TABLE I

Compound	R	Yield, %	M.P., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
I	n-C_4H_7	23	97	41.28	40.94	4.95	5.17	20.64	20.38
I	i-C_3H_7	16	98	41.28	41.42	4.95	5.11	20.64	20.75
II	CH_3	85	215–216	34.00	34.32	2.85	3.01	15.86	15.38
II	$C_6H_5CH_2$	99	207–208	52.27	52.43	3.95	4.01	11.09	11.34
III	CH_3	96	41–42	30.77	31.15	2.05	2.42	14.36	15.02
V	CH_3	90	191	41.85	41.54	4.68	4.82	16.27	16.01
VI	CH_3	75	132	66.21	66.42	5.23	5.41	18.17	17.94

obtained by the previously reported procedures. The reaction of dichloro compound (III) (1 mole) with aniline (2 moles) gave the 4,6-dianilino compound (VI).

Lythgoe *et al.*[3] pointed out that the reaction of 2-methylthio-4-chloro-6-aminopyrimidine (I, R $=CH_3$) with nitrous acid did not give the 5-nitrosopyrimidine, but they did not confirm that I (R$=CH_3$) gave the 6-pyrimidinol (II, R$=CH_3$). We found that both 2-methylthio-4-methoxy-6-aminopyrimidine (IV, R = CH_3),[4,5] and 2-alkylthio-4-chloro-6-aminopyrimidine (I),[4,6] when treated with sodium nitrite, gave a good yields of the corresponding 6-pyrimidinols (II, V). The preparation of II (R = CH_3) from III (R = CH_3) has been reported by Koppel *et al.*[1]

The methoxylation of compound I (R = CH_3) with sodium methoxide at 120° gave IV (R = CH_3), but compounds II did not give V by the same method at 120–160°. The 6-pyrimidinols II and V showed strong infrared absorption at 1660 cm.$^{-1}$.

Table I lists the data obtained with the above compounds.

EXPERIMENTAL

2-Alkylthio-4-chloro-6-aminopyrimidine (I). The compound I (R = CH_3) was made by previously described procedures.[4] Compounds I (R= $C_6H_5CH_2$, n-C_3H_7, i-C_3H_7) were synthesized in the presence of dimethylaniline.[6]

2-Methylthio-4-methoxy-6-aminopyrimidine (IV, R = CH_3).[5] A 5.0-g. sample of 2-methylthio-4-chloro-6-aminopyrimidine was dissolved in 50 ml. of methyl alcohol to which 1.2 g. of metallic sodium had previously been added. The mixture heated in a sealed vessel at 120° for 3 hr. The alcohol was removed by evaporation under reduced pressure and the residue was stirred with water and mixture was acidified with hydrochloric acid and filtered. The white residue was recrystallized from aqueous alcohol; yield 4.4 g.

2-Alkylthio-4-chloro(or methoxy)-6-pyrimidinols (II, V). To the 6-aminopyrimidines (I, V) (1 mole) dissolved in a minimal amount of glacial acetic acid was gradually added an excess of sodium nitrite (2 moles) at room temperature. During the addition the temperature was maintained at room temperature. The reaction mixtures were allowed to stand at room temperature for 40 hr. with occasional stirring and then filtered to give light-yellow solids. The crude products were recrystallized from aqueous alcohol. Yields and analyses are given in Table I.

2-Methylthio-4,6-dichloropyrimidine (III). Dimethylaniline (3.5 g.) was added to a suspension of 2-methylthio-4-chloro-6-pyrimidinol (5.0 g.) in phosphoryl chloride (50 ml.) and heated at boiling point for 2 hr. After removal of the excess of phosphoryl chloride under reduced pressure, the reaction mixture was poured on ice (100 g.) and filtered. The precipitate was extracted with three 100-ml. portion of ether, each of which was then used to extract the aqueous filtrate. The combined ether extract was washed with three 50-ml. portion of water and dried over anhydrous sodium sulfate. Upon evaporation of ether, crude crystals (5.0 g.) were obtained, m.p. 38–39°. After one recrystallization from aqueous alcohol, the m.p. was 41–42°.

2-Methylthio-4,6-dianilinopyrimidine (VI).—A mixture of 2-methylthio-4,6-dichloropyrimidine (1 g.), aniline (0.9 g.), glacial acetic acid (25 ml.), and concentrated hydrochloric acid (2 ml.) was heated at refluxing temperature for about 4 hr. The resulting solution was treated with charcoal for decolorization and filtered hot. The desired product precipitated partially on cooling, but for complete precipitation the solution was neutralized with 10*N* sodium hydroxide. The precipitate was filtered, thoroughly washed with water, and crystallized from 60% alcohol. Yield and analyses are given in Table I.

Acknowledgment. Thanks are due to the Microanalyst of the Department of Chemistry, Tohoku University, and the Spectral Operator of the Chemical Research Institute of Non-Aqueous Solution, Tohoku University, for their technical assistance.

DEPARTMENT OF AGRICULTURAL CHEMISTRY
FACULTY OF AGRICULTURE
TOHOKU UNIVERSITY
KITA-6-BANCHO, SENDAI
JAPAN

(3) B. Lythgoe, A. R. Todd, and A. Topham, *J. Chem. Soc.*, 1944, 315.

(4) T. B. Johnson and C. O. Johns, *Am. Chem. J.*, 34, 175 (1905).

(5) C. O. Johns and B. M. Hendrix, *J. Biol. Chem.*, 20, 153 (1915).

(6) British Patent 744,867 (1956); *Chem. Abstr.*, 51, 2063i (1957).

Azo and Hydrazo Compounds. I. An Attempt to Prepare the *N*-Oxide of 3,6-Diphenyl-1,2,4,5-tetrazine

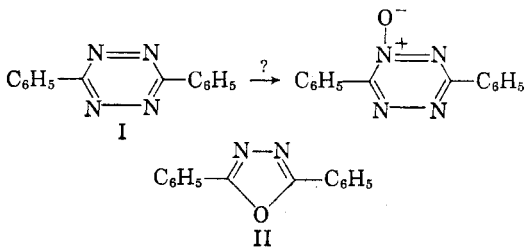
JOAN ALLEGRETTI,[1] JOHN HANCOCK, AND R. STEPHEN KNUTSON[1]

Received November 13, 1961

As part of an over-all study of new preparations and reactions of azo compounds, the synthesis of

(1) NSF Undergraduate Research Assistants, projects G12240 and G15694.

the *N*-oxide of a tetrazine was attempted—more particularly that of 3,6-diphenyl-1,2,4,5-tetrazine, which is fairly readily available. *N*-Oxides of this type have apparently not been described before, although several analogs are known in the triazine series.[2]



The starting material I, prepared by an improved method,[3] was allowed to react with an excess of peracetic acid at 50–60°: the initial red-purple color of I disappeared giving a colorless solution, from which 2,5-diphenyl-1,3,4-oxadiazole[4] (II) was isolated in good yield.

EXPERIMENTAL

1,2-Dihydro-3,6-diphenyl-1,2,4,5-tetrazine.[3] Ethyl benzimidoate hydrochloride was first prepared by passing dry hydrogen chloride through a cooled (ice bath) stirred mixture of benzonitrile (165.0 g.) and absolute ethanol (93.0 g.) until an increase in weight (91.0 g.) had occurred. The mixture was allowed to stand overnight at 3–5°, and the almost solid contents filtered under suction, washed with cold ethanol, then with ether, and dried *in vacuo* over phosphorus pentoxide. A second crop was collected from the filtrate: total yield, 182 g. (61%).

The dihydrotetrazine was prepared in the next step. To a stirred mixture of hydrazine hydrate (99–100%, 13.0 g.) in water (68.5 ml.) was gradually added the above benzimidoester hydrochloride (46.5 g.). Ethanol (37.5 ml.) was added and the mixture heated with stirring on the steam bath for 1 hr. (material began to precipitate after about 15 min.). The mixture was cooled in ice water, filtered, and the yellow residue washed successively with water, methanol, and ether. The dihydrotetrazine was oxidized (partially) to the red tetrazine on exposure to air when traces of solvent were present, but was more stable when dry. Additional material was obtained from the filtrate, and a total yield of 25.5 g. (76%) was obtained, m.p. (*in vacuo*), 183°. If the m.p. were determined in an open capillary, the substance turned red and melted at 191° (the m.p. of the parent tetrazine).

If the heating of the reaction mixture on the steam bath were prolonged (*e.g.*, to 20 hr., as in the original directions of Carboni and Lindsey[3]), then some of the dihydrotetrazine isomerized[5] to 4-amino-3,5-diphenyl-1,2,4,4*H*-triazole[8] (m.p. 264°), which could be isolated by a rather tedious fractional crystallization. The product as prepared above seemed to be free of this impurity (as determined by infrared analysis).

Oxidation of the dihydrotetrazine to the tetrazine. This followed very closely the method of Carboni and Lindsey[3,9]; the reaction seemed to be practically instantaneous. When dihydrotetrazine was used which was contaminated with the isomeric aminotriazole, the latter was oxidized to the colorless 3,5-diphenyl-1,2,4-triazole[10] m.p. 191°.

Oxidation of 3,6-diphenyl-1,2,4,5-tetrazine. To the tetrazine (1.00 g.) was added a mixture of peracetic acid (40% solution, 30 cc.) which had been buffered[11] to pH 5 with 3.0 g. of hydrated sodium acetate: the heterogeneous mixture was stirred at 50–60° for 24 hr., during which time there was feeble effervescence, and after which time all color had disappeared. Dilution of the mixture with water gave a colorless solid (0.70 g., 84%) which was shown to be 2,5-diphenyl-1,3,4-oxadiazole by infrared analysis and melting point comparisons with an authentic sample.[4]

Acknowledgment. We are very grateful to Dr. R. A. Carboni, E. I. du Pont de Nemours and Co., Inc., for having given us instructions for preparing 1,2-dihydro-3,6-diphenyl-1,2,4,5-tetrazine and the corresponding tetrazine. Messrs. Becco, Inc., supplied us with the peracetic acid free of charge. We wish to thank Mr. Guido Faux for early contributions to the general project, and the National Science Foundation, together with the donors of the Petroleum Research Fund (administered by the American Chemical Society), for financial support.

REED COLLEGE
PORTLAND 2, ORE.

(2) *Cf.*, for example, H. v. Euler, H. Hasselquist, and O. Heidenberger, *Chem. Ber.*, **92**, 2266 (1959).

(3) Based on that of R. A. Carboni and R. V. Lindsey, Jr., *J. Am. Chem. Soc.*, **81**, 4342 (1959); R. A. Carboni, private communication.

(4) T. Ikeda, S. Kanahara, and N. Nishikawa, *Ann. Rept. Fac. Pharm., Kanazawa Univ.*, **6**, 1 (1956); *Chem. Abstr.*, **51**, 3609^a (1957).

(5) Rearrangements of this type account for (a) confusion in the early literature[6] regarding structures of the products, and (b) the very low yields of dihydrotetrazines obtained when attempts were made to prepare them directly by heating hydrazine with various nitriles.[7]

(6) Compare the excellent account of the chemistry of 1,2,4,5-tetrazines in J. G. Erickson, P. F. Wiley, and V. P. Wystrach, "The Chemistry of Heterocyclic Compounds," Interscience, New York, 1956, Vol. 10, pp. 179–249.

(7) E. Müller and L. Herrdegen, *J. prakt. Chem.*, (2), **102**, 113–155 (1921).

(8) *Cf.* "Beilsteins Handbuch der Organischen Chemie," Vierte Auflage, Hauptwerk, **26**, 83.

(9) *Idem*, *J. Am. Chem. Soc.*, **80**, 5795 (1958).

(10) Ref. 8, p. 81.

(11) In original experiments this was omitted; however, it is known[7] that strong acids can cause transformation of diphenyltetrazine to the diphenyloxadiazole encountered in this work. In later experiments the buffer was added to obviate this possibility, since commercial peracetic acid can contain appreciable quantities of sulfuric acid. However, the addition of buffer seemed to have no effect on the reaction product.

3,4-Dihydroxyphenacyl Chloride Quaternary Salts of Heterocyclic Nitrogen Compounds[1]

CARL TABB BAHNER AND HAROLD KINDER

Received October 23, 1961

An early indication,[2] which was not confirmed by subsequent testing, that *N*-(3,4-dihydroxy-

(1) This research was supported by a research grant from the National Institutes of Health, U. S. Public Health Service.