benzoyl chloride has been found in the literature, the compound was analyzed. One-gram samples were hydrolyzed in an aqueous sodium hydroxide solution, acidified with nitric acid and the chloride precipitated as silver chloride which was weighed in a tared Jena crucible.

Anal. Calcd. for $C_7H_3O_3NFCl$: Cl, 17.42. Found: Cl, 17.32, 17.34.

Alkyl Esters of 2-Nitro-5-fluorobenzoic Acid.—2-Nitro-5-fluorobenzoyl chloride was refluxed in an excess of the appropriate alcohol for thirty minutes. The addition of water to the reaction mixture caused precipitation of the esters. The liquid esters were distilled under reduced pressure; the solid esters were recrystallized from dilute alcohol.

Dialkylaminoalkyl Ester Hydrochlorides of 2-Nitro-5-fluorobenzoic Acid.—The acid chloride was dissolved in anhydrous benzene and an equimolecular quantity of the appropriate alkylamino alcohol, also dissolved in anhydrous benzene, was added. In most instances the alkamine ester hydrochloride separated out immediately. The reaction mixture was refluxed for one hour. The dimethylaminoethyl and diethylaminoethyl ester hydrochlorides precipitated as solids at once; the diethylaminopropyl ester hydrochloride separated as an oily layer heavier than benzene but solidified upon refluxing; the di-*n*-propylaminoethyl and di-*n*-propylaminopropyl ester hydrochlorides separated as oily layers heavier than benzene which crystallized when the reaction mixtures were cooled in an ice–salt bath. The di-*n*-butylaminoethyl ester hydrochloride appeared to be completely soluble in the benzene since no layer separated; when the mixture was cooled, the ester crystallized out. The di-*n*-butylaminopropyl ester hydrochloride separated out as an oily layer lighter than benzene and crystallized when the reaction mixture was cooled in an ice–salt bath. The products were filtered off and washed with anhydrous ether; recrystallization was carried out by dissolving the products in a minimum of anhydrous ethanol and precipitating them from the cooled ethanol solution with anhydrous ether.

Alkyl Esters of 2-Amino-5-fluorobenzoic Acid.—These compounds were prepared by the reduction of the corresponding nitro esters with hydrogen, using a platinum oxide catalyst prepared according to the method of Adams.[5] No difficulty was experienced in purifying these esters.

The Dialkylaminoalkyl Esters of 2-Amino-5-fluorobenzoic Acid.—These compounds were also prepared by the reduction of the corresponding nitro esters. After the reduction, the catalyst was removed by filtration and the solution dried over anhydrous sodium sulfate. The anhydrous alcohol solution was then poured into anhydrous ether and the hydrochlorides separated as an amorphous mass which crystallized upon standing.

Summary

Several alkyl and alkamine esters of 2-nitro-5-fluorobenzoic acid and 2-amino-5-fluorobenzoic acid have been prepared. All of the esters of 2-amino-5-fluorobenzoic acid possess anesthetic properties. The toxicity of the procaine analog was slightly higher than that of procaine. All of the anesthetic esters were quite unstable and formed highly colored solutions. The compounds possess no practical value as anesthetics.

(5) Adams, Voorhees and Shriner, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1932, p. 452.

CHICAGO, ILLINOIS RECEIVED MARCH 17, 1944

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF WINTHROP CHEMICAL COMPANY, INC.]

Catalytic Hydrogenation of Pyridinols, Quinolinols and their Esters

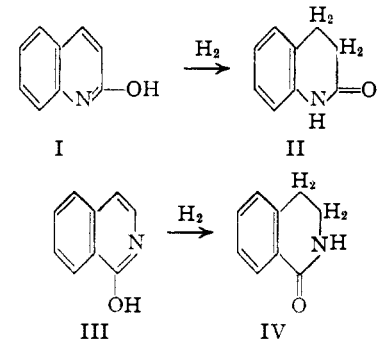
BY CHESTER J. CAVALLITO AND THEODORE H. HASKELL

In the continuation of some work on the preparation of phenolic acid esters described in a recent publication,[1] the attempt was made to prepare pyridinyl and quinolinyl esters of phenolic acids. The method consisted of treating the pyridinol or quinolinol with the benzyloxyaroyl chloride, followed by catalytic hydrogenolysis of the benzyl group. Instead of obtaining the corresponding pyridinyl or quinolinyl hydroxybenzoate, in several hydrogenations entirely unexpected reactions occurred, which varied with the position of the hydroxyl group on the pyridine or quinoline ring. In order to determine the types of hydrogenation which could take place, the isomeric pyridinols, quinolinols and certain of their esters were investigated.

Hydrogenation was carried out in a dioxane or ethanol solution of the compound at 25 and 55° with a palladium sponge catalyst[2] and with from one to three atmospheres of hydrogen super pressure in a modified[3] Parr low pressure hydrogenator. An Adams platinum or Raney nickel catalyst was ineffective in catalyzing these reactions under the conditions employed.

(1) Cavallito and Buck, THIS JOURNAL, **65**, 2140 (1943).
(2) Willstätter and Waldschmidt-Leitz, *Ber.*, **54**, 123 (1921).
(3) Buck and Jenkins, THIS JOURNAL, **51**, 2163 (1929).

Under the conditions of these experiments, 2-pyridinol yielded α-piperidone, whereas 3- and 4-pyridinols did not reduce. The 2-quinolinol (I) and 1-isoquinolinol (III) gave the 3,4-dihydroquinolones (II and IV) but the 3-, 5-, 6-, 7- and 8-



quinolinols yielded the corresponding 1,2,3,4-tetrahydroquinolinols. 4-Quinolinol, 2-methyl-4-quinolinol and 4-methyl-2-quinolinol did not reduce.

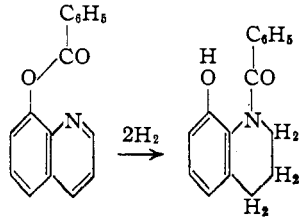
Under the conditions of reduction, naphthalene did not hydrogenate, and pyridine showed some hydrogen uptake; however, most of the starting material was recovered. Quinoline hydrogenated

more readily than isoquinoline. The introduction of hydroxyl groups in quinoline permitted hydrogenation to proceed more rapidly. 3-Quinolinol hydrogenated more slowly than the 5-, 6-, 7- or 8-derivatives, and 3-pyridinol was even more resistant, not hydrogenating under the experimental conditions.

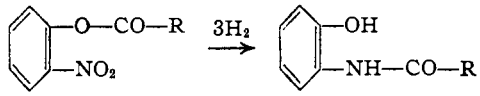
Of the aromatic esters prepared, the 3-pyridinyl and the 3-, 5-, 6-, 7- and 8-quinolinyl esters were fairly stable, whereas the 2-pyridinyl and 2-quinolinyl esters were more easily hydrolyzed. The 4-pyridinyl, 4-quinolinyl and 4-methyl-2-quinolinyl esters were very unstable, and could be prepared only under anhydrous conditions (compare 2-acetoxypyridine).[4] The esters of aromatic acids appear to be more stable than the aliphatic acid esters.

The 3-, 5-, 6- and 7-benzoxyquinolines hydrogenated as expected to yield the benzoxytetrahydroquinolines. With 3-benzoxypyridine, no reduction took place.

The 8-quinolinyl esters underwent hydrogenation to the 1,2,3,4-tetrahydro derivative, but the reaction was complicated by the subsequent migration of the acyl group to the nitrogen. The

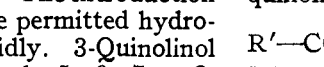


rearrangement is analogous to that which occurs in the reduction of carboxylic acid esters of *o*-nitrophenol.



Reductions of *o*-nitro esters of various types involving rearrangements have been reported using tin and hydrochloric acid.[5,6,7,8,9] Catalytic reductions of *o*-nitrophenyl benzoate with platinum or palladium catalysts at 25° gave the rearranged amide almost quantitatively. This appears to be a true intramolecular rearrangement. The *m*- and *p*-nitro esters yield the amino esters upon reduction. A mixture of nitrobenzene and phenyl benzoate yielded no benzanilide on reduction, nor did a mixture of aniline and phenyl benzoate yield benzanilide when heated to 55°. This indicates that no intermolecular reaction takes place in the rearrangement of ortho-amino esters.

The normally expected reduction products, the *o*-aminophenyl esters and 1,2,3,4-tetrahydro-8-quinolinyl esters, have in common the grouping



where R is H or some group which does not destroy the basic character of the nitrogen. This structure can undergo the rearrangement even though the rearranging components are bound to different rings.

Evidence for the structure of the rearranged N-acyl-tetrahydro-8-quinolinol is convincing. The esters of 1,2,3,4-tetrahydroquinolinols are soluble in acid, insoluble in alkali, are easily saponified, and give no color change with ferric chloride. N-Benzoyl-tetrahydro-8-quinolinol is soluble in alkalies, insoluble in acids, does not saponify, and gives a green color with ferric chloride (becoming red on warming). The N-benzoyl derivative on benzoylation yields N-benzoyl-8-benzoxy-1,2,3,4-tetrahydroquinoline which is identical with the product obtained by benzoylation of 1,2,3,4-tetrahydro-8-quinolinol.

The 2-benzoxy- and 2-β-naphthoxy derivatives of pyridine and quinoline undergo rapid hydrogenolysis to form toluene and β-methylnaphthalene, respectively, with liberation of 2-pyridinol or 2-quinolinol which is then further hydrogenated. With 1-benzoxyisoquinoline, toluene and 1-isoquinolinol are formed. It is possible to recover the major part of the hydroxy compound unchanged by stopping the reaction when the reduction rate becomes much slower, or after absorption of 3 molar equivalents of hydrogen. With 4-benzoxypyridine, 4-benzoxyquinoline, and 2-benzoxy-4-methylquinoline, the hydrogenation does not proceed at all after absorption of 3 molar parts of hydrogen.

The mild conditions (25°, one to two atmospheres of hydrogen superpressure) necessary to bring about the reduction of the 2-pyridinyl, 4-pyridinyl, 2-quinolinyl and 4-quinolinyl aromatic esters to hydrocarbons of the aroyl portion of the ester are unusual. This ease of hydrogenolysis appears to be associated with the weakness of the ester bond. Esters of aliphatic acids with 2-pyridinol are readily hydrolyzed by small amounts of moisture.[4] The aromatic esters are more stable, but not as stable as ordinary phenolic esters. Phenyl benzoate is unaffected by the reduction, and upon heating to 50° with aniline undergoes no change, whereas 2-benzoxypyridine, which is readily reduced, reacts quickly with aniline at 50° to yield benzanilide. The lability of this type of ester must be associated with the weakly phenolic character of 2-pyridinol and 2-quinolinol, as evidenced by their tendency to exist as pyridones and quinolones. The 4-hydroxy derivatives appear to be even less phenolic in character. The weak ester linkages are apparently cleaved by hydrogen to yield the original hydroxy compound, and the aldehyde of the acid. The aldehyde is further reduced to the alcohol, and in the case of the aromatic substituted

(4) Tschitschibabin and Szokow, *Ber.*, **58**, 2650 (1925).
(5) Böttcher, *ibid.*, **16**, 629, 1933 (1883).
(6) O. Widman, *J. prakt. Chem.*, **155**, 343 (1893).
(7) Einhorn and Pfyl, *Ann.*, **311**, 34 (1900).
(8) Auwers, *ibid.*, **332**, 159 (1904).
(9) J. H. Ransom, *Ber.*, **31**, 1055 (1898) to THIS JOURNAL, **36**, 390 (1914).

TABLE I

Compound	Appearance[a]	Yield, %	M. p.[b] °C.	Formula	Analyses,[c] % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
2-Benzoxypyridine	Prisms a	60 A	47 g	$C_{12}H_9O_2N$	...	...	..	..	7.04	7.27
3-Benzoxypyridine	Prisms a	65 A	51	$C_{12}H_9O_2N$	...	...	..	..	7.04	7.06
4-Benzoxypyridine	Plates a	50 B	79	$C_{12}H_9O_2N$	72.36	72.49	4.52	4.73	7.04	7.13
2-Benzoxyquinoline	Needles d	60 A	95	$C_{16}H_{11}O_2N$	...	...	..	..	5.62	5.69
3-Benzoxyquinoline	Prisms d	.. A	67	$C_{16}H_{11}O_2N$	77.11	77.34	4.42	4.80	5.62	5.77
4-Benzoxyquinoline	Prisms b	45 B	131	$C_{16}H_{11}O_2N$	...	...	..	...	5.62	5.68
5-Benzoxyquinoline	Prisms a	45 A	93	$C_{16}H_{11}O_2N$	77.11	76.78	4.42	4.65	5.62	5.96
6-Benzoxyquinoline	Prisms a	60 C	118 h	$C_{16}H_{11}O_2N$	77.11	76.98	4.42	4.17	5.62	5.90
7-Benzoxyquinoline	Needles a	40 C	85 j	$C_{16}H_{11}O_2N$	...	...	..	..	..	..
8-Benzoxyquinoline	Prisms d	97 A	118 k	$C_{16}H_{11}O_2N$	...	...	..	..	..	..
3-Benzoxy-1,2,3,4-tetrahydroquinoline	Granular crystals d	90 ±	106	$C_{16}H_{15}O_2N$	75.89	76.00	5.93	6.02	5.53	5.90
5-Benzoxy-1,2,3,4-tetrahydroquinoline	Granular crystals d	90 ±	107	$C_{16}H_{15}O_2N$	75.89	75.96	5.93	5.90	5.53	5.78
6-Benzoxy-1,2,3,4-tetrahydroquinoline	Prisms d	90 ±	102	$C_{16}H_{15}O_2N$	75.89	76.20	5.93	6.09	5.53	5.73
7-Benzoxy-1,2,3,4-tetrahydroquinoline	Plates d	90 ±	117	$C_{16}H_{15}O_2N$	75.89	76.20	5.93	6.20	5.53	5.65
2-Benzoxy-4-methylquinoline	Needles a	.. B	76	$C_{17}H_{13}O_2N$	77.59	77.65	4.94	4.91	5.32	5.65
2-β-Naphthoxyquinoline	Prism clusters d	55 A	125	$C_{20}H_{13}O_2N$	...	...	..	..	4.68	4.97
2-β-Naphthoxypyridine	Rhombohedral plates d	70 A	116	$C_{16}H_{11}O_2N$	...	...	..	..	5.62	5.68
2-(4-Benzyloxy)-benzoxypyridine	Prism clusters d	60 A	123–125	$C_{19}H_{15}O_3N$	...	...	..	..	4.59	4.57
2-(3,4,5-Tris-(benzyloxy)-benzoxy)-pyridine	Prism clusters d	80 A	116	$C_{33}H_{27}O_5N$	76.60	76.67	5.22	5.30	2.71	2.52
3-(3,4,5-Tris-(benzyloxy)-benzoxy)-pyridine	Needles d	80 A	120	$C_{33}H_{27}O_5N$	...	...	..	..	2.71	2.83
3-(3,4,5-Trihydroxy)-benzoxypyridine	Spheroids c	90 ±	180–185	$C_{12}H_9O_5N$	58.30	58.60	3.64	3.99	5.67	5.52
2-(3,4,5-Tris-(benzyloxy)-benzoxy)-quinoline	Needle clusters e	40 A	117	$C_{37}H_{29}O_5N$	78.31	78.67	5.11	5.26	2.47	2.32
N-Benzoyl-1,2,3,4-tetrahydro-8-quinolinol	Rhombohedral plates c	90 ±	174	$C_{16}H_{15}O_2N$	75.89	75.87	5.93	6.00	5.53	5.80
N-Benzoyl-8-benzoxy-1,2,3,4-tetrahydroquinoline	Prisms d	..	146	$C_{23}H_{19}O_3N$	77.31	77.68	5.32	5.01	3.92	3.90
8-(4-Benzyloxy)-benzoxyquinoline	Prism clusters d	60 A	163	$C_{23}H_{17}O_3N$	...	...	..	..	3.94	3.95
N-(4-Hydroxybenzoyl)-1,2,3,4-tetrahydro-8-quinolinol	Elongated plates (hydrates) c	90 ±	161	$C_{16}H_{15}O_3N$	71.38	71.60	5.58	5.61	5.21	5.40
8-Benzoxy-2-quinolinol	Elongated hexagonal plates d	20 A	208	$C_{16}H_{11}O_3N$	72.45	72.15	4.15	4.09	5.28	5.20
2,8-Bis-(benzoxy)-quinoline	Needles a	30–60 A	108	$C_{23}H_{15}O_4N$	74.79	74.45	4.07	3.79	3.79	3.73
8-Benzoxy-3,4-dihydro-2(1)-quinolone	Needles d	90 ±	167	$C_{16}H_{13}O_3N$	71.91	71.84	4.87	4.95	5.24	5.15
1-Benzoxyisoquinoline	Needles b	80 A	147	$C_{16}H_{11}O_2N$	77.11	77.25	4.42	4.45	5.62	5.57
N-Benzoyl-3,4-dihydro-1(2)-isoquinolone	Needles d	..	132	$C_{16}H_{13}O_2N$	76.45	76.61	5.17	5.04	5.57	5.45
2-(3,4,5-Tri-(acetoxy)-benzoxy)-quinoline	Very small needles c	40 B	133	$C_{22}H_{17}O_8N$	...	...	..	..	3.31	3.30

[a] Crystallization media: a, Skellysolve B; b, Skellysolve C; c, 70% ethanol; d, 95% ethanol; e, ethanol–dioxane. [b] Melting points: g, m. p. 42° by Tschitschibabin and Oparina, *Chem. Zentr.*, **97**, I, 938 (1926); h, m. p. 230° by Skraup, *Monatsh.*, **3**, 556, 567 (1882); j, m. p. 88° by Skraup, *ibid.*, **3**, 556, 567 (1882); k, m. p. 118–120° by Bedall and O. Fischer, *Ber.*, **14**, 1367 (1881). [c] The authors wish to thank the Misses E. Bass, A. Rainey and P. Curran for the microanalyses.

methanols (benzyl alcohol, β-naphthyl alcohol, etc.). the reduction proceeds to the hydrocarbon.

2,8-Quinolindiol formed a mono-ester and a di-ester with benzoyl chloride. Both esters yielded

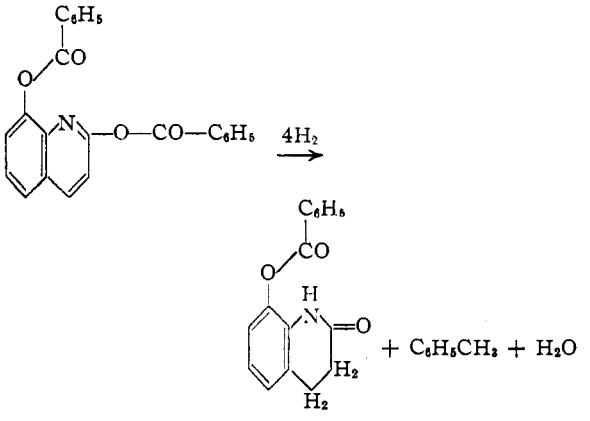
TABLE II

Compound	Literature m. p., °C.	M. p. observed, °C.	M. p., °C., of the quinolinol precursor	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
3,4-Dihydro-2(1)-quinolone	163[a]	160	200	73.47	73.64	6.12	6.40	..	..
3,4-Dihydro-1(2)-isoquinolone	71[b]	73	209	...	...	..	..	..	..
8-Hydroxy-3,4-dihydro-2(1)-quinolone	....	195	265 dec.	66.26	66.27	5.52	5.38	..	..
1,2,3,4-Tetrahydro-3-quinolinol	....	93	198	72.48	72.81	7.38	7.27	9.40	9.28
1,2,3,4-Tetrahydro-5-quinolinol	116–117[c]	116	225	...	...	..	..	..	..
1,2,3,4-Tetrahydro-6-quinolinol	160[d]	160	193	72.48	72.87	7.38	7.06	9.40	9.42
1,2,3,4-Tetrahydro-7-quinolinol	94– 95[e]	93	235	...	...	..	..	..	..
1,2,3,4-Tetrahydro-8-quinolinol	121–122[f]	119	76	...	...	..	..	..	..

[a] H. Meyer and Beer, *Monatsh.*, **34**, 1179 (1913). [b] Bamberger and Dieckman, *Ber.*, **26**, 1219 (1893). [c] Riemerschmied, *ibid.*, **16**, 723 (1883). [d] Miyamoto and Kataoka, *Chem. Abst.*, **33**, 9306 (1939). [e] v. Braun, *Ber.*, **47**, 499 (1914). [f] Bedall and O. Fischer, *ibid.*, **14**, 1368 (1881).

the same monobenzoyl-dihydro derivative on reduction, the di-ester also yielding toluene. This indicated that the mono-ester is the 8-ester. That is the normal expectation since the 8-hydroxyl group is more phenolic in its properties than the 2-hydroxyl. The physical properties are also in agreement. It was observed that 8-benzoxyquinoline melts higher than 8-quinolinol, whereas 2-benzoxyquinoline melts much lower than 2-quinolinol. The monobenzoate of 2,8-quinolindiol melts only slightly lower than the parent base, whereas the di-ester melts much lower, indicating that the 2-hydroxyl is esterified on going from the mono- to the di-ester.

Upon reduction of the dibenzoyl ester, the typical hydrogenolysis of the 2-ester occurs, but there is no migration of the 8-acyl group since the nitrogen in the adjacent ring is no longer basic in character. The reduction product is soluble in dilute alkalies, insoluble in dilute acids, yields no color change with ferric chloride, and is easily saponified to give benzoic acid and 8-hydroxy-3,4-dihydro-2(1)-quinolone.



Under the hydrogenation conditions described, acid chlorides absorb very little hydrogen. Benzoyl chloride, for example, absorbed less than 10% of the hydrogen required to yield toluene. The hydrogenation of the 2- and 4-aroyloxypyridine and -quinoline, on the other hand, yielded the hydrocarbon of the acid portion of the ester practically quantitatively.

Experimental

Analyses and properties of the esters and their hydrogenation products are presented in Table I. Melting points of the quinolinols and their reduction products are compared in Table II. Pertinent analyses are included.

Pyridinols and Quinolinols.—The 2-pyridinol (α-pyridone), 2-quinolinol (carbostyril), 8-quinolinol and 4-methyl-2-quinolinol were obtained from the Eastman Kodak Co.

4-Pyridinol (γ-pyridone), m. p. 148°, was obtained by the method of Koenigs and Greiner.[10]

3-Pyridinol was prepared by dissolving 15 g. of crude 3-aminopyridine in 18 cc. of concentrated sulfuric acid, to which sodium nitrite solution was added to slight excess. The solution was heated as long as nitrogen was evolved, then cooled, neutralized with sodium carbonate and extracted with ether. The ether was evaporated and the residue was recrystallized from hot water after decolorization with charcoal. The 3-aminopyridine was prepared from nicotinamide.[11] The over-all yield was 30% from nicotinamide and the m. p. 125° for the pyridinol.

3-Quinolinol was prepared by diazotization and hydrolysis of 3-aminoquinoline,[12] which was prepared from 3-bromoquinoline. The aminoquinoline was obtained by the procedure used for the preparation of 3-aminopyridine.[13]

The bromoquinoline was obtained by bromination of quinoline with S_2Br_2.[14] The over-all yield of quinolinol from the bromo derivative was 40%.

4-Quinolinol was prepared by a Conrad–Limpach type of reaction,[15,16] as modified by several workers.

To 500 cc. of glacial acetic acid was added 93 g. (1 mole) of aniline and 188 g. (1 mole) of diethyl oxalacetate. The solution was kept at 40 to 50° for four hours and then allowed to stand for fifteen hours at room temperature. The solution was poured over 2 kg. of ice and 35% sodium hydroxide solution was added until neutrality to litmus was reached, during which time an oily layer separated. Extraction was carried out with 2.5 liters of ether, removing the anil of diethyl oxalacetate. After drying over potassium carbonate, the ether solution was evaporated and the oily residue was added with stirring, during the course of five to ten minutes, to 1.5 liters of mineral oil at 250° to bring about ring closure. On cooling, white crystals separated which were filtered, washed with Skellysolve B, and dried. The yield of ethyl ester of kynurenic acid was about 60%, m. p. 210–215°.

The ester was saponified by refluxing 97 g. (0.47 mole) with one liter of 4% aqueous sodium hydroxide solution. After treating with charcoal, the solution was diluted to 1.5 liters with hot water and acidified while hot until acid

(10) Koenigs and Greiner, *Ber.*, **64**, 1055 (1931).
(11) Pollak, *Monatsh.*, **16**, 54 (1895).
(12) Mills and Watson, *J. Chem. Soc.*, **97**, 753 (1910).
(13) Maier-Bode, *Ber.*, **69**, 1536 (1936).
(14) Edinger, *J. prakt. Chem.*, **54**, 358 (1896).
(15) Conrad and Limpach, *Ber.*, **21**, 1965, 1970 (1888).
(16) Limpach, *ibid.*, **64**, 969 (1931).

TABLE III

Compound	Reduction product
2-Pyridinol	α-Piperidone[a]
3- and 4-pyridinols	Unchanged
1-Isoquinolinol	3,4-Dihydro-1(2)-isoquinolone
2-Quinolinol	3,4-Dihydro-2(1)-quinolone
3-Quinolinol	1,2,3,4-Tetrahydro-3-quinolinol
4-Quinolinol	Unchanged
5-, 6- 7- and 8-quinolinols	Corresponding 1,2,3,4-Tetrahydroquinolinols
4-Methyl-2-quinolinol	Unchanged
2-Methyl-4-quinolinol	Unchanged
2-Benzoxypyridine	Toluene[b] + α-piperidone
3-Benzoxypyridine	Unchanged
4-Benzoxypyridine	Toluene + 4-pyridinol
2-β-Naphthoxypyridine	β-Methylnaphthalene + α-piperidone
2-(4-Benzyloxy)-benzoxypyridine	*p*-Cresol[c] + α-piperidone
2-(3,4,5-Tris-(benzyloxy)-benzoxy)-pyridine	3,4,5-Trihydroxytoluene[d] + α-piperidone
3-(3,4,5-Tris-(benzyloxy)-benzoxy)-pyridine	3-(3,4,5-Trihydroxy)-benzoxypyridine
2-Benzoxyquinoline	Toluene + 3,4-dihydro-2(1)-quinolone
3-Benzoxyquinoline	3-Benzoxy-1,2,3,4-tetrahydroquinoline
4-Benzoxyquinoline	Toluene + 4-quinolinol
5-, 6- and 7-Benzoxyquinolines	Corresponding benzoxy-1,2,3,4-tetrahydroquinolines
8-Benzoxyquinoline	N-Benzoyl-1,2,3,4-tetrahydro-8-quinolinol
1-Benzoxyisoquinoline	Toluene + 3,4-dihydro-1(2)-isoquinolone + N-benzoyl-3,4-dihydro-1(2)-isoquinolone[e]
2-β-Naphthoxyquinoline	β-Methylnaphthalene + 3,4-dihydro-2(1)-quinolone
2-Benzoxy-4-methylquinoline	Toluene + 4-methyl-2-quinolinol
2-(3,4,5-Tris-(benzyloxy)-benzoxy)-quinoline	3,4,5-Trihydroxytoluene[d] + 3,4-dihydro-2(1)-quinolone
2-(3,4,5-Tri-(acetoxy)-benzoxy)-quinoline	3,4,5-Triacetoxytoluene[f] + 3,4-dihydro-2(1)-quinolone
8-(4-Benzyloxy)-benzoxyquinoline	N-(4-Hydroxybenzoyl)-1,2,3,4-tetrahydro-8-quinolinol
8-Benzoxy-2-quinolinol	8-Benzoxy-3,4-dihydro-2(1)-quinolone
2,8-Bis-(benzoxy)-quinoline	8-Benzoxy-3,4-dihydro-2(1)-quinolone + toluene

[a] Confirmed by preparation of N-benzoyl derivative, m. p. 110°. [b] Isolated by distillation and confirmed by oxidation to benzoic acid. [c] The *p*-nitrobenzoyl ester prepared, m. p. 225° dec. *Anal.* Calcd. for $C_{14}H_{11}O_4N$: N, 5.45. Found: 5.35. [d] Difficult to isolate pure in appreciable quantities. [e] A compound with such properties was obtained in small amounts. Alkaline hydrolysis yielded benzoic acid and 3,4-dihydro-1(2)-isoquinolone. [f] Granular crystals obtained by slow evaporation of a Skellysolve B solution; m. p. 105–106°.

to congo red. After cooling, the acid was filtered and dried; yield 96%, m. p. 280°.

Decarboxylation was carried out by adding the pulverized acid (80 g.) to one liter of paraffin oil at 270°, this temperature being maintained for five minutes. On cooling, a brown solid separated, which was ground, washed with Skellysolve B and recrystallized from dioxane; yield 93%, m. p. 200°.

2-Methyl-4-quinolinol was prepared by a reaction similar to that above. A mixture of 20 g. of aniline and 28 g. of ethyl acetoacetate was allowed to stand for five days, then extracted with ether. The ether solution was dried over sodium sulfate, then evaporated. The residue was added to paraffin oil at 250–260°. A brown oil separated which crystallized on cooling. The product was washed with Skellysolve B, dried and recrystallized from water after treatment with charcoal. The yield was 61% and the m. p. 230°.

5-Quinolinol was made from 5-aminoquinoline by diazotization and hydrolysis as described for 3-pyridinol. The amino compound was prepared according to Fieser and Hershberg.[17] The over-all yield from 5-nitroquinoline was 15%.

6-Quinolinol (60% yield from *p*-aminophenol) and 7-quinolinol (25% yield from *m*-aminophenol) were prepared by the Cohn modification[18] of the Skraup synthesis.

2,8-Quinolindiol was obtained by alkaline fusion of 8-quinolinol.[19]

(17) Fieser and Hershberg, THIS JOURNAL, **62**, 1644 (1940).

(18) Cohn, *ibid.*, **52**, 3685 (1930).

(19) Diamant, *Monatsh.*, **16**, 760 (1895).

TABLE IV

Compound	Grams reduced	Mmoles compd.	Time in min., for absorption of 10 mmoles of hydrogen	Time, in min., for complete hydrogenation
Benzyl alcohol	1.08	10.0	10	10
2-Benzoxypyridine	0.66	3.3	45	120
2-β-Naphthoxypyridine	.83	3.3	15	50
2-Benzoxyquinoline	.83	3.3	15	50
2-β-Naphthoxyquinoline	1.00	3.3	20	50

1-Isoquinolinol was prepared by diazotization and hydrolysis of the amino compound obtained by the action of sodamide on isoquinoline.[20]

Pyridinyl and Quinolinyl Esters.—Three general methods were used in the preparation of these esters:

Method A.—To 0.05 mole of the pyridinol or quinolinol dissolved in 25 cc. of pyridine, was added from 0.05 to 0.08 mole of the acid chloride desired, and the mixture was heated on a steam-bath for forty-five minutes. About 300 cc. of water was added to the cooled solution, and the product which separated was washed with 7% sodium bicarbonate solution, then with water.

Method B.—This is essentially the method of Conrad and Limpach.[16] To 0.05 mole of the dry sodium salt of the pyridinol or quinolinol suspended in 25 cc. of dry ether was slowly added 0.05 mole of the acid chloride. The mixture was shaken for thirty minutes, then filtered. The ether solution was evaporated and the ester obtained.

(20) Tschitschibabin and Oparina, *J. Russ. Phys.-Chem. Soc.*, **50**, 543, 548 (1920).

Method C.—A mixture of 0.05 mole of the quinolinol and 0.25 mole of the acid chloride was heated on an oil-bath at 150° for forty-five minutes. To the cooled product 100 cc. of water was added and the insoluble substance washed with 5% sodium carbonate solution. The product was dissolved in ether, dried over potassium carbonate and then the ether was evaporated.

The esters prepared by these methods are so indicated as A, B or C in the yield column of Table I. The products in each case are recrystallized from an organic solvent as referred to in the Appearance column of Table I.

The 4-benzyloxybenzoyl chloride and 3,4,5-tris-(benzyloxy)-benzoyl chloride were prepared according to reference 1. 3,4,5-Tri-(acetoxy)-benzoyl chloride was prepared by the method of Fischer.[21]

Catalytic Reduction of the Pyridinols, Quinolinols and their Esters.—An amount of the compound between 0.5 and 1.5 g. was dissolved in 100 cc. of ethanol or dioxane. Dioxane was used as a solvent for most of the esters. After addition of 200 mg. of Pd catalyst,[2] hydrogenation was carried out at 55° in the apparatus previously mentioned. The compounds tested and the reduction products obtained are outlined in Table III. The time required for the reductions varied from about one to three hours, most reductions requiring about two hours. The esters of the 2-benzoxypyridine type reduced in two stages as measured by the rate of hydrogen uptake. The rates of reduction are compared in Table IV. Benzyl alcohol is included as a reference standard.

2-Benzoxypyridine was reduced more slowly than the other esters. The first three molar equivalents of hydrogen were absorbed more rapidly since hydrogenolysis of the ester with subsequent reduction of the resulting aldehyde to the hydrocarbon proceeded more rapidly than reduction of the pyridinol or quinolinol rings.

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Summary

1. All three monohydroxypyridines and seven monohydroxyquinolines are capable of forming aromatic esters. Esters of the 2- and 4-hydroxy bases are more readily hydrolyzed than others; the 4-esters could be prepared only under anhydrous conditions. Introduction of a methyl group in the 4-position of quinoline reduced the strength of the ester linkage in the 2-position.

2. With a palladium catalyst, 2-pyridinol was reduced to α-piperidone; 3- and 4-pyridinols did not reduce. 2-Quinolinol reduced to the 3,4-dihydro derivative, 4-quinolinol did not reduce. 3-, 5-, 6-, 7- and 8-quinolinols reduced to the corresponding 1,2,3,4-tetrahydroquinolinol. The presence of a methyl group as in 4-methyl-2-quinolinol prevented reduction.

3. The benzoyl ester of 3-pyridinol did not hydrogenate. The 3-, 5-, 6- and 7-quinolinol benzoyl esters reduced to the corresponding 1,2,-3,4-tetrahydro- derivatives. The 2- and 4-pyridinol, 2- and 4-quinolinol, and 4-methyl-2-quinolinol aromatic acid esters reduced to yield the hydrocarbon of the aromatic acid with liberation of the hydroxypyridine or -quinoline which behaved according to its own nature toward further reduction. Esters of 8-quinolinol underwent reduction to the 1,2,3,4-tetrahydro derivative which rearranged to give the N-acyl derivative. This last case is similar to the rearrangement of ortho aminophenyl esters and appears to result when the grouping R′—CO—O—C=C— NHR occurs in a reaction, R being H or a group which does not destroy the basic character of the nitrogen.

4. Hydrogenation of 1-isoquinolinol yielded 3,4-dihydro-1(2)-isoquinolone; 1-benzoxyisoquinoline gave toluene, the dihydroisoquinolone and a small amount of a compound which appears to be N-benzoyl-3,4-dihydro-1(2)-isoquinolone.

(21) E. Fischer, Bergmann and Lipschitz, *Ber.*, **51**, 45 (1918).

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Heat Capacity and Entropy, Heats of Fusion and Vaporization and the Vapor Pressure of Trimethylamine. The Entropy from Spectroscopic and Molecular Data

BY JOHN G. ASTON, MALCOLM L. SAGENKAHN, GEORGE J. SZASZ, GUSTAVE W. MOESSEN AND HERBERT F. ZUHR

The Raman spectrum of trimethylamine shows a shift of 272 cm.$^{-1}$ which can be assigned to the hindered rotation of the methyl groups. Thus the determination of the entropy of trimethylamine from calorimetric data and the third law of thermodynamics is particularly desirable to compare with the entropy calculated from spectroscopic and molecular data as a verification of the assignment. Such a comparison has already been made for methylamine[1] and for dimethylamine,[2] but in those cases the comparison was used to estimate the potential barrier hindering internal rotation. The present paper records the results of calorimetric measurements on trimethylamine from 11°K. to the normal boiling point along with the other data necessary for calculating the entropy of the saturated vapor at several temperatures up to its normal boiling point. The entropy thus calculated is compared with that calculated from molecular and spectroscopic data whose assignment to the normal modes of vibration including the hindered rotation is discussed.

Preparation and Purification of Trimethylamine.—Trimethylamine was prepared by the reaction of para-

(1) (a) Aston, Siller and Messerly, THIS JOURNAL, **59**, 1743 (1937); (b) Aston and Doty, *J. Chem. Phys.*, **8**, 743 (1940).

(2) Aston, Eidinoff and Forster, THIS JOURNAL, **61**, 1539 (1939).