A 100-mg (0.26 mmol) sample of the mixture in 5 ml of glacial acetic acid and 4 ml of concentrated HCl was boiled under reflux for 4 days and poured into 40 ml of water, and the mixture was extracted with benzene (3 × 15 ml). The extract was washed with water until neutral, with 10 ml of saturated K_2CO_3 solution, and with water (4 × 10 ml) and dried ($MgSO_4$), and the solvent was removed to give 88 mg of white solid, nmr (CCl_4) δ 3.60 (C-3 $OCOCH_3$, half the area of the C-18 CH_3 at 0.67, indicating only about 50% hydrolysis). The mixture was taken up in 4 ml of glacial acetic acid and 4 ml of 48% hydrobromic acid and boiled under reflux for 2.5 days. After work-up as above 63 mg (70%) of a white solid was obtained; the nmr spectrum showed no methoxy absorption at δ 3.60. After recrystallization from methanol, 54 mg of 3α-methyl-*A*-nor-5α-cholestan-2-one (IIId) was obtained: double mp 124–125.5° and 131.5–133°; $[\alpha]_{589}$ +110°, $[\alpha]_{578}$ +113°, $[\alpha]_{546}$ +138°, $[\alpha]_{436}$ +296°, $[\alpha]_{365}$ +754° (*c* 0.15, $CHCl_3$); $T_R^{115°}$ 1.26; R_f 1.40; nmr ($CDCl_3$) δ 0.70 (s, C-18 CH_3), 0.83, 0.88, 0.93, and 0.97 (C-19 CH_3 and side chain CH_3's), and a new peak at 1.08 (part of doublet for C-3 CH_3); nmr (100 MHz) ($CDCl_3$) δ 0.70 (s, C-18 CH_3), 0.85, 0.90, 0.92, and 0.95 (s, C-19 CH_3 and side chain CH_3's), and 1.03 (d, J = 7 Hz, C-3 CH_3); mass spectrum (70 eV) *m/e* (rel intensity) 386 (68) (M^+) and 231 (base peak).

Anal. Calcd for $C_{27}H_{46}O$: C, 83.87; H, 11.99. Found: C, 83.65; H, 12.09.

Registry No.—Ia, 39010-42-9; Ib, 39010-43-0; Ic, 26654-59-1; IIb, 39010-45-2; IIc, 39010-46-3; IId, 39010-47-4; IIe, 39010-48-5; IIf, 39010-49-6; IIg, 39010-50-9; IIIa, 27460-19-1; IIIb, 39010-52-1; IIIc, 39010-53-2; IIId, 39010-54-3; 5α-pregnane-3,20-dione, 566-65-4; 2,3-secocholestane-2,3-dioic acid, 1178-00-3; dimethyl 2,3-secocholestane-2,3-dioate, 1180-24-1.

Hydride Reductions of Naphthalic Anhydrides[1]

JAMES CASON,* DON M. LYNCH, AND ANDREAS WEISS

Chemical Laboratories, University of California, Berkeley, California 94720

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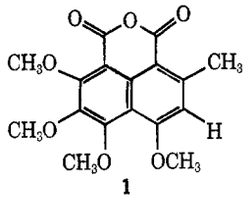
Diborane reduction, at room temperature, of 1,8-naphthalic anhydrides yields the corresponding cyclic ether (2,1,3-*peri*-naphthopyran) as sole isolable product. Reduction with diborane of 1,8-naphthalide also yields only the *peri*-naphthopyran, but in twice the yield obtained from the anhydride. If both the 2 and 7 positions in the anhydride are occupied, reduction fails to occur. Diborane reduction of 1,2-naphthalic anhydride, or of the adduct from anthracene and maleic anhydride, yields only the corresponding diol. Lithium aluminum hydride reduction, at room temperature, of 1,8-naphthalic anhydride yields no *peri*-naphthopyran, but a mixture of diol and 1,8-naphthalide; 1,2-naphthalic anhydride gives similar results. 2,7-Dimethoxy-1,8-naphthalic anhydride, on lithium aluminum hydride reduction in refluxing tetrahydrofuran, yields no diol but a mixture of naphthalide and cyclic ether, with increase in ratio of cyclic ether as reaction time is increased. The data indicate that the naphthalide (lactone) is a common intermediate for formation of either diol or cyclic ether and that diol is not an intermediate in cyclic ether formation. The first step in the sequence proceeds at a higher rate with lithium aluminum hydride, whereas the second step is faster with diborane. 7-Methyl-2,3,4,5-tetramethoxy-1,8-naphthalic anhydride (**1**), on lithium aluminum hydride reduction, yields only one of the two possible naphthalides; structure **7** has been assigned on the basis of nmr data.

In the course of our earlier investigation[2] of methods for synthesis of substituted 1,8-naphthalic anhydrides, it was discovered that diborane rapidly reduces this type of anhydride, at room temperature, to the corresponding cyclic ether, the 2,1,3-*peri*-naphthopyran. This result was unexpected, since diborane fails to reduce acid chlorides at room temperature,[3] and even sodium borohydride, used by us for preparation of the diborane *in situ*, reduces aromatic acid chlorides only slowly at steam bath temperature.[4] The present investigation is concerned with additional study of reductions with diborane and with lithium aluminum hydride.

1,8-Naphthalic anhydride, as well as 3-methoxy-1,8-naphthalic anhydride, give about the same yield (40%) on reduction at room temperature with diborane, and no other products could be isolated; however, when both the 2 and 7 positions were occupied, reduction failed to occur. Starting material was recovered when there was utilized either 2,7-dimethoxy-1,8-naphthalic anhydride or 7-methyl-2,3,4,5-tetramethoxy-1,8-naphthalic anhydride[5] (**1**). When the same reaction conditions were used for reduction of 1,8-naphthalide (**2**), 2,1,3-*peri*-naphthopyran was again obtained, but in



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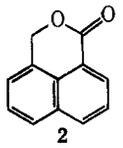

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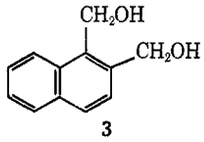
~80% yield.[6] Thus, the intermediacy of **2** in the reduction of 1,8-naphthalic anhydride is suggested.

When 1,2-naphthalic anhydride was subjected to diborane reduction, the sole product isolable from the reaction was the diol, **3**. Similarly, when the adduct of



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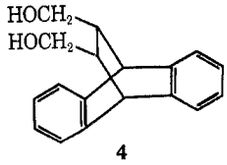

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maleic anhydride and anthracene was reduced, the only product obtained was diol **4**. Thus in absence of the notably stable 2,1,3-*peri*-naphthopyran system, cyclic ether is not formed. Much of the chemistry of the peri-substituted naphthalenes is dominated by the stability of this ring system. For example, 1,8-naphthalic anhydride fails to react with alcohols; indeed,

(1) This investigation was supported in part by a research grant (G-9866) from the National Science Foundation.

(2) J. Cason, A. Weiss, and S. A. Monti, *J. Org. Chem.*, **33**, 3404 (1968).

(3) H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, **82**, 681 (1960).

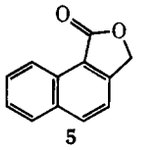
(4) S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 122 (1949).

(5) J. Cason and D. M. Lynch, *J. Org. Chem.*, **31**, 1883 (1966).

(6) There have been several reports of hydride reductions of esters, including lactones, to ethers. The pioneering report of reduction of lactones to tetrahydropyrans by diborane seems to be that of G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, **26**, 4557 (1961).

heating of 1,8-naphthalic acid with methanol or ethanol yields 1,8-naphthalic anhydride. Additional consistent behavior of peri-substituted naphthalenes is reported in the investigation[7] concerned with isolation of anhydride **1** as a degradation product of the naturally occurring pigment herqueinone.

In spite of the stability of the 2,1,3-*peri*-naphthopyran system, reduction of 1,8-naphthalic anhydride with lithium aluminum hydride at room temperature yields none of the cyclic ether. There results a mixture of naphthalide (**2**) and the diol, 1,8-bis(hydroxymethyl)naphthalene. Indeed, with this reducing agent, results with the 1,2-naphthalic anhydride are the same; products are diol **3** and the 1,2-naphthalide. In view of the significant hindrance exerted by an adjacent peri position in naphthalene, it seems safe to assume that the single 1,2-naphthalide obtained from the reaction has structure **5**. In further evidence of the



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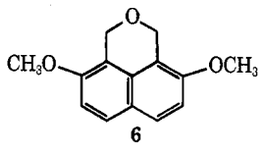

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impact of hindrance in this reaction, 2,7-dimethoxy-1,8-naphthalic anhydride is reduced by lithium aluminum hydride, after 3 hr at reflux in tetrahydrofuran, to yield the cyclic ether, 4,9-dimethoxy-2,1,3-*peri*-naphthopyran (**6**). After a brief period of reflux, the principal product is the intermediate 2,7-dimethoxy-1,8-naphthalide.

The experimental results indicate that the reaction sequence with lithium aluminum hydride also involves the naphthalide as a common intermediate, and the cyclic ether is not formed by dehydration of the diol. Formation of the cyclic ether *via* the diol is also contraindicated by the report[8] that the diol is obtained in good yield when the lithium aluminum hydride reduction of 1,8-naphthalic anhydride is carried out with 3 hr of heating under reflux in a benzene–ether mixture, with distillation of the ether toward the end of the reflux period. In diborane reduction of 3-methoxy-1,8-naphthalic anhydride, recovered alkali-soluble material consisted of starting material, not the naphthalide. Thus, our combined data reveal that with diborane the second step (lactone to cyclic ether) is the faster step, whereas with lithium aluminum hydride the second step is the slower one, regardless of whether the product is diol or cyclic ether.

Lithium aluminum hydride reduction of the highly substituted anhydride, **1**, proved to yield a single 1,8-naphthalide; careful examination failed to detect a second isomer. On the basis of the location of the resonance line in nmr (*cf.* Table I) for the methylene hydrogens at τ 4.23, structure of this lactone is assigned as **7**, with the methylene hydrogens on the side with methyl. 1,8-Naphthalide displays this line at τ 4.10, while 2,7-dimethoxy-1,8-naphthalide has it at τ 4.31. Thus, structure **7**, with the methylene hydrogens not adjacent to methoxyl, seems required, because the methylene hydrogens are significantly downfield from

(7) J. Cason, J. S. Correia, R. B. Hutchison, and R. F. Porter, *Tetrahedron*, **18**, 839 (1962).

(8) W. J. Mitchell, R. D. Topsom, and J. Vaughan, *J. Chem. Soc.*, 2526 (1962).

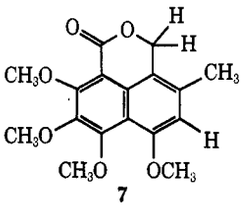
TABLE I

NMR SPECTRA OF ANHYDRIDE 1 AND LACTONE 7

Type H	τ values[a] (number of H's) 1	7
Ar H	3.20 (1)	3.12 (1)
Ar CH_2O		4.23 (2)
Ar OCH_3	5.83 (6)	5.77 (3)
Ar OCH_3	5.90 (3)	5.86 (6)
Ar OCH_3	5.97 (3)	5.93 (3)
Ar CH_3	7.11 (3)	7.00 (3)

[a] All lines are singlets.

the location in the 2,7-dimethoxy-1,8-naphthalide, where they must be adjacent to methoxyl. Buttressing effect of additional methoxyls in **7** might shift the



7

methylene hydrogens further upfield, but not downfield. In additional support of structure **7**, the resonance line for the aromatic methyl hydrogens in **7** is located at τ 7.00, as compared to 7.11 in anhydride **1** (Table I); so a different environment for the aromatic methyl in the two structures is revealed. No conclusions concerning structure may be reached by comparing positions of methoxyl hydrogens, on account of the relatively large effects of vicinal methoxyls on each other;[7] indeed, the lowest field line results from six methoxyl hydrogens in **1**, whereas six hydrogens are accounted for in the middle line of the three resonance lines in **7** (Table I).

Experimental Section[9]

Reduction of 1,8-Naphthalic Anhydride. A. With Diborane.—To a solution of 1.36 g (36 mmol) of $NaBH_4$ in 37 ml of purified diglyme, stirred at room temperature in an atmosphere of N_2, was added portionwise 3.96 g (20 mmol) of powdered 1,8-naphthalic anhydride. To the reddish turbid mixture was next added dropwise, during ~30 min, a solution of 6.8 g (48 mmol) of boron trifluoride etherate in 15 ml of purified diglyme. The ratio of $NaBH_4$:BF_3 is 3:4, as required stoichiometrically for formation of B_2H_6. Stirring at room temperature was continued for 2 hr. After about one-fourth of the BF_3 had been added, the initially reddish solution turned clear yellow, and, after about three-fourths of the addition, a precipitate began to separate. The reaction mixture was worked up by addition of 100 ml of ice–water, followed by filtration, washing, and drying of the precipitate. Crystallization from commercial mixed hexanes yielded 1.36 g (40%) of 2,1,3-*peri*-naphthopyran: mp 76–80° [sublimation raised this to 82–83° (lit.[10] mp 83–83.5°)]; ir clear in carbonyl region, aromatic absorption at 6.20 μ; **picrate** mp 176–178° (lit.[10,11] mp 177.5–178, 173.5–175°).

A similar run using double the ratio of $NaBH_4$ gave 50% yield, mp 82–84°.

B. With Lithium Aluminum Hydride.—To a suspension of 396 mg (2 mmol) of 1,8-naphthalic anhydride in 10 ml of purified tetrahydrofuran (THF), stirred in an atmosphere of N_2, there was added dropwise at room temperature, during 30 min, a solution of 228 mg (6 mmol) of $LiAlH_4$ in 20 ml of absolute ether.

(9) Melting points are corrected. Nmr spectra were recorded on a Varian A-60 instrument, in deuteriochloroform as solvent, with TMS as internal reference. Microanalyses were by the Analytical Laboratory, Department of Chemistry, University of California, Berkeley.

(10) A. J. Weinheimer, S. W. Kantor, and C. R. Hauser, *J. Org. Chem.*, **18**, 801 (1953).

(11) J. Cason and J. D. Wordie, *J. Org. Chem.*, **15**, 608 (1950).

After stirring had been continued for 1 hr, excess $LiAlH_4$ was destroyed by adding 15 ml of water, followed by 15 ml of 2 *M* H_2SO_4. The resultant two-phase solution was extracted with three portions of ether, and solvent was removed from the washed extracts. Repeated systematic crystallization of the residue from $CHCl_3$ yielded 100 mg (27%) of 1,8-bis(hydroxymethyl)naphthalene, mp 156–157° (lit.[10] mp 154–154.5°), ir and melting point identical with those of a sample synthesized by reduction of dimethyl 1,8-naphthalate with $LiAlH_4$. Combined mother liquors from isolation of the diol were evaporated to dryness, and the residue was systematically recrystallized from ethanol to yield 143 mg (39%) of 1,8-naphthalide (**2**), mp 159–161°, ir and melting point identical with those of an authentic sample,[11] but lit.[11] melting point of same sample is 156.6–157.2°. Another sample of **2**, purified *via* extraction into basic solution, had mp 157–161° (lit.[12,13] mp 156–157, 159–160°). The substance appears to be polymorphic.

Reduction of 1,8-Naphthalide (2) with Diborane.—Reduction of 184 mg of **2** by the same procedure described for 1,8-naphthalic anhydride, except that one-half the ratio of reducing agent was used, yielded, after crystallization, 135 mg (80%) of product, mp 80–83°.

Reduction of 3-methoxy-1,8-naphthalic anhydride[2] with diborane by the same procedure described for the unsubstituted anhydride yielded 43 mg of crude product from 72 mg of starting material. The crude product was heated under reflux for 15 min with 23 ml of 1 *N* NaOH (to dissolve any naphthalide present), and the cooled mixture was extracted with three portions of ether. Work-up of the alkaline solution yielded no naphthalide, but 10 mg of starting material, which, after crystallization from glacial acetic acid, had mp 246–250° (lit.[2] mp 249–250°). Product recovered from the ether extracts was recrystallized from hexane to yield 24 mg (38%), mp 80–83°, of **5-methoxy-2,1,3-*peri*-naphthopyran**. By sublimation and further recrystallization was obtained an analytical sample: mp 82–84°; ir clear in carbonyl region, aromatic absorption at 6.27 μ.

Anal. Calcd for $C_{13}H_{12}O_2$: C, 78.0; H, 6.0. Found: C, 77.6; H, 6.0.

Reduction of 1,2-Naphthalic Anhydride. A. With Diborane.—A 396-mg sample of 1,2-naphthalic anhydride,[14] mp 169–171°, was reduced as described for the 1,8 isomer. Recrystallization of the product from benzene yielded 240 mg (63%), mp 122–123°, of **1,2-bis(hydroxymethyl)naphthalene (3)**.

Anal. Calcd for $C_{12}H_{12}O_2$: C, 76.6; H, 6.4. Found: C, 76.6; H, 6.2.

B. With Lithium Aluminum Hydride.—A 396-mg sample of the anhydride was reduced as described for the 1,8 isomer, and the product was first crystallized from benzene to yield 170 mg (45%) of diol **3**, mp 122–123°, ir and melting point identical with those of sample from diborane reduction. Recrystallization from methanol of material recovered from the mother liquors yielded 84 mg, mp 157–158°, of **1,2-naphthalide**, assigned structure **5**.

Anal.[15] Calcd for $C_{12}H_8O_2$: C, 78.25; H, 4.4. Found: C, 78.3; H, 4.45.

Diol 4.—A 5.52-g sample of the adduct from anthracene and maleic anhydride was reduced with diborane as described for 1,8-naphthalic anhydride, and the product was crystallized from benzene to yield 3.6 g (68%) of diol **4**, mp 225–226° (lit.[16] mp 221°). In view of the minor discrepancy in melting point and the previous report in a patent,[16] a sample was analyzed.

Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.2; H, 6.9.

A 100-mg sample of diol **4** was converted to the **cyclic ether** by heating it under reflux for 20 hr with 5 ml of 35% H_2SO_4, yield 79 mg (85%), mp 182–183° from methanol (lit.[16] mp 180–181°).

2,7-Dimethoxy-1,8-naphthalic Anhydride.—Following the procedure previously developed[2] for synthesis of 3-substituted acenaphthenequinones, 3.04 g (16.2 mmol) of 2,7-dimethoxynaphthalene (from acid-catalyzed methylation of commercial diol, mp 139–141° from ethanol, lit.[17] mp 139°) and 4.48 g (16.2 mmol) of diphenyloxalimide chloride yielded 5.5 g of crude product containing 3,8-dimethoxyacenaphthenequinone. Since difficulty was encountered in extracting the quinone into aqueous bisulfite, as experienced[2] with another dimethoxyacenaphthenequinone, the crude product was oxidized in a mixture of 22 ml of 95% ethanol, 185 ml of 4 *N* NaOH, 185 ml of 30% H_2O_2, and 256 ml of water. After the reaction mixture had been allowed to stand for 30 min with occasional shaking, the large (3.15 g) dark precipitate which still remained was removed by filtration. The white precipitate obtained by acidification of the alkaline filtrate was recrystallized from ethylene glycol to yield 869 mg (21% from 2,7-dimethoxynaphthalene) of the desired anhydride, mp 346–348° (lit.[18] mp 340–344°).

Reduction of 2,7-Dimethoxy-1,8-naphthalic Anhydride.—Attempted reduction of 58 mg of this anhydride, with twice the normally used ratio of $NaBH_4$ to BF_3, resulted in recovery of 50 mg of starting material. Reduction of 100 mg of the anhydride with $LiAlH_4$ as described for the parent anhydride, except that the mixture was heated for 30 min under reflux, yielded 91 mg of crude product. This material was heated under reflux for 1 hr with 10 ml of 10% methanolic KOH (to saponify any naphthalide present), and the cooled and water-diluted solution was extracted with three portions of ether. The ether extracts yielded 27 mg of oily material, from which no pure product could be isolated. Acidification of the alkaline solution yielded 33 mg of product, which gave after crystallization from methanol 20 mg (21%) of 2,7-dimethoxy-1,8-naphthalide, mp 198–201°. After two additional crystallizations, the analytical sample had mp199–202°; uv (*cf.* Table II); ir ($CHCl_3$) 5.84 μ; nmr τ [*J* (for doublets) = 9 Hz] 2.05 (d, 1, Ar H), 2.23 (d, 1, Ar H), 2.77 (d, 1, Ar H) 2.83 (d, 1, Ar H), 4.31 (s, 2, Ar CH_2O), 5.85 (s, 3, Ar OCH_3), 5.99 (s, 3, Ar OCH_3).

TABLE II

UV ABSORPTION OF 1,8-NAPHTHALIDES[a]

1,8-Naphthalide	λ_{max}, nm[b] ($\epsilon \times 10^{-3}$)			
Parent	[c]	213 (42.0)	241 (23.1)	314 (7.1)
2,7-Di-OCH_3	218 (32.9)	232 (52.9)	255 (16.4)	344 (11.8)
7	224 (23.1)	254 (40.8)	...	338 (9.45)

[a] Solvent 95% ethanol. [b] λ_{min} in order of listing above: 262 (1.05), 282 (2.7), 279 (1.5). [c] Below range observable in ethanol solvent.

Anal. Calcd for $C_{14}H_{12}O_4$: C, 68.8; H, 4.95. Found: C, 68.4; H, 5.0.

In a similar reduction, except that twice the ratio of $LiAlH_4$ was used and heating was continued for 3 hr, the saponifiable material (naphthalide) amounted to only 6 mg and the neutral product was 39 mg. Recrystallization from methanol yielded 20 mg (22%) of **4,9-dimethoxy-2,1,3-*peri*-naphthopyran (6)**, mp 130–133°. Two crystallizations from methanol yielded analytical sample: mp 132.5–134°; ir ($CHCl_3$) clear in carbonyl region, aromatic absorption at 6.15 μ.

Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1. Found: C, 72.6; H, 6.2.

Uv of 1,8-Naphthalides.—Uv absorption of the naphthalides is shifted to longer wavelengths (Table II) by the methoxyl substitution adjacent to the ester function; however, additional methoxyl substitution (**7**) has little effect on the longest wavelength band, except to broaden it significantly on the low-wavelength side. The spectrum of **7** is also simplified, in that the band to be expected near 275 nm is entirely absent.

Reduction of Anhydride 1.[5]—Attempted reduction of 54 mg of **1** with diborane by the same procedure applied to 1,8-naphthalic anhydride led to recovery of 30 mg of starting material; no homogeneous reaction product could be isolated, even after diverse applications of liquid-phase column chromatography. Reduction, during 30 min, of 100 mg of **1** with $LiAlH_4$ and work-up *via* saponification with methanolic KOH followed the pro-

(12) R. C. Fuson and G. Munn, *J. Amer. Chem. Soc.*, **71**, 1870 (1949).

(13) G. Errera and G. Ajon, *Gazz. Chim. Ital.*, **44** (II), 92 (1914).

(14) P. A. S. Smith and R. O. Kan, *J. Amer. Chem. Soc.*, **82**, 4753 (1960). Details of experimental procedure were adapted from the preparation of homophthalic acid: P. A. S. Smith and R. O. Kan, *Org. Syn.*, **44**, 62 (1964).

(15) Classical combustion analysis tended toward low values for several of the compounds encountered in this investigation; however, this naphthalide gave unacceptably low values (highest C, 77.5%). The correct value was obtained, as for previously reported compounds,[2] by the method depending on combustion in a sealed tube; *cf.* C. W. Koch and E. Jones, *Mikrochem. Acta*, **4**, 734 (1963).

(16) H. Krzikalla, E. Woldan, and O. Dornheim, German Patent 736,024 (1943); *Chem. Abstr.*, **38**, 4620 (1944).

(17) H. Bunzly and H. Decker, *Ber.*, **38**, 3272 (1905).

(18) D. H. R. Barton, P. de Mayo, G. A. Morrison, and H. Raistrick, *Tetrahedron*, **6**, 48 (1959).

cedure described for 2,7-dimethoxy-1,8-naphthalic anhydride. No homogeneous product could be isolated from the base-insoluble fraction. After crystallization of the base-soluble material from methanol–water, there was obtained 17 mg (18%) of **lactone 7**, mp 112.5–114.5°. This material was combined with the products from two other similar runs, and, in solution in 10 ml of ether–hexane (2:3), was applied to a column of 10.6 g of Woelm alumina (activity III). Elution with ether–hexane, then with ether, while observing band movement in uv light, revealed only a single blue band, which was finally eluted with ether. Crystallization of the eluted product (49 mg) from hexane yielded 43 mg of white crystals, mp 115.0–116.5°; two additional crystallizations gave the analytical sample of **7**, mp 115.5–116.5°, ir 5.87 μ (carbonyl), uv (Table II), nmr (Table I).

Anal. Calcd for $C_{17}H_{18}O_6$: C, 64.1; H, 5.7. Found: C, 64.0; H, 5.9.

Registry No.—**1**, 6398-92-1; **2**, 518-86-5; **3**, 39050-28-7; **4**, 26495-88-5; **5**, 5657-01-2; **6**, 39050-31-2; **7**, 39050-32-3; $NaBH_4$, 16940-66-2; $LiAlH_4$, 16853-85-3; 1,8-naphthalic anhydride, 81-84-5; diborane, 19287-45-7; 3-methoxy-1,8-naphthalic anhydride, 5289-78-1; 5-methoxy-2,1,3-*peri*-naphthopyran, 39050-34-5; 1,2-naphthalic anhydride, 5343-99-7; 2,7-dimethoxy-1,8-naphthalic anhydride, 32432-09-0; 2,7-dimethoxy-1,8-naphthalide, 39050-37-8.

Notes

Addition of Amide Ion to Isoquinoline and Quinoline in Liquid Ammonia. Nuclear Magnetic Resonance Spectra of Anionic σ Complexes[1]

JOHN A. ZOLTEWICZ,* LARRY S. HELMICK, TERRY M. OESTREICH, ROY W. KING, AND PAUL E. KANDETZKI

Department of Chemistry, University of Florida, Gainesville, Florida 32601

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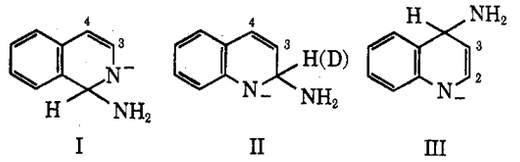
Anionic σ complexes are formed by the addition of nucleophiles to aromatic and heteroaromatic molecules.[2] Recent studies of such complexes, commonly called Meisenheimer-type complexes, have provided new insights into the effects of structure on the addition of nucleophiles to unsaturated carbon centers.

We wish to call attention to a class of anionic σ complexes long postulated[3] but largely uncharacterized. The complexes are formed by the reaction of amide ion with hetarenes.

We now report the first unambiguous evidence in the form of nmr spectra for the existence of anionic σ complexes I–III formed by the addition of amide ion to



I II III

isoquinoline and quinoline. Amide ion adds faster to C-2 than to C-4 of quinoline to give II but the C-4 adduct (III) is more stable; *i.e.*, kinetic and thermodynamic products are formed, respectively.

Complexes I–III have long been postulated to occur in the Chichibabin amination of isoquinoline and quinoline.[4,5] Some appear to have been isolated by Bergstrom in the 1930's, but owing to their instability in the solid state they were characterized only superficially.

Results and Discussion

In the presence of excess KNH_2, reaction with isoquinoline or quinoline is complete and rapid; no hetarene can be detected by nmr when mixtures are examined shortly after preparation. When substrate is present in excess, spectra of both complexed and free heterocycles are observed, and there is no evidence of signal averaging between these two, either in coupling constants or chemical shifts.

A significant change occurs in the pattern of a single multiplet of a complex as the amide ion concentration is varied. The multiplicity decreases as the concentration of KNH_2 increases. This means that amide ion catalyzes proton transfer between the amino group of an adduct and solvent, leading to spin decoupling.[7,8] When the amide ion concentration is low, this exchange is slow and spin coupling is observed. This multiplicity change serves as a useful way to recognize the proton signal of the tetrahedral center of the complex and provides direct evidence for a complex containing an amino group. In the absence of amide ion, isoquinoline and quinoline in NH_3 show no evidence of adduct formation.

Isoquinolines.—The spectrum of the complex between isoquinoline and amide ion at −10° shows a broad multiplet at τ 2.7–3.65, a triplet (J_{HCNH} = 7.0 Hz) at τ 4.66 which collapses to a singlet when amide ion is present in excess and a doublet ($J_{3,4}$ = 5.5 Hz) at τ 5.13. The triplet–singlet change and the lack of further splitting indicates that the adduct is formed by

(1) Presented in part at the Gordon Conference on Heterocyclic Chemistry, New Hampton, N. H., June 26–30, 1972.

(2) M. J. Strauss, *Chem. Rev.*, **70**, 667 (1970).

(3) K. Ziegler and H. Zeiser, *Chem. Ber.*, **63**, 1847 (1930).

(4) F. W. Bergstrom, *J. Amer. Chem. Soc.*, **56**, 1748 (1934); *Justus Liebigs Ann. Chem.*, **515**, 34 (1934); *J. Org. Chem.*, **2**, 411 (1937); *ibid.*, **3**, 233, 424 (1938).

(5) Simple ions are written here, but early conductance studies indicate that ion pairing is important in ammonia.[6]

(6) C. A. Kraus, *J. Phys. Chem.*, **58**, 673 (1954), and references cited therein.

(7) R. A. Ogg, Jr., *Discuss. Faraday Soc.*, **No. 17**, 215 (1954).

(8) T. J. Swift, S. B. Marks, and W. G. Sayre, *J. Chem. Phys.*, **44**, 2797 (1966).