Polynuclear Heterocycles. IX. The Formation of Ylidene Enol Betaines and Their Ring Closure to 2,3-Phthaloylpyrrocolines

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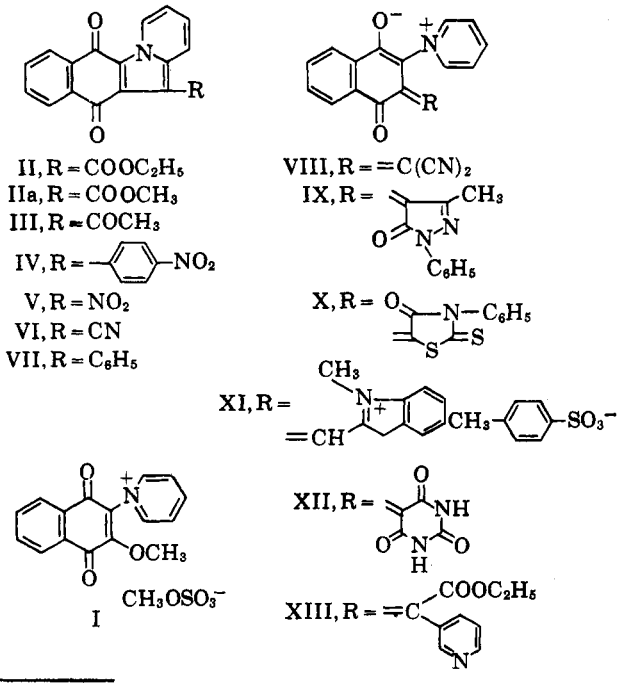
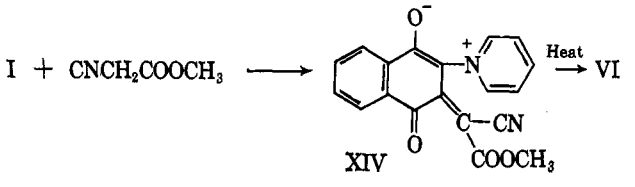
The reaction of N-(1,4-dioxo-2-methoxynaphthyl-3)pyridinium methosulfate (I) with active methylene compounds to yield ylidene enol betaines and substituted pyrrocolines is described. The cyclization of certain of the ylidene enol betaines to yield pyrrocolines was effected and the mechanism is discussed. Derivatives of I that contained substituents in the pyridinium moiety were prepared and allowed to react with active methylene compounds. The reaction between 2,3-dichloro-1,4-naphthoquinone, an active methylene compound, and a substituted pyridine was investigated.

In the preceding study[1] of this series, it was found that N-(1,4-dioxo-2-methoxynaphthyl-3)pyridinium methosulfate (I)[1] reacts with amines which are not weakly basic or sterically hindered to give products in which the methoxy group of I is replaced by an amino group. This reaction of I with nucleophilic agents has now been extended to include active methylene compounds. The active methylene compounds employed and the numbers of the formulas for the products formed are as follows: diethyl malonate gives II; ethyl benzoylacetate, II; dimethyl malonate, IIa; methyl acetoacetate, IIa; 2,4-pentanedione, III; ethyl *p*-nitrophenylacetate, IV; nitromethane, V; methyl cyanoacetate, VI; ethyl cyanoacetate, VI; deoxybenzoin, VII; malononitrile, VIII; 3-methyl-1-phenyl-2-pyrazolin-5-one, IX; 3-phenylrhodanine, X; 2,3-dimethylbenzothiazolium *p*-toluenesulfonate, XI; barbituric acid, XII; and ethyl 3-pyridylacetate, XIII. To effect these reactions, equivalent quantities of I and the methylene compound, and two or more equivalents of sodium acetate were refluxed for two hours in methanol. In all cases, highly colored blue solutions were immediately formed, and in examples VIII through XIII, the blue color persisted. The blue color obtained in examples II through VII, however, rapidly changed to brown after a short time.



The structures of compounds II, IIa, III, VI, and VII have been firmly established by Pratt, Rice, and Luckenbaugh[2] who prepared them from 2,3-dichloro-1,4-naphthoquinone and pyridine and ethyl acetoacetate, methyl acetoacetate, 2,4-pentanedione, ethyl cyanoacetate, and phenyl-2-propanone, respectively. The ultraviolet absorption spectra of II, IIa, III, VI, and VII of known structure have been determined and these spectra compared with those of IV and V. With due allowance for substituents, the spectra of IV and V are similar to the spectra of the known compounds (see Table I). These observations support the assigned structures.

In one instance the reaction of methyl cyanoacetate with I was conducted at 25–33° to give the deep blue dye XIV which, on heating alone or in an inert solvent, gave VI, demonstrating that XIV is an intermediate in the formation of VI. The thermal decomposition of



XIV gave small amounts of pyridine, hydrogen cyanide, and IIa, in addition to methyl formate and VI. These products were identified in the mass spectrometer by means of reference samples. The presence of IIa demonstrates that ring closure of XIV by the elimination of hydrogen cyanide does occur to a slight extent. The blue coloration which forms during all of the reactions and which changes to brown in the cases in which ring closure takes place is evidence that enol betaines similar to XIV are a common intermediate during the formation of the pyrrocolines, II through VII.

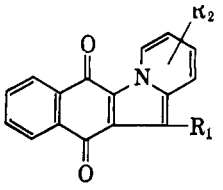
Our conception of the mechanism for these reactions is as follows: The first step is the replacement of the methoxy group by the ion of the active methylene compound. The carbon of I to which the methoxy group is attached is particularly subject to attack by an anion because of the positive charge induced on it by its proximity to the electron-withdrawing oxygen atoms and the pyridinium group. Thus the replacement of the methoxy group in I by methyl cyanoacetate would give A or its tautomer B which loses the elements of HX, in the presence of basic reagents, to give the enol betaine C which is isoelectric with D, and the latter undergoes

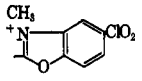
(1) G. A. Reynolds, R. E. Adel, and J. A. VanAllan, Part VIII, *J. Org. Chem.*, 2683 (1963).

(2) E. F. Pratt, R. G. Rice, and R. W. Luckenbaugh, *J. Am. Chem. Soc.*, **79**, 1212 (1957).

TABLE I

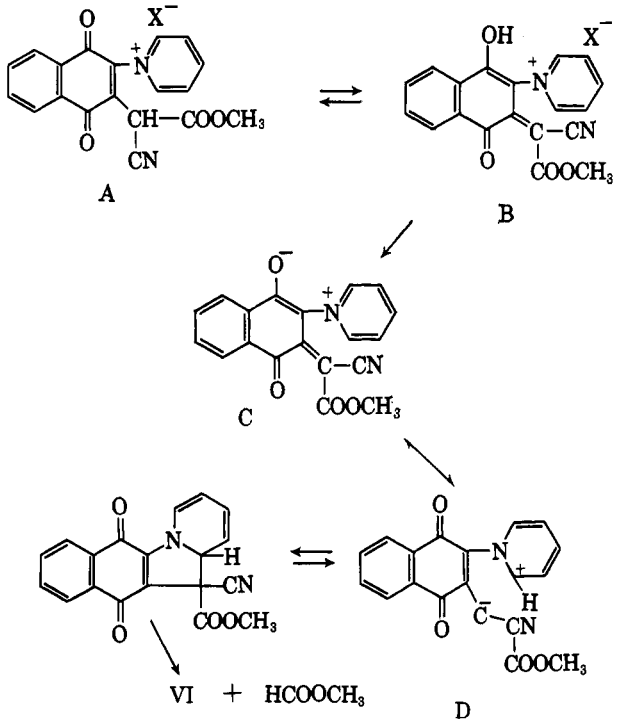
ULTRAVIOLET ABSORPTION DATA ON THE 2,3-PHTHALOYLPYRROCOLINES



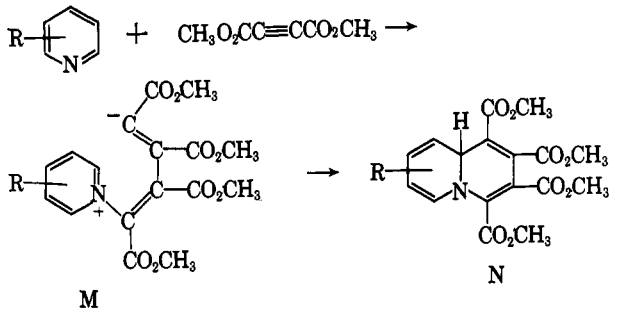
Compound no.	R_1	R_2	λ_1 (ϵ)[a]	λ_2 (ϵ)	λ_3 (ϵ)	λ_4 (ϵ)	λ_5 (ϵ)	Solvent
II	$-COOC_2H_5$	H	254 (42.0)	278 (22.0)	324 (15.0)	355 (7.2)	475 (6.2)	CH_3CN
IIa	$-COOCH_3$	H	255 (49.0)	~283 (15.8)	318 (13.9)	348 (7.5)	~416 (1.7) 492 (1.8)	CH_3CN
III	$-COCH_3$	H	259 (41.5)	~273 (25.0)	323 (14.1)	353 (7.0)	475 (6.4)	CH_3CN
IV	$4\text{-}NO_2C_6H_4-$	H			330 (10.0)	~375 (6.8)	498 (6.3)	DMF[b]
V	$-NO_2$	H			324 (11.0)	364 (8.1)	489 (6.8)	DMF
VI	$-CN$	H	257 (42.0)	277 (21.0)	325 (16.0)	354 (8.1)	476 (6.8)	CH_3CN
VII	$-C_6H_5$	H	256 (48.0)		300 (9.6)	370~354~	500 (8.4)	CH_3CN
XV	$-C(CH_3)=NNCOOC_2H_4OC_2H_5$	H	254 (37.0)		325 (10.3)	355 (5.5)	485 (6.8)	CH_3CN
XVII	$-CONHC_6H_5$	H		275 (35.0)	335 (15.4)	355 (9.6)	508 (6.0)	DMF
XIX	$-CONH_2$	H			325 (13.3) 333 (13.8)	354 (8.1)	492 (5.2)	DMF
XX		H	255 (33.0)	282 (23.7)	315 (14.4)	372 (11.3)	468 (7.0)	CH_3CN
XXVII	$-CONHC_6H_5$	6- or 8-CH_3			325 (12.3)	~337 (11.1) ~354 (6.8)	490 (6.45)	DMF
XXVIII	$-CONHC_6H_5$	$7\text{-}CH=CHC_6H_5$		275 (38.0) 269 (55.0)	325 (23.4) 340 (24.4)	365 (31.0) 385 (37.5)	530 (6.0)	DMF
XXIX	$-CONHC_6H_5$	7,8 benzo		279 (67.5)	310 (21.5)	340 (11.3)	462 (9.0)	DMF

[a] Extinction coefficients are reported as $\epsilon \times 10^{-3}$; λ reported in mμ. [b] Dimethylformamide.

ring closure, with the elimination of methyl formate, to give VI.



As precedents for this sequence of reactions, the following analogous cases are cited: Enol betaine salts of type B are readily converted to enol betaines by bases.[1] Thus, the salt B is converted to the enol betaine C by sodium acetate. A precedent for the ring closure of D to VI is to be found in the addition of dimethyl acetylenedicarboxylate to pyridine, since there is evidence[3] that compounds of type M are formed at low temperature and M cyclizes to N at room temperature. The

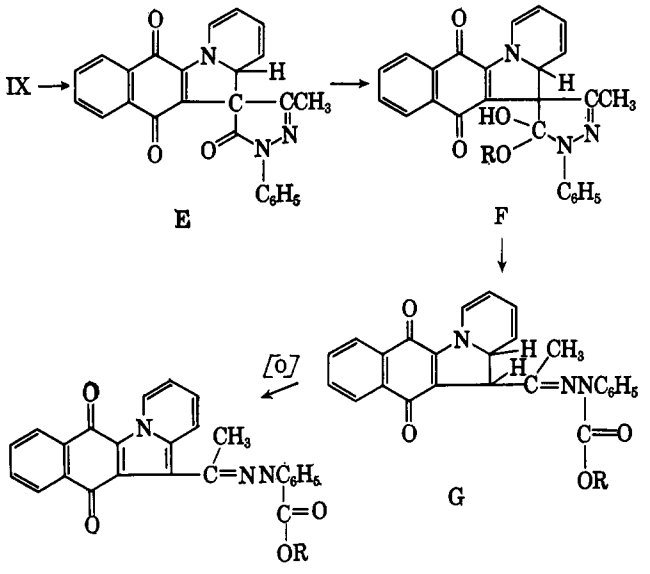


elimination of methyl formate to yield the aromatic pyrrocoline nucleus is irreversible and, therefore, drives the reversible intermediate steps of the cyclization to completion.

On the basis of mechanism, it appeared feasible that compounds VIII through XII should cyclize to pyrrocoline derivatives if they were subjected to more vigorous conditions than refluxing in alcohol. Accordingly, a sample of VIII was refluxed in 2-ethoxyethanol and in trichlorobenzene for 12 hr., but VIII was recovered. However, when a sample of VIII was heated to 400° in a pyrolysis cell and the resulting products were examined by means of a mass spectrometer, the cyclized product VI and hydrogen cyanide were identified.

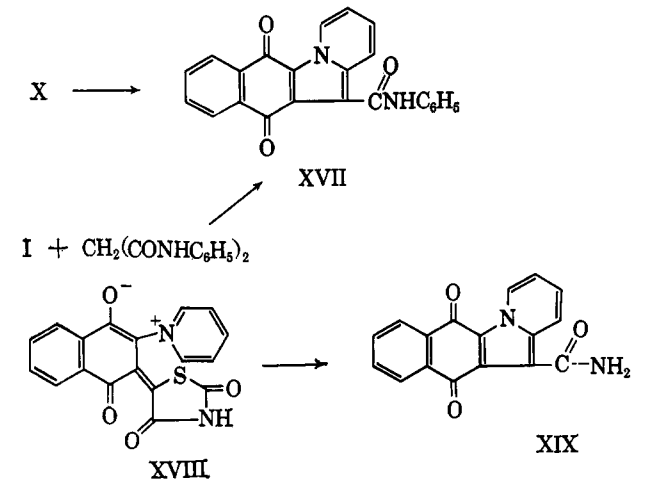
(3) L. M. Jackman, A. W. Johnson, and J. C. Tebby, *J. Chem. Soc.*, 1579 (1960).

Attempts to bring about ring closure of IX in refluxing 2-ethoxyethanol resulted in the formation of a compound which has an empirical composition corresponding to the addition of ethoxy–ethanol to IX. The infrared spectrum of this product has an absorption band at 5.82 μ indicative of an ester group and an ultraviolet absorption spectrum characteristic of the 2,3-phthaloylpyrrocolines (Table I). These observations suggest that the compound formed by the cyclization of IX has undergone reaction with the solvent to give XV. *n*-Amyl alcohol, in place of the 2-ethoxyethanol, gave the corresponding amyl ester XVI. The mechanism by which this occurs is believed to be as follows. The initial spirocyclization product E adds the alcohol to give the hemiacetal F which undergoes a reverse acylation to give G, followed by aerial oxidation of G to give XV or XVI.



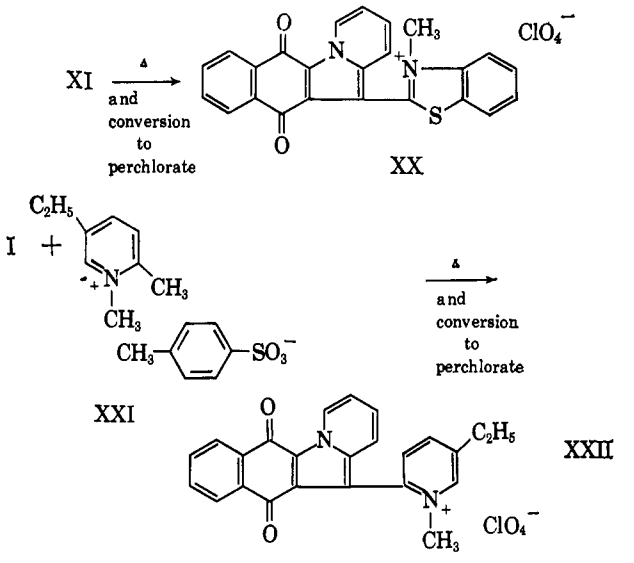
Hydrolysis of XV by hydrochloric acid gave 1-acetyl-2,3-phthaloylpyrrocoline (III), thus confirming the structure of XV.

Pyrolysis of X in 2-ethoxyethanol or preferably in dimethylformamide proceeds readily to give 1-phenylcarbamyl-2,3-phthaloylpyrrocoline (XVII), the elements of carbon disulfide having been eliminated during pyrolysis. Since XVII also has been prepared from malonanilide and I, the product of the pyrolysis of X is established as XVII.

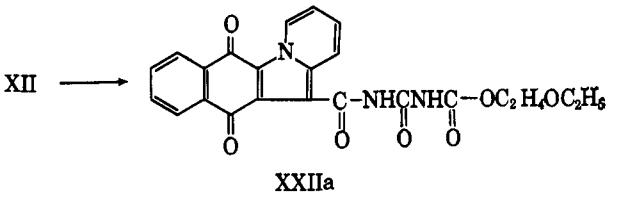


The dye XVIII, formed by the reaction of I with 2,4-thiazolidinedione, on heating in dimethylformamide, loses carbon oxysulfide to give the known 1-carboxamido-2,3-phthaloylpyrrocoline (XIX).[2]

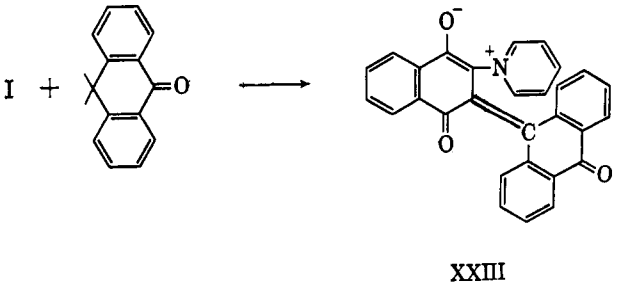
The ring closure of XI in 2-ethoxyethanol resulted in the formation of the pyrrocoline XX which also was found as a secondary product in the synthesis of XI. In a closely related reaction, 1,2-dimethyl-5-ethylpyridinium *p*-toluenesulfonate (XXI) reacts with I to give the pyrrocoline XXII.



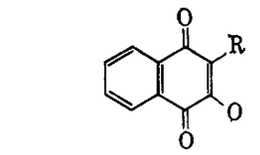
The ring closure of XII in 2-ethoxyethanol proceeded very slowly (24 hr. at reflux temperature) to give the pyrrocoline, XXIIa.

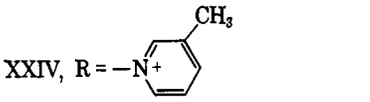


The condensation of anthrone with I gave a dye XXIII which was unchanged after refluxing for 24 hr. in 2-ethoxyethanol; *i.e.*, it does not undergo ring closure to a pyrrocoline.

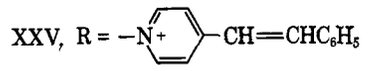


To study the effect of substituents in the pyridinium moiety of I, in regard to the reactions of these materials with active methylene compounds, the enol betaines XXIV,[1] XXV,[1] and XXVI[2] were prepared and converted to the corresponding quaternary salts, XXIVa → XXVIa.

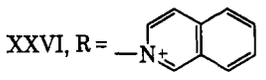




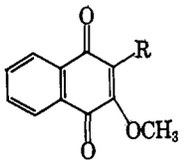
XXIV, R = —N⁺(CH₃)

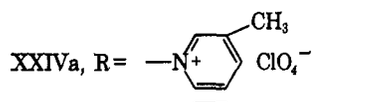


XXV, R = —N⁺—CH=CHC₆H₅

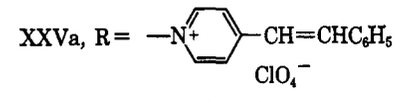


XXVI, R = —N⁺

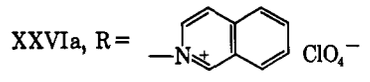




XXIVa, R = —N⁺(CH₃) ClO_4^-



XXVa, R = —N⁺—CH=CHC₆H₅ ClO_4^-



XXVIa, R = —N⁺ ClO_4^-

Attempts to effect reaction of 4-picoline with 2,3-dichloro-1,4-naphthoquinone gave a highly colored, very insoluble product of unknown constitution. If the methyl group of 4-picoline is blocked, as in 4-styrylpyridine, the desired betaine XXV is obtained. This observation suggests that the methyl group of the betaine which may have been obtained from 4-picoline has undergone further reaction. 2,3-Dichloro-1,4-naphthoquinone does not react with 2-picoline. The similarity of the ultraviolet absorption spectra of the betaines XXIV → XXVI with those of the parent 1,4-dioxy-3-pyridinium-2-naphthoxide and the spectra of the salts XXIVa → XXVIa with I indicates their close structural relationship (Table II).

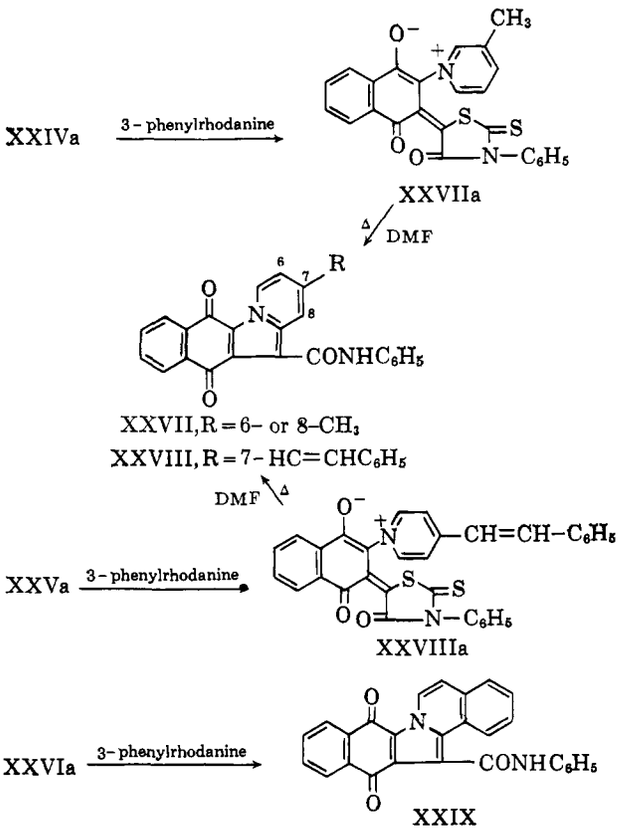
TABLE II

ULTRAVIOLET ABSORPTIONS OF THE BETAINES AND THEIR SALTS

Compound no.	λ(ε)[a]	λ(ε)	λ(ε)	λ(ε)	Solvent
I	250 (18.6)	280 (14.2)	335 (4.0)		CH_3OH
XXIV	222 (15.8)	263 (19.1)	322 (2.8)	377 (3.5)	CH_3CN
XXIVa	246 (14.8) 252 (14.8)	280 (18.4)	340 (3.5)		CH_3CN
XXV		268 (9.8)	336 (18.0)	415 (8.0)	CH_3CN
XXVa	243 (21.0)	279 (22.0)	355 (13.6) 357 (30.4)		CH_3CN
XXVI	228 (42.6)	265 (23.8)		400 (6.7)	CH_3CN
XXVIa	233 (45.0)	281 (19.5)	340 (8.0)		CH_3CN
XXXII	230 (17.0)	261 (22.4)	378 (5.0)		CH_3CN

[a] Extinction coefficients are reported as $\epsilon \times 10^{-3}$; λ reported in mμ.

3-Phenylrhodanine reacts with the quaternary salts XXIVa and XXVa in methanol to give the dyes XXVIIa and XXVIIIa, respectively, whereas XXVIa is converted directly to the pyrrocoline XXIX. The ring closure of the dyes XVIIa and XXVIIIa to the corresponding pyrrocolines XXVII and XXVIII was effected in dimethylformamide (DMF).



The pyrrocolines XXVII, XXVIII, and XXIX were also prepared from the quaternary salts XXIVa, XXVa, and XXVIa, and malonanilide as a confirmation of structure.

The method of Pratt[2] was extended to substituted pyridines. Thus, 2,3-dichloro-1,4-naphthoquinone reacts with diethyl malonate, methyl cyanoacetate, and 2,4-pentanedione in the presence of 3-picoline to give the pyrrocolines XXXa, XXXb, and XXXc, respectively; with methyl cyanoacetate in the presence of 4-picoline to give XXXd; with methyl cyanoacetate in the presence of 4-styrylpyridine and 4-(4-dimethylaminostyryl)pyridine to give the pyrrocolines XXXe, and XXXf, respectively. With ethyl cyanoacetate and 2,3-dichloro-1,4-naphthoquinone in the presence of 2-picoline or 2,6-lutidine the reaction takes a different course to give a compound whose empirical formula corresponds to XXXI and whose m.p. 204° and red color correspond to a compound of this structure obtained by the reaction 2,3-dichloro-1,4-naphthoquinone and ethyl cyanoacetate in the presence of sodium ethoxide.[4] The infrared spectrum and ultraviolet absorption spectrum of this substance are not in accord with this structure, but we have not established an alternate one. (See p. 3507, col. 2.)

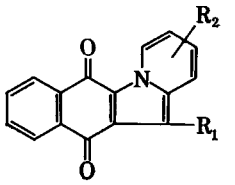
Methyl cyanoacetate reacts with the enol betaines XXVI and XXXII[5] in acetic anhydride to give the pyrrocolines XXXIII[2] and VI,[2] respectively, but this reaction does not appear to be a general one since other reactive methylene compounds failed to react.

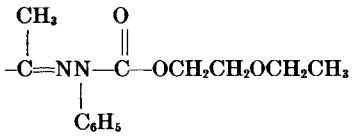
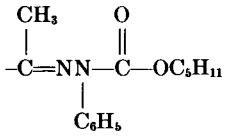
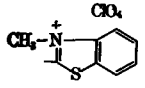
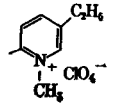
(4) C. Liebermann, *Ber.*, **32**, 918 (1899).

(5) J. A. VanAllan and G. A. Reynolds, Part VI, *J. Org. Chem.*, **28**, 1019 (1963).

TABLE III

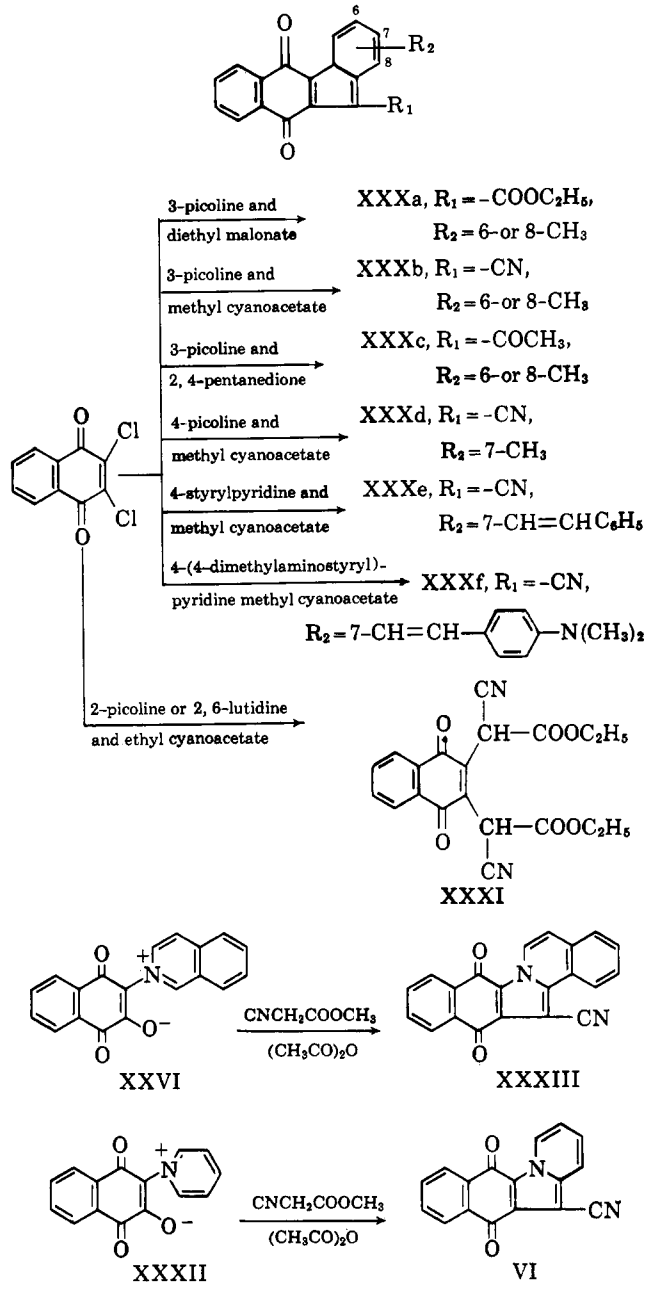
2,3-PHTHALOYLPYRROCOLINES



Compound no.	R_1	R_2	Empirical formula	M.p., °C.	Calcd. (found) C	H	N	Solvent of recrystn.	Method of preparation
II[a]	$-COOC_2H_5$	H	$C_{19}H_{13}NO_4$	156	71.3 (70.9)	4.1 (4.1)	4.4 (4.4)	2-Ethoxyethanol	A
IIa[a]	$-COOCH_3$	H	$C_{18}H_{11}NO_4$	190	70.8 (70.4)	3.6 (3.3)	4.6 (4.6)	Acetic acid	A
III[a]	$-COCH_3$	H	$C_{18}H_{11}NO_3$	206	74.7 (74.3)	3.8 (3.8)	4.8 (5.0)	2-Ethoxyethanol	A
IV	$4\text{-}NO_2C_6H_4-$	H	$C_{21}H_{12}N_2O_4$	332	70.7 (71.1)	3.4 (3.3)	7.9 (7.5)	2-Ethoxyethanol	A
V	$-NO_2$	H	$C_{16}H_8N_2O_4$	265	65.8 (65.9)	2.8 (3.2)	9.6 (9.2)	Acetic anhydride	A
VIa	$-CN$	H	$C_{17}H_8N_2O_2$	319	74.8 (74.5)	3.0 (2.8)	10.3 (10.4)	Dimethylformamide	A and D
VII[a]	$-C_6H_5$	H	$C_{22}H_{13}NO_2$	244	81.8 (82.1)	4.1 (4.3)	4.3 (4.3)	2-Ethoxyethanol	A
XV		H	$C_{29}H_{25}N_3O_5$	140	70.3 (70.3)	5.1 (5.1)	8.5 (8.4)	Ethanol	B
XVI		H	$C_{30}H_{29}N_3O_4$	158	72.8 (73.0)	5.9 (5.7)	8.5 (8.4)	Amyl alcohol	B
XVII	$-CONHC_6H_5$	H	$C_{23}H_{14}N_2O_3$	265	75.2 (74.8)	3.8 (4.1)	7.6 (7.7)	Dimethylformamide	A and B
XIX[a]	$-CONH_2$	H	$C_{17}H_{10}N_2O_3$	303	70.4 (70.0)	3.5 (3.4)	9.7 (9.7)	Nitrobenzene	B
XX		H	$C_{24}H_{15}ClN_2OS$	305	58.3 (58.2)	3.1 (2.9)	5.7 (5.6)	Acetonitrile	A and B
XXII[b]		H	$C_{24}H_{19}ClN_2O_6$	290	61.6 (61.2)	4.1 (3.9)	6.0 (5.7)	Acetonitrile	A

XXIIa	$-CONHCONHCOO(CH_2)_2OC_2H_5$	H	$C_{23}H_{19}N_3O_7$	>400	61.5 (61.7)	4.2 (3.9)	9.3 (9.5)		B
XXVII	$-CONHC_6H_5$	6- or 8-CH_3	$C_{24}H_{16}N_2O_3$	298	75.9 (75.6)	4.2 (4.2)	7.4 (7.4)	Dimethylformamide	A and B
XXVIII	$-CONHC_6H_5$	7-$-CH=CHC_6H_5$	$C_{31}H_{20}N_2O_3$	305	79.5 (79.8)	4.3 (4.3)	6.0 (5.8)	Dimethylformamide	A and B
XXIX	$-CONHC_6H_5$	7,8-Benzo	$C_{27}H_{16}N_2O_3$	372	77.9 (77.5)	3.9 (3.9)	6.7 (6.8)	Dimethylformamide	A
XXXa	$-COOC_2H_5$	6- or 8-CH_3	$C_{19}H_{15}NO_4$	178	71.1 (71.5)	4.7 (4.6)	4.4 (4.4)	Acetic anhydride	C
XXXb	$-CN$	6- or 8-CH_3	$C_{18}H_{10}N_2O_2$	278	75.6 (75.5)	3.5 (3.5)	9.8 (10.0)	Dimethylformamide	C
XXXc	$-COCH_3$	6- or 8-CH_3	$C_{19}H_{13}NO_3$	212	75.3 (75.2)	4.3 (4.6)	4.6 (4.6)	2-Ethoxyethanol	C
XXXd	$-CN$	7-CH_3	$C_{18}H_{10}N_2O_2$	323	75.6 (75.2)	3.5 (3.4)	9.8 (9.8)	Dimethylformamide	C
XXXe	$-CN$	7-$CH=CHC_6H_5$	$C_{25}H_{14}N_2O_2$	318	80.3 (79.9)	3.8 (3.8)	7.5 (7.4)	Dimethylformamide	C
XXXf	$-CN$	7-CH=CH-(4-$N(CH_3)_2$)	$C_{27}H_{19}N_3O_2$	*ca.* 290	77.8 (77.9)	4.6 (4.4)	10.1 (9.9)	Dimethylformamide	C
XXXIII[a]	$-CN$	7,8-Benzo	$C_{21}H_{10}N_2O_2$	350	78.3 (77.9)	3.1 (3.5)	8.7 (8.4)	1,2,3-Trichloropropane	D

[a] Lit. m.p., °C., *cf.* ref. 3: II, 157–158; IIa, 190–191; III, 205–206; VI, 307.5–308.5; VII, 244.5–245.5; XIX, 302–303; and XXXIII, 350–350.5. [b] Isolated the perchlorate by adding water and 70% perchloric acid to the reaction mixture.



In summary, pyridinium salts of type I react with active methylene compounds to give derivatives of 2,3-phthaloylpyrrocoline. The intermediate cyanine-type dyes may be isolated in favorable cases. Substituents in the pyridine moiety have little, if any, influence on the ease of cyclization.

Experimental

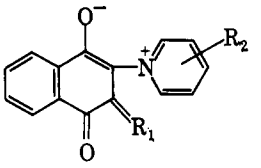
The following general methods illustrate the procedures used for the preparation of 2,3-phthaloylpyrrocolines. The analytical data are collected in Table III.

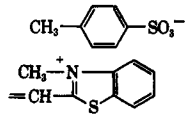
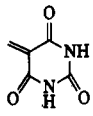
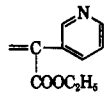
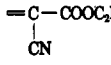
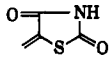
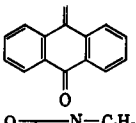
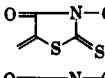
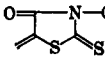
Method A.—A mixture of 0.01 mole of N-(1,4-dioxo-2-methoxynaphthyl-3)pyridinium methosulfate (I), 0.01 mole of the active methylene compound, 2 g. of sodium acetate, and 30 ml. of methanol was refluxed on the steam bath for 1.5 hr. The reaction mixture was cooled and the product was filtered. Crystallization of the product from a suitable solvent gave the 2,3-phthaloylpyrrocoline. This method also was used with compounds XXIVa, XXVa, and XXVIa in place of compound I.

Method B.—A mixture of 1.5 g. of ylidene pyridinium naphoxide and 25 ml. of dimethylformamide or 2-ethoxyethanol was heated until the original blue color changed to brown (0.5–24 hr.). The reaction mixture was allowed to cool to room temperature

TABLE IV

YLIDENE PYRIDINIUM NAPHTHOXIDES



Compound no.	R_1	R_2	Empirical formula	M.p., °C.	Calcd. (found) C	H	N	Solvent of recrystn.
VIII		H	$C_{18}H_9N_3O_2$	305	72.2 (71.8)	3.0 (3.3)	14.0 (13.9)	Acetic anhydride
IX[a]		H	$C_{25}H_{17}N_3O_2$	220	73.7 (73.6)	4.2 (4.1)	10.3 (10.3)	
X		H	$C_{24}H_{14}N_2O_3S_2$	240	65.0 (65.3)	3.2 (3.1)	6.3 (6.5)	Dimethylformamide–ethanol
XI[a]		H	$C_{31}H_{24}N_2O_6S_2$	243	65.7 (65.3)	4.2 (3.8)	4.9 (4.6)	
XII		H	$C_{19}H_{11}N_3O_5$	345	63.2 (62.9)	3.1 (3.4)	11.6 (11.2)	2-Ethoxyethanol
XIII		H	$C_{24}H_{18}N_2O_4$	250	72.3 (72.2)	4.6 (4.2)	7.0 (7.4)	Acetonitrile
XIV[a]		H	$C_{19}H_{12}N_2O_4$	249	68.9 (69.0)	3.6 (3.5)	8.4 (8.6)	
XVIII[a,b]		H	$C_{18}H_{10}N_2O_4S$		61.8 (61.5)	2.9 (2.5)	8.0 (7.9)	
XXIII		H	$C_{29}H_{17}NO_3$	*ca.* 330	81.5 (81.6)	4.0 (4.4)	3.3 (3.0)	
XXVIIa[a,b]		3-CH_3	$C_{25}H_{16}N_2O_3S_2$		65.8 (65.5)	3.5 (3.4)	6.1 (5.8)	
XXVIIIa[a,b]		4-CH=CHC$_6$H$_5$	$C_{31}H_{20}N_2O_3S_2$		70.0 (69.9)	3.8 (3.8)	5.3 (4.9)	

[a] These dyes could not be recrystallized because of rearrangement to the pyrrocolines in hot solvents in which they were soluble. [b] Rearranged to the pyrrocoline at approximately 200°.

and the product was filtered. Crystallization of the product from a suitable solvent gave the 2,3-phthloylpyrrocoline. When a solution of 2-(3-methyl-5-oxo-1-phenyl-2-pyrazolin-4-ylidene)-1-oxo-3-pyridinium-4-naphthoxide (IX) in 2-ethoxyethanol or *n*-amyl alcohol was heated, the solvents participated in the reaction and the products were XV and XVI, respectively. The solvent also takes part in the reaction of XII in 2-ethoxyethanol solution to yield XXIIa.

Method C.—To a warm suspension of 4.5 g. (0.02 mole) of 2,3-dichloro-1,4-naphthoquinone in 20 ml. of 1,2,3-trichloropropane containing 0.04 mole of a substituted pyridine was added 0.02 mole of an active methylene compound. Heating on the steam bath was continued for 1 hr. The reaction mixture was allowed to cool to room temperature and the product was filtered. Crystallization of the product from a suitable solvent gave the 2,3-phthaloylpyrrocoline.

Method D. For 1-Cyano-2,3-phthaloyl-7,8-benzopyrrocoline (XXXIII).—A mixture of 6.0 g. (0.02 mole) of 1,4-dioxo-2-isoquinolinium-3-naphthoxide (XXVI), 2.0 g. (0.02 mole) of methyl cyanoacetate, and 6.0 ml. of acetic anhydride was refluxed for 1 hr. The reaction mixture was allowed to cool to room temperature and the product was filtered. Crystallization from 1,2,3-trichloropropane gave the desired product, m.p. 350°.

1-Cyano-2,3-phthaloylpyrrocoline (VI) was prepared in a similar manner.

The following general method illustrates the procedure used for the preparation of ylidene pyridinium naphthoxides. The analytical data are collected in Table IV. A mixture of 0.01 mole of I, XXIVa, or XXVa, 0.01 mole of the active methylene compound, and 30 ml. of methanol was warmed on the steam bath until reflux temperature was reached. To the mixture was added 2 g. of sodium acetate and refluxing was continued for 15 min. The mixture was allowed to cool to room temperature and the product was filtered, washed well with water and dried. The product in some cases could not be crystallized because of rearrangement to the pyrrocolines in hot solvents in which they were soluble (*cf.* Table IV).

2-Carbomethoxycyanomethylene)-1-oxo-3-pyridinium-4-naphthoxide (XIV) was prepared at room temperature rather than in refluxing methanol because of the instability of the product in hot methanol.

N-(1,4-Dioxo-3-methoxynaphthyl-2)-3-methylpyridinium Perchlorate (XXIVa).—A suspension of 5.0 g. of 1,4-dioxo-2-(3-methylpyridinium)-3-naphthoxide (XXIV) in 25 ml. of dimethyl sulfate was heated on the steam bath until all of the naphthoxide had gone into solution (1 hr.). The solution was cooled to room temperature and poured into ether from which an oil separated. The solvent was decanted and the oil was dissolved in a minimum amount of warm methanol. One milliliter of 70% perchloric acid was added and the solution was chilled. The product was

filtered and crystallized from acetonitrile–methanol (m.p. 238°).

Anal. Calcd. for $C_{17}H_{14}ClNO_7$: C, 53.8; H, 3.7; N, 3.7. Found: C, 53.5; H, 3.7; N, 3.4.

N-(1,4-Dioxo-3-methoxynaphthyl-2)4-styrylpyridinium perchlorate (XXVa) also was prepared in this manner, m.p. 287° (from acetonitrile).

Anal. Calcd. for $C_{24}H_{18}ClNO_7$: C, 61.7; H, 3.9; N, 3.0. Found: C, 61.4; H, 4.0; N, 3.0.

N-(1,4-Dioxo-3-methoxynaphthyl-2)isoquinolinium perchlorate (XXVIa) was prepared similarly, m.p. 210° (from acetonitrile–methanol).

Anal. Calcd. for $C_{20}H_{14}ClNO_7$: C, 57.9; H, 3.5; N, 3.5. Found: C, 58.1; H, 3.2; N, 3.4.

1-Acetyl-2,3-phthaloylpyrrocoline (III) was prepared from the hydrolysis of XV or XVI. A suspension of 2 g. of XV or XVI in 20 ml. of hydrochloric acid (*d* 1.18) was warmed to 95–100°. Complete solution occurred in about 5 min. The initially deep red colored solution changed to light red and the product separated. After 2 hr., 20 ml. of water was added. The product was filtered and crystallized from alcohol to give 1.1 g. of III (m.p. 206°) which was identified by comparison of its infrared spectrum with that of an authentic sample.

2,3-Bis(α-carbethoxy-α-cyanomethyl)-1,4-naphthoquinone (XXXI).—A mixture of 4.5 g. of 2,3-dichloronaphthoquinone, 5 ml. of ethyl cyanoacetate, and 4.5 ml. of 2,6-lutidine in 25 ml. of 1,2,3-trichloropropane was heated to 95–100° for 3 hr. A small amount of insoluble material was filtered off, the solvent was evaporated under reduced pressure, and the residue was crystallized from alcohol to give 3.5 g. of XXXI, m.p. 206°.[4]

Photosensitized Oxidation of Carvomenthene[1]

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Carvomenthene (1-*p*-menthene) sensitized with chlorophyll absorbed oxygen rapidly when exposed to intense light. Yields of hydroperoxide based on oxygen absorption were good. The hydroperoxides were reduced to alcohols with sodium sulfite for separation by gas–liquid chromatography. The individual g.l.c. peaks were identified on the basis of physical properties, infrared spectra, and hydrogenation to the saturated alcohols. The products in order of emergence were: carvomenthene epoxide (3%), *trans*-2-*p*-menthen-1-ol (29%), *cis*-2-*p*-menthen-1-ol (9%), *cis*-piperitol (2%), 1(7)-*p*-menthen-*trans*-2-ol (17%), *trans*-carvotanacetol (15%), 1(7)-*p*-menthen-*cis*-2-ol (25%). The *cis*-piperitol is attributed to isomerization of the 2-*p*-menthen-1-ols and the epoxide formation to reaction of a peroxide radical with carvomenthene. The relative yields of the other products are in accord with a nonconcerted reaction mechanism involving random attachment of the oxygen at one end of the double bond, migration of an allylic hydrogen to the oxygen from an "axial" position *cis* to the initial point of attack, and concurrent shifting of the double bond. Hydrogen transfer and bond migration probably occur through a cyclic intermediate.

Photosensitized oxidation is a very useful synthetic tool which would be even more useful if its mechanism were sufficiently well defined to permit prediction of the products obtained from a given olefin. Schenck, *et al.*,[3] proposed the general mechanism in which the activated sensitizer forms a complex with oxygen which then "adds to one C-atom of the double bond, whereupon an H-atom migrates from the allylic position to the oxygen and the double bond is shifted." More recently it has been shown that in condensed ring systems the migrating hydrogen comes from a quasi-axial position *cis* to the newly formed C–O bond.[4,5] Both groups picture a cyclic intermediate in which the initial double bond is essentially intact and the oxygen is partially bonded to a double bond carbon and to an allylic hydrogen; but the available evidence was not considered adequate to support uniquely a concerted mechanism.[5] A somewhat different mechanism has been proposed by Sharp[6] who suggested the initial formation of a perepoxide ion by electrophylic attack of an activated oxygen molecule on the double bond. Product ratios in the case of unsymmetrical olefins with several allylic hydrogens should be of help in deciding among these mechanisms because the different mechanisms would lead to different product ratios.

The available data is meager and somewhat conflicting. Photosensitized oxidation of α-pinene has been reported to yield only *trans*-pinocarvyl hydroperoxide.[3] This implies a selective, stereospecific attack on the monosubstituted end of the trisubstituted double bond. On the other hand, the isolated trisubstituted double bond in myrcene is attacked predominantly but not exclusively at the disubstituted end.[7] Without giving any experimental details, Schenck further reported that 1-methylcyclohexene yielded a mixture of secondary and tertiary hydroperoxides but that carvomenthene (1-*p*-menthene) (I) and limonene yielded only tertiary hydroperoxides.[8]

Carvomenthene (I) was selected as the substrate for the present investigation because it is easily prepared by hydrogenation of commercial citrus limonene or of dipentene obtained by isomerization of the pinenes; its structure is well suited to the purpose; and the exclusive formation of the tertiary isomers as suggested by Schenck, if correct, would offer a very attractive route to synthetic menthol.[9] Carvomenthene has been shown to exist chiefly in the half-chair form with the isopropyl group in the equatorial position.[10] This conformer has quasi-axial hydrogens on C-3 *cis* to the isopropyl group and on C-6 *trans* to the isopropyl group. In addition the methyl group is free to rotate giving the equivalent of an axial hydrogen both *cis* and

(1) Presented in part at the 138th National Meeting of the American Chemical Society, New York, N. Y., September, 1960, Abstract, p. 79P.

(2) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(3) G. O. Schenck, H. Eggert, and W. Denk, *Ann.*, **784**, 177 (1953).

(4) W. H. Schuller and R. V. Lawrence, Southeastern Regional Meeting of the American Chemical Society, Richmond, Va., November 6, 1959; *Chem. Ind.* (London), 105 (1961).

(5) A. Nickon and J. F. Bagli, *J. Am. Chem. Soc.*, **81**, 1630 (1959); **83**, 1498 (1961).

(6) D. B. Sharp, Abstracts, 138th National Meeting of the American Chemical Society, New York, N. Y., September, 1960, p. 79P.

(7) R. L. Kenney and G. S. Fisher, *J. Am. Chem. Soc.*, **81**, 4288 (1959).

(8) G. O. Schenck, *Angew. Chem.*, **64**, 12 (1952).

(9) J. P. Bain, A. B. Booth, and W. Y. Gary (to The Glidden Co.). U. S. Patent 2,894,040 (1959).

(10) J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5493 (1959).