pared by heating the hexahydrate (Baker's Analyzed, special, low in cobalt) at 210° in a stream of dry hydrogen chloride.

Magnesium bromide and magnesium iodide were prepared in ether solution from the elements by the method of Menschutkin.[20] The halide was used *in situ* in the experiment involving magnesium bromide at a molar ratio of 2.25. In all other cases the magnesium halide solutions were filtered and stored as described below for the Grignard reagent; the solutions were analyzed by titration with standard silver nitrate solution using dichlorofluorescein as an indicator.[21]

Mesitoyl chloride,[22] b.p. 125–126° (30 mm.), was stored in 0.1-mole portions in sealed ampules which were opened just before use.

Methylmagnesium iodide was prepared, filtered, stored and analyzed as described previously.[5]

Acetomesitylene, b.p. 118–120° (18 mm.), was prepared in 96% yield by the reaction of acetic anhydride with excess mesitylene in the presence of anhydrous aluminum chloride. Redistillation through a 45 cm. × 1.2 cm. column packed with Helipaks yielded material, b.p. 134.5–135° (31 mm.), $n^{20}D$ 1.5158.

Ethyl mesitoate[23] was distilled through the above column, b.p. 143° (27 mm.), $n^{20}D$ 1.5008.

Reaction of Methylmagnesium Iodide with Mesitoyl Chloride.—The reactions were carried out under a dry nitrogen atmosphere in a 1-l. three-neck flask equipped in the usual manner. Mesitoyl chloride (0.1 mole), diluted to 380 ml. with ether, was placed in the flask and cooled in an ice-bath; the catalyst was then added and the mixture stirred for one-half hour. Two liquid phases formed when the magnesium halides and zinc chloride were used; stannic chloride caused the separation of a solid phase. Methylmagnesium iodide (0.29 mole), diluted to 290 ml., was added during 1.5 hours; the same rates of addition and stirring were maintained in all experiments. After addition was complete the ice-bath was removed, the mixture stirred for an additional hour, and allowed to stand overnight. The reaction mixture was then poured onto ice and hydrochloric acid, the layers separated, and the aqueous layer extracted with ether; the aqueous layer was then rejected. The combined ether layers were extracted with aqueous sodium bisulfite and then with successive portions of aqueous sodium carbonate until all mesitoic acid had been removed. The combined aqueous extracts were acidified with hydrochloric acid and the mesitoic acid collected on a filter, dried and weighed. The ether solution was dried over sodium sulfate and the ether removed on the steam-bath; the residue was distilled at reduced pressure from a 125-ml. Claisen flask. The liquid product distilled cleanly within a five degree range which varied from 115–120° (15 mm.) for pure acetomesitylene to 125–130° (15 mm.) for pure ethyl mesitoate. This distillate was analyzed by comparing its refractive index with those of a series of synthetic mixtures of ketone and ester. Any mesitil remained in the Claisen flask, and was taken up in a small amount of 85% ethanol, collected on a filter, dried and weighed. These yellow crystals, m.p. 99–103°, could be recrystallized from petroleum ether to yield material of m.p. 119–120°.

NEW YORK, N. Y.

(20) B. N. Menschutkin, *Z. anorg. Chem.*, **49**, 34 (1906).

(21) I. M. Kolthoff and E. B. Sandell, "Textbook of Inorganic Quantitative Analysis," The Macmillan Co., New York, N. Y., 1943, p. 571.

(22) R. P. Barnes, *Org. Syntheses*, **21**, 77 (1941).

(23) M. S. Newman, THIS JOURNAL, **63**, 2431 (1941).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

Monomer Synthesis.[1] Synthesis of a Vinyltriazine and a Study of the Reaction of Phenylbiguanide with Acrylate Esters

BY C. G. OVERBERGER AND SEYMOUR L. SHAPIRO[2]

RECEIVED AUGUST 27, 1953

Reaction of phenylbiguanide with acrylyl chloride in an alkaline aqueous acetonitrile solution gave I, X = $CH{=}CH_2$. The structure was determined by hydrogenation to give the known ethyl derivative, I, X = C_2H_5. The products of the reaction of phenylbiguanide with methyl, ethyl and octyl acrylates with alkoxide catalysts have been determined. Derivatives of I, X = $CH_2{-}CH_2OR$, have been obtained and it has been demonstrated that the β-alkoxy group is derived from the alkoxide catalyst. Reaction of methyl β-methoxypropionate and ethyl β-ethoxypropionate with phenylbiguanide gave the corresponding alkoxy compounds, I, X = $CH_2{-}CH_2OR$.

We have initiated a study of the polymerization of specific types of vinyl monomers within the body, particularly within the cell. These monomers are of the vinylpyrimidine or vinyltriazine type containing an amino or substituted amino group. This paper describes the preparation of a vinyltriazine and the course of the reaction and products from the reaction of phenylbiguanide with methyl, ethyl and octyl acrylates with alkoxide catalysts. Reactions of phenylbiguanide with β-alkoxypropionic acid esters with alkoxide catalysts are also described.

We have been able to prepare I, X = $CH{=}CH_2$, by the reaction of phenylbiguanide and acrylyl chloride in an alkaline aqueous acetonitrile solution. Quantitative hydrogenation gave the ethyl derivative, X = C_2H_5, identical with a known sample (infrared and physical properties). Infrared spectra indicated the disappearance of the double bond frequency at 10.15 μ and 6.1 μ[3] after hydrogenation.

As an alternate route to I, X = $CH{=}CH_2$, we investigated the reaction of I, R = C_2H_5, with N-bromosuccinimide and benzoyl peroxide according to the directions of Wenner[4] who prepared *o,o'*-bis-(bromomethyl)-biphenyl in this way. Miller and co-workers[5] have reported that phenylsuccinic anhydride was converted to phenylmaleic anhydride in 57–64% yield by a similar reaction. When I, X = C_2H_5, was treated under the above condi-

(1) This is the eighth in a series of articles concerned with the synthesis and polymerization of vinyl monomers. For the preceding paper, see S. L. Shapiro and C. G. Overberger, THIS JOURNAL, **76**, 97 (1954).

(2) A portion of a thesis by Seymour L. Shapiro, submitted to the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) F. C. Shaefer, J. R. Dudley and J. T. Thurston, THIS JOURNAL, **73**, 3004 (1951), have reported double bond frequencies for 2-N-vinylanilino-4-hydroxy-6-ethoxy-*s*-triazine at 3090 cm.$^{-1}$ (3.22μ) 1620 cm.$^{-1}$ (6.17μ) and 905–1000 cm.$^{-1}$ (10–11μ).

(4) W. Wenner, *J. Org. Chem.*, **17**, 523 (1952).

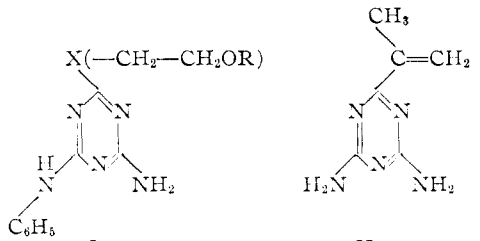
(5) L. E. Miller, H. B. Staley and D. J. Mann, THIS JOURNAL, **71**, 374 (1949).

tions, a 44% yield of monobromo product was obtained which proved to be the *p*-bromophenyl derivative identical with the compound prepared from *p*-bromophenylbiguanide and ethyl propionate.

The failure to achieve bromination of this aliphatic side chain by this reaction is consistent with the observations of Mariella and Belcher[6] who found that bromination of the alkyl substituent in the alkylated pyridines with *n*-bromosuccinimide did not take place when an amino or hydroxyl group was present in the pyridine ring.

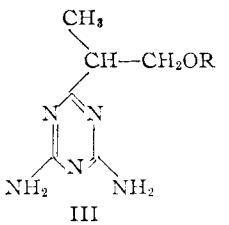
Dehydrohalogenation of I, X = $CHBr-CH_3$,[1] with phenylbiguanide as the base failed to give any vinyl product, although phenylbiguanide hydrobromide was formed.

Thurston[7] has reported the reaction of biguanide with methyl methacrylate in lower alcohols (ROH) without a catalyst to give II (61%) and III (20%) when R = CH_3.



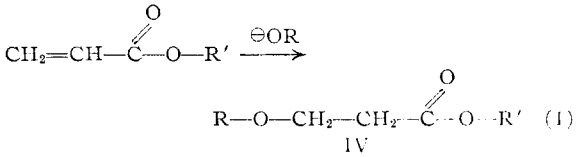
I

II



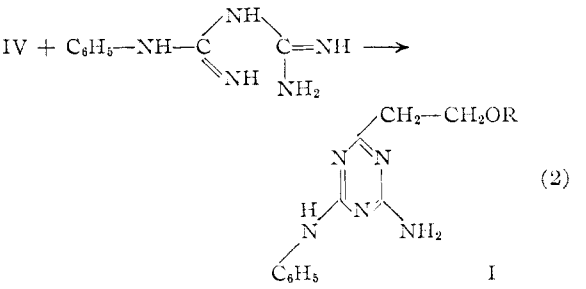
III

when a crotonic ester in an ROH medium was used without catalyst, only derivatives of type III were reported. The structure of these compounds was suggested without supporting evidence. Oldham[8] has reported the preparation of I, X = $CH_2-CH_2OCH_3$, from phenylbiguanide and methyl β-methoxypropionate with sodium methoxide in methanol using a 40% excess of the ester. We then decided to study the reaction between the more available phenylbiguanide and the acrylate esters to prepare compounds of type I, X = $CH=CH_2$, without the α-methyl group in the side chain. When no alkoxide catalyst was used the reaction between phenylbiguanide and the acrylate esters followed a different course and is not described here in detail (see formula VII). When molar quantities of sodium alkoxide were employed as a base the reactions took the course



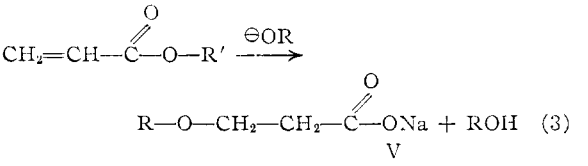
IV (1)

(6) R. P. Mariella and E. P. Belcher, THIS JOURNAL **74**, 1916 (1952).
(7) J. T. Thurston, U. S. Patent 2,461,943, Feb. 15, 1949.
(8) W. N. Oldham, U. S. Patent 2,309,663, February 2, 1943.



(2)

I



V (3)

V on acidification formed a 1:1 adduct with phenylbiguanide ($ROCH_2-CH_2-COOH\cdot PBG$, VI).

Reaction product I was isolated from the reaction mixture by precipitation of the acetic acid or trichloroacetic acid salt or by evaporation to dryness to obtain the free base directly. Evidence that the reaction proceeded as described was obtained in the following way.

In methanolic sodium methoxide, the product obtained by reaction of methyl, ethyl or octyl acrylate with phenylbiguanide was I, R = CH_3. Condensation of methyl β-methoxypropionate with phenylbiguanide using sodium methoxide in methanol gave I, R = CH_3. Condensation of methyl acrylate in ethanolic sodium ethoxide with phenylbiguanide gave I, R = C_2H_5. Reaction of ethyl β-ethoxypropionate and phenylbiguanide in methanolic sodium methoxide gave I, R = C_2H_5. Reaction of methyl acrylate and phenylbiguanide with sodium *n*-propoxide in *n*-propyl alcohol gave I, R = *n*-C_3H_7. There can be little doubt therefore that the β-alkoxy group of the triazine is derived from the alkoxide catalyst. That interchange of alkyl groups in the β-alkoxy esters probably does not take place under these conditions is amply demonstrated by the experiments cited. The synthesis of I using the β-alkoxy ester establishes the position of the alkoxide group in the β-position of the side chain in I. Reduction of the concentration of the alkoxide from one molar equivalent does not improve the yield of I.

The yield of I, R = CH_3, was considerably improved by the use of two equivalents of phenylbiguanide to one mole of acrylate or β-methoxypropionate. The use of two molar equivalents was suggested by the isolation, in the alkoxide-catalyzed reaction of phenylbiguanide and ethyl β-ethoxypropionate of a reaction product, apparently a readily dissociable molecular complex between phenylbiguanide and I, R = C_2H_5. That the entire yield of I, R = C_2H_5, is present in the form of this complex is indicated by the virtual identity of yield from the same reaction mixture when I, R = C_2H_5, is isolated in the form of the phenylbiguanide complex,[9] or as its trichloroacetic acid salt. The molecular complex was readily dissoci-

(9) Molecular compound formation between substituted biurets and isocyanurates recently has been reported (W. J. Close, THIS JOURNAL, **75**, 3619 (1953)) and our case may be similar.

TABLE I

YIELDS OF ALKOXYTRIAZINES, USING ALKOXIDE CATALYSTS

Ester	Solvent	Catalyst (equimolar)	Yield of alkoxy triazine (I) R	%	Method	Yield of phenylbiguanide salt of alkoxy acid (VI) R	%
Methyl acrylate	CH_3OH	OMe–	CH_3	46.5[b]	B		
Methyl acrylate	CH_3OH	OMe–	CH_3	36	C	CH_3[e]	26.7
Methyl β-methoxypropionate[a]	CH_3OH	OMe–	CH_3	36	C	CH_3	28.8
Ethyl acrylate	CH_3OH	OMe–	CH_3	50.5[b]	B		
Octyl acrylate	CH_3OH	OMe–	CH_3	12.3[b]	B		
Methyl acrylate	C_2H_5OH	OEt–	C_2H_5	31.4	C	C_2H_5[f]	22.9
Ethyl β-ethoxypropionate	CH_3OH	OMe–	C_2H_5	26.2	C	C_2H_5	14.8
Methyl acrylate	n-C_3H_7OH	OPr–	n-C_3H_7	41.5[c,d]	C		
Methyl β-methoxyacrylate	CH_3OH	OMe– (0.5 *M*)	CH_3	31.2	C	CH_3	12.0
Methyl β-methoxyacrylate	CH_3OH	OMe– (0.2 *M*)	CH_3	29.7	C	CH_3	12.5
Methyl β-methoxyacrylate	CH_3OH	OMe– (0.7 *M*)	CH_3	68.0[d]	A		
Methyl acrylate	CH_3OH	OMe– (0.7 *M*)	CH_3	59.0[d]	A		
Ethyl β-ethoxypropionate	CH_3OH	OMe– (0.7 *M*)	C_2H_5	39.8[d]	A		

[a] Oldham reported the preparation of I, from phenylbiguanide and methyl methoxypropionate in methanol, in about 39% yield, m.p. 118°. [b] Isolated as acetic acid salt. [c] Crude yield. [d] Isolated as trichloroacetic acid salt. [e] *Anal.* Calcd. for $C_{12}H_{19}N_5O_3$: C, 51.23; H, 6.81; N, 24.9. Found: C, 51.36; H, 6.81; N, 25.2., m.p. 150–152°. [f] *Anal.* Calcd. for $C_{13}H_{21}N_5O_3$: C, 52.86; H, 7.17; N, 23.7. Found: C, 53.12; H, 7.35; N, 24.0., m. p. 169–171°.

ated by aqueous picric acid into the constituent picrates which were fractionally isolated in proportionate yields to account for a complex.

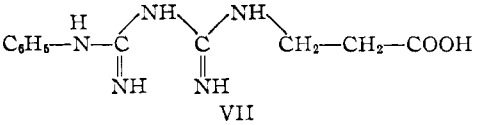
When equimolar amounts of I, R = C_2H_5, and phenylbiguanide were mixed in acetonitrile or methanol, the complex did not form and its exact nature is not understood, nor could an equivalent structure be isolated in reactions involving I, R = CH_3.

Step 3, saponification of the ester, was a competing reaction which could not be suppressed. The structure of the phenylbiguanide salts of VI, R = C_2H_5, was verified by synthesis using equimolar quantities of the β-ethoxypropionic acid and phenylbiguanide. Data pertaining to this reaction are given in Table I.

Compounds of Type I readily form salts with organic acids. With compound I, R = CH_3, the acetic acid could be removed at 80° or by recrystallization from water. The free bases and their salts are described in Table II.

Acetylation of I, R = CH_3, with acetic anhydride gave a mixture of acetates from which the pure monoacetate was isolated. Treatment of I, R = CH_3, C_2H_5 and n-C_3H_7, with hot 10% trichloroacetic acid gave largely resin and a small amount of I, X = CH_2–CH_2OH.

Evidence to demonstrate the structure I, X = CH_2–CH_2OH, was afforded by comparison with a product isolated from the reaction of phenylbiguanide with β-propiolactone. Previous workers[10] have demonstrated that amino groups will react with β-propiolactone to give β-hydroxy amides and β-amino acids dependent on whether the nucleophilic attack of the amino group is on the carbonyl group or on an adjacent carbon. Thus, compounds VII and I, CH_2–CH_2–OH, the compound derived from cyclization and aromatization of the β-hydroxyamide structure $C_6H_5NHC(=NH)$–NH–C(=NH)–NH–$COCH_2$–CH_2OH might be expected and both compounds were isolated, I, X = CH_2–CH_2OH (18%), and VII (9.7%). The melting point of I, X = CH_2CH_2OH, prepared in this way was not depressed when mixed with a sample obtained from the treatment of I with trichloroacetic acid. Compound VII was tentatively identified by comparison with a product isolated from a study of the non-catalyzed reaction between ethyl acrylate and phenylbiguanide and is not described here.



VII

In the Experimental section only one representative type of each transformation is included.

Experimental[11]

Preparation of 2-Amino-4-anilino-6-vinyl-*s*-triazine (I, X = CH=CH_2).—A suspension of 21.4 g. (0.1 mole) of phenylbiguanide hydrochloride in 50 g. of cracked ice, 50 ml. of acetonitrile and 1 g. of hydroquinone was prepared in a 1-l., three-necked flask equipped with a stirrer and two dropping funnels. Two solutions, one containing 8.0 g. (0.2 mole) of sodium hydroxide in 100 ml. of water and the other containing 9.05 g. (0.1 mole) of freshly distilled acrylyl chloride[12] in 100 ml. of acetonitrile were added simultaneously over a one-hour period to the stirred, chilled reaction mixture (ice-bath). A solid, 8.5 g., separated which was treated with 200 ml. of boiling water. The residue gave 0.83 g. of I, X = CH=CH_2, m.p. 176–179°, and concentration of the aqueous filtrate gave 7.5 g. of phenylbiguanide hydrochloride, m.p. 247–248°, a mixed melting point with an authentic sample was not depressed. The picrate of this product was identical with phenylbiguanide dipicrate monohydrate, m.p. 185–186°, mixed m.p. 185–187° (see later Experimental section). Concentration of the filtrate from the reaction mixture gave an additional 4.35 g. of I, X = CH=CH_2, m.p. 165–175°, yield of crude 5.18 g. (37.6% based on phenylbiguanide hydrochloride reacted). Purification was effected by recrystallization from an ethanol–water solution to give 2.35 g. of product, m.p. 177–178°, and was accompanied by large losses due to a brown impurity. An analytical sample melted at 180–181°. The compound was unaffected by light or oxygen.

Anal.[13]. Calcd. for $C_{11}H_{11}N_5$: C, 61.95; H, 5.20; N, 32.85. Found: C, 61.93; H, 5.17; N, 32.80.

(10) T. L. Gresham, J. E. Jansen, F. W. Shaver, R. A. Bankert and F. T. Fiedorek, THIS JOURNAL, **73**, 3168 (1951).

(11) All melting points are uncorrected.

(12) G. H. Stempel, R. P. Gross and R. P. Mariella, THIS JOURNAL, **72**, 2299 (1950).

(13) Analyses by Drs. Weiler and Strauss, Oxford, England.

The picrate was prepared in aqueous ethanol and recrystallized from water, m.p. 232–233°.

Anal. Calcd. for $C_{17}H_{14}N_8O_7$: C, 46.16; H, 3.19. Found: C, 46.28; H, 3.48.

The above reaction failed with biguanide under similar conditions.

Hydrogenation of I, X = CH=CH$_2$.—Hydrogenation of 200 mg. (0.00094 mole) of I, X = CH=CH$_2$, in ethanol was accomplished with 50 mg. of palladium-on-charcoal catalyst. Slightly more than the theoretical amount of hydrogen was absorbed. Concentration of the solution gave 185 mg. (91.5%) of I, X = C_2H_5, m.p. 154–157°. Recrystallization from a methanol–water solution gave a m.p. 158–160°, a mixture of this product with an authentic sample (m.p. 158–160°) melted at 158–160°. The infrared spectrum of I, X = C_2H_5, indicated the disappearance of the double bond frequency at 10.15 μ and 6.10 μ.[3]

Preparation of 2-Amino-4-(*p*-bromoanilino)-6-ethyl-*s*-triazine by Reaction of I, X = C_2H_5, with N-Bromosuccinimide.—A suspension of 2.15 g. (0.01 mole) of I, X = C_2H_5, in 25 ml. of carbon tetrachloride was treated with 1.8 g. (0.01 mole) of N-bromosuccinimide and 25 mg. of benzoyl peroxide. The solution was refluxed for four hours according to the general directions of Wenner.[4] The insoluble precipitate, 2.6 g., was removed and recrystallized from a methanol–water solution, 1.3 g. (44.3%), m.p. 174–176°. An analytical sample was recrystallized from acetonitrile, m.p. 179–181°.

Anal. Calcd. for $C_{11}H_{12}BrN_5$: C, 44.91; H, 4.11; N, 23.8. Found: C, 45.14; H, 3.92; N, 23.5.

No well-defined products could be isolated from the carbon tetrachloride solution.

Preparation of the *p*-Bromophenyl Derivative from *p*-Bromophenylbiguanide.—To a solution of sodium methoxide prepared from 0.46 g. (0.02 g. atom) of sodium and 10 ml. of methanol was added 2.93 g. (0.01 mole) of *p*-bromophenylbiguanide hydrochloride.[1] The solution was cooled and 1.02 g. (0.01 mole) of ethyl propionate added and the reaction mixture kept at room temperature for 72 hours and then diluted with 25 ml. of water. Filtration gave a product which was dissolved in 50 ml. of warm acetonitrile. On standing, crystals separated, 0.77 g. (26.2%), m.p. 180–182°; a mixture of this product with the sample obtained from N-bromosuccinimide (m.p. 179–181°) melted at 180–182°. These crystals turn to a golden color on exposure to light.

2-Amino-4-anilino-6-(β-methoxyethyl)-*s*-triazine (I, X = CH$_2$–CH$_2$OCH$_3$). **Procedure A.**—Methyl acrylate, 4.3 g. (0.05 mole) was slowly added to a cooled (−40°) sodium methoxide solution prepared from 1.65 g. (0.072 g. atom) of sodium and 65 ml. of anhydrous methanol. Phenylbiguanide, 17.7 g. (0.1 mole) was added at one time and the resultant slurry maintained at −10° overnight. The reaction mixture was allowed to stand at room temperature for from 4 to 8 days and then refluxed for 2 hours. The reaction mixture on cooling was poured into 500 ml. of 10% trichloroacetic acid. The salt precipitated on standing, 12.2 g. (59%), m.p. 137–138° dec.

Treatment of 5 g. of the trichloroacetic acid salt of I, X = CH$_2$–CH$_2$–OCH$_3$, with 60 ml. of 2.5 *N* sodium hydroxide gave 3.25 g. of crude free base, m.p. 110–114°. Recrystallization from a methanol–water solution gave 2.15 g. (72.5%), m.p. 119–120° (Table II).

Procedure B.—Phenylbiguanide, 100 g. (0.565 mole), was dissolved with cooling in a solution of sodium methoxide prepared from 15 g. (0.65 g. atom) of sodium in 450 ml. of anhydrous methanol followed by the addition of 75 g. (0.87 mole) of methyl acrylate. The reaction mixture was stoppered and allowed to stand at room temperature for 48 hours, at which time the mixture was poured into 2.5 l. of 10% acetic acid and allowed to stand in the ice-box overnight. The acetic acid salt was removed by filtration and recrystallized from 2.5 l. of 10% acetic acid at 80°, long thin needles, 80 g. (46.5%), m.p. 97–99° dec., of the acetic acid salt of I, X = CH$_2$–CH$_2$OCH$_3$.

Procedure C.—Methyl acrylate, 10 g. (0.16 mole), was slowly added to a solution of sodium methoxide prepared from 2.3 g. (0.1 g. atom) of sodium dissolved in 85 ml. of anhydrous methanol at −40°. Phenylbiguanide, 15 g. (0.085 mole), was added at one time and the resultant slurry maintained at −10° overnight and then stored at room temperature for 48 hours. The reaction mixture was then cooled and maintained at −20° during the addition of a solution of 8 ml. of concentrated hydrochloric acid diluted to 20 ml. with methanol. The reaction mixture was evaporated to give 28 g. of solid, which was extracted with two 150-ml. portions of acetone. From the acetone solution was obtained 5.3 g. of a light yellow oil which, after two recrystallizations from an acetone–water solution, gave 2.15 g. of I, X = CH$_2$–CH$_2$OCH$_3$. The residue from the acetone extraction was treated with 200 ml. of hot acetonitrile, the acetonitrile solution cooled and the solid removed by filtration. Removal of the acetonitrile gave a yellow oil which gave crystals from a methanol–water solution; 3.35 g. of crude I, X = CH$_2$–CH$_2$OCH$_3$. The solid, acetonitrile-insoluble residue, was again treated with 200 ml. of hot acetonitrile and any solid removed before cooling. The solution on cooling gave 2.95 g. of the phenylbiguanide salt of β-methoxypropionic acid. From the acetonitrile filtrate was obtained an additional 1.60 g. of I, X = CH$_2$–CH$_2$OCH$_3$. Further extraction of the solid residue with acetonitrile and absolute ethanol gave 3.32 g. of the phenylbiguanide salt. An additional 0.2 g. of I, X = CH$_2$–CH$_2$OCH$_3$ was obtained from the filtrates; total yield of I, X = CH$_2$–CH$_2$–OCH$_3$, 7.3 g. (36%); total yield of the phenylbiguanide salt of β-methoxypropionic acid, 6.27 g. (26.7%) (Table I).

The analytical data for the phenylbiguanide salts of β-methoxy- and β-ethoxypropionic acids are given in Table I.

2-Amino-4-anilino-(β-ethoxyethyl)-*s*-triazine (I, X = CH$_2$–CH$_2$OC$_2$H$_5$).—Procedure A was repeated with 7.3 g. (0.05 mole) of ethyl ethoxypropionate and 75 ml. of methyl alcohol. After storage for 3 days at room temperature the reaction mixture, 90 ml., was divided into 15-ml. and 75-ml. portions.

Portion I was poured into 150 ml. of 10% trichloroacetic acid and the white trichloroacetic acid salt was obtained; 1.4 g. (39.8%), m.p. 137–138° dec. (Table II). The salt was suspended in 20 ml. of 2.5 *N* sodium hydroxide and allowed to stand one hour with stirring. The white precipitate of I, X = CH$_2$–CH$_2$OC$_2$H$_5$, was removed by filtration, washed with water and dried; 0.74 g. (36.5%), m.p. 119–120° (Table II).

Portion II was evaporated and the residue, 20 g., extracted with 200 ml. of hot acetone. Filtration and removal of acetone gave 15 g. of white residue. Five grams of this residue was dissolved in 50 ml. of warm acetonitrile and the solution decolorized with Norite. On 3 hours standing, the precipitated crystals, an apparent phenylbiguanide adduct of I, X = CH$_2$–CH$_2$OC$_2$H$_5$, was removed by filtration, 2.6 g. (42.9%), m.p. 145–147°. Recrystallization was effected from acetonitrile, m.p. 146–148°. The exact nature of this adduct is unknown.

Anal. Calcd. for $C_{21}H_{28}N_{10}O$: C, 57.78; H, 6.40. Found: C, 57.50; H, 6.53.

The mixture of picrates obtained from 500 mg. of the phenylbiguanide adduct of I, X = CH$_2$–CH$_2$OC$_2$H$_5$, was heated briefly with 75 ml. of hot water which dissolved the phenylbiguanide picrate. From the aqueous solution was obtained 400 mg. (53.5%), m.p. 185–186°, of phenylbiguanide picrate; a mixture of this product with an authentic sample (m.p. 185–186°), melted at 185–186°. The relatively insoluble residue was recrystallized from water; 460 mg. (82.2%), m.p. 197–199°; a mixture of this product with an authentic sample of the picrate of I, X = CH$_2$–CH$_2$–OC$_2$H$_5$ (m.p. 197–198°) melted at 197–198°.

The picrate of phenylbiguanide for comparison, prepared in aqueous medium and recrystallized from water, was a dipicrate with one mole of water of crystallization.

Anal. Calcd. for $C_{20}H_{19}N_{11}O_{15}$: C, 36.76; H, 2.93. Found: C, 36.94, 36.91; H, 2.98, 2.85.

Phenylbiguanide Salt of β-Ethoxypropionic Acid.—Phenylbiguanide, 8.8 g. (0.05 mole), was dissolved in 300 ml. of acetonitrile and 6.8 g. (0.065 mole) of β-ethoxypropionic acid added dropwise. After standing for two hours, the dense precipitate was removed by filtration, 13.4 g. (91%), m.p. 169–171° after recrystallization from acetonitrile. A mixture of this product with the compound isolated from the reaction, Table I, footnote *c* (m.p. 169–171°) melted at 170–172°.

Other Salts of I, X = CH$_2$–CH$_2$OCH$_3$.—The acid salts of I, X = CH$_2$–CH$_2$OCH$_3$, were prepared from a methanolic solution of the base and precipitated with dilute aqueous acid. The hydrochloride was prepared by mixing a dry cold ether solution of hydrogen chloride with an ether

TABLE II

ALKOXYTRIAZINES AND SALTS

I, R	Compound HA	M.p., °C.	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CH_3[a]		119–120	$C_{12}H_{15}N_5O$	58.76	58.70	6.16	6.24
CH_3	Acetic[b]	97–99 d.	$C_{14}H_{19}N_5O_3$	55.07	54.91	6.27	6.08
CH_3	Picric[d]	205–206 d.	$C_{18}H_{18}N_8O_8$[e]				
CH_3	Trichloroacetic	137–138 d.	$C_{14}H_{16}N_5Cl_3O_3$	41.12	40.90	3.95	3.89
CH_3	Heptafluorobutyric	128–130 d.	$C_{15}H_{16}F_7N_5O_3$	40.27	40.38	3.61	3.83
CH_3	Hydrochloric[c]	143–144 d.	$C_{12}H_{16}ClN_5O$	51.15	51.42	5.73	5.88
C_2H_5[a]		120–121	$C_{13}H_{17}N_5O$	60.21	60.16	6.61	6.41[f]
C_2H_5	Acetic[b]	95–100 d.	$C_{15}H_{21}N_5O_3$	56.41	56.55	6.63	6.34
C_2H_5	Picric[d]	197–198 d.	$C_{19}H_{20}N_8O_8$	46.74	46.65	4.13	4.12
n-C_3H_7[a]		117–118	$C_{14}H_{19}N_5O$	61.52	61.79	7.01	6.93
n-C_3H_7	Picric[d]	191–193 d.	$C_{20}H_{22}N_8O_8$	47.81	47.68	4.41	4.63
n-C_3H_7	Trichloroacetic	128–129 d.	$C_{16}H_{20}Cl_3N_5O_3$	44.00	43.60	4.62	4.52

[a] Recrystallized from MeOH–H_2O. [b] Recrystallized from 10% acetic acid. [c] Recrystallized from CH_3CN. [d] Recrystallized from H_2O. [e] Calcd.: N, 23.6. Found: N, 24.2. [f] Calcd. N, 27.0. Found: N, 27.0.

solution of the base and the product recrystallized from acetonitrile (Table II).

Acetylation of I, X = CH_2–CH_2OCH_3.—Two grams (0.0065 mole) of I, X = CH_2–CH_2OCH_3, as the acetic acid salt was treated with 40 ml. of acetic anhydride, 2 drops of pyridine was added and the solution refluxed for 2 hours. The solvent was removed and the residual oil dissolved in ether and treated with Norite. From the ether solution was obtained 2.09 g. of product which on recrystallization from acetonitrile and water gave the monoacetate, m.p. 158–159°.

Anal. Calcd. for $C_{14}H_{17}N_5O_2$: C, 58.52; H, 5.96; N, 24.4. Found: C, 58.49; H, 5.66; N, 24.6.

2-Amino-4-anilino-6-(β-hydroxyethyl)-s-triazine. A. From β-Propiolactone.—Phenylbiguanide, 17.7 g. (0.1 mole), was dissolved in 100 ml. of hot acetonitrile and cooled to 38°. β-Propiolactone, 8.0 g. (0.11 mole), diluted to 25 ml. with acetonitrile was added slowly with stirring. Within 15 minutes a heavy yellow oil separated and the supernatant liquid was decanted from the oil and placed in the ice-box at 10°. The oil was triturated with ethanol to give 3.24 g. of white powder (VII), m.p. 195–197°, recrystallized from methanol, 2.7 g. (9.7%), m.p. 205–206°.

Anal. Calcd. for $C_{11}H_{15}N_5O_2$ (VII): C, 53.00; H, 6.07; N, 28.1. Found: C, 53.21; H, 6.26; N, 28.2.

The supernatant liquid after several weeks at ice-box temperature gave 6.0 g. of white crystals, m.p. 145–150°. Recrystallization from a methanol–water solution gave 4.2 g. (18.2%), m.p. 159–160° of I, X = CH_2–CH_2OH.

Anal. Calcd. for $C_{11}H_{13}N_5O$: C, 57.13; H, 5.67; N, 30.3. Found: C, 57.12; H, 5.46; N, 30.2.

The picrate was prepared in water and recrystallized from water, m.p. 224–225°.

Anal. Calcd. for $C_{17}H_{16}N_8O_8$: C, 44.37; H, 3.50; N, 24.3. Found: C, 44.17; H, 3.76; N, 23.9.

B. From I, X = CH_2–CH_2OCH_3.—Five grams (0.0164 mole) of I, X = CH_2–CH_2OCH_3, as the acetic acid salt was dissolved in 15 ml. of dioxane and the solution heated to reflux. To this was added 250 ml. of aqueous 10% trichloroacetic acid so that reflux was maintained. An oily product separated and the solution turned milky. Reflux was continued for two hours and the reaction mixture was decanted from the oily polymeric product, concentrated to 60 ml. and any solid removed by filtration. The filtrate was diluted with 30 ml. of methanol and treated with Norite. On standing, the solution gave small white pellets of I, X = CH_2–CH_2OH, 500 mg. (18.9%), m.p. 156–158°, mixed m.p. 156–159°.

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BROOKLYN, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

Monomer Synthesis. Methylation of 2-Aminopyrimidine[1]

BY C. G. OVERBERGER AND IRVING C. KOGON[2]

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Useful procedures for the methylation of 2-aminopyrimidine and 2-N-methylaminopyrimidine on the amine nitrogen have been developed and structures of methylated products determined by unequivocal synthesis. 2-N-Dimethylamino-4-hydroxypyrimidine and the 4-chloro derivative have been prepared and characterized. Reduction of the 4-chloro derivative gave the 2-N-dimethylaminopyrimidine. Reaction of n-butyllithium with 2-N-dimethylaminopyrimidine gave 2-N-dimethylamino-4-butylpyrimidine. With an excess of butyllithium the dibutyl product was obtained.

In connection with the synthesis of vinyl pyrimidines, it was necessary to investigate several model syntheses. This paper describes the synthesis of derivatives of 2-aminopyrimidine. In particular it was desirable to develop methods to methylate 2-aminopyrimidine on the amino nitrogen and not the ring nitrogen. Although one of the ultimate reasons for the synthesis of vinyl pyrimidines was for the purpose of studying internal cell induced polymerization and its effect on abnormal cell mitosis, some of these intermediates described here were also screened by the Sloan–Kettering group and found to be inactive.

N-Methylaminopyrimidine was prepared from 2-

(1) This is the ninth in a series of articles concerned with the synthesis of monomers and their polymerization; for the eighth, see C. G. Overberger and Seymour L. Shapiro, THIS JOURNAL, **76**, 1061 (1954).

(2) Public Health Research Fellow 1951–1953. This paper comprises a portion of a thesis presented by Mr. Irving C. Kogon in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.