reaction of the oxadiazole with two moles of methylamine) pumped off and 7.00 g. (95%) of 1,2-bis(N-methylperfluorobutyrimidoyl)hydrazine removed. After recrystallization from toluene, the product melted at 105.0–105.8°.

This product also was prepared in 93% yield by allowing 2,5-bis(perfluoropropyl)-1,2,4-oxadiazole to react with refluxing methylamine for 2 hr.

1,2-Bis(N-methylperfluoropropionimidoyl)hydrazine and 1,2-Bis(N-methylperfluoroacetimidoyl)hydrazine.—These two compounds were prepared by either method described for 1,2-bis(N-methylperfluorobutyrimidoyl)hydrazine. 1,2-Bis(N-methylperfluoropropionimidoyl)hydrazine was obtained in quantitative yield, m.p. 94.5–95.0°, as was 1,2-bis(N-methylperfluoroacetimidoyl)hydrazine, m.p. 99.0–99.5°.

3,5-Bis(perfluoropropyl)-4-methyl-1,2,4,4*H*-triazole.—1,2-Bis-(N-methylperfluorobutyrimidoyl)hydrazine, 3.0 g. (0.0066 mole), was placed in an 8-in. test tube, equipped with side arm and drying tube, and mixed with 3.0 g. of phosphorus pentoxide. A water-cooled cold-finger condenser was fitted in the reaction tube and the reaction mixture heated at 80–85° for 4 hr. A white, flaky solid, 3,5-bis-(perfluoropropyl)-4-methyl-1,2,4,4*H*-triazole, 2.4 g. (88%), m.p. 47.5–48.0°, was deposited on the condenser and sides of the reaction tube.

3,5-Bis(perfluoroethyl)-4-methyl-1,2,4,4*H*-triazole and 3,5-Bis(perfluoromethyl)-4-methyl-1,2,4,4*H*-triazole.—These two compounds were prepared by the procedure described for 3,5-bis(perfluoropropyl)-4-methyl-1,2,4,4*H*-triazole. 3,5-Bis(perfluoroethyl)-4-methyl-1,2,4,4*H*-triazole was obtained in 94% yield, m.p. 49.5–50.0°. 3,5-Bis(perfluoromethyl)-4-methyl-1,2,4,4*H*-triazole was distilled from the reaction mixture as a liquid (93% yield), b.p. 199.5–200°; d^{25} 1.613; n^{25} 1.3647.

1-(Perfluorobutyrimidoyl)-2-(N-methylperfluorobutyrimidoyl)hydrazine.—1-(Perfluorobutyrimidoyl)-2-(perfluorobutyryl)hydrazine (1.65 g., 0.0039 mole) was placed in a 50-ml. round-bottom flask equipped with a Dry Ice reflux condenser and 10 ml. of ethyl alcohol added. The reaction solution was frozen in liquid nitrogen, the flask pumped free of air, and excess methylamine condensed in the flask. The mixture was allowed to warm to the reflux temperature of methylamine and refluxed for 3 hr. at atmospheric pressure. Unchanged methylamine was removed under reduced pressure to give a white solid product. Recrystallization from toluene yielded 1.50 g. (90%) of 1-(perfluorobutyrimidoyl)-2-(N-methylperfluorobutyrimidoyl)hydrazine, m.p. 122.0–122.5°. Heating this product with an equal weight of phosphorus pentoxide at 150° for 2 hr. resulted in deamination and produced 3,5-bis(perfluoropropyl)-1,2,4-triazole in 80% yield.

Determination of pK_a of the Triazoles.—3,5-Bis(perfluoromethyl)-1,2,4-triazole, 0.0162 g., was dissolved in a mixture of 4 ml. of water (freshly distilled, free of carbon dioxide) and 4 ml. of dioxane (free of peroxides and acid). The solution was titrated with 0.0100 *N* sodium hydroxide and the pH determined by the potentiometric method. The change in pH was very rapid near the end point, and the curve had the characteristic shape of a strong acid–strong base titration. The pK_a value of 3.0 was taken from the curve at the point where one half of the triazole had been neutralized (where pH = pK_a). The molecular weight found by titration was 197; the calculated value is 205.

Titrations of 3,5 bis(perfluoroethyl)-1,2,4-triazole and 3,5-bis(perfluoropropyl)-1,2,4-triazole were carried out by the same procedure. The pK_a values of these two compounds were 2.72 and 3.10, respectively. Molecular weights found by titration were 304 (calcd. 305) and 395 (calcd. 405).

Acknowledgment.—The authors are indebted to Dr. Wallace S. Brey of the University of Florida for the n.m.r. measurements and interpretations.

1,2,4-Triazoles. VI.[1] The Synthesis of Some *s*-Triazolo[4,3-*a*]pyrazines

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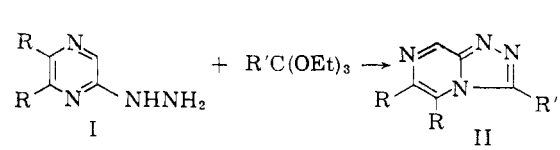
A series of *s*-triazolo[4,3-*a*]pyrazines has been synthesized by ring closure of 2-hydrazinopyrazines with ortho esters, a method superior to that of acidic cyclodehydration. The structures of several interesting by-products obtained in these reactions are discussed.

Of the two possible ring systems formed by the fusion of an *s*-triazole nucleus with a pyrazine nucleus, only one is known and that in the form of its benzo derivative, *s*-triazolo[4,3-*a*]quinoxaline.[3] This communication describes the preparation of the parent ring system itself, *s*-triazolo-[4,3-*a*]pyrazine, and several alkyl and aryl substituted members of this system.

The most efficient method of synthesis of the *s*-triazolo[4,3-*a*]pyrazine ring system (II) was found to be the ring closure of 2-hydrazinopyrazines (I) with ortho esters, a method analogous to the cyclization of 2-hydrazino derivatives of the pyridazine, pyrimidine, and quinoxaline ring systems to the corresponding fused *s*-triazole derivatives with these reagents.[3,4]



I II

The hitherto unknown 2-hydrazinopyrazines were readily prepared in good yield from the cor-

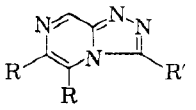
(1) Part V, K. T. Potts and T. H. Crawford, *J. Org. Chem.*, **27**, 2631 (1962).

(2) Department of Chemistry, University of Louisville.

(3) Den-itsu Shiho and S. Tagami, *J. Am. Chem. Soc.*, **82**, 4044 (1960).

(4) C. F. H. Allen, H. R. Beilfuss, D. M. Burness, G. A. Reynolds, J. F. Tinker, and J. A. van Allan, *J. Org. Chem.*, **24**, 787, 793 (1959).

TABLE I



3,5,6-TRISUBSTITUTED *s*-TRIAZOLO[4,3-*a*]PYRAZINES

Compound no.	R	R′	M.p., °C.	Yield, %	Solvent[a]	Formula	Found C	Found H	Found N	Calculated C	Calculated H	Calculated N
1	H	H	194–195	75	a	$C_5H_4N_4 \cdot 0.5H_2O$	46.6	4.1	43.0	46.5	3.9	43.4
2	CH_3	H	190	55	d	$C_7H_8N_4$	56.6	5.3	37.4	56.7	5.4	37.8
3	C_6H_5	H	187–188	72	d	$C_{17}H_{12}N_4$	74.8	4.5	20.7	75.0	4.4	20.6
4	H	CH_3	239	78	a	$C_6H_6N_4$	53.7	4.4	41.7	53.7	4.5	41.8
5	CH_3	CH_3	126–127	55	c	$C_8H_{10}N_4 \cdot H_2O$	53.6	6.7	31.2	53.3	6.7	31.1
6	C_6H_5	CH_3	200–201	43	d	$C_{18}H_{14}N_4$	75.4	5.0	19.3	75.5	4.9	19.6
7	H	C_2H_5	158	70	b	$C_7H_8N_4$	57.1	5.4	37.5	56.7	5.4	37.8
8	CH_3	C_2H_5	93–94	52	d	$C_9H_{12}N_4$	61.1	6.9	31.8	61.3	6.9	31.8
9	C_6H_5	C_2H_5	234–5	50	d	$C_{19}H_{16}N_4$	75.7	5.5	18.6	76.0	5.4	18.7

[a] All crystallized as white needles except 2 which separated as rectangular plates. a = methanol; b = benzene; c = petrol; d = benzene–petrol.

TABLE II

PICRATE DERIVATIVES OF 3,5,6-TRISUBSTITUTED *s*-TRIAZOLO[4,3-*a*]PYRAZINES

Compound no.	M.p., °C.	Solvent[a]	Formula	Found C	Found H	Found N	Calculated C	Calculated H	Calculated N
1	177 (decomp.)	a	$C_{11}H_7N_7O_7$	38.1	2.3	28.0	37.8	2.2	28.0
2	136–137	b	$C_{13}H_{11}N_7O_7$	41.7	3.1	25.7	41.4	2.9	26.0
3	145–146	c	$C_{23}H_{15}N_7O_7$	55.6	3.1	19.4	55.2	2.8	19.6
4	156–157	b	$C_{12}H_9N_7O_7$	39.9	2.8	26.7	39.7	2.5	27.0
5	134–135	c	$C_{14}H_{13}N_7O_7 \cdot 0.5C_6H_6$	47.2	3.8	23.3	47.4	3.8	22.8
6	158–159	c	$C_{24}H_{17}N_7O_7 \cdot 0.5C_6H_6$	58.7	3.9	17.3	58.5	3.6	17.7
7	100–101	c	$C_{13}H_{11}N_7O_7$	41.9	3.2	26.0	41.4	2.9	26.0
8	127–128	c	$C_{15}H_{15}N_7O_7$	44.7	4.1	23.8	44.4	3.7	24.2
9	132–133	c	$C_{25}H_{19}N_7O_7 \cdot 0.5C_6H_6$	59.6	3.9	16.9	59.2	3.9	17.3

[a] All crystallized as yellow needles except 2 and 3, which formed orange rhombs and orange rosettes, respectively. a = chloroform; b = benzene; c = benzene–petrol.

responding 2-chloropyrazines[5] by reaction with 98% hydrazine in boiling absolute alcohol (the use of hydrazine hydrate resulted in diminished yields), this method being similar to the well described displacement of the chloro group by ammonia used for the preparation of 2-aminopyrazines.[6] They were characterized as their picrates, which very tenaciously held one half mole of benzene of crystallization.

The *s*-triazolo[4,3-*a*]pyrazines prepared by this method are described in Table I. The ready availability of ortho esters from alkyl cyanides through the corresponding imino ester hydrochlorides[7] allows considerable variation of the substituent at position 3; we are at present extending this method to include more diversified variations of substituents in the pyrazine portion of the ring system. The structures of these products were assigned mainly on the basis of analytical and molecular weight determinations, compatibility of spectral data with such structures, chemical properties, and by analogy with other similar synthetic procedures. All the *s*-triazolo[4,3-*a*]-pyrazines were characterized as their picrates (Table II). We have consistently found that picrates provide a satisfactory means of characterizing *s*-triazole derivatives.[8] They are sometimes difficult to prepare and are often solvated, benzene especially being retained very tenaciously, and are best prepared in benzene solution.

Acidic cyclodehydration agents that were used so successfully in the pyrimidine series[9] were unsatisfactory in this series. 2-Hydrazinopyrazine itself with formic acid gave largely carbonaceous material, and 2,3-diphenyl-6-hydrazinopyrazine formed the corresponding 5,6-diphenyl-*s*-triazolo-[4,3-*a*]pyrazine (compound 3) in only 10% yield. (The use of dimethylformamide as the cyclization agent likewise gave this product in low yield.) Attempted cyclization with an acetic acid–acetic anhydride mixture gave instead of the 3-methyl isomer (compound 6), a complex acetylated product whose structure is discussed later. The cyclization of the corresponding acyl derivatives was also difficult to effect. N-Benzoyl-2,3-diphenyl-6-hydrazinopyrazine was converted into 3,5,6-triphenyl-*s*-triazolo[4,3-*a*]pyrazine (characterized only by spectral data) with phosphorus oxychloride in very minute yield; boiling phenol could not effect

(5) G. Karmas and P. E. Spoerri, *J. Am. Chem. Soc.*, **74**, 1580 (1952).

(6) G. W. H. Cheeseman, *J. Chem. Soc.*, 242 (1960); A. E. Erickson and P. E. Spoerri, *J. Am. Chem. Soc.*, **68**, 400 (1946).

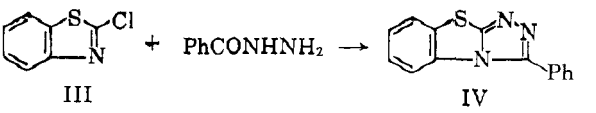
(7) S. M. McElvain and J. W. Nelson, *ibid.*, **64**, 1825 (1924).

(8) K. T. Potts, *J. Chem. Soc.*, 3461 (1954); D. R. Liljegren and K. T. Potts, *ibid.*, 518 (1961).

(9) N. Takahayashi, *J. Pharm. Soc. Japan*, **75**, 1242 (1955).

this cyclization. The action of polyphosphoric acid at 150° for three hours resulted in the formation of a product of as yet undetermined structure in good yield. On the basis of spectral data, we suspect this to be the required triphenyl compound but it has not yet been possible to characterize it completely. The ring closures with acids, and also with orthoesters, can be regarded as occurring through the attack of an intermediate carbonium ion on the nitrogen atom of the pyrazine ring. The ease of cyclization should thus be related to the basic strength of the nucleus. Pyrazine, with a pK_a value of 0.6 compared to that of pyrimidine 1.3, pyridazine 2.3, pyridine 5.2, and trimethylamine 9.8,[10] is a weak mono acid base whose salts are easily dissociated, but which can form a disalt under anhydrous conditions. The polarizations of the carbon-nitrogen double bonds are opposed to each other and the formation of a mono cation in acid solution would tend, by the strong inductive effect, to lower the availability of electrons at the second nitrogen, thus retarding cyclization. [It is interesting to note that 2-hydrazinopyridine is more readily converted into the fused *s*-triazole system with acidic cyclodehydration agents than with the corresponding orthoesters.[11]] However, derivatives of the *s*-triazolo[4,3-*a*]quinoxaline ring system can be obtained in good yields either by the action of acids or ortho esters on the appropriate 2-hydrazino compounds.[3] As the pK_a of the quinoxaline nucleus is also about 0.6, it is difficult to reconcile this ease of cyclization with the basicity of the nucleus. However, the presence of the benzene ring appears to impart special properties to the quinoxaline nucleus. It makes it very susceptible to attack by nucleophilic agents such as sodium bisulfite, hydrogen cyanide, and Grignard reagents which form addition compounds across the carbon-nitrogen double bonds, reactions which do not occur in the pyrazine series.[12] This can be attributed to the electronic influences exerted by the benzene ring. It also enables the second nitrogen to act as though it is not deprived of electrons in the mono cation present in the above acidic cyclodehydrations, so that cyclization occurs with ease.

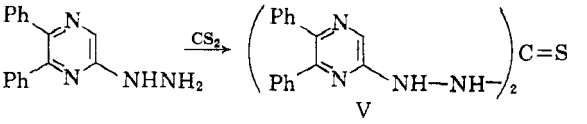
Fused *s*-triazole systems have also been prepared by the direct reaction of benzhydrazide with a suitable heterocyclic system containing a reactive chlorine atom. Thus, from 2-chlorobenzothiazole (III) 3-phenyl-*s*-triazolo[3,4-*b*]benzothiazole (IV) was obtained.[13] Application of this method to the 2-chloropyrazines did not yield the expected *s*-triazolopyrazines but instead self-condensation



III IV

products of benzhydrazide. From the reaction of benzhydrazide with 2,3-diphenyl-6-chloropyrazine in boiling phenol with a trace of sodium phenoxide, the major product isolated was identified as 3,5-diphenyl-*s*-triazole; a second product obtained in small quantities appeared to be 2,3-diphenyl-6-phenoxypyrazine, formed from the chloropyrazine and the small amount of sodium phenoxide added as a catalyst. Similarly, 2,5-diphenyl-1,3,4-oxadiazole was obtained from the reaction of 2,3-dimethyl-6-chloropyrazine with benzhydrazide under these conditions, and from a similar reaction between 2-chloropyrazine and benzhydrazide, dibenzoylhydrazine was formed. Benzhydrazide is a weaker nucleophile than primary amines or hydrazine and its inability to displace the chlorine atom at a faster rate than that at which it undergoes self-condensation at these elevated temperatures[14] may be attributed to this fact. It has been reported that the *s*-triazolo[4,3-*a*]quinoxalines were formed only in very poor yields by the above procedure.[3]

Several other incidental methods used for effecting ring closure of 2-hydrazinopyrimidines were also investigated in this series. With carbon disulfide, a 2-hydrazinopyrimidine gave the *s*-triazolopyrimidine with a mercapto group in the 3-position.[15] However, 2-hydrazinopyrazines did not cyclize under these conditions but gave a product derived from the condensation of two moles of the hydrazine with one of carbon disulfide. Thus the reaction of 2,3-diphenyl-6-hydrazinopyrazine with carbon disulfide yielded 1,3-di(2,3-diphenyl-6-pyrazinylamino)thiourea (V). The formation of this product is analogous to the formation of substituted thioureas from aromatic amines and carbon disulfide,[16] and the fact that di-condensation occurred in preference to ring closure may be also attributed to the low basicity of the pyrazine nucleus.



V

Phenyl isothiocyanate has also been used to obtain fused *s*-triazole systems with a 3-mercapto substituent, but when it reacted with 2,3-diphenyl-6-hydrazinopyrazine, the product isolated in very

(10) A. Albert, R. Goldacre, and J. Phillips, *J. Chem. Soc.*, 2240 (1948).

(11) H. Burton and K. T. Potts, unpublished results.

(12) For pertinent references see: Y. H. Peatt, in Elderfield's "Heterocyclic Chemistry," Vol. VI, John Wiley, New York, 1957, pp. 400, 477; A. Albert, W. L. F. Armarego, and E. Spinner, *J. Chem. Soc.*, 2689 (1961); W. L. F. Armarego, *ibid.*, 561 (1962).

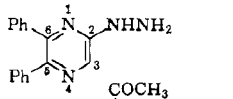
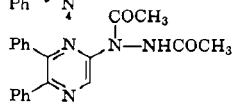
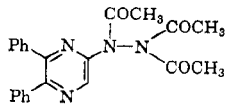
(13) G. A. Reynolds and J. A. van Allan, *J. Org. Chem.*, **24**, 1478 (1959).

(14) D. R. Liljegren and K. T. Potts, *Chem. Ind.*, 2049 (1961); D. R. Liljegren and K. T. Potts, *J. Chem. Soc.*, 518 (1961); K. T. Potts, *Chem. Rev.*, **87**, 100 (1961).

(15) (a) W. Markwald and M. Chain, *Ber.*, **33**, 1900 (1895); (b) C. F. H. Allen, H. R. Beilfuss, D. M. Burgess, G. A. Reynolds, J. F. Tinker, and J. A. van Allan, *J. Org. Chem.*, **25**, 361 (1960).

(16) A. W. Hofmann, *Ann.*, **70**, 142 (1849).

TABLE III

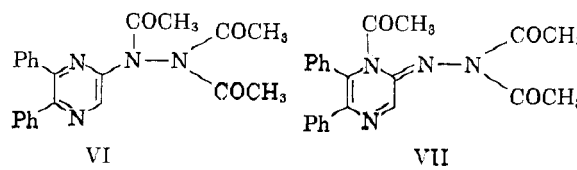
	Ultraviolet data,[a] Maxima		Infrared data,[b] ν Cm.⁻¹				N.M.R. data,[c] τ Values for protons		
	λ	ε	Bonded NH	NH	CO	Amide II	CH_3	Phenyl	C-3
	228	13,000	3390	3279	...	...	...	2.78(10)[d]	1.87(1)[d]
	293	16,000							
	350	7,000							
	229.5	24,900	3333	3252	1709	1471	7.72(3)[d]	2.72(10)[d]	0.78(1)[a]
	285	13,130					7.92(3)[d]		
	326	14,130							
	228	24,000	...	...	1733[e]	...	7.55(6)[d]	2.76(10)[a]	0.78(1)[d]
	283	12,000			1712(sh)		7.71(3)[d]		
	324	12,000							

[a] In ethanol. [b] See ref. 17. [c] See ref. 18. [d] Number of protons. [e] Broad absorption band.

poor yield was identified as 5,6-diphenyl-*s*-triazolo-[4,3-*a*]pyrazine. This elimination of a mercapto group from an *s*-triazole nucleus does not occur readily unless an oxidizing agent[4] or Raney nickel[15b] is present, and it probably occurred in this case during the drastic work-up procedure.

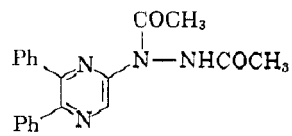
The product obtained from treatment of 2,3-diphenyl-6-hydrazinopyrazine with boiling acetic acid–acetic anhydride was found to be a triacetyl derivative of the hydrazine. Such a compound could be represented by structures VI and VII and, mainly on the basis of the spectral data shown in Table III, structure VI, 1,2,2-triacetyl-1-(2,3-diphenyl-6-pyrazinyl)hydrazine, is the more satisfactory. This triacetyl derivative readily lost an acetyl group and gave a diacetyl compound which was also obtained from the hydrazine and acetyl chloride in pyridine solution. Treatment of the hydrazine with the theoretical amount of acetyl chloride required for monoacetylation always gave this diacetyl product. Two isomeric diacetyl compounds (VIII) and (IX) are also possible; the former is preferred on mechanistic grounds and by analogy with the formation of 1,2-diacetyl-1-phenylhydrazine from 2-acetyl-1-phenylhydrazine and acetic anhydride.[19] The spectral data shown in Table III confirm the assignment of structure VIII to this product. 2-Hydrazinoquinoxaline likewise did not cyclize to the corresponding *s*-triazolo[4,3-*a*]quinoxaline with acetic anhydride but formed a diacetyl product.[3] On the basis of the above evidence this product is probably 1,2-diacetyl-1-(2-quinoxalinyl)hydrazine.

Several interesting features in the n.m.r. data of these compounds are worthy of further comment. The C-3 proton of VI occurs at very low field (τ 0.77) and this can be attributed to the strong deshielding effect[20] of the carbonyl function of the acetyl group attached to N-1. This is very strong evidence against structure (VII) since the carbonyl functions of the two acetyl groups attached to N-2 could not deshield this proton to any extent. Furthermore, this C-3 proton in VII should be similar to a pyridone C-3 proton which has been shown to give a signal at τ 3.43.[21] A further consequence of the deshielding property of this carbonyl function attached to N-1 is the effect it has on the methyl protons of the acetyl groups attached to N-2. These are deshielded to a small extent and result in a signal at lower field.

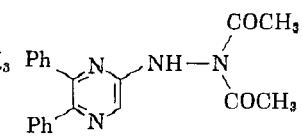


VI

VII



VIII



IX

Experimental[22]

Modified Method of Preparation of 2-Hydroxypyrazine.—A more satisfactory preparative procedure was obtained by varying the original method[5] as follows. The reaction mixtures from three runs were combined and concentrated to a volume of *ca.* 1 l. in a cyclone evaporator and the precipitated 2-hydroxypyrazine was separated and purified by extraction with chloroform in a Soxhlet apparatus. The above mother-liquor was evaporated to dryness in a film evaporator and a further quantity of 2-hydroxypyrazine was extracted from this dried residue with chloroform as above. The 2-hydroxypyrazine (40% yield) crystallized

(17) Measurements were made in 3-mm. cells using a Grubb-Parsons Model S4 double-beam spectrometer, at a concentraton of about 5 mg./ml. We thank Dr. R. A. Jones for these precise measurements.

(18) Determined on a Varian Model HR 60 Instrument in acetonitrile solution (satd. solution) at 60 Mc./sec. and calibrated by side-band technique, using tetramethylsilane as internal standard. We are indebted to Dr. T. H. Crawford for these measurements.

(19) R. Behrend and W Reinsberg, *Ann.*, **377**, 202 (1960); R. L. Hinman and D. Fulton, *J. Am. Chem. Soc.*, **80**, 1895 (1958).

(20) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, 1959, pp. 121–125.

(21) J. A. Elvidge and L. M. Jackman, *J. Chem. Soc.*, 859 (1961).

(22) Petrol refers to the fraction, b.p. 60–80°. All evaporations were carried out under reduced pressure on the water bath and melting point were determined in capillaries. Analyses were carried out by the C.S.I.R.O. Microanalytical Laboratory, Melbourne.

from the chloroform as light fawn needles, m.p. 181–185° (lit.,[6] m.p. 188–190°) and was sufficiently pure for use without further purification.

2-Chloro-5,6-diphenylpyrazine was obtained in satisfactory yield only by the following procedure. 2-Hydroxy-5,6-diphenylpyrazine (75 g.), phosphorus oxychloride (275 ml.), phosphorus pentachloride (75 g.), and several drops of conc. sulfuric acid were heated under reflux for 20 days. The phosphorus oxychloride was evaporated, methanol added, and the slurry filtered. This yielded 75 g. (93%) of crude chloro compound, m.p. 122–124°, raised to 126–127° on recrystallization from methanol (lit.,[5] m.p. 126–127°).

2-Hydrazinopyrazines. General Method of Preparation.—The crude 2-chloropyrazine (0.1 mole), 98% hydrazine (16 ml., 0.5 mole), and absolute ethanol (50 ml.) were heated under reflux for 4 hr. The ethanol was evaporated and the resulting solid recrystallized from benzene. 2-Hydrazinopyrazine (6.6 g., 60%), m.p. 108–110°, on further recrystallization from benzene, separated as cream needles, m.p. 112–113°. No worthwhile quantity of product was isolated from the mother liquor after work-up in the usual way.

Anal. Calcd. for $C_4H_6N_4$: C, 43.6; H, 5.5; N, 50.9. Found: C, 43.7; H, 5.4; N, 50.6.

The *picrate* crystallized from an acetone–petrol mixture as yellow plates, m.p. 155–156° (dec.).

Anal. Calcd. for $C_{10}H_9N_7O_7 \cdot 0.5C_6H_6$: C, 41.1; H, 3.5; N, 25.7. Found: C, 41.3; H, 3.2; N, 26.0.

2,3-Dimethyl-6-hydrazinopyrazine (7.6 g., 54%), m.p. 110–112°, on two recrystallizations from benzene, formed very pale yellow needles, m.p. 119–120°.

Anal. Calcd. for $C_6H_{10}N_4$: C, 52.2; H, 7.3. Found: C, 52.0; H, 7.2.

The **picrate** crystallized from ethanol as yellow needles, m.p. 169–170°.

Anal. Calcd. for $C_{12}H_{13}N_7O_7 \cdot 0.5C_6H_6$: C, 44.4; H, 4.0; N, 24.1. Found: C, 44.0; H, 4.2; N, 23.9.

2,3-Diphenyl-6-hydrazinopyrazine (17.2 g., 69%), m.p. 151–153°, on further crystallization from benzene, formed cream needles, m.p. 154–155°. Ultraviolet spectrum in ethanol: λ_{max} 228, 293, 350 mμ; ε 13,000, 16,000, 7,000.

Anal. Calcd. for $C_{16}H_{14}N_4$: C, 73.3; H, 5.4; N, 21.4. Found: C, 73.4; H, 5.4; N, 21.2.

The **picrate** crystallized from benzene as orange rhombs, m.p. 157° (dec.).

Anal. Calcd. for $C_{22}H_{17}N_7O_7 \cdot 0.5C_6H_6$: C, 56.6; H, 3.8; N, 18.5. Found: C, 56.2; H, 3.9; N, 18.7.

3,5,6-Trisubstituted-*s*-triazolo[4,3-*a*]pyrazines. General Method of Preparation.—The 2-hydrazinopyrazine (1 g.), the ortho ester (3 ml.), and dry xylene (10 ml.) were heated under reflux for 4 hr. All traces of solvent were evaporated and the resulting solid recrystallized from the solvents listed in Table I. The picrates were formed in benzene solution. The concentration of picric acid was sometimes critical and occasionally long heating on a hot plate was required before the picrate separated (compounds 5,6,9). The picrates were recrystallized from the solvents shown in Table II.

Attempted Reaction of Benzhydrazide with 6-Chloropyrazines. (a) The Isolation of 3,5-Diphenyl-1,2-4-triazole.—2,3-Diphenyl-6-chloropyrazine (1.0 g.), benzhydrazide (2.0 g.), and phenol (4.0 g.) containing a trace of sodium phenoxide were heated under reflux for 10 days. The phenol was removed by steam distillation and the remaining water evaporated. The solid residue (0.76 g.), m.p. 175–183°, was chromatographed on alumina (15 g.) using benzene as eluent. Repeated recrystallization of the resulting solid from benzene gave white needles, m.p. 187–189°. This was identified as 3,5-diphenyl-1,2,4-triazole (lit.,[23] m.p. 190°) by mixed m.p. determination and comparison of its infrared spectrum with that of an authentic specimen.[8]

Anal. Calcd. for $C_{14}H_{11}N_3$: C, 76.0; H, 5.0; N, 19.0. Found: C, 76.2; H, 5.1; N, 18.6.

(23) G. Pellizzarri, *Gazz. chim. ital.*, **41**, 20, 93 (1911).

In another experiment carried out on a smaller scale, the first product isolated, after chromatography on alumina in benzene, separated from petrol as small, white, irregular prisms (0.15 g.), m.p. 94–95°. This product is most likely 2,3-diphenyl-6-phenoxypyrazine.

Anal. Calcd. for $C_{22}H_{16}N_2O$: C, 81.5; H, 4.97. Found: C, 81.7; H, 4.93.

(b) The Isolation of 2,5-Diphenyl-1,3,4-oxadiazole.—When 2,3-dimethyl-6-chloropyrazine was used in the above reaction, 2,5-diphenyl-1,3,4-oxadiazole was isolated. It separated from petrol as white needles, m.p. 135–136° (lit.,[24] m.p. 138°). The infrared spectrum was identical with that of an authentic specimen which did not depress the m.p. of the product.

Anal. Calcd. for $C_{14}H_{10}N_2O$: C, 75.7; H, 4.5. Found: C, 75.5; H, 4.6.

(c) The Isolation of Dibenzoylhydrazine.—In the reaction of 2-chloropyrazine (1.0 g.) with benzhydrazide (1.2 g.) as above, the residue left after removing the phenol by steam-distillation was identified as dibenzoylhydrazine, 0.45 g. (51%), m.p. 234–235°. It crystallized from benzene-ethanol as fine, white needles, m.p. 240–241° (lit.,[25] m.p. 240–241°), not depressed on admixture with an authentic sample with which it had an identical infrared spectrum.

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C,70.0; H, 5.0; N, 11.7. Found: C, 70.0; H, 5.1; N, 12.0.

5,6-Diphenyl-*s*-triazolo[4,3-*a*]pyrazine. (a) Ring Closure of the Hydrazine with 98% Formic Acid.—2,3-Diphenyl-6-hydrazinopyrazine (1.0 g., 0.004 mole) and 98% formic acid (15 ml.) were heated under reflux for 3 hr. The formic acid was evaporated and the residue crystallized from benzene–petroleum ether. It separated as a very pale yellow microcrystalline powder, 0.1 g. (10%), m.p. 181–183°. The m.p. was not raised on further recrystallization, but the infrared spectrum was identical with that of the product obtained using ethyl orthoformate as the cyclization agent.

Heating 2-hydrazinopyrazine with formic acid under these conditions, or at 70°, gave mainly a carbonaceous product.

(b) Ring Closure with Dimethylformamide.—2,3-Diphenyl-6-hydrazinopyrazine (0.5 g., 0.002 mole) and dimethylformamide (20 ml.) were heated under reflux for 18 hr. The dimethylformamide was evaporated and the residue recrystallized from benzene–petrol. The pure product (0.01 g., 0.5%), m.p. 187–188°, was identical with the product from the ethyl orthoformate ring closure.

N-Benzoyl-2,3-diphenyl-6-hydrazinopyrazine, prepared from benzoyl chloride and the corresponding hydrazine in the presence of pyridine (15 hr.), separated as white needles (89%) from benzene–petrol, m.p. 189–190°.

Anal. Calcd. for $C_{23}H_{18}N_4O$: C, 75.4; H, 5.0; N, 15.3. Found: C, 75.6; H, 5.0; N, 15.2.

Ring Closure of N-Benzoyl-2,3-diphenyl-6-hydrazinopyrazine. (a) Using Phosphorus Oxychloride.—The benzoyl compound (0.5 g.) and phosphorus oxychloride (5 ml.) were heated under reflux for 2 hr. The reaction mixture was then poured into ice water and the solid material collected. This was identified as starting material. The aqueous phase was neutralized and the precipitated material collected and crystallized from benzene–petrol yielding 7 mg., m.p. 238–239°, of a product whose infrared spectral characteristics indicated that it was most likely 3,5,6-triphenyl-*s*-triazolo-[4,3-*a*]pyrazine.

(b) Using Phenol.—The benzoyl compound (0.4 g.) and phenol (1 g.) were heated and after 18 hr. reflux the phenol was removed by steam distillation. The residue (0.12 g.) crystallized from benzene–petrol as white needles, m.p. 186–187°. Analytical and spectral data identified the product as unchanged N-benzoyl-2,3-diphenyl-6-hydrazinopyrazine.

(24) R. Stollé, *J. prakt. Chem.*, **69** [2], 157 (1904).

(25) R. Stollé and A. Benrath, *ibid.*, **70** [2], 268 (1904); F. Arndt, L. Lowe, and L. Ergener, *Istanbul Univ. Fen Fek. Mecmuasi, Seri A*, **13**, 116 (1948).

Acetylation of 2,3-Diphenyl-6-hydrazinopyrazine. (a) Formation of 1,2,2-Triacetyl-1-(2,3-diphenyl-6-pyrazinyl)-hydrazine.—The hydrazinopyrazine (1.0 g., 0.004 mole), acetic anhydride (2 ml.), and acetic acid (2 ml.) were heated under reflux for 2.5 hr. The acetylation mixture was evaporated and the residue recrystallized from methanol (charcoal) from which it separated as colorless rhombs, m.p. 178–179°. Ultraviolet spectrum in ethanol: λ_{max} 228, 283, 324 mμ; ε 24,000, 12,000, 12,000.

Anal. Calcd. for $C_{22}H_{20}N_4O_3$: C, 68.0; H, 5.2; N, 14.4. Found: C, 68.2; H, 5.3; N, 14.6. Mol. wt.: calcd., 388; found, 400.

(b) Formation of 1,2-Diacetyl-1-(2,3-diphenyl-6-pyrazinyl)-hydrazine.—The hydrazinopyrazine (1.0 g., 0.004 mole), dissolved in dry pyridine (6 ml.), was treated with acetyl chloride (0.4 ml.; 0.004 mole) added dropwise. After 1 hr. at room temp. the reaction mixture was poured into ice water and the resulting solid collected. The crude diacetyl compound (0.85 g.) crystallized from benzene–petrol as small, white needles, m.p. 167–168° and repeated recrystallization was necessary to effect complete removal of the unchanged hydrazine present.

Anal. Calcd. for $C_{20}H_{18}N_4O_2$: C, 69.4; H, 5.2; N, 16.2. Found: C, 69.1; H, 5.2; N, 16.2.

This same product was obtained from the above triacetyl compound by dissolving it in methanol and evaporating the solution to dryness on the water bath. More methanol was added and the diacetyl derivative was first crystallized from methanol and then benzene–petrol. The triacetyl compound also tended to decompose slightly on prolonged boiling in toluene.

Attempted Synthesis of 3-Mercapto-5,6-diphenyl-*s*-triazolo[4,3-*a*]-pyrazine. (a) Using Carbon Disulfide.—2,3-Diphenyl-6-hydrazinopyrazine (1.0 g., 0.004 mole), carbon disulfide (2 ml., 0.025 mole), and pyridine (10 ml.) were heated under reflux until hydrogen sulfide ceased to be evolved (7 hr.). The solvent was evaporated and the residue recrystallized from a tetrahydrofuran–ethanol mixture. 1,3-Di(5,6-diphenyl-2-pyrazinylamino)thiourea separated in poor yield as a pale yellow, microcrystalline solid, m.p. 239–240°.

Anal. Calcd. for $C_{38}H_{26}N_8S\cdot0.5H_2O$: C, 68.8; H, 4.7; N, 19.6; S, 5.6. Found: C, 68.4; H, 4.5; N, 19.3; S, 5.9.

(b) Using Phenyl Isothiocyanate.—The above hydrazine (1.0 g., 0.004 mole), phenyl isothiocyanate (0.7 g., 0.005 mole), and trichlorobenzene (5 ml.) were heated under reflux for 5 hr. The solvent was removed (at 0.05 mm.) and, after attempts at purification by crystallization failed, the residue was sublimed at 150°/0.001 mm. The sublimate crystallized from benzene–petrol as white needles, m.p. 187–188° and was identified as 5,6-diphenyl-*s*-triazolo[4,3-*a*] pyrazine by mixed m.p. determination and comparison of its infrared spectrum with that of an authentic specimen.

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5-Trifluoromethyltetrazole and Its Derivatives

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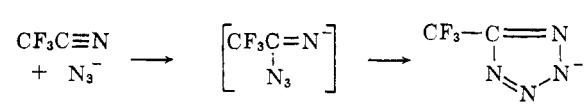
Sodium 5-trifluoromethyltetrazole was readily prepared from trifluoroacetonitrile and sodium azide. The salt was converted to the free tetrazole, which is a strong, stable, organic nitrogen acid, methylated to give 1- and 2-methyl-5-trifluoromethyltetrazole and chlorinated to give N-chloro-5-trifluoromethyltetrazole.

Trifluoroacetonitrile at atmospheric pressure and room temperature reacts exothermally with sodium azide in acetonitrile to give sodium 5-trifluoromethyltetrazole (I). These are the mildest conditions yet reported for the formation of a tetrazole from a nitrile and an inorganic azide.[1,2] The high reactivity of trifluoroacetonitrile is in agreement with the observation[1] that electronegative groups on the nitrile facilitate tetrazole formation; for example, *p*-nitrobenzonitrile, terephthalonitrile, and perfluorocaprylonitrile reacted readily with sodium azide at 100° in dimethylformamide to form 5-substituted tetrazoles. Benzonitriles with more electropositive substituents and aliphatic nitriles required higher temperatures and acid catalysis to give good yields of tetrazole.

These data and the results reported in this paper indicate that more than one mechanism is operating in tetrazole formation from nitriles and inorganic azides. Hence the general mechanism[3] as stated by Henry, Finnegan, and Lofquist[1] may be separated into two mechanisms: (1) In the case of electronegatively substituted nitriles no acid catalyst is needed and the reaction probably proceeds by attack of azide ion on the carbon of the nitrile



group followed by ring closure to give the salt of the tetrazole. The electronegative substituent on the nitrile facilitates initial attack by azide ion and stabilizes the negative charge of the intermediate by its inductive effect. The positively charged

(1) A variety of aromatic and aliphatic nitriles reacted with ammonium azide in dimethylformamide at 95–125° to give 5-substituted tetrazoles. [W. G. Finnegan, R. A. Henry, and R. Lofquist, *J. Am. Chem. Soc.*, **80**, 3908 (1958).]

(2) 5-Substituted tetrazoles were prepared from substituted acetonitriles and aluminum azide in refluxing tetrahydrofuran [H. Behringer and K. Kohl, *Ber.*, **89**, 2648 (1956).]

(3) "The general mechanism for the reaction appears to be a nucleophilic attack of azide ion on the carbon of the nitrile group, followed by ring closure of the imino azide to form the tetrazole ring."[1]