trichlorotoluene, 98-07-7; acetophenone, 98-86-2; chlorobenzene, 108-90-7; 2,4-dinitrotoluene, 121-14-2; methyl benzoate, 93-58-3; phenetole, 103-73-1; naphthalene, 91-20-3.

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Fluorinated Azo Dyes.[1a] II.[1b] Synthesis and Spectral Properties of 2,6-Difluoro- and 2,3,5,6-Tetrafluoro-4-aminoazobenzene and Their N-Methylated and 4′-Ethyl Derivatives

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A number of new polyfluorinated azo dyes have been synthesized: 2,6-difluoro-4-aminoazobenzene (and its N-methyl and N,N-dimethyl derivatives), 2,3,5,6-tetrafluoro-4-aminoazobenzene (and the N-methyl and N,N-dimethyl derivatives), the 4′-ethyl derivative of all of these dyes, and the 4′-ethyl-substituted derivatives of the 3,5-difluoro azo dyes reported earlier.[1b] Visible and ultraviolet spectra were studied; noteworthy photochromic effects and remarkably slow *cis* to *trans* relaxations are reported. From the spectra of protonated dyes, calculation has been made of the relative amounts of ammonium and azonium forms.

In continuation of our first study,[1b] and for reasons outlined in that paper, we have synthesized the compounds indicated in the above title. Systematic study of the carcinogenicity of various ring-substituted derivatives of 4-dimethylaminoazobenzene (DAB)[2] has led to considerable insight into structure–activity relations. This knowledge has been most significantly built up by Dr. J. A. Miller and Dr. E. C. Miller, McArdle Laboratory, University of Wisconsin, who have summarized much of what is known about many of these compounds.[3] This laboratory is contributing to the knowledge of this area by preparing symmetrically substituted difluoro- and tetrafluoro-AB[2] dyes. We have also synthesized the 4′-ethyl derivatives of these dyes, since this substituent markedly enhances the carcinogenicity (see, *e.g.*, papers by Miller[3] and Sugiura[4] and coworkers) of 4-N-methylaminoazobenzene (MAB)[2] and DAB itself.

In addition, we find that the ultraviolet and visible spectral properties of the new dyes, reported in this paper, are fully as interesting as the properties of the 3,5-difluoro-AB (and N-methyl and -dimethyl derivatives) examined in the earlier work. The marked photochromism[5] (phototropism) and slow *cis* to *trans* isomerization noted for the latter dyes, even in ethanol,[6,7] are still more noteworthy for a number of the dyes in the present series.

Synthesis of this group of intermediates, dyes, and derivatives (Table I) was carried out essentially as described previously,[1b] differences being noted in the Experimental Section. Since nitrosobenzene and 4′-ethylnitrosobenzene condense exclusively in the 4 position of 2,6-difluoro-*p*-phenylenediamine, giving the corresponding 3,5-difluoro-AB,[8] it was necessary to use the 4-N-acetyl derivative of this difluorodiamine[9] to promote condensation to the 2,6-difluoro-AB series (Scheme I). The latter condensations gave poor yields (*ca.* 33%) and were especially sluggish, increased temperature having no effect on this lethargy.

4-Ethylnitrosobenzene, whose properties have not been recorded before,[10] is less stable than nitrosobenzene or 4-methylnitrosobenzene. Since there is considerable decomposition upon steam distillation, the compound must instead be extracted from the reaction mixture and distilled under vacuum.

Synthesis of the tetrafluoro dyes was effected in a manner similar to that for the 2,6-difluoro series (Scheme I), except that the initial condensation took place between the nitroso compound and tetrafluoro-*p*-phenylenediamine. These were also slow reactions (7 days for maximum yields of 46–48%).

Attempts to formylate the 2,3,5,6-tetrafluoro-AB dyes failed; therefore, this route to the corresponding MAB dyes was impossible. We succeeded in methylating N-acetyl-2,3,5,6-tetrafluoro-AB, however, with subsequent hydrolysis of the acetyl group to give 2,3,5,6-tetrafluoro-MAB in very low overall yield. Acetylation of 4′-ethyl-2,3,5,6-tetrafluoro-AB gave only 44% N-acetyl dye. Attempted methylation of the latter and hydrolysis gave no N-monomethylated dye. Instead we recovered only a small amount of a ring-ethoxylated product.

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(1) (a) Supported in part by Grant CA-01744 from the National Cancer Institute and by Career Development Award 5-KO3-CA-14,991 (T. L. F.). (b) Part I: N. Ishikawa, M. J. Namkung, and T. L. Fletcher, *J. Org. Chem.*, **30**, 3878 (1965).

(2) The following abbreviations are used in this paper: AB, 4-aminoazobenzene, MAB, 4-N-methylaminoazobenzene; DAB, 4-N,N-dimethylaminoazobenzene.

(3) J. A. Miller, E. C. Miller, and G. C. Finger, *Cancer Res.*, **17**, 387 (1957).

(4) K. Sugiura, M. L. Crossley, and C. J. Kensler, *J. Nat. Cancer Inst.*, **15**, 67 (1954).

(5) See R. Lovrien and J. C. B. Waddington, *J. Amer. Chem. Soc.*, **86**, 2315 (1964), footnote 2.

(6) W. R. Brode, J. H. Gould, and G. W. Wyman, *ibid.*, **75**, 1856 (1953).

(7) M. N. Inscoe, J. H. Gould, and W. R. Brode, *ibid.*, **81**, 5634 (1959).

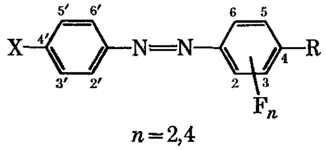
(8) The structure of 4′-ethyl-3,5-difluoro-AB was confirmed by deamination and unambiguous synthesis of the deaminated product by condensation of 4-ethylnitrosobenzene and 3,5-difluoroaniline (method A).

(9) We reported[1b] synthesis of this compound by reductive splitting of the azo group with 85% hydrazine hydrate and palladium on carbon, noting that this method appears to be new, but we later discovered that this type of reduction was reported earlier by S. Pietra, *Ann. Chim.* (Rome), **47**, 410 (1957).

(10) This compound was reported (a) by R. E. Lutz and M. R. Lytton [*J. Org. Chem.*, **2**, 73 (1937)], mp 22°, but described as impure; and (b) by this laboratory [M. E. Taylor and T. L. Fletcher, *J. Amer. Chem. Soc.*, **80**, 2246 (1958)], without physical constants or analyses. We now suspect that the compound was impure in our earlier preparation, because its use then resulted in an anomalous product. It had been steam distilled, and we now find that the compound is readily oxidized during this operation.

TABLE I

FLUORINATED 4-AMINOAZOBENZENE DERIVATIVES

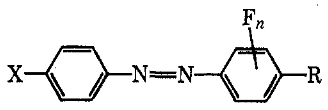


Positions of F_n	X	R	Registry no.	Method[a]	Mp, °C[b]	Yield, %	Formula	C, % Calcd	C, % Found[b]	H, % Calcd	H, % Found	F, % Calcd	F, % Found	N, % Calcd	N, % Found
3,5	Et	NH_2	22928-79-6	A	100–101	46	$C_{14}H_{13}F_2N_3$	64.36	63.95	5.02	4.97	14.54	14.67	16.08	15.98
3,5	Et	NHAc	22928-80-9	*c*	187–188	99	$C_{16}H_{15}F_2N_3O$							13.86	13.68
3,5	Et	NHCHO	22928-81-0	*d*	158–159	91	$C_{15}H_{13}F_2N_3O$	62.27	62.29	4.53	4.57				
3,5	Et	$NHCH_3$	22928-82-1	B	56–57	80	$C_{15}H_{15}F_2N_3$	65.44	65.54	5.49	5.38	13.80	13.88	15.27	15.03
3,5	Et	$N(CH_3)_2$	22955-94-8	C	49–50	96	$C_{16}H_{17}F_2N_3$	66.42	66.67	5.92	6.11	13.13	12.88	14.53	14.39
2,6	H	NH_2	22955-95-9	*e*	143–144	85	$C_{12}H_9F_2N_3$	61.80	61.73	3.80	3.80			18.02	17.82
2,6	H	NHAc	22955-96-0	D	199.5–200.5	35	$C_{14}H_{11}F_2N_3O$	61.08	61.39	4.03	4.28	13.81	13.70	15.27	15.15
2,6	H	NHCHO	22955-97-1	*d*	163–164	78	$C_{13}H_9F_2N_3O$							16.09	16.27
2,6	H	$NHCH_3$	22955-50-6	B	97–98[f]	44	$C_{13}H_{11}F_2N_3$	63.15	63.13	4.49	4.49	15.37	15.17	17.00	16.89
2,6	H	$N(CH_3)_2$	343-74-8	C	128–129[g]	51	$C_{14}H_{13}F_2N_3$	64.36	64.46	5.02	5.11	14.55	14.22	16.08	15.95
2,6	Et	NH_2	22955-52-8	*e*	113–114	94	$C_{14}H_{13}F_2N_3$	64.36	64.49	5.02	5.30			16.08	16.27
2,6	Et	NHAc	22955-53-9	D	196–197	33	$C_{16}H_{15}F_2N_3O$	63.36	63.23	4.98	4.98	12.53	12.73	13.86	14.20
2,6	Et	NHCHO	22955-54-0	*d*	159–160	92	$C_{15}H_{13}F_2N_3O$							14.53	14.82
2,6	Et	$NHCH_3$	22955-55-1	B	113–114[f]	60	$C_{15}H_{15}F_2N_3$	65.44	65.61	5.49	5.69	13.80	14.06	15.27	15.02
2,6	Et	$N(CH_3)_2$	22955-56-2	C	122.5–123.5	62	$C_{16}H_{17}F_2N_3$	66.42	66.52	5.92	5.99			14.53	14.39
2,3,5,6	H	NH_2	22955-57-3	A	128–129	46	$C_{12}H_7F_4N_3$	53.54	53.63	2.62	2.50	28.23	28.01	15.61	15.50
2,3,5,6	H	NHAc	22955-58-4	*h*	192–193	68	$C_{14}H_9F_4N_3O$							13.50	13.65
2,3,5,6	H	$NHCH_3$	22955-59-5	E	152–153	8	$C_{13}H_9F_4N_3$	55.13	55.21	3.20	3.34	26.83	27.29	14.84	14.62
2,3,5,6	H	$N(CH_3)_2$	22955-60-8	C	94–95	100	$C_{14}H_{11}F_4N_3$	56.57	56.60	3.73	3.71			14.13	14.29
2,3,5,6	Et	NH_2	22955-61-9	A	98–99	48	$C_{14}H_{11}F_4N_3$	56.57	56.51	3.73	3.73	25.57	25.29	14.13	14.32
2,3,5,6	Et	NHAc	22955-62-0	*h*	215–216	44	$C_{16}H_{13}F_4N_3O$					22.40	22.15	12.39	12.48
2,3,5,6	Et	$NHCH_3$	22955-63-1	*i*	90–91	4	$C_{15}H_{13}F_4N_3$	57.87	58.28	4.21	4.34	24.42	24.33	13.50	13.43
2,3,5,6	Et	$N(CH_3)_2$	22955-64-2	C	81–82	80[j]	$C_{16}H_{15}F_4N_3$	59.07	59.15	4.65	4.66			12.92	12.76

[a] Methods designated by capital letters are described in the Experimental Section. [b] Melting points were determined on a Fisher-Johns block and are corrected to standards. Microanalyses were determined by Dr. A. Bernhardt, Elbach über Engelskirchen, Germany, and by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. [c] Brief boiling of the corresponding amino compound with an equivalent amount of acetic anhydride gave the amide. [d] Obtained by boiling the corresponding amino compound with an excess amount of formic acid (98–100%) for 10 min. [e] Obtained by acid hydrolysis of the corresponding acetamido compound in alcoholic solution followed by basification. [f] Some preparations of 2,6-difluoro-MAB and 4′-ethyl-2,6-difluoro-MAB gave higher melting, unstable products which are under investigation. [g] This compound was first reported by Miller, *et al.*, mp 128–129°; see ref 3. [h] Acetylation required prolonged (2 hr) refluxing of the amine in a mixture of acetic acid and acetic anhydride. [i] Obtained from the second band in the chromatography of the dimethylation product of 4′-ethyl-2,3,5,6-tetrafluoro-AB. [j] A nearly quantitative yield was obtained when a small amount of the amine was dimethylated; when the batch size was increased tenfold, the yield was 80% and the monomethyl by-product was isolated (footnote *i*).

TABLE II

ABSORPTION MAXIMA[a] FOR 4-AB DERIVATIVES



$n = 2, 4$

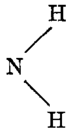
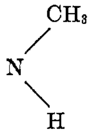
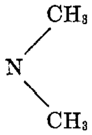
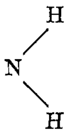
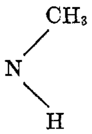
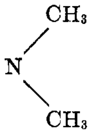
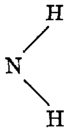
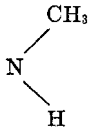
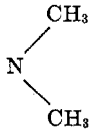
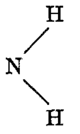
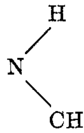
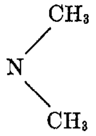
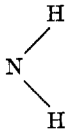
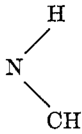
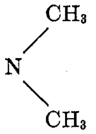
			Ethanol		Ethanol–hydrochloric acid[a]		
Positions of F_n	X	R	Solutions kept in the dark (*trans*), λ_{max}, mμ (log ε)	Solutions after illumination (*cis*), λ_{max}, mμ (log ε)	Band designation *b*	Band designation *c*	Solutions kept in the dark, λ_{max}, mμ (log ε)
3,5	C_2H_5		243 (4.10)	246 (4.09)			240 (3.76)
			299 (3.69) s[d]	364 (4.13)			264 (3.78)
			378 (4.48)	444 (3.65) s	K′	B	340 (4.11)
					Q	A	525 (4.55)
3,5	C_2H_5		245 (4.06)	247 (4.07)			237 (3.84)
			297 (3.72)	306 (3.70)			270 (3.70)
			389 (4.47)	382 (4.24)	K′	B	339 (4.26)
					Q	A	536 (4.36)
3,5	C_2H_5		238 (4.08)	242 (4.08)			237 (3.97)
			316 (3.97) s	313 (3.87) s	K′	B	339 (4.45)
			385 (4.34)	379 (4.07)	Q (?)	A (?)	436 (3.04)
2,6	H		246 (4.00)	250 (4.13)			261 (3.87)
			371 (4.42)	295 (3.70) s			313 (3.51)
			450 (3.65) s	355 (3.88)			476 (4.73)
				451 (3.68)			
2,6	H		248 (4.01)	253 (4.16)			263 (3.88)
			381 (4.44)	303 (3.68) s	K′	B	321 (3.32)
			450 (3.76) s	368 (3.97)	Q	A	486 (4.80)
				454 (3.73)			
2,6	H		252 (4.04)	257 (4.19)			266 (3.87)
			297 (3.70) s	295 (3.75)	K′	B	327 (3.26)
			385 (4.40)	373 (3.98)	Q	A	495 (4.81)
			452 (3.77) s	451 (3.73) s			
2,6	C_2H_5		245 (4.06)	251 (4.17)			265 (3.87)
			371 (4.49)	297 (3.82) s	K′	B	325 (3.60)
			443 (3.78) s	360 (3.92)	Q	A	491 (4.72)
				451 (3.73) s			
2,6	C_2H_5		247 (4.05)	252 (4.18)			268 (3.90)
			291 (3.74) s	272 (3.83) s	K′	B	328 (3.38)
			381 (4.49)	369 (4.01)	Q	A	498 (4.78)
			449 (3.82) s	452 (3.77) s			
2,6	C_2H_5		248 (4.09)	257 (4.21)			268 (3.95)
			292 (3.80)	293 (3.86) s	K′	B	331 (3.41)
			386 (4.45)	375 (4.03)	Q	A	507 (4.81)
			449 (3.86) s	450 (3.79)			
2,3,5,6	H		234 (4.05)	238 (4.11)			238 (3.86)
			364 (4.38)	306 (3.82)	K′	B	365 (4.31)
			435 (3.56) s	356 (3.87)	Q	A	491 (4.23)
				445 (3.55)			

TABLE II

(*Continued*)

			Ethanol		Ethanol-hydrochloric acid[a]		
Positions of F_n	X	R	Solutions kept in the dark (*trans*), λ_{max}, mμ (log ε)	Solutions after illumination (*cis*), λ_{max}, mμ (log ε)	Band designation *b*	Band designation *c*	Solutions kept in the dark, λ_{max}, mμ (log ε)
2,3,5,6	H		239 (4.04) 263 (3.88) s 377 (4.39) 449 (3.59) s	245 (4.13) 365 (3.87) 442 (3.58)	K′ Q	B A	256 (3.76) 379 (3.93) 505 (4.62)
2,3,5,6	H		235 (4.01) 268 (3.94) 378 (4.20) 452 (3.49) s	240 (4.01) 265 (4.04) 369 (3.80) 433 (3.50) s	K′ Q	B A	234 (3.89) 318 (4.29) 390 (3.47) s 514–555 (3.51)
2,3,5,6	C_2H_5		237 (4.08) 365 (4.44) 435 (3.56) s	240 (4.12) 306 (3.82) 356 (3.87) 445 (3.55)	K′ Q	B A	242 (3.91) 366 (4.32) 507 (4.29)
2,3,5,6	C_2H_5		241 (4.12) 303 (3.81) s 375 (4.49) 451 (3.71) s	247 (4.17) 297 (3.92) s 366 (3.88) 448 (3.65)	K′ Q	B A	253 (3.85) 373 (4.00) 522 (4.67)
2,3,5,6	C_2H_5		239 (4.05) 261 (3.91) s 307 (3.92) 376 (4.21) 450 (3.57) s	243 (4.04) 263 (4.03) 294 (3.92) s 369 (3.82) 435 (3.56) s	K′ Q	B A	238 (3.98) 334 (4.34) 545 (3.47)

[a] Ultraviolet and visible absorption spectra were obtained on a Beckman DK-1 automatic recording spectrophotometer in neutral absolute ethanol and in *ca.* 4 *N* hydrochloric acid in absolute ethanol. The 4 *N* solutions were conveniently made by adding 28.56 ml of 7 *N* HCl to an alcoholic solution of the dye in a 50-ml volumetric flask and then filling to the mark with alcohol. The concentration of the dyes in neutral solutions was 4×10^{-5} *M* in all cases. In acid solution the concentration was the same except for the following dyes, where it was 2×10^{-5} *M:* 2,6-difluoro-AB, MAB, and DAB; 4′-ethyl-2,6-difluoro-AB, MAB, and DAB; tetrafluoro-MAB; and 4′-ethyl-tetrafluoro-MAB. [b] G. E. Lewis, *Tetrahedron,* **10,** 129 (1960); A. J. Ryan, *ibid.,* **20,** 1547 (1964). [c] G. Cilento, E. C. Miller, and J. A. Miller, *J. Amer. Chem. Soc.,* **78,** 1718 (1956). [d] s = shoulder.

Dimethylation of the two tetrafluoro-AB dyes gave high yields of the corresponding DAB dyes. From the reaction mixture after N,N-dimethylation of 4′-ethyl-2,3,5,6-tetrafluoro-AB, we obtained a 4% yield of the corresponding, elusive MAB.

Spectra in visible and ultraviolet light were carried out as described in the first paper (Table II).[1b] In general, in neutral ethanol, maxima at *ca.* 245 mμ were shifted to slightly longer wavelengths (with the same or slightly increased absorbance) and those at 365–400 mμ to shorter wavelengths (with markedly decreased absorbance) by illumination. With the introduction of an ethyl group at the 4′ position, there is an increase in absorbance at the shoulder or maximum at *ca.* 300 mμ (3,5-difluoro-AB and -MAB), or *ca.* 290 mμ (2,6-difluoro-MAB and -DAB), but there is no such difference in the case of the tetrafluoro dyes.

Table III shows the per cent return of absorption maxima at *ca.* 375 mμ from the fully illuminated state to the relaxed form (in the dark) for given times; it clearly shows that the 2,6-difluoro[11] and tetrafluoro azo dyes change much more slowly from *cis* to *trans* than the 3,5-difluoro dyes. The latter, as pointed out earlier, are slower to transform than ordinary unfluorinated azo dyes.

Very little photochromic effect was observed with these dyes in acidic ethanol; the few solutions which we examined in this way could not be studied meaningfully, since irreversible deterioration was detectable shortly after illumination began.

As discussed in the literature,[1b,12] there is a reciprocal relationship in acidic solutions (indicating tautomeric forms) between the so-called K′ and Q[13,14] (or B and A[12]) bands (see Table II) which are located at 310–340[15] and 475–535 mμ, respectively. The first of these (K′ or B) is due to protonation of the amine group, and the second (Q or A) is due to protonation of the β nitrogen atom of the azo group. The latter band, in the spectrum of 4′-ethyl-3,5-difluoro-DAB, is located at 436 mμ with very low absorbance, indicating very little azonium ion formation. Table IV gives the results of calculating the percentages of each form of protonated dye by the method of Ryan.[14] By plotting the ε

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[11] See footnote *f*, Table I.

[12] G. Cilento, E. C. Miller, and J. A. Miller, *J. Amer. Chem. Soc.,* **78,** 1718 (1956).

[13] G. E. Lewis, *Tetrahedron,* **10,** 129 (1960).

[14] A. J. Ryan, *ibid.,* **20,** 1547 (1964).

[15] For the tetrafluoro dyes, described in this paper, this band is found at 334–390 mμ.

SCHEME I

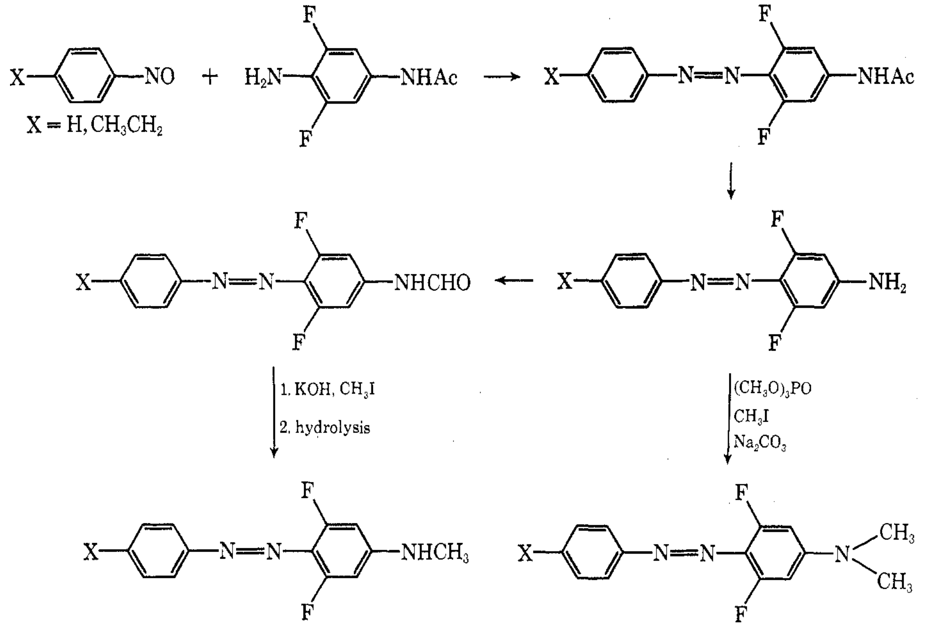
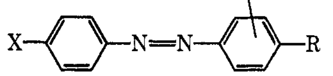


TABLE III

COMPARISON OF TIMES FOR *cis* TO *trans* REVERSION, AFTER ILLUMINATION, FOR FLUORINATED 4-AB DERIVATIVES[a,b]



$n = 2, 4$

Positions of F$_n$	X	R	Return, % 1 hr	2 hr	3 hr	4 hr
3,5	Et	NH$_2$	64	80	88	91
3,5	Et	NHCH$_3$	81	93	100	
3,5	Et	N(CH$_3$)$_2$	39	63	71	74
2,6	H	N(CH$_3$)$_2$	30	42	44	
2,3,5,6	Et	NH$_2$	17	23	26	28
2,3,5,6	Et	NHCH$_3$	10	15	19	25
2,3,5,6	Et	N(CH$_3$)$_2$	10	14	15	16
2,6	Et	NHCH$_3$	7	9	16	17
2,6	Et	N(CH$_3$)$_2$	12	15	17	18
2,3,5,6	H	NH$_2$	5	8	9	10
2,3,5,6	H	NHCH$_3$	2	5	10	13
2,3,5,6	H	N(CH$_3$)$_2$	1	3	6	9

[a] Per cent return = 100 (absorbance change for a given time interval)/[total absorbance change (*trans* → *cis*)], calculated for the peak between 365 and 400 mμ which showed the largest difference in absorbance upon prolonged illumination in neutral alcoholic solution. [b] In contrast, we have observed that the unfluorinated 4′-ethyl-DAB, for example, reverts to the extent of *ca.* 90% in 15–20 min.

values of the K′ bands, $\epsilon_{K'}$, against those of the Q bands, ϵ_Q, and drawing the line of best fit we obtained 24,000 and 67,000 as the limiting values for the K′ (B) and Q (A) bands, respectively, for the 4′-H dyes, and 28,000 and 68,000 as the corresponding values for the 4′-ethyl dyes. The ratios 100 ($\epsilon_{K'}$/lim. $\epsilon_{K'}$) and 100 (ϵ_Q/lim. ϵ_Q) then give the percentages of the ammonium and azonium forms, respectively, present in the equilibrium mixture.

Infrared data are as expected: ν_{max} 1391–1429 cm^{-1} (N=N)[16] and 1111–1178 cm^{-1} (CN=).[16] Tentative assignments for ν_{max} for the aryl CF bands (based on the literature[17] and previous work in this laboratory[17]) are as follows: for the difluorinated dyes, 1193–1316 and 1012–1139 cm^{-1}; for the tetrafluorinated dyes, 1294–1325 and 1168–1295 cm^{-1} and, in general, additional bands at 1156–1258 and 1005–1025 cm^{-1}.

Tlc data have been published elsewhere.[18]

Experimental Section[19]

***p*-Ethylnitrosobenzene.**—This was prepared essentially by the method of Lutz and Lytton[10a] with some modifications. The reaction medium for the reduction was a 2:1 (v/v) mixture of EtOH and CH$_3$OCH$_2$CH$_2$OH with NH$_4$Cl (rather than CaCl$_2$) in a little H$_2$O. The second step, oxidation to the NO group with cold aqueous FeCl$_3$, was followed by overnight refrigeration and separation of the crude oil. The latter was washed several

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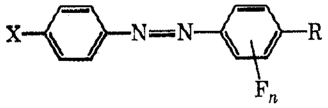
[16] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1958, p 272; P. Bassignaa and C. Cogrossi, *Tetrahedron*, **20**, 2361 (1964).

[17] See also M. J. Namkung and T. L. Fletcher, *J. Org. Chem.*, **26**, 2243 (1961); K. Suzuki, E. K. Weisburger, and J. H. Weisburger, *ibid.*, **24**, 1511 (1959); M. J. Namkung and T. L. Fletcher, *Can. J. Chem.*, **45**, 2569 (1967), footnotes 1, 12; ref 1b.

[18] N. K. Naimy, M. J. Namkung, and T. L. Fletcher, *J. Chromatog.*, **43**, 537 (1969).

[19] See footnote *b*, Table I.

TABLE IV
RELATIVE AMOUNTS[a] OF PROTONATED TAUTOMERS OF FLUORINATED 4-AB DERIVATIVES



$n = 2,4$

Positions of F_n	X	R	Ammonium form, %	Azonium form, %
3,5	H	NH_2	48	53
3,5	H	$NHCH_3$	65	30
3,5	H	$N(CH_3)_2$	100	5
3,5	Et	NH_2	46	52
3,5	Et	$NHCH_3$	65	34
3,5	Et	$N(CH_3)_2$	100	2
2,6	H	NH_2	14	81
2,6	H	$NHCH_3$	9	94
2,6	H	$N(CH_3)_2$	8	96
2,6	Et	NH_2	14	78
2,6	Et	$NHCH_3$	9	89
2,6	Et	$N(CH_3)_2$	9	97
2,3,5,6	H	NH_2	86	25
2,3,5,6	H	$NHCH_3$	35	63
2,3,5,6	H	$N(CH_3)_2$	82	5
2,3,5,6	Et	NH_2	75	28
2,3,5,6	Et	$NHCH_3$	35	67
2,3,5,6	Et	$N(CH_3)_2$	78	5

[a] Based as described in text on method of Ryan.[14]

times with H_2O, taken up in Et_2O, and dried over Na_2SO_4 and then molecular sieves (type 4A). The crude product from four batches of 30.2 g of 4-ethylnitrobenzene[20] was distilled at 4.5 mm under a blanket of N_2. The product (which decomposes when steam distilled) was collected at 64–65°: yield 33 g (30%); mp 17–18°; $n^{25}D$ 1.5550; ir (neat) 1508 cm^{-1}.

Anal. Calcd for C_8H_9NO: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.23; H, 6.67; N, 10.09.

3,5-Difluoro-4′-ethylazobenzene. A. Deamination of 3,5-Difluoro-4′-ethyl-AB.—The named AB was deaminated as described[1b] for 3,5-difluoro-AB in 45% yield, mp 81–82°.

Anal. Calcd for $C_{14}H_{12}F_2N_2$: C, 68.28; H, 4.91; N, 11.37. Found: C, 68.39; H, 4.95; N, 11.37.

B.—The foregoing compound was also synthesized by method A in the next paragraph in 64% yield (melting point, mixture melting point with product in previous paragraph, and ir spectra all identical).

Methods, as Indicated in Table I. A.—Arylene diamines were condensed with nitrosobenzene, or 4-ethylnitrosobenzene, in the general way described previously.[1b] For most of these condensations we used temperatures of 32–38°. For optimum yields of the tetrafluorinated[21] dyes the reaction was continued for 10 days at temperatures of 40–43°.

Method B.—4-Formamidoazo dyes were methylated with CH_3I in alcoholic KOH followed by hydrolysis in added aqueous NaOH.[1b]

Method C.—Dimethylation of aminoazo dyes was carried out in $(CH_3O)_3PO$, CH_3I, and Na_2CO_3.[1b,22]

Method D.—A mixture of 12 g of 4-acetamido-2,6-difluoroaniline[1b] and 5.7 g of nitrosobenzene[20] or 7.3 g of *p*-ethylnitrosobenzene in 30 ml of absolute ethanol and 15 ml of glacial acetic acid was flushed with N_2 and allowed to stand at 37° ± 2° for 14 days. The reaction mixture was stirred into water and the supernatant was decanted from gummy material. The latter was dried, dissolved in benzene, and put through an alumina column. After the eluent was evaporated, the product in the major red band was rechromatographed, giving the yields and melting points recorded in Table I.

Method E. 2,3,5,6-Tetrafluoro-MAB.—A mixture 2 g of 4-acetamido-2,3,5,6-tetrafluoroazobenzene, 20 ml of EtOH, 0.7 g of KOH, and 3 g of CH_3I was boiled under reflux for 4 hr; 10 ml of 20% aqueous NaOH was added; and refluxing was continued for 1 hr. The reaction mixture was poured into water and the red precipitate was filtered off and dried. The product was passed through an alumina column (C_6H_6). Upon evaporation of the solvent and addition of 1 drop of MeOH, red crystals formed, mp 141–153°. Recrystallization from alcohol raised the melting point (Table I).

Registry No.—*p*-Ethyl nitrosobenzene, 22955-65-3; 3,5-difluoro-4′-ethylazobeneze, 22955-66-4.

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(20) Aldrich Chemical Co., Milwaukee, Wis.

(21) Tetrafluoro-*p*-phenylenediamine was purchased from Whittaker Corp., San Diego, Calif.

(22) H.-L. Pan and T. L. Fletcher, *J. Org. Chem.*, **27**, 3639 (1962).

Electrolyte Effects upon the Reactions of Nitrohalobenzenes with Amines[1]

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Specific salt effects have been observed for reactions between 2,4-dinitrofluorobenzene and aniline or the anions of glycine, glycylglycine, and glycylglycylglycine in water, and for the reactions of 2,4-dinitrochlorobenzene and aniline or the glycylglycinate ion. The overall salt effects can be separated into those on the activity coefficient of the substrate, and on the relative activity coefficients of the nucleophile and the transition state. The transition-state effects are smaller for reactions of the amines than of hydroxide ion. Anions of high charge density, *e.g.*, SO_4^{2-}, assist reaction by destabilizing the substrate even though they destabilize the transition state relative to the nucleophile, whereas low charge density anions and cations, *e.g.*, ClO_4^- or $(CH_3)_4N^+$, stabilize both the substrate and the transition state.

The reactions between nucleophiles and 2,4-dinitrofluoro- and -chlorobenzene involve initial addition to give an intermediate which then loses the halide ion. For general discussions of these reactions, see ref 2. In polar hydroxylic solvents loss of the halide ion is generally rapid, so that the rate-limiting step is nucleophilic addition, but in favorable cases loss of fluoride ion may be slow,[2] and in one system slow loss of chloride has been observed.[3]

Aromatic substitutions by nucleophilic anions are subject to large specific salt effects,[4–6] whereas the Debye–Hückel relationship predicts that they should be absent, and the Hughes–Ingold extension of this

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[1] Support of this work by the National Science Foundation is gratefully acknowledged.

[2] J. F. Bunnett, *Quart, Rev.* (London), **12**, 1 (1958); S. D. Ross, *Progr. Phys. Org. Chem.*, **1**, 31 (1963); J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, **87**, 3875, 3879 (1965); J. Miller, *Aust. J. Chem.*, **22**, 921 (1969).

[3] R. L. Toranzo, R. V. Caneda, and J. Brieux, *J. Amer. Chem. Soc.*, **88**, 3651 (1966).

[4] J. D. Reinheimer, J. T. Gerig, and J. C. Cochran, *ibid.*, **83**, 2873 (1961), and references cited therein.

[5] C. A. Bunton and L. Robinson, *ibid.*, **90**, 3965 (1968).

[6] C. A. Bunton and L. Robinson, *J. Org. Chem.*, **34**, 780 (1969).