conformation has long been a source of concern, especially to protein crystallographers. Among small molecules, it has been found that the antibiotic cycloheximide incorporates both chair and twist-boat conformations of its 2,4-dimethylcyclohexanone moiety into the same crystal.[13] These conformations are estimated to differ by 2–3 kcal/mol and both may be populated in solution although evidence is not yet available on this point. Some steroids with aromatic A rings, such as 2,4-dibromoestradiol,[14] crystallize in two forms which differ in the conformation of the B ring, but in these cases the energy difference between conformations is quite small.[15] We view the conformational situation in **3** as a special case in which the molecular symmetry, substantial dipole moment, and potential for intermolecular interactions both in the symmetry plane of the molecule and perpendicular to it permit efficient packing of the axial conformation despite its increased energy.

Experimental Section

1,3,5-Trithiane 1-oxide (**3**), available from previous work,[1b] was crystallized slowly from dimethyl sulfoxide to give crystals suitable for X-ray diffraction.

X-ray Crystallographic Measurements, Crystal Data. The unit-cell symmetry was established from 25° precession photographs taken with Mo Kα radiation. The crystal system is orthorhombic, and systematic absences $0kl$ with $k + l$ odd and $hk0$ with h odd are compatible with space groups $Pnma$ (D_{2h}^{16}, No. 62) or $Pn2_1a$ (C_{2v}^{9}, No. 33, $b \rightleftarrows c$). The former group was chosen on the basis of the distribution of maxima in the Patterson function and, with only four molecules in the unit cell, requires that each molecule have mirror symmetry. Accurate unit-cell dimensions were derived from a least-squares fit to the observed values of $\pm 2\theta$ for 12 strong general reflections, measured from a crystal carefully centered on the diffractometer. They are as follows: a = 19.179 (9), b = 7.044 (4), and c = 4.629 (3) Å for λ = 1.5418 Å. For Z = 4, the calculated density is 1.638 g cm^{-3}. That observed by flotation in an ethyl iodide–hexane mixture is 1.65 g cm^{-3}. $F(000)$ is 320 and the absorption coefficient, μ, for Cu Kα radiation is 95 cm^{-1}. No absorption correction was made and most of the residual errors are attributable to this neglect.

Intensity Data. Measurements of intensity were made from a single-crystal prism 0.2 mm on a side and mounted with c^* parallel to the ϕ-axis of a Picker four-circle diffractometer operated under the control of an XDS Sigma 2 computer. Cu Kα radiation was used, made monochromatic by Bragg reflection of the direct beam from a highly oriented graphite crystal. Two symmetry-equivalent octants of reciprocal space, hkl and $\bar{h}kl$, were surveyed to 2θ = 120°. Intensity significantly above background [$I > 3\sigma(I)$] was measured at 833 of the 986 accessible reflections (493 independent data). Scintillation counting was used with pulse height analysis. The θ–2θ scan technique was used with a scan range of 4° and a scan speed of 2° min^{-1} in 2θ. Background measurements were made for 10 s at the beginning and end of each scan with both crystal and counter at rest. Stability of the experimental conditions was monitored by measurement of the intensity of two symmetry-equivalent reflections after every 50 scans. With a mean intensity of about 25 000 counts, the root-mean-square deviations of individual reflections from the mean were 1.1% in each case. Structure amplitudes were derived in the usual ways. The residual between the two sets of symmetry-equivalent data is 3.6%. Both octants were used in the later refinement.

Structure Determination and Refinement. The positions of the two independent sulfur atoms were derived from a three-dimensional Patterson function and the structure solved by the heavy-atom method. Block-diagonal least-squares refinement gave R = 0.12 when individual isotropic thermal parameters were used and R = 0.055 when anisotropic thermal parameters were used for S, O, and C. A conventional weighting scheme was used.[17] Hydrogen atoms were located from a three-dimensional difference electron-density map and their parameters included in the least-squares process. The refinement gave physically unreasonable parameters for the hydrogen atoms, however, and so fixed contributions for these atoms were taken instead, based on C–H distances of 1.08 Å and isotropic B values of 5.0 Å^2. At convergence [$\Delta(p) < 0.1\sigma(p)$] the usual unweighted and weighted residuals were 0.046 and 0.052. A final difference electron-density map showed residual peaks (±0.57 e/Å^3) close to the sulfur positions, most probably attributable to neglect of absorption corrections, but was otherwise structurally featureless. The scattering functions were taken from ref 16. All programs used were written in this laboratory for the XDS Sigma 2 computer, with the exception of ORTEP for which a CDC Cyber 172 computer was used.

Registry No. 3, 10349-03-8.

Supplementary Material Available: Listing of anisotropic thermal parameters (1 page). Ordering information is given on any current masthead page.

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Quinone Chemistry. Reaction of 2,3-Dichloro-1,4-naphthoquinone with Arylamines in Pyridine

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2,3-Dichloro-1,4-naphthoquinone (**1**) reacts with arylamines (**2**) in pyridine to afford 2-(arylamino)-3-chloro-1,4-naphthoquinone (**6**), 2-(arylamino)-1,4-naphthoquinone (**5**), 2-(arylamino)-1,4-naphthoquinone-3-pyridinium perchlorate (**4**), and 2-amino-1,4-naphthoquinone-3-pyridinium perchlorate (**7**), depending upon the nature of the substituent in **2**. 2-(4-Nitroanilino)-1,4-naphthoquinone-3-pyridinium chloride (**4e**, X = Cl) reacts with alkali to give 1-oxo-2-(4-nitrophenylimino)-3-pyridinium-4-naphthoxide (**9**), not the product reported[12] previously. Intermediate compounds have been isolated and characterized. A probable mechanism for the formation of the derivatives is discussed.

In continuation of our interest in quinone chemistry, we have synthesized indazolequinones,[1] benzoisoxazole-quinones,[2] quinazoline-5,8-quinones,[3,4] acridinequinones,[5] 2-(alkylamino)-5-(arylamino)-1,4-benzoquinones,[6] amino-

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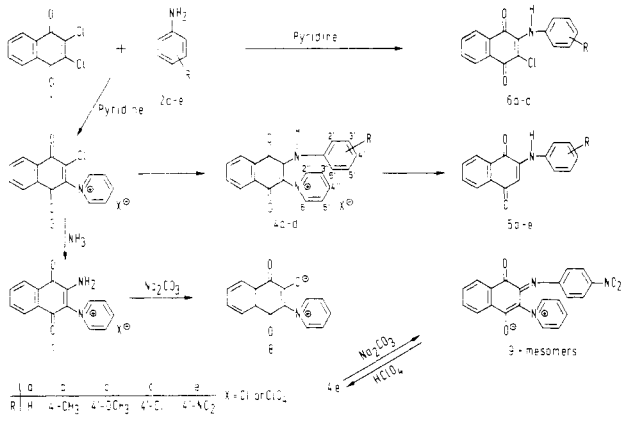
Table I. ^{1}H NMR Data of Substituted 1,4-Naphthoquinone-3-pyridinium Salts[a,b,f]

compd	pyridine ring: 2''-H, 6''-H	pyridine ring: 4''-H	3''-H, 5''-H, and naphthoquinone ring	2'-H, 6'-H	3'-H, 5'-H	NH(s)
3 (X = Cl)[e]	8.89	8.63	7.72-8.29			
4d (X = Cl)	8.84	8.52	7.88-8.28	7.04[c]	7.10[c]	10.35
4d (X = ClO_4)	8.77	8.50	7.88-8.35	6.97[c]	7.10[c]	10.41
10			7.95-8.31[d]	7.1 (not resolved)		10.41
4e (X = Cl)	8.94	8.50	7.95-8.30	7.29[c]	7.92[c]	10.72
4e (X = ClO_4)	8.83	8.48	7.96-8.32	7.20[c]	7.92[c]	10.57
4e (X = HSO_4)	8.86	8.47	7.95-8.32	7.25[c]	7.91[c]	10.54
4f (X = Cl)	8.72	8.41	7.74-8.22	7.07 (mc)[g]	6.68 (mc)[h]	10.05
				3.63 (s, OCH_3)		
4f (X = ClO_4)	8.68	8.39	7.74-8.24	7.07 (mc)[g]	6.69 (mc)[h]	10.03
				3.62 (s, OCH_3)		
9	8.97	8.52	7.64-8.18	6.74[g]	7.88[h]	
7	8.99	8.8	7.85-8.44			7.85-8.21 (br)
8	8.89	8.59	7.68-8.22			

[a] Data given in parts per million from Me_4Si (δ 0). [b] Me_2SO-d_6 solvent. [c] Doublet, J = 9 Hz. [d] Naphthoquinonoid ring. [e] In $CDCl_3$-D_2O. [f] br, broad; s, singlet; m, multiplet; mc, multiplet center. [g] For 3'-H and 5'-H. [h] For 4'-H and 6'-H.

Scheme I



arylquinones,[4] and phenanthridinequinones.[7] We have also examined[8] the reaction of 2,3-dichloro-1,4-naphthoquinone (1) with o-aminophenols under various reaction conditions. During the latter studies we became interested in studying in detail the reaction of 1 with aromatic amines, because there was a great similarity in the mechanism of formation for both types of reaction products.

Although many reactions of 1 with amines in alcohol have been described,[9-11] only a few reactions of 1 with amines in pyridine are recorded.[11-13] Van Allan and Reynolds have reported[12] that 1 reacts with 4-nitroaniline (**2e**) in pyridine to yield 2-(4-nitroanilino)-1,4-naphthoquinone (**5e**) and that 2-(4-nitroanilino)-1,4-naphthoquinone-3-pyridinium chloride (**4e**, X = Cl) reacts with alkali to give **5e** in quantitative yield (Scheme I). These unusual reactions in which a chlorine atom or pyridinium chloride is replaced by hydrogen seemed to be worthy of further investigation.

We have studied the reaction of 1 with aromatic amines **2** having electron-donating (CH_3, OCH_3) and electron-withdrawing (Cl, NO_2) substituents in pyridine to examine the nature and yields of the reaction products. Intermediate compounds have been identified, and a mechanism for the formation of all compounds is proposed. It was observed that structure and yields of the reaction products are affected by the substituent present in the arylamine: 1 reacts with arylamines of enhanced nucleophilicity (**2a–d**) to give **4–6** (Table II). With 4-chloroaniline (**2d**) in addition to these products 7 (X = ClO_4) is also found. With 4-nitroaniline (**2e**) 7 is the main product; in this case **5e** is present only in a small amount, and **6e** and **4e** could not be isolated. The results are summarized in Scheme I. The structures of **5** and **6** were confirmed by comparing them with authentic samples. The structures of **4** and **7** were established by microanalysis and ^{1}H NMR, UV, and IR spectra (Table I and Experimental Section). The NMR spectra of **4a–e** and **7** show the correct proton count and coupling constants and the expected value for the chemical shift. The structure of **7** was further confirmed by the reaction of an ethanolic solution of **3** (X = ClO_4) with concentrated ammonia.

From these data one can conclude that the reaction of 1 with **2** proceeds in two directions. (i) Initially nucleophilic attack of the amino group of **2** on the quinone 1 takes place with elimination of hydrochloric acid to form **6**. In this case pyridine acts only as an acid acceptor. The absence of **6e** in the reaction of 1 with **2e** is presumably due to the weak basicity of the amine. (ii) Simultaneously, pyridine reacts with 1 to form **3** (X = Cl), which, in presence of aromatic amine, subsequently reacts to give **4**. These assumptions are supported by the following experiments. Efforts have been made to isolate **3**. Despite several unsuccessful attempts to characterize this intermediate,[9-13] the product isolated was always described to be 1,4-dioxo-3-pyridinium-2-naphthoxide (**8**). It was argued that its formation was due to hydrolysis of **3** by atmospheric moisture. For the first time we now report the successful preparation of **3**. It was obtained from the reaction of 1 with absolute pyridine in dry chloroform under a nitrogen atmosphere, and it was recrystallized from acetonitrile–ether. The structure was proved by microanalysis, spectroscopic data (Table I), and chemical reactions. The quaternary salt **3** reacts further with arylamine to give **4**. An alternative possibility for the for-

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Table II. Reaction of 2,3-Dichloro-1,4-naphthoquinone (1) and Arylamines (2) in Pyridine[a]

	products (% yield)							
reactants	4[b]	mp, °C	5	mp, °C	6	mp, °C	7,[c]	mp, °C
1 + 2a	4a[13] (28)	298	5a[21] (11)	191	6a[13] (12)	210		
1 + 2b	4b (19)	348-350	5b[16] (14)	201	6b[26] (37)	195		
1 + 2c	4c (15)	352-354	5c[18] (8)	155-157	6c[17] (44)	222		
1 + 2d	4d (44)	304-306	5d[20] (6)	227	6d[19] (3)	268	7 (7)	
1 + 2e			5e[15] (3)	339			7 (23)	298

[a] Satisfactory analytical values (±0.3% for C, H, N, and Cl) were reported for all compounds. [b] In 4 (X = ClO_4). [c] Identical in melting point, mixture melting point, and IR and ^1H NMR spectra with the sample prepared from 3 and ammonia.

mation of 4 from 6 was ruled out as 6 does not react with pyridine. When 4a–e were heated in pyridine or chlorobenzene 5a–e were obtained, respectively, in very low yields. The mechanism of this process is not known.

Van Allan and Reynolds have reported[12] that reaction of 1 with 2e in the presence of 3 or more equiv of pyridine in 1,2,3-trichloropropane gave 5e. Repetition of their directions for the reaction gave in our hands only 4e (X = Cl) in excellent yield. In addition to this, the reported[12] reaction of 4e (X = Cl) with sodium carbonate to give 5e does not appear reasonable because most of the quaternary pyridinium salts having electron-withdrawing groups result in the formation of the corresponding amine derivatives or enol betaines.[14] Therefore the reaction of 4e with alkali was reinvestigated. A red-orange compound in quantitative yield was isolated from the reaction of 4e (X = Cl) with alkali and proved to be 9. Its structure was established by microanalysis, spectroscopic data, and salt formation. The ^1H NMR spectrum of 9 showed clearly the presence of a pyridine, naphthoquinone, and 4-nitroaniline ring in the molecule (Table I). Compound 9 was converted to 4e (X = ClO_4) by treatment with 70% perchloric acid. This behavior of 4e (X = Cl) toward alkali is consistent with the reported anomalous behavior of quaternary pyridinium salts.[14] Compound 7 also reacts with alkali to afford the expected 8.

The ^1H NMR spectral data of the pyridinium salts are listed in Table I. A combination of chemical shifts, spin–spin couplings, and integration data permits the identification of individual hydrogens in the aromatic rings. All NMR spectra contain the characteristic bands of the pyridinium cations and are in good agreement with those of reported quaternary pyridinium salts.[22-25] A proper analysis of the proton spectra for the pyridine ring implies an AB_2X_2 approach. The 2″-H and 6″-H atoms of the pyridine ring appear as a characteristic multiplet centered in the lowest region of the spectra at δ 8.68–8.99. In all the studied derivatives the 4″-H proton of the pyridine ring again shows a typical multiplet centered in the region δ 8.39–8.80. The 3″-H and 5″-H protons are assigned in the region at δ 7.64–8.44 as a multiplet and seem to be mixed with the naphthoquinonoid ring protons. This had been confirmed as 10, having a deuterated pyridine ring and showing the quinonoid ring protons at δ 7.95–8.31. Thus the position of 2″-H and 6″-H protons of the pyridine system and the protons of the quinone ring (H_5–H_8) cannot be distinguished. The NH proton is found in the region δ 10.03–10.72 as a singlet and is D_2O exchangeable.

Until now no systematic study has been reported to see the effect of increasingly bulkier anions (Cl^-, HSO_4^-, ClO_4^-, etc.) on the various protons of the molecule. Therefore, the ^1H NMR spectra of a few quaternary pyridinium salts having the same structure of the cation but only differing in the anion were measured in the same solvent under similar conditions. Chemical shifts of the 2″-H and 6″-H protons of the pyridine ring seem to be slightly dependent upon the nature of anions. These protons are shifted to higher field about 0.1 ppm in presence of bulkier anions. From inspection of Table I one can conclude that there is only a small effect of different anions on the chemical shift of the other ring protons. The IR and UV spectral data of the 2-(arylamino)-1,4-naphthoquinone-3-pyridinium salts 4 and 7 are listed in Tables III and IV (see the supplementary material).

Experimental Section

Melting points were obtained in open capillary tubes or in an aluminum block and are uncorrected. The following instruments were used for spectroscopic analysis: Perkin-Elmer 225 spectrophotometer (IR), potassium bromide pellets; Gilford 24 (UV/visible); Varian HA-100 and Bruker WH-90 (^1H NMR); Varian CH-7A (mass spectra, 70 eV). Elemental analyses were performed by the Peptide Chemistry Division of the Max-Planck-Institute of Biochemistry, Munich. The purity of the samples was ascertained by ascending TLC (silica gel) using chloroform as the solvent for the 2-(arylamino)-1,4-naphthoquinones and MeOH for the quaternary pyridinium salts. The pyridinium salts are highly hygroscopic. For analysis and spectroscopic investigations they were dried at 80–90 °C for 48 h under vacuum over phosphorus pentoxide. The yields of pyridinium salts are reported as perchlorates and they are obtained in 80–90% yield from the corresponding chlorides. For IR and UV data v = very, s = strong, m = medium, w = weak, br = broad, and sh = shoulder.

General Procedure for the Condensation of 1 with Arylamines in Pyridine. 2-(Arylamino)-1,4-naphthoquinone-3-pyridinium Perchlorate (4), 2-(Arylamino)-3-chloro-1,4-naphthoquinone (6), and 2-(Arylamino)-1,4-naphthoquinone (5). A mixture of 2.27 g (10 mmol) of 1 and substituted arylamine (11 mmol) in 20 mL of dry pyridine was heated at 110–130 °C with stirring for 4–5 h. After the mixture was kept overnight in the refrigerator, the precipitate was collected and dried over phosphorus pentoxide. It was dissolved in 200 mL of hot water and filtered. Most of the material was soluble in water, leaving some undissolved residue. To the filtrate was added 2 mL of 70% perchloric acid, and after the mixture cooled, the precipitated compound was filtered, washed with cold water, and dried. It was purified by repeated crystallization with acetonitrile–ether to provide the corresponding 2-(arylamino)-1,4-naphthoquinone-3-pyridinium perchlorate (4). The pyridine filtrate was poured into 250 mL of cold water and neutralized with concen-

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trated HCl. The resulting suspension was extracted with chloroform–acetone (1:1), and the organic phase was dried over anhydrous sodium sulfate and evaporated to dryness in vacuo. This and water-insoluble substances were dissolved in a minimum amount of chloroform and column chromatographed (silica gel, deactivated with 10% H_2O) with the same solvent as eluent. The first orange-red zone provided the corresponding 2-(arylamino)-3-chloro-1,4-naphthoquinone (**6**). Recrystallization from chloroform–hexane gave a clean product. The next band gave the corresponding 2-(arylamino)-1,4-naphthoquinone (**5**); the pure product was obtained by crystallization with $CHCl_3$–hexane. Structures of all the above quinones were confirmed by comparison (mixture melting point, IR and mass spectra) with the corresponding quinones of known orientation. The yields and melting points of the products are listed in Table II.

2-(4-Chloroanilino)-1,4-naphthoquinone-3-pyridinium Perchlorate (4d), 2-Amino-1,4-naphthoquinone-3-pyridinium Perchlorate (7), 2-(4-Chloroanilino)-3-chloro-1,4-naphthoquinone (6d), and 2-(4-Chloroanilino)-1,4-naphthoquinone (5d). The reaction of **1** and of 4-chloroaniline (**2d**) in dry pyridine as described in the general procedure gave a mixture of **4d** and **7**. The pyridinium perchlorate mixture was separated by preparative TLC (2-mm silica gel plates) using methanol as the developing system. The upper yellow band provided 2.05 g of **4d**, mp 304–306 °C. The second shining yellow band was assigned to 2-amino-1,4-naphthoquinone-3-pyridinium perchlorate (**7**) on the basis of R_f value comparison in several developing systems with the authentic sample from the reaction of **3** and ammonia. Compound **7** decomposes slowly on the thin-layer plate and therefore could not be isolated in pure form from the reaction of **1** and **2d**. The other products, yields, and melting points are listed in Table II.

2-Chloro-1,4-naphthoquinone-3-pyridinium Chloride (3, X = Cl). To a stirred solution of 4.54 g (20 mmol) of **1** in 100 mL of dry chloroform at 95 °C was added 9.48 g (120 mmol) of absolute pyridine. The resulting solution was stirred under a nitrogen atmosphere at 95–110 °C for 5 h. TLC (MeOH) established that it still contained a little **1** in the suspension. Another 1.58 g (20 mmol) of dry pyridine was added, and refluxing was continued for 2 h. The color of the solution changed from light yellow to dirty dark yellow. After the mixture was cooled at −2 °C for 24 h under a nitrogen atmosphere, a light yellow precipitate was isolated by filtration and washed with dry benzene to remove traces of unreacted naphthoquinone. It was dried over phosphorus pentoxide to yield 3.5 g of **3** (X = Cl), mp 175–178 °C. An additional 1.05 g of **3** was obtained from the mother liquor (total yield 74%). Recrystallization with absolute acetonitrile–ether under a nitrogen atmosphere gave an analytical sample: UV (acetonitrile) λ_{max} nm (log ϵ) 367.5 (3.49), 263 (4.27), 257 (sh, 4.27), 221 (sh, 4.15); IR (KBr) 3120 (w), 3060 (w), 2940 (w), 1675 (vs), 1636 (m), 1625 (s), 1589 (s), 1558 (s) cm^{-1}. The substance is sensitive to air and light. The carbon analysis of this salt was somewhat lower, although hydrogen, nitrogen, and chlorine values were satisfactory.

Anal. Calcd for $C_{15}H_9Cl_2NO_2$: C, 58.80; H, 2.96; N, 4.57; Cl, 23.12. Found: C, 58.24; H, 3.19; N, 4.58; Cl, 22.80.

2-Chloro-1,4-naphthoquinone-3-pyridinium Perchlorate (3, X = ClO_4). To a solution of 9.08 g (40 mmol) of **1** in 150 mL of dry chlorobenzene at 100–130 °C was added 15.8 g (200 mmol) of dry pyridine under a nitrogen atmosphere with stirring. The resulting solution was stirred at 95–120 °C for 7 h and concentrated on a rotatory evaporator. It was washed with 150 mL of dry benzene to remove the unreacted **1** and impurities. The residue was dissolved in 150 mL of acetonitrile and filtered. To the filtrate were added 3 mL of 70% perchloric acid and then 100 mL of methanol. Again it was concentrated in vacuo to 5 mL and diluted with 5 mL of acetone. The resulting light yellow precipitate, obtained by filtration, was washed with a little cold water and dried in vacuo to yield 10.23 g (69%) of **3** (X = ClO_4) as a light yellow substance, mp 225–257 °C. Repeated recrystallization with methanol–ether raised the melting point to 263 °C: UV (EtOH) λ_{max} nm (log ϵ) 212.5 (4.47), 245 (4.30), 283 (sh, 4.01), 325 (3.73); IR (KBr) 3130 (m), 3080 (m), 3048 (w), 1690 (vs), 1678 (s), 1627 (vs), cm^{-1}; ^1H NMR (Me_2SO-d_6) 9.16 (2 H, mc, 2′-H, 6″-H), 8.95 (1 H, mc, 4″-H), 8.02–8.61 (6 H, m, 3″-H, 5″-H, and H_5–H_8).

Anal. Calcd for $C_{15}H_9Cl_2NO_6$: C, 48.60; H, 2.45; N, 3.78; Cl, 19.15. Found: C, 48.53; H, 2.49; N, 3.95; Cl, 19.51.

***Condensation of* 1 with 4-Nitroaniline (2e) in Pyridine: 2-(4-Nitroanilino)-1,4-naphthoquinone (5e) and 2-Amino-1,4-naphthoquinone-3-pyridinium Perchlorate 7 (X = ClO_4).** A mixture of 2.27 g (10 mmol) of **1** and 1.38 g (10 mmol) of 4-nitroaniline (**2e**) in 20 mL of dry pyridine was treated at 120–140 °C for 3 h with stirring. The mixture was cooled overnight in the refrigerator, and the solid was filtered off and washed once with a little cold absolute methanol and several times with ether. The crude material was dissolved in 200 mL of boiling water and filtered, leaving some highly insoluble colored material. To the above filtrate was added 2 mL of 70% perchloric acid. The yellow precipitate, obtained by filtration, was washed with cold water and dried to give 0.83 g (23%) of **7**. Repeated crystallization from acetonitrile–ether provided the analytical sample as yellow needles, mp 298 °C. Anal. Calcd for $C_{15}H_{11}ClN_2O_6$: C, 51.06; H, 3.14; N, 7.94; Cl, 10.05. Found: C, 51.43; H, 3.22; N, 8.22; Cl, 9.78. It was identical in every respect (melting point, mixture melting point, IR, and ^1H NMR) with the sample prepared from **3** and ammonia. The water-insoluble material was column chromatographed (silica gel, 10% H_2O) with $CHCl_3$ as eluent. It yielded a yellow-orange zone which afforded 0.1 g (3%) of **5e**,[15] mp 339 °C.

2-(4-Chloroanilino)-1,4-naphthoquinone-3-pyridinium Chloride (4d, X = Cl) and 2-(4-Chloroanilino)-1,4-naphthoquinone-3-pyridinium Perchlorate (4d, X = ClO_4). A mixture of 2.27 g (10 mmol) of **1** and 3.95 g (50 mmol) of pyridine in 30 mL of 1,2,3-trichloropropane was heated at 110 °C for 0.5 h with stirring. Then 1.39 g (11 mmol) of 4-chloroaniline (**2d**) was added, and heating was continued for 2.5 h. The mixture was chilled, and the precipitate was isolated by filtration and dried in vacuo to give 3.5 g (87%) of **4d** (X = Cl). Crystallization with dry methanol–ether gave orange-red needles, mp 342–344 °C (it starts to change color at 240 °C).

Anal. Calcd for $C_{21}H_{14}Cl_2N_2O_2$: C, 63.48; H, 3.55; N, 7.05. Found: C, 63.48; H, 3.72; N, 7.00.

By the usual procedure **4d** (X = Cl) afforded 2-(4-chloroanilino)-1,4-naphthoquinone-3-pyridinium perchlorate (**4d**, X = ClO_4) as light orange-yellow powder: yield 91%; mp 304–306 °C.

Anal. Calcd for $C_{21}H_{14}Cl_2N_2O_6$: C, 54.66; H, 3.06; N, 6.07. Found: C, 54.62; H, 2.96; N, 6.10.

2-(2-Methoxyanilino)-1,4-naphthoquinone-3-pyridinium Chloride (4f, X = Cl). A mixture of 5.54 g (20 mmol) of **1**, 2.47 g (20 mmol) of 2-methoxyaniline (**2f**), and 4.74 g (60 mmol) of dry pyridine in 30 mL of 1,2,3-trichloropropane was heated at 95–110 °C for 2 h with stirring. It was cooled overnight, and the precipitate was collected, washed with a little cold ethanol and hexane, and dried over phosphorus pentoxide to give 6 g (62%) of **4f** (X = Cl). Recrystallization with methanol–ether furnished a light orange-yellow powder, mp 220 °C.

Anal. Calcd for $C_{22}H_{17}ClN_2O_3$: C, 67.26; H, 4.36; N, 7.13. Found: C, 66.97; H, 4.31; N, 6.97.

2-(2-Methoxyanilino)-1,4-naphthoquinone-3-pyridinium Perchlorate (4f, X = ClO_4). A mixture of 0.31 g (1 mmol) of **3** (X = Cl) and 0.246 g (2 mmol) of 4-methoxyaniline (**2f**) in 7 mL of 1,2,3-trichloropropane was heated at 95–100 °C for 2 h. It was chilled, and 2 mL of ether was added. The resulting product was isolated by filtration and washed with ether. This semisolid material was dissolved in 15 mL of methanol, 2 mL of 70% perchloric acid was added, the mixture was then diluted to 250 mL with water, and the precipitate was collected to give 0.3 g (66%) of **4f** (X = ClO_4). Crystallization with methanol–ether provided **4f** as yellow powder, mp 292 °C. Its structure was confirmed by comparing the IR with that of the sample prepared by method of Van Allan and Reynolds.[13]

Reaction of 2-Chloro-1,4-naphthoquinone-3-pyridinium Perchlorate (3) with Ammonia. 2-Amino-1,4-naphthoquinone-3-pyridinium Perchlorate (7). A mixture of 0.37 g (1 mmol) of **3** (X = ClO_4) and 0.06 g (4 mmol) of concentrated ammonia in 10 mL of ethanol was heated at 90–110 °C for 2 h. The solution was cooled for 18 h. The precipitate was filtered, washed with water, and dried and gave yellow **7**, mp 285 °C. This was dissolved in 250 mL of hot water and filtered to remove insoluble impurities. The filtrate on evaporation at reduced pressure gave 0.22 g (62%) of **7** as pure product. Recrystallization

with acetonitrile–ether provided 7 as yellow powder, mp 298 °C.

Anal. Calcd for $C_{15}H_{11}ClN_2O_6$: C, 51.06; H, 3.14; N, 7.94; Cl, 10.05. Found: C, 51.00; H, 3.24; N, 7.72; Cl, 9.69.

2-(4-Nitroanilino)-1,4-naphthoquinone-3-pyridinium Chloride (4e, X = Cl). A mixture of 2.27 g (10 mmol) of 1 and 1.51 g (11 mmol) of 4-nitroaniline (2e) in 20 mL of 1,2,3-trichloropropane was heated with stirring at 100 °C until a clear solution was obtained, 3.16 g (40 mmol) of dry pyridine was added, and heating was continued for 2 h. After the mixture cooled overnight, the precipitate was collected by filtration and dried in vacuo to yield 2.8 g of 4e (X = Cl). From the filtrate, an additional 0.35 g was isolated (total yield 77%). Crystallization from acetonitrile–ether provided 4e (X = Cl) as an orange-brown powder, mp 272 °C.

Anal. Calcd for $C_{21}H_{14}ClN_3O_4$: C, 61.80; H, 3.46; N, 10.30; Cl, 8.69. Found: C, 61.72; H, 3.53; N, 10.2; Cl, 8.50.

Crystallization of the above sample with water provided 4e·$2H_2O$ (X = Cl), mp 297 °C.

Anal. Calcd for $C_{21}H_{18}ClN_3O_6$: C, 56.83; H, 3.63; N, 9.47. Found: C, 57.08; H, 3.57; N, 9.68.

1-Oxo-2-(4-nitrophenylimino)-3-pyridinium-4-naphthoxide (9). To a solution of 0.81 g (2 mmol) of 4e (X = Cl) in 25 mL of water was added 15 mL of a saturated solution of sodium carbonate or 5 mL of 1 N NaOH (pH of the reaction mixture in latter case was 12.6). The reaction mixture became deep red and was heated at 50–60 °C with stirring for 1 h and cooled. The precipitate was collected by filtration, washed with water, and dried in vacuo to yield 0.7 g (94%) of 9. Recrystallization from chloroform–hexane provided 9 as deep orange-red crystals: mp 239 °C; UV (dioxane) λ_{max} nm (log ϵ) 221 (sh, 4.16), 278 (sh, 4.18), 334 (sh, 4.04), 352.5 (sh, 4.04), 471 (3.56); IR (KBr) 3180 (w), 3060 (w), 3016 (w), 1680 (vs), 1619 (m), 1589 (s), 1571 (s), 1515 (br s) cm^{-1}.

Anal. Calcd for $C_{21}H_{13}N_3O_4$: C, 67.90; H, 3.53; N, 11.32. Found: C, 67.53; H, 3.71; N, 11.12.

2-(4-Nitroanilino)-1,4-naphthoquinone-3-pyridinium Bisulfate (4e, X = HSO_4). To a solution of 0.37 g (1 mmol) of 9 in 50 mL of ethanol was added 2 mL of concentrated sulfuric acid. The resulting suspension was stirred at 50–60 °C for 1 h, concentrated under reduced pressure to 7 mL, and then poured into 200 mL of cold water. The precipitate was collected by filtration, washed thoroughly with water, and dried in vacuo to yield 398 mg (85%) of the pyridinium bisulfate, mp 184 °C. An analytical sample was obtained by crystallization with acetonitrile–ether as light yellow-orange leaflets.

Anal. Calcd for $C_{21}H_{15}N_3O_8S·1.5H_2O$: C, 50.80; H, 3.65; N, 8.47; S, 6.45. Found: C, 50.97; H, 3.24; N, 8.3; S, 6.51.

2-(4-Nitroanilino)-1,4-naphthoquinone-3-pyridinium Perchlorate (4e, X = ClO_4). Method A. To a solution of 0.07 g (0.2 mmol) of 9 in 10 mL of ethanol was added 0.5 mL of 70% perchloric acid. The resulting suspension was heated at 70–80 °C for 30 min with stirring and cooled. After dilution with 200 mL of water, the product was isolated by filtration, washed with water, and dried in vacuo to give 85 mg (90%) of 4e (X = ClO_4). Crystallization of this with methanol–ether gave 4e (X = ClO_4) as orange-yellow crystals, mp 323 °C.

Anal. Calcd for $C_{21}H_{14}ClN_3O_8$: C, 53.43; H, 2.99; N, 8.91. Found: C, 53.48; H, 2.99; N, 9.01.

Method B. To a solution of 0.41 g (1 mmol) of 4e (X = Cl) in 10 mL of ethanol was added 1 mL of 70% perchloric acid. This was poured into 500 mL of cold water. The precipitate was collected and dried in vacuo to yield 420 mg (89%) of 4e (X = ClO_4), mp 323 °C.

Method C. A mixture of 0.31 g (1 mmol) of 3 (X = Cl) and 0.14 g (1 mmol) of 4-nitroaniline (2e) in 7 mL of acetonitrile was heated at 90–100 °C with stirring for 2 h, and the precipitate was collected by filtration, washed with ether, dried in vacuo, and crystallized from acetonitrile–ether to give 0.26 g (64%) of 4e (X = ClO_4), mp 323 °C. IR and mixture melting point comparison indicated that the materials prepared by methods A, B, and C were identical.

Thermal Treatment of 2-(4-Chloroaniline)-1,4-naphthoquinone-3-pyridinium Chloride (4d, X = Cl) in Pyridine. 2-(4-Chloroanilino)-1,4-naphthoquinone (5d). A suspension of 403 mg (1 mmol) of 4d in 5 mL of dry pyridine was heated at 130–140 °C for 4 h. The resulting suspension was cooled, filtered, and washed with chloroform. The dry residue gave 350 mg of starting material (R_f value, mixture melting point). The filtrate was poured into 100 mL of water and neutralized with 2 N HCl. It was extracted with acetone–chloroform (1:1), and the organic layer was dried over sodium sulfate. The concentrated solution on being chromatographed twice by preparative TLC (silica gel, 2 mm thick; chloroform) afforded 4.2 mg (2%) of 2-(4-chloroanilino)-1,4-naphthoquinone (5d),[20] mp 227 °C. It is of interest to note that the yield of 5d in the above reaction is lower than that from the reaction of 1 and 2d in pyridine.

Reaction of 2-Amino-1,4-naphthoquinone-3-pyridinium Perchlorate (7) with Alkali. 1,4-Dioxo-3-pyridinium-2-naphthoxide (8). To a suspension of 100 mg (0.28 mmol) of 7 in 5 mL of water was added 4 mL of a saturated solution of sodium carbonate. The color of the suspension changed from yellow to orange-yellow. It was heated to 70–80 °C with stirring for 2.5 h and cooled. The precipitate was isolated by filtration, washed with 10 mL of cold water, and dried in vacuo to yield 65 mg (91%) of 8, crystallized from methanol–ether, mp 310 °C. It was found to be identical in every respect with an authentic sample.[12]

2-(4-Chloroanilino)-1,4-naphthoquinone-3-pyridinium-d_5 Chloride (10). A mixture of 0.227 g (1 mmol) of 1 and 0.24 g (3 mmol) of pyridine-d_5 in 3 mL of 1,2,3-trichloropropane was heated with stirring at 100 °C until a clear solution was obtained, and then 0.127 g (1 mmol) of 4-chloroaniline was added. Heating was continued for 2 h, and the resulting suspension was cooled overnight. The precipitate was collected by filtration, washed with chloroform, and dried in vacuo to yield 240 mg (60%) of 10 as an orange-red powder, mp 340–342 °C.

Registry No. 1, 117-80-6; 2a, 62-53-3; 2b, 106-49-0; 2c, 104-94-9; 2d, 106-47-8; 2e, 100-01-6; 2f, 90-04-0; 3 (X = Cl), 74292-48-1; 3 (X = ClO_4), 75112-53-7; 4a, 1920-78-1; 4b, 75112-55-9; 4c, 75112-57-1; 4d (X = Cl), 75112-58-2; 4d (X = ClO_4), 75112-60-6; 4e (X = Cl), 75112-61-7; 4e (X = ClO_4), 75112-63-9; 4e (X = HSO_4), 75112-64-0; 4f (X = Cl), 75125-20-1; 4f (X = ClO_4), 1920-77-0; 5a, 6628-97-3; 5b, 57182-49-7; 5c, 64505-52-8; 5d, 3144-89-6; 5e, 75112-65-1; 6a, 1090-16-0; 6b, 62101-46-6; 6c, 22359-32-6; 6d, 75112-66-2; 7, 75112-68-4; 8, 21758-86-1; 9, 75125-21-2; 10, 75112-69-5; pyridine, 110-86-1; pyridine-d_5, 7291-22-7.

Supplementary Material Available: UV (Table III) and IR (Table IV) spectral data for 4 (X = ClO_4, Cl, HSO_4) and 7 (2 pages). Ordering information is given on any current masthead page.