Synthesis of 1*H*-Naphth[2,3-*d*]imidazole-4,9-diones by Acid Catalyzed Cyclization of 2-Acylamino-3-amino-1,4-naphthoquinones (1)

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The conversion of 2-acylamino-3-amino-1,4-naphthoquinones (II) to the corresponding 2-substituted 1*H*-naphth[2,3-*d*]imidazole-4,9-diones (I) under both alkaline and acid catalyzed conditions has been effected and the results compared. Treatment of 3-(4′-chlorobutanonylamino)-3-amino-1,4-naphthoquinone (IIe) with aqueous ethanolic sodium hydroxide solution gives 1,2-butanonaphth[2,3-*d*]imidazole-4,9-dione (V); whereas, treatment of IIe with refluxing formic acid gave 2-(4′-chlorobutyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione. Treatment of 2-substituted 1*H*-naphth[2,3-*d*]imidazole-4,5-diones in DMF with alkyl halides in the presence of potassium carbonate affords the expected 1,2-disubstituted naphth[2,3-*d*]imidazole-4,9-diones (VI). The spectral properties of I, II, V and VI as well as those of some 2-acylamino-3-chloro-1,4-naphthoquinones IV are discussed.

1*H*-Naphth[2,3-*d*]imidazole-4,5-diones (I) are of interest as bacteriostatic agents (2). Previously, these compounds have been prepared by the alkaline catalyzed cyclization of the corresponding 2-acylamino-3-amino-1,4-naphthoquinone (II) (2-4). In this report we describe an acid catalyzed cyclization of II to I and compare the results to the alkaline catalyzed reaction.

Treatment of 2-amino-3-chloro-1,4-naphthoquinone (III) with an acid chloride in refluxing xylene or with an acid anhydride containing catalytic amounts of sulfuric acid at room temperature gave the 2-acylamino-3-chloro-1,3-naphthoquinones (IV) (Chart 1). The compounds prepared along with their spectral and analytical data are listed in Table I. The infrared spectral date of these compounds indicate that IVa-f exist in the form IVA. The infrared spectrum (potassium bromide) of the aroyl example IVg showed the absence of N-H and amide II absorption and showed absorption at 1712 cm^{-1} attributable to C=NCOR. This would indicate that this compound has the tautomeric form IVB. The fact that the UV spectrum of IVg does not show an absorption at 336 mμ present in the other examples and is almost colorless, whereas the derivatives IVa-f are bright yellow in color, is consistent with this assignment. When a warm dioxane or nitrobenzene solution of IV was treated with dry ammonia the corresponding 2-acylamino-3-amino-1,4-naphthoquinones (II) listed in Table II were obtained (5).

2-Substituted 1*H*-naphth[2,3-*d*]imidazole-4,9-diones (I) have generally been prepared by refluxing the corresponding 2-acylamino-3-amino-1,4-naphthoquinones (II) in ethanol containing 2*N* sodium hydroxide (2-4). However, it is reported that the cyclization of II to I does not take place under acidic conditions (2,4,6). If II was reduced to the hydroquinone, the cyclization could be effected in refluxing acetic acid and I could be obtained by the oxidation of the hydroquinone form of the imidazole (2). We have found that the substituted 1*H*-naphth[2,3-*d*]imidazole-4,9-diones (I) are conveniently synthesized by treating the corresponding 2-acylamino-3-amino-1,4-naphthoquinone (II) with refluxing formic acid without prior reduction of II. This procedure offers an attractive alternative to

CHART I

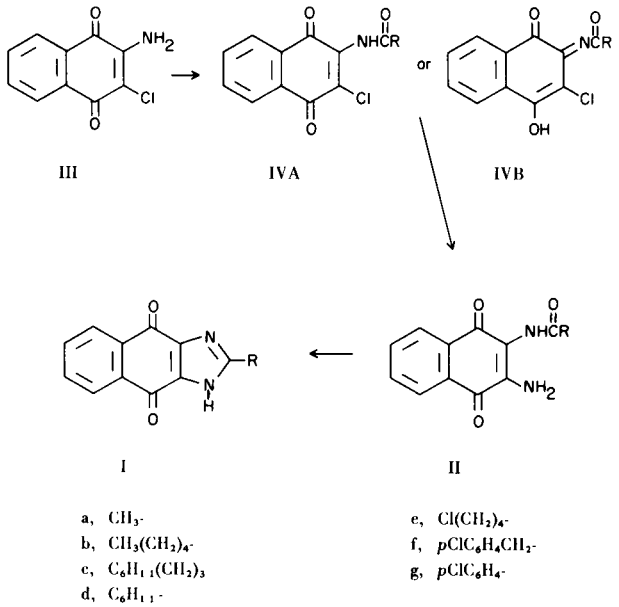


TABLE I

2-Acylamino-3-chloro-1,4-naphthoquinones

Compound (a)	Procedure (b)	Yield % (c)	M.p. °C	Ultraviolet abs. (d) λ max (methanol)	ε x 10^{-3}	Infrared Bands; ν max (KBr) cm^{-1} (e) N-H	Amide I	Quinone C=O	Amide II	Other	Molecular Formula	Calcd. % (Found %) C	H	N	Cl
IVa	A	95	216-218 (f)			3320	1712	1665	1485						
IVb	A	83	143-144 (g,h)	247	18.7	3265	1692	1668	1505		$C_{16}H_{16}ClNO_3$	62.85	5.28	4.58	11.59
				252	20.2							(62.51)	(5.18)	(4.13)	(11.83)
				286	9.2										
				336	3.3										
IVc	B	35	186-187	247	19.4	3278	1692	1670	1500		$C_{20}H_{22}ClNO_3$	66.75	6.16	3.89	9.88
				253	21.1							(66.77)	(6.19)	(3.84)	(9.98)
				286	9.4										
				336	3.3										
IVd	B	75	203-204 (i,j)	247	19.8	3270	1695	1670	1502		$C_{17}H_{16}ClNO_3$	64.25	5.08	4.41	11.16
				253	21.7	(3360)	(1717)	(1675)	(1465)			(64.20)	(4.82)	(4.59)	(11.38)
				287	9.6										
IVe	B	28	179-181 (k)	247	17.4	3263	1698	1668	1513		$C_{15}H_{13}Cl_2NO_3$	55.23	4.02	4.29	21.74
				252	20.5							(55.37)	(4.06)	(4.06)	(22.07)
				286	9.5										
				337	3.3										
IVf	B	42	215-223° (dec)	247	20.5	3242	1691	1670	1493		$C_{18}H_{11}Cl_2NO_3$	60.02	3.08	3.89	19.69
				252	20.8							(60.27)	(3.16)	(3.96)	(19.46)
				286	9.6										
				336	2.5										
IVg	B	13	206-209 (ℓ)	236	24.5			1680		1712 (m)	$C_{17}H_9Cl_2NO_2$	58.98	2.62		
				287	9.1							(58.64)	(2.47)		

(a) A typical procedure for each type preparation is given in the experimental section. (b) Procedure A, acid anhydride plus sulfuric acid; Procedure B, acid chloride in refluxing xylene. (c) Based on pure compound recrystallized from ethanol. (d) Only absorption above 230 mμ is given. (e) Values in parentheses were obtained in methylene chloride solution. (f) Lit. (ref. 2) m.p. 219°. (g) M.p. 143-144° resolidified and melted at 155-157°. (h) Lit. (ref. 2) m.p. 148-148.5°. (i) A crystal structure change was noted between 158-162°. (j) Recrystallized from ethyl acetate. (k) A crystal structure change was noted between 172-174°. (ℓ) Recrystallized from a *N,N*-dimethylformamide and methanol mixture. (m) Absorption due to $\geq C{=}N{-}COC_6H_4Cl$.

TABLE II

2-Acylamino-3- amino-1,4-naphthoquinones (II)

Compound (a)	Reaction Solvent (b)	Yield % (c)	M.P. °C	Ultraviolet abs. (d) λ max methanol	ε x 10^{-3}	Infrared Bands, ν max (KBr) cm^{-1} NH & NH_2	Amide I	Quinone C=O (e)	Amide II	Molecular Formula	Calcd. % (Found %) C	H	N	Cl
IIa	A	70	233-235 (f)											
IIb	B	88	149-151 (g)	268	21.4	3418	1688	1640-	1510	$C_{16}H_{18}N_2O_3$	67.11	6.34	9.79	
				323	2.1	3310		1608			(67.40)	(6.35)	(10.03)	
				452	2.4									
IIc	B	81	150-151	268	21.8	34.35	1672	1620	1525	$C_{20}H_{24}N_2O_3$	70.56	7.11	8.23	
				327	2.2	3320					(70.63)	(7.55)	(8.38)	
				452	2.4	3300								
IId	B	81	185-187	268	20.0	3420	1668	1645-	1505	$C_{17}H_{18}N_2O_3$	68.44	6.08	9.39	
				325	2.2	3310		1605			(68.20)	(5.96)	(9.58)	
				452	2,3									
IIe	A	63	169-169.5	268	21.3	3420	1698	1670-	1515	$C_{15}H_{15}ClN_2O_3$	58.73	4.93	9.13	11.56
				327	2.2	3225		1620			(58.49)	(4.93)	(9.19)	(11.50)
				452	2.4	3262								
IIf	A	68	241-243 (h)	268	22.9	3420	1690	1649-	1510	$C_{18}H_{13}ClN_2O_3$	63.44	3.84	8.22	10.41
				i		3302		1610			(62.95)	(3.83)	(8.35)	(10.59)
IIg	A	58	286-287.5	267	24.7	3393	1690	1670-	1570	$C_{17}H_{11}ClN_2O_3$	62.49	3.39	8.58	10.85
				i		3303		1570			(62.61)	(3.34)	(8.87)	(10.73
						3365								

(a) Typical procedures are given in the experimental section. (b) A = dioxane at 40-50°; B = nitrobenzene at 140-150°. (c) Based on pure compound recrystallized from ethanol. (d) Only absorption above 230 mμ is given. (e) There was usually a broad absorption consisting of 2-4 peaks for this absorption. (f) Lit. (ref. 2) m.p. 233-234°. (g) Lit. (ref 2) m.p. 139.4-140.1°. (h) Recrystallized from a *N,N*-dimethylformamide and methanol mixture. (i) This compound was too insoluble to obtain weaker absorption bands.

TABLE III

2-Substituted 1*H*-naphth[2,3-*d*]imidazole-4,9-diones (I)

Compound (a)	Recrystallization Solvent (b)	Yield % (c) Acid (d)	Yield % (c) Base (e)	M.p. °C	Molecular Formula	Calcd. % (Found%) C	H	N	Cl
Ia	A	90	63 (f)	>350° (g)					
Ib	A	58	68 (f) 45	191-192 (h)	$C_{16}H_{16}N_2O_2$	71.62 (72.03)	6.01 (6.04)	10.44 (10.65)	
Ic	A	57	72	201-203	$C_{20}H_{22}N_2O_2$	66.66 (66.81)	4.80 (4.80)	7.41 (7.41)	
Id	B	55	39	274-276	$C_{17}H_{16}N_2O_2$	72.83 (72.76)	5.75 (5.58)	10.00 (10.03)	
Ie	B	39	i	170-171	$C_{15}H_{13}ClN_2O_2$	62.39 (62.24)	4.54 (4.42)	9.70 (9.86)	12.28 (12.09)
If	B	67	5	287-291	$C_{18}H_{11}ClN_2O_2$	66.98 (66.57)	3.44 (3.41)	8.68 (8.60)	
Ig	C	30	10	344-346	$C_{17}H_9ClN_2O_2$	66.13 (65.95)	2.94 (2.84)	9.08 (9.31)	11.49 (11.31)

(a) Typical procedures are given in the experimental section. (b) A = ethyl alcohol; B = ethyl acetate; C = formamide. (c) Based on pure compound isolated. (d) The acid catalyzed cyclizations were carried out in refluxing formic acid (95-100%). (e) The alkaline catalyzed cyclizations were carried out according to the procedure reported in ref. 2. (f) Taken from ref. 2. (g) Lit. (ref. 2) m.p. 368°. (h) Lit. (ref. 2) m.p. 182.3-183.5°. (i) Compound V is obtained in 75% yield on treating IIe with base.

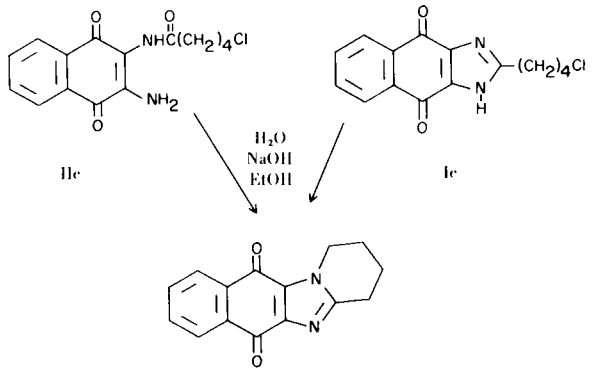
TABLE IV

Ultraviolet and Infrared Spectral Data of Naphth[2,3-*d*]imidazole-4,9-diones

	Ultraviolet Absorption								Infrared Bands		
	CH_3OH (b)		0.1*N* HCl		*p*H 7 (c)		0.1*N* NaOH		ν max, KBr		
Compound	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}	N-H	Quinone C=O	Other
Ia	244	38.0	249	sh (d)	247	40.5	261	37.3	(e)	1665	
	277 (f)	15.2	245	30.6	283	16.0					
	330	2.9	276	16.6							
Ib	246	42.3	245	31.7	248	43.8	264	40.8	3200	1675	
	277	14.5	250	41.5	283	14.5					
	332	3.0	278	16.2							
Ic	247	48.7	246	40.5	(g)		263	40.5		1670	
	273	25.4	250	52.8							
	277	25.0	277	sh							
	333	2.9	272	26.8							
Id	246	42.3	245	33.5	243	43.7	264	40.5	3280	1670	
	277 (f)	13.6	251	45.0	283	13.6					
	333	2.9	279	15.5							
Ie	246	41.6	246	32.3	247	43.9	262	39.0	3200	1675	
	275 (f)	14.4	251	40.8	281 (f)	14.4					
	279	15.0	278	16.2							
	332	2.9									
If	247	43.5	247	sh	248	44.5	263	43.0	3222	1665	
	277 (f)	14.5	251	42.7	277 (f)	14.5					
	329	3.0	275	14.5							
Ig	285	43.8	(g)		(g)		292	52.7	3234	1660	1650
	294	42.8									
	390	1.7									
V	247	43.8	244	31.3	248	45.6	249	44.8		1670	
	275 (f)	15.8	250	35.1	282	15.4	283	15.2			
	280	15.0	279	15.8							
	332	3.0									
VIa	248	47.0	(g)		(g)		(g)			1678	
	280	15.2								1661	
	332	3.3									
VIb	248	44.6	248	42.0	248	42.5	249	31.9		1677	
	275 (f)	14.4	280	15.4	283	14.2	283 (f)	14.3		1660	
	281	14.9									
	332	3.4									

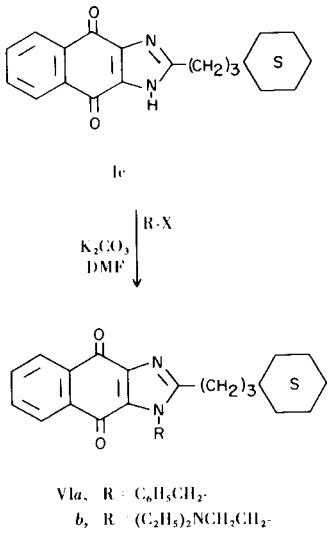
(a) Only absorption peaks above 230 mμ are recorded. (b) Absorption above 300 mμ were measured only in methanol. (c) Phosphate buffer. (d) sh = shoulder. (e) This compound showed a broad salt like absorption between 2700-2400 cm^{-1}. (f) A broad absorption band. (g) Insoluble in this solvent.

the base catalyzed route and is of particular value when II contains a group sensitive to alkaline or oxidizing and reducing agents. For example, treatment of 2-(5′-chloropentanoylamino)-3-amino-1,4-naphthoquinone (IIe) with hot aqueous-ethanolic sodium hydroxide gave 1,2-butanonaphth[2,3-*d*]imidazole-4,9-dione (V), and no 2-(4′-chlorobutyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione (Ie) was obtained. However, treatment of IIe with refluxing formic acid gave 39% of Ie. The 2-(4′-chlorobutyl)-1*H*-naphth-[2,3-*d*]imidazole-4,9-dione (Ie) is most probably an intermediate in the alkaline catalyzed conversion of IIe to V. The fact that Ie is rapidly and nearly quantitatively converted to V upon treatment with aqueous ethanolic sodium hydroxide solution is in agreement with this suggestion.



A comparison of the yields of I obtained from the alkaline and acid cyclization of several 2-acylamino-3-amino-1,4-naphthoquinones (II) is given in Table III. As mentioned in the previous paragraph when R = $Cl(CH_2)_4$, only the acid procedure gave Ie. When R = CH_3, C_6H_{11}, *p*-$ClC_6H_4CH_2$– or *p*-ClC_6H_4, the acid procedure gave yields superior to the alkaline route. If R = $CH_3(CH_2)_4$ or $C_6H_{11}(CH_2)_3$ both procedures gave respectable yields of I. Experimentally, both procedures are quite easy to carry out. In both cases minor side products are observed and pure products are best prepared by column chromatography on aluminum oxide (7).

Treatment of 2-(3′-cyclohexylpropyl)-1*H*-naphth[2,3-*d*]-imidazole-4,9-dione (Ic) with benzyl bromide or 2-diethylaminoethyl chloride in *N*,*N*-dimethylformamide in the presence of potassium carbonate gave the 1,2-dialkylnaphth[2,3-*d*]imidazole-4,9-diones, VIa and b, in excellent yield. 1,2-Disubstituted naphth[1,2-*d*]imidazole-4,9-dione have also been prepared by cyclization of the necessary 2-acylamino-3-alkylamino-1,4-naphthoquinone or 2-(*N*-alkyl-*N*-acylamino)-3-amino-1,4-naphthoquinone (4) and by pyrolysis of the requisite 1,2,3-trisubstituted naphth[2,3-*d*]-imidazolium salt (8). The procedure involving the



VIa, R = $C_6H_5CH_2$–
b, R = $(C_2H_5)_2NCH_2CH_2$–

alkylation of I appears to be simpler and would be much more general than the other two procedure.

The 1*H*-naphth[2,3-*d*]imidazole-4,9-diones prepared by either the acid or alkaline procedure were yellow crystalline compounds that were homogenous to thin layer chromatographic analysis (9). With the exception of Ie, which reacted to give V, they all formed red sodium salts that were soluble in aqueous alcohol. The 2-alkyl-1*H*-naphth[2,3-*d*]imidazole-4,9-diones (I) showed no absorption in the visible region. The UV spectrum (methanol) of 2-(3′-cyclohexylpropyl)-1*H*-naphth[2,3-*d*]imidazole-4,-9-dione (Ic) shows absorption at 247 mμ ($\epsilon \times 10^{-3}$ = 48.7), 273 (25.4), 277 (25.0) and 333 (2.9). In 0.1*N* sodium hydroxide Ic is converted to the anion and shows absorption at 263 mμ ($\epsilon \times 10^{-3}$ = 40.5). In 0.1*N* hydrochloric acid Ic is protonated and the 246 mμ and 277 mμ absorption peaks observed in methanol shows a bathochromic and hypsochromic shift, respectively. The infrared spectrum (potassium bromide) of Ic shows absorption at 1670 cm^{-1} (quinone carbonyl). The spectral data of other 1*H*-naphth[2,3-*d*]imidazole-4,9-diones are given in Table IV.

The 1,2-dialkylnaphth[2,3-*d*]imidazole-4,9-diones were yellow crystalline compounds that were more soluble in ethanol than the 2-alkyl-1*H*-naphth[2,3-*d*]imidazole-4,9-diones. The UV spectrum in methanol was quite similar to the spectra of the 2-alkyl-1*H*-naphth[2,3-*d*]imidazole-4,9-diones but showed no shift in 0.1*N* sodium hydroxide solution. The infrared spectrum showed the absence of NH absorption but showed a split carbonyl absorption between 1678 and 1660 cm^{-1}. The spectral date for these compounds are given in Table IV.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage microscope using a calibrated thermometer. Ultraviolet and visible spectra were measured on a Cary Model 14 Spectrophotometer. Nmr spectra were recorded on a Varian Model A-60, using tetramethylsilane as an internal standard. Infrared spectra were measured with a Perkin Elmer 221 Spectrophotometer; samples were prepared in the form of pressed potassium bromide disks. Mass spectra were determined on an AEI MS-902 spectrometer. Microanalyses were carried out by Micro-Tech Laboratories, Skokie, Illinois.

2-Amino-3-chloro-1,4-naphthoquinone.

This material was prepared by the procedure of Hoover and Day (2) from 2,3-dichloro-1,4-naphthoquinone, m.p. 201-203°; Lit. (2) 195-196°;

2-Hexanoylamino-3-chloro-1,4-naphthoquinone (Procedure A, Table I.).

This compound was prepared by a previously reported procedure (2). To a solution-suspention of 2-amino-3-chloro-1,4-naphthoquinone (8.3 g., 40 mmoles) in 80 ml. of hexanoic anhydride was added 8 drops of concentrated sulfuric acid. The mixture solidified to a solid mass. Methylene chloride (90 ml.) was added to the obtained solution. The solution was stirred at 25° for 1 hour. The solution was concentrated under vacuum, and the remaining solid taken up in hot ethanol. The cooled solution gave 10.13 g. (83%) of 2-hexanoylamino-3-chloro-1,4-naphthoquinone, m.p. 143-144°; resolidified and melted at 155-157°. The compound IVa listed in Table I was prepared by an analogous procedure.

2-(4′-Cyclohexylbutanoylamino)-3-chloro-1,4-naphthoquinone (Procedure B, Table I.)

Using a procedure similar to that reported by Hoover and Day (2) to prepare other 2-acylamino-3-chloro-1,4-naphthoquinones a mixture of 41.5 g. (0.2 mole) of 2-amino-3-chloro-1,4-naphthoquinone and 4-cyclohexylbutanonyl chloride [prepared by refluxing 35.8 g. (0.21 mole) of 4-cyclohexanebutyric acid with 100 ml. of thionyl chloride for 2 hours followed by concentration on a rotary evaporator at a bath temperature of 60°] in 150 ml. of xylene was treated with dry hydrogen chloride for 5 minutes and then refluxed for 3 hours. The cooled product was filtered and the resulting solid washed with hexane, dried and recrystallized from ethanol to give 26.1 g. (35%) of 2-(4′-cyclohexylbutanoylamino)-3-chloro-1,4-naphthoquinone, m.p. 186-187°. The compounds IVc-g listed in Table I were prepared by an analogous procedure.

2-(5′-Chloropentanoylamino)-3-amino-1,4-naphthoquinone (Procedure A, Table II).

Dry ammonia gas was passed into a warm solution (40-50°) of 7.18 g. (20.2 mmoles) of 2-(5′-chloropentanoylamino)-3-chloro-1,4-naphthoquinone for 2 hours. The reaction mixture was filtered and the filtrate concentrated by freeze-drying. The red solid obtained was recrystallized from ethanol to give 4.25 g. (63%) of 2-(5′-pentanoylamino)-3-amino-1,4-naphthoquinone, m.p. 169-169.5°. Compounds IIa and IIe-g listed in Table II were prepared by an analogous procedure.

2-(4′-Cyclohexylbutanoylamino)-3-amino-1,4-naphthoquinone (Procdure B, Table II).

Using a procedure similar to that used by Hoover and Day (2) to prepare other 2-acylamino-3-amino-1,4-naphthoquinone, dry ammonia gas was passed into a solution of 25.6 g. (0.071 mole) of 2-(4′-cyclohexylbutanoylamino)-3-chloro-1,4-naphthoquinone in 128 ml. of nitrobenzene for 1 hour while the temperature was maintained at 140-150° by means of an oil bath. The cooled reaction mixture was dissolved in hot ethanol and filtered. On cooling the filtrate gave 19.1 g. (81%) of 2-(4′-cyclohexylbutanoylamino)-3-amino-1,4-naphthoquinone, m.p. 150-151°. Compounds IIb and d were prepared by an analogous procedure.

2-(3′-Cyclohexylpropyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione (Alkaline Catalyzed Procedure).

This compound was prepared by a procedure similar to that used by Hoover and Day (2) to prepare other 1*H*-naphth[2,3-*d*]-imidazole-4,9-diones. To a hot solution of 15.3 g. (0.043 mole) of 2-(3′-cyclohexylbutanoylamino)-3-amino-1,4-naphthoquinone in 400 ml. of ethanol was added 100 ml. of 2*N* sodium hydroxide solution, and the mixture was refluxed for 30 minutes. The hot solution was treated with Norite and filtered through a short celite column. The filtrate was concentrated to 1/2 its original volume and adjusted to *p*H 8 with 2*N* sulfuric acid solution. The yellow product that separated was filtered, washed with water and dried under high vacuum. Recrystallization from ethanol gave 10.4 g. (72%) of 2-(3′-cyclohexylpropyl)-1*H*-naphth[2,3-*d*]imidazole-4,-9-dione, m.p. 201-203°. The results obtained with other examples are given in Table III. In many cases chromatography on aluminum oxide (7) was necessary in order to obtain a product that was homogenous to tlc analysis (9)

2-(*p*-Chlorophenyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione (Acid Catalyzed Procedure).

A solution of 1.66 g. (5.8 mmoles) of 2-*p*-chlorobenzoylamino-3-amino-1,4-naphthoquinone in 50 ml. of formic acid (97-100%) was refluxed for 6.5 hours. The cooled reaction mixture was diluted with water. The resulting orange solid was filtered, washed with water, recrystallized from formamide, and dried to give 0.45 g. (30%) of 2-(*p*-chlorophenyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione, m.p. 344-346°.

The results obtained with other examples are given in Table III. In several cases, chromatography on aluminum oxide (7) was necessary in order to obtain a product that was homogenous to tlc analysis (9).

Preparation of 1,2-Butanonaphth[2,3-*d*]imidazole-4,9-dione from 2-(5′-chloropentanoylamino)-3-amino-1,4-naphthoquinline.

To a hot solution of 2.5 g. (8.15 mmoles) of 2-(5′-chloropentanoylamino)-3-amino-1,4-naphthoquinone in 95 ml. of ethanol was added 25 ml. of 2*N* sodium hydroxide solution and the mixture was heated on a steam bath for 10 minutes. The cooled reaction mixture was filtered to give a green-yellow solid. Recrystallization from an ethanol and methylene chloride mixture gave 1.54 g. (75%) of 1,2-butanonaphth[2,3-*d*]imidazole-4,9-dione, m.p. 257-259°.

Anal. Calcd. for $C_{15}H_{12}N_2O_2$: C, 71.41; H, 4.80; N, 11.11. Found: C, 71.75; H, 4.81; N, 11.28.

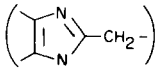
Preparation of 1,2-Butanonaphth[2,3-*d*]imidazole-4,9-dione from 2-(4′-Chlorobutyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione.

To a solution of 0.031 g. (0.107 mmole) of 2-(4′-chlorobutyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione in 2 ml. of ethanol was added 2 drops of 2*N* sodium hydroxide solution and the solution was heated on a steam bath for 0.5 hour. After cooling, a green-yellow precipitate separated. Filtration followed by washing of the solid with water and drying under high vacuum gave 0.027 g. (99%) of 1,2-butanonaphth[2,3-*d*]imidazole-4,9-dione, m.p. 255-

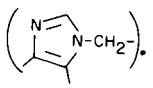
258°. An ir spectrum of this sample was identical to the spectrum of a product from the previous experiment.

1-Benzyl-2-(3′-cyclohexylpropyl)naphth[2,3-*d*]imidazole-4,9-dione.

A mixture of 0.322 g. (1.0 mmole) of 2-(3′-cyclohexylpropyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione, 0.138 g. (1.0 mmole) of anhydrous potassium carbonate and 0.171 g. (1.0 mmole) of benzyl bromide in 1 ml. of DMF was stirred at 25° for 2 hours. The reaction mixture was diluted with water and the resulting precipitate, filtered, washed with water, and dried to give 0.36 g. (88%) of 1-benzyl-2-(3′-cyclohexylpropyl)naphth[2,3-*d*]imidazole-4,9-dione, m.p. 149-150°. The analytical sample prepared by recrystallization from ethanol had m.p. 150-151°. Nmr (deuteriochloroform) showed an unsymmetrical triplet centered at δ 2.75



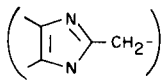
and a singlet at 5.73 ppm



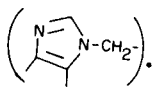
Anal. Calcd. for $C_{27}H_{28}N_2O_2$: C, 78.61; H, 6.84; N, 6.79. Found: C, 78.30; H, 6.80; N, 6.75.

1-(2′-Diethylaminoethyl)-2-(3′-cyclohexylpropyl)naphth[2,3-*d*]-imidazole-4,9-dione.

A mixture of 3.22 g. (10.0 mmoles) of 2-(3′-cyclohexylpropyl)-1*H*-naphth[2,3-*d*]imidazole-4,9-dione, 2.76 g. (10.0 mmoles) of anhydrous potassium carbonate and 1.72 g. (10.0 mmoles) of 2-diethylaminoethyl chloride hydrochloride in 10 ml. of DMF was stirred at 25° for 2 hours. The reaction mixture was diluted with water and extracted with benzene. The benzene extracts were dried (sodium sulfate), concentrated, dissolved in hexane and cooled in the freezer to give 3.40 g. (81%) of 1-(2′-diethylaminoethyl)-2-(3′-cyclohexylpropyl)naphth[2,3-*d*]imidazole-4,9-dione, m.p. 74-76°. The analytical sample prepared by further recrystallization from hexane had m.p. 75-77°. Nmr (deuteriochloroform) showed a triplet at 0.98, J = 7.0 cps (CH_3 of CH_2CH_2 group), a quartet at 2.60 (CH_2 of CH_3CH_2), a multiplet at 2.80 slightly overlapping the 2.60 resonance



and an unsymmetrical triplet at 4.45 ppm



Anal. Calcd. for $C_{26}H_{35}N_3O_2$: C, 74.07; H, 8.37; N, 9.97. Found: C, 74.35; H, 8.27; N, 10.30.

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(5) These compounds may exist as a mixture of tautomeric forms.

(6) The use of refluxing acetic acid (ref. 2) and alcoholic hydrogen chloride solution (ref. 4) were attempted. In contrast, 2-amino-3-acetylamino-1,4-naphthoquinones, containing an alkyl or phenyl substituent on either nitrogen atom are cyclized in acid medium to the corresponding 1-alkyl (or phenyl)-2-methylnaphth-[2,3-*d*]imidazole-4,9-dione (ref. 4).

(7) Woelm neutral aluminum oxide (activity grade III) was used, and the columns were eluted with chloroform. Compounds If and Ig were too insoluble for chromatography and were purified by recrystallization.

(8) P. Truitt, D. Hayes, and L. T. Creagh, *J. Med. Chem.*, 7, 362 (1964).

(9) Thin layer plates were prepared using Merck Aluminum Oxide HF and eluted with hexane:chloroform:methanol (4:4:1).

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