TABLE II

OPTICAL CRYSTALLOGRAPHIC DATA FOR SOME SALTS OF CINCHONINE

Cinchonine salt	Opt. char. (sign)	Sign of elongation	Refractive indices at 25°			2E, degrees	Rhombic dispersion	Extinction angle, degrees	Crystal system
			Alpha	Beta	Gamma				
Benzoate	+	±	1.547	1.596	1.684				Monoclinic
Bromate	−	+		1.636	1.670	53	$\nu > \rho$		Monoclinic
Chlorate	−	+	1.573	1.641	1.664	101	$\nu > \rho$		Monoclinic
o-Chlorobenzoate	+	−	1.519		1.625	Large			Monoclinic
Hydrobromide	−	+		1.649	1.691	Large	Weak		Orthorhombic?
Hydrochloride	−	+	1.545	1.617	1.661	Large	$\nu > \rho$	24	Monoclinic
Hydroiodide	−	+	1.596	1.649	1.684		$\rho > \nu$	19	Monoclinic
Iodate	−	+	1.600	1.660	>1.700	Large			Monoclinic
Nitrate	+	+	1.550	1.568	1.655	59	$\nu > \rho$	45	Monoclinic
Perchlorate	−	+	1.518	1.572	1.620	Large	$\nu > \rho$	12	Monoclinic
Sulfate	−	+	1.587	1.641	1.667		$\nu > \rho$	38	Monoclinic
Thiocyanate	−	−	1.554	1.651	1.700	Large	$\rho > \nu$		Monoclinic
Thiosulfate	−	±	1.578		1.690	82	$\nu > \rho$	35	Monoclinic

Optical Crystallographic Data.—The optical properties of the salts reported in Table I were obtained by the methods used in a similar study[6] for salts of strychnine. The refractive indices were determined in all cases by the immersion method. The temperature at which the indices were taken was 25 ± 1°, and the source of light was ordinary daylight from a window with a northern exposure. The extinction angle was determined by turning the crystal to extinction and measuring the angle between this position and the long edge of the crystal. Not all of the optical data could be obtained for each salt because of the difficulty involved in orienting properly the crystals. The refractive indices, together with the other optical data, are given in Table II.

Summary

1. Three new salts of cinchonine have been prepared and described.

2. The data in the literature concerning ten salts of cinchonine have been determined, and corrections have been made in the water of crystallization of the nitrate, chlorate and iodate.

3. The optical crystallographic data for thirteen salts of cinchonine have been determined.

BOULDER, COLORADO RECEIVED JANUARY 29, 1935

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[6] Poe and Sellers, THIS JOURNAL, **54**, 249 (1932).

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

A Further Study of Phenyl- and Diphenylarsines[1]

BY F. F. BLICKE AND J. F. ONETO[2]

In this investigation, which represents a continuation of our previous studies of phenyl- and diphenylarsine,[3] we have shown that phenylarsine reacts with phenylchloroethoxyarsine to form arsenobenzene and it might be expected that the arsine and triphenylchloromethane would react in an analogous manner to yield arsenobenzene and triphenylmethyl. However, in the latter instance the reaction products isolated were phenyldichloroarsine and triphenylmethane formed, probably, through decomposition of the initial reaction product, phenyl-bis-triphenylmethylarsine, by the hydrogen chloride formed during the reaction.

Diphenylarsine and chloroacetyl chloride yield diphenylchloroarsine as reported by Steinkopf, Schubart and Schmidt.[4] Diphenylchloroarsine was also obtained from diphenylarsine and chloroacetic acid (D), at an elevated temperature, with the intermediate formation of tetraphenyldiarsyl; since it has been shown, in a separate experiment,

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[1] This paper represents one part of a dissertation to be submitted to the Graduate School by Mr. Oneto in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

[2] Parke, Davis and Company Fellow.

[3] Blicke and Powers, THIS JOURNAL, **54**, 3353 (1932); *ibid.*, **55**, 315, 1161 (1933).

[4] Steinkopf, Schubart and Schmidt, *Ber.*, **61**, 679 (1928). Instead of a distillation of the crude reaction product we dissolved it in petroleum ether (30–60°), filtered the solution in air and allowed the solvent to evaporate. A 65% yield of diphenylchloroarsine was obtained; m. p. 40–41°.

that the diarsyl and chloroacetic acid react to form diphenylchloroarsine (C) we believe that the products in reaction D are formed through the intermediate reactions A, B and C.

$$\text{(A)}\quad (C_6H_5)_2AsH + ClCH_2COOH = (C_6H_5)_2AsCl + CH_3COOH$$

$$\text{(B)}\quad (C_6H_5)_2AsH + (C_6H_5)_2AsCl = (C_6H_5)_2As{-}As(C_6H_5)_2 + HCl^{5}$$

$$\text{(C)}\quad (C_6H_5)_2As{-}As(C_6H_5)_2 + 2ClCH_2COOH = 2(C_6H_5)_2AsCl + HOOCCH_2CH_2COOH^{6}$$

$$\text{(D)}\quad 2(C_6H_5)_2AsH + 3ClCH_2COOH = 2(C_6H_5)_2AsCl + CH_3COOH + HCl + HOOCCH_2CH_2COOH$$

In order to avoid the formation of a halogen acid in some of the reactions which we wished to study it was decided to use the arsines in the form of their MgBr derivatives.[7] The latter were prepared from the arsines with the aid of phenylmagnesium bromide[8] in a free radical bulb; triphenylmethylmagnesium bromide also converts diphenylarsine into its MgBr derivative.

Since the oily phenylarsylenemagnesium bromide, $C_6H_5As(MgBr)_2$, is more soluble in organic solvents than the crystalline diphenylarsylmagnesium bromide, $(C_6H_5)_2AsMgBr$, and consequently more difficult to purify, we investigated only reactions of the latter substance.

Diphenylarsylmagnesium bromide and mercuric chloride react in accordance with formulation E to form tetraphenyldiarsyl. In a separate experiment it was shown that the diarsyl and mercuric chloride interact, instantly, to produce diphenylchloroarsine (F). Consequently, mixed in the proportions shown by equation G, the arsylmagnesium bromide and mercuric chloride would yield diphenylchloroarsine.

$$\text{(E)}\quad 2(C_6H_5)_2AsMgBr + HgCl_2 = (C_6H_5)_2As{-}As(C_6H_5)_2 + 2MgClBr + Hg$$

$$\text{(F)}\quad (C_6H_5)_2As{-}As(C_6H_5)_2 + HgCl_2 = 2(C_6H_5)_2AsCl + Hg$$

$$\text{(G)}\quad 2(C_6H_5)_2AsMgBr + 2HgCl_2 = 2(C_6H_5)_2AsCl + 2MgClBr + 2Hg$$

When three molecular equivalents of diphenylarsylmagnesium bromide were allowed to react with arsenic trichloride diphenylchloroarsine and arsenic were produced.

Addition of iodine, as well as diphenyliodoarsine, to the magnesium bromide compound produced tetraphenyldiarsyl in practically quantitative yield. When 3,3′-dinitrodiphenyliodoarsine was used a small quantity of 3,3′,3″,3‴-tetranitrotetraphenyldiarsyl was isolated.[9] In connection with this experiment the 3,3′-dinitrodiphenylchloro-, bromo-, iodo- and hydroxyarsine were prepared and by means of a molecular weight determination it was shown that the hydroxyarsine possesses the formula $(NO_2C_6H_4)_2AsOH$, as suggested by Michaelis,[10] and not $(NO_2C_6H_4)_2As{-}O{-}As(C_6H_4NO_2)_2$.

From interaction of diphenylarsylmagnesium bromide with diphenylbromomethane there were obtained tetraphenyldiarsyl and tetraphenylethane.

The characteristic orange color of a triphenylmethyl solution developed when diphenylarsylmagnesium bromide reacted with triphenylbromomethane in benzene; the isolation of triphenylmethyl, in the form of its ethyl acetate addition product, and of triphenylmethyl peroxide proved that the trivalent carbon radical had been formed. When the original reaction mixture was treated with hydrogen chloride the solution became colorless and diphenylchloroarsine and triphenylmethane were isolated in good yield. In view of these results it seems that the initial reaction products, tetraphenyldiarsyl and triphenylmethyl, (H), may exist in equilibrium with triphenylmethyldiphenylarsine; the presence of the latter product would account for the transformation of the primary reaction products, by hydrogen chloride, into the chloroarsine and the methane (I). In a separate experiment it was shown that a mixture of tetraphenyldiarsyl and triphenylmethyl is converted into diphenylchloroarsine and triphenylmethane by hydrogen chloride.[11]

$$\text{(H)}\quad 2(C_6H_5)_2AsMgBr + 2(C_6H_5)_3CBr = (C_6H_5)_2As{-}As(C_6H_5)_2 + 2(C_6H_5)_3C{-} \rightleftharpoons 2(C_6H_5)_2As{-}C(C_6H_5)_3$$

$$\text{(I)}\quad 2(C_6H_5)_2As{-}C(C_6H_5)_3 + HCl = 2(C_6H_5)_2AsCl + 2(C_6H_5)_3CH$$

It was also shown that when a mixture of diphenylchloroarsine and triphenylmethyl is treated with hydrogen chloride, the chloroarsine can be recovered unchanged while the triphenylmethyl is converted into *p*-benzohydryltetraphenylmethane.

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(5) This reaction takes place readily at ordinary temperature [Blicke and Powers, This Journal, **54**, 3358 (1932)].

(6) We were unable to isolate succinic acid; the evolution of a gas during the reaction indicated that the acid may have been decomposed.

(7) These derivatives have been prepared by Job, Reich and Vergnaud [*Bull. soc. chim.*, [4] **35**, 1404 (1924)] but were studied by them only to a very limited extent.

(8) It was impossible to use ethylmagnesium bromide, employed by Job, Reich and Vergnaud, since ethylene is formed from this reagent.

(9) It is probable that a considerable amount of the MgBr compound was decomposed by interaction with the nitro groups.

(10) Michaelis, *Ann.*, **321**, 145 (1902).

(11) Hydrogen chloride has no effect on tetraphenyldiarsyl and it changes triphenylmethyl rapidly into *p*-benzhydryltetraphenylmethane [Gomberg, *Ber.*, **36**, 379 (1903)].

When mixed, diphenylarsylmagnesium bromide and triphenylmethyl do not interact. However, upon the addition of water an immediate reaction takes place due to the formation of diphenylarsine, a substance which interacts readily with triphenylmethyl to form tetraphenyldiarsyl and triphenylmethane.[12]

From benzophenone chloride and the arsylmagnesium bromide there were obtained tetraphenyldiarsyl and tetraphenylethylene.

From *o*-xylylene bromide ω,ω′-bis-(diphenylarsyl)-*o*-xylene, $C_6H_4[CH_2As(C_6H_5)_2]_2$, was produced. This product, in solution, absorbed oxygen slowly, reacted with iodine to yield diphenyliodoarsine and *o*-xylylene iodide and formed an addition product with mercuric chloride. Attempts to obtain the same compound from $C_6H_4(CH_2MgBr)_2$ and diphenylbromoarsine were unsuccessful.

Reaction with benzophenone yielded benzpinacol.

Experimental Part

All operations were carried out in a modified free radical apparatus,[13] in an atmosphere of nitrogen, at ordinary temperature unless otherwise indicated. In most instances the reaction mixtures were shaken for twenty-four hours. Absolute grades of alcohol and ether and 30–60° petroleum ether were employed except in specified cases. The melting point of tetraphenyldiarsyl was determined in a sealed tube filled with nitrogen.

Phenylarsine and Phenylethoxychloroarsine.—To 2.3 g. of phenylethoxychloroarsine,[14] dissolved in 5 cc. of benzene. there was added 1.1 cc. (1.54 g.) of phenylarsine. The hydrochloric acid formed was allowed to escape occasionally through the stopcock. After twenty-four hours the benzene layer was decanted, the crystalline arsenobenzene washed successively with sodium hydroxide solution, water, alcohol and ether; yield 2.9 g.; calcd. yield 3.0 g.; m. p. 207–209°.

Phenylarsine and Triphenylchloromethane.—A solution prepared from 2.2 g. of triphenylchloromethane and 5 cc. of benzene was added to 0.61 g. of phenylarsine, dissolved in 5 cc. of the same solvent. After twenty-four hours the crystalline deposit of triphenylmethane was washed three times with petroleum ether (30–60°); yield 1.45 g.; calcd. yield 1.95 g., m. p. 92–93° after recrystallization from alcohol.

Upon evaporation of the petroleum ether wash solution the oily phenyldichloroarsine was converted into phenylarsylene N-pentamethylenedithiocarbamate which melted at 183–184°[15] after recrystallization from ethyl acetate; yield 2.4 g.; calcd. yield 3.0 g.

Diphenylarsine and Chloroacetic Acid.—A mixture of 2.8 g. of chloroacetic acid and 4.6 g. of arsine was heated, gradually, to 160° in a bath. Hydrogen chloride was evolved and after one hour the mixture was cooled and low boiling petroleum ether added. After some time a mixture of oil and crystals separated. The petroleum ether was decanted, the crystals washed free from oil with alcohol and isolated in a carbon dioxide atmosphere. This product, tetraphenyldiarsyl, melted at 129–130° and weighed 0.2 g.

Upon evaporation of the petroleum ether 4.0 g. of diphenylchloroarsine was obtained; calcd. yield 5.2 g.; m. p. 39–40°.

Tetraphenyldiarsyl and Chloroacetic Acid.—Four grams of the diarsyl and 2 g. of chloroacetic acid were heated in a bath at 160° for one hour; a small amount of gas was evolved during the reaction. The mixture was cooled, extracted with low boiling petroleum ether, and the solvent allowed to evaporate. The diphenylchloroarsine obtained melted at 40–41° and weighed 3.0 g.; calcd. yield 4.7 g.

Diphenylarsylmagnesium Bromide.—Phenylmagnesium bromide was prepared from 3.9 g. of bromobenzene, 0.6 g. of magnesium and 20 cc. of ether in a 100-cc. round-bottomed flask fitted with a side arm. The solution of the reagent was poured into an evacuated radical bulb, cooled with ice, and 4.6 g. of diphenylarsine, dissolved in 10 cc. of benzene, added. The radical bulb was removed from the ice-bath and after about fifteen minutes the magnesium bromide compound began to precipitate. The mixture should now be shaken vigorously for a few minutes in order to avoid the formation of hard pellets. After twelve hours the liquid was decanted and the precipitate washed twice with 15 cc. of benzene; yield about 90% of the calcd. amount. This product, suspended in 20 cc. of benzene, was used in the experiments described below.

Reactions of Diphenylarsylmagnesium Bromide

Mercuric Chloride.—To diphenylarsylmagnesium bromide there was added 2.7 g. of mercuric chloride, dissolved in 70 cc. of ether. Heat developed and a gray precipitate formed immediately. After the mixture had been shaken for twelve hours, the radical bulb contained colorless, crystalline tetraphenyldiarsyl and globules of mercury. The liquid was decanted into a second bulb and the solvents removed under diminished pressure. The residue in the original bulb was extracted with hot benzene, the solution poured into the second bulb, shaken with ammonium chloride and then with water. The benzene layer was decanted into a third bulb, the solvent removed, the residue of the diarsyl washed with petroleum ether and then recrystallized from alcohol; m. p. 129–131°; yield 2.7 g.; calcd. yield 4.5 g.

Tetraphenyldiarsyl and Mercuric Chloride.—To 1.4 g. of tetraphenyldiarsyl, dissolved in ether, 0.81 g. of mercuric chloride, dissolved in the same solvent, was added. After two hours the mixture was filtered from the gray precipitate and the solvent allowed to evaporate. The yield of diphenylchloroarsine was 1.4 g.; m. p. 41–42°.

The reactions recorded in Table I were carried out in a manner similar to that illustrated in the first experiment described above.

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[12] Blicke and Powers, THIS JOURNAL, **55**, 1166 (1933).

[13] Blicke, Oakdale and Oneto, *ibid.*, **56**, 142 (1934), Fig. 1.

[14] McKenzie and Wood, *J. Chem. Soc.*, **117**, 410 (1920).

[15] Blicke and Oakdale, THIS JOURNAL, **54**, 2995 (1932); Blicke and Powers, *ibid.*, **55**, 317 (footnote 5)(1933).

TABLE I

REACTION OF DIPHENYLARSYLMAGNESIUM BROMIDE

In experiments 1 and 3 the reactant was dissolved in 50–70 cc. of ether, in all other experiments it was dissolved in 10–50 cc. of benzene.

	With	Reaction product	M. p., °C.	Yield, g.
1	$HgCl_2$ (2.7 g.)	$(C_6H_5)_2As{-}As(C_6H_5)_2$,[a] (Hg)	129–131[b]	2.7
2	$AsCl_3$ (1.1 g.)	$(C_6H_5)_2As{-}As(C_6H_5)_2$,[c] (As)		
3	I (2.1 g.)	$(C_6H_5)_2As{-}As(C_6H_5)_2$	129–131	3.5
4	$(C_6H_5)_2AsI$ (6.4 g.)	$(C_6H_5)_2As{-}As(C_6H_5)_2$	129–130	7.2
5	$(NO_2C_6H_4)_2AsI$ (8.0 g.)	$(NO_2C_6H_4)_2As{-}As(C_6H_4NO_2)_2$[d]	202–203[e]	0.75
6	$(C_6H_5)_2CHBr$ (3.5 g.)	$(C_6H_5)_2CH{-}CH(C_6H_5)_2$[f]	208–209[g]	1.0
		$(C_6H_5)_2As{-}As(C_6H_5)_2$	129–130	3.2
7	$(C_6H_5)_3CBr$ (5.8 g.)	$(C_6H_5)_3CH$[h]	91–92[i]	4.1
		$(C_6H_5)_2AsCl$[h]	41–42[j]	3.0
8	$(C_6H_5)_2CCl_2$ (1.6 g.)	$(C_6H_5)_2As{-}As(C_6H_5)_2$	128–129	2.1
		$(C_6H_5)_2C{=}C(C_6H_5)_2$[k]	219–221[l]	0.35
9	$C_6H_4(CH_2Br)_2$ (2.4 g.)	$C_6H_4[CH_2As(C_6H_5)_2]_2$[m]	104–105[n]	3.6
10	$(C_6H_5)_2CO$ (3.2 g.)	$(C_6H_5)_2C(OH)C(OH)(C_6H_5)_2$[o]	186–188[p]	2.5

[a] In some instances the diarsyl obtained was very pure, in others it was necessary to recrystallize it from alcohol or petroleum ether (90–100°). [b] Blicke, Weinkauff and Hargreaves [THIS JOURNAL, **52,** 782 (1930)], reported 129–130°. [c] The diarsyl was treated with iodine in ether and isolated as diphenyliodoarsine; yield, 3.0 g.; m. p. 40–42°. [d] Recrystallized from pyridine. [e] Reported to be 203–204°, Blicke, Oakdale and Oneto [*ibid*., **56,** 142 (1934)]. [f] Washed with alcohol. [g] Zagoumenny [*Ann*., **184,** 178 (1877)] reported 209°. [h] Obtained after treatment of the original reaction mixture with benzene saturated with hydrogen chloride. The methane was recrystallized from alcohol, the chloroarsine from acetic acid. [i] Melts at 92° according to Kekulé and Franchimont [*Ber*., **5,** 907 (1872)]. [j] Blicke and Smith [THIS JOURNAL, **51,** 1564 (1929)] reported 40–42°. [k] Recrystallized from a mixture of alcohol and benzene. [l] Behr [*Ber*., **3,** 753 (1870)] reported 221°. [m] This product was recrystallized from petroleum ether (90–100°) and then twice from alcohol in a radical bulb. *Anal*. Calcd. for $C_{32}H_{28}As_2$: As, 26.67; mol. wt., 562. Found: As, 26.56; mol. wt. 556 (benzene, cryoscopic method). The material is soluble in cold benzene. Dissolved in bromobenzene 0.94 g. of the product absorbed 44 cc. (N. T. P.) of oxygen in seven minutes and 54 cc. in twenty-four hours. The mercuric chloride addition product, prepared in ether, melted at 220–221°; when suspended in water and shaken with 10% sodium hydroxide solution yellow mercuric oxide and ω,ω′-bis-(diphenylarsyl)-*o*-xylene are formed immediately. [n] Determined in a sealed tube filled with nitrogen. [o] Recrystallized from a mixture of chloroform and alcohol. [p] According to Bachmann [THIS JOURNAL, **53,** 2761 (1931)] melts at 186–188°.

Tetraphenyldiarsyl, Triphenylmethyl and Hydrogen Chloride.—A solution of tetraphenyldiarsyl obtained from 4.3 g. of diphenylbromoarsine, 2 cc. of mercury and 60 cc. of benzene was added to a solution of triphenylmethyl prepared from 3.9 g. of triphenylchloromethane, 6 g. of molecular silver and 60 cc. of benzene. The orange solution was concentrated to a small volume and 100 cc. of benzene saturated with hydrogen chloride added. After the solution had become colorless the solvent was removed under diminished pressure and the mixture of oil and crystals filtered on a Jena filter. The crystalline product, triphenylmethane, weighed 2.5 g. and melted at 91–92° after recrystallization from alcohol. After some time the oily material solidified; it proved to be diphenylchloroarsine: yield 2.4 g.; m. p. 40–41° after recrystallization from acetic acid.

Diphenylchloroarsine, Triphenylmethyl and Hydrogen Chloride.—A mixture of 3.1 g. of diphenylchloroarsine and triphenylmethyl, prepared from 3.9 g. of triphenylchloromethane, 6 g. of molecular silver and 30 cc. of benzene, in a radical bulb, was treated with 75 cc. of benzene which had been saturated with hydrogen chloride. The orange colored mixture soon became colorless and after twelve hours the solvent was removed under diminished pressure; the crystalline residue was extracted with alcohol whereupon diphenylchloroarsine was removed. The crystalline *p*-benzohydryltetraphenylmethane which then remained weighed 2.3 g.; m. p. 226–227°[16] after recrystallization from a mixture of benzene and acetic acid.

3,3′-Dinitrodiphenylchloro-, -bromo-, -iodo- and -hydroxyarsine.—A hot mixture of 3,3′-dinitrodiphenylarsinic acid,[17] 90 cc. alcohol, 120 cc. of hydrochloric acid and two drops of hydriodic acid was treated with sulfur dioxide. The precipitated, oily chloroarsine soon became crystalline and melted at 113–115° after recrystallization from a mixture of benzene and petroleum ether (90–100°);[18] yield quantitative.

The bromoarsine was prepared from 5 g. of the nitro acid, 10 cc. of alcohol, 25 cc. of constant boiling hydrobromic acid and a drop of hydriodic acid as described above; m. p. 93–94°;[19] yield 5.7 g.

To prepare the iodoarsine 1 g. of the hydroxyarsine, described below, was dissolved in 10 cc. of hot acetic acid and 2 cc. of hydriodic acid (sp. gr. 1.70) added. The iodide precipitated slowly in crystalline form; m. p. 94–95° after recrystallization from acetic acid.

Anal. Calcd. for $C_{12}H_8O_4N_2AsI$: I, 28.46. Found: I, 28.24.

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(16) This melting point was reported by Gomberg [*Ber.*, **36,** 379 (1903)].

(17) Wieland and Rheinheimer, *Ann.*, **423,** 36 (1921).

(18) Prepared by another method Michaelis [*ibid.*, **321,** 142 (1902)] stated that the compound melted at 112°.

(19) Michaelis [*ibid.*, **321,** 143 (1902)] reported 93°.

The hydroxyarsine was obtained by addition of 600 cc. of ammonia water to 25 g. of the chloroarsine, dissolved in 450 cc. of hot alcohol. The oily precipitate, which soon crystallized, was recrystallized from 350 cc. of alcohol; yield 20 g.; m. p. 156–157°.[20]

Anal. Calcd. for $C_{24}H_{16}O_9N_4As_2$ (arsyl oxide): As, 22.92; mol. wt., 654. Calcd. for $C_{12}H_9O_5N_4As$ (hydroxyarsine): As, 22.57; mol. wt., 336. Found: As, 22.62, 22.66; mol. wt., 323 (solvent ethylene bromide).

Summary

Interaction between the following substances has been investigated: (a) phenylarsine with phenylethoxychloroarsine and triphenylchloroarsine, respectively; (b) diphenylarsine with chloroacetyl chloride and chloroacetic acid, respectively; (c) diphenylarsylmagnesium bromide with mercuric chloride, arsenic trichloride, iodine, diphenyliodoarsine, 3,3′-dinitrodiphenyliodoarsine, diphenylbromomethane, triphenylbromomethane, benzophenone chloride, *o*-xylylene bromide and benzophenone, respectively; (d) tetraphenyldiarsyl with chloroacetic acid and mercuric chloride.

ANN ARBOR, MICHIGAN RECEIVED JANUARY 31, 1935

(20) Michaelis [*Ann.*, **321**, 145 (1902)], who obtained the compound by a seemingly impossible method, reported the melting point as 149°.

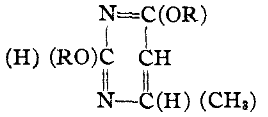
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Researches on Pyrimidines. CXLV.
Alkamine Ethers of the Pyrimidine and Quinazoline Series[1]

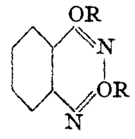
BY JOHN J. DONLEAVY AND MEARL A. KISE

During recent years it has been demonstrated clearly by many investigators that the physiological activity of a great variety of organic compounds can be enhanced greatly by the introduction of basic ether groups. The pharmacological effect of these groups does not appear to be specific in any real sense, since in different types of structures they enhance or produce markedly different physiological behaviors. Thus, *p*-β-diethylaminoethoxyanisole has a strong action upon the heart.[2] Upon the other hand, the hydrochloride of β-naphthyl-β-dimethylaminoethyl ether exerts a local anesthetic action.[3] More recently the alkamine ethers of the heterocyclic nuclei, pyridine, acridine and quinoline, have been found to possess marked physiological activity as antipyretics, etc.[4] In the light of these facts it was of interest to prepare several basic ethers of pyrimidine and quinazoline or benzopyrimidine, in order to note the pharmacological effect of the introduction of the basic ether configurations into these nuclei and to obtain data relative to the toxicity of pyrimidines of this general type.

The various alkamine ethers of pyrimidine and quinazoline listed below were prepared by treating the corresponding chloro compounds with the sodium salts of the requisite dialkylamino alcohols. The pyrimidine and quinazoline ethers are represented by the general types I and II, respectively.



I



II

The necessary chloro compounds, prepared from the corresponding oxy compounds, included 2,4-dichloropyrimidine,[5] 6-methyl-2,4-dichloro-pyrimidine,[6] 6-methyl-4-chloropyrimidine[7] and 2,4-dichloroquinazoline.[8]

Experimental

6-Methyl-2,4-dioxypyrimidine.—This pyrimidine was prepared by the following improved modification of the method of Biltz and Heyn.[6]

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(1) This, the first of several communications, was constructed in part from the dissertation presented to the faculty of the Graduate School of Yale University by Mearl A. Kise in June, 1933, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) Hahl, German Patent, 423,037 (1925); *Frdl.*, **15**, 1642 (1925).

(3) Clemo and Perkin, *J. Chem. Soc.*, **121**, 642 (1922).

(4) Miescher and Urech, U. S. Patent 1,881,236; *C. A.* **27**, 1096 (1933); Callsen and Hahl, German Patent 430,960 (1926); *Frdl.*, **15**, 1644 (1926); Hartmann and Isler, U. S. Patent 1,860,286 (1932); *C. A.* **26**, 3877 (1932); Mietzsch, German Patent 490,418 (1930); *Frdl.*, **16**, II, 2704 (1931).

(5) Davidson and Baudisch, THIS JOURNAL, [2] **48**, 2379 (1926); Johnson and Flint, *ibid.*, [1] **53**, 1079 (1931); Hilbert and Johnson, *ibid.*, [1] **52**, 1155 (1930).

(6) Behrend and Roosen, *Ann.*, **251**, 238 (1889); Biltz and Heyn, *ibid.*, **413**, 109 (1917); Gabriel and Colman, *Ber.*, [2] **32**, 1533 (1899).

(7) Gabriel and Colman, *ibid.*, [3] **32**, 2931 (1899).

(8) Bogert and Scatchard, THIS JOURNAL, [2] **38**, 1612 (1916); Lange, Roush and Asbeck, *ibid.*, **52**, 3696 (1930); Gabriel and Stelzner, *Ber.*, [2] **29**, 1300 (1896); Gabriel and Colman, *ibid.*, [3] **38**, 3559 (1905); Bogert and Scatchard, THIS JOURNAL, **41**, 2061 (1919).