solid then melted again at about 200°. The melting points varied with the duration of heating. This behavior is probably due to thermal rearrangement which has been reported[12] to occur in related triazoles.

Anal. Calcd. for $C_9H_9N_5O$: C, 53.19; H, 4.46; N, 34.47. Found: C, 52.94; H, 4.32; N, 34.32.

Spectral Data. λ_{max} in mμ (a_M) in absolute alcohol: 225 (10.2×10^3), 253 (shoulder) (9.50×10^3). The spectrum was similar to that of 1-phenyl-4-carbethoxy-5-amino-1,2,3-triazole, prepared according to Dimroth.[12]

4(5)-Carboxamido-5(4)-phenylamino-1,2,3-triazole. For rearrangement of 1-phenyl-4-carboxamido-5-amino-1,2,3-triazole, the conditions used were those reported by Dimroth[12] for the rearrangement of 1-phenyl-4-carbethoxy-5-amino-1,2,3-triazole to 4(5)-carbethoxy-5(4)-phenylamino-1,2,3-triazole. After the 1-phenyl derivative had been refluxed in pyridine for 3 hr., the reaction mixture was cooled and neutralized with hydrochloric or acetic acid to precipitate the triazole. The triazole, thus obtained in 75% yield, melted at 200–201° after being recrystallized from absolute ethanol. The elemental analysis was the same as that of the starting material. The ultraviolet absorption spectrum, determined in absolute ethanol, had maxima at 262 mμ (a_M, 10.2×10^3) and at 297 mμ (a_M, 9.93×10^3) and was similar to that found for 4(5)-carbethoxy-5(4)-phenylamino-1,2,3-triazole.[12]

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New Trifluoromethylphenothiazine Derivatives

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We wish to make a preliminary report of some physical and chemical data on aminoalkyl fluorine-substituted phenothiazines with pronounced pharmacological activity.[1,4] Phenothiazine drugs containing halogen or methoxyl substituents have been discussed by Viaud.[2] Smith has reported several trifluoromethylphenothiazines,[3] but no 10-aminoalkyl derivatives thereof have been described chemically. A preliminary report on the pharmacological activity of compounds 2 and 9 (Table III) has been presented.[4a,b] A brief clinical report[4c] on the antiemetic and psychotherapeutic effectiveness of com-

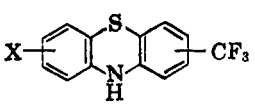
(1) The pharmacology of these drugs will be published in detail elsewhere by Dr. Leonard Cook and coworkers of these laboratories.

(2) P. Viaud, *J. Pharm. Pharmacol.*, **6**, 361 (1954).

(3) N. L. Smith, *J. Org. Chem.*, **15**, 1125 (1950).

(4) (a) J. C. Burke, H. L. Yale, G. L. Hassert, Jr., and J. P. High, Program, The American Society for Pharmacology and Experimental Therapeutics Meeting, French Lick, Ind., Nov. 8–10, 1956, p. 11. (b) J. J. Piala, J. P. High, K. Greenspan, and J. C. Burke, Program, The American Society for Pharmacology and Experimental Therapeutics Meeting, French Lick, Ind., Nov. 8–10, 1956, p. 11. (c) P. K. Conner, W. Fraser, S. I. Kinard, H. Bennett, and J. H. Moyer, *Clin. Res. Proc.*, **5** (1), 121 (1957).

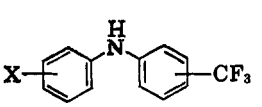
TABLE I



X	CF_3 (Position)	M.P., °C.[a]	Yield, %	Formula	Analysis Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
H[b]	4	71–72°	5	$C_{13}H_8F_3NS$	58.42	3.02	5.24	58.54	3.18	5.38
8-Cl	2	188–189°	8.5	$C_{13}H_7ClF_3NS$	51.75	2.34		52.10	2.59	
7-OCH_3	2	169–170°	19	$C_{14}H_{10}F_3NOS$	56.56	3.39	4.71	56.63	3.62	4.75

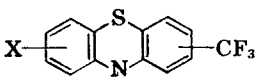
[a] Uncorrected. [b] Prepared by H. E. Reiff and J. Jaffe of these (SKF) Laboratories.

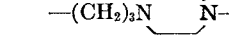
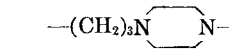
TABLE II



X	CF_3 (Position)	B.P., °C.	Yield, %	Formula	Analysis Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
3-Cl	3′	128–9°/0.05 mm.	57	$C_{13}H_9ClF_3N$	57.47	3.34	5.16	57.41	3.37	5.26
4-OCH_3	3′	m.p. 59–60°	41	$C_{14}H_{12}F_3NO$	62.92	4.53	5.24	63.00	4.65	5.16

TABLE III



No.	CF_3 (Position)	R	X	B.P., °C.	M.P., °C.[a]	Formula	Analysis Calcd. C	Calcd. H	Found C	Found H
1	2[b]	$-CH_2CH_2N(CH_3)_2$	H	152.5°/0.3 mm.	239.5–240° (HCl)	$C_{17}H_{18}ClF_3N_2S$	54.47	5.84	54.66	4.97
2	2	$-CH_2CH_2CH_2N(CH_3)_2H$	H	177–181°/1 mm.	176–177° (HCl)	$C_{18}H_{20}ClF_3N_2S$	55.59	5.21	55.70	5.22
3	2	$-(CH_2)_3N(CH_3)_2$	H		214–5° (HCl)	$C_{18}H_{20}ClF_3N_2OS$	53.39	4.98	53.11	5.08
4	2[c]		H	202–210°/0.7 mm.	193–194° (dimaleate)	$C_{29}H_{32}F_3N_3O_8S$	54.45	5.04	54.53	5.17
5	2[d]	 (sulfoxide)	H	—	173–175° di HCl	$C_{21}H_{26}Cl_2F_3N_3OS$ .3 H_2O	45.82	5.86	45.50	5.92
6	2	$-(CH_2)_3N(CH_3)_2$	7-OCH_3	205–210°/0.8 mm.	177.5–179° (HCl)	$C_{19}H_{22}ClF_3N_2OS$	54.47	5.29	54.77	5.53
7	2	$-(CH_2)_3N(CH_3)_2$	8-Cl	195–202°/1.3 mm.	114–116° (maleate)	$C_{22}H_{22}ClF_3N_2SO_4$	52.54	4.41	52.61	4.70
8	2	$-(CH_2)_3N(CH_3)_2$	8C-H_3	188–191°/0.5 mm.	153–154° (maleate)	$C_{23}H_{25}F_3N_2O_4S$	57.25	5.22	57.42	5.20
9	4	$-(CH_2)_3N(CH_3)_2$	H	185–190°/0.3 mm.	147–148° (HCl)	$C_{18}H_{20}ClF_3N_2S$	55.59	5.18	55.59	5.11

[a] Uncorrected (oil bath). [b] Prepared by A. M. Pavloff, SKF Laboratories. [c] Prepared by B. M. Lester, SKF Laboratories. [d] Prepared by E. L. Anderson, SKF Laboratories.

pounds 2 and 4 (Table III) has also been published recently.

The compounds in Table III were prepared by alkylation of the appropriate phenothiazine with a tertiary aminoalkyl halide in an inert solvent, using sodamide as a condensing agent.[5] In Table I are listed the parent trifluoromethylphenothiazines prepared in this work which have not been described elsewhere.

The substituted phenothiazines were prepared by the method of Bernthsen,[6] using the appropriately substituted diphenylamines. The diphenylamines which have not been described elsewhere are listed in Table II. An alternative route to the trifluoromethylphenothiazines is found in the Smiles rearrangement.[7]

The sulfoxides listed in Table III were prepared by the action of hydrogen peroxide on the oxalate salts of the parent compound.[8]

4-Trifluoromethylphenothiazine (m.p. 71–72°) was isolated in yields of less than 5% as a side-product in the thionation of 3-trifluoromethyldiphenylamine. Its configuration as the 4-isomer was indicated by the peak in infrared at 12.5 microns, found in 1,2,3-trisubstituted benzene[9] rings, and by the absence of a peak at 12–12.1 microns, found in 2-trifluoromethylphenothiazine[3] and other 1,2,4-trisubstituted benzene compounds.[9]

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Preparation of 2,2′-Diaminobiphenyl by Reduction of 2,2′-Dinitrobiphenyl

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Attempts to prepare 2,2′-diaminobiphenyl from 2,2′-dinitrobiphenyl by chemical reduction according to methods reported in the literature and by various modifications of these methods gave erratic results. Occasionally good yields of the diamine were obtained, but frequently the products were unreacted dinitrobiphenyl, tar, benzo[*c*]cinnoline-5-oxide, or benzo[*c*]cinnoline-5,6-dioxide or various mixtures.

Catalytic reductions in general were more satisfactory. The procedure of S. D. Ross, Kahan, and Leach[1] using ethanol-ethyl acetate (1 v.: 3 v.) and Adams catalyst gave uniformly good yields. The amount of catalyst and time of reduction can be reduced if the hydrogenation is carried out at an elevated temperature. Thus a solution of 12 g. of 2,2′-dinitrobiphenyl in 200 cc. of mixed solvent with 0.006 g. of platinum oxide, which was placed in the hydrogenator at 60°, was reduced in 20 min., whereas a run of the same size using 0.1 g. of catalyst which was started at room temperature required 30 min. The addition of six drops of 6*N* acetic acid had no effect on the rate at room temperature. The addition of six drops of 6*N* aqueous sodium hydroxide greatly reduced the rate of hydrogenation for about 25 min., but then the rate approached that of the neutral or acidic runs. Evidently alkali decreases the rate but is removed by reaction with the ethyl acetate. Reductions in ethanol[2] have the disadvantage that only about 1 g. of dinitrobiphenyl can be dissolved in 200 cc. and that the rate of reduction is somewhat slower than in the mixed solvent. Neither acid nor base has an appreciable effect on the rate in this solvent.

Everett and W. C. J. Ross[3] report that catalytic reduction of an ethanol solution of 2,2′-dinitrobiphenyl in ethanol in the presence of Raney nickel gave benzo[*c*]cinnoline. The present work shows, however, that under the proper conditions W-2 Raney nickel[4] gives excellent yields of 2,2′-diaminobiphenyl. An initial gauge pressure of around 50 p.s.i. is preferred. At pressures of 600 p.s.i. and at 2000 p.s.i. the results were erratic, tars and benzo-[*c*]cinnoline-5-oxide being among the products obtained. The ethanol-ethyl acetate (1 v.:3 v.) mixture was preferable as a solvent to methanol, ethanol, or dioxane. The usual concentration in this solvent was 12 g. per 200 cc. The rate of reduction definitely was dependent on the age of the catalyst. In a series of standard runs using 4 cc. of catalyst mush, starting with the solution at 60° and using catalyst that was 0, 6, 12, 20, and 24 months old, the time for complete reduction of 12 g. was 20,

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