nal as shown by X-ray diffraction patterns. Prolonged exposure to light or heat (100° or above) causes slow decomposition though the compounds are stable for months at room temperature in the dark. Phosphazo compounds are hydrolyzed very slowly by water or dilute alkalies but the reaction is rapid in warm dilute acids.

$$R—N=P—NHR + 2HCl + 3H_2O \longrightarrow 2RNH_2\cdot HCl + H_3PO_3$$

General Procedure for Preparation of Amides.—A 3-necked flask equipped with stirrer and reflux condenser is mounted in an oil-bath. To the flask is added 0.2 mole of a monocarboxylic acid or 0.1 mole of a dicarboxylic acid and a phosphazo compound (equivalent to 0.2 mole of a monoamine or 0.1 mole of a diamine) dissolved in 150–200 ml. of toluene. This mixture is stirred, heated to boiling (oil-bath at 130°) and agitation continued at this temperature for two hours. The reaction proceeds readily at the reflux temperature with the separation of metaphosphorous acid (HPO_2) as an orange gummy precipitate. In most cases, the desired amide is soluble in the hot toluene and can be conveniently separated from the orange precipitate by decantation or filtration. The crude amide is then isolated by one of three methods, as follows.

Procedure 5.—Direct crystallization from the toluene on cooling.

Procedure 6.—Treatment with 150 ml. of a 20% solution of sodium carbonate and removal of the toluene by steam-distillation. If the amide is a solid, it is separated by filtration and washed with water; if a liquid, it is extracted with ether, the ether is then evaporated, and the residue is distilled at reduced pressure.

Procedure 7.—Procedure 6 is followed without first decanting the toluene from the orange precipitate.

If purification of the amide is desired, the product can be recrystallized from 95% alcohol, dilute alcohol or other suitable solvent. In many cases the crude products are sufficiently pure to render recrystallization unnecessary.

X-Ray Diffraction Patterns.—Diffraction patterns obtained from powdered samples of phenylphosphazoanilide and related products were made in order to characterize the pure powders and to prove identity of samples prepared by different procedures. A brief history of the material used for each pattern follows.

Pattern (1).—Phenylphosphazoanilide (m. p. 251–253°) prepared by the interaction of aniline and phosphorus trichloride.

Pattern (2).—Phenylphosphazoanilide (m. p. 248–253°) prepared from aniline and phenylphosphazo chloride, $C_6H_5N=P—Cl$.

Pattern (3).—Same material as used in pattern (1) but recrystallized from chloroform; hard, translucent crystals melting at somewhat lower temperature and with more pronounced decomposition than product (1).

Pattern (4).—Pure aniline phosphite, $C_6H_5NH_2\cdot H_3PO_3$; a hydrolysis product of phenylphosphazoanilide.

Pattern (5).—Hydrate of phenylphosphazoanilide, $(C_6H_5NH_2)POH$, previously described by Michaelis and Schroeter.

Summary

1. The interaction of carboxylic acids and primary amines in the presence of phosphorus trichloride to form N-substituted amides is given a new interpretation. An intermediate formation of phosphazo compounds is proposed and substantiated by experiment.

2. Phosphazo compounds of the general formula, R—N=P—NHR, are described for the first time. They are prepared by the interaction of phosphorus trichloride and primary amines in inert solvents such as toluene.

3. This new class of phosphazo compounds can be used to prepare N-substituted amides by treatment with carboxylic acids in boiling toluene.

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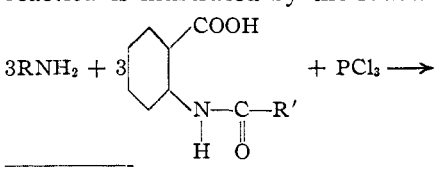
[CONTRIBUTION FROM THE CENTRAL RESEARCH LABORATORY OF GENERAL ANILINE AND FILM CORPORATION]

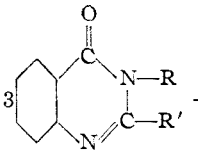
A New Synthesis of 4-Quinazolones

BY H. W. GRIMMEL, A. GUENTHER AND JACK F. MORGAN

Methods previously employed to prepare 4-quinazolones include, among others, the heating of N-acylanthranilanilides at 200°[1] and the interaction of primary amines with the moisture sensitive acylanthranils at low temperatures.[2]

A new synthesis of 4-quinazolones has been found which allows the preparation of these compounds in one simple operation at moderate temperatures from stable starting materials. When primary amines are condensed with N-acylanthranilic acids in toluene or other suitable solvents with the aid of phosphorus trichloride, 4-quinazolones are formed, generally in good yields. This reaction is illustrated by the following equation.





$+ H_3PO_3 + 3HCl + 3H_2O$ (1)

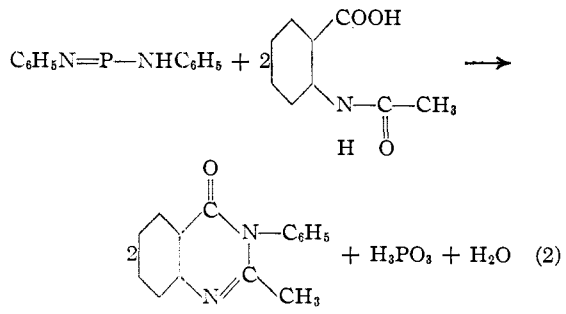
It will be noted that, according to equation (1), the formation of three moles of quinazolone is accomplished by one mole of phosphorus trichloride whereas the employment of two moles of this condensing agent might normally have been expected for this condensation. Quinazolone yields were not increased when two moles of phosphorus trichloride were employed.

It was also found that 4-quinazolones could be prepared from organic phosphazo compounds.[3] For example, an 82% yield of 2-methyl-3-phenyl-4-quinazolone resulted from the interaction of phenylphosphazoanilide and N-acetylanthranilic acid in boiling toluene. This reaction may be illustrated as

(1) Körner, *J. prakt. Chem.*, [2] **36**, 165 (1900).

(2) Original paper, Bogert and Chambers, THIS JOURNAL, **27**, 649 (1905).

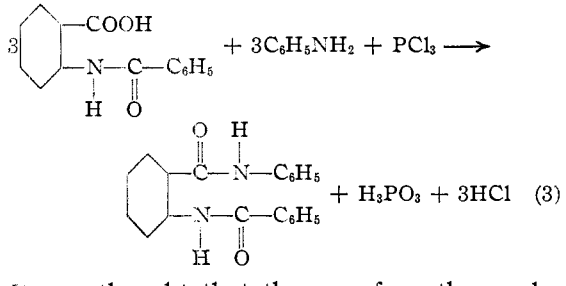
(3) H. W. Grimmel, A. Guenther and Jack F. Morgan, *ibid.*, **68**, 539 (1946).



The method of preparing quinazolones from N-acylanthranilic acid and a primary amine in the presence of phosphorus trichloride is of fairly general application. This reaction can be used successfully to prepare quinazolones from aromatic amines, aralkyl amines, aliphatic amines or arylhydrazines. Nuclear substituted derivatives of N-acylanthranilic acid may also be used. In addition, it is possible to carry out the reaction using phosphorus oxychloride in place of the trichloride although the yields and purity of products suffer somewhat.

Certain limitations of the method were found; α-naphthylamine, allylamine, 2-amino-pyridine and 2-amino-6-ethoxybenzothiazole failed to yield quinazolones under the conditions of experiment employed and in each case the starting material N-acetylanthranilic acid was recovered almost quantitatively. Also, no simple identifiable quinazolone resulted when aniline and N-acetoacetylanthranilic acid were employed as starting materials. The difficulty in this latter instance is attributed to the reaction of aniline with the acetoacetyl side chain.

Somewhat unexpected results were obtained in two cases. N-Acetylanthranilic acid reacted with cyclohexylamine to yield *o*-acetamidohexahydrobenzanilide. The reaction between N-benzoylanthranilic acid and aniline gave *o*-benzamidobenzanilide in 57.3% yield, and again no formation of quinazolone was observed.



It was thought that the use of another mole of phosphorus trichloride in the reaction might accomplish quinazolone formation; however, when twice the indicated amount of phosphorus trichloride was employed, the sole product was N-benzoylanthranil.

Experimental

The general procedure for preparing quinazolones is illustrated by the following example.

In a 500-ml. 3-necked flask equipped with stirrer, reflux condenser, dropping funnel and mounted in an oil-bath were placed 17.9 g. (0.1 mole) of N-acetylanthranilic acid, 12.75 g. (0.1 mole) of *p*-chloroaniline and 175 ml. of toluene. The mixture was stirred and treated dropwise with a solution of 4.6 g. (0.0334 mole) of phosphorus trichloride in 25 ml. of toluene over a period of fifteen minutes. The resulting suspension was heated to the reflux temperature of the solvent (oil-bath at 130°) and agitation maintained at this temperature for two hours. The contents of the flask were transferred to a larger flask and treated with 200 ml. of a 10% sodium carbonate solution. After removing the toluene by steam distillation, the white solid in the boiler was removed by filtration, washed with water and dried at 60°; yield 21.6 g. (80%); m. p. 155–158°. When crystallized from 75 ml. of 95% ethanol, there resulted 18.6 g. (69%) of white crystalline 2-methyl-3-*p*-chlorophenyl-4-quinazolone; m. p. 157–158°.

Anal. Calcd. for $C_{15}H_{11}ON_2Cl$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.74; H, 4.14; N, 10.52.

Analyses for other new quinazolones prepared by the above method are given below.

2-Methyl-3-*o*-nitrophenyl-4-quinazolone.—*Anal.* Calcd. for $C_{15}H_{11}O_3N_3$: C, 64.05; H, 3.94. Found: C, 64.19; H, 3.88.

TABLE I

PREPARATION OF 4-QUINAZOLONES USING PHOSPHORUS TRICHLORIDE

	2-Methyl-4-quinazolone	Yield,[a] %	M. p.,[a] °C.
1	3-Phenyl-	86	145–147
2	3-*p*-Toluyl-	68	147–149
3	3-*p*-Anisyl-	70	167–169
4	3-*p*-Phenetyl-	66	145–148
5	3-*o*-Nitrophenyl-	76	169–171[b]
6	3-*m*-Nitrophenyl-	66	127–129[b]
7	3-*p*-Nitrophenyl-	78	191–193[b]
8	3-*p*-Chlorophenyl-	80	157–158[b]
9	3-β-Naphthyl-	56	173–175
10	3-Anilino-	63	207–209
11	3-Benzyl-	32	230–232[c]
12	3-Dodecyl-	68	90– 92[b]
13	3-Phenyl-6-chloro-	61	181–182[b]
14	3-*p*-Phenetyl-6-chloro-	61	150–152[b]

[a] Represents crude product. [b] Represents recrystallized material. [c] Represents hydrochloride.

2-Methyl-3-*m*-nitrophenyl-4-quinazolone.—*Anal.* Calcd. for $C_{15}H_{11}O_3N_3$: N, 14.94. Found: N, 14.95.

2-Methyl-3-lauryl-4-quinazolone.—*Anal.* Calcd. for $C_{21}H_{32}ON_2$: N, 8.53. Found: N, 8.33.

2-Methyl-3-phenyl-6-chloro-4-quinazolone.—*Anal.* Calcd. for $C_{15}H_{11}ON_2Cl$: C, 66.55; H, 4.10; N, 10.35. Found: C, 66.06; H, 4.13; N, 10.24.

2-Methyl-3-*p*-phenethyl-6-chloro-4-quinazolone.—*Anal.* Calcd. for $C_{17}H_{15}O_2N_2Cl$: N, 8.90. Found: N, 9.16.

Summary

Two new methods of preparing 4-quinazolones are described.

1. Primary amines react with N-acetyl-anthranilic acid or certain of its derivatives at moderately elevated temperatures in the presence of phosphorus trichloride or phosphorus oxychloride to form various 4-quinazolones.

2. Phosphazo compounds, R—N=P—NHR, derived from primary amines and phosphorus trichloride, react with N-acetylanthranilic acid to form various 4-quinazolones.

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