756. *Naphthaquinone Chemistry. Part III.*[1] *New Derivatives of* 1,2- *and* 1,4-*Naphthaquinone.*

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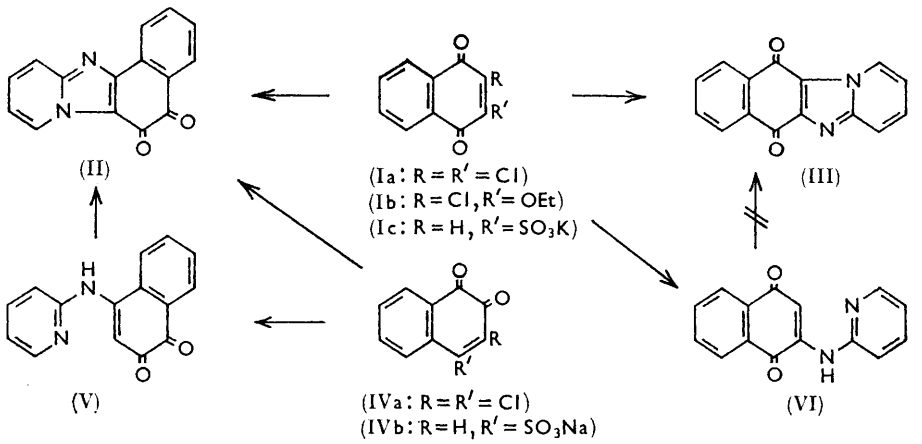
Various substituted naphthaquinones were prepared, often by nucleophilic displacement reactions on chloro- or sulpho-quinones. The convenient preparation of three quinone diazo-oxides is described.

In Parts I and II [1] the preparation was described of the quinones either (II) or (III), depending upon the nature of R′ in the quinones (Ia) and (Ib). The reaction of either quinone (Ia) or (IVa) with 2-aminopyridine yields exclusively (II), whilst (Ib) gives exclusively (III).



At room temperature, sodium 1,2-naphthaquinone-4-sulphonate (IVb) reacts with 2-aminopyridine in water to give (V), as reported by Carrara and Bonacci [2] [who, however, give the melting point as 225—228° (decomp.)]. If, however, the reaction mixture is boiled, product (II) is produced; this is the most convenient, although not the most efficient method of preparing it. Also, it was found that potassium 1,4-naphthaquinone-2-sulphonate yielded the isomeric compound (VI). In this instance, however, cyclization to (III) could not be induced. While quinone (IVb) reacted with 2-aminopyrazine to give a mixture of the cyclic and open homologues of (II) and (V), it did not react with 2-aminopyrimidine under these conditions, and the *para*-isomer (Ic) failed to react with either 2-aminopyrazine or 2-aminopyrimidine. Both quinones (Ic) and (IVb) reacted with 3-aminopyridine, and (IVb) yielded a normal product with 4-aminopyridine, but (Ic) gave a dark blue, high-melting insoluble product which could not be purified for analysis. Both

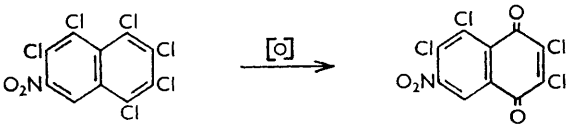
[1] Part II, Mosby, *J. Org. Chem.*, 1961, **26**, 1316.
[2] Carrara and Bonacci, *Chimica e Industria (Milan)*, 1944, **26**, 75.

salts reacted with benzhydrazide, and (IVb) (but not Ic) gave a product with 1,1-dimethylhydrazine, but both were decomposed by treatment with hydrazine. The products of these reactions of (Ic) and (IVb) with various nucleophiles in aqueous solution are listed in Tables 1 and 2.

Various new naphthaquinones are listed in Table 3.

Fries and Ochwat [3] reported the reaction of 2,3-dichloronaphthaquinone with sodium acetate in ethanol to yield 2-acetoxy-3-chloronaphthaquinone. Fieser [4] and Brown used this same method to prepare 2-alkoxy-3-chloronaphthaquinones, and we have confirmed that the resulting product is indeed 2-chloro-3-ethoxynaphthaquinone, not the acetoxy-derivative. The methoxy-homologue was obtained similarly. Acetylation of 2-chloro-3-hydroxynaphthaquinone afforded the 2-acetoxy-compound.

Oxidation of perchloronaphthalene with fuming nitric acid in a sealed tube was reported [5] to yield hexachloronaphthaquinone. However simply refluxing the mixture afforded a 70% yield of the quinone. Hexachloronaphthaquinone and 2,3-dichloronaphthaquinone were used to prepare the series of amino- and azido-naphthaquinones in Tables 3 and 4.



(VII) (VIII)

Treatment of 2,3-dichloro-5-nitronaphthaquinone [6] with ammonia gave a mixture of amines (compounds Nos. 29 and 30, Table 3) with two distinct crystal types. These were separated by hand, and acetylated. It is not clear which product corresponds with which structure, hence the ambiguous entries in the Table.

Oxidation of the known 2,3-diethoxycarbonyl-1,4-dihydroxynaphthalene [7] with lead

TABLE 1.

4-Substituted 1,2-naphthaquinones.

Cpd.	4-Substituent	Yield (%) pure	M. p.	Found C	Found H	Found N	Found O	Calculated C	Calculated H	Calculated N	Calculated O
1	2-Pyridylamino-	41	236·5—237·0°	71·9	4·00	11·2	12·6	72·0	4·00	11·2	12·8
2	3-Pyridylamino-	36	242—244	71·9	4·01	11·2	12·8	,,	,,	,,	,,
3	4-Pyridylamino-	32	231—232	71·9	4·04	11·1	12·8	,,	,,	,,	,,
4	4-(1-Methylpyridinium)-amino benzene sulphonate	42	218—219	62·3	4·29	6·77	18·7	62·6	4·26	6·64	18·9
5	N:C<(CH:CH)$_2$>NMe	14	278—279	72·0	4·90	9·85	12·1	72·7	4·55	10·6	12·1
6	2-Pyrazinylamino-	20	254·0—255·5	67·1	3·60	16·7	12·6	67·0	3·59	16·7	12·8
7	NH·NH·Bz	41	280—281	69·7	4·44	9·56	16·4	69·9	4·11	9·59	16·4
8	NH·NMe$_2$	21	138·0—138·5	66·5	5·62	12·9	14·8	66·7	5·55	12·9	14·8
9	4-Azido	25	d. 126	60·2	2·68	21·0	16·1	60·3	2·51	21·1	16·1

[1] Crystallized from dichlorobenzene or nitromethane. Carrara and Bonacci (ref. 2) give m. p. 225—228 (decomp.). [2] Crystallized from glycol diacetate. [3] Crystallized from glycol diacetate. [4] Obtained by quaternizing (3) with methyl benzenesulphonate. Crystallized from methanol. [5] Prepared from (4) by treatment with aqueous sodium hydroxide. Crystallized from nitromethane. [6] Crude reaction product was extracted with warm pyridine, diluted with water, and filtered. The filtrate was acidified with acetic acid and the resulting precipitate was crystallized from acetic acid. [7] Crystallized from acetic acid. [8] Crystallized from nitromethane. [9] Chromatographed in ethyl acetate solution upon acid washed alumina. Compound is photosensitive.

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[3] Fries and Ochwat, *Ber.*, 1923, **56**, 1291.
[4] Fieser and Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 3609.
[5] Schvemberger and Gordon, *J. Gen. Chem.*, 1932, **2**, 921.
[6] Fries, Pense, and Peeters, *Ber.*, 1928, **61**, 1395; Ger. Pat. 468,507; *Friedländer*, 1931, **16**, 520.
[7] Schwerin, *Ber.*, 1894, **27**, 104; Homeyer and Wallingford, *J. Amer. Chem. Soc.*, 1942, **64**, 798.

tetra-acetate readily gave 2,3-diethoxycarbonylnaphthaquinone. Treatment of this ester with ammonia afforded the cyclic imide (compound 28, Table 3). Condensation of diethyl phthalate with succinonitrile produced, after oxidation, 2,3-dicyanonaphthaquinone (compound 26, Table 3). Attempts to obtain this nitrile by displacement reactions of various metal cyanides upon dichloronaphthaquinone were not successful.

TABLE 2.

N-Substituted 2-amino-1,4-naphthaquinones.

Cpd.	*N*-Substituent	Yield (%) pure	M. p.	Found C	Found H	Found N	Found O	Calculated C	Calculated H	Calculated N	Calculated O
10	2-Pyridyl	20	200·5—201·5°	71·6	4·24	10·8	12·5	72·0	4·00	11·2	12·8
11	3-Pyridyl	29	247 (Inst.)	72·0	3·99	11·2	12·9	,,	,,	,,	,,
12	NHBz	27	228—229 d.	69·7	4·33	9·54	16·3	69·7	4·44	9·56	16·4

[10] Crystallized from *o*-dichlorobenzene. [11] Crystallized from glycol diacetate. [12] Crystallized from acetic acid.

TABLE 3.

Di- and tri-substituted naphthaquinones.

Cpd.	Substituent at position 2	3	5	Yield (%) pure	M. p.	Found C	Found H	Found N	Found O	Calc. C	Calc. H	Calc. N	Calc. O
13	OMe	Cl	H	89	148—149°	59·2	2·90	15·8	21·7	59·3	3·14	15·9	21·6
14	OAc	Cl	H	54	142·5—143·5	57·5	2·41	14·0	25·2	57·5	2·79	14·2	25·5
15	OMe	NH_2	H	50	142·7—143·2	64·7	4·47	6·81	23·9	65·0	4·44	6·91	23·7
16	OMe	N_3	H	17	93—94 d.	58·7	3·07	18·8	19·0	57·7	3·06	18·4	21·0
17	NAc_2	Cl	H	40	160—161	57·3	3·56	4·71	12·4 (Cl)	57·6	3·43	4·80	12·2 (Cl)
18	NH·Ac	OCH_3	H	65	183—184	63·7	4·59	5·77	—	63·7	4·50	5·72	—
19	NH·Ac	N_3	H	55	d. ~200	56·2	2·92	21·8	18·8	56·3	3·11	21·9	18·8
20	NAc_2	N_3	H	69	141—142 d.	56·3	3·42	18·7	21·6	56·4	3·35	18·8	21·5
21	NHAc	NHAc	H	77	248·5—251·0 d.	61·7	4·24	10·2	23·6	61·8	4·40	10·3	23·5
22	NH·NHBz	NHAc	H	40	209·5—210·5	64·9	4·20	12·2	18·3	65·3	4·30	12·0	18·3
23	NH·NH·Bz	NAc_2	H	16	195—196 d.	64·5	4·25	10·7	—	64·5	4·35	10·8	—
24	OH	N_3	H	57	121° d. (Inst.)	55·8	2·52	19·4	22·3	55·8	2·32	19·5	22·3
25	OH	CN	H	12	190—193 d.	66·8	3·07	—	24·5	66·4	2·51	—	24·5
26	CN	CN	H	4·8	272·0—273·5	69·2	1·81	13·9	15·3	69·3	1·92	13·5	15·4
27	CO_2Et	CO_2Et	H	85	53·7—54·7	63·6	4·52	—	31·7	63·6	4·64	—	31·7
28	2 + 3 = CO·NHCO		H	21	131·2—132	63·5	2·45	6·11	28·0	63·5	2·20	6·17	28·2
29	Cl (or NH_2)	NH_2 (or Cl)	NO_2	10	266·5—267·2	47·5	1·92	11·2	14·2 (Cl)	47·5	1·98	11·1	14·0 (Cl)
30	NH_2 (or Cl)	Cl (or NH_2)	NO_2	14	244·0—245·5	47·4	2·05	11·1	14·2 (Cl)	,,	,,	,,	,,
31	Cl (or NHAc)	NHAc (or Cl)	NO_2	90	234·5—235·5	49·2	2·17	10·1	12·3 (Cl)	48·9	2·38	9·53	12·0 (Cl)
32	NHAc (or Cl)	Cl (or NHAc)	NO_2	82	231·5—232·5	49·0	2·75	9·85	12·2	,,	,,	,,	,,
33	NHAc	NHAc	NO_2	34	239—240 d.	52·8	3·36	13·0	—	53·0	3·47	13·2	—
34	N_3	N_3	NO_2	64	121—122 d.	42·1	1·03	34·1	22·2	42·1	1·05	34·4	22·4
35	N_3	N_3	NH_2	—	134 d.	46·6	1·63	37·6	12·8	47·1	1·96	38·4	12·6
36	NH_2	NH_2	NH_2	11	~260 d.	58·9	4·09	20·0	—	59·1	4·43	20·7	—
37	N_3	N_3	NHAc	74	130—131 d.	48·7	2·30	32·5	—	48·5	2·38	33·0	—

[13] Prepared from (Ia) and sodium acetate in methanol. [14] Obtained from 2-chloro-3-hydroxynaphthaquinone, acetic anhydride, and pyridine. Crystallized from ethyl acetate, or chromatographed in ethyl acetate on acid-washed alumina. [15] Obtained by vatting (16) followed by air-oxidation. Chromatographed in benzene on acid-washed alumina, developing with 1 : 4 ethyl acetate–benzene. [16] Prepared from (13) and sodium azide in dimethylformamide. Some 2,3-bisazidonaphthoquinone is also formed. Crystallized from ethyl acetate–cyclohexane. [17] Obtained by heating the amine with excess of acetic anhydride and a drop of sulphuric acid. Recrystallized twice from ethanol. [18] From the reaction of sodium methoxide on 2-acetamido-3-chloronaphthaquinone. Crystallized from methanol. [19] Obtained from the acetamido-chloro-compound by reaction with sodium azide in dimethylformamide. Crystallized from ethyl acetate. [20] From (17) and sodium azide in dimethylformamide. Crystallized from ethyl acetate–ligroin. [21] Obtained by acetylation of 2-acetamido-3-aminonaphthoquinone. Crystallized from ethyl acetate, then from nitromethane. [22] Prepared by treating 2-acetamido-3-chloronaphthaquinone with benzhydrazide in dimethylformamide. Crystallized from nitromethane. [23] Prepared in the same way as (22), but from (17). Crystallized from nitromethane. [24] Obtained from (XI) by reaction with sodium azide in dimethylformamide. Crystallized from ethyl acetate. [25] From (XI) and sodium and cuprous cyanides in ethanol. Crystallized from ethyl acetate. [26] Synthesized by the Dieckmann condensation of ethyl phthalate with succinonitrile and oxidation of the quinol with ferric chloride. [27] Obtained by oxidation of the quinol[7] with lead tetra-acetate in toluene. Crystallized from cyclohexane. [28] From the treatment of (27) with ammonium hydroxide. Chromatographed in ethyl acetate upon acid-washed alumina. [29] Prepared along with (30) by treating 2,3-dichloro-5-nitronaphthaquinone [6] in ethanol with ammonia. Crystallized the mixture from nitromethane and separated the two crystal types by hand. [31] Obtained by acetylating (29). [32] Obtained by acetylating (30). [33] The mixture of (29) and (30) was acetylated and the mixed acetamido-chloro-nitronaphthoquinones was treated with ammonia in nitrobenzene at 135—145°. The resulting mixture of amines was acetylated, and the crude product was crystallized from acetonitrile, methanol, or acetic acid. [34] From 2,3-dichloro-5-nitronaphthaquinone and sodium azide in dimethylformamide. Crystallized from ethyl acetate. [35] Prepared by treating 5-amino-2,3-dichloronaphthaquinone [6] with sodium azide in dimethylformamide. [36] Obtained by vatting (34), followed by air-oxidation and crystallization from nitromethane. [37] Prepared by the reaction of 5-acetamido-2,3-dichloronaphthaquinone (Wilbur and Day, *J. Org. Chem.*, 1960, **25**, 753) with sodium azide in dimethylformamide. Crystallized from nitromethane.

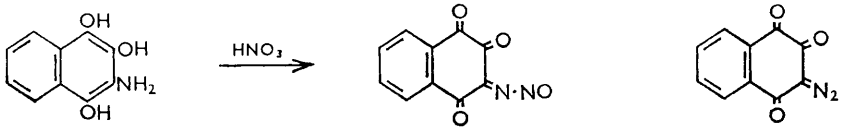
TABLE 4.

5,6,7,8-Tetrachloro-1,4-naphthaquinones; products from hexachloronaphthaquinone.

Cpd.	Subst. at position 2	3	Yield (%) pure	M. p.	Found C	H (Cl)	N (Cl)	O	Calc. C	H (Cl)	N (Cl)	O
38	OEt	Cl	50	156—160° d.	38·1	1·56	48·1 (Cl)	12·6	38·4	1·34	47·4 (Cl)	12·8
39	NH_2	Cl	80	227·0—228·0	35·0	0·76	4·14	9·56	34·7	0·58	4·06	9·28
40	NHAc	Cl	63	235·0—236·2 d.	36·6	0·98	3·68	12·7	37·2	1·06	3·62	12·4
41	NAc_2	Cl	59	187·5—189·0	38·9	1·50	3·37	15·0	39·2	1·40	3·26	14·9
42	NH_2	NH_2	46	264·0 (inst.)	36·8	0·87	8·56	43·8 (Cl)	36·8	1·23	8·59	43·6 (Cl
43	NHAc	NH_2	67	271·0—272·0	38·9	1·94	7·41	37·9 (Cl)	39·2	1·66	7·61	38·6 (Cl)
44	NHAc	NHAc	51	d. ~ 290	41·0	2·00	6·84	15·8	41·0	1·95	6·85	15·6
45	N_3	N_3	97	134·0—136·0	31·5	37·2 (Cl)	22·3	8·69	31·7	37·5 (Cl)	22·2	8·46

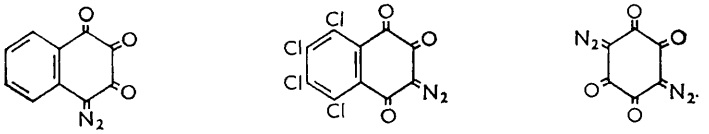
[38] Perchloronaphthaquinone was refluxed with sodium acetate in ethanol. The photosensitive product was crystallized from methylcyclohexane and chromatographed in ethyl acetate solution upon acid-washed alumina. [39] A slurry of perchloronaphthaquinone in boiling ethanol was treated under reflux with ammonia gas. The product was crystallized from chlorobenzene or from nitromethane. [40] Treated, at room temperature, a slurry of (39) in a slight excess of acetic anhydride with a drop of sulphuric acid. Crystallized twice from nitromethane. [41] Obtained as was (40), but the reaction mixture was boiled. Crystallized from either acetic acid or acetic anhydride. [42] Obtained by vatting (45), followed by air-oxidation. Crystallized from nitromethane. [43] Treated a solution of (40) in a small volume of nitrobenzene at 100° with ammonia gas. [44] Treated (43) with acetic anhydride and a drop of sulphuric acid in nitromethane at the b. p. Recrystallized from nitromethane. [45] Obtained from perchloronaphthaquinone and sodium azide in dimethylformamide.

Oxidation of 1,2,3,4,5,6-hexachloro-7-nitronaphthalene (VII) with nitric acid gave the quinone (VIII).



(IX) (X) (XI)

By treating compound (IX) with nitric acid, Kehrmann [8] obtained a product to which he assigned structure (X). However, Beilstein [9] suggests structure (XI) as a possible alternative for this substance. We have found that the diazo-oxide (XI) is readily obtained, in nearly quantitative yield, by treating 2-amino-3-chloro-1,4-naphthaquinone with nitrosylsulphuric acid (or sodium nitrite in sulphuric acid). Curiously, a similar treatment of 4-amino-3-bromo-1,2-naphthaquinone gave none of the isomeric quinone diazo-oxide (XII), and the amine was recovered. However, the perchloro-compound (XIII) was obtained from 2-amino-3,5,6,7,8-pentachloro-1,4-naphthaquinone, and (XIV), previously obtained [10] by other methods, was easily prepared from 2,5-diamino-3,6-dichlorobenzo-



(XII) (XIII) (XIV)

quinone. When compound (XI) was allowed to react with sodium azide and with sodium cyanide, the corresponding 3-substituted 2-hydroxynaphthaquinones (compounds 24 and 25, Table 3) were obtained.

EXPERIMENTAL

Melting points were taken in Pyrex capillaries using a Hershberg apparatus and Anschütz thermometers.

2,3,5,6-*Tetrachloro*-7-*nitro*-1,4-*naphthaquinone* (VIII).—Hexachloro-2-nitronaphthalene (from the Fundamental Research Co., Berkeley, California; 5·00 g.) and fuming (90%) nitric acid (35 ml.) were stirred and boiled under reflux for 10 min. The resulting solution was cooled and

[8] Kehrmann, *Ber.*, 1888, **21**, 1781.
[9] Beilstein, " Handbuch der Organischen Chemie," 4er. Aufl., Springer, Berlin, 1933, Vol. 16, p. 541.
[10] Henle, *Annalen*, 1906, **350**, 335.

diluted with ice and filtered, giving a solid (3·83 g., 93%), m. p. 187·5—188·5°, yellow needles (from methylcyclohexane), m. p. 188·0—188·9°, overall yield (84%) (Found: C, 35·2; H, 0·4; Cl, 41·6; N, 4·25; O, 18·7. Calc. for $C_{10}HCl_4NO_4$: C, 35·2; H, 0·3; Cl, 41·6; N, 4·11; O, 18·8%).

1,4-*Naphthaquinone* 2,3-*Diazo-oxide* (XI).—2·08 g. of 2-amino-3-chloronaphthaquinone in 20 ml. of 1M-nitrosylsulphuric acid (in sulphuric acid) was stirred at 45° for ¼ hr. and then was diluted with water. The solid was filtered off, washed well with water and with methanol, and dried, giving the diazo-oxide in quantitative yield as a bright yellow powder. The compound has no definite m. p., and decomposes vigorously but irregularly when put into the bath above 100°; it may, however, be heated slowly from below 100 to 165° without melting. Attempts to recrystallize the diazo-oxide gave a less pure product (Found C, 60·0; H, 2·2; N, 13·9; O, 24·0. Calc. for $C_{10}H_4N_2O_3$: C, 60·0; H, 2·0; N, 14·0; O, 24·0%.)

Perchloro-1,4-*naphthaquinone* 2,3-*diazo-oxide* (XIII). To 15·0 ml. of nitrosylsulphuric acid (1M in sulphuric acid) was added 1·00 g. of 2-aminoperchloronaphthaquinone. The deep red solution was stirred at 30—35° for 5 min. then poured on ice and filtered. The pale orange solid was washed well with water and then with methanol and dried in air, affording a quantitative yield. When put into the m. p. bath below 108°, it was unmelted below 150°, but if put in at 108·5° or higher, it decomposed vigorously. The compound could not be recrystallized satisfactorily (Found: C, 35·2; Cl, 42·0; N, 7·9. Calc. for $C_{10}Cl_4N_2O_3$: C, 35·5; Cl, 42·0; N, 8·3%).

1,4-*Bisdiazocyclohexanetetraone* (XIV).—A solution of 2·07 g. of 2,5-diamino-3,6-dichlorobenzoquinone in 50 ml. of nitrosylsulphuric acid (1M-solution in sulphuric acid) was warmed to 50° for 1 hr., then was cooled an diluted with ice until turbid and filtered. The solid was washed well with water and dried, giving 1·85 g. (96·4% yield). It explodes at about 85°, and the infrared spectrum shows strong bands at 4·65 μ (diazo-group) and 6·10 μ (carbonyl group).

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