UNCLASSIFIED

AD NUMBER
AD351275
CLASSIFICATION CHANGES
TO: **UNCLASSIFIED**
FROM: **CONFIDENTIAL**
LIMITATION CHANGES
TO: **Approved for public release; distribution is unlimited.**
FROM: **Distribution authorized to U.S. Gov't. agencies and their contractors; Administrative/Operational Use; MAY 1964. Other requests shall be referred to Chemical Research and Development Labs., Edgewood Arsenal, MD.**
AUTHORITY
ARDEC/ECBC ltr dtd 27 May 2009 ARDEC/ECBC ltr dtd 27 May 2009

THIS PAGE IS UNCLASSIFIED

UNCLASSIFIED

AD NUMBER
AD351275
CLASSIFICATION CHANGES
TO confidential
FROM secret
AUTHORITY
31 May 1976 per Grp-3 document marking

THIS PAGE IS UNCLASSIFIED

AD- 351275

SECURITY REMARKING REQUIREMENTS

DOD 5200.1-R, DEC 78

REVIEW ON 28 MAY 84

351275

SECRET

U. S. Army
Chemical Research and Development Laboratories
Technical Report

CRDLR 3213

Some Chemical Reactions of BZ (U)

351275

CATALOGED BY DDC
AS AD No.

by
Brennie E. Hackley, Jr.
Chappelle C. Cochrane
Ethel B. Hackley

May 1964

DDC
RECEIVED
DDC-IRA D

EDGEWOOD ARSENAL, MD

Group 3

Downgraded at 12 Year Intervals;
Not Automatically Declassified.

01380

Copy ___ of ___ Copies

CRDL-Pub-42-S-63

SECRET

Defense Documentation Center Availability Notice

Qualified requesters may obtain copies of this report from Headquarters, Defense Documentation Center, Attn: TISIA-2, Cameron Station, Alexandria, Virginia.

SECRET

May 1964 CRDLR 3213

SOME CHEMICAL REACTIONS OF BZ (U)

by

Brennie E. Hackley, Jr.
Chappelle C. Cochrane
Ethel B. Hackley

Physiology Division

Recommending Approval:

JOSEPH R. BLAIR
Colonel, MC
Director of Medical Research

Approved:

S. D. SILVER
Technical Director

U. S. Army Edgewood Arsenal
CHEMICAL RESEARCH AND DEVELOPMENT LABORATORIES
Edgewood Arsenal, Maryland

SECRET

(U) **FOREWORD**

This work was conducted under Task 4C08-03-016-14, Biochemical Action of Chemical Agents (U). The experimental data are contained in notebooks MN-1452, MN-1465, MN-1440, MN-1400, and MN-1587. The work was started in March 1961 and completed in April 1962.

Acknowledgments

The authors wish to acknowledge the technical assistance of Messrs. David E. Renard, Clifford Shiblom, Kenneth E. Stine, and Robert L. Green.

Notices

This document contains information affecting the national defense of the United States within the meaning of the Espionage Laws, Title 18, U. S. C., sections 793 and 794. The transmission or the revelation of its contents in any manner to an unauthorized person is prohibited by law.

Reproduction of this document in whole or part is prohibited except with the permission of the issuing office; however, DDC is authorized to reproduce the document for U. S. Governmental purposes

Disposition

When this document has served its purpose, DESTROY it in accordance with AR 380-5 DO NOT return the document to U. S. Army Chemical Research and Development Laboratories.

(C) DIGEST

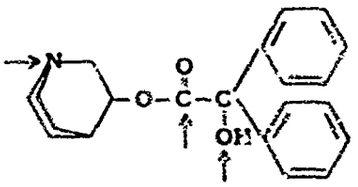
A fundamental study of the chemistry of BZ was conducted to assist in problems that may arise in detection, decontamination, biochemical mechanism of action, and metabolism. BZ reacts with (a) substituted phenyl isocyanates to yield 2, 4-oxazolidinediones, (b) nitriles to produce amides (Ritter reaction), and (c) alkyl halides to give quaternary ammonium salts. Analysis of BZ can be accomplished by quaternization in acetonitrile, separation of reactants, and assaying spectrally.

(S) SOME CHEMICAL REACTIONS OF BZ (U)

(S) INTRODUCTION

(U) BZ is a compound that has been type classified as an incapacitating chemical agent. To assist in the evaluation of the biological properties of the agent, and problems of manufacture, storage stability, detection, decontamination, biochemical mechanism of action, and metabolism, a fundamental study of the chemistry of BZ has been made.

(S) In the chemical structure of BZ there are three primary reactive sites: (a) the tertiary alcohol, (b) the ester linkage, and (c) the quinuclidinyl



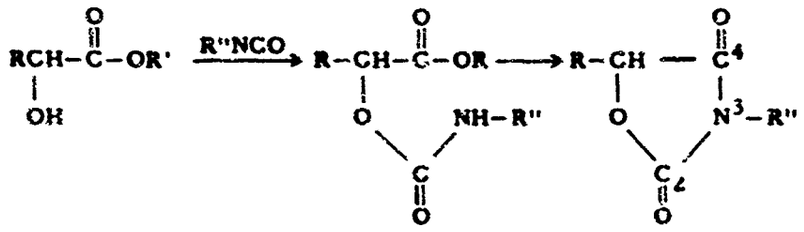
nitrogen atom. A survey of the literature (open and classified) on benzilate esters containing a tertiary nitrogen in the β-position of the alcohol moiety[1, 2, 3, 4] shows that most attention has been directed to reactions at the tertiary nitrogen, i.e., quaternization and salt formation, while little has been done on the direct reactions of the hydroxyl function. A considerable effort has been expended in these Laboratories on the hydrolytic cleavage of BZ. The purpose of this research was to study reactions of the tertiary hydroxyl group as well as reactions specific for benzilate esters that involve a bi functional or two centered attack on the alcohol and ester linkage. In addition, some previously unreported quaternary salts were prepared as models to assist in the analysis and identification of BZ and its metabolic products.

II (S) PROCEDURES AND RESULTS.

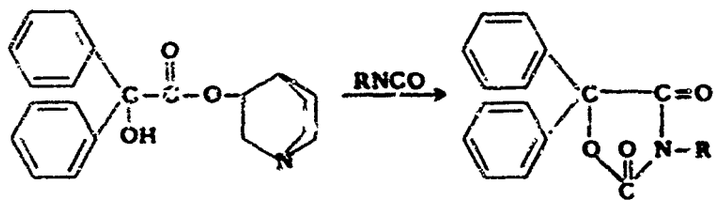
A. (S) 2,4-Oxazolidinediones.

(S) One of the classic modes of formation of 2,4-oxazolidinediones results from the reaction of an α-hydroxy ester and an isocyanate to form the

corresponding urethane, which is subsequently cyclized by heat or alkaline catalysts to the requisite oxazolidinedione.[5]



(S) In the special case of benzilate esters, the oxazolidinediones are formed spontaneously, even at low temperatures, on reaction with an isocyanate.[6] This type of two-centered attack would be specific for benzilate esters such as BZ. By judicious selection of the isocyanate, the N-substituted-5,5-diphenyl oxazolidinedione (obtained as a single product) could possibly be analyzed by fluorescent, colorimetric, infrared, or other physical



analytical means that would provide an unequivocal assay of the benzilate to the total exclusion of other metabolic fragments.

1. (U) General Procedure for the Preparation of Oxazolidinediones From BZ.

A mixture of 1 gm (0.003 mole) of BZ, 0.003 mole of isocyanate, and 10 ml of dry benzene was refluxed for 1 hr. The cooled benzene solution was filtered and the filtrate evaporated to dryness under vacuum. The residue crystallized from isopropyl alcohol afforded the oxazolidinedione

2 (U) Results.

The oxazolidinediones prepared are listed in table 1 They all exhibit characteristic infrared absorptions in the regions of 5.5μ (urethane) and 5.7μ (amide).

B (S) Ritter Reaction Products

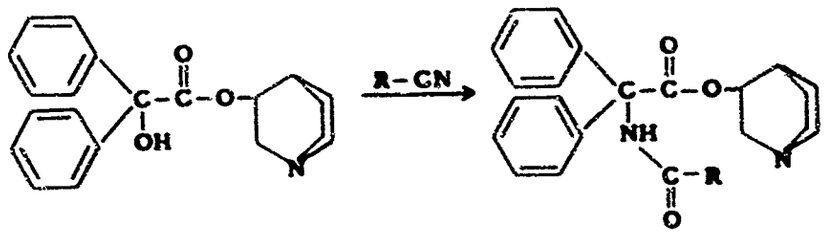
(S) Ritter et al[7] reported the reaction of nitriles with alkenes or tertiary alcohols to form N t-alkyl amides The presence of a tertiary alcohol group in BZ suggested the possible application of this reaction to BZ.

1 (U) General Procedure for the Ritter Reaction.

A solution of 1 gm (0.003 mole) of BZ and 0.004 mole of nitrile in 10 ml of glacial acetic acid was chilled in an ice bath and 15 ml of concentrated sulfuric acid added dropwise at a rate such that the temperature was maintained between 5° to 10°C. The reaction mixture was stirred cold for 1 hr and at room temperature for 2 hr The solution was poured onto crushed ice and neutralized with saturated potassium carbonate solution, then extracted with chloroform. The extract was dried over anhydrous potassium carbonate or sodium sulfate and the solvent removed. The residue was crystallized from benzene or benzene petroleum ether (bp 30° to 60°C) to yield the desired products

2 (S) Results

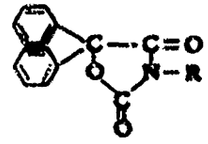
Table 2 lists the Ritter products prepared They are colorless, crystalline solids with definite melting points and show no unusual characteristic absorptions upon infrared analysis

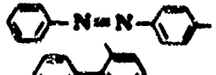
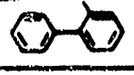


(U)

TABLE I

2,4-OXAZOLIDINEDIONES



R-	Melting point	Formula	Yield	Carbon		Hydrogen	
				Calculated	Found	Calculated	Found
	°C		%	%			
	141-143	$C_{21}H_{15}O_3N$	87	76.6	75.9	4.6	4.6
Br	131-132	$C_{21}H_{14}O_3NBr$	81	61.8	61.4	3.4	3.4
CH_3	117-118	$C_{22}H_{17}O_3N$	87.5	76.9	76.9	5.0	5.0
CH_3O	129	$C_{22}H_{17}O_4N$	09	73.5	73.1	4.8	4.4
NO_2	148-149	$C_{21}H_{14}O_5N_2$	90	67.4	67.2	3.3	3.8
$(CH_3)_2N$	155-156	$C_{23}H_{20}O_3N_2$	80	74.2	72.9	5.4	5.3
	148-150	$C_{25}H_{17}O_3N$	61	79.1	77.6	4.5	5.4
	153-154	$C_{27}H_{19}O_3N_3$	72	74.8	74.8	4.4	4.6
	136-138	$C_{27}H_{19}O_3N$	83	80.0	80.4	4.7	5.2

2 (U) Results

The oxazolidinediones prepared are listed in table 1 They all exhibit characteristic infrared absorptions in the regions of 5 5μ (urethane) and 5.7μ (amide).

B (S) Ritter Reaction Products

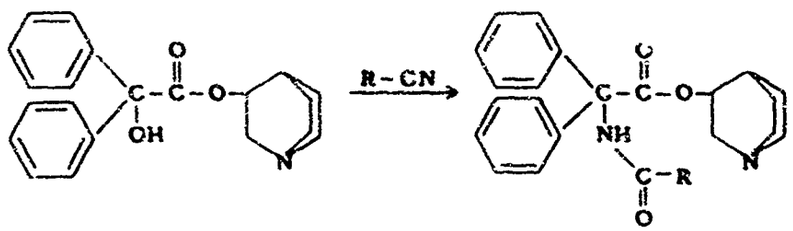
(S) Ritter et al[7] reported the reaction of nitriles with alcohols or tertiary alcohols to form N -alkyl amides The presence of a tertiary alcohol group in BZ suggested the possible application of this reaction to BZ.

1 (U) General Procedure for the Ritter Reaction.

A solution of 1 gm (0.003 mole) of BZ and 0.004 mole of nitrile in 10 ml of glacial acetic acid was chilled in an ice bath and 15 ml of concentrated sulfuric acid added dropwise at a rate such that the temperature was maintained between 5° to 10°C The reaction mixture was stirred cold for 1 hr and at room temperature for 2 hr The solution was poured onto crushed ice and neutralized with saturated potassium carbonate solution, then extracted with chloroform. The extract was dried over anhydrous potassium carbonate or sodium sulfate and the solvent removed The residue was crystallized from benzene or benzene petroleum ether (bp 30° to 60°C) to yield the desired products

2 (S) Results

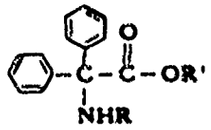
Table 2 lists the Ritter products prepared They are colorless, crystalline solids with definite melting points and show no unusual characteristic absorptions upon infrared analysis

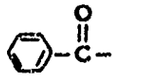


(U)

TABLE 2

RITTER REACTION PRODUCTS



R-	R'	Melting point	Yield	Formula	Carbon		Hydrogen	
					Calculated	Found	Calculated	Found
		°C	%		%			
$CH_3-\overset{O}{\overset{\|\|}{C}}-$	Quinuclidine	179-180	76	$C_{23}H_{26}O_3N_2$	73.0	73.8	6.9	7.1
$CH_3CH_2-\overset{O}{\overset{\|\|}{C}}-$	Quinuclidine	214-215	69	$C_{24}H_{28}O_3N_2$	73.44	73.6	7.2	6.9
	Quinuclidine	96-99	50	$C_{28}H_{28}O_3N_2$	76.3	73.6*	6.4	5.9*
$NH_2-\overset{O}{\overset{\|\|}{C}}-CH_2-\overset{O}{\overset{\|\|}{C}}-$	Quinuclidine	112-113	66.5	$C_{24}H_{27}O_4N_3$	71	70.9	6.7	6.7
$CH_3-\overset{O}{\overset{\|\|}{C}}-$	Methyl	169-172	95		72.1	71.8	5.9	5.1

* The carbon and hydrogen analyses of this reaction product deviate from theory; no attempt was made to further purify the substance.

C. (S) Quaternary Ammonium Compounds.

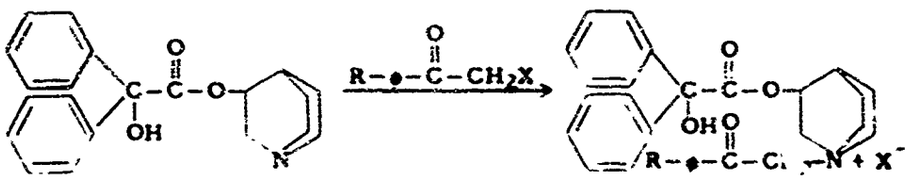
(C) When a tertiary base is quaternized with an alkylhalide, the differences in solubility of the salt-like product and the starting materials should be sufficient to allow spectral determination of the base. Several substituted phenacyl bromide quaternaries of BZ were prepared

1 (C) General Procedure for Preparation of Quaternary Salts.

A mixture of 1 gm (0.003 mole) of BZ, 0.004 mole of the phenacyl bromide, and 75 ml of chloroform was allowed to stand at room temperature for 18 hr. The solvent was removed under vacuum and the residue was crystallized from ethanol-ether, acetonitrile-ether or ethanol-1,2 dimethoxyethane.

2. (S) Results.

These products, typical high-melting crystalline solids, are listed in table 3



D. (C) BZ Acetate.

As part of this overall program, the authors were interested in preparing the acylated derivatives of BZ. In this connection attempts were made to acetylate BZ with acetic anhydride and with acetyl chloride in pyridine to no avail. The infrared spectrum of BZ indicates strong intramolecular, or intermolecular hydrogen bonding, which is absent in its salts. The nonreactivity observed with the usual acetylating reagents may be due to this bonding as well as to steric factors. Thus, treatment of the p-toluenesulfonic acid salt of BZ with isopropenyl acetate afforded the acetate quite smoothly.

(C) TABLE 3

PHENACYL BROMIDE QUATERNARY SALTS OF BZ (C)

Alkyl halide	Melting point	Yield	Carbon		Hydrogen	
			Calculated	Found	Calculated	Found
	°C	%	%			
p-Phenylphenacyl bromide	214-215	92	68.68	68.9	5.4	5.7
p-Nitrophenacyl bromide	190-191	99	59.9	58.3	5.1	5.3
p-Bromophenacyl bromide	170-175	90	56.6	56.6	4.8	4.8
β-Naphthacyl bromide	220-224	93	67.7	67.5	5.5	5.4

A mixture of 2 gm (0.0039 mole) of the p-toluenesulfonic acid salt of BZ, mp 180° to 182°C, 20 ml of isopropenyl acetate and a few crystals of p-toluenesulfonic acid was refluxed; acetone was distilled off slowly over a period of 5 hr. The mixture was homogeneous at this time. The excess isopropenyl acetate was removed under vacuum and the residue made alkaline with cold saturated potassium carbonate solution. This was extracted with chloroform, dried over anhydrous sodium sulfate, and the solvent removed under reduced pressure. The residue was refluxed with diethyl ether, filtered, and cooled to room temperature, it yielded 0.68 gm, 44.5%, of the acetate, mp 121° to 123°C.

Calculated: C, 72.8; H, 6.64
Found. C, 72.7 H, 6.7

E. (C) Spectrophotometric Determination of Small Quantities of BZ

p-Bromophenacyl bromide reacts readily with BZ in acetonitrile forming a quaternary salt. Since quaternary salts have relatively high solubility in water, one may separate the product from reactants and thus determine the amount of tertiary amine originally present. A plot of absorbancy versus concentration follows Beer's law. Detailed procedures for the determination of BZ in (a) acetonitrile, (b) water, and (c) in human whole blood follow.

Reagents: Recrystallized p-bromophenacyl bromide, spectro-grade acetonitrile, chloroform, CP, 0.1 M tris(hydroxymethyl)aminomethane (tris) buffer (pH 8.5), cyclohexane, and BZ.

1 (C) Determination of BZ in Acetonitrile.

(C) To 0.1 ml of 10^{-2} M solution of p-bromophenacyl bromide in acetonitrile in a glass-stoppered bottle is added 1 to 40 μg of BZ dissolved in 1 ml of acetonitrile. The solution is mixed and heated in a 50°C water bath for 10 min. After cooling the solution to room temperature 2 ml of 0.1 M KCl and 5 ml of cyclohexane are added and the mixture is mechanically shaken for 5 min. A portion of the aqueous phase is read spectrophotometrically at 265 mμ and the adherence to Beer's law demonstrated (table 4, figure 1).

(U) TABLE 4

DETERMINATION OF BZ IN ACETONITRILE

BZ	Absorbancy*
μg/ml	
0	0.066
2.6	0.205
5.2	0.328
7.8	0.456
10.4	0.597
13.0	0.738

* Average of five determinations

2. (C) Determination of BZ in Aqueous Solutions.

(C) To 2-ml aqueous solutions of BZ (5 to 40 μg) are added 0.2 ml of tris buffer (pH 8.5) and 3 ml of chloroform. The mixture is shaken mechanically for 5 min and the aqueous layer removed. An aliquot of the chloroform layer is air evaporated and the residue dissolved in 1 ml of acetonitrile. The analysis is then made in the manner reported above (E.1.) (table 5, figure 2).

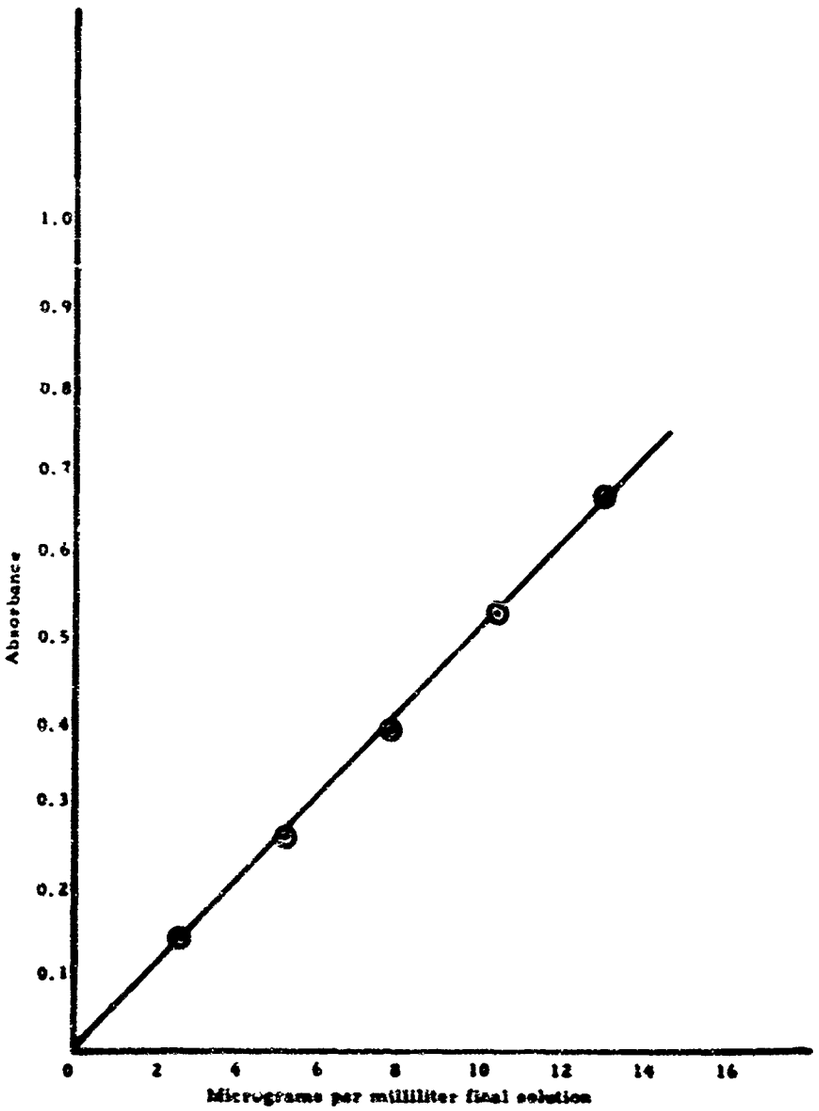


FIGURE 1

DETERMINATION OF BZ IN ACETONITRILE

(U) TABLE 5

DETERMINATION OF BZ IN AQUEOUS SOLUTIONS

BZ	Absorbancy*
ug/ml	
0.62	0.018
1.25	0.058
2.5	0.101
5.0	0.253
7.5	0.391
10.0	0.517
12.5	0.649

* Average of five determinations.

3. (C) Determination of BZ in Human Whole Blood.

(C) To 1 ml of human whole blood is added a 1-ml aqueous solution of BZ. The mixture is diluted to 7 ml and thoroughly mixed. One milliliter of 50% $ZnSO_4$ is added, mixed, and followed by 1 ml of 0.3 N $Ba(OH)_2$. Chloroform (10 ml) is added and the mixture is shaken mechanically for 10 min. It is then transferred to a glass-stoppered centrifuge tube and spun at 2500 rpm for 10 min. A 4-ml aliquot of the chloroform layer is air evaporated and the analysis performed in acetonitrile as above (table 6, figure 3).

(U) TABLE 6

DETERMINATION OF BZ IN WHOLE BLOOD

BZ	Absorbancy*
ug/ml	
1.7	0.062
3.4	0.148
5.1	0.230
5.9	0.280
6.8	0.317
8.5	0.388
10.2	0.478

* Average of four determinations.

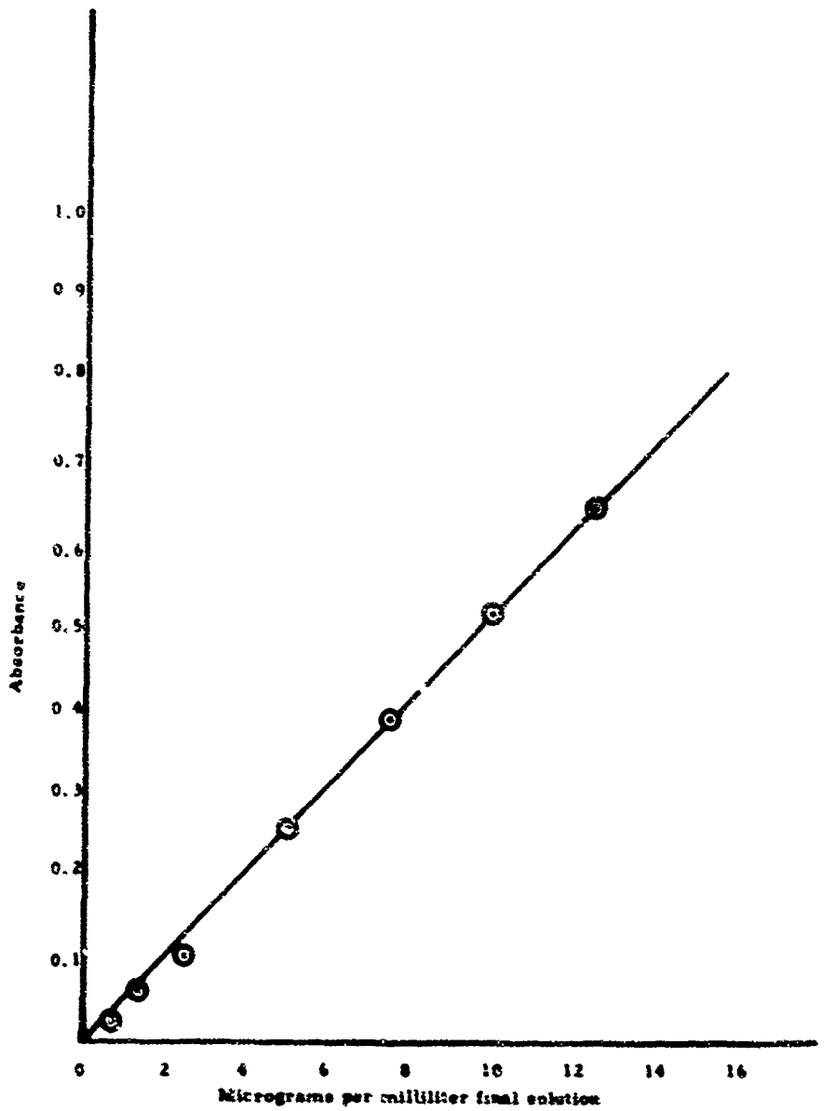


FIGURE 2

ANALYSIS OF BZ IN AQUEOUS SOLUTIONS

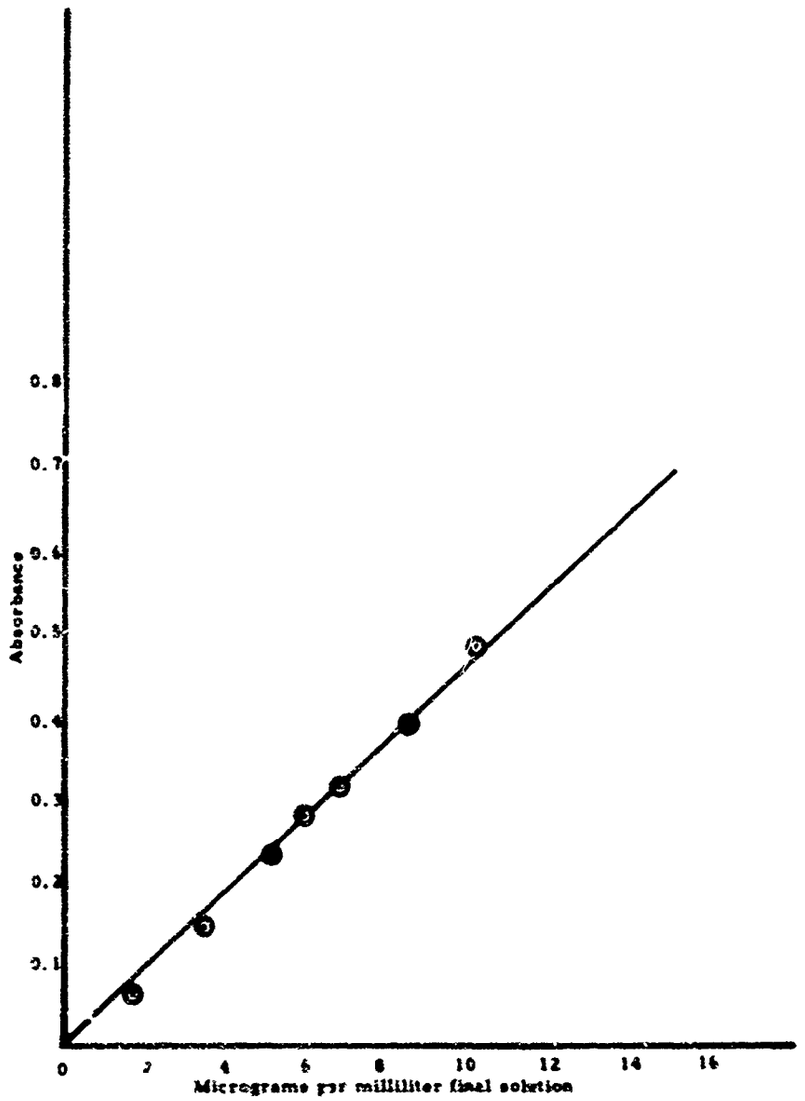


FIGURE 3

ANALYSIS OF BZ IN BLOOD

III. (C) CONCLUSIONS.

A fundamental study of the chemistry of BZ was conducted to assist in problems that may arise in detection, decontamination, biochemical mechanism of action, and metabolism. BZ reacts with (a) substituted phenyl isocyanates to yield 2,4-oxazolidinediones, (b) nitriles to produce amides (Ritter reaction), and (c) alkyl halides to give quaternary ammonium salts. Analysis of BZ can be accomplished by quaternization in acetonitrile, separation of reactants, and assaying spectrally.

(U) LITERATURE CITED

1. Ford-Moore, A. H., and Ing, H. R. Synthetic Mydriatics. J. Chem. Soc. (London) 55 (1947).

2. Sternbach, L. H., and Kaiser, S. Antispasmodics III Esters of Bicyclic Alcohols and Their Quaternary Salts. J. Am. Chem. Soc 75, 6068 (1953).

3 Sass, Samuel, Master, Irwin, Ludemann, William D., Martin, John J , Bratt, Martin, Sp-4, and Matoushek, Ralph, PFC. Technical Memorandum 13-14. Colorimetric and Spectrophotometric Estimation of EA 2277 and Similar Compounds, Some Chemistry on the Decomposition of EA 2277 (U) June 1960 SECRET Memorandum

4 U. S. Army Chemical Research and Development Laboratories. CRDL Special Publication 4-28 EA 2277 (U). A Summary Report as of 15 March 1961 March 1961 SECRET Report.

5 Clark-Lewis, J. W. 2,4 Oxazolidinedione Chem Revs 58, 63 (1958)

6 Rekker, R. F., Faber, A. C., Tom, D. H. E., Verleur, H., and Nauta, W Th. Rec. trav chim 70, 11d (1951).

7. Ritter, J., and Kalish, J J. Am Chem Soc 70, 4048 (1948).

DISTRIBUTION LIST NO. 5

No. of copies made 150

Copies

1	Mail and File Record Center, CRDL (Record Copy)
2- 8	CRDL Library, CRDL, Bldg 3330
9-11	Biomedical Research Lib, CRDL, Bldg 3220
12-15	Publications Section, Technical Releases Branch, TID
16	Director of Medical Research, CRDL
17-18	Chief, Physiology Division, CRDL
19-25	Australian Army Staff (W), ATTN: Lt. Col P. D. Yonge, 2001 Connecticut Avenue, N. W., Washington 8, D. C.
26-31	Canadian Liaison Officer (CBR), Building 5101, Edgewood Arsenal, Maryland
32	Chief, Bureau of Medicine and Surgery, Department of the Navy, ATTN: Code 74, Washington D. C. - 20390
33	Chief, Bureau of Naval Weapons, Code CS-3, Washington, D. C. 20380
34	Chief, Bureau of Naval Weapons, Code FWAM-12, Washington, D. C. - 20380
35-36	Chief, Field Office, USA Foreign Science and Technology Center, Building 4585 (483), Edgewood Arsenal, Maryland - 21010
37	Chief, Foreign Technology Division, ATTN TD-EWA, Wright-Patterson AFB, Ohio - 45433
38	Chief of Research and Development, Department of the Army, ATTN: Life Sciences Division, Washington, D. C. - 20310
39-40	Chief, Preventive Medicine Division, Directorate of Professional Service, Office of The Surgeon General, Washington, D. C. - 20315
41	Commandant, U. S. Army CBR Weapons Orientation Course, Dugway Proving Ground, Dugway, Utah - 84022
42	Commandant, U. S. Army Chemical School, ATTN: Training Media Division, Fort McClellan, Alabama - 36205
43	Commandant, U. S. Army Command & General Staff College, ATTN: Library Division, Fort Leavenworth, Kansas - 66027
44	Commandant, U. S. Army War College, ATTN: Library, Carlisle Barracks, Pennsylvania - 17013
45-46	Commander-in-Chief, U. S. Atlantic Fleet, Box 100, Division 30, ATTN: Code 313A, Norfolk, Virginia - 23511
47	Commander-in-Chief, U. S. Pacific Fleet, Navy No. 128, Box 11, c/o Fleet Post Office, San Francisco, California - 94135

DISTRIBUTION LIST NO. 5 (Contd)

48 Commander, Hq, RTD (RTNW), Bolling Air Force Base, Washington, D. C. - 20332

49 Commander (Code 88), U. S. Naval Ordnance Test Station, China Lake, California - 93557

50 Commander (Code 753), U. S. Naval Ordnance Test Station ATTN: Technical Library, China Lake, California - 93557

51 Commander, U. S. Naval Weapons Laboratory, (Code WWB KRT), ATTN: Technical Library, Dahlgren, Virginia

52 Commanding General, Aircraft, Fleet Marine Force, Marine Corps Air Station, El Toro, Santa Ana, California - 92709

53 Commanding General, Deseret Test Center, Fort Douglas, Utah - 84113

54 Commanding General, Fleet Marine Force, Atlantic, Norfolk, Virginia - 23511

55 Commanding General, 1st Marine Brigade, Fleet Marine Force, c/o FPO, San Francisco, California - 96601

56 Commanding General, 2d Marine Aircraft Wing, MCAS, Cherry Point, N. C. - 28533

57 Commanding General, U. S. Army Combat Developments Command Experimentation Center, ATTN: CDED-GC, Fort Ord, California - 93941

58 Commanding General, U S Army Materiel Command, ATTN: AMCAD-S, Washington, D. C. - 20315

59 Commanding General, U. S. Army Materiel Command, ATTN: Chemistry and Materials Branch Research Division, Washington, D. C. - 20315

60 Commanding General, U. S. Army Materiel Command, Research and Development Directorate, Development Division, CB Branch Building T7, Washington, D. C. -20315

61-62 Commanding General, U. S Army Medical Research & Development Command, ATTN. Chief, Records & Reports Branch, Main Navy Building, Washington, D. C. 20315

63 Commanding General, U. S. Army Munitions Command, ATTN: AMSMU-RE, Dover, New Jersey - 07801

64 Commanding General, U. S. Army Munitions Command, ATTN: AMSMU-RE-EP, Dover, New Jersey - 07801

65 Commanding General, U. S. Army Munitions Command, ATTN: AMSMU-SS-SC, Dover, New Jersey -07801

66 Commanding General, U. S. Army Natick Laboratories, ATTN: Technical Library, Natick, Massachusetts - 01762

DISTRIBUTION LIST NO. 5 (Contd)

67 Commanding General, U. S. Army Supply and Maintenance Command, ATTN: AMSSM-SO-A, Washington, D. C. - 20315

68 Commanding General, U. S. Army Test & Evaluation Command, ATTN: AMSTE-NBC, Aberdeen Proving Ground, Maryland - 21005

69 Commanding Officer, 392d Aerospace Medical Group, ATTN: SUAM-3, Vandenberg AFB, California

70 Commanding Officer, Detachment 4, ASD (ASQWC), Eglin Air Force Base, Florida - 32542

71-72 Commanding Officer, Dugway Proving Ground, ATTN: Technical Library, Dugway, Utah - 84022

73 Commanding Officer, Picatinny Arsenal, ATTN: SMUPA-VA6, Dover, New Jersey - 07801

74-75 Commanding Officer, Technical Training Center (TS-OF), Lowry Air Force Base, Colorado

76 Commanding Officer, USAF School of Aerospace Medicine (SMOTL), ATTN: Documents Librarian, Brooks Air Force Base, Texas - 78235

77 Commanding Officer, Air Proving Ground Center (PGAPI), Eglin Air Force Base, Florida -32542

78-79 Commanding Officer, U. S. Army Ballistic Research Laboratories, ATTN: AMXBR-T (Mr. William Kokinakis), Aberdeen Proving Ground, Maryland - 21005

80-81 Commanding Officer, U. S. Army Biological Laboratories, ATTN: Documents, Technical Library, Fort Detrick, Frederick, Maryland - 21701

82 Commanding Officer, USA CDC Artillery Agency, ATTN: CAGAT-RW, Fort Sill, Oklahoma - 73504

83 Commanding Officer, U. S. Army Combat Developments Command CBR Agency, Fort McClellan, Alabama - 36205

84 Commanding Officer, U. S. Army Combat Developments Command Intelligence Agency, Fort Holabird, Maryland - 21219

85 Commanding Officer, U. S. Army Combat Developments Command Medical Service Agency, Fort Sam Houston, Texas - 78234

86 Commanding Officer, U. S. Army Limited War Laboratory, ATTN: Technical Director, Aberdeen Proving Ground, Maryland

87 Commanding Officer, U. S. Naval Unit, Edgewood Arsenal, Maryland - 21010

88 Director, Air University Library, ATTN: AUL3T-8879, Maxwell Air Force Base, Alabama - 36112

DISTRIBUTION LIST NO 5 (Contd)

89 Director, Biological Sciences Division (Code 440), Office of Naval Research, Department of the Navy, 17th & Constitution Avenue, N. W., Washington 25, D. C.

90 Director of CBR Operations, Office of the Assistant Chief of Staff for Force Developments, Dept of the Army ATTN: FOR CMSR, Washington, D. C. - 20310

91-92 Director of Engineering & Industrial Services, ATTN: Publications Clerk, U. S. Army Edgewood Arsenal, Edgewood Arsenal, Maryland - 21010

93 Director, U. S. Army Edgewood Arsenal, Operations Research Group, Edgewood Arsenal, Maryland- 21010

94 Director, U. S. Naval Research Laboratory, ATTN: Army Liaison Officer, Code 1071, Washington, D C. 20390

95 Director, Walter Reed Army Institute of Research, Division of Neuropsychiatry, Washington, D. C. - 20012

96 Director, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. - 20012

97 Division of Health Mobilization, U. S. Public Health Service, ATTN: Mr. Charles H. Harp, Deputy Chief, Research Branch, Room 1216, Tempo "R" Building, Washington 25, D. C.

98-103 Dr D. F. Downing, Defense Research Staff, Munitions/TW, British Embassy, 3100 Massachusetts Avenue, N. W. Washington 8, D C.

104 Executive Director, EA CBR Advisory Council, Room 272, Building 5101, Edgewood Arsenal, Maryland - 21010

105 Headquarters, AFLC (MCD), Wright-Patterson AFB, Ohio-45433

106 Headquarters, AFMTC, Deputy for Bioastronautics (MTX), ATTN: Col. William H Lee, USAF, MSC, Patrick Air Force Base, Florida - 32925

107 Headquarters, AFSC (SCGB), ATTN. B. E. Flaherty, Lt. Col., USAF, MC. Andrews Air Force Base, Washington, D. C. - 20331

108 Headquarters, U. S. Army Combat Developments Command Combat Service Support Group, Fort Lee, Virginia - 23801

109 Headquarters, U. S. Army Munitions Command, Marine Corps Representative. ATTN: AMSMU-LM, Dover, New Jersey - 07801

110 Hq. U. S. Air Force, (AFMSPA-Bionucleonics), ATTN: Special Weapons Defense Officer), Washington, D. C. - 20333

DISTRIBUTION LIST NO 5 (Contd)

89 Director, Biological Sciences Division (Code 440), Office of Naval Research, Department of the Navy, 17th & Constitution Avenue, N. W., Washington 25, D. C.

90 Director of CBR Operations, Office of the Assistant Chief of Staff for Force Developments, Dept of the Army ATTN: FOR CMSR, Washington, D. C. - 20310

91-92 Director of Engineering & Industrial Services, ATTN: Publications Clerk, U. S. Army Edgewood Arsenal, Edgewood Arsenal, Maryland - 21010

93 Director, U. S. Army Edgewood Arsenal, Operations Research Group, Edgewood Arsenal, Maryland- 21010

94 Director, U. S. Naval Research Laboratory, ATTN: Army Liaison Officer, Code 1071, Washington, D C. 20390

95 Director, Walter Reed Army Institute of Research, Division of Neuropsychiatry, Washington, D. C. - 20012

96 Director, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington, D. C. - 20012

97 Division of Health Mobilization, U S Public Health Service, ATTN: Mr. Charles H. Harp, Deputy Chief, Research Branch, Room 1216, Tempo "R" Building, Washington 25, D. C.

98-103 Dr D. F. Downing, Defense Research Staff, Munitions/TW, British Embassy, 3100 Massachusetts Avenue, N. W. Washington 8, D C.

104 Executive Director, EA CBR Advisory Council, Room 272, Building 5101, Edgewood Arsenal, Maryland - 21010

105 Headquarters, AFLC (MCD), Wright-Patterson AFB, Ohio-45433

106 Headquarters, AFMTC, Deputy for Bioastronautics (MTX), ATTN: Col. William H Lee, USAF, MSC, Patrick Air Force Base, Florida - 32925

107 Headquarters, AFSC (SCGB), ATTN. B. E. Flaherty, Lt. Col., USAF, MC, Andrews Air Force Base, Washington, D. C. - 20331

108 Headquarters, U. S Army Combat Developments Command Combat Service Support Group, Fort Lee, Virginia - 23801

109 Headquarters, U. S. Army Munitions Command, Marine Corps Representative, ATTN: AMSMU-LM, Dover, New Jersey - 07801

110 Hq. U. S. Air Force, (AFMSPA-Bionucleonics), ATTN: Special Weapons Defense Officer), Washington, D. C. - 20333

DISTRIBUTION LIST NO. 5 (Contd)

111	Headquarters, U.S. Marine Corps, ATTN: Staff Medical Officer (Code AM), Washington, D. C. - 20360
112	Institute for Cooperative Research, University of Pennsylvania, ATTN: Security Officer, TO: Librarian, Project Summit. 3634 Walnut Street, Philadelphia, Pennsylvania - 19104
113	Office, Chief of Research and Development, Department of the Army, Room 3E 440, ATTN: Chemical-Biological Office, Washington 25, D. C. - 20301
114	Office of the Chief of Engineers, Department of the Army, ENGMC-ED, ATTN: Mr. James E. Malcolm, Washington, D.C. 20315
115	Officer in Charge, NBC Defense Department, U. S. Naval Schools Command, Treasure Island, San Francisco 30, California
116 - 117	PHS Liaison Officer, Fort Detrick, Frederick, Maryland - 21701
118	President, U. S. Army Airborne, Electronics & Special Warfare Board, Fort Bragg, North Carolina - 28307
119	President, U. S. Army Arctic Test Board, APO 733, Seattle, Washington
120	Research Analysis Corporation, ATTN: Library, McLean, Virginia - 22101
121	Stanford Research Institute, ATTN: External Reports, G-037 (for Dr. Wilbur Benson), Menlo Park, California - 94025
122	Surgeon, U. S. A. Rocky Mountain Arsenal, Denver, Colorado - 80240
123	The RAND Corporation, 1700 Main Street, ATTN: Library, Santa Monica, California - 90406
124	U. S. Army Scientific Liaison and Advisory Group (8744), ATTN: Dr. Don L. Isenberg, The Pentagon, Washington, D. C. -20310
125 - 126	U. S. Army Standardization Group, UK, ATTN: CBR Representative, Box 65, USN 100, FPO, New York, New York - 09599
127 - 130	USA CDC Liaison Officer, Hq. U. S. Army Munitions Command, Dover, New Jersey - 07801
131 - 150	Defense Documentation Center, Cameron Station, Alexandria, Virginia - 22314

CONFIDENTIAL

ABSTRACT

1 Originating Activity

Physiology Division
U S Army Chemical Research
and Development Laboratories
Edgewood Arsenal, Maryland

2a Report Security Classification

SECRET

2b Group (for DDC use only)

3 Report Title SOME CHEMICAL REACTIONS OF BZ (U)

4 Descriptive Notes The work was started in March 1961 and completed in April 1962

5. Authors Hackley Brennie E Jr Cochrane, Chappelle C. Hackley, Ethel B

6 Publication Date May 1964

7 Total No. of Pages 24

8 Originator's Report No

CRDLR 3213

9 Task 4C08-03 016 14

10. Other Report Nos.

11 Supplementary Notes (for DDC use only)

12. Release Statements (for DDC use only)

CONFIDENTIAL

13. Author's Key Terms - Unclassified Only

BZ	Mechanism of action
Chemical reactions	Amides
Detection	Ritter reaction
Decontamination	Alkyl halides
Biochemistry	Ammonium salts
Metabolism	Quaternization
Substituted compounds	Acetonitrile
Phenyl isocyanates	Spectrum
Chemical agents	2,4-oxazolidinediones
Nitriles	Biochemical action
Incapacitating agents	

14. DDC Descriptors (for DDC use only)

15 Identifiers - Unclassified Only

16. Body of Abstract

(C) The purpose of this work was to conduct a fundamental study of the chemistry of BZ, to assist in problems that may arise in detection, decontamination, biochemical mechanism of action, and metabolism. BZ reacts with (1) substituted phenyl isocyanates to yield, 2,4-oxazolidinediones, (2) nitriles to produce amides (Ritter reaction), and (3) alkyl halides to give quaternary ammonium salts. Analysis of BZ can be accomplished by quaternization in acetonitrile, separation of reactants, and assaying spectrally.

17. Indexing Annotation

Fundamental study of the chemistry of BZ to assist in the solution of problems of manufacture, storage, detection, decontamination, and biochemical mechanism of action.

CONFIDENTIAL

ABSTRACT

1. Originating Activity

Physiology Division
U. S. Army Chemical Research
and Development Laboratories
Edgewood Arsenal, Maryland

2a. Report Security Classification

SECRET

2b. Group (for DDC use only)

3. Report Title SOME CHEMICAL REACTIONS OF BZ (U)

4. Descriptive Notes The work was started in March 1961 and completed in April 1962.

5. Authors Hackley, Brennie E., Jr. Cochrane, Chappelle C. Hackley, Ethel B.

6. Publication Date May 1964

7. Total No. of Pages 24

8. Originator's Report No.

CRDLR 3213

9. Task 4C08-03-016-14

10. Other Report Nos.

11. Supplementary Notes (for DDC use only)

12. Release Statements (for DDC use only)

CONFIDENTIAL

13. Author's Key Terms - Unclassified Only

BZ	Mechanism of action
Chemical reactions	Amides
Detection	Ritter reaction
Decontamination	Alkyl halides
Biochemistry	Ammonium salts
Metabolism	Quaternization
Substituted compounds	Acetonitrile
Phenyl isocyanates	Spectrum
Chemical agents	2,4-oxazolidinediones
Nitriles	Biochemical action
Incapacitating agents	

14. DDC Descriptors (for DDC use only)

15. Identifiers - Unclassified Only

16. Body of Abstract

(C) The purpose of this work was to conduct a fundamental study of the chemistry of BZ, to assist in problems that may arise in detection, decontamination, biochemical mechanism of action, and metabolism. BZ reacts with (1) substituted phenyl isocyanates to yield, 2,4-oxazolidinediones, (2) nitriles to produce amides (Ritter reaction), and (3) alkyl halides to give quaternary ammonium salts Analysis of BZ can be accomplished by quaternization in acetonitrile, separation of reactants, and assaying spectrally

17. Indexing Annotation

Fundamental study of the chemistry of BZ to assist in the solution of problems of manufacture, storage, detection, decontamination, and biochemical mechanism of action

CONFIDENTIAL

ABSTRACT

1. Originating Activity

Physiology Division
U. S. Army Chemical Research
and Development Laboratories
Edgewood Arsenal, Maryland

2a. Report Security Classification

SECRET

2b. Group (for DDC use only)

3. Report Title SOME CHEMICAL REACTIONS OF BZ (U)

4. Descriptive Notes The work was started in March 1961 and completed in April 1962.

5. Authors Hackley, Brennie E., Jr. Cochrane, Chappelle C. Hackley, Ethel B.

6. Publication Date May 1964

7. Total No. of Pages 24

8. Originator's Report No.

CRDLR 3213

9. Task 4C08-03-016-14

10. Other Report Nos.

11. Supplementary Notes (for DDC use only)

12. Release Statements (for DDC use only)

CONFIDENTIAL

13. Author's Key Terms - Unclassified Only

BZ	Mechanism of action
Chemical reactions	Amides
Detection	Ritter reaction
Decontamination	Alkyl halides
Biochemistry	Ammonium salts
Metabolism	Quaternization
Substituted compounds	Acetonitrile
Phenyl isocyanates	Spectrum
Chemical agents	2,4-oxazolidinediones
Nitriles	Biochemical action
Incapacitating agents	

14. DDC Descriptors (for DDC use only)

15 Identifiers - Unclassified Only

16. Body of Abstract

(C) The purpose of this work was to conduct a fundamental study of the chemistry of BZ, to assist in problems that may arise in detection, decontamination, biochemical mechanism of action, and metabolism. BZ reacts with (1) substituted phenyl isocyanates to yield 2,4-oxazolidinediones, (2) nitriles to produce amides (Ritter reaction), and (3) alkyl halides to give quaternary ammonium salts Analysis of BZ can be accomplished by quaternization in acetonitrile, separation of reactants and assaying spectrally.

17 Indexing Annotation

Fundamental study of the chemistry of BZ to assist in the solution of problems of manufacture, storage, detection, decontamination, and biochemical mechanism of action

DEPARTMENT OF THE ARMY
US ARMY RESEARCH, DEVELOPMENT AND ENGINEERING COMMAND
EDGEWOOD CHEMICAL BIOLOGICAL CENTER
5183 BLACKHAWK ROAD
ABERDEEN PROVING GROUND, MD 21010-5424

REPLY TO
ATTENTION OF

AMSRD-ECB-TD

27 MAY 2009

MEMORANDUM FOR Army Declassification Activity, 8850 Richmond Highway, Suite 300, IMP Building, Alexandria, VA 22309

SUBJECT: Declassification Review

1. References:

a. Executive Order 12958, Classified National Security Information, dated 17 April 1995.

b. Executive Order 13292, Classified National Security Information, dated 25 March 2003.

c. AR 380-5, DA Information Security Program, dated 31 October 2000.

2. In accordance with the references listed above, the purpose of this memorandum is to provide the recommendation made by the Edgewood Chemical Biological Center (ECBC) Security Classification Review Board (SCRB), regarding declassification and downgrading of the below listed documents.

a. Isokinetic Sampling of H Aerosol, (ADA Case 08019), (as Produced by the Comings Candle), February 1946. Downgrade from Confidential to Unclassified/Unlimited.

b. Dugway Proving Ground Research and Development Weekly Report (Part A), Medical Research Laboratory Weekly Report (Part B), Dugway Proving Ground Mobile CWS Unit Weekly Report (Part C), (ADA Case 08024), February 1945. Distribution authorized to U.S. Government agencies and their contractors. Downgrade from SECRET to Unclassified/Unlimited.

c. Dugway Proving Ground Research and Development Weekly Report (Part A), Medical Research Laboratory Weekly Report (Part B), Dugway Proving Ground Mobile CWS Unit Weekly Report (Part C), (ADA Case 08023), January 1945. Downgrade from SECRET to Unclassified/Unlimited.

d. Counter-Insurgency and Air Power: Report of a Rand Ad Hoc Group, (ADA Case 07078), June 1962. Downgrade from SECRET to Unclassified/Unlimited.

e. The Role of Chemical and Biological Weapons in the Defense Strategy of the United States, (ADA Case 08002), December 1964. Retain at Confidential. 07-M-2839

07-M-2825, 07-M-2831,
07-M-2834 through 07-M-2838
07-M-2842

Printed on Recycled Paper

AMSRD-ECB-TD
SUBJECT: Declassification Review

f. Special Report: The Increment Flow Regulation Valve, (ADA Case 08020), 3 December 1945. Distribution authorized to US Government agencies only.

g. Interim Report: Development of Decontamination Solution Unit, 3-Gallon, E8R2, (ADA Case 08003), 15 February 1954. Retain at Confidential. 07-M-2836

h. Chemistry of BZ.I. Reaction of BZ with Iodine in Aqueous and Organic Solution, (ADA Case 08007), November 1962. Downgrade from Confidential to US Government Agencies and their contractors. 07-M-2837

i. Interim Report: Decontamination of Airplanes (F.Y. 53), (ADA Case 08006), 19 November 1953. Retain at Confidential.

j. Chemical Defense Experimental Establishment Portion, (ADA Case 08010), 4 December 1954. This document contains Foreign Government Information (British) and the decision should be deferred to them.

k. An Evaluation of the Relative Efficacy of Five Self-Injection Ampoules, (ADA Case 08011), December 1952. This document contains Foreign Government Information (British) and the decision should be deferred to them.

l. Infrared Spectra and Absorption Coefficients for GA, GB, GD, VM, VX, and the G analog (Reaction Product of VX and Conversion Filter), (ADA Case 08000), August 1966. Retain as US Government Agencies and their contractors. 07-M-2825

m. Estimate of Minimal Effective Dose of BZ by the Intramuscular Route in Man, (ADA Case 08004), November 1965. Downgrade from Confidential to Unclassified, US Government agencies and their contractors. 07-M-2831

n. Stability Testing of M138 BZ Bombs, (ADA Case 08008), August 1966. Downgrade from Confidential to Unclassified, US Government agencies and their contractors. 07-M-2835

o. Some Chemical Reactions of BZ, (ADA Case 08009), May 1964. Downgrade from Confidential to Unclassified/Unlimited. 07-M-2838

3. The point of contact is Mr. Jeremy Taylor at 410-436-6810 or jeremy.taylor2@us.army.mil.

for RICHARD W. DECKER, II
Technical Director