preliminary reaction with mercuric chloride, undergoes a subsequent irreversible denaturation. Possibly a similar series of reactions is involved in the inactivation of the enzyme by arsonic acids.

TABLE IV

FAILURE OF BAL TO REVERSE THE INACTIVATION OF CHOLINESTERASE BY *o*-BROMOBENZENEARSONIC ACID[a]

o-$BrC_6H_4AsO_3H_2$[b] (moles/l.)	BAL[c] (moles/l.)	Inhibition (%)
7.5×10^{-4}	1.5×10^{-3}	90
7.5×10^{-4}	0	87
0	1.5×10^{-3}	0[d]

[a] Inhibitor and enzyme were incubated at 23° for 20 minutes and then dialyzed for 24 hours as described in Table III. After the dialysis, 6-ml. aliquots of the dialyzed solutions were mixed with 1 ml. of water or BAL solution and allowed to stand at 23° for 20 minutes. Then substrate solution (1 ml. of 0.032 *M* acetylcholine bromide in 0.2 *M* phosphate of *pH* 7.0) was added to determine the residual activity of the enzyme. [b] Concentration that would have been present in the final reaction mixture if the dialysis had not been performed. [c] Concentration present in the final reaction mixture; *i.e.*, after the addition of substrate. [d] E. C. Webb and R. van Heyningen, *Biochem. J.*, 41, 74 (1947), reported that 0.005 *M* BAL has no effect on the activity of horse serum cholinesterase.

The results obtained in this investigation suggest that phosphonic, phosphinic and arsinic acids inhibit plasma cholinesterase by the same mechanism and that arsonic acids inhibit by another mechanism.

Acknowledgments.—The authors wish to thank Mrs. Barbara Stanley for performing the analyses necessary for this research and Mr. Edward L. Petit for invaluable technical assistance. Appreciation is due also to Dr. Harold J. Magnuson for advice in planning the experiments.

VENEREAL DISEASE EXPERIMENTAL LABORATORY
U. S. PUBLIC HEALTH SERVICE, SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF NORTH CAROLINA
CHAPEL HILL, NORTH CAROLINA

Sodium Amide Cleavage of 1-Alkylcyclobutyl Phenyl Ketones

BY K. E. HAMLIN AND URSULA BIERMACHER

RECEIVED AUGUST 3, 1955

1-Alkylcyclohexyl and 1-alkylcyclopentyl phenyl ketones are cleaved by sodium amide under conditions of the Haller–Bauer reaction to yield the corresponding 1-alkylcyclohexane- and 1-alkylcyclopentanecarboxamides.[1,2] On the other hand, 1-alkylcyclopropyl phenyl ketones have given variable results. Haller and Benoist[3] reported that 1-methylcyclopropyl phenyl ketone gave benzamide on sodium amide cleavage whereas 1-benzylcyclopropyl phenyl ketone afforded the expected 1-benzylcyclopropanecarboxamide.[4]

The cleavage of 1-alkylcyclobutyl phenyl ketones with sodium amide has not been reported in the literature. To determine their behavior under conditions of the Haller–Bauer reaction, 1-methyl- and 1-ethylcyclobutyl phenyl ketones were prepared by the alkylation of cyclobutyl phenyl ketone. In both cases, the alkylated ketones were cleaved normally to yield the corresponding cyclobutanecarboxamides.

Piehl and Brown[4] reported extensive sodium amide cleavage of cyclopropyl phenyl ketone to cyclopropanecarboxamide and benzamide. Only unreacted ketone was obtained when cyclobutyl phenyl ketone was treated with sodium amide under similar conditions.

Experimental

Cyclobutyl phenyl ketone[5] was prepared by condensation of cyclobutanecarbonyl chloride with benzene in the presence of anhydrous aluminum chloride.

1-Methylcyclobutyl Phenyl Ketone.—The sodio derivative was prepared in toluene from 48 g. (0.3 mole) of cyclobutyl phenyl ketone and 11.7 g. (0.3 mole) of sodium amide. This mixture was stirred and cooled in an ice-bath while 85 g. (0.6 mole) of methyl iodide was added in one portion. Reaction was immediate causing rapid refluxing of the mixture. Stirring at room temperature was continued for 22 hours after which the toluene solution was washed with water and distilled. The 1-methylcyclobutyl phenyl ketone boiled at 103° at 3 mm., $n^{25}D$ 1.5368, yield 41 g. (79%).

Anal. Calcd. for $C_{12}H_{14}O$: C, 82.72; H, 8.10; O, 9.18. Found: C, 83.14; H, 8.08; O, 9.31.

1-Ethylcyclobutyl Phenyl Ketone.—A suspension of the sodio derivative of 48 g. (0.3 mole) of cyclobutyl phenyl ketone in toluene, prepared as in the example above, was stirred at 75° while 46.8 g. (0.3 mole) of ethyl iodide was added dropwise. The mixture was heated at 75–80° for an additional 7 hours, was washed with water and was distilled. The desired 1-ethylcyclobutyl phenyl ketone distilled at 115–116° at 3 mm., $n^{25}D$ 1.5304, yield 19 g. (34%).

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.82; H, 8.81.

1-Methylcyclobutanecarboxamide.—A suspension of 15.5 g. (0.4 mole) of sodium amide in 200 ml. of anhydrous toluene was treated with 34.8 g. (0.2 mole) of 1-methylcyclobutyl phenyl ketone. The mixture was refluxed while stirring for 5 hours, was cooled to room temperature and was washed with water. Following distillation of the toluene *in vacuo*, 18 g. of crystalline product was obtained. After two recrystallizations from benzene, the 1-methylcyclobutanecarboxamide melted at 165° and weighed 12 g. (50% yield).

Anal. Calcd. for $C_6H_{11}NO$: C, 63.68; H, 9.80. Found: C, 63.42; H, 10.05.

1-Ethylcyclobutanecarboxamide.—In the manner described above, 1-ethylcyclobutyl phenyl ketone was cleaved with sodium amide to afford a 60% yield of product twice recrystallized from toluene, m.p. 136.5–137.5°.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.09; H, 10.32. Found: C, 66.40; H, 10.74.

Acknowledgment.—We are indebted to E. F. Sehlberg, Chief Microanalyst, and his staff for the analytical data.

ABBOTT LABORATORIES
NORTH CHICAGO, ILLINOIS

ar-2-Tetralol Derivatives

BY ROBERT L. HULL

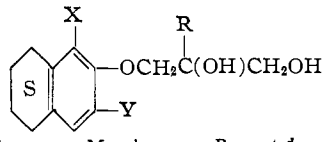
RECEIVED JUNE 10, 1955

In light of a recent publication[1] claiming the ar-2-tetralyl ether of glycerol to be more potent and

(1) K. E. Hamlin and M. Freifelder, THIS JOURNAL, **75**, 369 (1953).
(2) G. Wash, B. Shive and H. L. Lochte, *ibid.*, **63**, 2975 (1941).
(3) A. Haller and E. Benoist, *Ann. chim.*, [9] **17**, 25 (1921).
(4) The latter reaction was recently confirmed by F. J. Piehl and W. G. Brown, THIS JOURNAL, **75**, 5023 (1953).
(5) H. R. Henze and C. W. Gayler, *ibid.*, **74**, 3615 (1952).

(1) T. Kariyone, H. Yamada, M. Takahashi, T. Omiya, K. Okamoto and Y. Kashihara, *J. Pharm. Soc. Jap.*, **72**, 1545 (1952); *C. A.*, **47**, 9314 (1953).

TABLE I

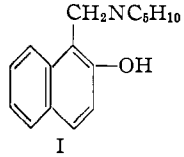


R	X	Y	Yield,[a] %	M.p.,[b] °C.	Recryst.[d] solvent	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
H	CH_3	H	42	109–110	A	71.16	71.06	8.53	8.55
CH_3	CH_3	H	34	91.5–92.5	B	71.97	72.21	8.86	8.71
CH_3	H	H	70	80–81	C	71.16	71.11	8.53	8.48
H	Br	H	31	120–121	B	51.84	51.98	5.69	5.83
H	Br	Br	42	104.5–105.5	A	41.08	41.38	4.24	4.28
H	CH_3	Br	29	85.5–86.5	B	53.34	53.65	6.08	6.38
H	CH_3	Cl	24	81–82	B	62.10	62.10	7.07	7.29
CH_3	CH_3	Br	51	102.5–103.5	D	54.72	54.88	6.43	6.60
H	H	$CH_2CH{=}CH_3$	21	66–67	B	73.25	73.36	8.45	8.69
H	H	*n*-C_3H_7	47	88–89	B	72.69	72.37	9.15	9.04
CH_3	H	$CH_2CH{=}CH_3$	44	175–180[c]	..	73.88	74.38	8.75	8.85
CH_3	Br	Br	23	81–82	C	42.66	42.98	4.60	4.61
H	Br	*n*-C_3H_7	51	86–87	B	55.98	56.19	6.75	6.70
CH_3	Br	*n*-C_3H_7	23	80–81	C	57.15	57.01	7.05	7.37

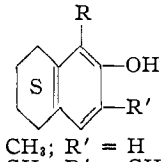
[a] Analytically pure product. [b] Uncorrected. [c] B.p. at 0.5 mm. [d] A = benzene; B = benzene–ligroin (b.p. 60–70°); C = ligroin (b.p. 60–70°); D = diisopropyl ether–ligroin b.p. (60–70°).

less toxic than mephenesin (3-*o*-toloxy-1,2-propanediol) as a muscle relaxant, it seemed desirable to prepare a number of similar ar-2-tetralyl ethers substituted in the aromatic nucleus. Especially was it desirable to prepare compounds of this type substituted *ortho* to the ether linkage since these types generally have shown improved mephenesin-like (spinal depressant) activity.[2] Several ethers of this type were prepared. In addition, a few oxazoles, derived from the parent ar-2-tetralols, were synthesized to investigate their muscle relaxing properties, since various benzazoles have been shown to have outstanding activity in this respect.[3]

A method more convenient than those previously published[4] for the preparation of 1-methyl-ar-2-tetralol (II) was found in the hydrogenation of the Mannich base, 1-(1′-piperidylmethyl)-2-naphthol (I), at 60–80° in acetic acid solution over a palladium-on-charcoal catalyst. Compound I reacted with three molecular equivalents of hydrogen at a pressure of 3–4 atmospheres to produce II in good yield.



I



II, R = CH_3; R′ = H
III, R = CH_3; R′ = $CH_2NC_5H_{10}$

The hydrogenation proceeded at a uniform rate and no attempt was made to stop it at an intermediate stage. However, the Mannich base, 1-methyl-3-(1′-piperidylmethyl)-ar-2-tetralol (III), prepared from II did not react with hydrogen under identical conditions.

The preparation of the various substituted chloro- and bromo-ar-2-tetralols was carried out by halogenation of the appropriate tetralol with sulfuryl chloride and bromine, respectively, in carbon tetrachloride.

In general, the preparation of the glyceryl and β-methylglyceryl ethers (Table I) was carried out according to standard procedures.[5] In the preparation of the ethers of 1,3-dibromo-ar-2-tetralol, the acetate was used as a starting material since it was more easily purified, the tetralol being generated *in situ*. No attempt was made to determine the conditions of optimum yield. In many instances the purification of the ether was difficult and several recrystallizations were necessary to obtain the product in an analytically pure state.

The oxazoles were prepared by nitration of a suitable tetralol, catalytic reduction of the nitro group, followed by cyclization of the aminophenol with formic acid and reaction with hydroxylamine to form the oxazole and 2-aminoöxazole, respectively.

All of the final products were found by Dr. G. M. Chen and staff of the Research Department to have no spinal depressant activity in mice at an oral dose level of 500 mg./kg.

Experimental[6]

1-Methyl-ar-2-tetralol (II).—A solution of 72.4 g. (0.30 mole) of 1-(1′-piperidylmethyl)-2-naphthol[7] in 200 ml. of glacial acetic acid and 3.0 g. of 5% palladium-on-charcoal was shaken with hydrogen at 50 p.s.i. at 60°. The uptake of hydrogen ceased when the calculated amount had reacted (20 hours). The reaction mixture was filtered into 1 l. of ice-water; the resulting precipitate was removed by filtration and shaken with 300 ml. of ether and 300 ml. of water. The ether extract was dried over anhydrous sodium sulfate and evaporated. The solid residue was recrystallized from ligroin (b.p. 60–70°) to give 29.4 g. (60%) of colorless needles, m.p. 113–114° (rep. 113.5–114.5°).[4]

A sample was completely soluble in 2% aqueous sodium hydroxide. A mixture melting point with authentic 1-methyl-ar-2-tetralol[4] showed no depression.

(2) (a) F. M. Berger, *J. Pharmacol. Exptl. Therap.*, **93**, 470 (1948); (b) A. F. Lindenstruth, J. H. Fellman and C. A. VanderWerf, THIS JOURNAL, **72**, 1886 (1950); (c) J. P. Lambooy, *ibid.*, **73**, 349 (1951).

(3) E. F. Domino, K. R. Unna and J. Kerwin, *J. Pharmacol. Exptl. Therap.*, **105**, 486 (1952).

(4) R. H. Martin and R. Robinson, *J. Chem. Soc.*, 491 (1943).

(5) (a) H. Gilman and A. H. Blatt, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 296; (b) B. J. Ludwig, W. A. West and W. E. Currie, THIS JOURNAL, **74**, 1935 (1952).

(6) Microanalytical data were supplied by Mr. C. E. Childs and staff. The melting points are uncorrected.

(7) K. Auwers and A. Dombroski, *Ann.*, **344**, 289 (1906).

1-Methyl-3-(1'-piperidylmethyl)-ar-2-tetralol (III).—To a solution of 16.2 g. (0.10 mole) of II and 8.5 g. (0.10 mole) of piperidine in 50 ml. of ethanol was added 8.2 g. of 36–38% aqueous formaldehyde. The solution warmed spontaneously; it was allowed to stand overnight at room temperature. On cooling in an ice-bath a colorless oil separated which crystallized on standing. The product was removed by filtration and washed with cold ethanol; yield 18.1 g., m.p. 57–59°. An additional 6.8 g., m.p. 57–59°, was obtained on concentration of the mother liquor; total yield, 24.9 g. (96%). A sample purified for analysis by recrystallization from ethanol melted at 60.5–61.5°.

Anal. Calcd. for $C_{17}H_{25}NO$: C, 78.71; H, 9.72. Found: C, 78.92; H, 9.65.

3-Chloro-1-methyl-ar-2-tetralol.—To a stirred suspension of 32.4 g. (0.20 mole) of II in 200 ml. of carbon tetrachloride was added dropwise over a period of 15 minutes 27.0 g. (0.20 mole) of sulfuryl chloride. Stirring was continued for two hours. The resulting solution was washed in turn with 300 ml. of water, 300 ml. of 5% sodium bicarbonate solution and 300 ml. of water. After drying over Drierite, the carbon tetrachloride was evaporated on a steam-bath and the residual oil distilled at reduced pressure. The fraction boiling at 90–115° (0.5 mm.), which solidified in the receiver, was recrystallized from 75 ml. of 70% ethanol to give 21.0 g. (53%) of colorless needles, m.p. 53–55°. A sample purified for analysis by recrystallization from ethanol melted at 57–58°.

Anal. Calcd. for $C_{11}H_{13}ClO$: C, 67.15; H, 6.66. Found: C, 66.96; H, 6.57.

3-Bromo-1-methyl-ar-2-tetralol.—A solution of 32 g. (0.20 mole) of bromine in 50 ml. of carbon tetrachloride was added dropwise, at such a rate that the color was discharged, to a stirred suspension of 32.4 g. (0.20 mole) of II in 150 ml. of carbon tetrachloride. The resulting solution was stirred an additional 30 minutes and then washed in turn with 300 ml. of water, 300 ml. of 5% sodium bicarbonate solution and 300 ml. of water. After drying over Drierite, the carbon tetrachloride was removed by distillation. Recrystallization of the solidified residue from 70% ethanol gave 36.5 g. (76%) of colorless needles, m.p. 67–69°. A sample purified for analysis by recrystallization from 70% ethanol melted at 69–70°.

Anal. Calcd. for $C_{11}H_{13}BrO$: C, 54.79; H, 5.43. Found: C, 55.28; H, 5.72.

1-Bromo-3-*n*-propyl-ar-2-tetralol.[8]—This compound was prepared in the same manner as above by the bromination of 3-*n*-propyl-ar-2-tetralol with bromine in carbon tetrachloride; yield 53%, m.p. 62.5–64°. A sample recrystallized from 70% ethanol melted at 64.5–65.5°.

Anal. Calcd. for $C_{13}H_{17}BrO$: C, 58.00; H, 6.37; Br, 29.68. Found: C, 58.30; H, 6.43; Br, 29.41.

α-Glyceryl and α-(β-Methylglyceryl) Ethers of ar-2-Tetralols (Table I). General Procedure.—A solution of 0.05 mole of the appropriate ar-2-tetralol in 25 ml. of absolute alcohol was added to a solution of 1.15 g. (0.05 g. atom) of sodium in 20 ml. of absolute alcohol. To this was added 0.05 mole of either glycerol α-monochlorohydrin or β-methylglycerol α-monochlorohydrin and the solution was heated at reflux for three hours. The reaction mixture was filtered to remove sodium chloride and the filtrate evaporated *in vacuo*. The residual solid or oil was either recrystallized several times from an appropriate solvent or fractionally distilled under reduced pressure.

α-Glycerol and α-(β-Methylglyceryl) Ethers of 1,3-Dibromo-ar-2-tetralol.—Ten and four-tenths grams (0.030 mole) of 1,3-dibromo-ar-2-tetralyl acetate[9] was added to a solution of 2.8 g. (0.070 mole) of sodium hydroxide in 40 ml. of 70% ethanol. The mixture was heated at reflux for one hour. To the resulting solution was added 0.040 mole of the appropriate glycerol monochlorohydrin, the solution was heated at reflux for three hours, and then evaporated *in vacuo* at 50°. The gummy residue was extracted with 100 ml. of hot benzene. The benzene extract was evaporated and the residue recrystallized several times from an appropriate solvent.

(8) This compound was reported as a liquid, b.p. 157–159° (8 mm.), prepared by hydrogenation of 3-allyl-1-bromo-ar-2-tetralol by S. I. Sergievskaya and A. E. Gavrilova, *J. Gen. Chem. (U.S.S.R.)*, **11**, 1027 (1941); *C. A.*, **39**, 4601 (1945).

(9) G. Schroeter, *Ann.*, **426**, 127 (1922).

1-Methyl-3-nitro-ar-2-tetralol.—A mixture of 34.5 g. (0.213 mole) of II and 20 ml. of concentrated sulfuric acid was heated on a steam-bath for 30 minutes. The deep-red solution was diluted with 150 ml. of water and cooled in an ice-bath. Concentrated nitric acid (14 ml.) was added dropwise with stirring. The resulting solution was heated on a steam-bath for ten minutes, diluted with an equal volume of water, and cooled in an ice-bath. The yellow precipitate was removed by filtration and washed with water. Recrystallization from ethanol yielded 26.4 g. (60%) of yellow needles, m.p. 116–118°. A sample recrystallized from ethanol melted at 118–119°.

Anal. Calcd. for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.63. Found: C, 63.88; H, 6.65.

1-Nitro-3-*n*-propyl-ar-2-tetralol.—This compound was prepared by nitration of 3-*n*-propyl-ar-2-tetralol as above; yield 60% of yellow needles, m.p. 101–103°. A sample prepared for analysis by recrystallization from ethanol melted at 104–105°.

Anal. Calcd. for $C_{13}H_{17}NO_3$: C, 66.36; H, 7.28. Found: C, 66.25; H, 7.25.

3-Amino-1-methyl-ar-2-tetralol.—A suspension of 10.4 g. (0.05 mole) of 1-methyl-3-nitro-ar-2-tetralol and 0.1 g. of platinum oxide in 200 ml. of absolute ethanol was shaken with hydrogen at 50 p.s.i. at room temperature. In ten minutes, the calculated amount of hydrogen had been taken up and hydrogenation ceased. The catalyst was removed by filtration and the filtrate diluted with four volumes of water. The slightly colored precipitate was removed by filtration and dried; yield 8.5 g. (95%), m.p. 142–144°. A sample was prepared for analysis by recrystallization from ligroin (b.p. 60–70°), m.p. 144–145°.

Anal. Calcd. for $C_{11}H_{15}NO$: C, 74.54; H, 8.53. Found: C, 75.02; H, 8.63.

1-Amino-3-*n*-propyl-ar-2-tetralol.—This compound was prepared by catalytic hydrogenation of 1-nitro-3-*n*-propyl-ar-2-tetralol as above; yield, after recrystallization from aqueous ethanol, 71%, m.p. 92–95°. A sample recrystallized for analysis melted at 95–96°.

Anal. Calcd. for $C_{13}H_{19}NO$: C, 76.05; H, 9.33. Found: C, 76.20; H, 9.22.

5,6,7,8-Tetrahydro-9-methylnaphth[2,3]oxazole.—A mixture of 8.1 g. (0.046 mole) of 3-amino-1-methyl-ar-2-tetralol and 25 ml. of 98% formic acid was heated at reflux for one hour. The excess formic acid and water were removed by distillation and the residue heated at 140–150° for four hours. The cooled solid was extracted with two 50-ml. portions of hot 2,2,4-trimethylpentane, and the combined extract cooled in an ice-bath. The yield of off-white crystalline solid was 5.7 g. (66%), m.p. 90–93°. A sample prepared for analysis by recrystallization from ethanol gave colorless crystals, m.p. 94–95°.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00. Found: C, 76.48; H, 6.76.

6,7,8,9-Tetrahydro-4-*n*-propylnaphth[1,2]oxazole.—This compound was prepared by ring closure of 1-amino-3-*n*-propyl-ar-2-tetralol with formic acid as above. It was obtained as a colorless oil, b.p. 99–101° (0.1 mm.), yield 60%.

Anal. Calcd. for $C_{14}H_{17}NO$: C, 78.10; H, 7.96. Found: C, 78.16; H, 7.87.

2-Amino-5,6,7,8-tetrahydro-9-methylnaphth[2,3]oxazole.—To a solution of 0.8 g. (0.02 mole) of sodium hydroxide in 25 ml. of water and 30 ml. of ethanol was added 1.3 g. (0.018 mole) of hydroxylamine hydrochloride and 3.4 g. (0.018 mole) of 5,6,7,8-tetrahydro-9-methylnaphth[2,3]-oxazole. The mixture was heated at reflux for 30 minutes. The resulting clear solution was diluted with an equal volume of water and cooled in an ice-bath. The cream-colored solid was removed by filtration and dried; yield 2.6 g. (72%), m.p. 156–158°. A sample prepared for analysis by recrystallization from ethanol–benzene gave cream-colored crystals of a monohydrate, m.p. 159–160°.

Anal. Calcd. for $C_{12}H_{14}N_2O \cdot H_2O$: C, 65.43; H, 7.32; N, 12.72. Found: C, 65.41; H, 7.24; N, 12.30.

2-Amino-6,7,8,9-tetrahydro-4-*n*-propylnaphth[1,2]oxazole.—This compound was prepared by the reaction of 6,7,8,9-tetrahydro-4-*n*-propylnaphth[1,2]oxazole with hydroxylamine as above. One recrystallization from benzene–

ligroin (b.p. 60–70°) gave the product in 64% yield, m.p. 172–174°. A sample recrystallized for analysis melted at 174–175°.

Anal. Calcd. for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88. Found: C, 73.31; H, 7.82.

DETROIT 32, MICHIGAN

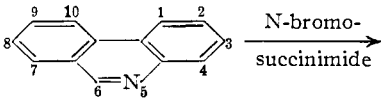
The Bromination of Phenanthridine

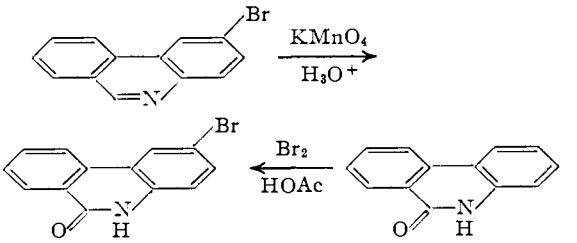
BY HENRY GILMAN AND JOHN EISCH

RECEIVED JULY 5, 1955

In the study of the substitutional chemistry of phenanthridine in relation to other aza-aromatic heterocycles, it was considered of interest to attempt the bromination of this heterocycle. Contrasted with the nitration and sulfonation of quinoline which occur in the benzenoid ring, the bromination of quinoline takes place preferentially in the pyridinoid ring beta to the nitrogen.[1] Since the pyridinoid ring in phenanthridine has no available position beta to the nitrogen, the position assumed by the entering bromine atom might help to elucidate the factors determining the exceptional selectivity of bromination.

As no previous direct bromination of phenanthridine has been reported in the literature, the observation that phenanthridine and N-bromosuccinimide afforded a moderate yield of a monobromophenanthridine is significant. The proof of structure of this compound was accomplished by oxidation with potassium permanganate in acid solution to give the corresponding bromophenanthridone.[2] The latter compound was shown to be identical with 2-bromophenanthridone by a mixed melting point determination and comparison of infrared spectra. The authentic 2-bromophenanthridone was obtained by the bromination of phenanthridone. That phenanthridone yields the 2-isomer upon bromination was recently demonstrated by Mosby[3] and confirmed by independent studies in this Laboratory.[4] These reactions leading to the conclusion that the monobromophenanthridine is the 2-isomer are summarized in the following equations[5]





The bromination of phenanthridine is still under study in order to determine optimal preparative conditions and to search for isomeric bromophenanthridines.[6] However, it can be noted at this stage that bromination of phenanthridine seems more selective than nitration where as many as six mononitrophenanthridines result.[2] It is also probable that the actual bromination of the heterocycle is of an electrophilic nature. If the bromination were to proceed by a free-radical mechanism, one would expect 6-bromophenanthridine to be a major product, by analogy with pyridine and quinoline.[7] In addition, the pyrolysis of phenanthridine hydrobromide perbromide has also resulted in the formation of 2-bromophenanthridine.[8]

Experimental[9]

2-Bromophenanthridone.—This compound was prepared by the bromination of phenanthridone in essential accordance with the directions of Mosby.[3] After two recrystallizations from nitrobenzene the white solid melted at 325.5–326.5°.

2-Bromophenanthridine.—In a 500-ml., 3-necked flask fitted with condenser and sealed stirrer were placed 17.9 g. (0.100 mole) of phenanthridine, 17.8 g. (0.100 mole) of N-bromosuccinimide and 125 ml. of carbon tetrachloride. The contents were stirred under reflux for 41 hours,[10] during which time the original cream-colored suspension changed to a reddish-brown solution and the walls of the flask were coated with an orange gum. An acidified sample still gave a positive blue color test with starch–iodide paper at the end of this period.

After 50 ml. of benzene was added, the reaction mixture was warmed and filtered. The golden orange filtrate was concentrated to 100 ml. and set aside to cool. A cream-colored crop of needles weighing 10.2 g. (40%) was obtained which melted over the range 140–155°. Two recrystallizations from 95% ethanol raised the melting point to 160–162.5°. An analytical sample crystallized as colorless needles from the same solvent, m.p. 162.0–163.0°. It was insoluble in warm sodium hydroxide solution, but soluble in warm, dilute hydrochloric acid.

Anal. Calcd. for $C_{13}H_8BrN$: Br, 30.96; N, 5.43. Found: Br, 30.98, 30.96; N, 5.50, 5.29.

Oxidation of 2-Bromophenanthridine.—2-Bromophenanthridine (2.0 g.), 5 ml. of concentrated sulfuric acid and 55 ml. of water were warmed to attain solution. Over a 30-minute period 3.2 g. of solid potassium permanganate was added portionwise. The color of the permanganate was continuously discharged upon warming the stirred mixture. Effervescence and the odor of free bromine indicated that oxidative degradation of the molecule occurred as a side reaction. After two hours the brown suspension was filtered. When the solid was thoroughly dried, it was ex-

(1) 3-Bromoquinoline results from heating quinoline with bromine and sulfur (A. Edinger, *J. prakt. Chem.*, [2] **54**, 357 (1896)) or from heating quinoline hydrochloride perbromide (W. LaCoste, *Ber.*, **14**, 915 (1881)). Higher temperatures favor attack at the 2-position; *cf.* reference 6a.

(2) A procedure employed to convert nitrophenanthridines to nitrophenanthridones by A. G. Caldwell and L. P. Walls, *J. Chem. Soc.*, 2156 (1952).

(3) W. L. Mosby, THIS JOURNAL, **76**, 936 (1954).

(4) The authors have found that Walls' "yellow 2-bromophenanthridone" (obtained by dichromate oxidation of 2-bromo-6-methylphenanthridine) is highly impure 2-bromophenanthridone. By careful purification white 2-bromophenanthridone was isolated and found to be identical with the bromination product of phenanthridone. The yellow impurity in Walls' product is a substance melting at 301–303°. Its infrared spectrum has a pronounced carbonyl band at 5.9 μ and lacks an –N–H band in the 2.9–3.1 μ region.

(5) The numbering system for phenanthridine employed in this paper is that of *Chemical Abstracts*.

(6) The reaction of N-bromosuccinimide with acridine was found to give a difficultly separable mixture of bromoacridines and succinimidoacridines. *Cf.* H. Schmidt and W. E. Leutenegger, *Helv. Chim. Acta*, **30**, 1965 (1947).

(7) (a) J. P. Wibaut and H. J. Den Hertog, *Rec. trav. chim.*, **64**, 55 (1945); (b) H. E. Jansen and J. P. Wibaut, *ibid.*, **56**, 699 (1937).

(8) Unpublished studies of this Laboratory.

(9) All melting points were taken in capillaries inserted in an electrically heated copper block and are corrected.

(10) In certain runs a 100-watt bulb was employed to illuminate the reaction mixture, but a subsequent run from which light was rigidly excluded gave comparable results.