absorption shows a hypochromic and hypsochromic effect in 1 *N* hydrochloric acid (Fig. 2).

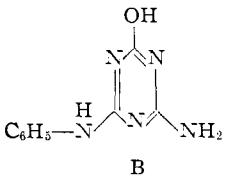
These effects are in accord with the suggestion that there is an increasing tendency for the triazine to be present in the conjugate acid form. The cationoid state results in a decrease of absorption in our unsymmetrical system.

A similar effect is observed on comparing II and I and Nachod and Steck[7] also observed a hypochromic effect in 0.01 *N* hydrochloric acid as compared to the neutral solution as shown in 3 and 5. A similar effect[4] has been noted with the unsymmetrical amine, aniline and its conjugate acid although there is a pronounced hypsochromic effect on going to the salt in this case.[4,8]

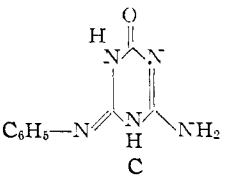
Consideration of structure XXVI shows the marked influence of acetylation on the spectrum. There is very little relationship to be seen between XXVI and XII, the parent product. There has been a large increase in intensity and a new type of absorption and it would appear that a new chromophore has been introduced (Fig. 1). For brevity, diagrams showing possible electronic paths are omitted.

The acetylation of I to yield XXVII does not give the extensive changes in the spectrum of the parent product as noted in the previously described acetylated product. There are, however, some marked bathochromic and hyperchromic effects.

The substitution of hydrogen by hydroxyl attached to the triazine ring as in XXVIII yields essentially a hyperchromic effect. Since the compound was examined as the hydrochloride, it is likely that the form most nearly representing the structure is B instead of a tautomeric structure such as C



B



C

Acetylation of XXVIII yielded a monoacetate XXIX which in view of its resultant hypochromic and hypsochromic effect compared to the spectrum of compound XXVIII is believed to reflect O-acetylation.

While the instrument used in this study was incapable of resolution of bands beyond 220 mμ, it is of interest to note that the minima reported of virtually all of the diaminotriazine compounds in this series was in the vicinity of 232 to 238 mμ reflecting a decrease in absorption from a maximum in the far ultraviolet. Hirt and Salley,[9] in a recent study of simple diaminotriazine, also indicate a minimum at about 237 mμ for their compounds with the maximum still not resolvable at about 200 mμ. It would appear, therefore, that extension of the ultraviolet study of the diaminotriazines in the neighborhood of 200 mμ would yield pertinent information particularly relevant to the triazine ring system.

The spectra were all determined with a model DU Beckman spectrophotometer using 1-cm. cells.

Acknowledgment.—We are grateful to Dr. Louis Freedman of the U. S. Vitamin Corporation for his generosity in allowing one of us to use the facilities of their laboratories. We are also grateful to Dr. E. I. Becker of the Polytechnic Institute of Brooklyn for helpful discussions.

(7) F. C. Nachod and E. A. Steck, THIS JOURNAL, **70**, 2819 (1948).

(8) See also E. J. Modest and H. Kangur, Abstracts of 124th A.C.S. Meeting, page 26-O for a similar effect with 1,2-dihydro-*s*-triazines.

(9) R. C. Hirt and D. J. Salley, *J. Chem. Phys.*, **21**, 1181 (1953).

BROOKLYN, NEW YORK

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION, LABORATORY OF ADVANCED RESEARCH, REMINGTON RAND, INC.]

Azidopyrimidines[1]

BY FREDERIC R. BENSON, LAWRENCE W. HARTZEL AND ELIZABETH A. OTTEN

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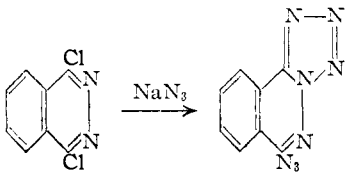
Attempts have been made to prepare ditetrazolo[a,c]pyrimidines; reactions designed to lead to this ring system have produced instead the isomeric 2,4-diazido pyrimidines. Evidence favoring the diazide structure of these compounds has been secured from their behavior toward hydrolysis, from heating at high temperature, and from their ultraviolet absorption spectra.

The preparation of ring systems containing two tetrazole groups fused to a single ring has been studied by Stollé and Storch.[2] These investigators attempted to obtain such compounds by the reaction of sodium azide with dichloroquinazoline, dichloroquinoxaline and dichlorophthalazine. In all cases it was found possible to effect ring closure with the formation of a tetrazole ring in only one position, a mixed tetrazolo–azido compound being obtained.

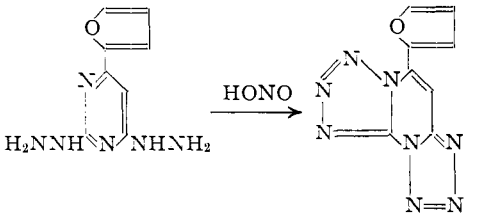


More recently, Andrisano[3] has described the preparation of 6-furylditetrazolo[a,c]pyrimidine from 6-furyl-2,4-dihydrazinopyrimidine and nitrous acid. Proof of structure of this compound was not given. Alternative structure possibilities for this compound include 2,4-diazido-6-furylpyrimidine or the two

(1) This work was performed under a subcontract from Arthur D. Little, Inc., by Remington Rand, Inc., in connection with an Army Ordnance Corps project. This article has been approved for publication by the Public Information Division, National Military Establishment.

(2) R. Stollé and H. Storch, *J. prakt. Chem.*, **135**, 128 (1932).

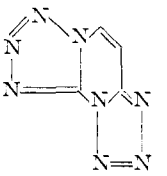
(3) R. Andrisano, *Boll. sci. facolta chim. ind. univ. Bologna*, **5**, 48 (1944–1947); *C. A.*, **44**, 3904i (1950).



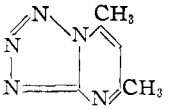
possible monoazidomonotetrazolo derivatives. Ring-chain isomers of the imide–azide–tetrazole type are known,[4] the case of guanyl azide and 5-aminotetrazole having received the most attention.[5] The preparation of the alleged 6-furylditetrazolo-[a,c]pyrimidine was repeated in this Laboratory. It was found, however, that instead of the compound melting at 122° as described by Andrisano a substance melting at 93° was obtained. This latter compound had the correct analysis for Andrisano's product. No evidence was found of a product melting at 122°. The product melting at 93° was also obtained by refluxing the dichloropyrimidine with sodium azide, a standard procedure for securing tetrazoles.[2,6,7] To establish the structure of this compound, it was subjected to two tests described by Stollé.[2] One test used involved refluxing with sodium ethoxide, thus liberating the azide group as sodium azide, but not destroying the fused tetrazole ring. A second test involved heating the compound in tetralin at about 200° wherein one mole of nitrogen was liberated from an azide group but not from a tetrazole ring. These tests were applied to the product obtained according to the procedure of Andrisano. Approximately two moles of nitrogen was liberated on heating in tetralin. Somewhat more than two equivalents of titratable material were liberated by treatment with sodium ethylate followed by acidification and distillation, the extra amount presumably being due to extra acid derived from breakdown of the furan ring. A qualitative test for the presence of azide in the distillate was positive. The results are suggestive, therefore, that the compound is 2,4-diazido-6-furylpyrimidine rather than the anticipated ditetrazolo compound. Additional confirmation was found in the ultraviolet absorption spectrum of the compound which will be discussed later in this article.

The same series of reactions described for the preparation of the furyl derivative was applied to 2,4-dichloropyrimidine. A compound melting at 92° was obtained by diazotizing 2,4-dihydrazinopyrimidine, by interaction of hydrazoic acid and the dichloro compound in a sealed tube at 100° and by refluxing with alcoholic sodium azide. Identical material resulted from each of these reactions. From the preparative standpoint, refluxing with sodium azide was the simplest procedure. In like manner, 2,4-dichloro-6-methylpyrimidine and 2,4-dichloro-6-phenylpyrimidine were treated with sodium azide yielding analogous products. In all cases, on heating in tetralin, 88% or more of the theoretical nitrogen for two moles of azide per pyrimidine ring was obtained. When these materials were treated with sodium ethoxide, followed by acidification and distillation of liberated hydrazoic acid 63% or better of the hydrazoic acid calculated for two azide groups per pyrimidine ring was obtained. The data for these tests of the products are summarized in Table I. The sodium ethoxide and tetralin tests are probably valid methods for distinguishing between isomeric imide azides and fused tetrazole rings. Nevertheless, the possibility does exist that under the test conditions a tetrazole group could be converted to an azide. Under such conditions these tests would be without significance as far as the structure of the original compound was concerned. Accordingly, the ultraviolet absorption spectra of these compounds were determined to provide relevant data for structure assignments.

Reference to the formula for ditetrazolo[a,c]pyrimidine reveals one isolated tetrazole ring and one other tetrazole ring, the unsaturation of which is



conjugated with the one double bond remaining within the pyrimidine moiety. There is ample evidence in the literature to show that a tetrazole ring without substituents capable of effecting a bathochromic shift has no ultraviolet absorption, at least above 220 mμ.[8,9] No information is available on the absorption of a tetrazole which bears a single exocyclic unsaturation conjugated with the ring unsaturation. Spectral data are available, however, for 2-(5-tetrazolyl)-thiophene. This compound with two conjugated exocyclic unsaturations coupled to the tetrazole ring, shows a maximum at 255 mμ.[9] The sole absorption spectrum measurement reported in the literature for fused ring tetrazolopyrimidines is for 5,7-dimethyltetrazolo[a]pyrimidine.[10] In neutral solution in alcohol this compound has an absorption maximum at 265 mμ; it will be noted from the accompanying formula that the ring system contains four conjugated double bonds. Since ditetrazolo[a,c]pyrimidine has only one exocyclic unsaturation conjugated with the unsaturation in the tetrazole portion it



would be expected that any maximum would be at a lower wave length than that found for these compounds with two conjugated exocyclic unsaturations. Data are available in the literature for the absorption spectra of ethyl azide and phenyl azide.[11]

(4) R. Stollé and F. Helworth, *Ber.*, **47**, 1139 (1914).
(5) A. Hantzsch and A. Vagt, *Ann.*, **314**, 357 (1901); K. A. Hofmann, H. Hock and H. Kirmreuther, *ibid.*, **380**, 135 (1911).
(6) M. O. Forster, *J. Chem. Soc.*, **95**, 184 (1909).
(7) J. v. Braun and W. Rudolph, *Ber.*, **74**, 264 (1941).
(8) F. W. Schueler, S. C. Wang, R. M. Featherstone and E. G. Gross, *J. Pharmacal. Exptl. Therap.*, **97**, 266 (1949).
(9) B. Elpern and F. C. Nachod, THIS JOURNAL, **72**, 3379 (1950).
(10) F. C. Nachod and E. A. Steck, *ibid.*, **70**, 2819 (1948).
(11) "International Critical Tables," Vol. V, McGraw-Hill Book Co., New York, N. Y., p. 373.

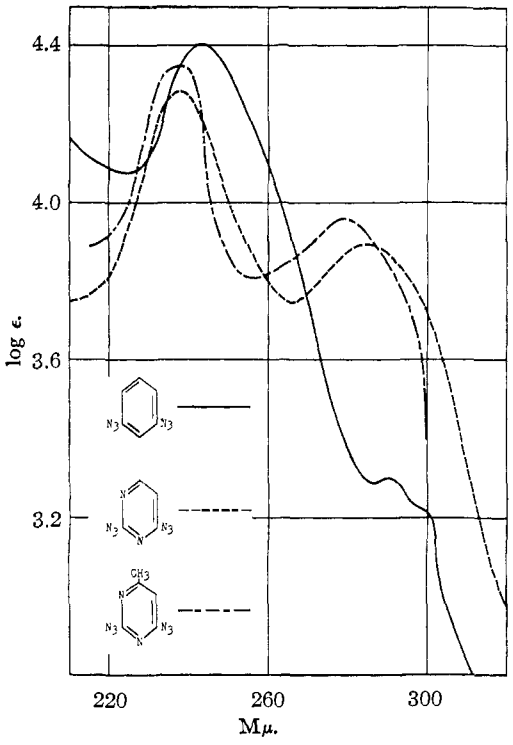
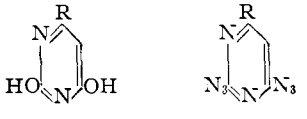


Fig. 1.—Absorption spectra of *m*-diazidobenzene, 2,4-diazidopyrimidine and 2,4-diazido-6-methylpyrimidine in 95% ethanol.

Ethyl azide has a maximum at 285 mμ; phenyl azide has maxima at 250 and 285 mμ. It is probable from these data that absorption in the neighborhood of 285 mμ is characteristic of the azide group. To make certain of this point *m*-diazidobenzene was prepared[12] and its absorption determined (Fig. 1). Aside from the absorption at 244 mμ, evidently due to the benzene ring, a maximum was found at 290 mμ. The absorption spectrum of the compound now presumed to be 2,4-diazidopyrimidine was determined; maxima were found at 239 and 285 mμ. That at 239 mμ is due to the pyrimidine ring.[13] The maximum at 285 mμ is clearly due to the azide groups. Similar results were found with the compound now presumed to be 2,4-diazido-6-methylpyrimidine (Fig. 1). Directly pertinent to this discussion are the spectra of the corresponding 6-substituted uracils.[14] Table I shows the uracil maxima and those of the presumed diazides.

TABLE I



R	A	B	C	$(A - B)^{\Delta\lambda}$	$(C - A)^{\Delta\lambda}$
H	258.5	239.0;	285	19.5	26.5
CH_3	260.0	239.0;	279	21.0	19.0
2-Furyl	272.5; 311.0	249.5; 291.5;	331	19.5	20.0
Phenyl	285.0	248.0;	309		24.0

(12) M. O. Forster and H. E. Fierz, *J. Chem. Soc.*, **91**, 1953 (1907).

(13) F. F. Heyroth and J. R. Loofbourow, THIS JOURNAL, **56**, 1728 (1934); F. M. Uber and R. Winters, *ibid.*, **63**, 137 (1941).

(14) R. Andrisano and G. Modena, *Gazz. chim. ital.*, **81**, 393 (1951).

The presumed diazides all have one more maximum than do the corresponding uracils. It is probable that the higher maxima (column C) for the presumed diazides are associated with the azide group. It is of interest that the wave length shifts between the two series are relatively constant. Presumably the lowest maxima in the furyl and phenyl derivatives are the result of a bathochromic shift of some much lower band of the pyrimidine, furane or benzene ring due to their mutual interaction. In the case of the 6-furyl derivative a bathochromic shift appears to have occurred resulting in absorption for the azide group at a somewhat higher wave length. Two maxima appear to have been combined in the case of both phenyluracil and the presumed diazidopyrimidine (Fig. 2). The effect of a phenyl substituent in reducing fine structure and in obscuring neighboring bands in spectra is well known.[15] The conclusion appears, therefore, to be inescapable that the ditetrazolo[a,c]pyrimidine ring system would not absorb in the vicinity of 280 mμ or higher and that a diazido pyrimidine would absorb in these regions. Accordingly, it is deduced that the compounds are in fact diazidopyrimidines and in particular that the alleged furylditetrazolopyrimidine described by Andrisano is probably 2,4-diazido-6-furylpyrimidine.

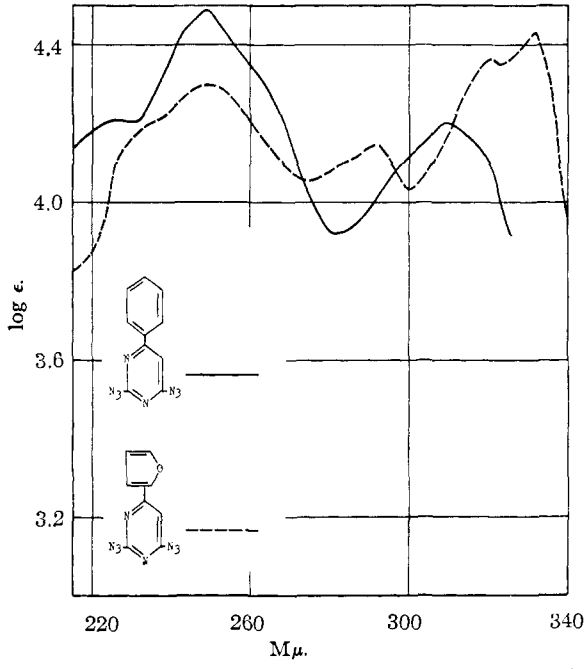


Fig. 2.—Absorption spectra of 2,4-diazido-6-phenylpyrimidine and 2,4-diazido-6-furylpyrimidine in 95% ethanol.

Thermochemical values for guanyl azido nitrate and 5-aminotetrazole nitrate as well as for nitroguanyl azide and 5-nitroaminotetrazole indicate that these imide azides contain about 11 kg. cal./mole more energy than the corresponding tetrazoles.[16] Since these rearrangements were accom-

(15) R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 18-19; Buraway in *Disc. Faraday Soc.*, No. 978 (1950).

(16) W. S. McEwen and M. W. Rigg, THIS JOURNAL, **73**, 4725 (1951).

panied by a liberation of energy, isomerization of the azides obtained in the present work appeared possible. Stollé had effected a conversion of an open chain imide azide to a 1,5-disubstituted tetrazole merely by refluxing in alcohol.[4] Efforts were made, therefore, to effect isomerization of these azides to ditetrazolo[a,c]pyrimidines, or at least to monotetrazolomonoazidopyrimidines. These experiments involved refluxing in ethyl alcohol, in *n*-butyl alcohol, in tertiary amyl alcohol, as well as repeated melting and remelting. In all cases unchanged diazide was recovered. On refluxing in pyridine, the compound was completely destroyed, no isolatable product being secured. Similarly, refluxing with sodium bicarbonate solution destroyed the compound. It is evident that considerable reluctance to form a ditetrazolo[a,c]pyrimidine ring system exists.

Experimental

All melting points are uncorrected.

2,4-Diazido-6-furylpyrimidine from 2,4-Dichloro-6-furylpyrimidine and Sodium Azide.—2,4-Dichloro-6-furylpyrimidine[17] (2 g.) and sodium azide (2 g.) were refluxed in 80 ml. of 3A alcohol for 3 hours on the steam-bath. The product was filtered off and washed with water. The filtrate was evaporated to dryness and the residue washed with water. The combined precipitates were recrystallized from 3A alcohol with charcoal and dried in a vacuum oven at 35–40° overnight. The melting point was 93–93.5° and the yield 1.5 g. *Anal.* Calcd. for $C_8H_4ON_8$: C, 42.11; H, 1.77; N, 49.11. Found: C, 42.39; H, 1.63; N, 49.05.

2,4-Diazido-6-furylpyrimidine from 6-Furyl-2,4-dihydrazinopyrimidine.—6-Furyl-2,4-dihydrazinopyrimidine[3] (1.5 g.) was dissolved in 150 ml. of water and 15 ml. of concentrated sulfuric acid. The solution was chilled in an ice–salt-bath (sulfate precipitated out) and poured into 4.2 g. of sodium nitrite in 35 ml. of water. The precipitate which formed was filtered off and recrystallized from 3A alcohol. The melting point was 93–93.5°; a mixed melting point with the product from the sodium azide preparation was 93–93.5°. The mother liquor was treated with water until no more solid precipitated and then filtered. The melting point was 83–93°. On recrystallization from alcohol the product melted at 93–93.5°. The total yield was 0.4 g.

2,4-Dihydrazinopyrimidine.—2,4-Dichloropyrimidine[18] (6 g.) in 170 ml. of 3A alcohol and 25 ml. of 100% hydrazine hydrate in a 500-ml. round bottom flask were refluxed one hour on the steam-bath. The reaction mixture was chilled in ice and the precipitate formed was filtered off, washed with alcohol and recrystallized from 95% alcohol. The solid (3 g.) melted at 206–207°. Attempts to recrystallize from absolute alcohol proved unsuccessful. The material was very difficult to dissolve and decomposition seemed to take place; the solution turned brown and fractions which seemed to be hydrazine dihydrochloride were obtained. Charcoal could not be used to absorb the brown color since it adsorbed the dihydrazinopyrimidine as well. When the alcohol was diluted with a little water the product dissolved readily. In most cases precipitation had to be induced by scratching. *Anal.* Calcd. for $C_4H_8N_8$: C, 34.28; H, 5.75; N, 59.97; equiv. wt., 70. Found: C, 34.34; H, 5.79; N, 60.35; equiv. wt., 139. It is evident that only one of the hydrazine groups is titratable.

2,4-Diazidopyrimidine from 2,4-Dihydrazinopyrimidine.—2,4-Dihydrazinopyrimidine (1.4 g.) was dissolved in 200 ml. of water and 15 ml. of acetic acid and chilled to 5°. To this solution was added 2.8 g. of sodium nitrite in 50 ml. of cold water. The temperature rose several degrees and most of the sodium nitrite was added before getting a positive test for nitrous acid. Needles appeared on standing in an ice–salt-bath. These were filtered and recrystallized from water to which a small amount of alcohol was added. After solution, the alcohol was evaporated off on a hot-plate and the solution chilled. Crystals appeared having a melting point of 92°, which gave no depression in mixed melting point determination with diazide from the hydrazoic acid preparation. The mother liquor from the original crystals was evaporated and chilled giving additional crystals.

2,4-Diazidopyrimidine from 2,4-Dichloropyrimidine and Sodium Azide.—2,4-Dichloropyrimidine (19 g., 0.13 mole) and sodium azide (25 g.) were refluxed in 700 ml. of 3A alcohol in a one-liter round-bottom flask for 3 hours on the steam-bath. The mixture was cooled, the salt filtered off and the filtrate evaporated to dryness at room temperature. The crude material was recrystallized from 250 ml. of 20% acetone with charcoal. The product was dried in a vacuum oven at 35–40° for 20 hours. The yield was 10.3 g. Evaporation of the mother liquor and recrystallization of the product gave an additional 1.5 g. The total yield was 11.8 g. (56% of theoretical). The melting point was 92–92.5°.

Anal. Calcd. for $C_4H_2N_8$: C, 29.63; H, 1.25; N, 69.12. Found: C, 29.90; H, 1.02; N, 68.70.

2,4-Diazidopyrimidine from 2,4-Dichloropyrimidine and Hydrazoic Acid.—2,4-Dichloropyrimidine (8 g., 0.055 mole) and 80 cc. of 15% hydrazoic acid in benzene (*ca.* 0.24 mole) were heated in a soda bottle on a steam-bath overnight. The salt was filtered off and the filtrate evaporated to dryness. The residue was washed with four portions of petroleum ether and then recrystallized from 20% acetone with charcoal and dried in a vacuum oven at 40° for 5 hours. The solid (about 3 g.) melted at 92° and proved to be the diazide.

The petroleum ether washings were evaporated to dryness leaving white crystals with a naphthalenic odor, the color turning pink on standing in the sun. (The azide has a sharp odor and turns yellow.) The yield was about 1.5 g. A small amount of the residue was heated in water and filtered. The water-soluble fraction turned yellow and the water insoluble turned pink. Melting points showed neither fraction to be pure. Another small amount was washed twice with hot water, dissolved in acetone and chromatogrammed through alumina. A yellow band formed in the alumina. The same yellow band was obtained when ethyl acetate was used as a solvent. When yellow diazide was chromatogrammed no color was removed. The acetone was evaporated to dryness giving crystals which turned pink in the sun. These were dissolved in acetone, treated with charcoal and then most of the acetone evaporated off. When almost dry the crystals were filtered off and dried; the melting point was 97.5–98.5°; a mixed melting point with diazide gave 79–85°. *Anal.* Found for naphthalenic-like substance: C, 26.27; H, 0.99; N, 54.12. Calcd. for 2,4-diazidopyrimidine ($C_4H_2N_8$): C, 29.63; H, 1.25; N, 69.12. Calcd. for azidomonochloropyrimidine ($C_4H_2N_6Cl$): C, 28.33; H, 1.19; N, 49.57.

2,4-Diazido-6-methylpyrimidine.—2,4-Dichloro-6-methylpyrimidine[19] (12.5 g., 0.077 mole) and 15 g. of sodium azide were refluxed in 600 ml. of 3A alcohol for 3 hours. After standing overnight a mixture of small white crystals and large yellow ones separated out. They were filtered and washed with water to remove salt. The filtrate was evaporated under reduced pressure, the precipitate being removed from time to time and washed with water. The crude product was recrystallized twice from 3A alcohol. The solid weighed 8 g. and melted at 126–126.5°. Evaporation of mother liquor yielded about 2 g. more of crude product.

Anal. Calcd. for $C_5H_4N_8$: C, 34.09; H, 2.29; N, 63.62. Found: C, 34.13; H, 2.10; N, 63.66.

2,4-Diazido-6-phenylpyrimidine.—A mixture of 2,4-dichloro-6-phenylpyrimidine[20] (13 g., 0.058 mole) and 17.5 g. of sodium azide was refluxed in 450 ml. of 3A alcohol for 3 hours, cooled and filtered. The precipitate which formed in the filtrate was filtered off and the filtrate evaporated to dryness. Both precipitates were washed thoroughly with water to remove salt, then combined and recrystallized from 3A alcohol with charcoal. After drying under vacuum the pure product (8.5 g.) melted at 92.5–93.5°. *Anal.* Calcd. for $C_{10}H_6N_8$: C, 50.42; H, 2.54; N, 47.04. Found: C, 50.48; H, 2.45; N, 46.72.

Treatment of Diazides with Sodium Ethoxide (Table II).—The sample was refluxed in excess sodium ethoxide solution for 5 hours. After evaporation of the alcohol, the residue

(17) R. Andrisano, *Gazz. chim. ital.*, **77**, 502 (1947).

(18) D. J. Brown, *J. Soc. Chem. Ind.*, **69**, 353 (1950).

(19) S. Gabriel and J. Colman, *Ber.*, **32**, 1533 (1899).

(20) E. Warmington, *J. prakt. Chem.*, [2] **47**, 205 (1893).

TABLE II

TESTS FOR AZIDE GROUP

Pyrimidine	Sodium ethoxide test: Sample, wt.	Hydrazoic acid, meq. Found	Calcd.	Theory, %	Tetralin test: Sample, wt.	Nitrogen, ml. Found	Calcd.	Theory, %
2,4-Diazido	1.00	12.8	12.4	103	1.00	245	276	88
2,4-Diazido-6-methyl	0.50	3.6	5.7	63	1.00	249[a]	254	98
2,4-Diazido-6-phenyl	0.50	3.5	4.2	82	0.44	78	83	94
2,4-Diazido-6-furyl	0.50	5.6	4.4	127[b]	0.35	70	69	101

[a] The first 150 ml. was collected in 10 minutes, the remainder in 6 hours, compared to a total of about 15 minutes for the other samples. The slow rate of decomposition may account for the low results in the sodium ethoxide test. [b] The furyl ring is opened by dilute acids and the resulting hydroxyl group oxidized to an acid under oxidizing conditions. Such formation of acid and its steam distillation would account for the high results.

was treated with dilute sulfuric acid followed by steam distillation of the hydrazoic acid formed; collection of the distillate was made in excess 0.1 *N* NaOH, which was then back titrated with 0.1 *N* HCl. The distillates were tested qualitatively with ferric chloride and in all cases were found to contain azide.

Decomposition of Diazides in Tetralin.—The samples were heated in tetralin (about 25 ml./g.) to 200°, and held there until no appreciable amount of gas was given off. In a blank run 5 ml. of gas was collected and this was subtracted from all results.

Attempts to Convert Diazides to Ditetrazoles (2,4-Diazidopyrimidine Was Used in All Experiments).—Diazide (0.8 g.) was refluxed in 30 ml. absolute alcohol overnight. On evaporation of the alcohol only the unchanged diazide was recovered.

Diazide (1.0 g.) was refluxed in 30 ml. of *t*-amyl alcohol for 8 hours; no gas was given off. On evaporation of the alcohol only the diazide was obtained.

Diazide (1.0 g.) was refluxed in *n*-butyl alcohol for 6 hours. On evaporation of the alcohol only the diazide was recovered.

About 0.1 g. of diazide and 2 g. of $NaHCO_3$ in 40 ml. of water refluxed for 3 hours. A very slight dark brown precipitate formed. The mixture was filtered and the filtrate evaporated to dryness. All efforts to isolate azide from this residue were unsuccessful. Similar results were obtained when pyridine was used.

All absorption spectra were determined using a Model DU Beckman spectrophotometer. The following list tabulates the concentrations used for each wave length region. The absorption spectra were determined in 95% ethanol.

Compound	Concn., moles/l.	Wave length, mμ
m-Diazidobenzene	2.2×10^{-5}	210–270
	1.8×10^{-4}	270–310
2,4-Diazidopyrimidine	8.3×10^{-5}	265–310
	4.1×10^{-5}	210–310
2,4-Diazido-6-methylpyrimidine	3.4×10^{-5}	215–290
	6.8×10^{-5}	215–225 and 255–300
2,4-Diazido-6-phenylpyrimidine	2.45×10^{-5}	215–325
	4.9×10^{-5}	270–330
2,4-Diazido-6-furylpyrimidine	2.4×10^{-5}	215–340

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF IRWIN, NEISLER & COMPANY]

Bis-ammonium Salts. Derivatives of Fluorene, Carbazole and Phenothiazine

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A series of bis-quaternary salts of the type, $R'-\overset{R}{\underset{R}{\overset{|\oplus}{N}}}-(CH_2)_x-\overset{R}{\underset{R}{\overset{|\oplus}{N}}}-R'\ 2Br^{\ominus}$, in which x = 6 or 10, R = methyl or ethyl and R′ is benzhydryl, 9-fluorenyl, 2-fluorenyl, 9-fluorenylethyl, 9-carbazylethyl, or 10-phenothiazinylethyl has been prepared. Quaternization of bis-(dialkylamino)-alkanes with benzhydryl bromide and 9-bromofluorene proceeded in excellent yield provided that solvolytic conditions were avoided. The compounds have been examined for neuromuscular blocking action, and several found to possess considerable activity. In particular, the bis-9-fluorene derivatives, IV and VI, in which x is 6, were unusually potent. The biological data are interpreted in terms of possible structure–activity relationships, and the enhancing effect of the large, planar, lipophilic 9-fluorenyl group on the neuromuscular blocking activity of bis salts is indicated.

During the past five years, a very large number of synthetic neuromuscular blocking agents have been reported and excellent reviews of the subject are available.[1-4] With very few exceptions, the most active compounds contain two quaternary nitrogen atoms situated at a maximum distance from one another of approximately 15 Å. Compounds with more than two quaternary groups appear to depend for high activity upon an optimum steric relationship between two of these groups.[5] With monoquaternaries, only in a series of quinone derivatives have compounds as active as the related bis quaternaries been reported.[6]

In the present report, a series of α,ω-bis-quaternary substituted alkanes is described in which the groups bound to each of the quaternary nitrogen atoms consist of two methyl or ethyl groups and one larger substituent of lipophilic character.

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