HETEROCYCLIC QUINONES FROM 2,3-DICHLORO-1,4-NAPHTHOQUINONE

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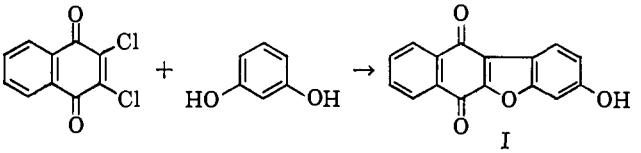
CONTENTS

I. INTRODUCTION

Most of the early work on the reactivity of the halogen atoms of 2,3-dihalo-1,4-naphthoquinone deals with the formation of mono and disubstituted compounds by replacement of one or both of the halogen atoms. Cyclization with the formation of a heterocyclic ring involving both halogens was reported first in 1899 by Liebermann (48) who prepared 3-hydroxybenzo(*b*)naphtho[2,3-*d*]furan-6,11-dione (I).



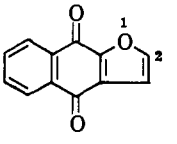
I

However, from 1899 to about 1940, very little interest had been shown in the cyclization reactions of 2,3-dichloro-1,4-naphthoquinone, hereinafter abbreviated as 2,3-DCNQ. The discovery that several heterocyclic quinones possess attractive properties as dyes (50, 65, 75, 90), catalysts (6, 85) and drugs (36, 80, 88) led to a renewed attention to their synthesis from 2,3-dihalo-1,4-naphthoquinone.

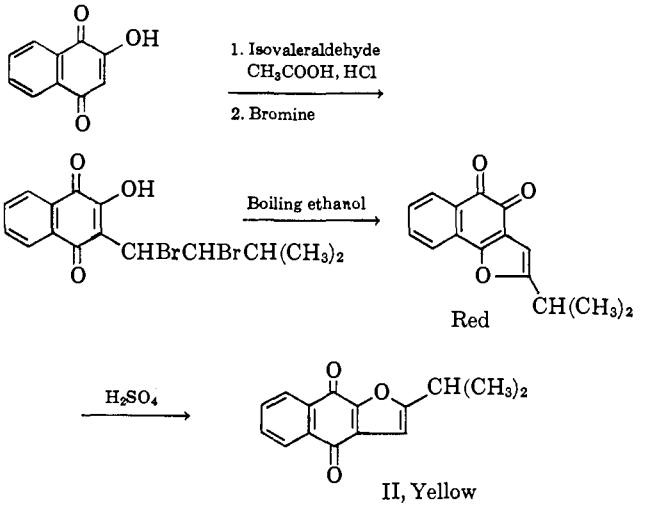
Cyclization involving the halogens of 2,3-dihalo-1,4-naphthoquinone can yield 5- and 6-membered heterocyclic rings. This review is concerned with the chemistry of polynuclear quinones containing a 5-membered heterocyclic ring fused with the naphthoquinonyl radical. Quinones containing a 6-membered heterocyclic ring are not included.

The literature is reviewed through the first half of 1960 (Volume 54—January to June) of *Chemical Abstracts*. Selected papers that have appeared in the literature in 1961 and 1962 also are included.

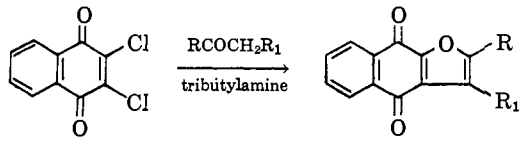
II. NAPHTHO[2,3-*b*]FURAN-4,9-DIONES



The first representative of this system, the 2-isopropylnaphtho[2,3-*b*]furan-4,9-dione (II), was obtained in 1896 starting from 2-hydroxy-1,4-naphthoquinone by a method involving several steps (33)

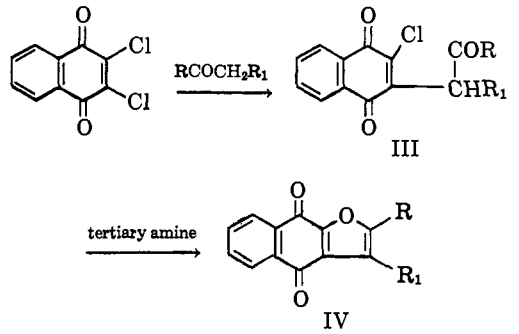


The first preparation of a naphtho[2,3-*b*]furan-4,9-dione from 2,3-DCNQ was carried out in 1957 by condensing 2,3-DCNQ with an active methylene compound in ethanol and in the presence of tributylamine (63)



This one-step method is not of general application. Acetone, acetophenone, phenylacetone, ethyl acetoacetate, ethyl benzoylacetate and dibenzoylmethane do not form naphthofurandiones following this method (63, 69).

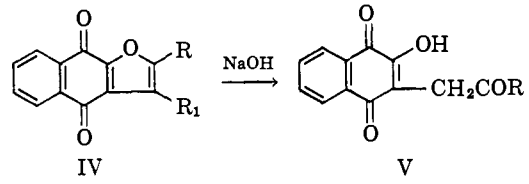
A more general method, known as the two-step method, involves the condensation of 2,3-DCNQ with the active methylene compound to form 2-chloro-3-(disubstituted methyl)-1,4-naphthoquinone (III), and the cyclization of this naphthoquinone (III) to the naphthofurandione (IV) in the presence of a tertiary amine (63).



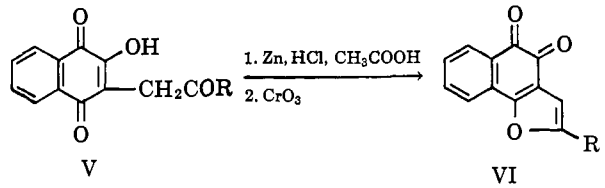
Very probably the one-step method also proceeds *via* the same intermediate.

The preparation of the intermediate III is carried out either by adding 2,3-DCNQ to a boiling solution of the active methylene compound in ethanol, in which sodium was previously dissolved (92), or by adding the sodium salt of the active methylene compound to a suspension of 2,3-DCNQ in ethanol (54). According to Pratt and Rice (63), the former procedure proved to be superior in the preparation of 3-(acetylcarbethoxymethyl)-2-chloro-1,4-naphthoquinone. The above naphthoquinone intermediates (III) are cyclized by refluxing their ethanol solution in the presence of tributylamine. Yields varying from 13 to 67% are reported (63).

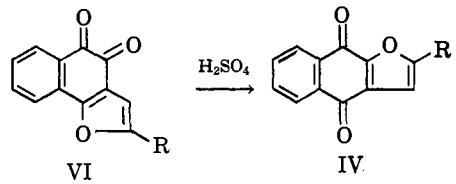
Evidence for the structure assigned to IV is based on the following reactions, which are characteristic of the naphtho[2,3-*b*]furan-4,9-dione system (34, 69): (a) Cleavage of the furan ring of IV upon alkaline hydrolysis (accompanied by loss of R_1, when R_1 is an acyl radical)



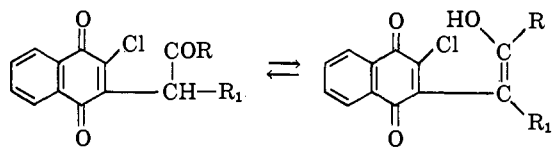
(b) Cyclization of the obtained hydroxyquinone (V) to naphtho[1,2-*b*]furan-4,5-dione (VI)



(c) Isomerization of VI to naphtho[2,3-*b*]furan-4,9-dione



The positions of the R and R_1 groups in the naphthofurandiones listed in Table I were determined by the direction of the enolization of the intermediate 2-chloro-3-(disubstituted methyl)-1,4-naphthoquinones.

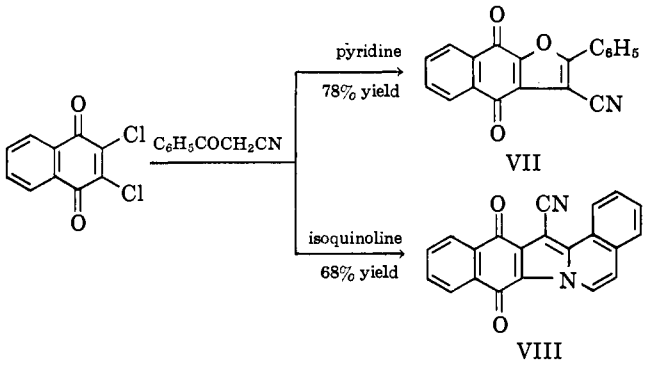


In the particular case of 3-(acetylbenzoylmethyl)-2-chloro-1,4-naphthoquinone, where two different enol forms are plausible, the structure of the resulting naphthofurandione (2-methyl-3-benzoyl rather than 2-phenyl-3-acetyl) was more conclusively demonstrated on the basis of the ultraviolet absorption spectra (63).

2-Bromo-3-hydroxy-1,4-naphthoquinone has been used in place of 2,3-DCNQ in the one-step method. A 34% yield of 2-phenyl-3-cyanonaphtho[2,3-*b*]furan-4,9-dione was obtained in the condensation with benzoylacetonitrile, using pyridine as the base (63). No reaction, however, was observed when 2-bromo-3-hydroxy-1,4-naphthoquinone was condensed with acetylacetone in pyridine (69).

In the preparation of 2-phenyl-3-cyanonaphtho-[2,3-*b*]furan-4,9-dione from 2,3-DCNQ and benzoylacetonitrile, pyridine or 4-picoline can be used in place of tributylamine. No reaction was observed, however, when tributylamine was replaced with *N*,*N*-dimethylaniline or with quinoline (69). It is interesting to note that whereas in the presence of pyridine, benzoylacetonitrile reacts with 2,3-DCNQ to give a 78% yield of

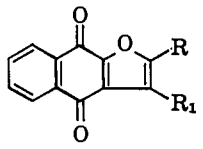
2-phenyl-3-cyanonaphtho[2,3-*b*]furan-4,9-dione VII, in the presence of isoquinoline and under the same conditions it gives a 68% yield of 14-cyanobenzo[*g*]-naphth-[2,3-*b*]indolizine-8,13-dione VIII (Table VII, note *c*). The formation of the benzonaphthindolizinedione system is described in section IX.



The active methylene compounds used successfully in these condensations and the naphthofurandiones obtained are listed in Table I.

TABLE I

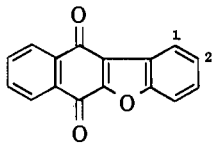
NAPHTHO[2,3-*b*]FURAN-4,9-DIONES (63, 69)



Active methylene compound used	Product R	Product R_1	Melting point, °C.	Yield, % One-step method	Yield, % Two-step method[a]
Acetylacetone	$-CH_3$	$-COCH_3$	202–203	15	43
Ethyl acetoacetate	$-CH_3$	$-COOEt$	163–163.5	..[b]	13
Benzoylacetone	$-CH_3$	$-COC_6H_5$	252.5–253.5	13	30
Benzoylacetonitrile	$-C_6H_5$	$-CN$	252–253	59[c]	67[d]
Dibenzoylmethane	$-C_6H_5$	$-COC_6H_5$	231.0–231.5	..[b]	26

[a] From the intermediate 2-chloro-3-(disubstituted methyl)-1,4-naphthoquinone. [b] This compound could not be prepared by the one-step method. [c] This yield increases to 78% by using pyridine and to 81% by using 4-picoline, in place of tributylamine. [d] Pyridine was used in place of tributylamine.

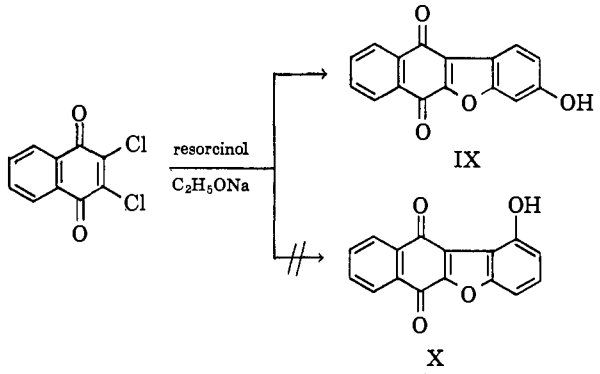
III. BENZO[*b*]NAPHTHO[2,3-*d*]FURAN-6,11-DIONES



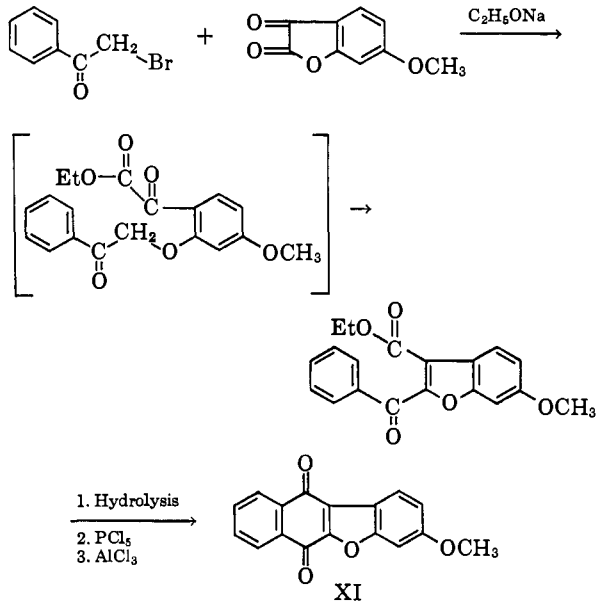
This system has also been called brazanquinone.

The first benzo[*b*]naphtho[2,3-*d*]furan-6,11-dione was prepared in 1899 by condensing 2,3-DCNQ with resorcinol in the presence of sodium ethoxide (48). Two isomers, IX and X, can be expected from this condensation.

Without offering substantial evidence, structure IX

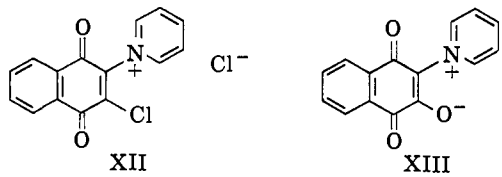


was preferred by Liebermann (48) first and by Kostanecky and Lampe (43) later. The accuracy of this choice was confirmed by Chatterjea (24), who prepared the methoxy derivative XI by an unambiguous route

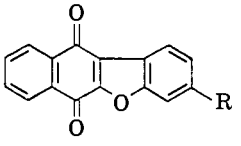


and found that the properties of XI are the same as those of the product obtained by alkylation of IX (43).

Benzo[*b*]naphtho[2,3-*d*]furan-6,11-diones are usually prepared by heating at 100° a mixture of 2,3-DCNQ and the phenol in pyridine. A 76% yield of 3-hydroxybenzonaphthofurandione is reported in the condensation with resorcinol (25). Mixtures of ethanol and pyridine, ethanol and sodium hydroxide (25), or ethanol and sodium ethoxide (48) have been used in place of pyridine. When pyridine is used, a by-product (XII) is formed, which is separated from the reaction mixture as the inner salt XIII, by extraction with boiling water (25, 95).

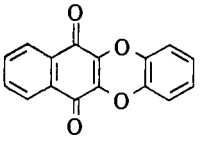


The formation of the benzonaphthofurandione system from 2,3-DCNQ and phenols is characteristic of phenolic compounds having a reactive *ortho* position. Derivatives of *m*-aminophenol, such as *m*-dimethylaminophenol and *m*-anilino-phenol react very easily with 2,3-DCNQ to give XIV and XV, respectively



XIV, R = $-N(CH_3)_2$
XV, R = $-NHC_6H_5$

whereas *p*-nitrophenol does not react (25). Pyrocatechol gives, in the presence of *N,N*-diethylaniline, benzo[*b*]-naphtho[2,3-*e*]-*p*-dioxine-6,11-dione (96)



2,3-Dichloro-5-nitro-1,4-naphthoquinone has been condensed with *m*-methoxyphenol, in the presence of pyridine, to yield a mixture of 3-methoxy-7(and 10)-nitrobenzo[*b*]-naphtho[2,3-*d*]furan-6,11-diones. Amino- and bromo-3-methoxy-benzo[*b*]naphtho[2,3-*d*]-furan-6,11-diones have been prepared from the above nitro derivatives (74).

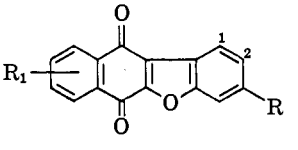
Direct nitration of 3-methoxybenzo[*b*]naphtho[2,3-*d*]-furan-6,11-dione(XI) gives nitro derivatives with nitro groups in the benzene ring containing the methoxy group (44, 74).

The benzonaphthofurandiones prepared are listed in Table II. Some of these compounds are reported in the patent literature as dyes for synthetic fibers (75).

Related systems are the naphtho[2′,3′-4,5]furo[3,2-*c*]-pyridine-1,6,11(2*H*)trione (XVI) and the 1*H*-naphtho[2′,3′-4,5]-furo[2,3-*c*]pyrazole-4,9-dione (XVII).

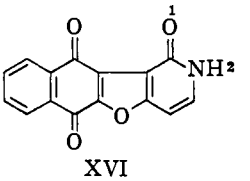
TABLE II

BENZO[*b*]NAPHTHO[2,3-*d*]FURAN-6,11-DIONES

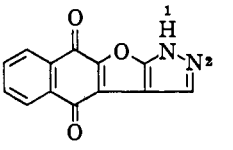


R	R_1	Color	Melting point, °C.	References
OH	H	Orange	320	(48, 43, 25)
OCH_3	H	Yellow	290–292	(43, 74)
OCH_3	7-NO_2	Yellow	318–320	(74)
OCH_3	10-NO_2	Orange	316–318	(74)
OCH_3	7-NH_2[a]	Red	282–284	(74)
OCH_3	10-NH_2[a]	Violet-brown	278–279	(74)
OCH_3	7-Br[b]	Orange	278	(74)
OCH_3	10-Br[b]	Scarlet	238–240	(74)
$N(CH_3)_2$	H	Violet-blue	310	(25)
$NH(C_6H_5)$	H	Blue	>310	(25)

[a] From the nitro derivative by reduction. [b] From the amino derivative by Sandmeyer reaction.



XVI



XVII

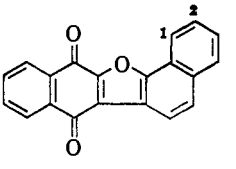
The parent compound (XVI) is unknown. The 2,3-dimethyl derivative is obtained by refluxing an alcoholic solution of 2,3-DCNQ and 1,6-dimethyl-4-hydroxy-2(1*H*)-pyridone in the presence of pyridine (25).

XVII is unknown. The 3-methyl-1-phenyl derivative is reported to have been obtained by refluxing 2,3-DCNQ and 3-methyl-1-phenyl-5-pyrazolone in ethanol and in the presence of pyridine (25).

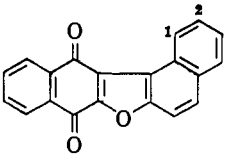
IV. DINAPHTHOFURANDIONES

This system has been called benzobrazanquinone.

2,3-DCNQ reacts with 1- and 2-naphthol, in the presence of pyridine or other acid-binding agents, to give dinaphthofurandiones of structures XVIII and XIX, respectively (10, 25, 26, 90).



Dinaphtho[1,2-2′,3′]furan-7,12-dione (XVIII)



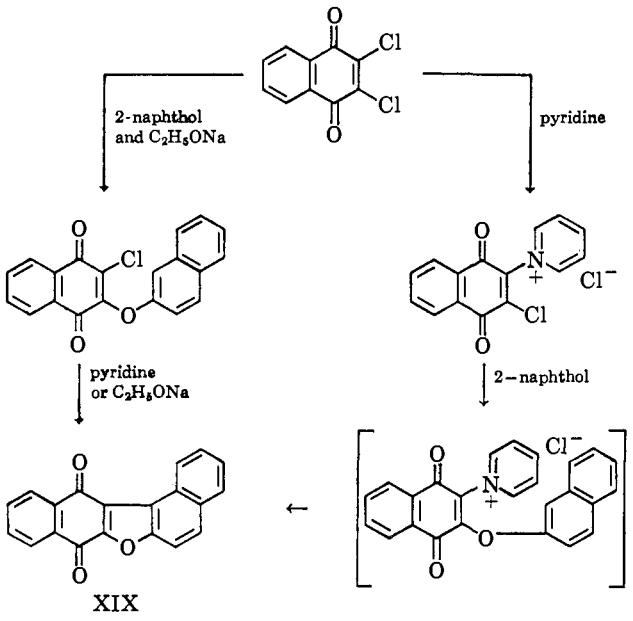
Dinaphtho[2,1-2′,3′]furan-8,13-dione (XIX)

It has been demonstrated that in the case of 2-naphthol the furan ring is formed with the adjacent 1 position and not with the adjacent 3 position (90).

The formation of the dinaphthofurandiones, as applied to XIX, can be represented as in Fig. 1 (3).

Dinaphthofurandiones are generally prepared by heating at 100° a mixture of 2,3-DCNQ and the naphthol in the presence of pyridine. A 60% yield of XVIII (26, 90) and a 50–55% yield of XIX are reported (3, 25). Mixtures of ethanol with pyridine (39), with sodium ethoxide or with sodium acetate (39) have been used in place of pyridine alone. Mixtures of toluene with *N,N*-diethylaniline or with pyridine also have been tried (90). As in the preparation of the benzonaphthofurandiones, when pyridine is used, the dinaphthofurandiones are obtained in mixture with the by-product XII, which can be separated by extraction with boiling water (3, 95).

The formation of dinaphthofurandiones from 2,3-



XIX

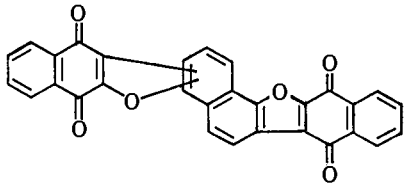
Figure 1.

DCNQ is characteristic of 1-naphthol derivatives having the adjacent position free and of 2-naphthol derivatives having the adjacent 1-position free or substituted by an easily removable substituent, such as bromine (90).

Substituted 2,3-DCNQ's, such as 5-nitro- and 5-chloro-, have been condensed with 1- and with 2-naphthol in the presence of pyridine (71, 73). From 2,3-dichloro-5-nitro-1,4-naphthoquinone mixtures of about equal amounts of 8-nitro and 11-nitrodinaphtho[1,2-2′,3′]furan-7,12-dione are formed in the condensation with 1-naphthol and mixtures of 9-nitro- and 12-nitrodinaphtho[2,1-2′,3′]furan-8,13-dione in the condensation with 2-naphthol. Amino, benzamido and bromodinaphthofurandiones have been obtained from the nitro derivatives described above (70).

The dinaphthofurandiones prepared from 2,3-DCNQ are listed in Tables III and IV with some of their properties.

The condensation of 2 moles of 2,3-DCNQ with one mole of certain naphthalenediols bearing the hydroxy groups in two different rings, gives dinaphthonaphthodifurantetrones. With 1,5- and 1,6-naphthalenediol compounds of the formula XX were obtained (4)

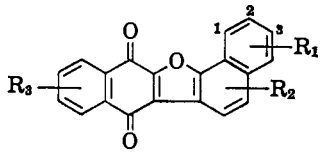


XX

whereas with 1,7- and 2,7-naphthalenediol, derivatives of the formula XXI were obtained (4).

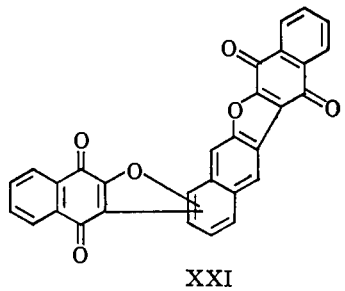
TABLE III

DINAPHTHO[1,2-2′,3′]FURAN-7,12-DIONES



R_1	R_2	R_3	Color	Melting point, °C.	References
H	H	H	Orange	229–230	(26, 90)
H	5-CH_3	H	Orange	275	(14)
H	5-Benzyl	H	Yellow	265	(12)
2-CH_3	6-CH_3	H	Yellow	292	(13)
2-OH	H	H	Red	301–302	(4)
4-OH	H	H	Brown	315	(15)
2-OCH_3[a]	H	H	Yellow	255	(4)
4-OCH_3	H	H	Orange	305	(15)
H	5-Cl	H	...	...	(39)
H	H	8-NO_2	Yellow	322	(70)
H	H	11-NO_2	Orange	344	(70)
H	H	8-NH_2	Brown	362	(70)
H	H	11-NH_2	Red	302	(70)
H	5-SO_3H	H	Yellow	...	(39)

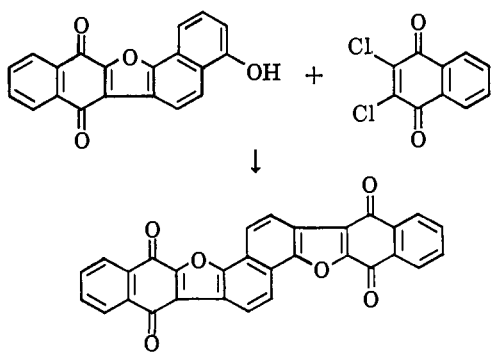
[a] Obtained by methylation of the 2-hydroxy derivative.



XXI

According to Buu-Hoï (10), the condensation of 2,3-DCNQ with 2,6- or with 2,7-naphthalenediol yields 3- or 2-hydroxydinaphtho[2,1-2′,3′]furan-8,13-diones, regardless of whether one or two moles of 2,3-DCNQ are used.

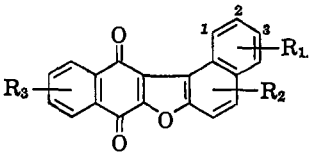
A two-step method for the synthesis of the dinaphtho-[2,3-*d*-2′,3′-*d*′]naphtho[1,2-*b*-5,6-*b*′]difuran-5,9,-14,18-tetrone (XXII) also was developed. It involves the condensation of one mole of 1,5-naphthalenediol with one mole of 2,3-DCNQ and the condensation of the obtained 4-hydroxydinaphtho[1,2-2′,3′]furan-7,12-dione with another mole of 2,3-DCNQ (4).



XXII

TABLE IV

DINAPHTHO[2,1-2′,3′]FURAN-8,13-DIONES

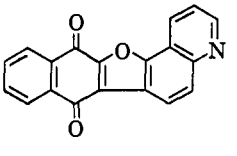


R_1	R_2	R_3	Color	Melting point, °C.	References
H	H	H	Orange-yellow	271–272	(10, 25, 90)
3-CH_3	H	H	Orange-yellow	270	(10)
3-*n*-Propyl	H	H	Orange	212	(10, 18)
2-*tert*-Butyl	H	H	Orange-yellow	283	(22)
3-*n*-Butyl	H	H	Yellow	223	(18)
3-*tert*-Butyl	H	H	Yellow	239–240	(10)
3-(Methyldiethyl)-methyl	H	H	Orange-yellow	231	(21)
2-CH_3, 3-CH_3	H	H	Orange	291	(13)
2-CH_3	6-CH_3	H	Orange-yellow	269	(13)
3-CH_3	6-CH_3	H	Orange	274	(13)
3-α-Phenylethyl	H	H	Yellow	230	(20)
2-OH	H	H	Red	>340	(10)
3-OH	H	H	Orange	317–318	(10)
4-OH	H	H	Brown-red	303–304	(11)
H	6-OH[a]	H	Dark red	>345	(17)
3-OH-4-CH_3	H	H	Brown-red	233–234	(14)
2-OCH_3	H	H	Orange	255–256	(10)
3-OCH_3	H	H	Orange-yellow	281–282	(10)
4-OCH_3	H	H	Orange-red	261–262	(11)
H	6-OCH_3	H	Red	295	(4)
3-Methylcyclopentyl	H	H	Orange-yellow	239	(21)
3-Methylcyclohexyl	H	H	Yellow	243	(19)
3-Br	H	H	Orange-yellow	308	(10)
H	H	9-Br	Orange	330–332	(70)
H	H	9-NO_2	Yellow	342–344	(70)
H	H	12-NO_2	Orange	314–316	(70)
H	H	9-NH_2	Violet	298–300	(70)
H	H	12-NH_2	Brown	338–340	(70)
H	6-Carboxanilide	H	Yellow	315–316	(39, 90)

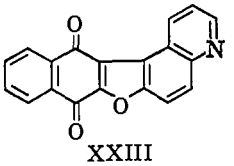
[a] Obtained by demethylation of the 6-OCH_3 derivative.

Derivatives of dinaphthonaphthodifurantetrones, such as dinitro and diamino, have been prepared from 2,3-dichloro-5-nitro-1,4-naphthoquinone and naphthalenediols (68).

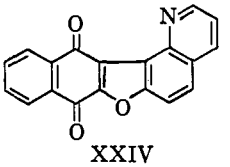
The reactivity of the chlorine atoms of 2,3-DCNQ toward phenolic groups appears to be greater than that toward heterocyclic nitrogen. Thus 2,3-DCNQ reacts with 5-quinolinol in the presence of pyridine to give a 57% yield of naphtho[2,3-*d*]furo[2,3-*f*]quinoline-7,12-dione.



Replacement of 5-quinolinol with 6- and 7-quinolinol gives naphtho[2,3-*d*]furo[3,2-*f*]quinoline-8,13-dione (XXIII) and naphtho[2,3-*d*]furo[2,3-*h*]quinoline-8,13-dione (XXIV), respectively (77).

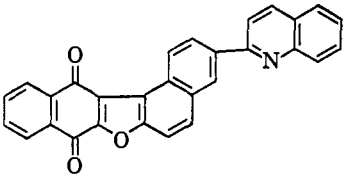


XXIII



XXIV

The condensation of 6-(2-quinolyl)-2-naphthol with 2,3-DCNQ gives 3-(2-quinolyl)-dinaphtho[2,1-2′,3′]-furan-8,13-dione (10).



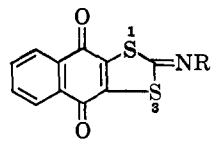
2,3-DCNQ also has been condensed with 1- and 2-anthrol, 1,5- and 1,8-anthradiol (38), hydroxybenzocoumarins (16), 4′-chloro-2-hydroxy-3-carbazolecarboxanilide (91), and 3′-hydroxybenzocarbazole (81) to give the corresponding naphthofurandiones.

A characteristic property of the dinaphthofurandiones is the color of their solutions in concentrated sulfuric acid (96%). A deep blue color is obtained with the dinaphtho[1,2-2′,3′]furan-7,12-diones, while a turquoise color is obtained with the dinaphtho[2,1-2′,3′]furan-8,13-diones (14). This color test has been suggested for the identification of a 2-naphthol radical having the adjacent 1 position free (10).

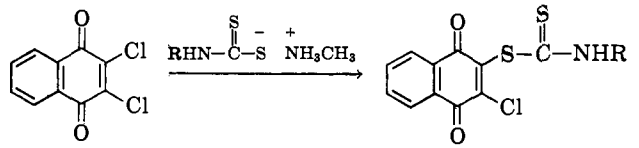
Several patents have been issued describing the preparation and properties of various dinaphthofurandiones. These compounds are reported as being useful

as dyes for natural and synthetic fibers (38, 39, 66, 67, 71, 72, 76, 84) and to possess interesting properties as catalysts for the reduction of aromatic nitro compounds (6, 85).

V. NAPHTHO[2,3]-1,3-DITHIOLE-4,9-DIONES

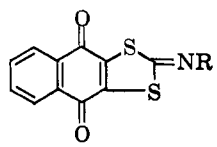


Treatment of 2,3-DCNQ with an equimolar amount of methylammonium monoalkyldithiocarbamates in water yields products reported to have the formula XXV (86).



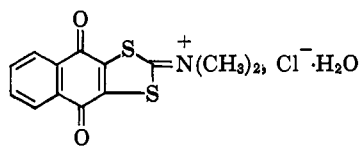
XXV

It is claimed that these products, when refluxed in ethanol, are cyclized to 2-alkyliminonaphtho[2,3]-1,3-dithiole-4,9-diones (XXVI) (86, 87).

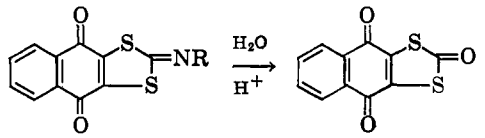


XXVI

Replacement of the methylammonium monoalkyldithiocarbamates with dimethylammonium dimethyldithiocarbamate gives a quaternary salt of the formula (88).



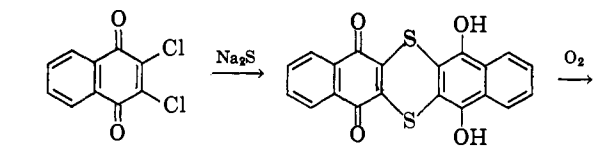
Evidence that the diones XXVI have a 1,3-dithiole structure is given by their ready transformation to naphtho[2,3]-1,3-dithiol-2,4,9-trione (XXVII) by acid hydrolysis (86).



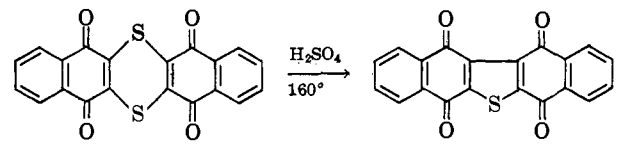
XXVII

The methyl (m.p. 185–186°) and ethyl (m.p. 192–193°) derivatives of XXVI are dark red products and are reported to possess fungicidal activity (87).

A related system, the dinaphtho[2,3-2′,3′]thiophene-5,7,12,13-tetrone (XXX) is also obtained from 2,3-DCNQ.



XXVIII

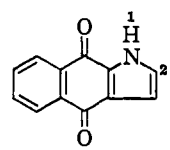


XXIX XXX

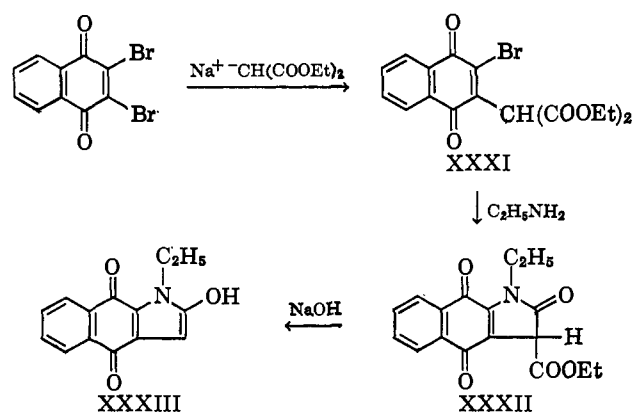
Treatment of an aqueous suspension of 2,3-DCNQ (1 mole) with sodium sulfide (1.5 moles) gives the monosodium salt of XXVIII, which when heated under reflux with a dilute solution of nitric acid or chromic acid is oxidized to dibenzo[*b*,*i*]thianthrene-5,7,12,14-tetrone (XXIX). By heating this tetrone with concentrated sulfuric acid at 150–170° or by refluxing it in nitrobenzene, XXX is formed (9).

Tetrone XXIX also is obtained by condensing 2,3-DCNQ with equimolar amounts of ammonium dithiocarbamate in water (86).

VI. 1*H*-BENZ[*f*]INDOLE-4,9-DIONES

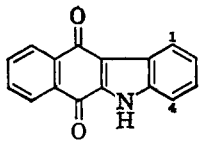


The 1*H*-benz[*f*]indole-4,9-dione system is also referred to in the early literature (*Chemical Abstracts* prior to 1936) as *β*,*β*-naphthazole-4,9-dione. Representatives of this system are obtained from 2,3-dibromo-1,4-naphthoquinone, through the intermediate 3-bromo-2-naphthoquinonylmalonic ester (XXXI) (47). This ester readily reacts with amines, such as ethylamine, to form 1-ethyl-3-carbethoxybenz[*f*]indoline-2,4,9-trione (XXXII) which, by treatment with an excess of 20% sodium hydroxide solution at reflux, gives 1-ethyl-2-hydroxy-1*H*-benz[*f*]-indole-4,9-dione (XXXIII) (49). 1-Methyl- and 1-benzyl-2-hydroxy-1*H*-benz[*f*]indole-4,9-dione also have been prepared (42, 49).

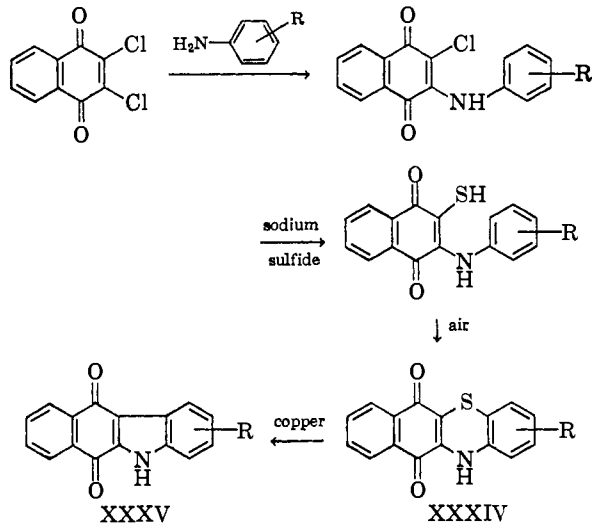


XXXI XXXIII XXXII

VII. 5*H*-BENZO[*b*]CARBAZOLE-6,11-DIONES



Compounds of this class are prepared from 2,3-DCNQ according to the scheme

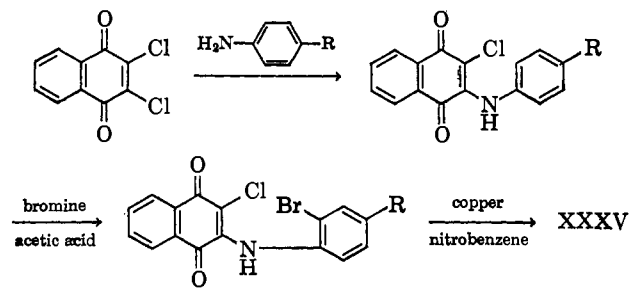


XXXV XXXIV

R = H, 3-CH_3 or 2-OCH_3

The intermediate benzo[*b*]phenothiazine-6,11-dione XXXIV is obtained by oxidizing with air 2-anilino-3-mercapto-1,4-naphthoquinone in boiling alcohol (29). The formation of the carbazole ring is effected by heating XXXIV with an agent capable of splitting out sulfur, as for example potassium ferricyanide, copper powder or potassium dichromate and in the presence of a diluent, such as nitrobenzene or naphthalene. Almost quantitative yields are obtained in this last step (45).

An alternative method for the synthesis of these benzocarbazolediones involves (1) the preparation of the 2-anilino-3-chloro-1,4-naphthoquinone, (2) the halogenation of this anilino derivative to form XXXVI and (3) the cyclization of XXXVI to XXXV by dehalogenation (40, 55).

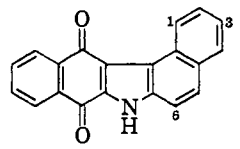


XXXVI

R = Cl,-CH_3 or -C_6H_5

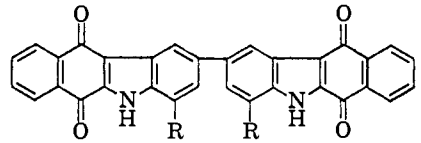
Replacement of 2,3-DCNQ in the latter method with 5-nitro-2,3-dichloro-1,4-naphthoquinone gives 5*H*-benzo[*b*]-carbazole-6,11-diones containing a nitro group in the naphthoquinone moiety (40).

Replacement of the anilino derivative in the above methods with 2-naphthylamine gives 7*H*-dibenzo[*b*,*g*]-carbazole-8,13-dione (40, 45).



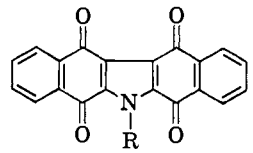
The 12-amino derivative of the above dibenzocarbazoledione is also described (40).

Replacement of the aniline derivative with benzidine (56) or with *o*-dianisidine (40) gives 2,2′-bi-5*H*-benzo-[*b*]-carbazole-6,6′,11,11′-tetrones.



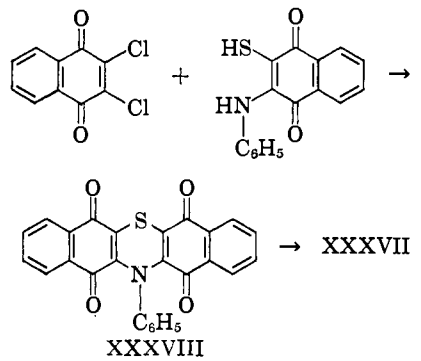
R = H or -OCH_3

A related system is the 6*H*-dibenzo[*b*,*h*]carbazole-5,7,12,13-tetrone XXXVII.



XXXVII

The 6-phenyl derivative is obtained from 2,3-DCNQ and 2-anilino-3-mercapto-1,4-naphthoquinone.

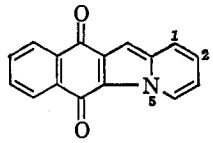


XXXVIII

The last step of this synthesis is effected by heating under reflux a solution of the intermediate 6-phenyldibenzo[*b*,*i*]-phenothiazine-5,7,12,14-tetrone XXXVIII in nitrobenzene (30). This step is similar to that involved in the preparation of dinaphtho[2,3-2′,3′]thiophene-5,7,12,13-tetrone (XXX) from dibenzo[*b*,*i*]-thianthrene-5,7,12,14-tetrone (XXIX) where separation of one atom of sulfur is observed (9).

The benzocarbazolediones are described as useful vat dyes (45, 55, 56).

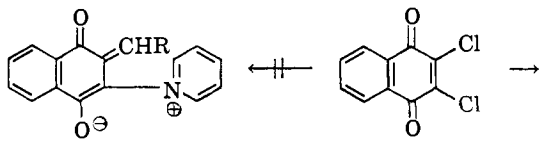
VIII. NAPHTH[2,3-*b*]INDOLIZINE-6,11-DIONES



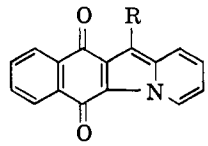
The names naphtho[2,3-*b*]pyrrocoline-6,11-diones (*Chemical Abstracts* prior to 1957) and 2,3-phthaloylpyrrocolines also have been used.

The first naphthindolizinediones were prepared independently by Luckenbaugh (52) and by Suryanarayana and Tilak (89), while investigating the reaction of 2,3-DCNQ with active methylene compounds and pyridine.

Evidence for the indolizine structure (XXXIX) was given by Luckenbaugh (52) and was substantiated later by Acharya, Suryanarayana and Tilak (2). The dipolar structure XL, first supported by Suryanarayana and Tilak (89, 93), was later withdrawn in favor of the indolizine one (2).

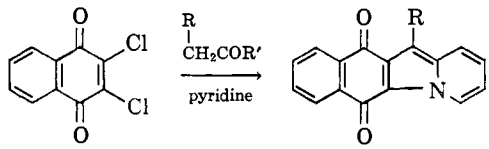


XL



XXXIX

The synthesis of 12-substituted naphth[2,3-*b*]indolizine-6,11-diones is usually effected by heating under reflux a mixture of 2,3-DCNQ, the active methylene compound and pyridine (52, 89), either in absolute ethanol (62) or in excess pyridine (93). Yields varying from 10 to 58% are obtained when ethanol is used.



The radical R is one of the electron attracting groups of the active methylene compound. The other group, generally the more electron attracting one, is cleaved during the reaction. As in the preparation of the benzonaphthofurandiones in the presence of pyridine, a by-product (presumably XII) is formed, which is separated from the reaction mixture as the inner salt XIII, by extraction with water (2, 64).

The formation of the 12-substituted naphth[2,3-*b*]indolizine-6,11-diones, as applied to the 12-carbethoxy derivative, can be represented as in Fig. 2 (52).

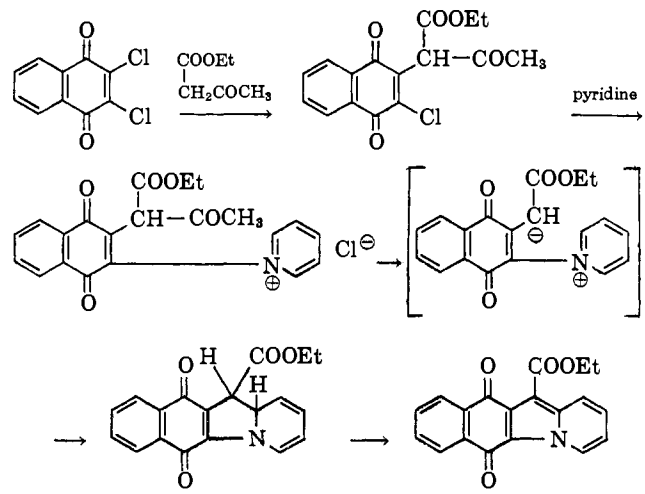


Figure 2.

A rather wide variety of active methylene compounds has been used, such as acetoacetic esters, cyanoacetic esters and acetylacetone. Weakly activated methylene compounds, such as phenylacetone, and singly activated methylene compounds, such as nitroethane, also give naphthindolizinediones (64).

Acetonitrile, propionitrile, diethyl malonate, acetophenone, ethyl *n*-butylacetoacetate, ethyl phenylacetate and dibenzoylmethane do not form the corresponding naphthindolizinediones by reaction with 2,3-DCNQ and pyridine, in absolute ethanol, but give the inner salt XIII (52, 62, 69). According to Acharya, Suryanarayana and Tilak (2), however, naphthindolizinediones are obtained, although in poor yields, from diethyl malonate, acetophenone and dibenzoylmethane, by carrying out the reaction in boiling pyridine.

Nitro, halo, and acylamino 2,3-dichloro-1,4-naphthoquinones have been used, in place of 2,3-DCNQ, in the reaction with acetoacetic esters and pyridine. From 5-nitro-2,3-dichloro-1,4-naphthoquinone and ethyl acetoacetate, a mixture of 7-nitro- and 10-nitro-12-carbethoxynaphth[2,3-*b*]indolizine-6,11-dione is obtained. Amino and diamino-12-carbethoxynaphth[2,3-*b*]indolizine-6,11-diones also have been prepared (50).

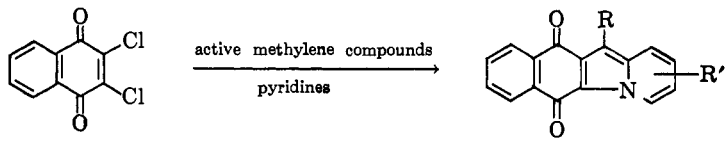
Besides pyridine, several substituted pyridines have been used successfully in this reaction, such as 4-picoline (53, 69), collidines (52), phenylpyridine (50) and 4-carbethoxypyridine (53). 2-Chloropyridine instead gives unreacted 2,3-DCNQ (69).

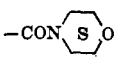
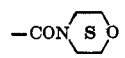
The naphth[2,3-*b*]indolizine-6,11-diones prepared from 2,3-DCNQ are listed in Table V.

An alternative route to 12-substituted naphth[2,3-*b*]-indolizine-6,11-diones involves the condensation of 2,3-DCNQ with 2-pyridylmethyl ketones in the presence of sodium ethoxide (64).

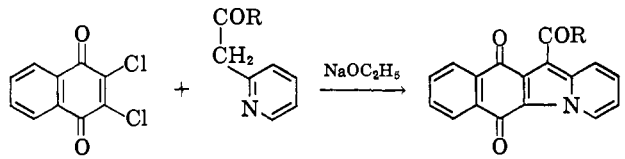
TABLE V

NAPHTH[2,3-*b*]INDOLIZINE-6,11-DIONES



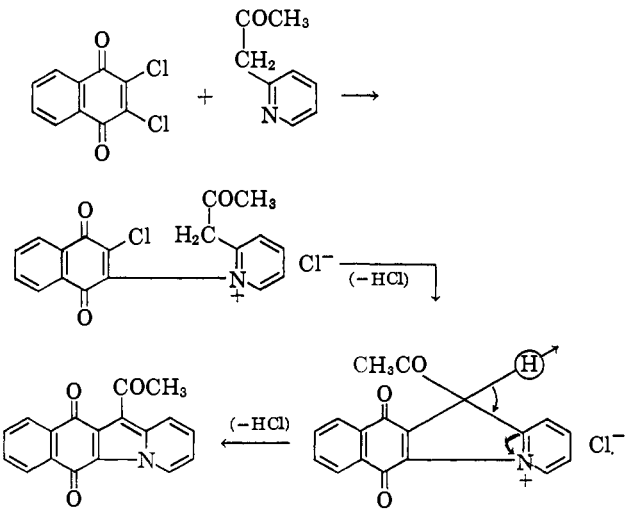
	Active methylene compound used	Product R	Product R′	Color	Melting point, °C.	Yield, %	References
1	2-Picoline	H	H	Orange	239.5	Poor[a]	(2, 53)
2	Nitroethane	$-CH_3$	H	Red	245.5–246.0	23	(69)
3	Acetylacetone	$-COCH_3$	H	Red	205–206	58	(64)
4	Acetylacetone	$-COCH_3$	CH_3[b]	Red	248–250.5	23	(69)
5	Acetylacetone	$-COCH_3$	$(CH_3)_2$[c]	Maroon	218–219	22	(52)
6	Phenylacetone	$-C_6H_5$	H	Red	244.5–245.5	14[e]	(69)
7	Benzoylacetone	$-COC_6H_5$	H	Maroon	256.5–257.5	10[j]	(52, 64)
8	Methyl acetoacetate	-COOMe	H	Yellow	190–191	51	(52)
9	Ethyl acetoacetate	-COOEt	H	Orange	157–158	49[f]	(52)
10	Ethyl acetoacetate	-COOEt	CH_3[b]	Red	186–187		(53)
11	Ethyl acetoacetate	-COOEt	$(CH_3)_2$[c]	Red	266 (dec.)	36	(52)
12		-COOH	H	Maroon	313.5–314.5	[g]	(62, 64)
13		$-CONH_2$	H	Orange	313.5–314.5	[h]	(62, 64)
14	Ethyl cyanoacetate	-CN	H	Orange	307–308.5	53[l]	(52)
15	Acetylacetone	$-COCH_3$	-COOEt[d]	Orange-yellow	210–211		(53)
16	Ethyl acetoacetate	-COOEt	-COOEt[d]	Yellow	186–187		(53)
17		-COOH	-COOH	Orange	>350	[k]	(53)
18				Red-orange	312–313	[i]	(53)
19	Ethyl cyanoacetate	-CN	-COOEt[d]	Yellow	272–273		(53)
20	Acetoacetanilide	$-CONHC_6H_5$	H	Violet	255		(93)

[a] Also prepared by decarboxylation of 17 and by hydrolysis and decarboxylation of 9. [b] Using 4-picoline in place of pyridine. [c] Using crude collidine in place of pyridine. [d] Using 4-carbethoxypyridine in place of pyridine. [e] Also prepared in poor yield from benzyl ethyl ketone (64). [f] Also prepared from diethyl malonate in excess of pyridine (93). [g] Prepared from compound 9 (62). [h] Prepared from compound 14 (64). [i] Prepared from compound 17 (53). [j] Also prepared in poor yields by using acetophenone or dibenzoylmethane in place of benzoylacetone (2). [k] Prepared from compound 16 (53). [l] Also prepared from methyl cyanoacetate (64).

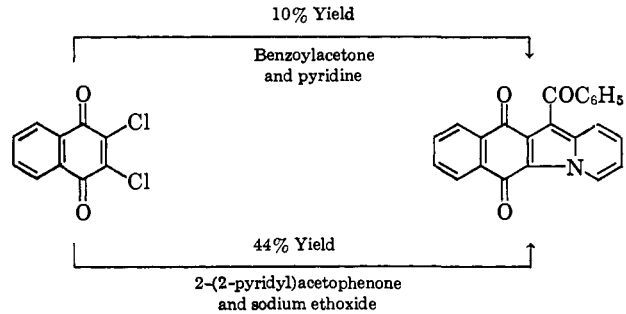


Yields varying from 40 to 44% have been obtained (Table VI).

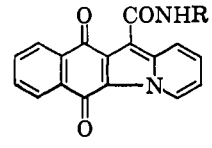
A mechanism, as applied to 12-acetylnaphth[2,3-*b*]-indolizine-6,11-dione, has been suggested (69)



This method of preparation is of special value in those cases where the method from active methylene compounds and pyridine gives poor yields, as in the preparation of 12-benzoylnaphth[2,3-*b*]indolizine-6,11-dione (69)

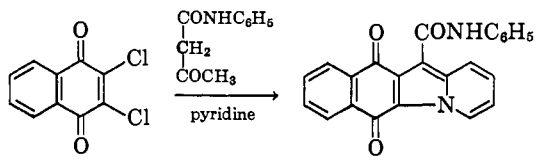


Interest in naphthindolizine chemistry was stimulated by the discovery that several derivatives of this class are useful as dyes for natural and synthetic fibers. Among the most investigated derivatives are the 12-carboxamides of the general formula

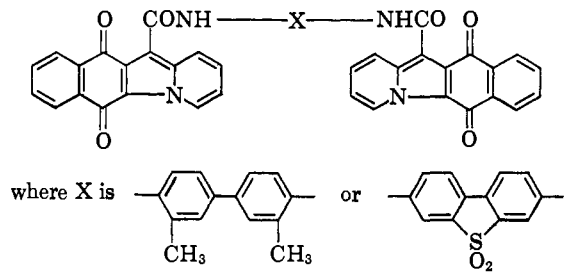


where R is an alkyl, cycloalkyl or aryl radical. These carboxamides are obtained by treating 6,11-dihydro-6,11-dioxonaphth[2,3-*b*]indolizine-12-carbonyl chloride with alkyl-, cycloalkyl-, or arylamines (50, 51, 53, 65).

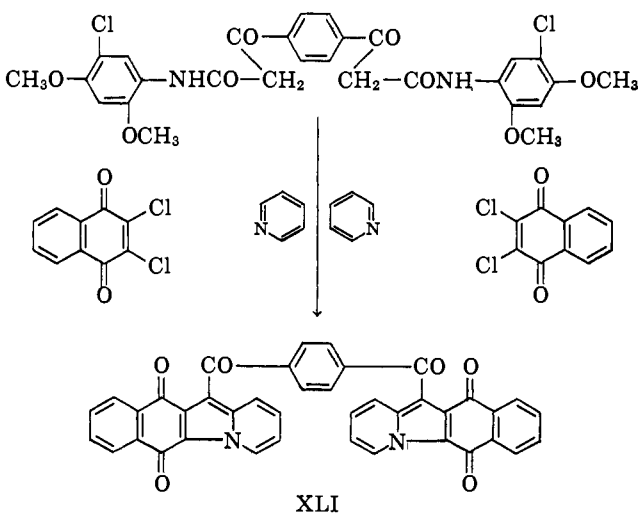
An alternative method for preparing these carboxamides involves the condensation of 2,3-DCNQ with *N*-aryl acetoacetamides in pyridine (82, 89, 93).



Replacement of the *N*-aryl acetoacetamides with biaryl analogs, such as 4,4′-bi-*o*-acetoacetotoluidide, *N*,*N*′-bis(acetoacetyl)benzidine sulfone, etc. (one mole for 2 moles of 2,3-DCNQ and excess pyridine) gives bis-carboxamides of the general formula (82).



Bis-naphth[2,3-*b*]indolizine-6,11-diones, such as 12,12′-terephthaloylbis-naphth[2,3-*b*]indolizine-6,11-dione (XLI), are obtained by treating two moles of 2,3-DCNQ with one mole of terephthaloylbis-(5-chloro-2,4-dimethoxyacetanilide) in pyridine, the leaving group being the carboxamide in this case (1, 2, 89)

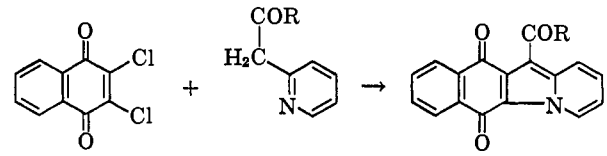


XLI

Nitro, amino and halo derivatives of XLI are also reported (83).

TABLE VI

12-SUBSTITUTED NAPHTH[2,3-*b*]INDOLIZINE-6,11-DIONES FROM PYRIDYLMETHYL KETONES



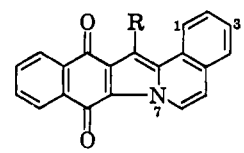
Pyridylmethyl ketone used	Product R	Melting point, °C.	Yield, %	Reference
1-(2-Pyridyl)-2-propanone	$-CH_3$	206–207	40	(64)
2-(2-Pyridyl)acetophenone	$-C_6H_5$	257–257.5	44	(64)
2-(2-Pyridyl)-4′-methoxyacetophenone	$-C_6H_4OCH_3$-p	226.5–227.5	43	(69)

IX. BENZONAPHTHINDOLIZINEDIONES

Several methods of numbering and naming this system are encountered in the literature. Prior to 1957 *Chemical Abstracts* used the name benzonaphthopyrrocolinediones, which was changed to benzonaphthindolizinediones for the years 1958 and 1959. In 1960 *Chemical Abstracts* started to name these compounds benzindoloquinoline- and benzindoloisoquinolinediones. However, in order to conform with the nomenclature used in the preceding chapter the name benzonaphthindolizinedione is used here.

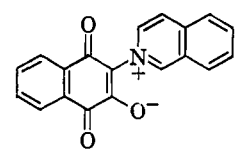
1. *Benzo[g]naphth[2,3-b]indolizine-8,13-diones*

When in the condensation of 2,3-DCNQ with active methylene compounds in ethanol, as described in the preceding chapter, synthetic isoquinoline is used in place of pyridine, benzo[*g*]naphth[2,3-*b*]indolizine-8,13-diones are formed (53, 64).



The yields vary from 7 to 55%. In place of synthetic isoquinoline, coal tar isoquinoline or coal tar quinoline (which contains isoquinoline) can be used in these condensations. It is reported that coal tar isoquinoline gives greater yields than synthetic isoquinoline (see Table VII).

Sometimes mixtures of benzonaphthindolizinediones and the by-product XLII are obtained in these condensations (64).

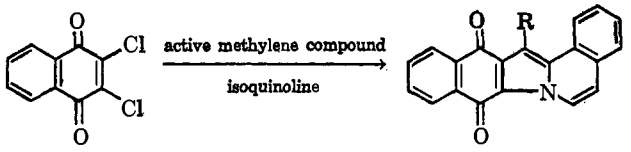


XLII

The active methylene compounds which reacted successfully with 2,3-DCNQ in the presence of synthetic

TABLE VII

BENZO[g]NAPHTH[2,3-b]INDOLIZINE-8,13-DIONES



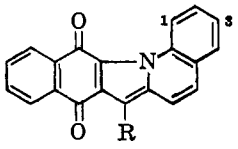
	Active methylene compound used	Product: R	Product: Melting point, °C.	Product: Color	Yields, %: Syn. isoquin.	Yields, %: Coal tar isoquin.	References
1	Nitromethane	H[a]	295–296	Red		9	(64)
2	Nitroethane	$-CH_3$	292.5–293.0	Red	13	26	(64)
3	1-Nitropropane	$-C_2H_5$	240–240.5	Red		29[d]	(64)
4	Methyl acetoacetate	-COOMe	246.5–247.5	Orange	54	64	(64, 69)
5	Ethyl acetoacetate	-COOEt[b]	239–239.5	Orange	52	64	(53, 64, 69)
6	Ethyl cyanoacetate	-CN[c]	350–350.5	Yellow		80	(64)
7	Acetylacetone	$-COCH_3$	281–282	Orange	55	72	(64)
8	Phenylacetone	$-C_6H_5$	314.5–315.5	Red-orange	7	19	(64)
9	Benzoylacetone	$-COC_6H_5$	307.5–308.5	Orange	38	43	(64)

[a] Also obtained in 36% yield from the compound listed under 5 (64). [b] Also obtained from ethyl benzoylacetate (yield 61%) (64). [c] Also obtained from methyl cyanoacetate (yield 72%) and from benzoylacetonitrile (yield 68%) (64). [d] Coal tar "quinoline" was used in place of coal tar isoquinoline.

isoquinoline or coal tar isoquinoline are listed in Table VII with the properties of the benzonaphthindolizine-diones obtained. Acetonitrile, propionitrile, dimethyl malonate and ethyl benzyl ketone in the presence of coal tar isoquinoline give only the by-product XLII (69).

2. *Benzo[e]naphth[2,3-b]indolizine-8,13-diones*

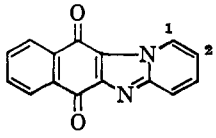
When synthetic quinoline is used in place of synthetic isoquinoline in the reaction with 2,3-DCNQ and an active methylene compound, the expected 7-substituted benzo[e]naphth[2,3-b]indolizine-8,13-diones are not formed (64, 69).



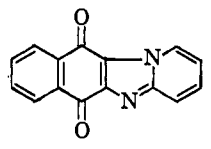
These derivatives are obtained by a route analogous to the alternative route to 12-substituted naphth[2,3-b]indolizine-6,11-diones, namely, from 2,3-DCNQ and 2-quinolylmethyl ketones (Table VIII). This reaction is carried out by refluxing an ethanolic solution of 2,3-DCNQ with the 2-quinolyl methyl ketone and sodium ethoxide. The yields vary from 12 to 47%. A long refluxing time (48 hours) and the omission of sodium ethoxide increase the yield of 7-benzoylbenzo[e]naphth-[2,3-b]indolizine-8,13-dione to 57% (69).

X. NAPHTHIMIDAZOPYRIDINEDIONES

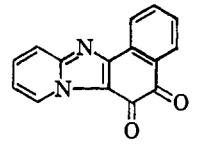
1. *Naphth[2',3'-4,5]imidazo[1,2-a]pyridine-6,11-dione*



Truit, Cooper and Wood (94) described the condensation of 2,3-DCNQ with 2-aminopyridine and assigned to the obtained product the linear 1,4-naphthoquinone structure (XLIII).



XLIII



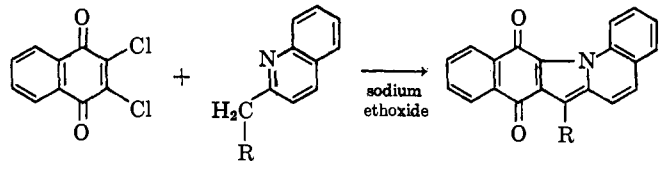
XLIV

The alternative angular 1,2-naphthoquinone structure (XLIV) was not selected by the above workers, because of their failure to obtain a phenazine derivative of the quinone by treatment with *o*-phenylenediamine.

The method used by Truit, Cooper and Wood (94) involves the condensation of 2,3-DCNQ with 2-aminopyridine in ethanol to form 2-chloro-3-(2-pyridylamino)-1,4-naphthoquinone (23), and ring closure of this intermediate by heating in acetic acid. An alternative

TABLE VIII

BENZO[e]NAPHTH[2,3-b]INDOLIZINE-8,13-DIONES



	Quinolylmethyl ketone used	Product: R	Product: Melting point, °C.	Product: Color	Yield, %	Reference
1.	1-(2-Quinolyl)-2-propanone	$-COCH_3$	278.5–279	Orange-red	47	(64)
2.	2-(2-Quinolyl)acetophenone	$-COC_6H_5$	279–279.5	Orange	12–57[a]	(69)
3.		-COOH[b]	310.5–311.5	Brown		(64)
4.		H[c]	240.5–241.5	Brown		(64)

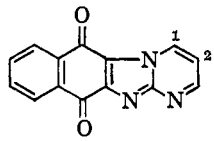
[a] Prepared without using sodium ethoxide. [b] Obtained from compound 1. [c] Obtained from compound 3.

method consists in refluxing a solution of 2-acetamido-3-chloro-1,4-naphthoquinone and 2-aminopyridine in 1-butanol. A 50% yield of orange needles of m.p. 306° is reported (94).

Mosby and Boyle (60) found that under the conditions of the above methods the angular quinone XLIV rather than the linear XLIII was formed. According to Mosby (59) the linear isomer XLIII is obtained by refluxing 2-chloro-3-ethoxy-1,4-naphthoquinone [prepared from 2,3-DCNQ, ethanol and sodium acetate (26)] with 2-aminopyridine in ethylene glycol dimethyl ether. A 34% yield of XLIII as golden-tan needles of m.p. 297–298° is reported. 2-Chloro-3-hydroxy(or acetoxy)-1,4-naphthoquinone can be used in place of the corresponding 3-ethoxy derivative.

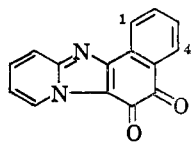
Evidence that the compound obtained by Mosby from 2-chloro-3-ethoxy-1,4-naphthoquinone has the structure XLIII is provided by the reduction of this compound to the known 1,2,3,4-tetrahydronaphth-[2′,3′-4,5]imidazo[1,2-*a*]pyridine-6,11-dione (58) and by the failure to obtain a phenazine derivative by treatment with *o*-phenylenediamine (59).

Replacement of 2-aminopyridine in the above condensations with 2-aminopyrimidine and with 2-aminopyrazine was also investigated. Mathur and Tilak (53) reported the formation of naphth[2′,3′-4,5]imidazo[1,2-*a*]pyrimidine-6,11-dione



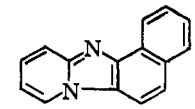
from 2-aminopyrimidine and 2,3-DCNQ in ethanol. No proof of this structure is given. Under the conditions of Mosby's method 2-chloro-3-ethoxy-1,4-naphthoquinone reacts with 2-aminopyrimidine or with 2-aminopyrazine to give only carbonaceous matter (59).

2. *Naphth[1′,2′-4,5]imidazo[1,2-a]pyridine-5,6-diones*



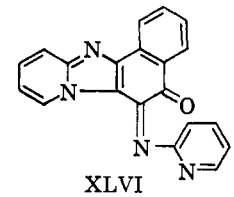
The first representative of this system was obtained by heating under reflux 2,3-DCNQ with 2-aminopyridine in ethanol and in the presence of sodium carbonate. A 46% yield of XLIV as orange crystals of m.p. 299.5°–301.5° is reported (60). An alternative method of preparing XLIV involves the condensation of 2,3-DCNQ with 2-acetamidopyridine in methyl Cellosolve at the reflux (60).

Evidence that the quinone obtained as above has structure XLIV is provided by the formation of a phenazine derivative of this quinone by treatment with *o*-phenylenediamine and by the preparation of the same quinone by the alternative route from 2-aminopyridine and 3,4-dichloro-1,2-naphthoquinone. The similarity of the spectral characteristics of derivatives of the reduced form of XLIV with those of derivatives of XLV, prepared by an unambiguous route (5, 57), strengthens the argument in favor of structure XLIV (60).



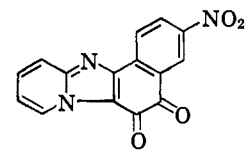
XLV

Other acid acceptors have been used in this condensation, such as sodium bicarbonate or, preferably, a second molar equivalent of 2-aminopyridine. When four or more molar equivalents of 2-aminopyridine were used in this reaction with 2,3-DCNQ, a vattable red-brown compound was obtained as a major product, for which structure XLVI was suggested (60).



XLVI

A large variety of substituted 2-aminopyridines, such as methyl-, chloro-, ethoxy-, 5-nitro- and 3,5-dinitro-2-aminopyridine may be used in place of 2-aminopyridine to yield naphthimidazopyridinediones with substituents in the pyridine ring (8). Derivatives of 2,3-DCNQ, such as 5-nitro-, 5-bromo-, and 5,8-dichloro-, and derivatives of 2,3-dibromo-1,4-naphthoquinone, such as the 5-hydroxy-, have been condensed with 2-aminopyridine to yield nitro, bromo, chloro and hydroxy derivatives of naphth[1′,2′-4,5]imidazo[1,2-*a*]-pyridine-5,6-dione, with the above substituents in the naphthoquinone moiety (8). A mixture of 1- and 4-nitronaphth[1′,2′-4,5]imidazo[1,2-*a*]pyridine-5,6-dione is formed from 2-aminopyridine and 2,3-dichloro-5-nitro-1,4-naphthoquinone, whereas direct nitration of XLIV gives a mononitro derivative, to which structure XLVII has been assigned (8, 60).



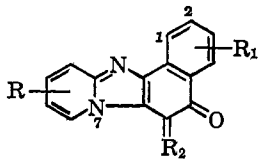
XLVII

Some of the naphth[1′,2′-4,5]imidazo[1,2-*a*]pyridine-5,6-diones prepared are listed in Table IX.

Aza analogs of XLIV have been obtained by con-

TABLE IX

NAPHTH[1',2'-4,5]IMIDAZO[1,2-*a*]PYRIDINE-5,6-DIONES (60)

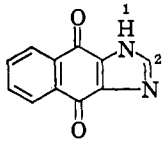


R	R_1	R_2	Color	Melting point, °C.
H	H	=O	Orange	299.5–301.5
H	H	=$NCOCH_3$	Orange	271.5–272.5
H	H	=N-2-pyridyl	Red-brown	245–245.5
H	1 (or 4)-NO_2	=O	Orange-red	292–293
H	4 (or 1)-NO_2	=O	Orange	322–324
H	3-NO_2	=O	Orange	>360
H	1,4-dichloro	=O	Orange	319–320.7
8-CH_3	H	=O	Yellow	280.8–283

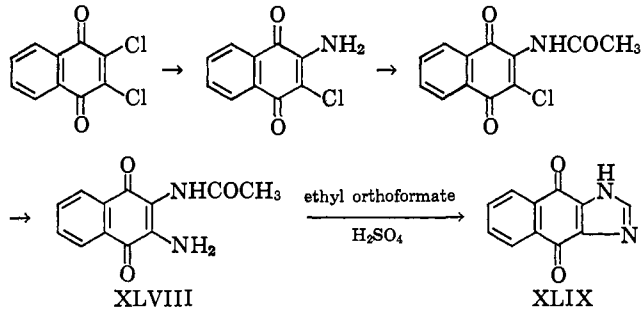
densing 2,3-DCNQ with 2-aminopyrimidine, with 2-aminoquinoline and with 2-aminothiazole. No proof of the structure of the quinones obtained from the last two amino compounds is given (60).

Derivatives of XLIV are reported to be useful as vat dyes and as pigments (8).

XI. 1*H*-NAPHTH[2,3-*d*]IMIDAZOLE-4,9-DIONES

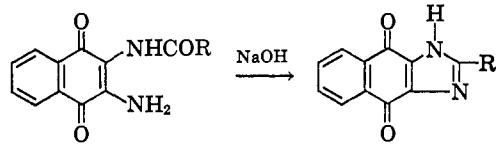


The parent compound, the 1*H*-naphth[2,3-*d*]imidazole-4,9-dione (XLIX), first prepared from 2,3-naphthalenediamine and formic acid, then oxidation of the formed naphth[2,3-*d*]imidazole (31), was obtained recently from 2,3-DCNQ through the intermediate 2-acetamido-3-amino-1,4-naphthoquinone



The last step was effected by treating XLVIII with ethyl orthoformate in the presence of sulfuric acid as the catalyst. A nearly quantitative yield of 1*H*-naphth[2,3-*d*]imidazole-4,9-dione from XLVIII is reported (35, 36). The cyclization step of this method is not of general application. Attempts to prepare the homolog, the 2-methyl-1*H*-naphth[2,3-*d*]-imidazole-4,-9-dione, by treating XLVIII with ethyl orthoacetate were unsuccessful (35).

2-Substituted 1*H*-naphth[2,3-*d*]imidazole-4,9-diones are generally prepared by heating under reflux 2-acylamino-3-amino-1,4-naphthoquinones in ethanol containing 15% of 2 *N* sodium hydroxide (36).



The reaction is usually completed within 15 to 30 minutes as evidenced by the change in the color of the reaction mass from red-violet to orange-brown (35). This method is an adaptation of the method used by Fries and Billig (27) to prepare 2-methyl-1-phenyl-1*H*-naphth[2,3-*d*]imidazole-4,9-dione from 2-acetamido-3-anilino-1,4-naphthoquinone.

Replacement of 2,3-DCNQ with 5-nitro- and 5-amino-2,3-dichloro-1,4-naphthoquinone, in the method outlined above for the preparation of the unsubstituted 1*H*-naphth[2,3-*d*]imidazole-4,9-dione (XLIX), gives 5-nitro- and 5-amino-1*H*-naphth[2,3-*d*]imidazole-4,9-dione, respectively. The 5-nitro derivative was also obtained by direct nitration of XLIX. A 75% yield is reported (98).

In the preparation of 2-(dialkylaminomethyl)-1*H*-naphth-[2,3-*d*]imidazole-4,9-diones from 2-(dialkylaminoacetamido)-3-amino-1,4-naphthoquinones, the cyclization is carried out with better results in acetic acid and in the presence of palladium black and hydrogen as reducing agents, followed by oxidation of the hydroquinone moiety of the naphthimidazole to the quinone structure (36).

Prolonged refluxing in a high boiling solvent was used to cause the cyclization of 2-acetamido-3-(*p*-carboxyanilino)-1,4-naphthoquinone and of 2-acetamido-3-(*p*-sulfamoylanilino)-1,4-naphthoquinone (97).

Some of the 1*H*-naphth[2,3-*d*]imidazole-4,9-diones prepared are listed in Table X.

The 1*H*-naphth[2,3-*d*]imidazole-4,9-diones of Table X are yellow crystalline compounds. They are unaffected by prolonged heating with 2 *N* sodium hydroxide or 6 *N* hydrochloric acid. The 1-alkyl derivatives are more basic than those with hydrogen in the 1 position. The 2-methyl derivatives do not show the active methylene character exhibited by many other 2-methyl azoles (36).

The naphthimidazolediones display pronounced inhibitory properties against *E. coli* 113–3 and against *E. coli* B 96 (36).

Bis-1*H*-naphth[2,3-*d*]imidazole-4,9-diones of the for-

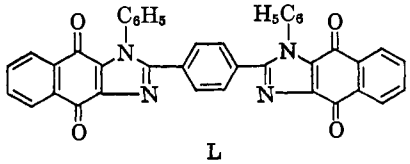


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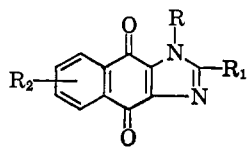
TABLE X

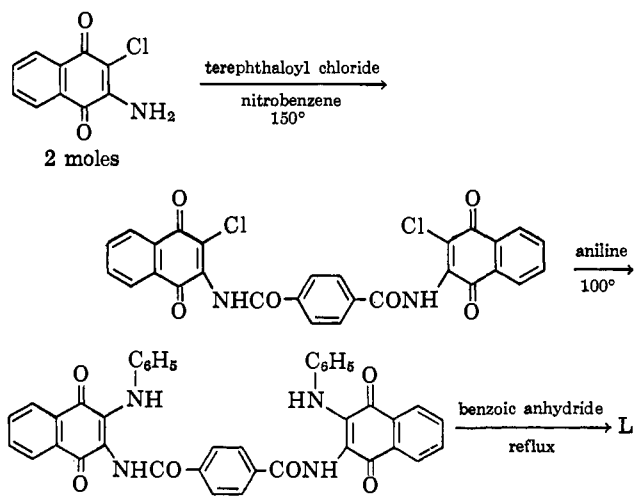
1*H*-NAPHTH[2,3-*d*]IMIDAZOLE-4,9-DIONES



R	R_1	R_2	Melting point, °C.	Yield,[a] %	References
H	H	H	370	95	(31, 36)
H	$-CH_3$	H	368	63[b]	(31, 36)
H	$-C_2H_5$	H	304.4–305	70	(36)
H	$-C_3H_7$-*n*	H	221.8–222.2	65	(36)
H	$-C_4H_9$-iso	H	250–251.4	57	(36)
H	$-C_5H_{11}$-*n*	H	182.3–183.5	68	(36)
H	$-C_{11}H_{23}$-*n*	H	127.5–129	71.5	(98)
H	$-CH(C_2H_5)_2$	H	240.7–242	81	(36)
H	$-CH_2C_6H_5$	H	279–280.3	62	(36)
H	$-CH{=}CH-C_6H_5$	H	340–343	27.6	(98)
H	$-CH_2OH$	H	276–278	79	(98)
H	$-CH_2N(C_2H_5)_2 \cdot HCl$	H	264.2–265.4	76	(36)
H	$-(CH_2)_4COOH$	H	267–268	74	(98)
H	$-(CH_2)_4CONH_2$	H	235–236	50[c]	(98)
C_6H_5	$-CH_3$	H	239		(27)
C_6H_4COOH-*p*	$-CH_3$	H	317	Poor	(97)
Naphthyl	$-CH_3$	H	222		(27)
H	H	5-NO_2	320–330	44[d]	(98)
H	H	5-NH_2	420 dec.	89	(98)
H	$-CH_3$	5-NH_2	440 dec.	79	(98)

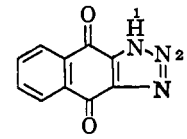
[a] From the corresponding 2-acylamino-3-aminonaphthoquinones. [b] A 94% yield is obtained from 2,3-diacetamido-1,4-naphthoquinone (98). [c] Obtained from the corresponding carboxy acid. [d] A 75% yield is obtained by direct nitration of 1*H*-naphth[2,3-*d*]-imidazole-4,9-dione (98).

mula are reported as being useful as vat dyes (46). Their synthesis involves the steps

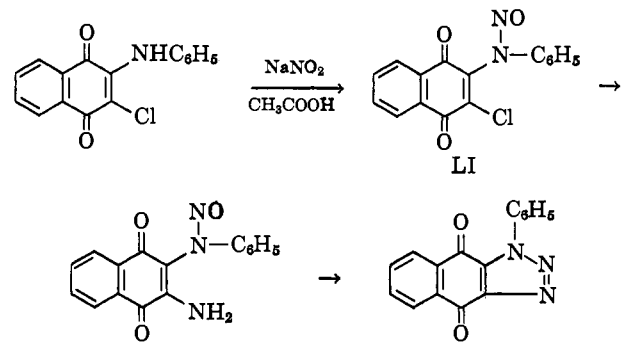


By using 5-nitro-2-amino-3-chloro-1,4-naphthoquinone (m.p. 240°) or 8-nitro-2-amino-3-chloro-1,4-naphthoquinone (m.p. 260°), in place of the 2-amino-3-chloro-1,4-naphthoquinone, the corresponding derivatives of L are obtained. These nitro compounds by reduction with an alkaline solution of sodium hydrosulfite, followed by oxidation of the hydroquinone moiety, give the corresponding amino derivatives (46).

XII. 1*H*-NAPHTHO[2,3-*d*]TRIAZOLE-4,9-DIONES



The 1-substituted 1*H*-naphtho[2,3-*d*]triazole-4,9-diones were prepared from 2,3-dichloro-1,4-naphthoquinone by Fries and Billig (27), who found that nitrosation of 2-anilino-3-chloro-1,4-naphthoquinone to 2-(*N*-nitrosoanilino)-3-chloro-1,4-naphthoquinone (LI) makes the chlorine atom reactive toward amines. Thus they obtained, by treatment of LI with ammonia in ethanol, 2-(*N*-nitrosoanilino)-3-amino-1,4-naphthoquinone, which easily cyclizes to 1-phenyl-1*H*-naphtho-[2,3-*d*]triazole-4,9-dione by heating in acetic acid. Quantitative yields are reported (27).

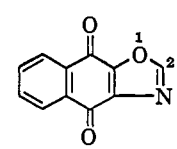


An alternative method of preparation involves the heating at 100° of an acetic acid solution of 2-amino-3-anilino-1,4-naphthoquinone with sodium nitrite (28).

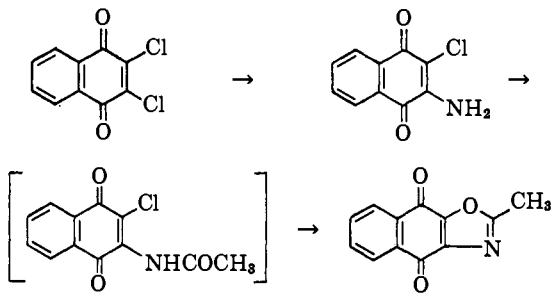
In addition to 1-phenyl-1*H*-naphtho[2,3-*d*]triazole-4,9-dione (yellow crystals of m.p. 241°), the 1-*p*-tolyl derivative (greenish-yellow crystals of m.p. 212°) is reported (28).

Nitro, amino, diamino, amino-bromo, and amino-nitro derivatives of 1-methyl-, 1-ethyl- and 1-butyl-1*H*-naphtho[2,3-*d*]triazole-4,9-diones have been prepared. They are reported as being useful intermediates for vat dyes (78, 79).

XIII. NAPHTH[2,3-*d*]OXAZOLE-4,9-DIONES



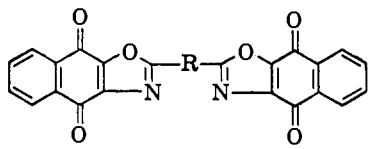
2-Methylnaphth[2,3-*d*]oxazole-4,9-dione is prepared from 2,3-DCNQ through the intermediate 2-amino-3-chloro-1,4-naphthoquinone



The cyclization is effected by refluxing a solution of 2-amino-3-chloro-1,4-naphthoquinone in acetic anhydride and in the presence of small amounts of sulfuric acid (30).

The naphth[2,3-*d*]oxazole-4,9-diones are pale yellow compounds of fairly high melting points. Unlike the analogous naphth[2,3-*d*]imidazole-4,9-diones, the naphthoxazoles are decomposed with formation of 2-amino-3-hydroxy-1,4-naphthoquinone, when heated with dilute caustic or concentrated sulfuric acid in ethanol solution (30).

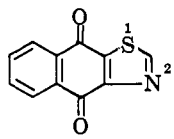
Bis-naphthoxazolediones of the general formula



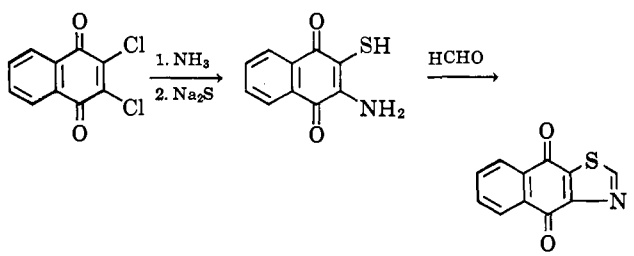
where R is a phenylene, a biphenylene or a naphthylene radical are prepared by condensing 2-amino-3-chloro-1,4-naphthoquinone (2 moles) with terephthaloyl chloride, 4,4'-biphenyldicarbonyl chloride or 1,4-naphthalenedicarbonyl chloride (1 mole), respectively, in nitrobenzene at reflux. Nitro, amino, and benzamido derivatives of bis-naphth[2,3-*d*]-oxazole-4,9-diones are vat dyes of good fastness properties on cotton (46).

The 2-methylnaphth[2,3-*d*]oxazole-4,9-dione is reported to be effective against strains of tuberculosis bacteria resistant to Neoteben-thiosemicarbazone (80).

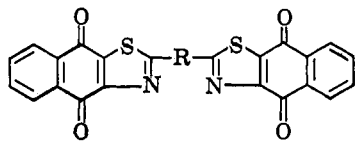
XIV. NAPHTHO[2,3-*d*]THIAZOLE-4,9-DIONES



This system is also called β,β-naphthothiazole-3,8-dione. The parent compound of this system was obtained from 2-amino-3-mercapto-1,4-naphthoquinone and formaldehyde (7, 30).



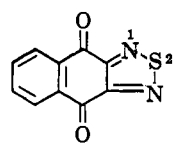
Derivatives with substituents in the 2 position have been prepared by using other aldehydes, such as acetaldehyde, glyoxal, benzaldehyde, dimethylaminobenzaldehyde, naphthaldehyde and terephthalaldehyde (37). When dialdehydes are used (1 mole with two moles of 2-amino-3-mercapto-1,4-naphthoquinone), bis-naphthothiazolediones are obtained (32)



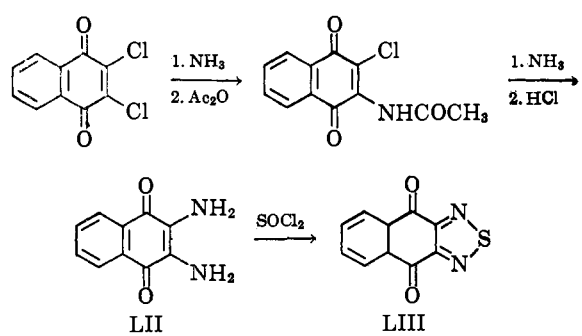
The preparation of the naphthothiazolediones is carried out by refluxing an aqueous suspension of 2-amino-3-mercapto-1,4-naphthoquinone and the aldehyde in the presence of small amounts of acetic acid. The intermediate thiazoline derivatives are transformed into the naphthothiazolediones by the action of atmospheric oxygen during the isolation step (32).

The naphthothiazolediones are yellow compounds, which give a characteristic yellow solution in concentrated sulfuric acid. Treated with alkaline solutions of sodium hydrosulfite, they produce the soluble, reduced derivative or "vat," from which cotton is dyed in yellow shades (32). The 2-methyl derivatives have weak basic properties and do not form quaternary salts with dialkyl sulfates (41).

XV. NAPHTHO[2,3-*c*](1,2,5)THIADIAZOLE-4,9-DIONE



The reaction of 2,3-diamino-1,4-naphthoquinone (LII) and thionyl chloride is described by Neeff and Bayer, who assigned to the condensation product the formula LIII. The intermediate, 2,3-diamino-1,4-naphthoquinone, is obtained from 2,3-DCNQ according to the sequence of reactions (36, 61)



The preparation of LIII is carried out by heating at 75° for a half hour a mixture of LII with an excess of

thionyl chloride. A 64% yield of a pale yellow compound (m.p. 246.5°) is obtained, which gives a green vat solution by treatment with an alkaline solution of sodium hydrosulfite (61).

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