[CONTRIBUTION FROM THE RESEARCH LABORATORIES, TENNESSEE EASTMAN CO., DIVISION OF EASTMAN KODAK CO.]

Azo Dyes from Substituted 2-Aminothiazoles[1]

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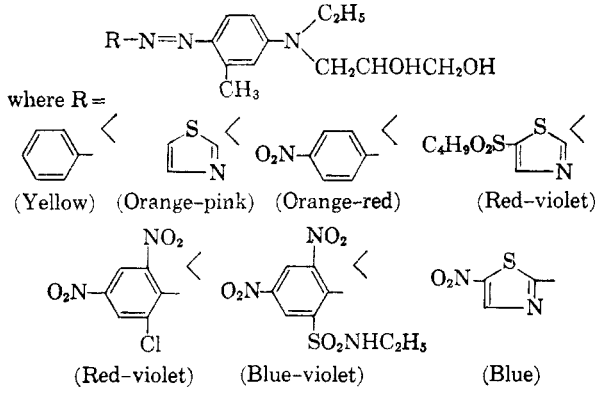
A series of 2-thiazolylazo dyes for cellulose acetate was prepared. Substituents in the 4-position have little effect on the color of 2-thiazolylazo dyes. The color of the dyes containing various groups in the 5-position deepens in the order of increasing negativity of the substituent. Thus, dyes containing the nitro group in the 5-thiazolyl position are blue to greenish blue; these dyes have superior dyeing and fastness properties. The bathochromism of the 2-thiazolylazo dyes is illustrated by comparison of the blue dyes from 2-amino-5-nitrothiazole with dyes from the benzene analog, *p*-nitroaniline; dyes from the latter are red.

The bathochromism of the 2-thiazolylazo dyes is discussed in terms of the influence of the 2-thiazolylazo structure and of substitution on the coupler and diazonium constituents.

The preparation and properties of new 2-aminothiazole intermediates are described. Certain problems encountered in nitration and oxidation reactions are discussed.

This paper concerns the effects of the position and nature of substituents in 2-aminothiazoles on the color of azo dyes prepared from them. Of primary interest is the color shift from the red of azo dyes derived from nitroanilines to the blue of analogous azo dyes[3-5] derived from 2-amino-5-nitrothiazoles. This pronounced shift exhibited by 5-nitro-2-thiazolylazo dyes is illustrated by the following series of azo dyes listed in the order of increasing deepening of color on cellulose acetate. The visible absorption spectra of certain of these dyes are shown in Fig. 1.



The 2-aminothiazoles used in this investigation are listed in Table I. Physical properties and analyses are given for new compounds. Known compounds used are listed with literature references.

2-Aminothiazole and most of its 5-substituted, 4-substituted, and 4,5-disubstituted derivatives were prepared by the reaction of thiourea with the appropriate α-halo aldehyde[6,7] (or 1,2-dichloroethyl ethyl ether[8]), α-halo ketone, or α-halo-β-keto ester. Derivatives of 2-aminothiazole containing the thio or sulfonyl group in the 5-position[9] generally were prepared by the reaction of 2-acetamido-5-bromothiazole[10] or 2-amino-5-bromothiazole[11] with the appropriate sodium mercaptide to yield initially the 5-thio compound. Oxidation of the 2-acetamido-5-alkylthiothiazole followed by hydrolysis of the acetamido group yielded the 5-sulfonyl compound.[12] The 2-amino-5-nitrothiazoles were prepared by dissolving the 2-aminothiazoles, or their acetyl derivatives, in concentrated sulfuric acid and nitrating[13] with one equivalent of fuming nitric acid at about 10°. The nitrations of 2-aminothiazole and 2-amino-4-trifluoromethylthiazole have been described.[14]

The difficulty of forming stable diazonium salts of both 2-aminothiazole and 2-amino-5-nitrothiazole has been described in connection with replacing the diazo group with halogen.[15] In the present work, 2-aminothiazole and its derivatives were diazotized

(1) Presented in part at the 131st National Meeting of the American Chemical Society, Miami, Fla., April 1957.

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(3) J. B. Dickey and E. B. Towne (to Eastman Kodak Co.), U. S. Patents **2,659,719** (1953); **2,683,708** (1954); **2,683,709** (1954); **2,730,523** (1956); **2,746,953** (1956).

(4) E. B. Towne and H. M. Hill (to Eastman Kodak Co.), U. S. Patent **2,726,247** (1955).

(5) E. B. Towne, J. B. Dickey, and M. S. Bloom (to Eastman Kodak Co.), U. S. Patent **2,839,523** (1958).

(6) M. N. Shchukina, *Zhr. Obshchei Khim.* (*J. Gen. Chem.*), **18**, 1653 (1948); *Chem. Abstr.*, **43**, 2575 (1949).

(7) O. Yu. Magidson and V. N. Sokolova, U.S.S.R. Patent **66,044** (1946); *Chem. Abstr.*, **41**, 1713 (1947).

(8) V. Traumann, *Ann.*, **249**, 31 (1888).

(9) L. L. Bambas, *J. Am. Chem. Soc.*, **67**, 671 (1945); L. L. Bambas (to Parke, Davis, and Co.), U. S. Patent **2,389,126** (1945); E. Hoggarth, *J. Chem. Soc.*, 110 (1947).

(10) H. J. Backer and J. A. K. Buisman, *Rec. trav. chim.*, **63**, 226 (1944).

(11) R. Dahlbom and T. Ekstrand, *Svensk Kem. Tidskr.*, **57**, 229 (1945).

(12) Hydrogen peroxide oxidation of an unacetylated 2-amino-5-alkylthiothiazole, however, gave a hydrogen peroxide derivative involving the amino group. Treatment of this derivative with dilute acid yielded the 2-amino-5-alkylsulfonylthiazole.

(13) K. Ganapathi and A. Venkataraman, *Proc. Indian Acad. Sci.*, **22A**, 343 (1945). See especially p. 354.

(14) J. B. Dickey, E. B. Towne, and G. F Wright, *J. Org. Chem.*, **20**, 499 (1955).

(15) K. Ganapathi and A. Venkataraman, *Proc. Indian Acad. Sci.*, **22A**, 362 (1945). See especially p. 365.

TABLE I

2-AMINOTHIAZOLES[a]

Thiazole Derivative	M.P., °C.	Yield, %[b]	Analyses							
			Calcd., %				Found, %			
			C	H	N	S	C	H	N	S
2-Amino-4-(*p*-nitrophenyl)-	266	44	48.87	3.17	19.00	14.48	48.81	3.58	18.24	13.94
2-Amino-4-(*p*-acetamidophenyl)-	240–243	64	56.65	4.72	18.03		56.62	4.87	17.91	
2-Amino-4-(2,5-dichlorophenyl)-	170–172	47	44.08	2.49	11.43		44.26	2.73	11.28	
2-Amino-5-methylthio-	130–133	53	32.88	4.11	19.18		33.64	4.27	19.06	
Acetyl derivative	192–195	95	38.29	4.25	14.89		38.94	4.46	14.62	
2-Amino-5-methylsulfonyl-	176–178	92								
Acetyl derivative	270–271	35	32.73	3.64	12.73	29.09	33.13	3.84	12.65	28.86
2-Amino-5-butylthio-	66–68	51	44.60	6.40	14.90	34.00	44.54	6.36	14.81	33.91
Acetyl derivative	143–144	95	46.96	6.09	12.17	27.82	47.00	6.12	11.98	27.82
2-Amino-5-butylsulfonyl-	94–95	72[c]	38.18	5.45	12.73	29.09	38.59	5.53	12.77	28.76
Acetyl derivative	242–243	45[c]	41.22	5.34	10.68	24.43	42.43	5.52	10.59	23.79
2-Amino-5-phenylthio-	120–121	85	51.92	3.84	13.46	30.77	52.08	4.07	13.28	29.95
Acetyl derivative	221–225	83	52.80	4.00	11.20	25.60	53.29	4.53	11.08	25.98
2-Amino-5-phenylsulfonyl-	205–215	95								
Acetyl derivative	274	82[c]	46.81	3.55	9.93	22.69	46.86	4.07	9.91	22.78
2-Amino-4-phenyl-5-methylthio-	83–90	63[c]								
Acetyl derivative	204	95	54.54	4.54	10.60	24.24	55.00	4.98	10.51	24.63
2-Amino-4-(*p*-nitrophenyl)-5-nitro-	251–252	70	40.60	2.26	21.05	12.03	40.69	2.51	21.02	12.05
2-Amino-4-(*m*-nitrophenyl)-5-nitro-	236–237	63	40.60	2.26	21.05	12.03	40.68	2.53	20.25	11.64
2-Amino-4-(2,5-dichlorophenyl)-5-nitro-	192–193	50.1	37.24	1.72	14.48		37.49	2.21	14.03	
Ethyl 2-amino-5-nitro-4-thiazolecarboxylate	178–181	19.4	33.20	3.22	19.30	14.70	33.31	3.40	19.28	15.00

[a] The following 2-aminothiazoles were also prepared: 2-amino-;[8] 2-amino-4-methyl-;[8,51] 2-amino-4-trifluoromethyl-;[14] ethyl 2-amino-4-thiazolecarboxylate;[41] 2-amino-4-phenyl-[8,33] 2-amino-4-(*m*-nitrophenyl)-;[33] 2-amino-5-methyl-;[50] 2-amino-5-thiocyanato-;[29] 2-amino-5-(*p*-nitrophenylthio)-,[9] 2-amino-5-(*p*-nitrophenylsulfonyl)-;[9] 2-amino-5-(*p*-nitrophenylazo)-;[26] 2-amino-5-bromo-;[11] 2-amino-4-phenyl-5-thiocyanato-;[29] 2-amino-4-phenyl-5-(*p*-nitrophenylthio)-;[28a] 2-amino-4-phenyl-5-(*p*-nitrophenylsulfonyl)-;[28a] ethyl 2-amino-4-trifluoromethyl-5-thiazolecarboxylate;[4] 2-amino-5-nitro-;[13] 2-amino-4-methyl-5-nitro-;[18] 2-amino-4-trifluoromethyl-5-nitro-;[14] 2-amino-4-tert-butyl-5-nitro-;[14] 2-amino-4-(butylsulfonyl)-5-nitro-.[5] [b] Purified product. [c] Crude product.

satisfactorily at 0–5° by adding the solid aminothiazole to nitrosylsulfuric acid in either acetic acid or 50% sulfuric acid solution. The resulting diazonium salt solutions were generally used within a few hours since they decomposed on long standing, even when cold. Coupling was usually accompanied by some evidence of decomposition; however, by careful addition of the diazonium salt solution at 0–5° to a solution of the coupler in an acetic-propionic acid mixture, 60–80% yields of dye were usually obtained. With a few couplers the yields of dye were as low as 40%.

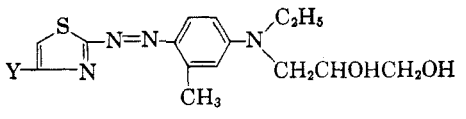
A few simple azo dyes have been prepared from 2-aminothiazole and phenols[8] and from anilines.[16,17] A yellowish red dye prepared from 2-amino-4-methylthiazole and *N*,*N*-bis(2-hydroxyethyl)-aniline has also been described.[18]

DISCUSSION

Dyes from 2-aminothiazole and 4-substituted 2-aminothiazoles. In the present work, dyes from 2-aminothiazole and 4-substituted 2-aminothiazoles were prepared using a typical aniline coupler, *N* - ethyl - *N* - (2,3 - dihydroxypropyl) - *m* - toluidine. These dyes, listed in Table II, have good gas fastness but only fair light fastness.

TABLE II

EFFECT OF 4-SUBSTITUTION ON THE COLOR OF DYES FROM 2-AMINOTHIAZOLES



Y	Color on Acetate	$\lambda_{max}^{CH_3OH}$, Mμ
H-	Orange-pink	502
CH_3-	Orange-pink	506
CF_3-	Red-pink	510
C_2H_5OOC-	Red-pink	514
2,5-$Cl_2C_6H_3$-	Red-pink	514
C_6H_5-	Red-pink	514
p-$O_2NC_6H_4$-[a]	Pink-red	517
m-$O_2NC_6H_4$-	Pink-red	517
p-$CH_3CONHC_6H_4$-	Pink-red	517

[a] Analytical Sample. *Anal.* Calcd. for $C_{21}H_{23}N_5O_4S$: C, 57.14; H, 5.21. Found: C, 56.65; H, 5.81. Spectroscopic data: λ_{max} 517 mμ, ϵ_{max} 4.57×10^4.

(16) V. Traumann, *Ber.*, 21, 938 (1888).

(17) G. T. Morgan and G. V. Morrow, *J. Chem. Soc.*, 107, 1291 (1915).

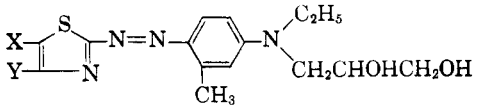
(18) J. H. Helberger and C. Taube (to General Aniline Works), U. S. Patent 2,149,051 (1939).

The dyes from 4-substituted 2-aminothiazoles are orange-pink to pink-red with absorptions of 506–517 mμ. The parent 2-aminothiazole dye absorbs at 502 mμ, hence, the influence of substitution in the 4-position is negligible. The failure of 4-substituents to effect expected color shifts in 2-thiazolylazo dyes may result from the inability of the 4-substituent to enter effectively into the resonance of the dye molecule.

Dyes from 5-substituted 2-aminothiazoles and 4,5-disubstituted 2-aminothiazoles. These dyes, listed in Table III, are red-orange to blue-violet having absorptions of 504 to 563 mμ. Although most of the dyes have only moderate light fastness, those containing a methylsulfonyl or butylsulfonyl group have good light fastness.

TABLE III

EFFECT OF 5- AND 4,5-SUBSTITUTION ON THE COLOR OF DYES FROM 2-AMINOTHIAZOLES



X	Y	Color on Acetate	$\lambda_{max}^{CH_3OH}$, Mμ
CH_3-	H-	Red–orange	504
Br-	H-	Pink–red	524
C_6H_5S-	H-	Pink–violet	530[b]
NCS-	H-	Red–violet	535
p-$O_2NC_6H_4S$-	H-	Red–violet	539
CH_3SO_2-	H-	Red–violet	544[b]
NCS-	C_6H_5-	Red–violet	545
$C_4H_9SO_2$-	H-[a]	Red–violet	550
$C_6H_5SO_2$-	H-	Violet	553[b]
C_2H_5OOC-	CF_3-	Bluish–violet	556[c]
p-$O_2NC_6H_4SO_2$-	C_6H_5-	Bluish–violet	560[b]
p-$O_2NC_6H_4SO_2$-	H-	Blue–violet	563

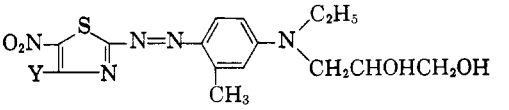
[a] Analytical Sample. *Anal.* Calcd. for $C_{19}H_{23}N_4O_4S_2$: C, 51.82; H, 6.36. Found: C, 51.17; H, 6.52. Spectroscopic data: λ_{max} 551 mμ, ϵ_{max} 4.85 × 10^4. [b] *N,N*-Bis(2-hydroxyethyl)-*m*-toluidine coupler. [c] *N*-Ethyl-*N*-(2,3-dihydroxy-2-methylpropyl)-*m*-toluidine coupler.

In contrast to the negligible effect of 4-substituents on color, 5-substituents cause a marked effect. As would be expected from resonance considerations, the color of the dyes containing the various groups in the 5-position deepens in the order of increasing negativity of the substituent; for example, the dye from 2-amino-5-thiocyanatothiazole is red-violet (535 mμ), whereas the corresponding dye from 2-amino-5-(*p*-nitrophenylsulfonyl)thiazole is blue-violet (563 mμ).

Dyes from 2-amino-5-nitrothiazole and 4-substituted 2-amino-5-nitrothiazoles. All of these dyes, listed in Table IV, are blue. They vary somewhat in tinctorial power on cellulose acetate, however. This series, like that in Table II shows that the nature of the group in the 4-position of the aminothiazole has little effect on the color of the dye. Dyes from 2-amino-5-nitrothiazole itself give good exhaustion and level dyeing and excellent affinity at dye bath temperatures as low as 40–50°. They color cellulose acetate deep, bright, blue shades. The dyed fabrics have good gas fastness, fair light fastness, and excellent dischargeability.

TABLE IV

EFFECT OF 5-NITRO SUBSTITUTION ON THE COLOR OF DYES FROM 2-AMINOTHIAZOLES



Y	Color on Acetate	Tinctorial Power on Acetate	$\lambda_{max}^{CH_3OH}$, Mμ
H-[a]	Blue	High	593
CH_3-	Blue	High	590
$(CH_3)_3C$-	Blue	Medium	590
p-$O_2NC_6H_4$-[b]	Greenish blue	Medium	600
m-$O_2NC_6H_4$-	Greenish blue	Medium	600
2,5-$Cl_2C_6H_3$-	Greenish blue	Medium	605
C_2H_5OOC-	Greenish blue	Medium	606
CF_3-	Greenish blue	Weak	613
$C_4H_9SO_2$-	Greenish blue	Weak	599[c]

[a] Analytical Sample. *Anal.* Calcd. for $C_{15}H_{19}N_5O_4S$: C, 49.32; H, 5.21. Found: C, 49.95; H, 5.74. Spectroscopic data: λ_{max} 596 mμ, ϵ_{max} 4.83 × 10^4. [b] Analytical Sample. *Anal.* Calcd. for $C_{21}H_{22}N_6O_6S$: C, 51.85; H, 4.53. Found: C, 51.74; H, 4.89. Spectroscopic data: λ_{max} 603 mμ, ϵ_{max} 3.10 × 10^4. [c] *N,N*-Bis(2-hydroxyethyl)-*m*-toluidine coupler.

Effect of coupler. The color of the 2-thiazolylazo dyes is affected not only by substituents in the thiazole ring but also by substituents in the coupler constituent. Thus, electron displacement can be enhanced by electron-donating substituents on the coupler constituent. The resulting increased polarizability should result in bathochromism. Apparently this is demonstrated; thus, for example, compared to the simple aniline coupler (*N*-ethyl-*N*-2,3-dihydroxypropyl-*m*-toluidine), *N,N*-bis(2-hydroxyethyl)-2-methoxy-5-acetamidoaniline yields a 5-nitro-2-thiazolylazo dye with a bathochromic shift of 33 mμ in the λ_{max} value.[19]

Electron-attracting substituents on the coupler cause hypsochromic shifts in the dye. Thus, *m*-chloroaniline couplers, relative to *m*-toluidine couplers, shift the color of the azo dye toward red.[20] Electron-attracting substituents in the dialkylamino group of the coupler also produce hypsochromic shifts. The following series of 5-nitro-2-thiazolylazo dyes incorporating fluorine-containing couplers[21] shows this hypsochromic shift. The shift is in the order predicted from the effect of fluorine on physical properties (*e.g.*, boiling point, basicity). The change in color is from blue to violet and suggests increasing interference with the

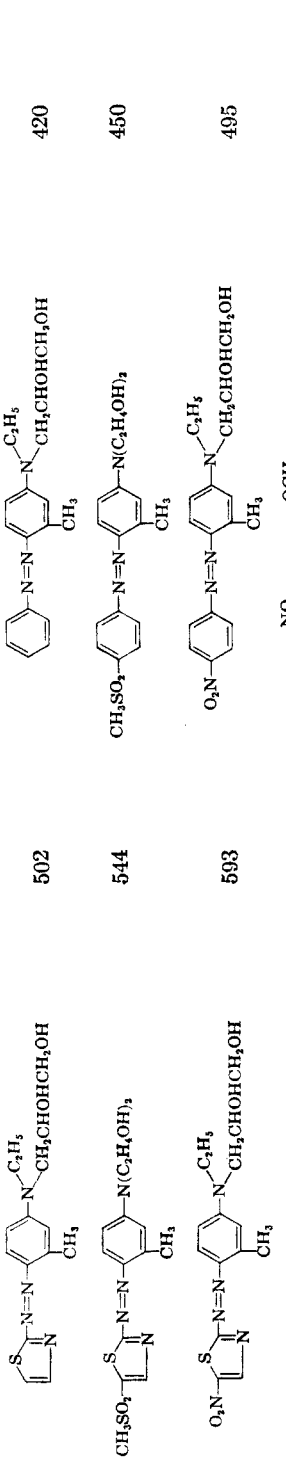
(19) J. B. Dickey, E. B. Towne, M. S. Bloom, W. H. Moore, B. H. Smith, Jr., D. G. Hedberg, *J. Soc. Dyers and Colourists*, **74**, 123 (1958).

(20) Unpublished results.

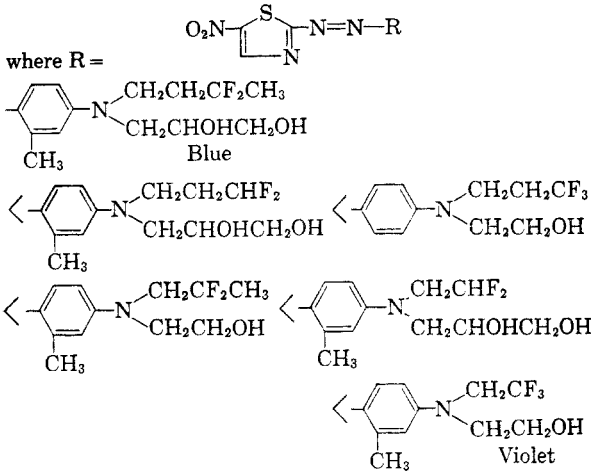
(21) J. B. Dickey, *et al.*, *Ind. Eng. Chem.*, **46**, 2213 (1954).

TABLE V

BATHOCHROMISM OF 2-THIAZOLYLAZO DYES

	$\lambda_{max}^{CH_3OH}$, mμ	$\lambda_{max}^{CH_3OH}$, mμ	$\Delta\lambda_{max}^{CH_3OH}$, mμ
	502	420	+82
	544	450	+94
	593	495	+98
		597	—

electron-donating properties of the dialkylamino group, the interference being dependent on the number of fluorine atoms and the proximity to the amino nitrogen atom.



Significance of the 2-thiazolylazo structure. The greatest significance of this work is the color shift from the red of azo dyes derived from *p*-nitroaniline to the blue of analogous azo dyes derived from 2-amino-5-nitrothiazole. It should be emphasized, however, that bathochromism relative to the benzene analogs is exhibited by all the 2-thiazolylazo dyes studied. Negative groups strategically placed in the thiazole ring are not required in order to bring about a bathochromic shift; for example, dyes from 2-aminothiazole display this effect.

As shown in Table V by the comparison of analogs incorporating a simple aniline coupler, the bathochromism of the 2-thiazolylazo dyes is an inherent property of the thiazole system itself; the bathochromism does not derive from the substituent groups. However, the greater polarizability of the thiazole system (relative to the benzene system), in addition to effecting a general bathochromism in 2-thiazolylazo dyes, also allows a greater electronic displacement to be effected by electronegative substituents. This displacement results in an increased absorption shift from the benzene analog in the 5-methylsulfonyl-2-thiazolylazo dye (+94 mμ) and the 5-nitro-2-thiazolylazo dye (+98 mμ) compared to the 2-thiazolylazo dye (+82 mμ).

The bathochromism displayed by the 2-thiazolylazo dyes is not unique. For example, a bathochromic shift characterizes the chalcone derivatives of thiophenes described by Buu-Hoï.[22] Triarylmethane dyes containing a thiophene ring exhibit a shift in absorption of the y-band to longer wave lengths.[23] However, the magnitude of the bathochromic shift (80–100 mμ) exhibited by the 2-

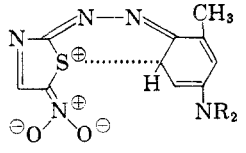
(22) N. P. Buu-Hoï, N. Xuong, and M. Sy, *Bull. soc. chim. France*, 1646 (1956).

(23) V. V. Ghaisas, B. J. Kane, and F. F. Nord, *J. Org. Chem.*, **23**, 560 (1958).

thiazolylazo dyes and the recently described 2-thienylazo dyes[19] is remarkable. To illustrate, a blue dye (λ_{max} 593 mμ) is obtained in the 5-nitro-2-thiazolylazo series with a simple aniline coupler. A blue phenylazo dye (λ_{max} 597 mμ) is obtained only in certain cases, for example, when the diazonium constituent contains three highly negative groups and when the coupler is one conferring a pronounced bathochromic effect (Table V). The dye from 2-amino-5-nitrothiazole and this coupler is, however, much greener (λ_{max} 628 mμ).

To effect the bathochromism of these thiazolylazo and thienylazo dyes, the energy difference between the ground states and the excited states must be less than for the analogous phenylazo dyes. On the basis of the presumably greater polarizability of the 2-thiazolyl system than the phenyl system, the 2-thiazolylazo dyes would be expected to have greater resonance stabilization of the excited states than analogous phenylazo dyes. However, the lower energy difference of the 2-thiazolylazo dyes (and the 2-thienylazo dyes) may be due to less resonance stabilization of the ground state: the 2-thienylazo dyes[19] are also bathochromic and the resonance energy of thiophene is less than that of benzene.[24] The possibility that both more excited-state stabilization and less ground-state stabilization participate in the bathochromism of 2-thiazolylazo and 2-thienylazo dyes cannot be disregarded.

In addition to conventional excited-state structures which involve polarized *trans* configurations, there is a novel structural possibility for the 2-thiazolylazo and 2-thienylazo dyes which provides an alternative explanation for the bathochromic shift. The decreased difference in energy levels between ground and excited states may be attributed to additional resonance stabilization of the excited state through contributions of a cyclic form.



(24) L. Pauling, *The Nature of the Chemical Bond*, Cornell University Press, Ithaca, N. Y., 1942, pp. 136, 138.

(25) The cyclic structure requires that the azo compound assume the cis configuration. Although comparison of *cis-trans* isomers of azobenzenes[45] indicates that the *cis*-2-thiazolylazo configuration should be less stable than the trans configuration, the cyclic structure, which cannot exist for the *cis*-azobenzenes, would possibly tend to overcome this instability. However, from the configuration of *cis*-azobenzene[45] it would be inferred that the *cis*-2-thiazolylazo configuration would not be coplanar nor would the C-S distance be such as to suggest effective interaction to yield a cycle. By comparison with *cis-trans* isomers of azobenzene[46-49] it would be expected that dyes with the *cis*-2-thiazolylazo configuration would absorb less intensely than those with the *trans*. The high intensity of the absorption by the 2-thiazolylazo dyes thus does not support the postulated *cis* form.

In addition to other objections,[25] the bathochromism of triarylmethane dyes containing a thiophene[23] ring seems an effective argument against such a structure, since these dyes are bathochromic, but presumably would not form an analogous cyclic structure. Attempts to evaluate the possibility of the existence of the cyclic form by the preparation of certain 2-thiazolylazo dyes have been inconclusive. The introduction of electron-donating or electron-attracting groups at suitable positions in the coupler ring should modify the tendency for the formation of the cyclic structure and thereby modify the absorption characteristics of the dyes. All modifications examined produced hypsochromic shifts. The introduction of a nitro group did not confer the required bathochromism. The hypsochromism caused by methyl and methoxyl groups is common to analogous phenylazo dyes as well. Thus, although in agreement with the expected effect, this hypsochromism cannot unequivocally be ascribed to the existence of the cyclic form.

Orientation upon nitration of 2-amino-4-phenylthiazoles. The nitration of 2-aminothiazoles having a phenyl or a substituted phenyl group in the 4-position has not been previously described. Attempts to nitrate 2-acetamido-4-phenylthiazole were reported unsuccessful.[26] The nitration of bis-(4-phenyl-2-thiazolyl)amine reportedly yields bis-(4-phenyl-5-nitro-2-thiazolyl)amine as the only nitration product.[27] The possible effect of the particular nitration conditions (concentrated nitric acid, concentrated sulfuric acid, and boiling acetone) on the orientation was not investigated in the present study.

In a previous paper,[14] the behavior of certain 2-amino-4-alkylthiazoles upon nitration was described. In the course of synthesizing dye intermediates for the present work, the behavior of certain 2-amino-4-phenylthiazoles upon nitration was studied.

The composition of the nitration products was established by chemical studies in addition to elemental analysis and comparison with reference compounds by infrared spectroscopy, ion exchange paper chromatography, and melting point determination. Thus, 2-amino-4-(*p*-nitrophenyl)thiazole, formed by nitration of 2-amino-4-phenylthiazole, was compared with the authentic sample prepared from *p*-nitrophenacyl bromide and thiourea. The nitration product from 2-acetamido-4-phenylthiazole was hydrolyzed to 2-amino-4-(*p*-nitrophenyl)-thiazole. The dinitration product from 2-amino-4-phenylthiazole and the mono-nitration product from 2-amino-4-(*p*-nitrophenyl)thiazole were compared by oxidation to *p*-nitrobenzoic acid. No dinitrobenzoic acid was detected, thus confirming the formation of the 5-nitrothiazolyl compound.

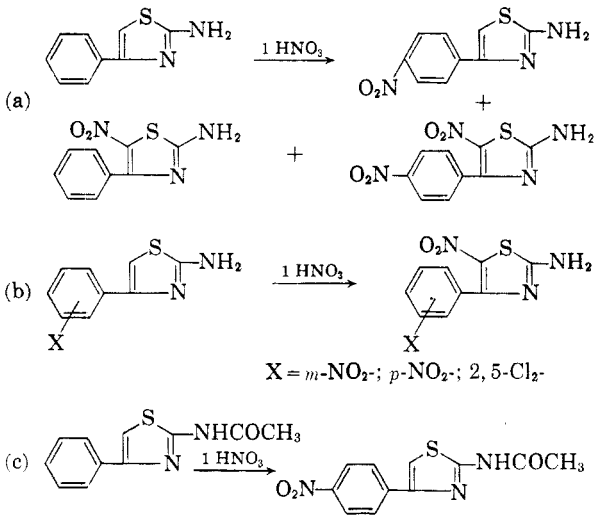
(26) M. T. Bogert and M. Chertcoff, *J. Am. Chem. Soc.*, 46, 2864 (1924).

(27) H. Beyer and G. Berg, *Ber.*, 89, 1602 (1956).

An authentic sample of 2-amino-4-phenyl-5-nitrothiazole was not available; its identity was inferred from infrared spectroscopic data.

It was also found convenient and feasible to convert the crude nitration products to azo dyes for paper chromatography. The R_f values were compared with those of reference dyes for identification. In fact, just from the color of the chromatography zones of separated azo dyes, the general nature of the 2-aminothiazole could be inferred. If the zone was blue, the dye contained a 5-nitrothiazolyl moiety and possibly also was nitrated in the phenyl group; if the zone was red, the dye was nitrated, if at all, only in the phenyl group. These inferences could also be drawn, although less exactly, from the color of the dye in solution or on cellulose acetate.

The incorporation of a phenyl group or a substituted phenyl group into 2-aminothiazole made the formation of mixtures on nitration with one equivalent of nitric acid a possibility; that is, nitration could take place on the phenyl ring, the thiazolyl ring, or both. In the case of 2-amino-4-phenylthiazole, such a mixture was formed. However, the 2-amino-4-(substituted phenyl)-thiazoles nitrated only in the 5-thiazolyl position, and 2-acetamido-4-phenylthiazole nitrated only in the *p*-phenyl position.



Bromination,[28] thiocyanation,[29] nitrosation,[30] and mercuration[31] of 2-amino-4-phenylthiazoles and 2-acetamido-4-phenylthiazoles reportedly yield 5-thiazolyl substitution exclusively. In these reactions the orientation is not affected by the nature of the attacking reagent or by the nature of the thiazole compound. Therefore, in this present work, the orientation of 2-amino-4-phenylthiazole (in part) and 2-acetamido-4-phenylthiazole on nitration to yield the *p*-phenyl-substituted product is anomalous to their other substitution reactions. The 2-amino-4(substituted phenyl)thiazoles studied did, however, yield only the 5-thiazolyl derivatives, but it is not unexpected that the 2-aminothiazolyl moiety nitrates preferentially compared to the *p*-nitrophenyl group, the *m*-nitrophenyl group, or the 2,5-dichlorophenyl group. Investigation of the nitration product from 2-amino-4-(*p*-acetamidophenyl)-thiazole was inconclusive since no pure compound could be isolated.

The orientation upon nitration of 2-acetamido-4-phenylthiazole to yield the *p*-nitrophenyl derivative suggests that the phenyl group is more reactive than the 2-acetamidothiazolyl moiety. Nitration of the phenyl group would not be expected in view of the orientation to the 5-thiazolyl position in other substitution reactions of 2-amino-4-phenylthiazole and 2-acetamido-4-phenylthiazole. However, the 2-acetamido group should be less effective than the 2-amino group in activating the 5-thiazolyl position, and thus orientation on nitration could be different.

The major components of the nitration product of 2-amino-4-phenylthiazole and one equivalent of nitric acid were 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole and 2-amino-4-(*p*-nitrophenyl)thiazole. Some 2-amino-4-phenyl-5-nitrothiazole was also formed, and some starting material was recovered. Similar nitration conditions, except for shorter reaction time, gave essentially the same products. The use of only 0.75 equivalent of nitric acid, however, gave a nitration product in which 2-amino-4-phenyl-5-nitrothiazole was not detected by infrared spectroscopy. Nitration with two equivalents of nitric acid yielded the expected 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole, together with a small amount of an unidentified compound. Conversion of the nitration product to the azo dye yielded only the dye from 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole.

EXPERIMENTAL[32]

Preparation of intermediates. Procedures for the preparation of new compounds illustrate the various types of 2-aminothiazoles used in this work. The properties of new compounds are reported in Table I; known compounds used are listed.

2-Amino-4-(p-nitrophenyl)thiazole. This compound was prepared in 44% yield by an adaptation of the method for the preparation of the *m*-nitrophenyl compound[33] by treating *p*-nitroacetophenone[34,35] and thiourea with bromine on

(28) (a) E. Hoggarth, *J. Chem. Soc.*, 114 (1947); (b) Y. Garreau, *Compt. rend.*, **222**, 963 (1946); (c) G. N. Mahapatra, *J. Am. Chem. Soc.*, **79**, 988 (1957).

(29) C. D. Hurd and H. L. Wehrmeister, *J. Am. Chem. Soc.*, **71**, 4007 (1949).

(30) H. Beyer and H. Drews, *Ber.*, **87**, 1500 (1954).

(31) G. Travagli, *Gazz. chim. ital.*, **78**, 598 (1948); M. K. Raut, *J. Indian Chem. Soc.*, **33**, 741 (1956); B. Das, *J. Sci. Ind. Research (India)*, **15B**, 613 (1956).

(32) Melting points are uncorrected.

(33) R. M. Dodson and L. C. King, *J. Am. Chem. Soc.*, **67**, 2242 (1945).

(34) H. G. Walker and C. R. Hauser, *J. Am. Chem. Soc.*, **68**, 1386 (1946).

(35) A. H. Ford-Moore and H. N. Rydon, *J. Chem. Soc.*, 679 (1946).

a steam bath. Recrystallization from a pyridine-water mixture gave a product melting at 266°.

In another preparation in which *p*-nitrophenacyl bromide was used, an improved yield (72%) was obtained. This method was adapted from the method of Hurd and Kharasch[36] for the preparation of the corresponding *m*-nitrophenyl compound.

2-Amino-5-butylsulfonylthiazole. A mixture of 18 g. (0.2 mole) of 1-butanethiol and 8 g. (0.2 mole) of sodium hydroxide in 140 ml. of water was stirred under nitrogen on a steam bath. A solution of 52 g. (0.2 mole) of 2-amino-5-bromothiazole hydrobromide[11] in 120 ml. of water and 120 ml. of ethyl alcohol was added. To this mixture a solution of 8 g. (0.2 mole) of sodium hydroxide in 20 ml. of water was then added. After the mixture had been stirred and refluxed for 4 hr., it was concentrated under reduced pressure, then cooled in ice to yield 27 g. (72%) of a sticky, brown solid. The 2-amino-5-butylthiothiazole was purified by continuous extraction with pentane in a Soxhlet apparatus. The extract yielded 19 g. (51%) of light tan platelets, m.p. 66–68°.

A mixture of 6.8 g. (0.036 mole) of 2-amino-5-butylthiothiazole, 4.1 g. (0.036 mole) of acetic anhydride, and 25 ml. of acetic acid was allowed to stand overnight at room temperature. After being heated on a steam bath for 30 min., the solution was poured onto ice to yield 8.4 g. (100%) of 2-acetamido-5-butylthiothiazole, m.p. 141–143°. Recrystallization from hexane gave the analytical sample, m.p. 143–144°.

A mixture of 7.8 g. (0.034 mole) of 2-acetamido-5-butylthiothiazole, 17 g. (0.14 mole) of a 30% solution of hydrogen peroxide, and 75 ml. of acetic acid was allowed to stand overnight at room temperature. After being heated on a steam bath for 2 hr., the reaction mixture was cooled and filtered. The product was recrystallized from ethyl alcohol to obtain 4 g. (45%) of 2-acetamido-5-butylsulfonylthiazole, m.p. 242–243°. The filtrate was concentrated to yield 1.7 g. of starting material, m.p. 140–143°.

A mixture of 20 ml. of concentrated hydrochloric acid, 10 ml. of water, and 2 g. (0.0076 mole) of 2-acetamido-5-butylsulfonylthiazole was refluxed with stirring for 2 hr. The solution was diluted with an equal volume of cold water and brought to a *p*H of 6 with solid sodium acetate. The resulting white solid was filtered and washed with water to yield 1.2 g. (72%) of 2-amino-5-butylsulfonylthiazole, m.p. 94–95° after recrystallization from benzene.

Hydrogen peroxide derivative of 2-amino-5-butylsulfonylthiazole. In an attempt to prepare 2-amino-5-butylsulfonylthiazole directly[37] from 2-amino-5-butylthiothiazole by oxidation with hydrogen peroxide, a product different from the authentic compound derived from 2-acetamido-5-butylthiothiazole was obtained. Oxidation of 9.4 g. of 2-amino-5-butylthiothiazole with hydrogen peroxide in acetic acid gave 7 g. of a white solid, m.p. 166–167° after recrystallization from ethyl alcohol. The melting point and analysis do not agree with those of authentic 2-amino-5-butylsulfonylthiazole (see Table I). Although in poor agreement with calculated values, the analysis indicates the addition of four oxygen atoms and the empirical formula $C_7H_{14}N_2O_4S_2$.

Anal. Calcd. for $C_7H_{14}N_2O_4S_2$: C, 33.0; H, 5.5; N, 11.0; O, 25.2; S, 25.2. Found: C, 31.32; H, 4.95; N, 10.41; S, 27.76.

The same compound (m.p. 170–171°) was obtained by using the same oxidation conditions with authentic 2-amino-5-butylsulfonylthiazole, m.p. 94–95°. The melting point of a mixture of the two hydrogen peroxide derivatives was undepressed, m.p. 168–170°.

(36) C. D. Hurd and N. Kharasch, *J. Am. Chem. Soc.*, 68, 653 (1946).

(37) J. Goerdeler and P. Linden [*Ber.*, 89, 2742 (1956)] reported the direct oxidation of 5-amino-3-ethylthio-1,2,4-thiadiazole to the corresponding sulfoxide and sulfone. The conditions used (monoperoxyphthalic acid in chloroform at −30°) may account for their success.

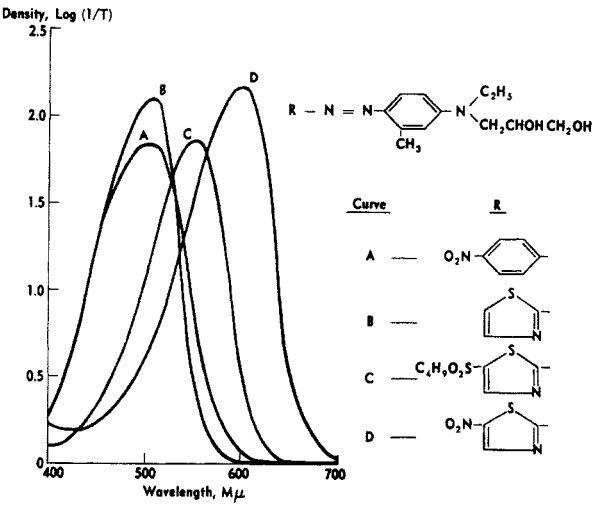


Fig. 1. Color-deepening effect of 5-substitution in 2-thiazolylazo dyes

A melting point of a mixture with authentic 2-amino-5-butylsulfonylthiazole was depressed, m.p. 94–163°. The analysis of the hydrogen peroxide derivative obtained from 2-amino-5-butylsulfonylthiazole was the same as that obtained from 2-amino-5-butylthiothiazole.

Anal. Found: C, 31.36; H, 5.01; N, 10.40; S, 27.81; O, 23.76.

The standard peroxide test (KI/HOAc) demonstrated only trace amounts of peroxide in the hydrogen peroxide derivative. However, refluxing the hydrogen peroxide derivative in deaerated acetic anhydride (under nitrogen) in the presence of potassium iodide resulted in a strong peroxide test. Similar procedures with dilute hydrochloric acid also resulted in a strong peroxide test. It is noteworthy that these two reactions were found to convert the hydrogen peroxide derivative to 2-amino-5-butylsulfonylthiazole or its acetyl derivative.

The hydrogen peroxide derivative is characterized by the following infrared absorption bands: 6.25, 8.37, 9.05, 9.30, 9.65, 9.80, 10.40, 10.55, 11.2, 11.5, and 14.4μ. The 2-amino-5-butylsulfonylthiazole hydrogen peroxide derivative shows marked pertubation of the NH_2 stretching absorption. There is a shift of these absorptions from 2.95 and 3.00μ for 2-amino-5-butylsulfonylthiazole to a broad absorption centered at 3.06μ. This shift suggests amino group involvement in the structure of the hydrogen peroxide derivative (in confirmation of its chemical behavior) possibly by hydrogen bonding of the amino group with the oxygen.

The infrared spectrum shows no relation to that of urea hydroperoxidate, amine oxides, or gramine oxide-hydrogen peroxide derivative.[38]

Acetylation of the hydrogen peroxide derivative of 2-amino-5-butylsulfonylthiazole gave a good yield of a white solid, m.p. 242–244° after recrystallization from ethyl alcohol. The melting point of a mixture with authentic 2-acetamido-5-butylsulfonylthiazole (m.p. 242–243°) was not depressed, m.p. 241–243°. These compounds were also shown to be identical by infrared spectroscopy.

A sample of the hydrogen peroxide derivative of 2-amino-5-butylsulfonylthiazole was refluxed for 2 hr. with 10% hydrochloric acid solution to yield a white solid, m.p. 91–94° after recrystallization from benzene. The melting point of a mixture with authentic 2-amino-5-butylsulfonylthiazole (m.p. 94–95°) was undepressed, m.p. 92–94°.

In another reaction which also involved cleavage of the hydrogen peroxide derivative, diazotization converted it to

(38) D. W. Henry and E. Leek, *J. Am. Chem. Soc.*, 79, 5254 (1957).

a dye which paper chromatography showed to be identical to the dye from 2-amino-5-butylsulfonylthiazole.

2-Amino-5-methylsulfonylthiazole. To a solution of 20 g. (0.5 mole) of sodium hydroxide in 200 ml. of water was added 20 g. (0.1 mole) of 2-acetamido-5-thiocyanatothiazole.[29,39] The thiazole was hydrolyzed[40] under a nitrogen atmosphere on a steam bath for 1 hr.; the color of the solution changed from orange-red to cherry red. The stirred solution was cooled to 0°, and 12.6 g. (0.1 mole) of dimethyl sulfate was added dropwise. During the addition, a brown-buff, crystalline solid separated. The reaction mixture was allowed to stand at room temperature overnight under nitrogen. The solid was then collected on a filter, washed with water until neutral, and dried. The brown-buff crystals of 2-amino-5-methylthiothiazole weighed 7.8 g. (53% yield) and melted at 125–130°. A sample recrystallized from hexane melted at 130–133°.

A solution of 7.4 g. (0.05 mole) of 2-amino-5-methylthiothiazole and 5.7 g. (0.055 mole) of acetic anhydride in 25 ml. of acetic acid was allowed to stand overnight at room temperature. The solution was concentrated and poured onto ice. The precipitate was filtered, washed with water, and dried to obtain 8.9 g. (95%) of 2-acetamido-5-methylthiothiazole, m.p. 192–195° after recrystallization from ethyl alcohol.

To a suspension of 7 g. (0.037 mole) of 2-acetamido-5-methylthiothiazole in 50 ml. of acetic acid was added 17 g. (0.15 mole) of a 30% solution of hydrogen peroxide. The temperature of the reaction mixture rose to 40° and solution was effected. The solution was allowed to stand overnight at room temperature, and then it was warmed on a steam bath for several hours. The solution was concentrated to yield 2.8 g. (35% yield) of 2-acetamido-5-methylsulfonylthiazole, m.p. 270–271° after recrystallization from ethyl alcohol. A mixture of 10 ml. of concentrated hydrochloric acid, 5 ml. of water, and 2.5 g. (0.01 mole) of 2-acetamido-5-methylsulfonylthiazole was refluxed for 2 hr. When the solution had cooled, colorless crystals formed. After the cold solution had been neutralized, the product was collected on a filter, washed with water, and dried to yield 1.8 g. (92%) of 2-amino-5-methylsulfonylthiazole, m.p. 176–178° after recrystallization from ethyl alcohol.

By the use of the hydrolysis method of Bellavita and Vantaggi,[40] 2-amino-4-phenyl-5-thiocyanatothiazole[29] was similarly converted to the sodium mercaptide derivative, which was directly methylated by the above method to yield 2-amino-4-phenyl-5-methylthiothiazole (63%). It was quantitatively acetylated to yield 2-acetamido-4-phenyl-5-methylthiothiazole, m.p. 204° after recrystallization from ethyl alcohol.

2-Amino-4-(p-nitrophenyl)-5-nitrothiazole. 2-Amino-4-(*p*-nitrophenyl)thiazole (4.4 g., 0.02 mole) was slowly dissolved in 20 ml. of concentrated sulfuric acid which was stirred and kept at 10–12°. While the sulfuric acid solution was stirred at 4°, 1 ml. (0.02 mole) of 90% nitric acid was added at such a rate that the temperature remained constant. The stirred reaction mixture was then allowed to warm to room temperature. After standing overnight, it was poured into ice water with stirring. The resulting precipitate was collected on a filter and washed with water until neutral to yield 5.2 g. (98%), m.p. 251–252° after recrystallization from acetic acid.

Ethyl 2-amino-5-nitro-4-thiazolecarboxylate. It has been reported that the nitration of either ethyl 2-amino-4-thiazolecarboxylate or its acetyl derivative yields only unreacted starting material.[18] In the present work nitration was satisfactorily effected, although in some runs the crude nitration product tended to decompose.

To 50 ml. of concentrated sulfuric acid, kept below 15° by means of an ice bath, 17.2 g. (0.1 mole) of ethyl 2-amino-4-thiazolecarboxylate[41] was added. Then 5 ml. of fuming nitric acid was added while the temperature was kept below 15°. After the acid had been added, the bath was allowed to warm to room temperature overnight. The yellow solution was poured onto ice, and the yellow solid that separated was collected by filtration. Neutralization of the filtrate with ammonium hydroxide yielded more solid. The combined solids were recrystallized from ethyl alcohol to yield 4.0 g. (19.4%) of ethyl 2-amino-5-nitro-5-thiazolecarboxylate, m.p. 178–181°.

Determination of products from nitration of 2-amino-4-phenylthiazole. I. Nitration with one equivalent of nitric acid: long reaction time. To 47 ml. of concentrated sulfuric acid in a 100-ml. three-necked flask, 8.8 g. (0.05 mole) of 2-amino-4-phenylthiazole was added at 10–14° with stirring. The stirred solution was treated at 3–5° over a period of 30 min. with a mixture of 3.5 g. (0.05 mole) of fuming nitric acid (sp. gr. 1.49–1.50) and 3 ml. of concentrated sulfuric acid. Stirring was continued for 15 min. at this temperature. After the stirred reaction mixture warmed to room temperature, it was allowed to stand overnight protected from moisture.

The reaction mixture was poured into 500 ml. of an ice-water mixture, yielding a reddish solid which was collected on a filter. The product was washed with cold water, then with saturated sodium acetate solution until it was neutral to Congo Red paper. After the product, Fraction A, was washed with water and dried in air, it weighed 6.4 g., m.p. 228–230° (dec.).

The combined filtrate and washings from Fraction A, after being neutralized to Congo Red paper, were chilled to yield 1.2 g. of a yellow solid, Fraction B, m.p. 192–200° (dec.).

The filtrate from Fraction B was neutralized to litmus paper with 20% sodium hydroxide solution yielding 1.7 g. of a solid, Fraction C, m.p. 143–145°.

Fraction A was shown by infrared spectroscopy to be a mixture of 2-amino-4-(*p*-nitrophenyl)thiazole and 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole. The mononitro compound is characterized by absorption bands at 7.55, 8.3, 9.6, 11.85, and 13.85μ. The dinitro compound is characterized by bands at 7.85, 11.55, 12.15, 13.43, and 14.1μ.

In another nitration experiment the material corresponding to Fraction A was studied by paper chromatography and by ion exchange paper chromatography (see *Chromatographic Methods*). By comparison of the nitration product with concurrently chromatographed reference compounds, again both 2-amino-4-(*p*-nitrophenyl)thiazole and 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole were identified. The crude dye incorporating the *m*-toluidine coupler was prepared, and by concurrently chromatographing reference dyes, the dyes from both 2-amino-4-(*p*-nitrophenyl)thiazole and 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole were identified. Evidence for the presence of 2-amino-4-phenyl-5-nitrothiazole in very low concentration was found in both the ion exchange paper chromatogram of the nitration product and in the paper chromatogram of the dye prepared from this mixture.

Fraction B was identified by infrared spectroscopy as a mixture of 2-amino-4-(*p*-nitrophenyl)thiazole and possibly 2-amino-4-phenyl-5-nitrothiazole. Infrared absorption bands at 8.8, 12.6, and 14.3μ characterize the compound tentatively identified as 2-amino-4-phenyl-5-nitrothiazole. The ion exchange paper chromatogram of Fraction B confirmed the presence of 2-amino-4-(*p*-nitrophenyl)thiazole and the compound tentatively identified as 2-amino-4-phenyl-5-nitrothiazole. A trace amount of 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole was also detected.

In Fraction C, the starting material, 2-amino-4-phenylthiazole, which is characterized by infrared absorption bands at 9.7, 10.95, 14.5, 14.95, and 15.2μ, was identified.

(39) V. Bellavita, *Ann. chim. appl.*, **38**, 449 (1948); *Chem. Abstr.*, **44**, 154 (1950).

(40) V. Bellavita and L. Vantaggi, *Ann. chim. (Rome)*, **41**, 194 (1951); *Chem. Abstr.*, **46**, 486 (1952).

(41) H. Erlenmeyer and C. J. Morel, *Helv. Chim. Acta*, **30**, 1201 (1947).

II. *Nitration with one equivalent of nitric acid: short reaction time.* This experiment was similar to I. It differed only in reaction time. Instead of allowing the reaction mixture to stand overnight, it was poured into an ice-water mixture after stirring at 2–5° for 10 min. following the addition of nitric acid. The nitration product was fractionated as described in I.

Fraction A, m.p. 223° (dec.) weighed 7.7 g. It was identified by infrared spectroscopy as a mixture of 2-amino-4-(*p*-nitrophenyl)thiazole and 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole. Oxidation of a portion of Fraction A by sodium dichromate yielded a main fraction of pure *p*-nitrobenzoic acid; a small second fraction consisted of *p*-nitrobenzoic acid and an unidentified nonacidic compound. Benzoic acid was not detected in these fractions by infrared spectroscopy.

Fraction B, m.p. 187–190° (dec.), weighed 0.6 g. and was identified by infrared spectroscopy as a mixture of 2-amino-4-phenylthiazole, the compound tentatively identified as 2-amino-4-phenyl-5-nitrothiazole, 2-amino-4-(*p*-nitrophenyl)thiazole, and 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole. The paper chromatogram of the dye from Fraction B showed the presence of the azo dyes from all four of the amines that infrared spectroscopy had indicated.

Fraction C, m.p. 139–142°, weighed 1.4 g. It was shown by infrared spectroscopy to contain 2-amino-4-phenylthiazole.

III. *Nitration with 0.75 equivalent of nitric acid.* This experiment was also similar to I. It differed only in that the amount of nitric acid used (2.6 g., 0.0375 mole) was 75% of the theoretical amount.

Fraction A, m.p. 202–203°, weighed 5.1 g. It was identified by infrared spectroscopy as a mixture of 2-amino-4-(*p*-nitrophenyl)thiazole and 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole.

Fraction B, m.p. 138–142°, weighed 1.9 g. It was shown by infrared spectroscopy to contain principally 2-amino-4-phenylthiazole.

IV. *Nitration with two equivalents of nitric acid.* This experiment was also similar to I. It differed in that two equivalents (7.0 g., 0.10 mole) of nitric acid were used. The crude product, m.p. 221–226°, weighed 11.9 g. and represented an 89.5% yield of 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole. A sample recrystallized from a benzene–ethyl alcohol mixture melted with decomposition at 250–251°, in agreement with the melting point of the authentic compound.

The azo dye from the crude nitration product was shown by paper chromatography to be identical with the authentic dye from 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole. No other components were detected. However, by infrared spectroscopy the crude nitration product was shown to be a mixture consisting mainly of 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole. A small amount of an unknown compound characterized by an infrared absorption band at 12.63μ was also present. The failure of the unknown compound to form the azo dye suggests that it may not be a primary aromatic amine.

The recrystallized nitration product was found by infrared spectroscopy to be pure 2-amino-4-(*p*-nitrophenyl)-5-nitrothiazole.

Preparation of dyes, dyeing and testing. The 2-aminothiazoles were diazotized using nitrosylsulfuric acid and the resulting diazonium compounds were coupled in a propionic-acetic acid mixture, anhydrous sodium acetate being added to neutralize to Congo Red paper.[19]

Dyeings of 10-g. samples of jersey fabric knit from dull cellulose acetate filament yarn were made using 33.3-mg. dye samples.[19]

All fastness tests were in accordance with the procedures of the American Association of Textile Chemists and Colorists.[42]

Chromatographic methods. For paper chromatography of azo dyes, Whatman 3MM paper was used for samples of 10 to 20 μg., and Whatman seed-test paper[43] was used for samples of 10 to 100 mg. The samples were applied in acetone solution, the small samples being applied as spots, and the large samples being applied as streaks. Ascending development was more convenient than descending development and gave sharper separation of zones. Circular paper chromatography was found to be a useful and rapid method for determining the composition of crude dyes and for determining the best developer composition.

For these azo dyes an acetone-heptane mixture (3:7 v/v) was found to be generally very satisfactory for development. This developer caused satisfactorily rapid migration with requisite separation of zones.

To identify an azo dye, it was run concurrently on a strip of Whatman 3MM paper with reference dyes. From the color of spots and from their rate of migration from the base line (compared to that of reference dyes), it was possible to assign structures. Mixtures of dyes, such as those from the nitration product of 2-amino-4-phenylthiazole, did not cause difficulties in identification.

For ion exchange paper chromatography of 2-aminothiazoles, H. Reeve Angel Ion Exchange Paper, Grade SA-1 was used.[44] This strong acid ion exchange paper was furnished in Na^+ form. The H^+ form was regenerated by acidification with dilute hydrochloric acid (1:1) then treated with distilled water to remove mineral acid. After the paper had been dried, the samples in acetone solution were applied in spots. The top phase of a mixture of 250 ml. of butyl alcohol, 250 ml. of water, and 2 ml. of concentrated hydrochloric acid was used to obtain the chromatogram by ascending development.

Amines were identified by comparing their rates of migration with those of reference amines concurrently chromatographed on a strip of ion exchange paper.

Determination of visible absorption spectra. The absorption spectra given in Fig. 1 were obtained using a General Electric recording spectrophotometer. The dyes were studied as solutions in butyl alcohol at a concentration of 1 part in 50,000 by weight.

The λ_{max} values given in the tables were determined with a Cary recording spectrophotometer (Model 14) using a 1-cm. cell. The dyes were dissolved in anhydrous methanol, in a concentration giving a satisfactorily high absorbance. The dyes used for this determination were not given rigorous purification. However, careful purification by chromatography did not significantly affect the λ_{max} values.

For ϵ_{max} value determination and elemental analysis, dyes were purified by repeated paper chromatography. The ϵ_{max} values were obtained with a Cary recording spectrophotometer (Model 14) using a 1-cm. cell. The dyes were dissolved in anhydrous methanol in 7.5×10^{-6} mole/l. concentration.

Determination of infrared absorption spectra. The infrared absorption spectrograms were recorded on a Baird Infrared Recording Spectrophotometer (Model AB2) using the potassium bromide pressed-pellet technique.

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Ethyl *N*-Methyl-2-pyridone-4-carboxylate and Derivatives

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The alkaline potassium ferricyanide oxidation of *N*-alkylpyridinium salts has been used as a method for the preparation of 4-carboxy-*N*-methyl-2-pyridone which was converted into its ethyl ester and several other derivatives.

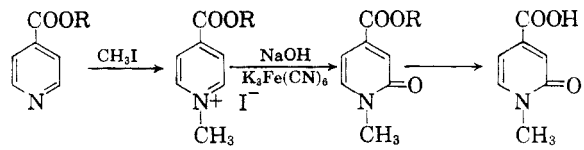
Although the 3-, 5-, and 6-, carboxy-*N*-methyl-2-pyridones have been reported in the literature,[2–5] we have found no report of *N*-methyl-4-carboxy-2-pyridone (I). The preparation of ethyl *N*-methyl-2-pyridone-4-carboxylate was undertaken in order to test the analgesic activity of this compound and several of its derivatives.

The alkaline potassium ferricyanide oxidation of *N*-methylpyridinium iodide to *N*-methyl-2-pyridone is a well established reaction.[6] Sugasawa and Suzuta[7] oxidized 1-(3,4-methylenedioxyphenethyl)-4-carbethoxypyridinium bromide with alkaline potassium ferricyanide to *N*-(3,4-methylenedioxyphenethyl)-4-carboxy-2-pyridone. M. L. Peterson[8] reported the alkaline ferricyanide oxidation of 2,5-dicarbomethoxy-*N*-methylpyridinium methosulfate and its betaine to *N*-methyl-5-carboxy-2-pyridone.

The alkaline ferricyanide oxidation of *N*-methyl-3-carboxamidopyridinium iodide has been widely studied. Most recently Pullman and Colowick[9] have demonstrated that both the 2- and 6-pyridones of *N*-methyl-3-pyridine carboxamide are formed upon oxidation.

Thyagarajan[10] has recently reviewed the alkaline potassium ferricyanide oxidation reaction.

The attempted alkaline potassium ferricyanide oxidation of both *N*-methyl-4-carboxypyridinium iodide and its betaine under the usual conditions[5,6] failed to yield any 2-pyridone, starting material being recovered. However the oxidation of the methiodides of isonicotinic acid esters were studied with greater success. The product isolated was the 4-carboxy-*N*-methyl-2-pyridone; the ester was never detected.



R = CH_3, CH_2CH_3, $CH(CH_3)_2$

It is generally accepted[10–12] that the oxidation takes place *via* the pseudo base. A more detailed postulation of the mechanism of the ferricyanide oxidation of *N*-alkylpyridinium hydroxides to form *N*-alkyl-2-pyridones is proposed by Bradlow and Vanderwerf.[13]

The yield of *N*-methyl-4-carboxy-2-pyridone depended on the rate of addition of the reagents to the reaction mixture. The sodium hydroxide solution was added to a concentrated aqueous solution

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