \cdot 2H_2O$ (10)	3·1	4·9	56
$C_8O_2(OH)_4$ (9)	4·8	6·8	57

Croconic acid and rhodizonic acid are quite soluble in water and moderately soluble in oxygenated organic compounds. Squaric acid, on the other hand, is insoluble in organic solvents and sparingly soluble (2%) in water, probably because of strong hydrogen bonding in the solid. The infrared spectra of all of the oxocarbon acids provides evidence for extensive hydrogen bonding. Croconic and rhodizonic acids give normal tests for the carbonyl group, i.e. with phenylhydrazines. However in squaric acid, both carbonyl groups are 'vinylogous carboxyl' carbonyls, and hence they do not react with carbonyl reagents[37]. All of the oxocarbon acids give colours with ferric chloride characteristic of enols.

The alkali metal salts of the oxocarbon acids are all stable substances soluble only in water. The colour deepens from squarate (colourless) to croconate (yellow) to rhodizonate salts; the latter are strongly dichroic, appearing green by reflected light but red by transmitted light or when very finely ground[30].

IV. STRUCTURES OF THE OXOCARBON ANIONS: AROMATICITY

A. Squarate, Croconate and Rhodizonate Anions

A resonance-stabilized structure for the croconate anion was first suggested in 1958 by Yamada and Hirata[49,58], reasoning from the

high acid strength of croconic acid and the lack of infrared absorption in the usual carbonyl region in croconate ion. A delocalized formulation for the squarate ion was proposed on the basis of the same sort of evidence by Cohen, Lacher and Park[37]. These observations led to the suggestion that the anions in question were aromatic species, and to the generalization of the oxocarbons as an aromatic series[1,2].

Aromaticity implies a symmetrical structure for the oxocarbon anions. The first definite evidence for symmetry came from vibrational spectroscopic studies, which indicated that squarate and croconate ions, in their alkali metal salts, are planar species in which all the carbon atoms and all the oxygen atoms are equivalent[2,59]. Detailed normal coordinate analysis of the infrared and Raman spectra of dipotassium squarate and croconate showed, moreover, that there must be substantial π bonding between the ring carbon atoms[59]. Table 2 lists C—O and C—C stretching force constants for the oxocarbon anions and for some related species. The data show that the C—C stretching force constants in the oxocarbons are distinctly greater than for C—C single bonds, though less than for benzene. Moderate multiple bond character (π bonding) between carbon atoms in the oxocarbon rings is indicated.

More recently, the detailed structure of dipotassium squarate monohydrate[60], diammonium croconate[61], and dirubidium rhodizonate[62] have been determined by single-crystal x-ray investigations. Results show that in all of these salts the anions have symmetrical planar structures. The observed C—C bond lengths (Table 3) confirm the existence of substantial delocalized multiple bonding between ring carbon atoms. Differences among the three anions are small,

TABLE 2. Stretching force constants[a].

Species	K_{CC} (mdyne/Å)	K_{CO} (mdyne/Å)
$C_4O_4^{2-}$	3·95	5·60
$C_5O_5^{2-}$	3·50	6·72
C—C	2·0–2·3	
Benzene	5·17	
C=C	~7	
C—O		2·8
Acetate ion	2·46	7·20
C=O		10·8

[a] Urey–Bradley force field.

and may result from crystal forces rather than differences in the free anions. It is interesting that the C—O bond lengths are very short, particularly in rhodizonate ion, indicating a C—O bond order of nearly 2 for this species.

TABLE 3.   Bond lengths in oxocarbon salts

Species	r_{CC}(Å)	r_{CO}(Å)	Reference
$K_2C_4O_4 \cdot H_2O$	1·469	1·259	60
$(NH_4)_2C_5O_5$	1·457	1·262	61
$Rb_2C_6O_6$	1·488	1·213	62

Molecular orbital calculations have been carried out on a variety of oxocarbon anions, including more complex types as well as monocyclics, using the simple Hückel method[1]. Some results are given in Table 4. Even the simplest calculations give remarkably good agreement with experiment in most respects. Thus the bond orders are fairly close to those predicted, and the electronic spectra of the oxocarbon anions, which show bathochromic shifts as ring size increases, are well correlated by the MO calculations. More elaborate SCF calculations have also been attempted, particularly for $C_6O_6^{n-}$ ions[63-65]. Hückel and Pariser-Parr-Pople MO calculations have also been carried out for the oxocarbon acids[65a].

TABLE 4.   Results of simple Hückel MO calculations for oxocarbon anions

Species	$D\epsilon/\pi^a$	Mobile Bond Order		Charge Density	
		C—C	C—O	C	O
$C_3O_3^{2-}$	0·280	0·594	0·416	+0·187	−0·854
$C_4O_4^{2-}$	0·240	0·471	0·542	+0·236	−0·736
$C_5O_5^{3-}$	0·231	0·447	0·598	+0·234	−0·634
$C_6O_6^{2-}$	0·227	0·444	0·626	+0·241	−0·571
$C_7O_7^{2-}$	0·223	0·436	0·636	+0·253	−0·539
$C_8O_8^{2-}$	0·220	0·427	0·651	+0·264	−0·513
$C_6O_6^{4-}$	0·209	0·527	0·455	+0·074	−0·741

^{a} Delocalization energy (resonance energy) per π electron.

The alternation of aromatic stabilization with ring size, found for the cyclic polyenes, is not predicted (or observed) for oxocarbons. The unknown monocyclic oxocarbons $C_3O_3^{2-}$, $C_7O_7^{2-}$ and $C_8O_8^{2-}$

should all be aromatic[1]. Moreover, most polycyclic oxocarbon anions, regardless of symmetry or ring size, are predicted to have substantial aromatic stabilization[1] (Table 4).

B. The Tetraanion of Tetrahydroxyquinone

Molecular orbital calculations also suggest aromatic properties for oxocarbon anions with charges other than $2-$. However, the lowest-lying unfilled π energy level in all of the monocyclic oxocarbon dianions is *degenerate*, according to the simple Hückel calculations. Therefore, species $C_nO_n^{4-}$ should have two unpaired electrons occupying the degenerate orbitals and should be a triplet state, paramagnetic species[1].

These molecular orbital considerations led directly to the preparation of the only known oxocarbon anion with charge other than $2-$, $C_6O_6^{4-}$, from tetrahydroxyquinone[66]. When tetrahydroxyquinone is treated with base such as potassium hydroxide, the insoluble dipotassium salt $K_2C_6O_4(OH)_2$ is usually produced. $K_4C_6O_6$ was finally obtained by working with dilute anhydrous methanolic solutions of $KOCH_3$ and tetrahydroxyquinone, with rigid exclusion of oxygen[66]. The product is a black solid with absorption throughout the visible region. It is possible that earlier workers had this material in hand, but in quite impure form[12]. In air, it undergoes rapid oxidation to dipotassium rhodizonate. $K_4C_6O_6$ is a probable intermediate in the oxidation of $K_6C_6O_6$[12].
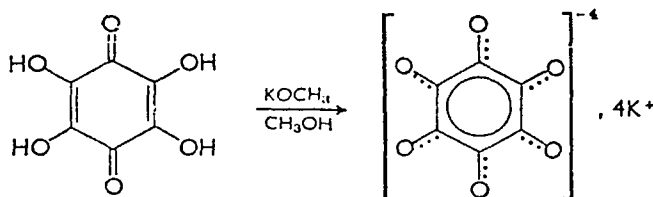
The black solid $K_4C_6O_6$ is diamagnetic, in contradiction to the prediction from Hückel MO theory. The diamagnetism could be explained by distortion of the anion, or by electron correlation neglected in the simple MO approach. The simple infrared spectrum of $K_4C_6O_6$ is consistent with a symmetrical formulation for the anion[31,66] but there is as yet no firm evidence for the structure of the compound.

C. Oxocarbon Radicals

Upon oxidation in air, the diamagnetic $K_4C_6O_6$ gave a dark green, strongly paramagnetic substance giving a single e.s.r. line at

$g = 2 \cdot 003$[66]. This intermediate could not be isolated pure, but underwent rapid quantitative oxidation to give dipotassium rhodizonate. The formulation $C_6O_6^{3-}$ was suggested for the intermediate radical, which would thus be a delocalized oxocarbon anion radical.

Further evidence for oxocarbon anion radicals is given by an e.s.r. study of the products from the potassium–carbon monoxide reaction. When the products were heated to 250°, a single-line e.s.r. spectrum was observed[67], attributed to $C_6O_6^{5-}$. Other such delocalized oxocarbon anion radicals are likely to be discovered in the future.

V. REACTIONS OF THE OXOCARBONS

A. Oxidation Products: Triquinoyl, Leuconic Acid and Octahydroxycyclobutane

It has been known for more than a century that rhodizonic and croconic acids undergo oxidation to give triquinoyl octahydrate $(C_6H_{16}O_{14})$ and leuconic acid $(C_5H_{10}O_{10})$ respectively. The analogous four-membered ring compound, $C_4(OH)_8$ was prepared only in 1963[40].

Triquinoyl octahydrate was first prepared by the oxidation of hexahydroxybenzene with nitric acid[11,12]. It can be made by the bromine oxidation of rhodizonic acid, or, somewhat more conveniently, by oxidation of tetrahydroxyquinone with bromine or nitric acid[6]. The compound forms colourless prisms, decomposing at 99°c. In water, it behaves as a weak acid, but basic solutions undergo rapid degradation[68]. Reduction with sulphur dioxide gives rhodizonic acid[12].

Leuconic acid is easily obtained by oxidation of a solution of croconic acid or an alkali metal croconate with chlorine or nitric acid[6,6a,69]. With SO_2, it is reduced back to croconic acid. Leuconic acid crystallizes as colourless needles decomposing at 158–160°[6]. Like triquinoyl, it is a weak acid which undergoes decomposition to open-chain compounds in basic solution[70,71]. A sodium leuconate $NaC_5H_9O_5$, thought to be cyclic, has been prepared[70].

The oxidation product of squaric acid, $C_4(OH)_8$, was obtained by treatment of squaric acid with bromine or nitric acid at 0°[40]. The product can be precipitated from aqueous solution by addition of acetone. It is a colourless solid decomposing at 140°, and reducible to squaric acid with sulphur dioxide.

The structure of $C_4(OH)_8$ is definitely known to be that of octa-hydroxycyclobutane (27). This structure was proposed from study of the infrared and Raman spectra of this compound and its octa-deutero analogue $C_4(OD)_8$, which strongly suggest that the molecule has a fourfold axis of symmetry (D_{4h} structure)[40]. Recently, Bock has carried out a single-crystal x-ray determination on $C_4(OH)_8$ and has confirmed the hydroxycyclobutane structure[72]. The cyclobutane ring is planar, with bond lengths 1·358 Å (C—O) and 1·562 Å (C—C); all of the hydroxyls are involved in a network of hydrogen bonding.

The infrared spectra of octahydroxycyclobutane, leuconic acid, and triquinoyl octahydrate are all quite similar, and all three compounds are now believed to have the fully hydroxylated structures 27, 28 and 29[40]. The fact that triquinoyl octahydrate and leuconic


(27)   (28)   (29)
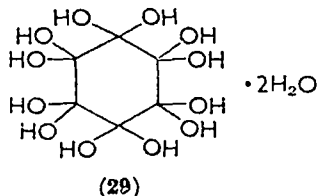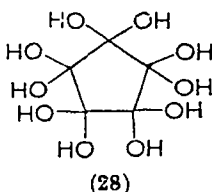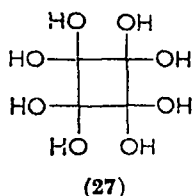
acid show no strong absorption in the carbonyl region of the infrared spectrum is consistent with this assignment[40,73]. The slow rate of reduction of triquinoyl observed in polarographic studies suggests that triquinoyl, but not its reduction product rhodizonic acid, is fully hydrated in solution also[74].

It would be of special interest to obtain unhydrated forms of these polyhydroxy compounds, which would then be neutral polymers of carbon monoxide, $(CO)_n$. Several attempts have been made to prepare these, but with inconclusive results. An anhydrous triquinoyl was claimed by Henle[75], who obtained a yellow syrup by shaking the octahydrate with ether and phosphorus pentoxide, or by treating silver rhodizonate with bromine in dry ether. The yellow solutions gave reactions typical of triquinoyl, but no pure compound was isolated. Later, Bergel prepared a dehydrated form of triquinoyl by warming the octahydrate over P_2O_5 in a vacuum[76]. The material so obtained analysed for $C_6O_6 \cdot 1-2\ H_2O$, but could *not* be converted back to triquinoyl octahydrate on addition of water. A partially dehydrated form of leuconic acid analysing for $C_5H_8O_9$ has also been prepared[12].

Several reactions of the polyhydrated oxocarbons are of interest. Leuconic acid was reported to give a tetra and a pentaoxime with hydroxylamine[12,77]. Leuconic acid[78] and triquinoyl[79] both undergo condensation reactions with *o*-toluenediamine to give derivatives formulated, on the basis of analysis only, as **30** and **31** respectively.


(30)   (31)
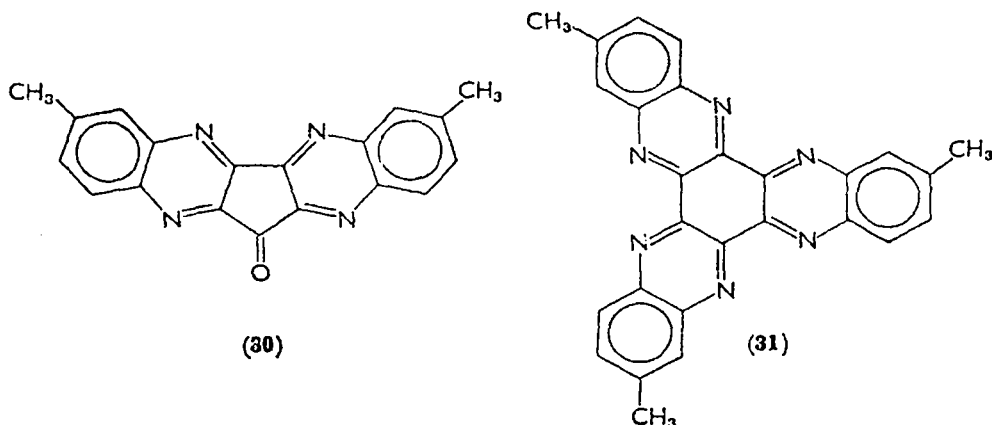
Preparation of the condensed ring compounds **32** and **32a** by ultraviolet photolysis of triquinoyl is claimed in a patent[80], but no structural evidence is given. Recently leuconic acid has been photolysed to a dimer believed to have structure **33**[80a].

(32)   (32a)

(33)
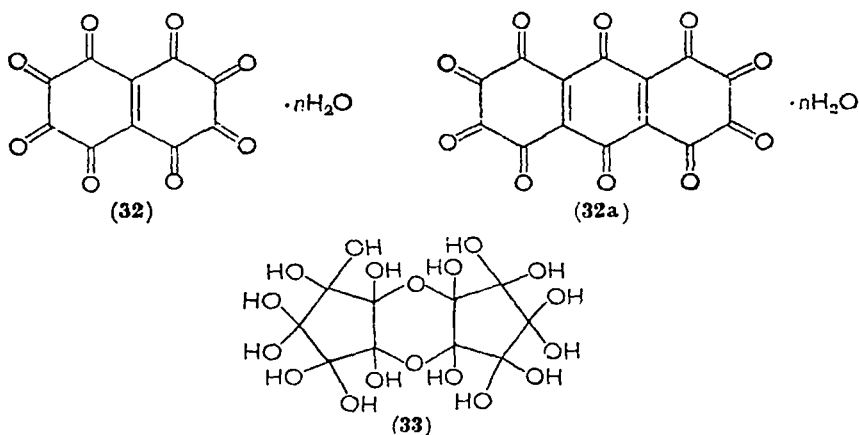
B. Reduction Products

The six-membered ring oxocarbons are the only ones whose reduction has been carefully studied. Rhodizonate ion or rhodizonic acid can be reduced, for instance with SO_2[12], to tetrahydroxyquinone and ultimately to hexahydroxybenzene (Scheme 1). Potentiometric oxi-

dation-reduction titrations have been carried out by Priesler and his coworkers[30,57] and by Tatibouet and Souchay[74] which show that the reduction takes place in two 2-electron steps and is largely reversible. The reduction potentials, E^0 at pH $= 0$, for the systems rhodizonic acid–tetrahydroxyquinone, tetrahydroxyquinone–hexahydroxybenzene and rhodizonic acid–hexahydroxybenzene were estimated to be $+0.426$, $+0.350$ and $+0.388$ volt respectively[57]. The electrochemistry was also studied as a function of pH. The measurements explain the
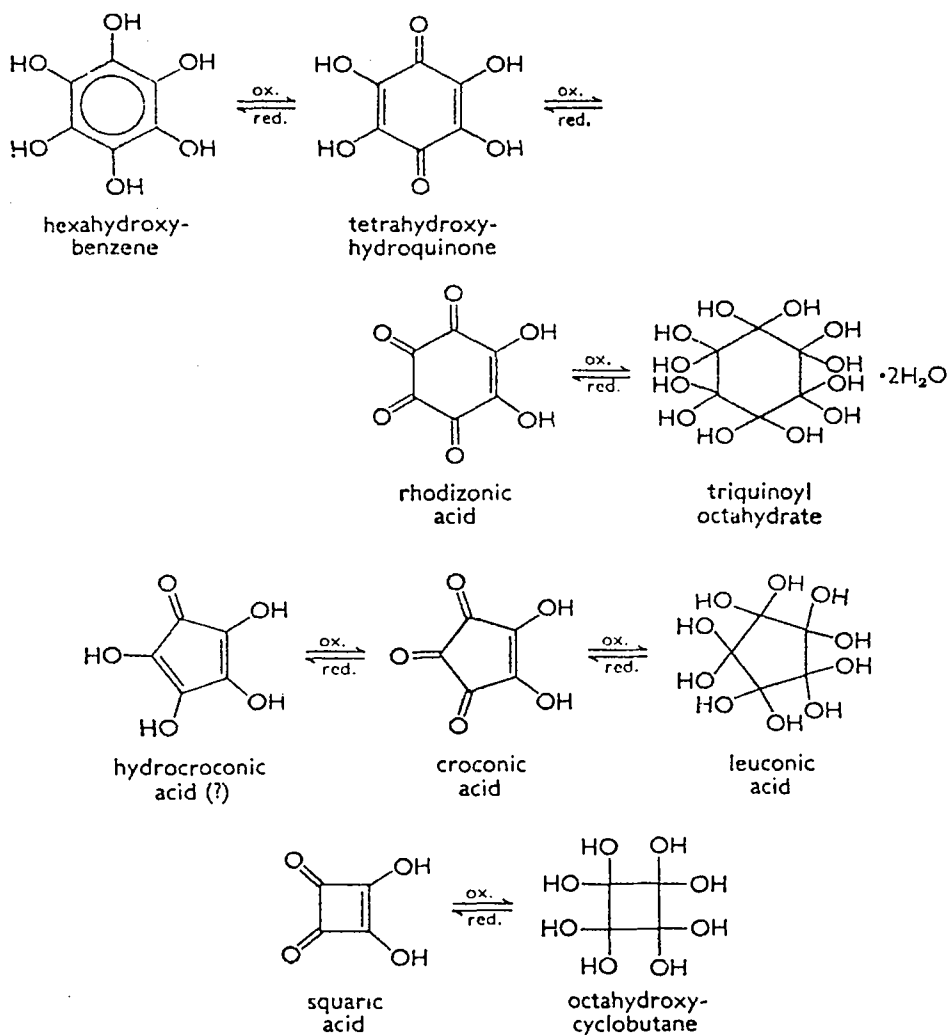

Scheme 1. Oxidation–Reduction Equilibra Among the Oxocarbons.

exclusive precipitation of dipotassium rhodizonate in an acetate buffer, which results from the dismutation of tetrahydroxyquinone to rhodizonate and $C_6(OH)_6$.

The reduction of croconic acid is not nearly so well understood. The reduction of dipotassium croconate with HI was studied as early as 1862 by Lerch[11], who isolated a yellow-brown reduction product which gave red salts formulated as $K_2C_5H_2O_5$ and $BaC_5H_2O_5$. Later, Nietzki and Benckiser[12] showed however that reduction of croconic acid with SO_2, Zn, or $SnCl_2$ gives colourless solutions which are easily reoxidized to yellow croconic acid[12]. They formulated their reduced material as 'hydrocroconic acid', 34. Solutions of this

(34)   (35)   (36)
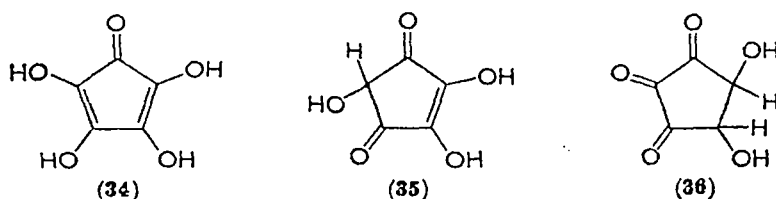
material were unstable and it could not be isolated. Later, the reduction of croconic acid was studied electrochemically, and shown to take place in no less than three distinct two-electron steps[17]. The two-electron reduction product was apparently different from that obtained by Nietzki and Benckiser[12], but was again assigned structure 34. A barium salt was isolated but not studied structurally[17]. More recent electrochemical studies by Fleury, Souchay and coworkers indicate that croconic acid undergoes stepwise reduction by one, two, three or four electrons[71a]. Structure 35, a tautomer of hydrocroconic acid, was suggested for the two-electron reduction product; another possible tautomeric structure is 36. The one-electron reduction product, isolated as a free acid and as the tetrasodium salt, is believed to have the bimolecular pinnacol-like structure 37[71a]. The hydrogen iodide reduction of croconic acid has recently been reinvestigated,

(37)   (38)
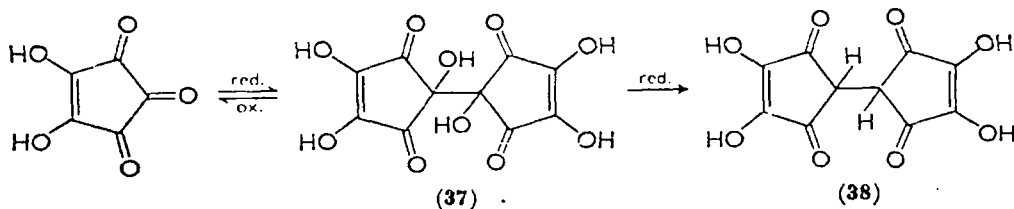
bimolecular products 37 and 38 being reported[81,82]. Both compounds are reported to have four enolic protons; tetramethyl enol ethers of
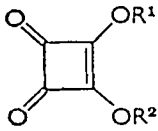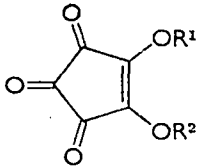
37 and **38** and a hexaacetyl derivative of **37** are also reported. Further work on the reduction products of croconates would be useful.

Scheme 1 summarizes oxidation–reduction relationships among the neutral oxocarbons. It is apparent that the systematics are best developed for the six-membered ring compounds, next for five-membered rings, and least in the four-membered series. Squaric acid is not expected to be stable in reduced form, in that the product would be tetrahydroxycyclobutadiene. The tetraanion of tetrahydroxycyclobutadiene might be isolable, however.

C. Esterification

A number of 'esters', actually enol ethers, are known for squaric and croconic acids (Table 5). The dimethyl and diethyl esters of croconic acid can be prepared by the reaction of methyl or ethyl iodide with silver croconate[58,83]. The esters are orange-red solids stable to 200°, but rapidly hydrolysed by moist air to croconic acid. Unlike croconic acid, they are soluble in most organic solvents.

TABLE 5. 'Esters' (enol ethers) of oxocarbon acids

| R^1	R^2	m.p. (°c)	b.p. (°c)/p (torr)	Reference
CH_3	CH_3	58		84
CH_3	H	132–4		84
C_2H_5	C_2H_5		89–91/0·4?	84
n–C_3H_7	n–C_3H_7			44
n–C_4H_9	n–C_4H_9		139/0·5	42, 43
CH_3	CH_3	114–5	250/740	83, 58
C_2H_5	C_2H_5	58	174–5/3	83
C_2H_5	H	150 d.	19/747	83

A colourless diethyl acetal, **39**, is obtained when either croconic acid or silver croconate is treated with alcoholic hydrogen chloride.

Diazomethane converts this acetal to its dimethyl ester (**40**), a stable yellow liquid[83].

When croconic acid itself is treated with diazomethane in ether, an interesting ring expansion takes place yielding trimethoxy-*p*-benzoquinone (**42**)[58]. The reaction must involve CH_2 insertion into a ring carbon–carbon bond, and presumably takes place through the intermediate **41**.

(39)   (40)
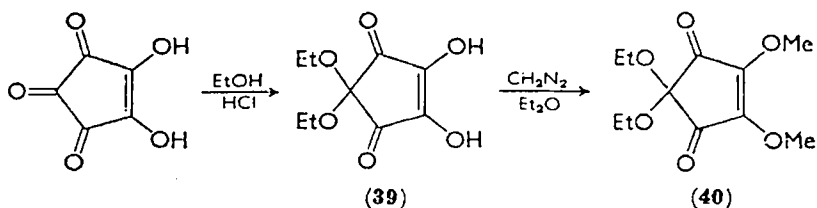
Diethyl[43] and dibutyl[42,43] squarate have been made simply by heating the corresponding alcohol with squaric acid, which serves as its own acid catalyst for esterification. Dibutyl squarate has also been made by alcoholysis of perchlorocyclobutenone, and other esters such as di-*n*-propyl squarate have been obtained by alcoholysis of dichlorocyclobutenedione (section V.D)[44]. These esters are colourless liquids, easily hydrolysed to squaric acid by water.

(41)   (42)
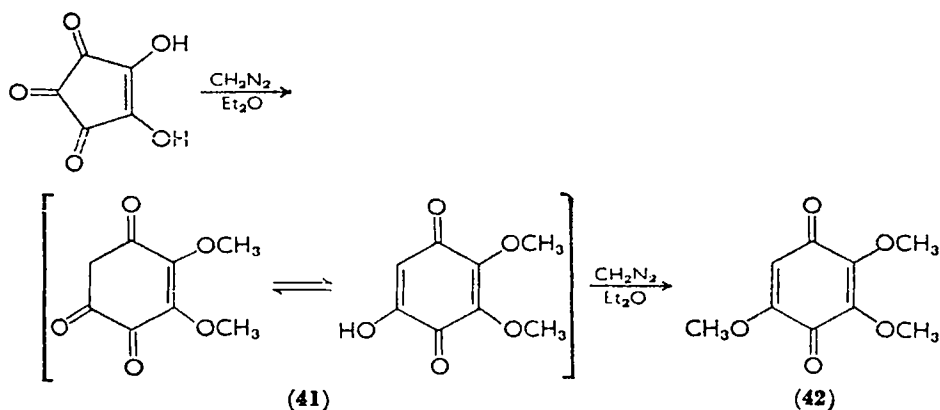
When squaric acid is heated with methanol, the half-ester 1-hydroxy-2-methoxycyclobutenedione (**43**), is obtained instead of the dimethyl ester. Compound **43** was also observed in the controlled hydrolysis of dimethyl squarate[84]. Dimethyl squarate itself can be synthesized from silver squarate and methyl iodide, or from squaric acid and diazomethane[84]. In the latter reaction, an orange by-product is also obtained, which may be a ring-enlargement product formed in a

reaction similar to that obtained with croconic acid and diazomethane. Unlike the other diesters of squaric acid which are liquid, dimethyl squarate is a low-melting solid. Heating with ethanol in the presence of ethoxide ion converts it to the diethyl ester[84], and other esters could probably be made similarly by transesterification.

Esters of rhodizonic acid do not seem to have been isolated, but should be accessible by the same routes described above.

(43)
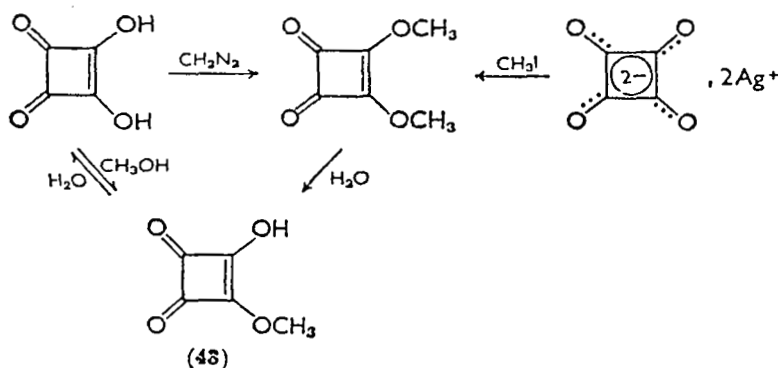
D. Derivatives of Squaric Acid

It is curious that much more is now known of the chemistry of squaric acid, isolated only in 1959, than about the other oxocarbons which are more than 100 years older. The chemistry of squaric acid derivatives has been reviewed by Maahs[44], and so will be treated only briefly here.
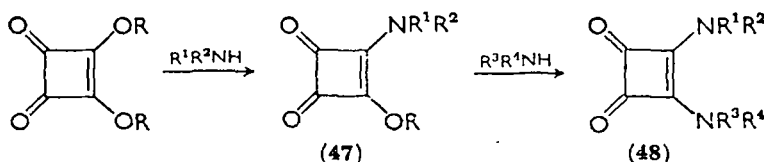
'Squaryl dichloride', dichlorocyclobutenedione (44), can be prepared by the action of SO_3 or oleum on perchlorocyclobutenone, 21 (section II.C.)[43]. It forms yellowish-green crystals melting at 51–52°, and has chemical properties typical for an acyl chloride.

(21)   (44)   (45)   (46)

R = H, Et, n-Pr
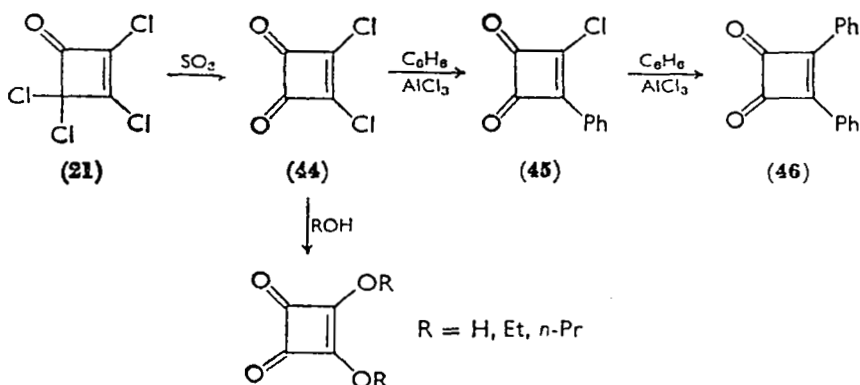
Compound **44** is easily solvolysed by water to squaric acid and by alcohols to diesters of squaric acid. With benzene, **44** undergoes Friedel–Crafts reactions to give phenylchloro- (**45**) or diphenylcyclo-butenedione (**46**) with catalytic or stoichiometric amounts of $AlCl_3$, respectively[44].

Ammonolysis of dimethyl squarate with gaseous ammonia in ether yields the monoester monoamide which precipitates out of solution. With aqueous ammonia in methanol or ether, or gaseous ammonia in methanol (in which the monoamide is soluble) the diamide of squaric acid can be obtained in good yield[84, 84a]. The diamide is a colourless solid decomposing at 320°.

Reaction of squaric esters with substituted amines also leads to mono (**47**) or diamides (**48**), depending on the amount of amine used. Mixed diamides can also be obtained by treating the monoester mono-

amides with other amines[44, 86]. Examples of compounds in this series are listed in the review by Maahs and Hegenberg[44].

Squaric acid diacetate (diacetoxycyclobutenedione, m.p. 63–65°) has been synthesized from squaric acid and acetic anhydride. This compound is very reactive and is solvolysed to squaric acid by water or alcohols[85].

Similar acid chlorides, amides, and acyloxy compounds could probably be made from croconic and rhodizonic acids, but up to now they are unknown.

E. Condensation Reactions

I. Of rhodizonic and croconic acids

Condensations involving rhodizonic and croconic acids with amines have been known for some time. In 1887 Nietzki and Kehrmann first condensed rhodizonic acid with 3,4-diaminotoluene to give a 1:1 product[79]. In the following year, Nietzki and Schmidt condensed rhodizonic acid with aniline and o-phenylenediamine[87]. The product with aniline was reported to have a structure of $H_2C_6O_5{=}NC_6H_5 \cdot C_6H_5NH_2$. With o-phenylenediamine, a condensed product with a 1:1 ratio of acid to amine was reported. Rhodizonic acid was also condensed with one and two molecules of N-phenyl-o-phenylene-

(49)

(50)

(51)
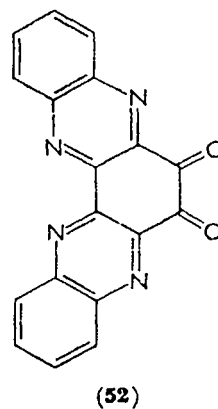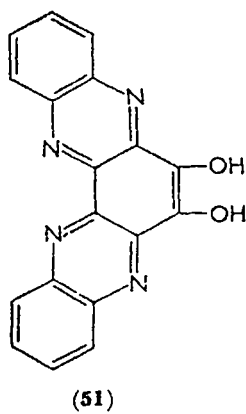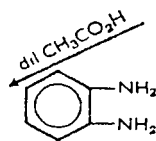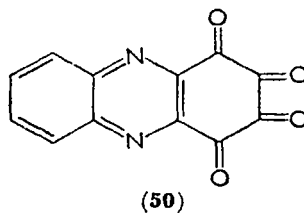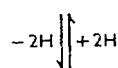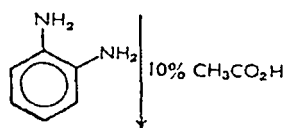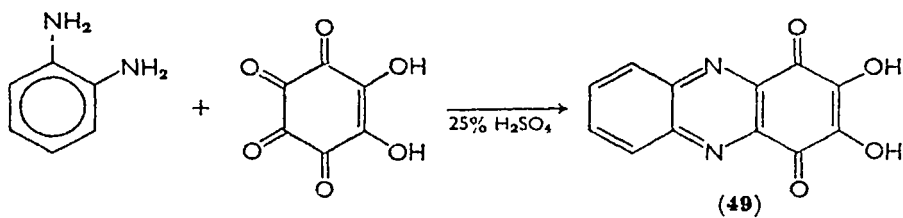
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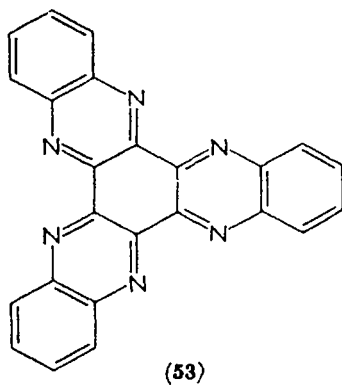
(53)

diamine to yield products of empirical formulae $C_{18}H_{12}O_4N_2$ and $C_{30}H_{18}O_2N_4$ [88].

More recently, detailed studies on the condensation of o-phenylene-diamine with rhodizonic acid to give phenazine derivatives have been carried out by Eistert, Fink and Werner[89]. These workers reacted rhodizonic acid with o-phenylenediamine in the presence of 25% sulphuric acid and obtained an almost quantitative yield of a 1:1 product, **49**, oxidizable to a tetraketone, **50**. In the presence of 10% acetic acid, however, a 1:2 product, **51**, resulted. The latter compound was isolated in yellow, greenish and violet modifications which are apparently tautomers with one or both protons located on nitrogen instead of oxygen. The oxidation product of **51**, the dicarbonyl compound **52**, reacts further with o-phenylenediamine to give the trisphenazine **53**, probably similar to the derivative obtained much earlier from triquinoyl (**31**, section V.A). Other derivatives of these interesting compounds are discussed in the paper by Eistert and coworkers[89].

(54)   (55)
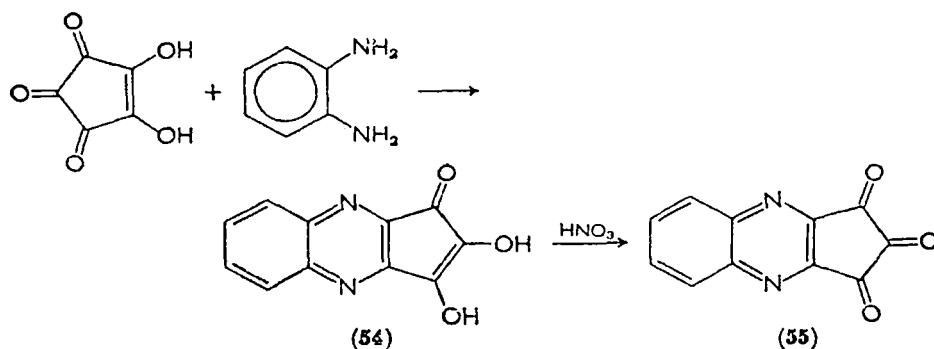
Nietzki studied the condensation of croconic acid with aromatic amines during the 1880's. Aniline reacts to give a diadduct $H_2C_5O_3-(NC_6H_5)_2$, and a monoadduct was obtained with 3,4-diaminotoluene[12]. These reactions have been clarified by recent work of Eistert and coworkers[89], who obtained the quinoxaline **54** and its oxidation product **55** (as monohydrates) from croconic acid and o-phenylene-
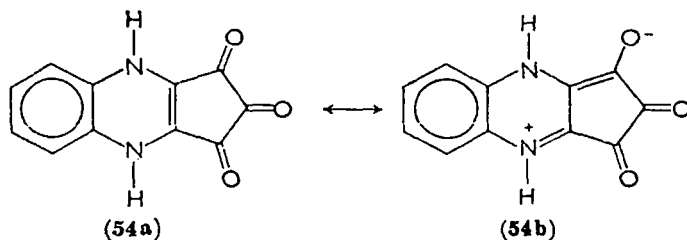
(54a)   (54b)

diamine. It is possible that compound **54** exists in the tautomeric form **54a ↔ 54b** with hydrogen bound to nitrogen[89]. Compound **55**, actually a derivative of leuconic acid, was also obtained by thermal decomposition of **50**, which takes place with disproportionation and with oxidative ring contraction (see section II.B.).
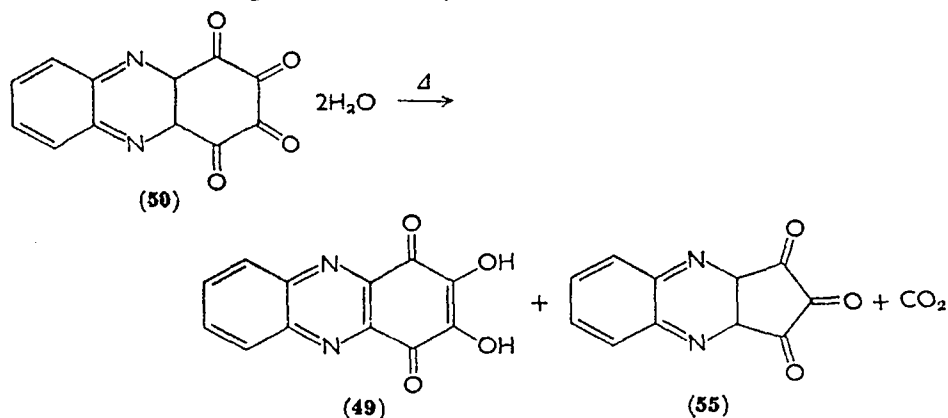
Related dihydropyrazine derivatives in the croconate series were studied by Prebendowski and Malachowski[83], who condensed a diketal of croconic acid (**56**) with ethylenediamine to give both a 2:1 adduct, formulated as **57**, and a 1:1 compound thought to be the dihydropyrazine **58**. On hydrolysis, **58** is converted to the diketo
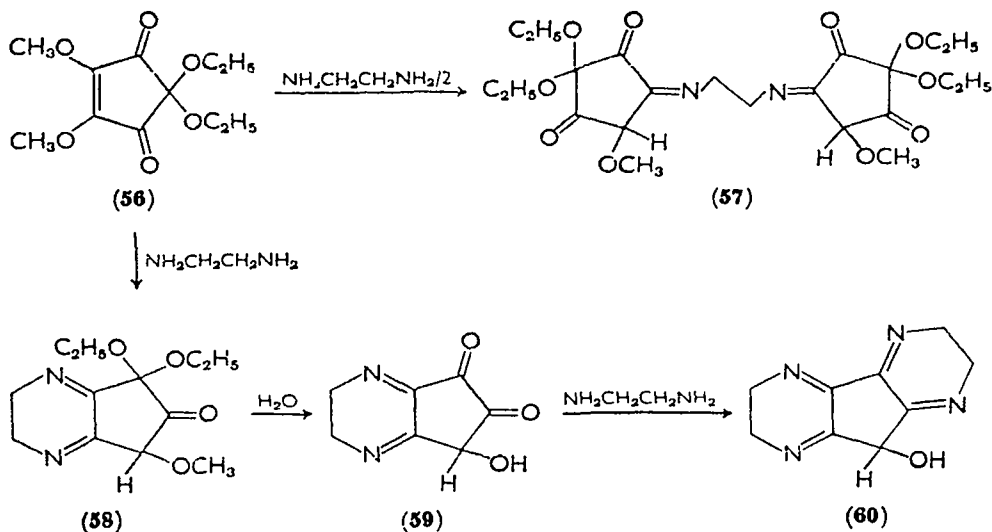
compound **59**, which reacts further with another mole of ethylene-diamine to give **60**. For all of these products, the structures were

deduced only from the elemental analysis. The dimethyl ester of croconic acid (section V.C.) was also condensed with *o*-phenylenediamine to give **61**, the dimethyl enol ether of **54**.

(61)
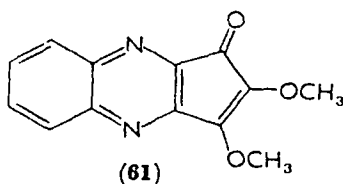
2. Of squaric acid

Recently, a number of extremely interesting condensation products have been obtained from squaric acid and its esters[90-93]. Some of these are discussed in the review on squaric acid by Maahs and Heyenberg[44], and in a more recent review on 'cyclobutenediylium dyes' by Sprenger and Zeigenbein[92a].

The condensation of squaric acid with activated, 5-substituted pyrroles gives red-violet dyes, formulated as cyanines (**62**) by Triebs and Jacob on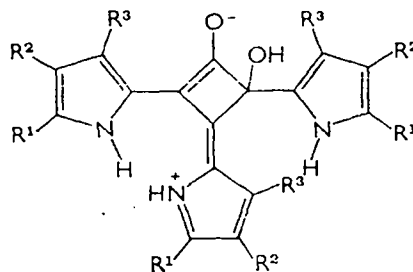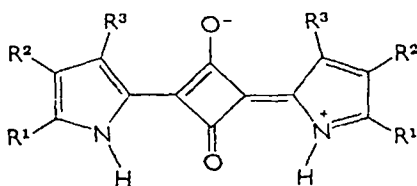 the basis of their electron absorption, which corresponds well with those of other cyclotrimethine dyes with betaine structure[94,95]. With excess pyrrole pale yellow tripyrrylcyclobutene derivatives (**63**) are formed. No products are obtained if the pyrrole rings are substituted in both the 2 and 5 positions. If neither position

(62)   (63)

is substituted, blue-green dyes are formed, apparently with polymeric structure[90].

Many other reactive aromatic and heterocyclic molecules will condense with squaric acid to give highly coloured betaine-like products, 1,3 substituted on the cyclobutene ring. For instance, *N*,*N*-dialkylanilines[92] condense to give deeply coloured products formulated as **64** (or **65**). Related condensation products are obtained with phloroglucinol[90], α-substituted indoles[91], azulenes[92], barbituric acid[92a]

and the betaine bases derived by loss of HI from 2-methyl substituted quinolinium, benzothiazolium and benzoselenazolium iodides[93].

(64)

(65)
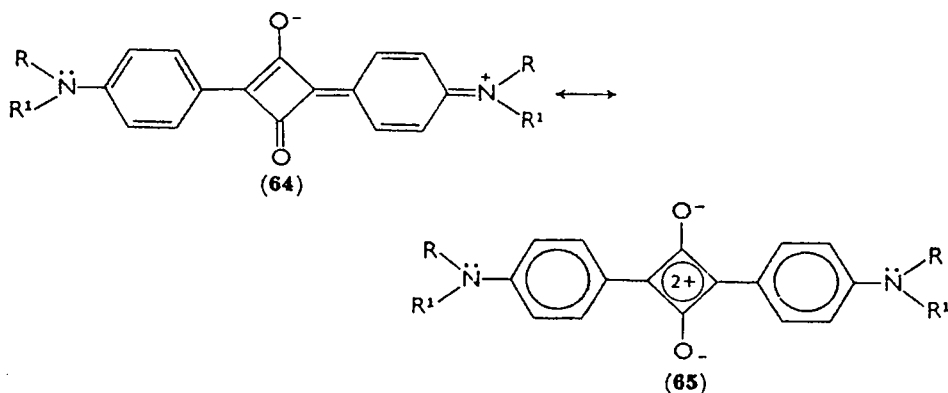
Sprenger and Ziegenbein[93] have questioned the structures **64** proposed for these dyes by Triebs and Jacob[90,91], and instead suggest that they be formulated as cyclobutenediylium derivatives (**65**). The question however is really one of relative contribution of different limiting structures to the resonance hybrid, which cannot be settled until information about the electron distribution in the dyes is available. To these reviewers, it seems likely that the cyanine form **64** is much more important than the cyclobutenediylium structure **65**.

Squarate esters also undergo condensation with 2- or 4-methyl-pyridinium, quinolinium or benzothiazolium iodides. However, in this case 1,2 rather than 1,3 substitution takes place on the four-membered ring[93]. Sprenger and Ziegenbein formulate the product from N-ethyl-4-methylpyridinium iodide as a cyclobutadienylium compound (**66**), but we can write additional and more probable resonance structures such as **67**. Analogous formulae can be written for other members of this series.

(66)   **(67)**
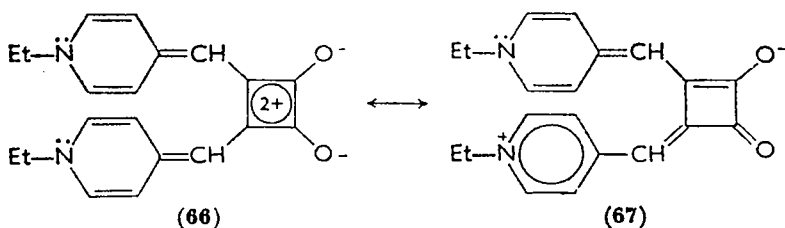
Although tertiary aromatic amines and heterocyclic nitrogen compounds condense with squaric acid to form bonds through carbon to the four-membered ring, primary and secondary aromatic amines

react quite differently, becoming attached through nitrogen to give yellow-coloured betaine compounds of type **68** (only a single limiting structure is written)[93a]. Finally, malonodinitrile reacts with dibutyl squarate and sodium butoxide in butanol to give deep yellow salts

(68)
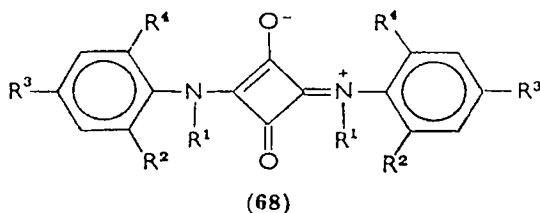
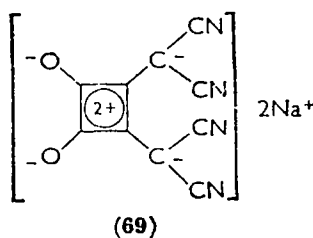which Sprenger and Ziegenbein formulate as **69**[93]. Other condensation products with novel structures will probably be made from oxocarbons in the future.

(69)

VI. APPLICATIONS OF THE OXOCARBONS

Rhodizonic acid and the alkali rhodizonates have long been useful in chemical analysis, because of the strongly coloured complexes which rhodizonate forms with many metal ions[94,95]. The analytical uses of rhodizonates have been reviewed by Feigl and Suter[96,96a]. Rhodizonate is useful in spot tests as well as quantitative determinations for metal ions such as Ba^{2+}, Sr^{2+}, Pb^{2+}, with which it forms insoluble red precipitates. Barium rhodizonate is more soluble than barium sulphate, and adsorbs strongly on the sulphate, so rhodizonate can be used as an adsorption indicator in the titrimetric determination of sulphate with standard barium solutions[97]. The end-point is observed by the change in colour of the precipitated $BaSO_4$ from white to rose-red, as barium rhodizonate begins to form. Barium and rhodizonate are also used in turbidimetric determination of small amounts of sulphate[98,98a]. Rhodizonate also forms precipitates with rare earth elements, and can be used to separate them into subgroups[99,99a-b].

Croconate ion has also been suggested[100] as a precipitating reagent in the determination of Ca^{2+}, Sr^{2+} and Ba^{2+}, and the solubility products of the alkaline earth croconates have recently been measured[101].

In biochemistry, rhodizonic acid is also found to have some activity. It serves as a replacement for myoinositol as the substrate for growth of the sugar mould *Saccharomyces carlsbergensis*[102,102a]. Probably because of its capabilities for oxidation and reduction, rhodizonic acid provides some protection to yeasts against damage from radiation[103,103a]. Rhodizonic acid will also prevent the photodecomposition of cystine[104], perhaps because of its ability to reoxidize sulphhydryl groups, i.e. in cysteine, to disulphide linkages[105].

According to patents, rhodizonic acid will increase serum levels of tetracycline antibiotics[106], and rhodizonic and croconic acids will both increase the effectiveness of chlorophyll as an oral deodorant in toothpastes, etc.[107] Several polycarbonyl compounds, including oxocarbons, are reported to be antidiabetic agents[108] and to have *in vitro* activity against influenza virus[109].

In the future, derivatives of squaric acid are likely to find technological application as drugs, dyestuffs, or in other ways. The remarkable new condensation products obtained from squaric acid (section V.E) are likely to lead to a reawakening of interest in derivatives of the other oxocarbons as well.

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