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).