ethyl chlorocarbonate to form **2-arsono-6-carbethoxyaminonaphthalene.** A sealed flask reaction with ethylene oxide in 0.5 *N* sodium carbonate solution gave **2-arsono-6-β-hydroxyethylaminonaphthalene.**

These arsenicals were white, difficultly soluble in water, and did not melt or decompose below 250°.

Summary

1. 2-Amino-6-nitronaphthalene was prepared by the method of Saunders. A study of the reaction over a range of temperatures showed that the ratio of the isomers formed was not altered.

2. The structure of this isomer was confirmed by reduction to 2,6-diaminonaphthalene. A new derivative, 2-benzoylamino-6-nitronaphthalene, was described.

3. 2-Arsono-6-nitronaphthalene was formed by the Bart reaction. Reduction of this compound with ferrous hydroxide yielded 2-arsono-6-aminonaphthalene. Three derivatives, formed by reaction of the amine with acetic anhydride, ethylene oxide and ethyl chlorocarbonate, were described.

LINCOLN, NEBRASKA RECEIVED JUNE 28, 1934

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF NEBRASKA]

Arsenated Phenoxyalkanols

BY LEON A. SWEET[1] AND CLIFF S. HAMILTON

β-4-Arsonoanilinoethanol and γ-4-arsonoanilinopropanol[2] have been prepared by condensing arsanilic acid with ethylene and trimethylene chlorohydrins. Similarly, the oxygen analogs were prepared by condensation with 4-hydroxyphenylarsonic acid.[3] In the present investigation two series of arsenated phenoxyalkanols were derived from the parent compounds, β-4-arsonophenoxyethanol and γ-4-arsonophenoxypropanol.

Condensations of ethylene and trimethylene chlorohydrins with 4-hydroxyphenylarsonic acid were readily effected by refluxing with 6 *N* sodium hydroxide. Under similar conditions ethylene chlorohydrin and 3-nitro-4-hydroxyphenylarsonic acid did not condense.

Nitration of β-4-arsonophenoxyethanol using three molecular proportions of nitric acid (sp. gr. 1.50) in an excess of concentrated sulfuric acid resulted in a mixture of β-2-nitro-4-arsonophenoxyethyl nitrate and the mono- and di-nitro compounds. Heating at 95° yielded a mixture of β-2,6-dinitro-4-arsonophenoxyethanol and 2,6-dinitro-4-arsonophenol. The use of nitric acid (sp. gr. 1.50) alone resulted in a complete conversion to the nitro ester and further reaction introduced one nuclear nitro group. Oxidation of the side chain to the corresponding acid accompanied nitration whenever sulfuric acid was not used. After reaction for twenty-four hours at room temperature the only product was 2-nitro-4-arsonophenoxyacetic acid. γ-4-Arsonophenoxypropanol behaved in a similar manner, although oxidation occurred more readily than with the ethanol homolog, necessitating a lower temperature and a longer time of reaction for the preparation of γ-2-nitro-4-arsonophenoxypropyl nitrate.

β-2-Nitro-4-arsonophenoxyethyl nitrate and γ-2-nitro-4-arsonophenoxypropyl nitrate were readily hydrolyzed by refluxing with 3 *N* hydrochloric acid. Reduction of the hydrolysates by means of alkaline ferrous hydroxide gave the corresponding amines.

Newbery, Phillips and Sticklings[4] observed that reduction of 2-nitro-4-arsonophenoxyacetic acid led to the cyclic compound 3-hydroxy-1,4-benzisoxazine-6-arsonic acid. In connection with our work on arsenated phenyl ethers it seemed of interest to prepare methyl-2-nitro-4-arsonophenoxyacetate to determine whether on reduction a straight chain or cyclic compound would result. Esterification did not prevent ring closure, the intermediate 2-amino compound losing a molecule of methanol to form 3-hydroxy-1,4-benzisoxazine-6-arsonic acid.

Experimental

β-4-Arsonophenoxyethanol[5] and its Sodium Salt.—To a solution of 218 g. of 4-hydroxyphenylarsonic acid in 500

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(1) Parke, Davis & Company Fellow.

(2) Hamilton, THIS JOURNAL, **45**, 2751 (1923).

(3) Unpublished work, Chemical Laboratory, Northwestern University. The compounds β-4-arsonophenoxyethanol, γ-4-arsonophenoxypropanol and β-2-acetylamino-4-arsonophenoxyethanol are identified by the numbers 141, 132 and 133, respectively, in our arsenical series. The last mentioned has appeared recently in the patent literature; Benda and Sievers, German Patent 552,267; English Patent 373,071.

(4) Newbery, Phillips and Sticklings, *J. Chem. Soc.*, **130**, 3056 (1928).

(5) Prepared by Cislak and Hamilton, Chemical Laboratory, Northwestern University.

cc. of 9 *N* sodium hydroxide, cooled to 25°, was added 400 g. of 40% (by weight) ethylene chlorohydrin. The solution was warmed gently to 40–50°, and after vigorous reaction ceased it was refluxed for five hours. It was filtered, cooled and the arsonic acid precipitated by adding 200 cc. of 12 *N* hydrochloric acid.

The acid was dissolved in sufficient 2 *N* sodium hydroxide to yield a solution neutral to litmus and was filtered into absolute ethanol. The monosodium salt separated as small white rods.

β-2-Nitro-4-arsonophenoxyethyl Nitrate.—β-4-Arsonophenoxyethanol (20 g.) was stirred with 40 cc. of nitric acid (sp. gr. 1.50) and 8 cc. of concd. sulfuric acid for three hours at 20°. The product was precipitated by pouring into cold water.

β-2-Nitro-4-Arsonophenoxyethanol.—β-2-Nitro-4-arsonophenoxyethyl nitrate (40 g.) was hydrolyzed by refluxing two hours with 165 cc. of 2.5 *N* hydrochloric acid. The solution was concentrated under vacuum to 100 cc., and made neutral to Congo red paper with 6 *N* sodium hydroxide. Upon cooling the nitro compound crystallized from solution; weight, 31 g.

β-2-Amino-4-arsonophenoxyethanol and its Hydrochloride and Sodium Salt.—β-2-Nitro-4-arsonophenoxyethanol (35 g.) was dissolved in 60 cc. of 2 *N* sodium hydroxide. It was shaken with a ferrous hydroxide suspension formed by dissolving 240 g. of ferrous chloride ($FeCl_2 \cdot 4H_2O$) in 300 cc. of water and adding sufficient 6 *N* sodium hydroxide to neutralize to litmus paper, plus the excess necessary to obtain a 2% concentration of sodium hydroxide. The mixture was filtered and the residue extracted with 100 cc. of 2% sodium hydroxide. The combined filtrates were made neutral to litmus, concentrated *in vacuo* to a saturated salt solution, and made faintly acid to Congo red paper with 6 *N* hydrochloric acid. The solution was warmed, decolorized with charcoal and filtered. The amine crystallized as a mass of needles and was twice recrystallized from 150 cc. volumes of water. Dried *in vacuo* over calcium chloride it retained one molecule of water of crystallization. Drying this monohydrate four hours at 105° caused the loss of two molecules of water. Presumably loss of the extra mole of water represented dehydration of the arsonic acid, since there was no loss of water upon heating the corresponding sodium salt at 120°.

TABLE I

	Name	Crystal form	Yield, %	M. p., °C.	Formula	As analyses, %	
						Calcd.	Found
1	β-4-Arsonophenoxyethanol	Colorless hexagonal plates[a]	60–64	147–148[b]	$C_8H_{11}O\ As$	28.60	28.60
2	Sodium salt of 1	Small colorless rods[c]	95	.....	$C_8H_{10}O_5AsNa \cdot 2H_2O$[d]	23.42	23.43
3	β-2-Nitro-4-arsonophenoxyethyl nitrate	Colorless needles[a]	90	217–218 (dec.)[e]	$C_8H_9O_9N_2As$	21.30	21.33
4	β-2-Nitro-4-arsonophenoxyethanol	Colorless rectangular plates[a]	90	138	$C_8H_{10}O_7NAs$	24.41	24.40
5	β-2-Amino-4-arsonophenoxyethanol	Colorless needles[a]	63	96–98[f]	$C_8H_{12}O_5NAs \cdot H_2O$	25.40	25.45
6	Arsonic anhydride of 5	....	100	208–210 (dec.)[g]	$C_8H_{10}O_4NAs$	28.93	28.85
7	Hydrochloride of 5	Colorless irregular masses[h]	96	171–172 (dec.)	$C_8H_{12}O_5NAs \cdot HCl$[i]	23.90	23.81
8	Sodium salt of 5	Colorless plates[h]	98	.....	$C_8H_{11}O.NAsNa$	25.06	25.08
9	β-2-Acetylamino-4-arsonophenoxyethanol	Long colorless needles[a]	71	207 (dec.)	$C_{10}H_{14}O_6NAs$[j]	23.49	23.59
10	β-2,6-Dinitro-4-arsonophenoxyethanol	Pale yellow rhomboids[a]	30	212–215 (dec.)	$C_8H_9O_9N_2As$	21.30	21.32
11	2,6-Dinitro-4-arsonophenol	Yellow plates[a]	45	>275	$C_6H_5O_8N_2As$[k]	24.33	24.32
12	β-2,6-Diamino-4-arsonophenoxyethanol	Colorless rods[a]	37	205 (dec.)	$C_8H_{13}O.N_2As$	25.66	25.68
13	β-2,6-Dinitro-4-arsonophenoxyethyl nitrate	Colorless hexagonal plates[a]	87	188–189	$C_8H_8O_{11}N_3As$	18.87	18.95
14	β-4-Arsonophenoxyethyl nitrate	Colorless needles[a]	82	145	$C_8H_{10}O_7NAs$	24.41	24.42
15	β-2-Chloro-4-arsonophenoxyethanol	Colorless rectangular plates[a]	18–35	141	$C_8H_{10}O_5ClAs$[l]	25.27	25.50
16	β-2-Chloro-4-arsonophenoxyethyl nitrate	Long colorless needles[a]	73	205 (dec.)[m]	$C_8H_9O_7NClAs$	21.94	21.92
17	2-Nitro-4-arsonophenoxyacetic acid	Yellow prisms[a]	70	>250	$C_8H_8O_8NAs$	23.34	23.39
18	3-Hydroxy-1,4-benzisoxazine-6-arsonic acid	Colorless rhombs[a]	72	>300	$C_8H_8O_5NAs$	27.45	27.51

[a] By recrystallization from water. [b] Softened at 127°. [c] From alcohol. [d] Calcd. for $2H_2O$: 11.25. Found: 11.13. [e] Softened above 160°. [f] Without water of crystallization, m. p. 156–157°. [g] Softened at 145–150°. [h] From alcohol-ether. [i] Calcd.: neut. eq. 157. Found: 158. [j] Absorbed one molecule of water of crystallization on standing in air. Calcd. for H_2O: 5.43. Found: 5.36. [k] Calcd. for N: 9.09. Found: 9.00. [l] Calcd. for Cl: 11.96. Found: 10.93. [m] Softened at 136°.

To a solution of 5 g. of the amine monohydrate in 20 cc. of absolute ethanol was added one equivalent of a solution of hydrogen chloride in absolute ethanol. The solution was filtered into 300 cc. of technical ethyl ether to precipitate the hydrochloride. It was filtered, washed with ether and air-dried, yielding a white powder; weight, 5.1 g.

A neutral solution was made by dissolving the amine in an equivalent quantity of 2 *N* sodium hydroxide. It was filtered into cold 95% ethanol and the monosodium salt separated.

Reaction of the monosodium salt with acetic anhydride formed β-2-acetylamino-4-arsonophenoxyethanol.

β-2,6-Dinitro-4-arsonophenoxyethanol.—A solution of 10 g. of β-4-arsonophenoxyethanol in 25 cc. of concd. sulfuric acid and 7 cc. of nitric acid (sp. gr. 1.50) was heated at 95° for thirty minutes, cooled, mixed with 200 g. of ice and β-2,6-dinitro-4-arsonophenoxyethanol crystallized from solution. A solution of this compound in dilute alkali was violet in color.

The mother liquor yielded 2,6-dinitro-4-arsonophenol.[6]

β-2,6-Diamino-4-arsonophenoxyethanol.—β-2,6-Dinitro-4-arsonophenoxyethanol was reduced to the diamine by means of alkaline ferrous hydroxide.

β-2,6-Dinitro-4-arsonophenoxyethyl nitrate was formed by reaction of the dinitro compound with nitric acid (sp. gr. 1.50). It gave a colorless solution in dilute alkali.

β-4-Arsonophenoxyethanol was converted to the nitrate ester by stirring with nitric acid (sp. gr. 1.50).

β-2-Chloro-4-arsonophenoxyethanol.—Impure samples of β-2-nitro-4-arsonophenoxyethyl nitrate, which contained β-4-arsonophenoxyethyl nitrate, were boiled with 6 *N* hydrochloric acid. The combination of nitric acid (formed by hydrolysis of the esters) and hot concentrated hydrochloric acid constituted a chlorinating agent which partially converted the last-named arsenical into β-2-chloro-4-arsonophenoxyethanol. After conversion of the nitro compound to the corresponding amine by reduction with ferrous hydroxide, separation was readily effected and the halogen compound was isolated. It was purified by repeated recrystallization from water.

This compound was converted to the nitrate by reaction with nitric acid (sp. gr. 1.50). Upon refluxing with 3 *N* hydrochloric acid, β-2-chloro-4-arsonophenoxyethanol was again obtained; m. p. 141°. The nuclear position of the halogen was further indicated by failure to hydrolyze with hot dilute alkali.

β-4-Arsonophenoxyethanol in nitric acid (sp. gr. 1.50) for twenty-four hours at 25–30° yielded 2-nitro-4-arsonophenoxyacetic acid. Reduction of the compound to 3-hydroxy-1,4-benzisoxazine-6-arsonic acid served to check its identity.

Three arsenious oxides were prepared from the corresponding arsonic acids by reduction with sulfurous acid, employing hydriodic acid as a catalyst. Purified by reprecipitating at 0° with dilute hydrochloric acid from their solutions in dilute alkali, they were obtained as white amorphous powders which did not melt below 250°.

TABLE II

SUBSTITUTED PHENYLARSENIOUS OXIDES

Substituent	Formula	As analyses, %		
		Calcd.	Found	
4-β-Hydroxyethoxy-	$C_8H_9O_3As$	32.86	32.42	32.36
3-Chloro-4-β-hydroxyethoxy	$C_8H_8O_3ClAs$	28.54	28.80	28.76
3-Amino-4-β-hydroxyethoxy	$C_8H_{10}O_3NAs$	30.83	30.60	30.64

3-Amino-4-β-hydroxyethoxyphenyldichloroarsine Hydrochloride.—The crude oxide was extracted with 75 cc. of warm butanol, filtered, diluted with 400 cc. of ether and filtered again. To the filtrate was added three molecular proportions of hydrogen chloride in absolute ethanol, and a pasty mass separated. After one hour the mixture was filtered. The partially crystallized product was triturated with a solution of hydrogen chloride in ether, filtered, washed with ether and the small white crystals were dried at 50° in a vacuum oven; weight, 7.5 g. or 71% yield; m. p. 174°.

Anal. Calcd. for $C_8H_{11}O_2NAsCl_3$: As, 22.40; Cl, 31.81; neut. eq., 111.5. Found: As, 22.30, 22.26; Cl, 31.81, 31.88; neut. eq., 114.0, 114.3.

Three arseno compounds were prepared by reduction of the corresponding arsonic acids with 25% hypophosphorous acid solutions at 95°. They were isolated as yellow powders.

TABLE III

Name	Formula	As analyses, %		
		Calcd.	Found	
Arseno-3,3′-dinitro-4,4′-di-β-phenoxyethyl nitrate	$C_{16}H_{14}O_{12}N_4As_2$	24.81	24.70	24.66
Arseno-3,3′-dinitro-4,4′-di-β-phenoxyethanol	$C_{16}H_{16}O_8N_2As_2$	29.16	29.13	29.08
Arseno-3,3′-diamino-4,4′-di-β-phenoxyethanol	$C_{16}H_{20}O_4N_2As_2$	33.01	32.64	32.67

γ-4-Arsonophenoxypropanol[7] was prepared in a manner analogous to that used with the ethanol homolog. It crystallized from water as white bobbin-shaped crystals. Reaction with fuming nitric acid at 15° for six hours produced **γ-2-nitro-4-arsonophenoxypropyl nitrate,** which crystallized from water as thin white plates. The latter was hydrolyzed by refluxing three hours with 3 *N* hydrochloric acid, yielding **γ-2-nitro-4-arsonophenoxypropanol.** The solution was neutralized and reduced to the amine (without isolating the intermediate hydrolysis product) by ferrous hydroxide After removal of the salt by evaporation to dryness and successive extractions of the amine with methanol and butanol, ethanol saturated with hydrogen chloride was added to precipitate **γ-2-amino-4-arsonophenoxypropanol hydrochloride.** The light tan oil thus formed changed slowly to a crystalline solid.

TABLE IV

SUBSTITUTED γ-PHENOXYPROPANOLS

Substituent	Yield, %	M. p., °C.	Formula	As analyses, %	
				Calcd.	Found
4-Arsono-	51	146	$C_9H_{13}O_5As$	27.15	27.08
Nitrate of 2-nitro-4-arsono-	78	207	$C_9H_{11}O_9N_2As$	20.46	20.53
Hydrochloride of 2-amino-4-arsono-	32	136	$C_9H_{14}O_5NAs \cdot HCl$	22.88	22.70

Methyl-2-nitro-4-arsonophenoxyacetate.—To a solution of 50 g. of anhydrous 2-nitro-4-arsonophenoxyacetic acid

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(6) Benda and Bertheim, *Ber.*, **44**, 3448 (1911).

(7) Prepared by Cislak and Hamilton, Chemical Laboratory, Northwestern University.

in 185 cc. of methanol was added 15 g. of concd. sulfuric acid and the solution was refluxed for two hours. Upon dilution with 200 cc. of water the ester separated; yield, 82% (43.5 g.). It was recrystallized from water, forming long rod-like crystals; m. p. 225–226°.

Anal. Calcd. for $C_9H_{10}O_8NAs$: As, 22.37. Found: As, 22.43, 22.45.

Reduction of this methyl ester with cold ferrous hydroxide yielded 3-hydroxy-1,4-benzisoxazine-6-arsonic acid; yield, 66%. It crystallized from water as white diamond-shaped crystals.

Anal. Calcd. for $C_8H_8O_3NAs$: As, 27.45. Found: As, 27.45, 27.50.

Summary

1. 4-Hydroxyphenylarsonic acid was condensed with ethylene and trimethylene chlorohydrins to form β-4-arsonophenoxyethanol and γ-4-arsonophenoxypropanol.

2. Nitration of β-4-arsonophenoxyethanol and γ-4-arsonophenoxypropanol was characterized by three types of reactions. Treatment with nitric acid (sp. gr. 1.50) resulted in the introduction of one or two nuclear nitro groups meta to the arsonic acid group, conversion of the alcohol group to its nitro ester, or oxidation of the alcohol group to the corresponding acid. Depending upon the conditions employed these reactions occurred either separately or simultaneously. Satisfactory methods for preparation and separation of the nitration products were devised.

3. β-2-Nitro-4-arsonophenoxyethyl nitrate and γ-2-nitro-4-arsonophenoxypropyl nitrate were hydrolyzed with 3 *N* hydrochloric acid to yield the corresponding mono-nitro compounds.

4. β-2-Amino-4-arsonophenoxyethanol, β-2,6-diamino-4-arsonophenoxyethanol and γ-2-amino-4-arsonophenoxypropanol were obtained by reduction of the corresponding nitro compounds. Some of the derivatives of the first compound were prepared.

5. Arseno-3,3′-dinitro-4,4′-di-β-phenoxyethyl nitrate, arseno-3,3′-dinitro-4,4′-di-β-phenoxyethanol and arseno-3,3′-diamino-4,4′-di-β-phenoxyethanol were prepared from the corresponding arsonic acids by reduction with hypophosphorous acid.

6. 3-Amino-4-β-hydroxyethoxyphenylarsenious oxide, 3-chloro-4-β-hydroxyethoxyphenylarsenious oxide, and 4-β-hydroxyethoxyphenylarsenious oxide were prepared from the corresponding arsonic acids by reduction with sulfurous acid, employing hydriodic acid as a catalyst. 3-Amino-4-β-hydroxyethoxyphenyldichloroarsine hydrochloride was prepared from the corresponding oxide.

LINCOLN, NEBRASKA RECEIVED JUNE 28, 1934

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE WASHINGTON SQUARE COLLEGE OF NEW YORK UNIVERSITY]

The Addition of Phenols to Arylenes. The Synthesis of Phenylthymol and its Isomers

BY JOSEPH B. NIEDERL AND CHARLES H. RILEY[1]

Theoretical Part

As the addition of phenols to unsaturated compounds of the acyclic series has been shown to be a general reaction[2] it was therefore considered highly desirable to extend these studies to the aromatic hydrocarbons. In the series of aromatic hydrocarbons with an unsaturated side-chain only styrene appears to have been subjected to such studies, yielding *x*-phenyl-α-(*p*-hydroxyphenyl)-ethane and α-phenyl-α-(*o*-hydroxyphenyl)-ethane, respectively.[3]

It was decided to study higher hydrocarbons with longer side chains and phenylpropylene ($C_6H_5—CH═CH—CH_3$) was chosen for this purpose with the expectation that interesting aryl derivatives of thymol would result. Phenylpropylene ($C_6H_5—CH═CH—CH_3$) prepared from phenylethylcarbinol by dehydration was therefore condensed with the cresols and a condensation product was obtained in each case. The condensing agent was a mixture of concentrated sulfuric acid and glacial acetic acid and the reac-

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(1) From the thesis presented by Charles H. Riley to the Faculty of the Graduate School, of New York University, in partial fulfilment of the requirement for the degree of Master of Science, 1933.

(2) Niederl and co-workers, THIS JOURNAL, **50**, 2230 (1928); **51**, 2426 (1929); **53**, 272, 806, 1928, 3390 (1931); **54**, 1063 (1932); **55**, 284, 2571, 3025, 4151, 4549 (1933); **56**, 1966 (1934); *Monatsh.*, **51**, 1028 (1929); **60**, 150 (1932); *Z. angew. Chem.*, **44**, 467 (1931); **46**, 395 (1933).

(3) Koenigs, *Ber.*, **23**, 3144 (1890); Koenigs and Carl, *ibid.*, **24**, 3889 (1891); Koenigs and Mai, *ibid.*, **25**, 2650 (1892).