Synthesis of 1,2-Disubstituted Naphth[1,2-*d*]imidazole-4,5-diones (1a,b)

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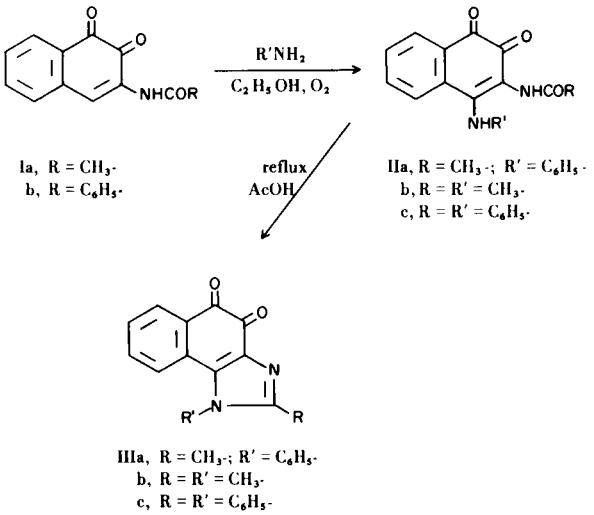
A convenient synthesis of 3-acylamino-1,2-naphthoquinones (I) is presented. The addition of aromatic and aliphatic amines to I followed by exposure to oxygen gives the corresponding 4-arylamino- or 4-alkylamino-3-acylamino-1,2-naphthoquinones (II). The addition of 4-cyclohexylbutylamine to 3-trichloroacetamino-1,2-naphthoquinone took an anomalous course and 1-(4′-cyclohexylbutyl)-3(*H*)-naphth[1,2-*d*]imidazoline-2,4,5-trione (VII) was obtained.

Treatment of II with refluxing acetic acid gave 1,2-disubstituted naphth[1,2-*d*]imidazole-4,5-diones (III). The reaction was successful with a variety of 4-substituted amino-3-acylamino-1,2-naphthoquinones (II) and usually occurred in excellent yield. However, the cyclization of II to III is subject to steric limitation and attempts to cyclize 4-*tert*-butylamino-3-acetamino-1,2-naphthoquinone to the corresponding imidazole derivative was unsuccessful. The infrared, ultraviolet and nuclear magnetic resonance spectra of I, II, and III are discussed in relation to their structures.

The interesting chemical and spectral properties of heterocyclic quinones in combination with the discoveries that certain of these compounds show attractive properties as medicinal agents, catalysts and dyes have led to a renewed interest in their synthesis (2). However, prior to the initiation of our study, only three 1,2-disubstituted naphth[1,2-*d*]imidazole-4,5-diones had been reported, and their spectral properties had not been studied. In 1898 Kehrmann and Zimmerli (3) reported that the addition of aniline or methylamine to 3-acetamino-1,2-naphthoquinone (Ia) followed by air oxidation gave the corresponding 4-phenylamino-3-acetamino-1,4-naphthoquinone (IIa) and 4-methylamino-3-acetamino-1,4-naphthoquinone (IIb). Treatment of IIa and IIb with refluxing acetic acid gave 1-phenyl-2-methylnaphth[1,2-*d*]imidazole-4,5-dione (IIIa) and 1,2-dimethylnaphth[1,2-*d*]imidazole-4,5-dione (IIIb), respectively. Forty years later Goldstein and Genton (4) reported the preparation of 1,2-diphenylnaphth[1,2-*d*]imidazole-4,5-dione (IIIc) by a similar procedure starting with 3-benzoylamino-1,2-naphthoquinone (Ib) (see Chart I). Since the latter report in 1938, no additional 1,2-disubstituted naphth[1,2-*d*]imidazole-4,5-diones have been reported. In this report, a variety of aromatic and aliphatic amines have been added to Ia as well as other 3-acylamino-1,2-naphthoquinones (I). The cyclization of the resulting 4-alkyl- or 4-arylamino-3-acylamino-1,2-naphthoquinones (II) to the corresponding 1,2-disubstituted naphth[1,2-*d*]imidazole-4,5-diones (III) has been studied in an effort to define the scope and limitations of this reaction.

CHART I



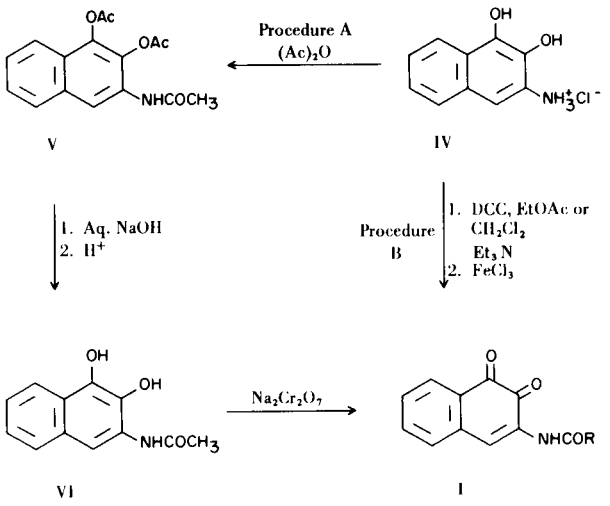
Ia, R = CH_3-
b, R = C_6H_5-

IIa, R = CH_3-; R′ = C_6H_5-
b, R = R′ = CH_3-
c, R = R′ = C_6H_5-

IIIa, R = CH_3-; R′ = C_6H_5-
b, R = R′ = CH_3-
c, R = R′ = C_6H_5-

The starting 3-acetamino-1,2-naphthoquinone (Ia) was initially prepared by the procedure reported by Kehrmann and Zimmerli (3) and outlined in Chart II (Procedure A). Attempts to extend this procedure to the preparation of other 3-acylamino-1,2-naphthoquinones (I) by using other acid anhydrides or acid chlorides was either unsuccessful or gave the desired 3-acylamino-1,2-naphthoquinone in low yield. A more satisfactory general route to 3-acylamino-1,2-naphthoquinones (I) involves treatment of 3-amino-1,2-naphthohydroquinone hydrochloride (IV) with the appropriate carboxylic acid in the presence of dicyclohexylcarbodiimide and triethylamine followed by oxidation (ferric chloride) of the crude intermediate 3-acyl-

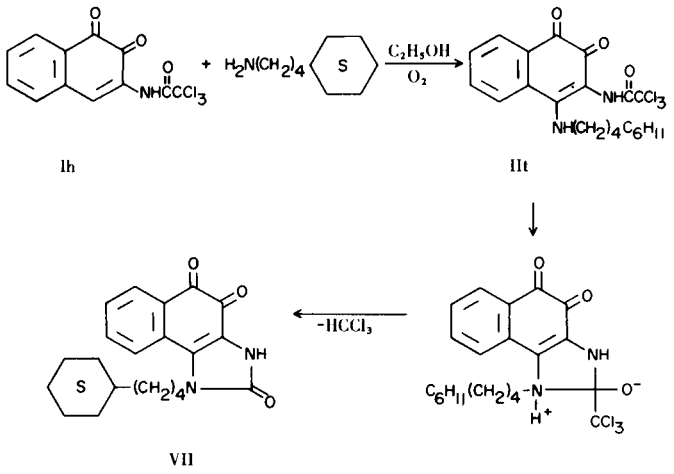
CHART II



amino-1,2-naphthohydroquinone (Chart II, Procedure B). This method gives specific mono-acylation on the nitrogen function of IV and thus eliminates the necessity of a hydrolysis step. The reaction can be carried out in one reaction vessel without isolation of the intermediate naphthohydroquinone. The results obtained with a number of acids are given in Table I.

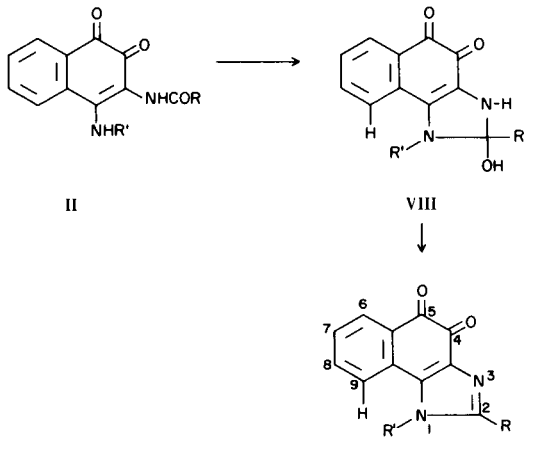
The addition of ammonia as well as a variety of aromatic or aliphatic amines to 3-acetamino-1,2-naphthoquinone proceeded quite cleanly to give after exposure to oxygen the corresponding 4-arylamino- or 4-alkylamino-3-acetamino-1,2-naphthoquinone. Similarly, the addition of 4-cyclohexylbutylamine to Ic-f, and the addition of methyl-, pentyl- and benzylamine to Ig, proceeded quite smoothly. The high yields of 4-alkylamino-3-chloroacetamino-1,2-naphthoquinone obtained from Ig, along with the absence of any products resulting from displacement of chloride from the α-chloroamide function, shows the extreme reactivity of the Δ^4-double bond of these 3-acylamino-1,2-naphthoquinones. The results of these addition reactions are summarized in Table II.

The addition of 4-cyclohexylbutylamine to trichloroacetamino-1,2-naphthoquinone (Ih) took an anomalous course and gave 1-(4′-cyclohexylbutyl)-3(*H*)-naphth[1,2-*d*]-imidazoline-2,4,5-trione (VII). The reaction presumably proceeds through the expected adduct IIt since TLC's at the beginning of the reaction show spots attributable to this adduct (5). The initial intermediate IIt then may react intramolecularly to give a cyclic intermediate which subsequently yeilds VII on loss of chloroform. The structural assignment of VII was based on the elemental analysis and the infrared spectrum which showed absorption at 3120 (NH), 1712 (imidazoline carbonyl; the carbonyl absorption in benzimidazolines is reported at 1720 cm^{-1}) (6) and 1645 cm^{-1} (quinone carbonyl).



The cyclization of the 4-arylamino- and 4-alkylamino-3-acylamino-1,4-naphthoquinones (II) to the corresponding naphth[1,2-*d*]imidazole-4,5-diones (III) was carried out in refluxing acetic acid. The results obtained from the cyclization of 4-arylamino- and 4-alkylamino-3-acetamino-1,4-naphthoquines to the corresponding 4-alkyl-3-methylnaphth[1,2-*d*]imidazole-4,5-dione shows the effect of the 4-alkylamino group of II on the cyclization reaction.

When R′ = H the cyclization did not take place, and there was quite a difference in the ease with which the individual compounds enter into the cyclization reaction. The results summarized in Table IIIA indicate that the cyclization is subject to steric influences. When R′ was an aryl group containing electron donating or electron withdrawing group (s) or when R′ was *n*-hexyl or benzyl the cyclization proceeded rapidly and nearly quantitatively. When R′ = isopropyl and R′ = cyclopentyl, 64% and 44% of the corresponding imidazole III was obtained in ½ and 1 hour, respectively. If R′ was *t*-butyl, none of the cyclization product could be isolated.



The increased reaction times and lower yields obtained as the 4-alkylamino group increased in size is probably due to serious steric interaction between the 1-substituent with the 9-hydrogen and the 2-methyl substituent of the more rigid intermediate VIII or the 1,2-disubstituted naphth[1,2-*d*]imidazole-4,5-dione (III) that is being formed. The close proximity of the large R′ group with the 9-hydrogen and the 2-methyl function is apparent from a comparison of the nmr spectra of some of these naphth-[1,2-*d*]imidazole-4,5-diones (Figure 1). For example, the

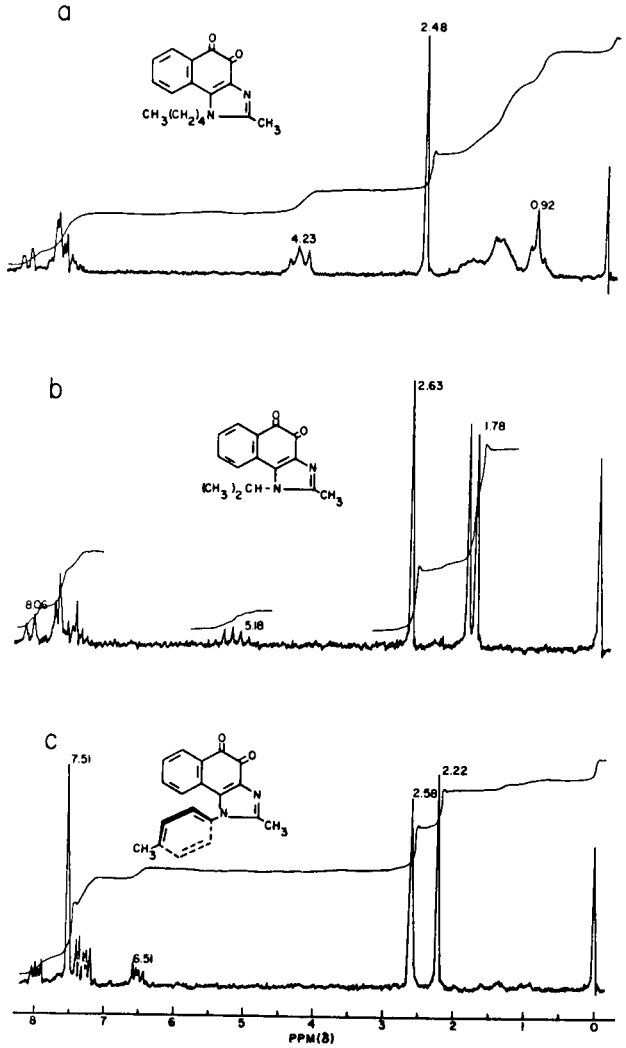


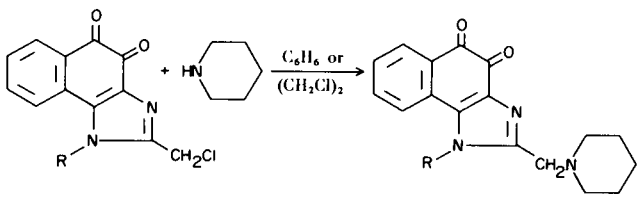
Figure 1: NMR spectrum of (a) 1-pentyl-2-methylnaphth-[1,2-*d*]imidazole-4,5-dione, (b) 1-isopropyl-2-methylnaph-th[1,2-*d*]imidazole-4,5-dione, and (c) 1-(*p*-tolyl)-2-methyl-naphth[1,2-*d*]imidazole-4,5-dione.

resonance of the 2-methyl group of 1-isopropyl-2-methyl-naphth[1,2-*d*]imidazole-4,5-dione (IIIk) appears at δ 2.63 whereas the same group shows a resonance at 2.48 ppm in 1-pentyl-2-methylnaphth[1,2-*d*]imidazole-4,5-dione (IIIh). This shift is undoubtedly due to increased shielding of the 2-methyl group in IIIk by the methyl groups of the 1-isopropyl function. The unusually low field position of the N–CH_2 group of IIIh and the methine group of IIIk is due at least in part to increased deshielding by the sterically close aromatic ring of the naphthoquinone moiety. Inspection of Corey-Pauling molecular models of these compounds also shows extreme steric crowding. It is particularly interesting that it is impossible to make a model of 1-(*t*-butyl)-2-methylnaphth[1,2-*d*]imidazole-4,5-dione (IIIℓ) using these models.

An examination of the nmr spectrum of 1-(*p*-tolyl)-2-methylnaphth[1,2-*d*]imidazole-4,5-dione (IIId) indicates that the correct structure has the *p*-tolyl group perpendicular to the imidazole ring (see Figure 1c). This assignment is based on the fact that the resonance of the 9-hydrogen and the 2-methyl group are shifted up field to δ 6.51 and 2.58 ppm, respectively, by the anisotropy of the aryl group. A Corey-Pauling molecular model of this compound shows the *p*-tolyl group is perpendicualr to the heterocyclic ring and is unable to rotate freely around the N–C bond due to steric interactions between the 9-hydrogen and the 2-methyl groups.

The effect of the 3-acylamino group of II on the cyclization of II to III is revealed in the results summarized in Table IIIB on treating IIm-s with refluxing acetic acid. Except for the formation of 1-(4′-cyclohexylbutyl)-2-*t*-butylnaphth[1,2-*d*]imidazole-4,5-dione (IIIp) the cyclization proceeded in good yield. These results indicate that the cyclization of II to III is subject to steric limitations in the 3-acylamino moiety as well as the 4-alkylamino group. The fact that IIp could be converted to the corresponding imidazole IIIp, albeit in low yield, whereas IIℓ resisted cyclization, would indicate that the size of the 4-alkylamino group is of more importance than that of the 3-acylamino group. This results from the 4-alkylamino moiety being subject to steric interactions with the 9-hydrogen of VIII or III in addition to the steric interaction between the two groups with each other.

Treatment of 1-pentyl-2-chloromethylnaphth[1,2-*d*]-imidazole-4,5-dione (IIIr) with excess piperidine in refluxine benzene effected a very smooth displacement and 82%

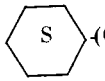


IIIr, R = $CH_3(CH_2)_4$-
q, R = CH_3-
s, R = $C_6H_5CH_2$-

IIIt, R = $CH_3(CH_2)_4$-
u, R = CH_3-
v, R = $C_6H_5CH_2$-

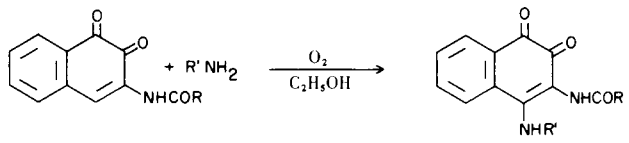
TABLE I

3-Acylamino-1,2-naphthoquinones

Compound (a) No.	R	Reaction Solvent	Recryst. Solvent	M.p. °C	% Yield (b)	Molecular Formula	Calcd., % C	H	N	Found, % C	H	N
Ia	CH_3-	CH_2Cl_2	EtOH	208-213 (c) (dec)	57	---	---	----	----	---	----	----
c		EtOAc	EtOH	161-163	25	$C_{20}H_{23}NO_3$	73.82	7.12	4.30	73.85	7.12	4.35
d	3,4,5-tri (CH_3O)$C_6H_2CH_2$-	EtOAc	EtOH	177-180 (dec)	60	$C_{21}H_{19}NO_6$	66.13	5.02	3.67	66.10	5.01	3.79
e	$(CH_3)_3C$-	EtOAc	EtOH	161-163	20	$C_{15}H_{15}NO_3$	70;02	5.88	5.44	70;07	5.78	5.62
f	C_6H_5CH=CH-	EtOAc	EtOH	203-208 (dec)	28	$C_{19}H_{13}NO_3$	75.24	4.32	4.67	75.67	3.93	4.83
g	$ClCH_2$-	CH_2Cl_2	DMF-MeOH	221-226 (dec)	70	$C_{12}H_8ClNO_3$	57.73	3.23	5.61	57.58	3.30	5.67
h	Cl_3C-	EtOAc	EtOH	195-197	46	$C_{12}H_6Cl_3NO_3$ (d)	45.24	1.90	4.40	45.34	1.79	4.41

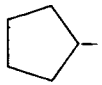
(a) A typical procedure is given in the Experimental Section. (b) Based on pure compound isolated from 3-amino-1,2-naphthohydroquinone hydrochloride. (c) Lit. (ref. 3) m.p. 214-216°. (d) Calcd. Cl, 33.39; Found Cl, 33.55.

TABLE II



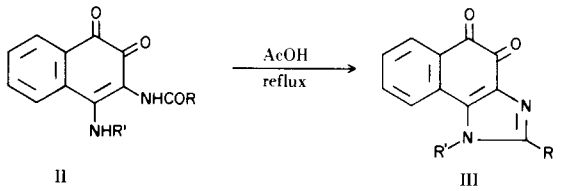
I II

4-Arylamino and 4-Alkylamino-3-acylamino-1,2-naphthoquinones (II)

Compound (a) No.	R'	R	Recryst. Solvent	M.p. °C	% Yield (b)	Molecular Formula	Calcd., % C	H	N	Found, % C	H	N
a	C_6H_5-	CH_3-	EtOH	313-314 (c,d)	76	$C_{18}H_{12}N_2O_3$	---	---	---	---	---	---
d	*p*-CH_3-C_6H_4-	CH_3-	EtOH	300-302 (d)	83	$C_{19}H_{16}N_2O_3$	71.23	5.04	8.75	71.23	5.15	8.74
e	*p*-Cl-C_6H_4-	CH_3-	EtOH	(d)	76	$C_{18}H_{13}ClN_2O_3$	63.44	3.84	8.22	63.53	3.77	8.40
f	3,4,5-tri(CH_3O)C_6H_2-	CH_3-	MeOH	(d)	81	$C_{21}H_{20}N_2O_6$	63.63	5.09	7.07	63.94	5.06	7.21
g	H-	CH_3-	EtOH	217-222 (e) (dec)	61	$C_{12}H_{10}N_2O_3$	---	---	---	---	---	---
h	$C_6H_5CH_2$-	CH_3-	DMF-MeOH	267-270	71	$C_{19}H_{16}N_2O_3$	71.23	5.04	8.75	71.52	4.97	8.64
i	$CH_3(CH_2)_4$-	CH_3-	DMF	190-192	97	$C_{17}H_{20}N_2O_3$	67.98	6.71	9.33	67.61	6.80	9.52
j		CH_3-	CH_2Cl_2-MeOH	227-230	91	$C_{17}H_{18}N_2O_3$	68.44	6.08	9.39	68.58	6.07	9.69
k	$(CH_3)_2CH$	CH_3-	EtOH	223-225	59	$C_{15}H_{16}N_2O_3$	66.15	5.92	10.29	66.23	5.94	10.32
l	$(CH_3)_3C$	CH_3-	(f)	(f)	21	$C_{16}H_{18}N_2O_3$	67.11	6.34	9.79	66.92	6.31	9.30
m	$C_6H_{11}(CH_2)_4$-	3,4,5-tri(CH_3O)$C_6H_2CH_2$-	C_6H_6	154-158 (dec)	51	$C_{31}H_{38}N_2O_6$	69.64	7.16	5.24	69.78	7.19	5.16
n	$C_6H_{11}(CH_2)_4$-	$C_6H_{11}(CH_2)_3$-	C_6H_6	170-173	88	$C_{30}H_{42}N_2O_3$	75.27	8.85	5.85	74.86	8.91	5.92
o	$C_6H_{11}(CH_2)_4$-	C_6H_5CH=CH-	EtOH	188-190	53	$C_{29}H_{32}N_2O_3$	76.28	7.07	6.14	76.01	6.98	6.35
p	$C_6H_{11}(CH_2)_4$	$(CH_3)_3C$-	EtOAc	177-180	55	$C_{25}H_{34}N_2O_3$	73.14	8.35	6.83	73.00	8.30	6.78
q	CH_3-	$ClCH_2$-	DMF-MeOH	220-223 (dec)	86	$C_{13}H_{11}ClN_2O_3$ (g)	56.03	3.98	10.05	55.78	4.10	10.05
r	$CH_3(CH_2)_4$-	$ClCH_2$-	EtOH	164-166	81	$C_{17}H_{19}ClN_2O_3$ (h)	60.98	5.72	8.36	60.96	5.63	8.44
s	$C_6H_5CH_2$-	$ClCH_2$-	DMF-MeOH	177-179	91	$C_{19}H_{15}ClN_2O_3$ (i)	64.32	4.26	7.90	64.51	4.19	8.00

(a) A typical procedure is given in the Experimental Section. (b) Based on pure compound isolated. (c) Lit. (ref. 3) m.p. 308°. (d) These compounds change to the corresponding imidazole before melting. (e) Lit. (ref. 3) m.p. 222°. (f) Non-crystalline compound that was purified by chromatography on aluminm oxide using chloroform as the eluent. (g) Calcd. Cl, 12.72. Found, 12.71. (h) Calcd. Cl, 10.60. Found, 10.61. (i) Calcd. Cl, 9.99. Found, 10.01.

TABLE III



II III

A. 1-Aryl or 1-Alkyl-2-methylnaphth[1,2-*d*]imidazole-4,5-dione (III)

Compound No. (a)	R'	R	Reaction Time	Recryst. Solvent	M.p. °C	% Yield (b)	Molecular Formula	Calcd., % C	H	N	Found, % C	H	N
a	C_6H_5-	CH_3-	2 min	AcOH	314-315 (c)	99	$C_{18}H_{12}N_2O_2$	74.98	4.20	9.72	74.55	4.29	9.66
d	*p*-$CH_3C_6H_4$-	CH_3-	2 min	CH_2Cl_2MeOH	301-303	99	$C_{19}H_{14}N_2O_2$	75.47	4.66	9.27	75.41	4.73	9.44
e	*p*-ClC_6H_4-	CH_3-	2 min	EtOH	315-317	100	$C_{18}H_{11}ClN_2O_2$	66.98	3.43	8.68	66.96	3.59	8.79
f	3,4,5-tri(CH_3O)-C_6H_2-	CH_3-	2 min	CH_2Cl_2-MeOH	290-293	96	$C_{21}H_{18}N_2O_5$	66.66	4.80	7.41	66.81	4.80	7.44
g	H	CH_3-	1 hr	---	---	0	---	---	---	---	---	---	---
h	$C_6H_5CH_2$-	CH_3-	10 min	EtOH	248-249	90	$C_{19}H_{14}N_2O_2$	75.48	4.67	9.27	75.57	4.55	9.31
i	$CH_3(CH_2)_4$-	CH_3-	10 min	C_6H_6	158-159	99	$C_{17}H_{18}N_2O_2$	72.32	6.43	9.92	72.18	6.40	9.98
j		CH_3-	1 hr	EtOH	242-245	44	$C_{17}H_{16}N_2O_2$	72.83	5.75	10.00	73.03	5.75	9.94
k	$(CH_3)_2CH$-	CH_3-	30 min	EtOH	250-253	64	$C_{15}H_{14}N_2O_2$	70.85	5.55	11.02	70.95	5.56	11.14
l	$(CH_3)_3C$-	CH_3-	1 hr	---	---	0	---	---	---	---	---	---	---
m	$C_6H_{11}(CH_2)_4$-	3,4,5-tri-(CH_3O)-$C_6H_2CH_2$-	20 min	EtOH	212-216	74	$C_{31}H_{36}N_2O_5$	72.07	7.02	5.42	71.78	6.97	5.38
n	$C_6H_{11}(CH_2)_4$-	$C_6H_{11}(CH_2)_3$-	15 min	EtOH	150-152	95	$C_{30}H_{40}N_2O_2$	78.22	8.75	6.08	77.79	8.72	6.09
o	$C_6H_{11}(CH_2)_4$-	C_6H_5CH=CH-	25 min	EtOH	252-253	57	$C_{29}H_{30}N_2O_2$	79.42	6.90	6.39	79.11	6.83	6.32
p	$C_6H_{11}(CH_2)_4$-	$(CH_3)_3C$-	1 hr	EtOAc	233-234	37	$C_{25}H_{32}N_2O_2$	76.49	8.22	7.14	76.55	8.29	7.22
q	CH_3-	$ClCH_2$-	30 min	CH_2Cl_2-MeOH	217-219	86	$C_{13}H_9ClN_2O_2$ (e)	59.90	3.48	10.75	60.01	3.59	10.79
r	$CH_3(CH_2)_4$-	$ClCH_2$-	20 min	EtOH	180-184 (dec)	88	$C_{17}H_{17}ClN_2O_2$ (d)	64.45	5.41	8.85	64.70	5.48	8.85
s	$C_6H_5CH_2$-	$ClCH_2$-	30 min	AcOH	222-224	85	$C_{19}H_{13}ClN_2O_2$ (f)	67.76	3.89	8.32	67.65	3.85	8.41

(a) A typical procedure is given in the Experimental Section. (b) Based on pure compound isolated. (c) Lit. (ref. 3) m.p. 305-306°. (d) Calcd. Cl, 11.19. Found Cl, 11.29. (e) Analytical sample dried at 100°. (f) Calcd. Cl, 10.53. Found Cl, 10.75.

TABLE IV

Ultraviolet Absorption Spectra of
1,2-Disubstituted Naphth[1,2-*d*]imidazole-4,5-diones (a)

Compound No.	CH_3OH (b)		0.1*N* HCl		*p*H 7		0.1*N* NaOH	
	λ max, mμ	ε x 10^{-3}	λ max, mμ	ε x 10^{-3}	λ max, mμ	ε x 10^{-3}	λ max, mμ	ε x 10^{-3}
IIIa	251	sh						
	261	27.2 (c)	254	28.0	261	23.6	241	sh
	268	26.9	258	sh	267	22.9	258	sh
	444	1.6					267	sh
IIId	252	sh						
	262	27.7	254	28.2	262	27.4	241	sh
	269	28.1	258	sh	250	sh	258	sh
	446	1.6			267	sh	267	sh
IIIe	241-250	p						
	262	26.8	254	27.4	247	sh		
	268	27.0			262	26.5	258	sh
	443	1.6			267	sh		
IIIf	247	23.0	254	35.2	250	sh		
	261	24.1	258	sh	261	35.2	258	23.6
	268	24.6			268	35.1		
	444	1.6						
IIIh	251	sh	253	27.3	252	sh	238	sh
	259	27.0	258	sh	261	26.1	258	sh
	267	26.7			266	sh		
	447	1.6						
IIIi	249	sh						
	260	27.2	252	26.7	249	sh	237	19.5
	268	27.3			261	25.6	260	15.8
	450	1.5			267	sh	266	sh
IIIj	252	sh						
	261	26.2	253	26.7	253	sh	241	23.3
	268	26.0	258	sh	261	26.3	258	sh
	448	1.4			267	sh		
IIIk	252	sh						
	261	25.2	254	25.2	252	sh	239	20.3
	268	25.0	258	sh	261	24.8	257	sh
	448	1.3			267	sh		
IIIm	251	30.7	(d)		(d)		(d)	
	259	31.6						
	268	29.7						
	445	1.5						
IIIn	252	sh	(d)		(d)		(d)	
	261	29.1						
	269	28.6						
	451	1.5						

TABLE IV - continued.

IIIo	274	26.3	(d)		(d)		(d)	
	327	37.8						
	480	1.2						
IIIp	252	sh	253	26.9	(d)		(d)	
	261	29.4						
	268	27.8						
	454	1.5						
IIIq	258	31.8	258	31.1	258	30.3	238	20.2
	263	sh						
	433	1.3	269	sh	264	sh	255	sh
IIIr	260	34.0	259	22.3	260	33.5	240	22.4
	265	sh						
	434	1.4	266	sh	265	sh	256	sh
IIIs	260	33.0	259	34.2	259	33.8	238	20.3
	268	sh	268	sh	268	sh	255	sh
	433	1.5						
IIIt	259	30.0	258	32.2	259	30.7	241	24.8
	267	29.3	264	sh	265	sh	257	sh
	442	1.5					266	sh
IIIu	252	sh						
	258	30.2	257	32.6	258	31.5	238	24.6
	266	28.5	263	sh			255	sh
	442	1.5						
IIIv	252	sh						
	258	31.4	257	31.4	258	29.8	238	23.0
	267	27.6	263	36.0	265	sh	257	sh
	439	1.5						

(a) Only absorption peaks above 230 mμ are recorded. (b) The visible spectra were obtained only in methanol. (c) sh = shoulder, p = plateau. (d) Compound insoluble in the solvent.

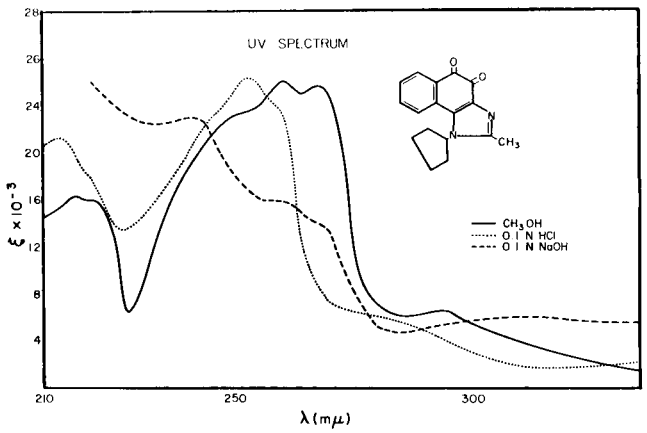


Figure 2: UV spectrum of 1-cyclopentyl-2-methylnaphth-[1,2-*d*]imidazole-4,5-dione.

of 1-pentyl-2-(*N*-piperidinomethyl)naphth[1,2-*d*]imidazole-4,5-dione (IIIt) was obtained. In a similar fashion but using ethylene dichloride as the solvent the 1-alkyl-2-(*N*-piperidinomethyl)naphth[1,2-*d*]imidazoles IIIu and IIIv were prepared.

All the 1,2-disubstituted naphth[1,2-*d*]imidazole-4,5-diones (III) were red crystalline compounds that were homogeneous to tlc analysis (7). With the exception of the compound having a styryl- group in the 2-position the naphth[1,2-*d*]imidazole-4,5-diones (III) showed similar electronic absorption curves. The visible spectrum showed λ max (methanol), 433-452 mμ (ϵ x 10^{-3} = 1.4-1.8). The UV spectrum of 1-cyclopentyl-2-methylnaphth[1,2-*d*]-imidazole-4,5-dione shown in Figure 2 is a typical example. The fact that the electronic spectral properties of the 1-aryl-2-alkylnaphth[1,2-*d*]imidazole-4,5-diones are similar to the 1-alkyl analogs indicates that the aromatic ring is

twisted out of the plane from the rest of the structure (see Table IV). This is in agreement with the nmr spectral data discussed earlier. The infrared spectrum of these compounds all showed carbonyl absorption between 1678-1668 cm^{-1}. As discussed earlier, the nmr spectrum of the naphth[1,2-*d*]imidazole-4,5-diones (III) were useful in establishing steric interactions between the 1-substituent with the 9-hydrogen and the substituent in the 2-position (see Figure 1a-c). The mass spectra of these compounds show in addition to a peak for the molecular ion (m) a (m + 2) peak. This phenomenon has also been observed by other workers (8).

Most of the 4-alkylamino-3-acylamino-1,2-naphthoquinones (II) were red-brown crystalline compounds. The visible spectrum of the 4-arylamino-3-acetamino-1,2-naphthoquinones showed λ max (methanol), 472-482 mμ, whereas the 4-alkylamino-3-acetamino-1,2-naphthoquinones showed λ max (methanol), 447-464 mμ. This type of shift is typical of *N*-substituted 4-amino-1,2-naphthoquinones. The UV spectra of II were similar; however, differences in absorption maximum and intensities were noted between the 4-arylamino and 4-alkylamino-3-acylamino-1,2-naphthoquinones. The infrared spectrum showed in addition to NH absorption, amide I, quinone carbonyl, and amide II absorption bands.

The absorption spectrum of 3-acetamino-1,2-naphthoquinone (Ia) showed λ max (methanol), 264 mμ ($\epsilon \times 10^{-3}$ = 26.0), 272 (24.8), 344 (2.0) and 458 (1.8). With the exception of If, which showed λ max (methanol), 287 (27.3) and 452 (3.2), the other 3-acylamino-1,2-naphthoquinone showed absorption spectra similar to Ia. The infrared spectra of I showed the expected amide NH, amide I and II bands and quinone carbonyl absorption.

EXPERIMENTAL (9)

3-Acetamino-1,2-naphthoquinone (Ia).

To a suspension of 16.96 g. (80 mmoles) of 3-amino-1,2-naphthohydroquinone hydrochloride (10) and 4.80 g. (80 mmoles) of acetic acid in 240 ml. of methylene chloride was added 8.08 g. (80 mmoles) of triethylamine followed by 19.8 g. (96 mmoles) of dicyclohexylcarbodiimide. The mixture was stirred at 25° under a slow stream of nitrogen for 6 hours. The mixture was filtered and the filtrate concentrated on a rotary evaporator. The remaining residue was dissolved in 200 ml. of ethanol, cooled in an ice bath and treated with a cold solution of 48 g. of ferric chloride hexahydrate in 400 ml. of water containing 4 ml. of concentrated hydrochloride acid. The resulting solid was separated by filtration, and recrystallized from ethanol to give 9.8 g. (57%) of 3-acetamino-1,2-naphthoquinone, m.p. 208-213° dec., Lit (3) 214-216°. See Table I for yield and analytical data on other examples.

4-Pentylamino-3-acetamino-1,2-naphthoquinone (IIi).

To a solution-suspension of 0.108 g. (0.5 mmoles) of 3-acetamino-1,2-naphthoquinone in 3 ml. of ethanol was added 0.044 g. (0.5 mmoles) of *n*-pentylamine in 2 ml. of ethanol. The violet colored starting material was gradually displaced and a terra-cotta solid precipitated. After stirring 3 hours (exposed to the atmosphere), the solid was separated by filtration, dried under high vacuum and recrystallized from ethanol to give 0.145 g. (97%) of crystals, m.p. 190-192°; ν max (potassium bromide), 3270 cm^{-1} (NH protruding from a broad absorption at 3600-3050), 1692 (Amide I), 1665 (quinone C=O), 1615 and 1590 (C=C) and 1530 cm^{-1} (Amide II); λ max (methanol), 238 mμ ($\epsilon \times 10^{-3}$ = 17.6), 277 (18.6) and 456 (1.9); λ max (pH 7), 238 (15.0), 272 (17.2), 300 (10.0, shoulder); λ max (0.1*N* sodium hydroxide), 234 (17.4) and 272 (10.8). The compound reacts in 0.1*N* hydrochloric acid to give the corresponding imidazole derivative. The yield and analytical results with other examples are given in Table II.

1-Pentyl-2-methylnaphth[1,2-*d*]imidazole-4,5-dione (IIIi).

A solution-suspention of 0.13 g. (0.43 mmoles) of 4-pentylamino-3-acetamino-1,2-naphthoquinone in 3 ml. of acetic acid was refluxed for 10 minutes. On heating, the solid dissolved and the solution lightened in color. The acetic acid was removed by freeze-drying to give 0.123 g. (100%) of a red crystalline compound, m.p. 153-156°. Recrystallization from benzene gave 0.12 g. (99%) of 1-pentyl-2-methylnaphth[1,2-*d*]imidazole-4,5-dione, m.p. 158-159°. The results obtained with other examples are given in Table III.

1-Pentyl-2-(*N*-piperidinomethyl)naphth[1,2-*d*]imidazole-4,5-dione (IIIt).

A solution of 2.41 g. (7.6 mmoles) of 1-pentyl-2-chloromethylnaphth[1,2-*d*]imidazole-4,5-dione and 1.94 g. (22.8 mmoles) of piperidine in 140 ml. of benzene was heated on a steam bath for 0.5 hour. The cooled reaction mixture was washed twice with 25 ml. portions of water. The benzene solution was dried (sodium sulfate), concentrated and the residue dried under high vacuum to give 2.86 g. of red crystals. Recrystallization from ethyl acetate gave 2.58 g. (90%) of red crystals, m.p. 168-171°. The analytical sample prepared by recrystallization from ethyl acetate had m.p. 169-171°; ν max (potassium bromide), 1675 cm^{-1} (C=O); the nmr spectrum showed a triplet at δ 0.98, J = 5.5 cps (CH_3-), a broad singlet at 1.51 (protons at the 3 and 4 positions of piperidine ring), a broad singlet at 2.42 (protons at position 2 of piperdine ring) a sharp singlet at 3.64 (-CH_2-piperidine), an AB quartet at 4.39, J = 5 cps (imidazole N–CH_2), a multiplet at 7.3-7.8 (7, 8 and 9-H of aromatic ring) and a multiplet at 8.03 ppm, $J_{6,7}$ = 5.5 cps, $J_{6,8}$ = 0.5 cps (6-H of aromatic ring).

Anal. Calcd. for $C_{22}H_{27}N_3O_2$: C, 72.30; H, 7.45; N, 11.50. Found: C, 72.67; H, 7.53; N, 11.54.

1-Methyl-2-(*N*-piperidinomethyl)naphth[1,2-*d*]imidazole-4,5-dione (IIIu).

A solution of 1.54 g. (5.92 mmoles) of 1-methyl-2-chloromethylnaphth[1,2-*d*]imidazole-4,5-dione and 3.05 g. (35.5 mmoles) of piperidine in 100 ml. of ethylene dichloride was refluxed for 0.5 hour. The cooled solution was filtered. The filtrate was washed with water, dried (sodium sulfate) and concentrated. The residue was recrystallized from ethanol and dried at 100° to give 1.27 g. (69%) of 1-methyl-2-(*N*-piperidinomethyl)naphth[1,2-*d*]-imidazole-4,5-dione, m.p. 184-186°. The analytical sample prepared by recrystallization from ethanol followed by drying at 100° had m.p. 192-196° dec.; ν max (potassium bromide), 1675 cm^{-1} (C=O).

Anal. Calcd. for $C_{18}H_{19}N_3O_2$: C, 69.88; H, 6.19; N, 13.58. Found: C, 69.57; H, 6.07; N, 13.58.

A sample dried at 60° analyzed for the monohydrate, m.p. 184-186°.

Anal. Calcd. for $C_{18}H_{19}N_3O_2 \cdot H_2O$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.33; H, 6.01; N, 12.85.

1-Benzyl-2-(*N*-piperidinomethyl)naphth[1,2-*d*]imidazole-4,5-dione (IIIv).

A solution of 2.16 g. (6.42 mmoles) of 1-benzyl-2-chloromethylnaphth[1,2-*d*]imidazole-4,5-dione and 3.27 g. (38.5 mmoles) of piperidine in 100 ml. of ethylene dichloride was refluxed for 0.5 hour. The cooled reaction mixture was filtered. The filtrate was washed with water, dried (sodium sulfate) and concentrated to give 2.75 g. of a red solid. Recrystallization from ethanol gave 1.99 (81%) of 1-benzyl-2-(*N*-piperidinomethyl)naphth[1,2-*d*]imidazole-4,5-dione, m.p. 190-195°. The analytical sample prepared by recrystallization from ethanol had m.p. 195-197°; ν max (potassium bromide), 1678 cm^{-1} (C=O).

Anal. Calcd. for $C_{24}H_{23}N_3O_2$: C, 74.78; H, 6.01; N, 10.90. Found: C, 74.43; H, 6.03; N, 10.80.

1-(4′-Cyclohexylbutyl)-3(*H*)-naphth[1,2-*d*]imidazoline-2,4,5-trione (VII).

To a solution of 5.11 g. (16.05 mmoles) of trichloroacetamino-1,2-naphthoquinone in 250 ml. of ethanol was added 2.50 g. (16.05 mmoles) of cyclohexanebutylamine, and the mixture was stirred 7 hours at 25°. The solid that had separated was filtered and dried under high vacuum to give 2.27 g. (44%) of 1-(4′-cyclohexylbutyl)-3(*H*)-naphth[1,2-*d*]imidazoline-2,4,5-trione, m.p. 252-255°. The analytical sample prepared by recrystallization from *N*,*N*-dimethylformamide had m.p. 244-247°; λ max (methanol), 222 mμ (ϵ x 10^{-3} = 15.8), 278 (26.9) and 523 (2.2).

Anal. Calcd. for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95. Found: C, 71.10; H, 6.73; N, 8.13.

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