6(5*H*)-Phenanthridinones. III. Halo-6(5*H*)phenanthridinones (1,2)

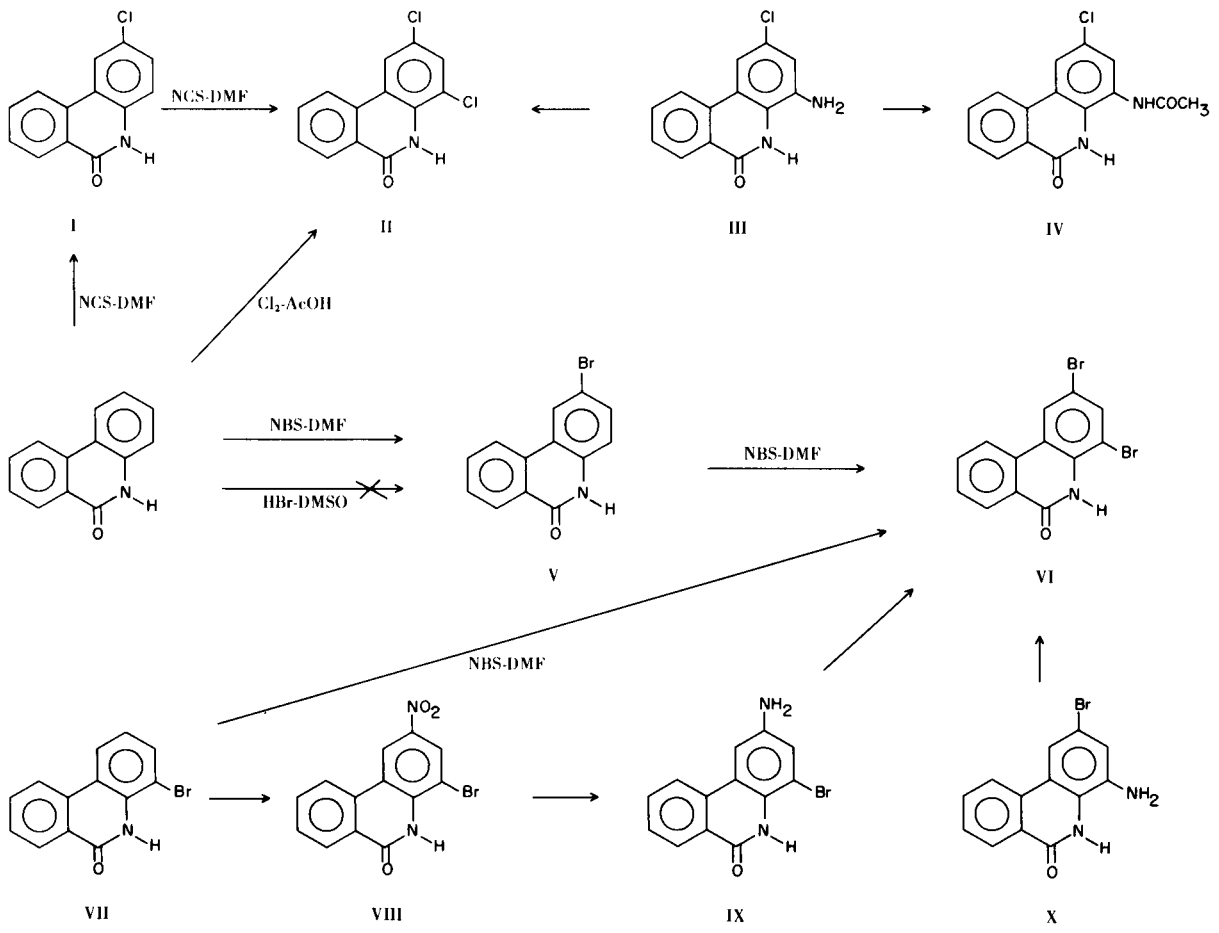
Hsi-Lung Pan and T. Lloyd Fletcher

Chemistry Research Laboratory of the Department of Surgery
School of Medicine, University of Washington

Halogenation of 6(5*H*)-phenanthridinone or its 3,8-dihalo derivatives with *N*-bromo or *N*-chlorosuccinimide in dimethylformamide gives the corresponding 2-halophenanthridinones (I,V,XI-XIV). Further halogenation of 2-halo-6(5*H*)-phenanthridinone with the appropriate *N*-halosuccinimide, in the same medium, gives the corresponding 2,4-dihalo derivatives (II,VI). NXS/DMF is found to be a very convenient halogenating system in these preparations. 1,3,8-Trihalo-6(5*H*)-phenanthridinones (XIX,XX) are prepared from the 1-nitro derivatives which are obtained by a Schmidt rearrangement of 2,7-dihalo-4-nitro-9-oxofluorenes. Similarly, rearrangement and further reaction of 2-nitro-5-chloro-9-oxofluorene (XXI) leads to 3,10-dichloro-6(5*H*)-phenanthridinone (XXIV). UV absorptions as well as selected IR absorptions of these 6(5*H*)-phenanthridinones are described.

Arylacetamides (3,4) and arylamines (5) have been successfully halogenated in the aromatic ring by means of *N*-halosuccinimides in dimethylformamide. We have found this halogenating system advantageous in the preparation

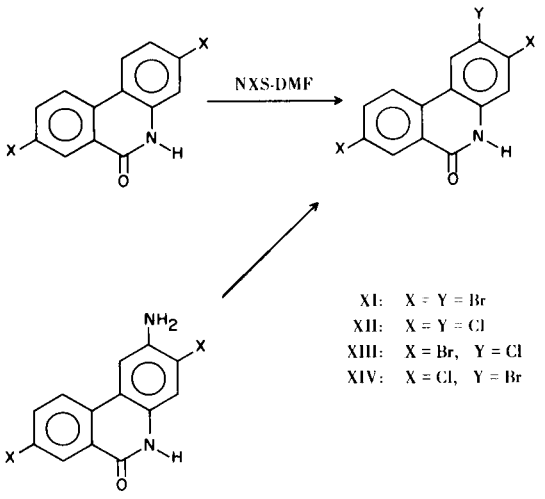
SCHEME I



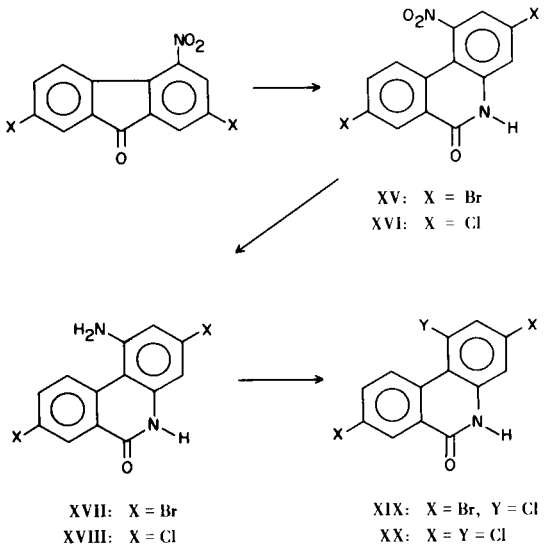
of halo-6(5*H*)-phenanthridinones, partly because of favorable solubility of these compounds in DMF. Furthermore, monohalo derivatives are often the sole product and the halogen atom invariably goes to the 2-position. Thus, with *N*-chlorosuccinimide, 2-chloro-6(5*H*)-phenanthridinone (I) (6) is formed in excellent yields, and 2-bromo-6(5*H*)-phenanthridinone (V) (6,7) is the only product found in the reaction with *N*-bromosuccinimide. Under forced conditions, however, 2,4-dihalo compounds [II, VI (8)] are formed in relatively low yields. We also prepared compound II by chlorinating 6(5*H*)-phenanthridinone with excess chlorine in acetic acid, or by converting 2-chloro-4-amino-6(5*H*)-phenanthridinone (III) through a Sandmeyer reaction. The structure of VI was substantiated by conversion of both 2-amino-4-bromo-6(5*H*)-phenanthridinone (IX) and 4-amino-2-bromo-6(5*H*)-phenanthridinone (X) to the dibromo compound. A weak halogenating agent, 48% aqueous hydrobromic acid in dimethyl sulfoxide, (9,10), fails to brominate phenanthridinone (Scheme I).

That the 2-position of the 6(5*H*)-phenanthridinone molecule, as mentioned above and also found in earlier work (2,6), is the most favorable site for electrophilic substitution, is also demonstrated in reactions involving 3,8-disubstituted-6(5*H*)-phenanthridinones. For example, nitration of 3-chloro-, 8-chloro-, or 3,8-dihalo-6(5*H*)-phenanthridinones, leads to the corresponding 2-nitro derivatives (2). Likewise, nitration of 4-halo-6(5*H*)-phenanthridinones gives the corresponding 2-nitro-4-halo-6(5*H*)-phenanthridinones (Scheme I). Halogenation of 3,8-dihalo-6(5*H*)-phenanthridinones with NXS/DMF, leads to 2,3,8-trihalo derivatives (XI-XIV). The fact that the halogen atom goes to the 2-position with NXS/DMF was substantiated by conversion of the 2-amino-3,8-dihalo-6(5*H*)-phenanthridinones to the 2,3,8-trihalo compounds (Scheme II).

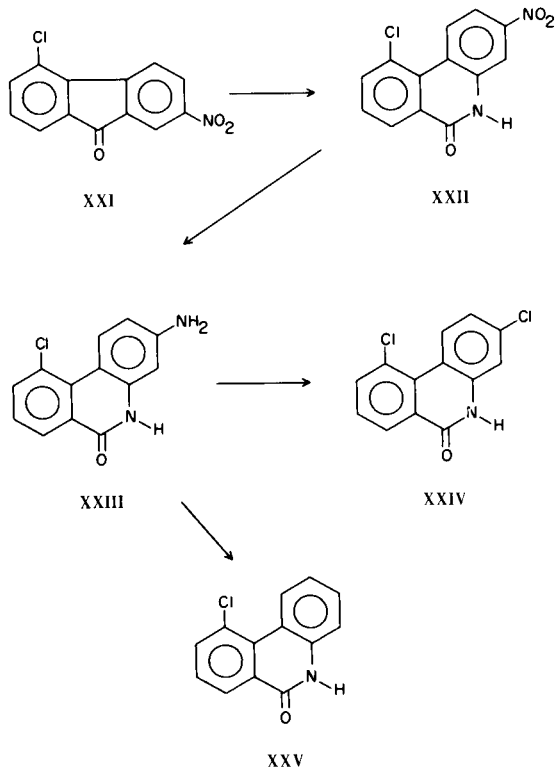
SCHEME II



SCHEME III



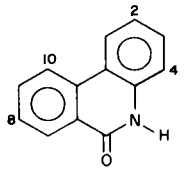
SCHEME IV



1,3,8-Trihalo-6(5*H*)-phenanthridinones (XIX,XX) were prepared from the 1-amino compounds (XVII,XVIII) which, in turn, were obtained by Raney nickel-hydrazine hydrate reduction of 1-nitro-3,8-dihalo-6(5*H*)-phenanthridinones (XV,XVI). The latter compounds were made by

TABLE I

Halogeno-6(5*H*)-phenanthridinone Derivatives



Compound No.	Substituent(s)	M.P., °C	Formula	Analyses, % Calcd. (Found)			
				C	H	N	X
I	2-Cl	322.5-323.5 (a)	$C_{13}H_8ClNO$				15.44(15.45) (b)
II	2,4-Cl_2	270-272	$C_{13}H_7Cl_2NO$				26.85(26.78) (b)
III	2-Cl, 4-NH_2	334-335 dec	$C_{13}H_9ClN_2O$			11.45(11.37)	
IV	2-Cl, 4-$NHCOCH_3$	298-299 dec	$C_{15}H_{11}ClN_2O_2$	62.84(62.79)	3.87(3.83)		
V	2-Br	323-324 (c)	$C_{13}H_8BrNO$				29.15(29.08) (d)
VI	2,4-Br_2	266-267 (e)	$C_{13}N_7Br_2NO$	44.23(44.31)	2.00(1.81)	3.96(3.84)	45.28(45.13) (d)
VII	4-Br	241-241.5	$C_{13}H_8BrNO$	56.96(57.14)	2.94(2.53)		29.15(29.38) (d)
VIII	2-NO_2, 4-Br	326-327	$C_{13}H_7BrN_2O_3$	48.93(48.71)	2.21(2.12)	8.78(8.61)	25.04(24.95) (d)
IX	2-NH_2, 4-Br	259-260	$C_{13}H_9BrN_2O$	54.00(53.92)	3.14(2.98)	9.69(9.50)	
X	2-Br, 4-NH_2	335-336 dec	$C_{13}H_9BrN_2O$	54.00(53.97)	3.14(3.08)	9.69(9.84)	
XI	2,3,8-Br_3	>360	$C_{13}H_6Br_3NO$	36.15(36.43)	1.40(1.54)	3.24(3.27)	55.50(55.20) (d)
XII	2,3,8-Cl_3	>360	$C_{13}H_6Cl_3NO$	52.30(52.41)	2.26(2.31)	4.70(4.74)	35.62(35.57) (b)
XIII	2-Cl, 3,8-Br_2	>360	$C_{13}H_6Br_2ClNO$	40.30(40.50)	1.56(1.75)		9.15(9.21) (b)
							41.25(41.20) (d)
XIV	2-Br, 3,8-Cl_2	>360	$C_{13}H_6BrCl_2NO$	45.52(45.66)	1.76(1.92)		20.67(20.61) (b)
							23.30(23.12) (d)
XV	1-NO_2, 3,8-Br_2	353-354 dec	$C_{13}H_6Br_2N_2O_3$	39.23(39.08)	1.52(1.42)	7.04(7.14)	
XVI	1-NO_2, 3,8-Cl_2	348-349	$C_{13}H_6Cl_2N_2O_3$	50.51(50.57)	1.96(1.91)	9.06(9.18)	
XVII	1-NH_2, 3,8-Br_2	317-318	$C_{13}H_8Br_2N_2O$	42.42(42.53)	2.19(2.04)	7.61(7.61)	43.42(43.48) (d)
XVIII	1-NH_2, 3,8-Cl_2	308-309 dec (f)	$C_{13}H_8Cl_2N_2O$	55.94(56.21)	2.89(2.96)	10.04(9.87)	
XIX	1-Cl, 3,8-Br_2	331-332	$C_{13}H_6Br_2ClNO$	40.30(40.23)	1.56(1.53)		9.15(9.33) (b)
							41.25(41.35) (d)
XX	1,3,8-Cl_3	349-350 dec	$C_{13}H_6Cl_3NO$	52.30(52.48)	2.26(2.26)		35.62(35.38) (b)
XXII	3-NO_2, 10-Cl	310-312	$C_{13}H_7ClN_2O_3$	56.85(56.88)	2.57(2.69)	10.20(10.34)	
XXIII	3-NH_2, 10-Cl	304-305 dec	$C_{13}H_9ClN_2O$	63.81(63.95)	3.71(3.82)		
XXIV	3,10-Cl_2	328-329	$C_{13}H_7Cl_2NO$	59.12(59.22)	2.67(2.81)		26.85(26.75) (b)
XXV	10-Cl	270-272	$C_{13}H_8ClNO$	67.99(68.10)	3.51(3.59)		15.44(15.20) (b)
XXVI	1-Cl	279-280 dec	$C_{13}H_8ClNO$	67.99(67.82)	3.51(3.61)		15.44(15.24) (b)

(a) Lit. (6), m.p. 327-328°. (b) X = Cl. (c) Lit. (6), m.p. 328.5-329°; Lit. (7), m.p. 323.5-324.5°. (d) X = Br. (e) Lit. (8), m.p. 356-357° dec. (f) With bath pre-heated at 300°. Without pre-heating the bath the compound melted at 301-302° dec.

rearrangement of 2,7-dihalo-4-nitro-9-oxofluorenes with hydrazoic acid in sulfuric acid (2) (Scheme III). Both XV and XVI, upon reduction and dehalogenation with palladium on carbon and hydrazine hydrate, gave 1-amino-6(5*H*)-phenanthridinone (2), a known compound, thus establishing the route of formation of XV and XVI in the rearrangement reactions.

Rearrangement of 2-nitro-5-chloro-9-oxofluorene (XXI) gave 10-chloro-3-nitro-6(5*H*)-phenanthridinone (XXII). Raney nickel and hydrazine hydrate reduction of the latter compound afforded 3-amino-10-chloro-6(5*H*)-phenanthridinone (XXIII) which was converted to 3,10-dichloro-6(5*H*)-phenanthridinone (XXIV). Compound XXIII was also deaminated to 10-chloro-6(5*H*)-phenahthri-

TABLE II

Ultraviolet Absorptions of Derivatives of 6(5H)-Phenanthridinone (a)

Compound	Substituent(s)	λ max, mμ (ε max)
XXVI	1-Cl	236(49,820), 261(16,640), 300(4,680), 312(b)(4,840), 325(6,520), 338(6.040)
I	2-Cl	230(55,200), 235(59,360), 260(16,600), 269(b)(10,480), 308(b)(5.140), 315(b)(5,660), 328(8,340), 342(7,720)
XXV	10-Cl	232(b)(53,240), 236(57,640), 253(b)(18,480), 262(18,600), 302(b)(5,820), 312(b)(6,460), 327(7,680), 338(b)(6,840)
V	2-Br	231(51,820), 236(56,400), 242(b)(39,980), 260(17,420), 268(b)(11,200), 308(b)(5,220), 315(b)(5,620), 328(8,320), 342(7,840)
VII	4-Br	226(b)(38,860), 232(45,460), 239(42,080), 260(16,080), 276(b)(8,520), 290(b)(3,540), 302(b)(5,060), 308(b)(5,240), 321(8,060), 336(7,380)
(c)	4-I	229(44,180), 233(b)(43,440), 261(15,680), 278(b)(8,280), 290(b)(4,080), 302(5,440), 312(b)(5,440), 323(8,420), 338(7,800)
(c)	4-NH_2	209(37,180), 238(32,640), 246(b)(25,440), 254(b)(18,880), 278(12,560), 308(8,340), 337(b)(3,680)
(c)	4-NO_2	221(41,920), 244(22,600), 248(b)(22,240), 256(21,940), 279(b)(8,760), 300(6,140), 311(6,460), 370(6,200)
(c)	3,8-F_2	225(50,970), 229(b)(47,050), 246(15,430), 256(17,270), 264(b)(10,840), 305(b)(6,870), 311(b)(7,110), 325(8,410), 339(6,440)
II	2,4-Cl_2	236(b)(56,820), 239(58,180), 261(17,780), 276(b)(10,080), 294(b)(3,620), 304(4.980), 316(b)(4,940), 329(7,760), 343(7,400)
(c)	3,8-Cl_2	215(b)(26,920), 226(b)(36,140), 232(38,960), 237(37,480), 245(b)(24,040), 255(b)(14,600), 264(10,380), 278(13,060), 314(7,880), 329(9,720), 344(8,240)
XXIV	3,10-Cl_2	240(43,360), 255(15,840), 264(15,760), 276(b)(10,380), 309(b)(5,300), 316(5,580), 330(7,700), 344(6,660)
VI	2,4-Br_2	210(22,640), 236(b)(59,020), 239(59,940), 262(20,040), 278(b)(9,800), 294(b)(4.060), 305(5,500), 318(b)(5,340), 330(8,460), 344(8,270)
(c)	3,8-Br_2	224(45,600), 232(46,120), 238(b)(44,880), 266(26,600), 272(b)(21,800), 281(18,440), 315(10,340), 330(12,960), 344(11,040)
(c)	2,4-$(NH_2)_2$	219(42,660), 248(32,940), 286(10,560), 312(b)(7.920), 362(6,320)

Compound	Substituent(s)	λ max, mμ (ε max)
(c)	3,8-$(NO_2)_2$	215(b) (29,420), 223(b) (27,700), 246(25,180), 272(b) (13,660), 280(14,540), 309(19,000), 377(9,980)
XXIII	3-NH_2, 10-Cl	224(32,800), 229(32,760), 269(b) (14,560), 286(b) (11,840), 320(11,300), 346(b) (8,000)
III	4-NH_2, 2-Cl	216(34,520), 244(b) (33,440), 247(33,680), 256(b) (22,640), 280(b) (11,120), 309 (8,720), 338(b) (3,840)
IV	4-$NHCOCH_3$,2-Cl	240(53,020), 260(b) (17,480), 295(b) (4,240), 306(5,560), 331(7,680), 344(7,020)
IX	2-NH_2, 4-Br	214(31,660), 235(36,940), 242(39,420), 311(b) (4,420), 360(6,060)
X	4-NH_2, 2-Br	216(39.040), 245(b) (35,880), 248(36,400), 281(b) (12,740), 298(b) (9,720), 309(10,160), 338(b) (4,400)
(c)	2-NH_2, 4-NO_2	224(b) (41,800), 229(45,040), 244(39,240), 265(b) (20, 820), 310(7,880), 455(4,740)
(c)	2-$NHCOCF_3$, 4-NO_2	228(36,560), 253(42,840), 300(b) (7,840), 315(6,400), 392(6,560)
XXII	10-Cl, 3-NO_2	221(34,380), 236(28,740), 268(17,480), 277(16,640), 306(14,220), 360(7,700)
VIII	4-Br, 2-NO_2	226(32,180), 252(21,360), 268(23,600), 278(b) (18,800), 304(11,500), 328(12,360), 338(b) (11,400)
XX	1,3,8-Cl_3	210(b) (26,880), 240(52,040), 248(b) (39, 540), 367(22,560), 281(b) (14,400), 308(b) (6,460), 316(7,020), 330(9,340), 344(8,980)
XII	2,3,8-Cl_3	210(b) (26,720), 227(b) (43,280), 234(49,640), 240(51,940), 248(b) (31,560), 266(23,980), 280(b) (14,800), 320(7,520), 334(11,580), 349(11,020)
XI	2,3,8-Br_3	230(b) (44,800), 238(48,080), 240(48,240), 251(b) (31,480), 268(28,240), 284(17,880), 321(8,040), 335(12,460), 350(12,100)
XIX	1-Cl, 3,8-Br_2	214(27,720), 242(51,200), 268(24,720), 284(b) (16,240), 308(6,980), 316(7,440), 331(10,340), 346(10,100)
XIII	2-Cl, 3,8-Br_2	228(44,300), 234(47,100), 240(46,900), 250(b) (30,140), 268(26,380), 283(17,520), 321(b) (8,080), 335(12,480), 350(12,000)
XIV	2-Br, 3,8-Cl_2	228(b) (43,980), 234(48,560), 240(48,760), 250(32,600), 266(24,860), 279(b) (15,080), 319(7,640), 334(11,600), 349(11,160)
XVII	1-NH_2, 3,8-Br_2	218(41,700), 242(b) (34,320), 348(37,560), 296(16,720), 330(b) (6,920), 348(7,540)
XVIII	1-NH_2, 3,8-Cl_2	213(47,200), 241(b) (34,780), 246(36,440), 294(18,060), 346(7,060)
XV	1-NO_2, 3,8-Br_2	234(52,180), 260(b) (20,300), 279(b) (16,120), 334(b) (9,000), 345(9,620)

Compound	Substituent(s)	λ max, mμ (ε max)
XVI	1-NO_2, 2,8-Cl_2	231(53,890), 258(b)(18, 600), 276(b)(14,280), 332(b)(8,320), 343(8,730)

(a) The absorptions were measured in absolute ethanol and are the average figures of two or three independent measurements. (b) Shoulder. (c) Ref. 13.

dinone (XXV) (Scheme IV). The other possible product from the rearrangement of XXI, 1-chloro-8-nitro-6(5*H*)-phenanthridinone, would have given 1-chloro-6(5*H*)-phenanthridinone (XXVI) after reduction and deamination. However, we prepared XXVI from known 1-amino-6(5*H*)-phenanthridinone, and it is clearly different from XXV as indicated by a depressed mixture melting point. The foregoing rearrangements follow the pattern described and discussed in the preceding paper in this series (2). A number of new halo-6(5*H*)-phenanthridinones as well as other substituted phenanthridinones are presented in Table I.

The ultraviolet absorption pattern of these phenanthridinones, as we found previously (2), is characteristically complex, with the major absorption maximum in the 215-240 mμ region and, in general, with progressively lesser maxima toward the longer wave-lengths (Table II). The halo-6(5*H*)-phenanthridinones have several of these lesser maxima, well-defined, in the range from 300 mμ to 360 mμ. However, when there is, additionally, a chromophore (*e.g.*, nitro) or an auxochrome (*e.g.*, amino) in the 2- or 4-position, there is no longer a well-defined group of lesser peaks, but a more or less overlapping group, or a single broad band. In addition, these latter compounds have a maximum in the 370-460 mμ region.

The infrared absorption bands of the lactam group and of the aromatic ring hydrogens have been assigned and are given in the Experimental section.

All of these compounds have been submitted for antitumor screening and their biological activities will be reported elsewhere.

EXPERIMENTAL

The ultraviolet absorption spectra were run on a Beckman DK-1 recording spectrophotometer and the infrared absorptions were measured in potassium bromide disks on a Beckman IR-5. The melting points above 250° were determined with a Hoover capillary melting point apparatus and are uncorrected. Melting points below 250° were taken on a Fisher-Johns block and are corrected to standards. Analyses were done by A. Bernhardt, Elbach über Engleskirchen, West Germany, and by Schwarzkopf Laboratories, Woodside, N. Y.

2-Chloro-6(5*H*)-phenanthridinone (I) (6).

6(5*H*)-Phenanthridinone (19.5 g., 0.1 mole), prepared either from 9-oxofluorene by a Schmidt reaction (11) or from the rearrangement of 9-oxofluorene oxime in polyphosphoric acid (12,13), was dissolved in dimethylformamide (500 ml.) by heating. To the stirred warm solution (~60°) *N*-chlorosuccinimide (Aldrich Chemical Co.) (15 g., 0.11 mole) was added in several portions. The mixture was stirred for 10 minutes and then allowed to stand at room temperature for 24 hours. The white needles were separated by filtration, washed with water, and dried, giving 16.2 g. (70%), m.p. 322-323°.

One recrystallization from acetic acid gave the analytical sample. A second crop (2.8 g., 12%) was obtained by water dilution of the dimethylformamide filtrate and recrystallization from acetic acid; ir cm^{-1}, ν max (-CONH-)3170, 1660; (one isolated ring hydrogen) 867; (two adjacent hydrogens) 826; (four adjacent hydrogens) 772.

2,4-Dichloro-6(5*H*)-phenanthridinone (II).

(a) From 6(5*H*)-Phenanthridinone and Chlorine.

6(5*H*)-Phenanthridinone (7.8 g., 0.04 mole) was suspended in acetic acid (500 ml.) containing anhydrous ferric chlorice (2 g.). To the stirred suspension a solution of chlorine (7.1 g., 0.01 mole) in acetic acid (100 ml.) was added dropwise over a period of 30 minutes. After all the chlorine solution had been added the reaction mixture was stirred at 50-55° for 2 hours, cooled, and diluted with water. The product was collected on a filter, washed with water, and recrystallized from acetic acid giving 6.3 g. (60%) of shiny white leaflets; ir cm^{-1}, ν max (-CONH-) 3220, 1660; (one isolated ring hydrogen) 858; (four adjacent hydrogens) 772.

(b) From 2-Chloro-6(5*H*)-phenanthridinone (I) and *N*-Chlorosuccinimide.

2-Chloro-6(5*H*)-phenanthridinone (I) (4.6 g., 0.02 mole) was dissolved in hot dimethylformamide (100 ml.). *N*-Chlorosuccinimide (5.3 g., 0.04 mole) was then added in one portion to the hot solution (~75°). The mixture was heated on a steam bath with occasional shaking for 2 hours, cooled, and diluted with water. The solid was separated by filtration and recrystallized twice from acetic acid giving 2.5 g. (47%) of the product. No melting point depression was observed when the product was mixed with the compound obtained in (a), and the infrared spectra of the two products are identical.

(c) From 2-Chloro-4-amino-6(5*H*)-phenanthridinone (III).

2-Chloro-4-amino-6(5*H*)-phenanthridinone (III) (1.2 g., 0.005 mole), prepared below, and concentrated sulfuric acid (30 ml.) were mixed and stirred while nitrosyl sulfuric acid, prepared from sodium nitrite (0.7 g., 0.01 mole) and concentrated sulfuric acid (5 ml.), was added in one portion, and the reaction mixture was stirred at room temperature for 4 hours. Crushed ice (100 g.) and a solution of freshly prepared cuprous chloride (5 g.) in concentrated hydrochloric acid (20 ml.) were added. This mixture was heated at 60-65° (bath temperature) for 30 minutes, and then diluted with water. The precipitate was collected, washed with some concentrated hydrochloric acid and then with water and dried. The yield was 1.2 g. (91%). Recrystallization from acetic acid gave shiny white blades. The melting point, the mixture

melting point with the compound prepared in (a), and the infrared spectra showed that the two compounds are identical.

2-Chloro-4-amino-6(5*H*)-phenanthridinone (III).

2-Chloro-4-nitro-6(5*H*)-phenanthridinone (6) (5.5 g., 0.02 mole) and stannous chloride dihydrate (50 g.) were mixed thoroughly by grinding. The mixture was boiled with concentrated hydrochloric acid (350 ml.) and 95% ethanol (30 ml.), with stirring, for 30 minutes, cooled, and treated with 2 *N* sodium hydroxide (800 ml.). The amine was filtered, washed well with water, and dried giving 4.7 g. (96%), m.p. 326-327° dec. An analytical sample was prepared by recrystallizing the product from acetone.

2-Chloro-4-acetamido-6(5*H*)-phenanthridinone (IV).

A mixture of acetic anhydride (1.5 g., 0.015 mole) and acetic acid (5 ml.) was added dropwise over a 15-minute period to a warm solution of III (2.5 g., 0.01 mole) in acetic acid (200 ml.). The reaction mixture was stirred for 1 hour, heated to 85° and cooled. The lustrous white needles were collected on a filter, washed with water, and dried to give 2.9 g. (100%). Recrystallization from acetic acid gave an analytical sample.

2-Bromo-6(5*H*)-phenanthridinone (V) (6).

This compound was prepared with *N*-bromosuccinimide in a similar manner as in the preparation of the chloro compound I; an 80% yield of a crude product was obtained. Recrystallization from acetic acid gave white needles; ir cm^{-1}, ν max (-CONH-) 3175, 1660; (one isolated ring hydrogen) 870; (two adjacent hydrogens) 816; (four adjacent hydrogens) 772.

2,4-Dibromo-6(5*H*)-phenanthridinone (VI) (8).

(a) From 2-Bromo-4-amino-6(5*H*)-phenanthridinone (X).

2-Bromo-4-amino-6(5*H*)-phenanthridinone (X) (1.5 g., 0.005 mole), prepared below, in concentrated sulfuric acid (20 ml.) and water (10 ml.), was diazotized at 5-10° with a saturated aqueous solution of sodium nitrite (0.5 g.). The diazotization mixture was stirred at 0-5° for 1 hour and then a refrigerated solution of cuprous bromide (4 g., 0.014 mole) in 48% hydrobromic acid (7 ml.) was added all at once. The mixture was continuously stirred without heating for 1 hour, then heated on a steam bath for another hour and cooled. After dilution with water, the solid was collected by filtration, treated with 9 *N* hydrochloric acid (80 ml.) and collected. It was washed successively with water, concentrated hydrochloric acid, and water, then dried and recrystallized from acetic acid giving 1.6 g. (91%) of lustrous white needles; ir cm^{-1}, ν max (-CONH-) 3240, 1670; (one isolated ring hydrogen) 890; (four adjacnet hydrogens) 774.

(b) From 2-Amino-4-bromo-6(5*H*)-phenanthridinone (IX).

The amine (IX) (0.2 g.), prepared below, was diazotized as described in the preceding procedure in 50% sulfuric acid (8 ml.) with sodium nitrite (0.1 g.), and the diazotization mixture was treated with a solution of cuprous bromide (1 g.) in 48% hydrobromic acid (2 ml.). The crude product was recrystallized from acetic acid and then chromatographed through a short alumina column with benzene as eluent giving snow white needles (0.05 g.). Melting point and mixture melting point determinations, as well as the infrared spectra, showed that this product and the compound obtained in (a) are identical.

(c) From 4-Bromo-6(5*H*)-phenanthridinone (VII).

By a procedure similar to IIb, this dibromo compound was obtained in 86% yield, using 1.2 equivalents of *N*-bromosuccinimide and 1 equivalent of VII, Recrystallization from acetic acid gave shiny needles. The product and the compound prepared in (a) are identical as shown by undepressed mixture melting point and infrared spectra.

(d) From 2-Bromo-6(5*H*)-phenanthridinone (V).

Compound V was converted to VI by using 2 equivalents of *N*-bromosuccinimde.

4-Bromo-6(5*H*)-phenanthridinone (VII).

A procedure similar to VIa was used in converting 4-amino-6(5*H*)-phenanthridinone (13) to VII in 62% yield. Chromatography through a short alumina column with benzene as eluent gave shiny rhombic crystals; ir cm^{-1}, ν max (-CONH-) 3280, 1640; (three adjacent hydrogens) 762; (four adjacent hydrogens) 750.

2-Nitro-4-bromo-6(5*H*)-phenanthridinone (VIII).

Compound VII (4.9 g., 0.018 mole) was added in small amounts to a stirred mixture of acetic acid (60 ml.) and 90% nitric acid (60 ml.) at 40-45° within 5 minutes. After all the bromo compound had been added the reaction solution was continuously stirred at 45-50° for 10 minutes and cooled. The product precipitated as lustrous needles which were collected, washed with a little acetic acid then with water and dried, to yield, 3.4 g. (60%), m.p. 324-326°. An analytical sample was prepared by recrystallization of the product from acetic acid.

2-Amino-4-bromo-6(5*H*)-phenanthridinone (IX).

The above nitro compound (VIII) was reduced with excess stannous chloride dihydrate and concentrated hydrochloric acid as described in the preparation of III, to give a 92% yield of IX. Recrystallization from 95% ethanol gave glistening yellowish-white needles.

2-Bromo-4-amino-6(5*H*)-phenanthridinone (X).

2-Bromo-4-nitro-6(5*H*)-phenanthridinone (6) (16 g.), toluene (1000 ml.), 95% ethanol (1000 ml.), 85% hydrazine hydrate (20 ml.) and Raney nickel (~ 0.5 g.) were mixed and boiled for 30 minutes and then more hydrazine hydrate (10 ml.) and Raney nickel (~ 0.2 g.) were added. Boiling was continued for 20 minutes and sufficient ethanol was added to the reaction mixture to bring the organic solids into solution. It was filtered hot and the filtrate was concentrated to obtain 10.9 g. (75.5%) of the product. Recrystallization from 95% ethanol gave white needles.

2,3,8-Tribromo-6(5*H*)-phenanthridinone (XI).

(a) From 3,8-Dibromo-6(5*H*)-phenanthridinone (13).

To a warm solution of 3,8-dibromo-6(5*H*)-phenanthridinone (13) (7.1 g., 0.02 mole) in dimethylformamide (150 ml.), *N*-bromosuccinimide (3.9 g., 0.022 mole) was added in several portions over a period of 5 minutes. The solution was heated on a steam bath with occasional shaking for 30 minutes and then set aside overnight. The precipitate was collected on a filter, washed with some dimethylformamide and then with water and dried to yield 5.6 g. of XI (65%), m.p. $> 360°$. Recrystallization from acetic acid gave white needles; ir cm^{-1}, ν max (-CONH-) 3200, 1670; (one isolated ring hydrogen) 875; (two adjacent hydrogens) 820.

(b) From 2-Amino-3,8-dibromo-6(5*H*)-phenanthridinone (2).

The amine (2) was diazotized and then reacted with cuprous bromide in the same manner as described in IIc. A yield of 92% was obtained, m.p. $> 360°$. Recrystallization from acetic acid gave fibrous needles. The products from (a) and (b) are identical as shown by their infrared spectra.

2,3,8-Trichloro-6(5*H*)-phenanthridinone (XII).

(a) From 3,8-Dichloro-6(5*H*)-phenanthridinone (13).

Compound XII was prepared from the dichloro compound (13) and *N*-chlorosuccinimide in a manner similar to XIa, giving a 77% yield, m.p. >360°. Recrystallization from acetic acid gave white needles; ir cm^{-1}, ν max (-CONH-) 3150, 1670; (one isolated ring hydrogen) 870; (two adjacent hydrogens) 821.

(b) From 2-Amino-3,8-dichloro-6(5*H*)-phenanthridinone (2).

2-Amino-3,8-dichloro-6(5*H*)-phenanthridinone (2) (1.4 g., 0.005 mole) was diazotized at 25° in a mixture of acetic acid (35 ml.) and concentrated sulfuric acid (25 ml.) with nitrosyl sulfuric acid. The latter was prepared from sodium nitrite (1 g.) and sulfuric acid (5 ml.) at 40-42°. After 4 hours of stirring the diazotization mixture was diluted with crushed ice (50 g.) and then treated at 50-55° with freshly prepared cuprous chloride (1.5 g.) in 10% hydrochloric acid (40 ml.). This was stirred for 30 minutes, heated to 55°, diluted with water, and the product was isolated, 1.1 g. (73.5%), m.p. > 360°. The infrared spectrum of this product and that of the compound obtained in (a) are identical.

2-Chloro-3,8-dibromo-6(5*H*)-phenanthridinone (XIII).

(a) From 3,8-Dibromo-6(5*H*)-phenanthridinone (13).

A mixture of the dibromo compound (13) and *N*-chlorosuccinimide was reacted in a manner similar to XIa giving a 92% yield of XIII. Two recrystallizations from acetic acid gave an analytically pure product; ir cm^{-1}, ν max (-CONH-) 3200, 1670; (one isolated ring hydrogen) 876; (two adjacent hydrogens) 820.

(b) From 2-Amino-3,8-dibromo-6(5*H*)-phenanthridinone (2).

In a procedure similar to IIc, compound XIII was prepared from this amine (2) in 95% yield. The product was recrystallized from acetic acid giving small needles. The product and the compound prepared by procedure (a) are identical as shown by their infrared spectra.

2-Bromo-3,8-dichloro-6(5*H*)-phenanthridinone (XIV).

(a) From 3,8-Dichloro-6(5*H*)-phenanthridinone (13).

3,8-Dichloro-6(5*H*)-phenanthridinone (13) was brominated as described in procedure XIa. The product (41% yield), m.p. > 360°, was recrystallized from acetic acid giving thin white needles; ir cm^{-1}, ν max (-CONH-) 3180, 1670; (one isolated ring hydrogen) 878; (two adjacent hydrogens) 821.

(b) From 2-Amino-3,8-dichloro-6(5*H*)-phenanthridinone (2).

The aminophenanthridinone (2) was converted to XIV as described in the preparation of XI, giving 0.6 g. (87%) of fibrous needles (from acetic acid), m.p. > 360°, identical with the compound obtained in (a) as indicated by the infrared spectra.

1-Nitro-3,8-dibromo-6(5*H*)-phenanthridinone (XV).

A solution of 2,7-dibromo-4-nitro-9-oxofluorene (4) (19.2 g., 0.05 mole) in concentrated sulfuric acid (800 ml.) was cooled in ice while a saturated aqueous solution of sodium azide (4.6 g., 0.07 mole) was introduced dropwise with stirring over a period of 2.5 hours. The reaction mixture was stirred further in the ice for an additional 2.5 hours and the cooling bath was removed. The mixture was stirred again for 40 hours, diluted with icewater, and the solid, 19.2 g. (96%), m.p. 330-339°, was recrystallized from acetic acid giving small light yellow needles.

1-Nitro-3,8-dichloro-6(5*H*)-phenanthridinone (XVI).

In the same manner as described in the preceding paragraph, 14.7 g. of 2,7-dichloro-4-nitro-9-oxofluorene (4) was converted to 15.1 g. (97%) of XVI, m.p. 330-338°; recrystallization from acetic acid gave small needles.

Reduction-Dehalogenation of XV and XVI to 1-Amino-6(5*H*)-phenanthridinone (2,14).

Compound XV (0.5 g.) was refluxed for 7.5 hours in 95% ethanol (100 ml.) with 5% palladium on carbon (0.05 g.) and 85% hydrazine hydrate (2 ml.) and filtered hot. Evaporation of the filtrate gave 0.2 g. (85%) of 1-amino-6(5*H*)-phenanthridinone (2) as indicated by the melting point, mixture melting point with an authentic sample, and infrared spectra. Compound XVI (0.5 g.) gave 0.25 g. (80%) of 1-amino-6(5*H*)-phenanthridinone.

1-Amino-3,8-dibromo-6(5*H*)-phenanthridinone (XVII).

A mixture of XV (4 g., 0.01 mole), toluene (500 ml.), 95% ethanol (500 ml.), 85% hydrazine hydrate (5 ml.) and Raney nickel (~ 0.2 g.) was slowly heated to boiling and continuously boiled with frequent shaking and addition of small amounts (about 0.1 g. portions) of Raney nickel for 30 minutes. A second portion of 85% hydrazine hydrate (3 ml.) was then added, and the mixture was boiled for another 30 minutes and filtered. Evaporation of the filtrate gave the amine, 2.9 g. (78%), as lustrous white rods.

1-Amino-3,8-dichloro-6(5*H*)-phenanthridinone (XVIII).

As described in the preceding paragraph, compound XVI was reduced to the amine, (90%), which was crystallized as stubby bars from toluene-ethanol.

1-Chloro-3,8-dibromo-6(5*H*)-phenanthridinone (XIX).

Diazotization of XVII (2.4 g.) with nitrosyl sulfuric acid as described previously, and reaction with freshly prepared cuprous chloride gave, after recrystallization from acetic acid and 95% ethanol, 1.3 g. (52%) of small crystals. Chromatography through a short alumina column with hot benzene as eluent gave snow-white needles; ir cm^{-1}, ν max (-CONH-) 3205, 1660; (one isolated ring hydrogen) 873; (two adjacent hydrogens) 826.

1,3,8-Trichloro-6(5*H*)-phenanthridinone (XX).

Diazotization of compound XVIII and reaction with cuprous chloride gave the product (93% yield). Recrystallization twice from acetic acid gave white prisms; ir cm^{-1}, ν max (-CONH-) 3175, 1670; (one isolated ring hydrogen) 878; (two adjacent hydrogens) 828.

2-Nitro-5-chloro-9-oxofluorene (XXI).

2-Nitro-5-amino-9-oxofluorene (15) (4.8 g., 0.02 mole) was diazotized at 5-10° in 30% hydrochloric acid (125 ml.) with a saturated aqueous solution of sodium nitrite (2.1 g., 0.03 mole). After 1 hour of stirring at 0-5° a solution of freshly prepared cuprous chloride (~ 5 g.) in concentrated hydrochloric acid (20 ml.) was added. The mixture was stirred at room temperature overnight and then heated on a steam bath for 15 minutes and diluted with water. The solid was collected and chromatographed through an alumina column with benzene as eluent giving 3.4 g. (65.5%) of small yellow needles, m.p. 188-188.5°; uv λ max (ethanol) 232 (shoulder) (ϵ, 20,040), 240 (ϵ 21,040), 282 (ϵ, 24,960), 310 (ϵ, 12,020), 322 (shoulder) (ϵ, 7,320), 374 mμ (ϵ, 1,780).

Anal. Calcd. for $C_{13}H_6ClNO_3$: C, 60.13; H, 2.33; N, 5.39; Cl, 13.66. Found: C, 60.03; H, 2.32; N, 5.53; Cl, 13.71.

3-Nitro-10-chloro-6(5*H*)-phenanthridinone (XXII).

The above chloro-nitrofluorenone (XXI) (2.6 g., 0.01 mole)

was reacted with sodium azide (1.5 g., 0.023 mole) in concentrated sulfuric acid (30 ml.) in the same way as described in the preparation of XV. The crude product, 2.6g. (96%), was recrystallized from acetic acid giving yellowish needles.

3-Amino-10-chloro-6(5*H*)-phenanthridinone (XXIII).

Compound XXII was reduced with Raney nickel and 85% hydrazine hydrate, in the same way as in the preparation of XVII, giving a 92% yield of needles. Two recrystallizations from 95% ethanol gave an analytical sample as thin white needles.

3,10-Dichloro-6(5*H*)-phenanthridinone (XXIV).

Amine XXIII was converted to XXIV by the reaction described in IIc. The crude product (92% yield) was recrystallized first from acetic acid, then from toluene, giving light yellow crystals; ir cm^{-1}, ν max (-CONH-) 3205, 1670; (one isolated ring hydrogen) 868; (two adjacent hydrogens) 826; (three adjacent hydrogens) 770.

10-Chloro-6(5*H*)-phenanthridinone (XXV).

Amine XXIII (3.4 g., 0.014 mole) in 6 *N* hydrochloric acid (150 ml.) was diazotized at 0-5° with a saturated aqueous solution of sodium nitrite (2 g., in excess). The mixture was stirred at 0° for 1 hour and then urea (0.9 g.) was added. After brief stirring, 50% hypophorphorous acid (60 ml.) was added all at once to the diazotization mixture, which was stirred in an ice bath for 30 minutes, and at ambient temperature for several hours; it was then diluted with water. The solid was filtered off, washed with water and dried giving 3.1 g. (97%) of a crude product. One recrystallization from acetic acid and two recrystallizations from 95% ethanol gave an analytical sample as orange crystals; ir cm^{-1}, ν max (-CONH-) 3170, 1660; (three adjacent hydrogens) 790; (four adjacent hydrogens) 760.

1-Chloro-6(5*H*)-phenanthridinone (XXVI).

1-Amino-6(5*H*)-phenanthridinone (2) (10.5 g., 0.05 mole) was converted to XXVI through a Sandmeyer reaction as described in (b) in the preparation of XII with the amounts of reagents proportionally increased. The product was recrystallized from acetic acid-water giving 7 g. (61%) of grayish crystals. A second recrystallization (ethanol) gave off-white stubby rods. A mixture of XXV and XXVI melted below the m.p. of the lower of the two (see Table I); ir cm^{-1}, ν max (-CONH-) 3170, 1660; (three adjacent hydrogens) 790; (four adjacent hydrogens) 762. In addition the uv spectra of XXV and XXVI have appreciable differences.

Attempted Bromination of 6(5*H*)-Phenanthridinone with 48% Hydrobromic Acid in Dimethyl Sulfoxide

6(5*H*)-Phenanthridinone (2 g., 0.01 mole) was dissolved in dimethyl sulfoxide (50 ml.). To the solution 48% hydrobromic acid (3.6 ml., ~0.03 mole) was added in one portion. The mixture was heated under reflux at 105-110° for 1 hour and cooled. The suspension was diluted with water and the solid collected giving 2 g. (100% recovery) of the unreacted 6(5*H*)-phenanthridinone, m.p. and mixture m.p. 288-289° (lit. m.p. 285-286°) (16).

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