solid, m.p. 209–210° after recrystallization from 99% isopropyl alcohol.

The same product was obtained when 2 g. of 4-*p*-nitrophenylsemicarbazide was boiled under reflux with 50 ml. of acetic anhydride for 20 hr. Since the material was not identical with either V or VI, it was not further characterized.

*B.* Following the technique described by Hoggarth[9] 10 g. of 1-acetyl-4-phenylthiosemicarbazide[16] was dissolved in 50 ml. of *N* sodium hydroxide. A solution of 7.6 g. of methyl iodide in 10 ml. of 99% isopropyl alcohol was added and the mixture shaken thoroughly for 5 min. The precipitate of *S*-methyl derivative was filtered off and air dried, yield 4.2 g. (39%), m.p. 121–124°. The crude *S*-methyl derivative (3 g.) was dissolved in 60 ml. of 99% isopropyl alcohol and boiled under reflux for 20 hr. Evaporation of the solvent gave a small amount of 2-methyl-5-phenylamino-1,3,4-oxadiazole, m.p. 174–175°, dense, pyramidal prisms, after several crystallizations from isopropyl alcohol.

*Anal.* Calcd. for $C_9H_9N_3O$: C, 61.7; H, 5.2; N, 24.0. Found: C, 61.6; H, 5.2; N, 23.9.

The major product of the thermal decomposition was always a sulfur containing material that was soluble in dilute acids but insoluble in bases. The material crystallized from isopropyl alcohol as transparent prisms, m.p. 119–120°. Elemental analysis indicated that the product might be 3-methylmercapto-4-phenyl-5-methyl-1,2,4-triazole.

*Anal.* Calcd. for $C_{10}H_{11}N_3S$: C, 58.5; H, 5.4; N, 20.5; S, 15.6. Found: C, 58.3; H, 5.7; N, 20.7; S, 15.3.

*C.* In an attempt to adapt the procedure of Stollé and Fehrenbach[10] 3.3 g. of 1-acetyl-4-phenylthiosemicarbazide was heated with stirring for 26 hr. with 3.5 g. of lead oxide suspended in 150 ml. of 95% ethanol. The lead oxide failed to darken beyond a faint gray. From the hot ethanolic filtrate 2 g. of a sulfur containing product was isolated, m.p. 217–218° after several crystallizations from 95% ethanol. Elemental analysis and the solubility of the compound in dilute aqueous alkalies suggested that the compound might be 3-mercapto-4-phenyl-5-methyl-1,2,4-triazole. The isomeric 2-methyl-5-phenylamino-1,3,4-thiadiazole structure has already been assigned to a compound, m.p. 193–194°.[11]

*D.* A mixture of 15 g. of 1-acetyl-4-phenylthiosemicarbazide and 15.5 g. of yellow mercuric oxide suspended in 800 ml. of toluene was boiled under reflux with stirring for 20 min. The mercuric oxide darkened rapidly and became black a few minutes after the toluene started to boil. The hot suspension was filtered rapidly. The colorless needles that separated from the filtrate on cooling were recrystallized from 99% isopropyl alcohol, yield 8 g. (64%), m.p. 175°, dense, pyramidal prisms. Mixture m.p. with 2-methyl-5-phenylamino-1,3,4-oxadiazole (see *B* above) not depressed.

Finely powdered 2-methyl-5-phenylamino-1,3,4-oxadiazole (16.8 g.) was added in small portions with stirring to an ice cold mixture of 25 ml. each of concentrated sulfuric and nitric acids. Stirring and cooling were continued until the solid dissolved completely. The nitration mixture was poured onto 400 g. of ice. The yellow, flocculent precipitate was filtered off, washed with water and dried at room temperature under reduced pressure. The crude product (21 g.) was extracted with several portions of cold chloroform. The insoluble portion was recrystallized several times from absolute methanol, pale, yellow needles, m.p. 232–233°. The mixture m.p. with V was not depressed.

The chloroform extracts were evaporated to dryness. The yellow residue was separated manually from a trace of orange material on the sides of the flask and recrystallized several times from absolute methanol, m.p. 218–219°. The product proved to be 2-methyl-5-(2′,4′-dinitrophenylamino)-1,3,4-oxadiazole.

*Anal.* Calcd. for $C_9H_7N_5O_5$: C, 40.8; H, 2.7; N, 26.4. Found: C, 40.7; H, 2.7; N, 26.9.

On hydrolysis of a small amount of the dinitro compound with boiling hydrochloric acid, 2,4-dinitroaniline, m.p. and mixture m.p. 178–180°, separated from the aqueous hydrolyzate. On standing the filtrate deposited crystals of hydrazine dihydrochloride, m.p. 195–200° with gas evolution; benzalazine, m.p. and mixture m.p. 92–93° was formed with benzaldehyde in alcoholic solution.

The 2-methyl-5-*p*-nitrophenylamino-1,3,4-oxadiazole (1.5 g.) synthesized above was acetylated by boiling for 8.5 hr. with 30 ml. of acetic anhydride. After dilution with isopropyl alcohol the reaction mixture was evaporated to dryness on a steam bath. The residue was extracted with chloroform. The chloroform soluble acetyl derivative was recrystallized several times from absolute methanol, m.p. and mixture m.p. with VI 157–159°.

*Anal.* Calcd. for $C_{11}H_{10}N_4O_4$: C, 50.4; H, 3.8; N, 21.4. Found: C, 50.2; H, 3.9; N, 21.6.

EAST LANSING, MICH.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DE PAUL UNIVERSITY]

# Relative Acidities of 5-(Substituted Phenyl)amino-4-phenyl-1,2,3-triazoles

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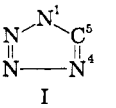
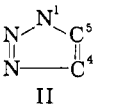
The relative acidities of 5-(substituted phenyl)amino-4-phenyl-1,2,3-triazoles have been studied by ultraviolet absorption spectrophotometry and electrometric titrations in dimethylformamide. The results are in agreement with the electronic mechanism proposed earlier, for the equilibria in the substituted amino tetrazoles and triazoles.

There is considerable evidence that the tetrazole ring, I, is electronegative and about as strongly so as an acetyl group.[1] Considering the electronegativities of carbon and nitrogen, one would expect the 1,2,3-triazole ring, II, to be less electronegative than in the tetrazole ring. One principal difference




I

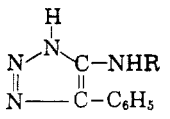



II

between structures I and II is that the latter is able to have different substituents in the 4-position. In this communication a further study of the electrical effects of these two ring systems is reported, involving an investigation of the acidities of 5-(substi-

(1) R. A. Henry, W. G. Finnegan, and E. Lieber, *J. Am. Chem. Soc.*, **77**, 2264 (1955); C. N. R. Rao, *J. Sci. Ind. Research (India)*, **17B**, 89 (1958).

tuted phenyl)amino-4-phenyl-1,2,3-triazoles, III, determined both by ultraviolet absorption spectrophotometry and by electrometric titrations in non-aqueous medium. It will be noted that in structure III, position -4 is maintained constant



III (R = substituted phenyl)

by means of a phenyl group. The influence of position -5 on the acidity of this ring system is discussed.

## EXPERIMENTAL

*5-(Substituted phenyl)amino-4-phenyl-1,2,3-triazoles* (III). The series of III used in the present investigation were prepared by the method reported earlier.[2]

*Spectrophotometric measurements.* The spectrophotometric determination of the acidic dissociation constants of III were determined by a modification of the procedure of Flexser, Hammett, and Dingwall,[3,4] using 18% (by weight) ethanol as solvent. A mixture of water-ethanol had to be used as the solvent because of the extreme insolubility of compounds of type III in water alone. While the presence of ethanol precludes the possibility of obtaining correct absolute thermodynamic values of the $pK_a$, the relative values of the compounds were obtained with a good degree of accuracy. It should also be mentioned that the alkaline solutions of compounds III slowly develop a pink color. All the spectra were recorded using a Cary recording spectrophotometer. The $pK_a$ values obtained by this method are summarized in Table I.

TABLE I

SPECTROPHOTOMETRIC DETERMINATION OF THE ACIDITIES OF 5-(SUBSTITUTED PHENYL) AMINO-4-PHENYL-1,2,3-TRIAZOLES IN 18% ETHANOL

| III; R = | $pK_a$[a] |
|---|---|
| 4-$CH_3OC_6H_4$ | 7.91 |
| 4-$CH_3C_6H_4$ | 7.72 |
| $C_6H_5$ | 7.58 |
| 3-$ClC_6H_4$ | 7.23 |
| 4-$O_2N$-$C_6H_4$ | 6.60 |

[a] A mean of at least three measurements.

*Electrometric titrations in dimethylformamide.* In view of the difficulty of obtaining values of the dissociation constants in water alone, the relative values obtained by ultraviolet spectrophotometry were checked by titrations in dimethylformamide taking the e.m.f. values at the half-neutralization points as a measure of the acidity of the compounds. Advantage was then taken of the fact that a linear relationship can be obtained between the e.m.f. values at the half-neutralization points in a nonaqueous solvent and the $pK_a$ of known substances in water.

Fritz,[5] Hall,[6] and Rochlin[7] have found relationships between the e.m.f. values of half-neutralization points in nonaqueous media and the thermodynamic $pK_b$ values in water. In the present investigation, pure phenol ($pK_a$ = 9.89) and benzoic acid ($pK_a$ = 4.2) were used as standard substances. By assuming a linear relation between the e.m.f. values at the half-neutralization points in dimethylformamide and the $pK_a$ values in water, the $pK_a$ values of the compounds of type III were estimated. These extrapolated values are in reasonable agreement with the values obtained by spectrophotometry.

The procedure described by Fritz[8] using dimethylformamide as solvent and sodium methoxide in 1:6 methanol:benzene as titrant, was employed. The instrumentation comprised of a Bechman *p*H meter fitted with antimony and calomel electrodes. This system gave steady potentials and relatively large breaks at the end point. The results of the electrometric titrations are summarized in Table II.

TABLE II

ELECTROMETRIC TITRATIONS OF 5-(SUBSTITUTED PHENYL)-AMINO-4-PHENYL-1,2,3-TRIAZOLES IN DIMETHYLFORMAMIDE

| III; R = | E.M.F. at the Half-neutralization Point,[a] Mv. | Extrapolated $pK_a$ |
|---|---|---|
| 4-$CH_3OC_6H_4$ | 314 | 8.2$_0$ |
| 4-$CH_3C_6H_4$ | 310 | 7.9$_4$ |
| 3-$CH_3C_6H_4$ | 309 | 7.8$_8$ |
| 4-$ClC_6H_4$ | 308 | 7.8$_0$ |
| 3-$ClC_6H_4$ | 305 | 7.5$_5$ |
| 3-$O_2N$-$C_6H_4$ | 295 | 6.8$_0$ |
| 4-$O_2N$-$C_6H_4$ | 294 | 6.7$_0$ |

[a] Phenol and benzoic acid gave the half-neutralization points at 335 and 261 mv., respectively.

## DISCUSSION

The 5-(substituted phenyl)amino-4-phenyl-1,2,3-triazoles, IV, may be considered either as derivatives of the 1,2,3-triazole ring, II, or as derivatives of aniline, V. Structure IV differs from the corresponding 5-(substituted phenyl)aminotetrazoles, VI, in the substituent in 4-position. Fig. 1 shows a plot of the $pK_a$ values of IV, obtained spectrophotometrically, versus Hammett's sigma-values ($\sigma$)[9] for groups. The extrapolated $pK_a$ values from the electrometric titrations in dimethylformamide also gave a similar linear relation. On the same graph (Fig. 1) are plotted the data previously obtained by Henry, Finnegan, and Lieber[10] for 5-(substituted phenyl)aminotetrazoles (VI) and the monosubstituted anilines (V.)[11] It will be noted from Fig. 1 that the rho-value ($\rho$)[12] for the triazole derivative,

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(12) J. Hine, *Physical Organic Chemistry*, McGraw-Hill Book Company, Inc., New York, N. Y., 1956, page 71.

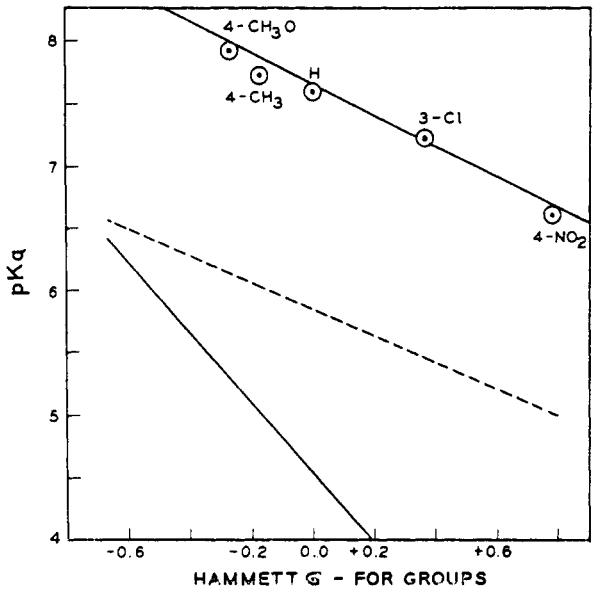


Fig. 1 Correlation of $pK_a$ values with Hammett sigma values of groups ⊙——⊙ 4-phenyl-5-(substituted phenyl) amino-1,2,3-triazoles. - - - - - - - 5-(substituted phenyl) aminotetrazoles. ——Mono-substituted anilines

IV, is similar to that of the tetrazoles. From the previous study by Lieber, Rao, and Chao,[13] it has been concluded that it is the heterocyclic proton rather than the proton on the exo-nitrogen atom that is the source of the acidity of types IV and VI compounds. The correspondence of the rho-values in these two systems is therefore easily understood.

Both IV and VI undergo thermal isomerizations which involve an equilibrium.[1,2,14] A plot of the $pK_a$ values of IV *vs.* the equilibrium constants for IV ⇌ VII at 458°K. in purified ethylene glycol as solvent is essentially linear and similar to the tetrazole system.[10] Generally, as the electronegativity of the substituent increases, the $pK_a$ of IV decreases (Fig. 1) and the position of equilibrium shifts favoring the formation of IV. These results are similar to those obtained for the equilibrium VI ⇌ VIII by Henry, Finnegan, and Lieber.[1] Accordingly, these data confirms the common electronic mechanism suggested[14] for these two equilibria.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

# Nitriles in Nuclear Heterocyclic Synthesis. II

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Reaction of 2,5-dimethyl-2,5-hexanediol, 2,4-dimethyl-2,4-pentanediol, and methallyl mercaptan with nitriles in concentrated sulfuric acid yields $\Delta^1$-pyrrolines, dihydropyridines, and 2-thiazolines, respectively. This new heterocyclic ring-closure has been accomplished with a variety of nitriles.

Previously reported nuclear syntheses of nitrogen heterocycles from nitriles have been limited in number. Dilthey[2] and Janz[3] have succeeded in condensing nitriles with dienes at elevated temperatures. The formation of a dihydroisoquinoline from methyleugenol and veratronitrile was reported by Ritter and Murphy.[4] Quilico[5] and

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