water, and dried. Recrystallization of the product from methanol gave the trienone (0.5 g.), m.p. 140–144°, λ_{max} 282–289 mμ (ε 3250).

Anal. Calcd. for $C_{20}H_{26}O_3$: C, 76.4; H, 8.3. Found: C, 76.2; H, 8.1.

The same trienone was obtained by hydrogenation over 10% palladized charcoal in ethanol of the tetraenone IX.

(±)-2,3-Dihydroxyestra-1,3,5(10)-trien-17-one (X).—The trienone VIII (0.3 g.) was stirred for 30 min. under nitrogen in molten pyridine hydrochloride at 185–195°. The cooled melt was added to 3 *N* HCl and the mixture was extracted with ether. Recrystallization of the product from ether gave the trienone, m.p. 220–230°, λ_{max} 290 mμ (ε 4100).

Anal. Calcd. for $C_{18}H_{22}O_3$: C, 75.3; H, 7.7. Found: C, 75.1; H, 7.5.

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Derivatives of Imidazole. II. Synthesis and Reactions of Imidazo[1,2-*a*]pyrimidines and Other Bi- and Tricyclic Imidazo Derivatives with Analgesic, Antiinflammatory, Antipyretic, and Anticonvulsant Activity

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The synthesis and pharmacological properties of some derivatives of imidazo[1,2-*a*]pyrimidine, 1H-imidazo[1,2-*d*]tetrazole, imidazo[2,1-*b*]thiazole, 1H-imidazo[1,2-*b*]-*s*-triazole, and imidazo[1,2-*b*]pyridazine are described. The results have been compared with those obtained under the same conditions with acetylsalicylic acid, aminopyrine, phenylbutazone, and chlortenoxazine. Some members of the series display activities in one or more of the pharmacological tests; the most interesting compounds are 2-(*p*-methylthiophenyl)-3-(morpholinomethyl)imidazo[1,2-*a*]pyrimidine (**7**), 2-(*p*-methylthiophenyl)-3-[4-(2-hydroxyethyl)-1-piperazinylmethyl]-imidazo[1,2-*a*]pyrimidine (**8**), and 2-(*p*-methylsulfonylphenyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzothiazole hydrochloride (**17**).

The first paper in this series[2] described the synthesis of a series of substituted imidazo[1,2-*a*]pyridines examined for analgesic, antiinflammatory, antipyretic, and anticonvulsant (muscle-relaxant) activity. The most active compounds were 2-(*p*-methylsulfonylphenyl)imidazo[1,2-*a*]pyridine hydrochloride and its dimethylaminomethyl Mannich base.

In order to study whether modification in the heterocyclic ring might result in a different spectrum or order of pharmacological activity, we synthesized a series of new imidazo[1,2-*a*]pyrimidines (Table I) which are closely related to the compounds described in the first paper. Other heterocyclic derivatives of imidazole were also synthesized (Table II) in order to extend the pharmacological screening to imidazo derivatives with an atom of nitrogen in angular position. Since earlier studies[2] have shown that substitution in R with a methylsulfonyl group seemed to be necessary for a broad spectrum of activity, this group was kept constant in these compounds.

Substituted 2-arylimidazo[1,2-*a*]pyrimidines (**1–5**) were prepared by condensation of 2-aminopyrimidine and 2-amino-5-methoxypyrimidine[3] with ω-bromoacetophenones, substituted in the *para* or *ortho* position with a methylthio, methylsulfoxy, or methylsulfonyl group.[2] Mannich bases **6–13** were obtained in acetic acid as previously described for imidazo[1,2-*a*]pyridines.[2]

2-(*p*-Methylsulfonylphenyl)-1H-imidazo[1,2-*d*]tetrazole (**14**) was obtained from 5-amino-1H-tetrazole and ω-bromo-*p*-methylsulfonylacetophenone. Other products reported in Table II (**15–22**) were prepared by the same method, starting from 2-aminothiazole, 2-amino-4,5,6,7-tetrahydrobenzothiazole,[4] 2-amino-5,6-dihydro-4H-cyclopentathiazole,[4] 3-amino-1,2,4-triazole, 3-aminopyridazine, 3-amino-6-chloropyridazine, and 3-amino-6-methoxypyridazine, respectively.

The rings of imidazo[1,2-*b*]pyridazine,[5] 1H-imidazo[1,2-*b*]-*s*-triazole, and 6,7-dihydro-5H-imidazo[2,1-*b*]-cyclopentathiazole are not recorded in "The Ring Index."[6]

Pharmacological Studies.—LD_{50} values in mice were determined, and analgesic, antiinflammatory, antipyretic, and anticonvulsant activities were investigated in several basic screening procedures as previously described.[2] The pharmacological results are presented in Table III as are the results of the standard drugs (acetylsalicylic acid, aminopyrine, phenylbutazone, and chlortenoxazine) and the most active compound of the earlier series (2-(*p*-methylsulfonylphenyl)imidazo[1,2-*a*]pyridine hydrochloride) for comparison.

Analgesic Activity.—Among the 22 compounds examined, significant analgesic activity was displayed only by the 2-phenylimidazo[1,2-*a*]pyrimidine analogs. Although several compounds of this series showed analgesic properties in one or more of the tests employed, this effect was accentuated in those substances where R = *o*-SO_2CH_3 (**1**) and *p*-$SOCH_3$ (**3**). Introduction of a

(1) To whom all inquiries concerning pharmacology should be sent.

(2) L. Almirante, L. Polo, A. Mugnaini, E. Provinciali, P. Rugarli, A. Biancotti, A. Gamba, and W. Murmann, *J. Med. Chem.*, **8**, 305 (1965).

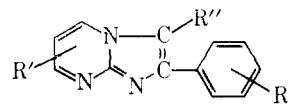
(3) H. Priewe and K. Gutsche, German Patent 1,145,622 (1963).

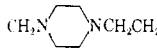
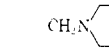
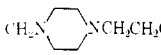
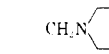
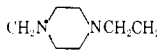
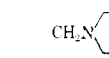
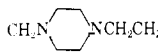
(4) H. Erlenmeyer and W. Schoenauer, *Helv. Chim. Acta*, **24**, 172–9E (1941).

(5) After the termination of this paper we had notice of the preparation of similar compounds by F. Yoneda, T. Otaka, and Y. Nitta [*Chem. Pharm. Bull.* (Tokyo), **12**, 1351 (1964); *Chem. Abstr.*, **62**, 5273*g* (1965)].

(6) A. M. Patterson, L. T. Capell, and D. F. Walker, "The Ring Index," American Chemical Society, Washington, D. C., 1960; Supplements, 1963 1964.

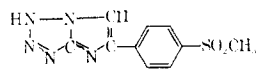
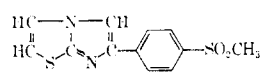
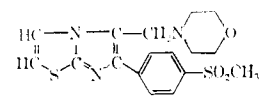
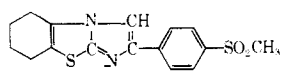
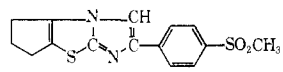
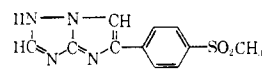
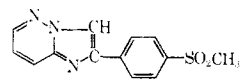
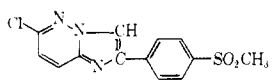
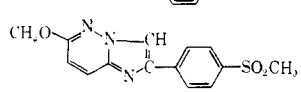
TABLE I



No.	R	R'	R''	Derivative[a]	Recrystn. solvent	M.p., °C.	Formula
1	*o*-SO_2CH_3	H	H	A	Ethanol	202–205	$C_{13}H_{11}N_3O_2S$
2	*p*-SCH_3	H	H	A	95% ethanol	222–224	$C_{13}H_{11}N_3S$
3	*p*-$SOCH_3$	H	H	A	Ethanol	282–284	$C_{13}H_{11}N_3OS$
4	*p*-SO_2CH_3	H	H	A	Ethanol	276–277	$C_{13}H_{11}N_3O_2S$
5	*p*-SO_2CH_3	6-OCH_3	H	A	Ethanol	265–267	$C_{14}H_{13}N_3O_3S$
6	*o*-SO_2CH_3	H		A	Ethanol	117–122	$C_{20}H_{25}N_5O_3S$
7	*p*-SCH_3	H		A	95% ethanol	139–141	$C_{18}H_{20}N_4OS$
8	*p*-SCH_3	H		A	Ethanol	187–188	$C_{20}H_{25}N_5OS$
9	*p*-$SOCH_3$	H		A	Ethanol	225–227	$C_{18}H_{20}N_4O_2S$
10	*p*-$SOCH_3$	H		B	Ethanol	222–225	$C_{20}H_{28}Cl_3N_5O_2S$
11	*p*-SO_2CH_3	H	$CH_2N(CH_3)_2$	C	95% ethanol	235–241	$C_{16}H_{20}Cl_2N_4O_2S$
12	*p*-SO_2CH_3	H		A	N,N-Dimethylformamide	270–272	$C_{18}H_{20}N_4O_3S$
13	*p*-SO_2CH_3	H		A	N,N-Dimethylformamide	248–249	$C_{20}H_{25}N_5O_3S$

[a] A, base; B, trihydrochloride; and C, dihydrochloride.

TABLE II

No.	Compd.	Derivative[a]	Recrystn. solvent	M.p., °C.	Formula
14		A	10% aq. HCl	235–238 dec.	$C_{10}H_{10}ClN_5O_2S$
15		B	Acetic acid	252–254 dec.	$C_{12}H_{10}N_2O_2S_2$
16		B	Acetic acid	209–211 dec.	$C_{17}H_9N_3O_3S_2$
17		A	10% aq. HCl	248–253 dec.	$C_{16}H_{17}ClN_2O_2S_2$
18		B	Acetic acid	246–248 dec.	$C_{15}H_{14}N_2O_2S_2$
19		B	Acetic acid	286–291 dec.	$C_{11}H_{10}N_4O_2S$
20		C	10% aq. HBr	270–272 dec.	$C_{13}H_{12}BrN_3O_2S$
21		B	Acetic acid	251–253 dec.	$C_{13}H_{10}ClN_3O_2S$
22		B	Acetic acid	216–219	$C_{14}H_{13}N_3O_3S$

[a] A, hydrochloride; B, base; and C, hydrobromide.

dialkylamino group at position R'' of the *p*-methylthio- and the *p*-methylsulfonyl-substituted derivatives further increased the intensity of analgesic activity (**7**, **8**, *vs.* **2**; **11**, **12** *vs.* **4**).

Finally it appeared that the analgesic activity in the electric stimulus test could be separated from the analgesic effect in the Randall and Selitto[7] procedure according to the nature of the substituent in R''; *i.e.*,

(7) L. O. Randall and J. J. Selitto, *Arch. intern. pharmacodynam.*, **111**, 409 (1957).

Mol. wt.	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found	O, % Calcd.	O, % Found	S, % Calcd.	S, % Found
273.3	57.13	56.64	4.05	4.28	15.38	15.69				
241.3	64.70	65.31	4.59	4.65	17.41	17.11				
257.3	60.88	60.67	4.31	4.35	16.33	16.28	6.22	6.32	12.46	12.53
273.3	57.13	56.96	4.05	4.06	15.38	15.24	11.71	12.01	11.73	11.87
303.3	55.43	54.94	4.32	4.25	13.85	13.98				
415.5	57.80	57.32	6.07	6.25	16.86	16.51				
340.4	63.50	63.38	5.92	5.94	16.46	16.81				
383.5	62.64	63.25	6.57	6.79	18.26	18.77				
356.5	60.66	59.67	5.66	5.67	15.72	15.66				
500.8	47.96	47.64	4.03	4.00	13.98	13.87				
403.3	47.65	47.82	5.00	5.00	13.89	13.73	6.39	6.48	6.40	6.51
372.4	58.05	58.05	5.41	5.65	15.05	14.97	12.89	13.01	8.60	8.71
415.5	57.81	57.63	6.06	6.27	16.86	16.75	11.55	11.32	7.71	7.63

Mol. wt.	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found	O, % Calcd.	O, % Found	S, % Calcd.	S, % Found
299.7	40.07	40.32	3.36	3.39	23.37	23.35	10.68	10.51	10.70	10.59
278.3	51.78	51.75	3.62	3.67	10.07	10.05	11.50	11.73	23.04	22.92
377.5	54.09	53.88	5.07	5.20	11.13	11.05	12.72	12.50	16.99	16.67
368.9	52.09	52.61	4.65	4.71	7.59	7.68	8.69	8.75	17.38	17.61
318.5	56.58	57.20	4.43	4.60	8.80	8.95	10.06	10.19	20.14	20.35
262.3	50.37	51.02	3.84	3.69	21.36	21.31	12.20	12.41	12.27	12.18
354.2	44.06	44.24	3.41	3.56	11.87	11.61	9.03	9.19	9.04	8.91
307.6	50.75	50.54	3.27	3.49	13.66	13.60	10.40	10.71	10.42	10.11
303.3	55.44	55.81	4.32	4.17	13.86	13.70	15.82	15.40	10.57	10.39

introduction of a dialkylamino group leads to a weaker activity in the electric stimulus test (**6** *vs.* **1**; **9** *vs.* **3**; **11**, **12** *vs.* **4**) and/or enhances the action in the Randall and Selitto procedure (**7**, **8** *vs.* **2**; **9** *vs.* **3**; **11**, **12** *vs.* 4). Substitution in R′ with a 6-OCH_3 group did not alter the activity (**4** *vs.* **5**).

With the exception of compound 8, the introduction of a hydroxyethylpiperazinylmethyl group in R″ diminished or abolished the analgesic activity in all tests (**6**, **10**, and **13**).

Antiinflammatory Activity.—The compounds with the highest activity were the 2-phenylimidazo[1,2-*a*]-

TABLE III

PHARMACOLOGICAL ACTIVITIES OF DERIVATIVES OF IMIDAZOLE

Compd.	Analgesic activity: Randall and Selitto[a] Inflamed foot	Randall and Selitto[a] Control foot	Hot plate[b]	Electric stimulus[b]	Tail clip[c]	Phenylquinone[d]	Antiinflammatory activity: Rat-foot edema[e] Yeast	Rat-foot edema[e] Carrageenan
1	49	33	37	137	41	0	25	19
2	0	0	37	0	0	60	0	0
3	16	0	46	46	70	60	10	40
4	0	0	20	46	0	0	13	47
5	0	0	31	39	0	30	18	20
6	0	0	0	0	45	30	0	0
7	133	53	34	0	25	50	39	32
8	98	65	38	21	69	50	45	15
9	53	10	32	16	35	60	0	0
10	0	0	0	0	0	0	0	0
11	28	0	36	−30	60	50	18	12
12	27	0	65	0	0	40	27	0
13	0	0	0	0	0	0	0	0
14	0	0	28	0	0	0	0	0
15	22	7	18	0	16	40	0	21
16	43	0	0	0	0	70	19	0
17	0	0	0	28	25	40	0	0
18	0	0	0	0	0	0	−19	−43
19	0	0	0	37	30	30	0	0
20	0	0	0	0	0	0	0	23
21	18	0	0	0	55	0	0	18
22	0	0	0	0	0	0	0	0
S-488[g]	143	22	57	49	30	85	68	59
Acetylsalicylic acid	20	0	0	0	18	65	33	62
Aminopyrine	108	25	89	0	53	100	65	62
Phenylbutazone	16	0	43	23	32	84	15	48
Chlortenoxazine	37	0	92	−17	24	63	22	40

[a] Per cent increase of pain threshold at 0.25LD_{50}, rat *p.o.*. [b] Per cent increase of pain threshold at 0.33LD_{50}, mouse i.p. [c] Per cent of animals insensitive at 0.33LD_{50}, mouse i.p. [d] Per cent of animals insensitive at 0.50LD_{50}, mouse *p.o.* [e] Per cent edema inhibition at 0.25LD_{50}, rat *p.o.* [f] Amount of reduction of fever in degrees, compared with controls, caused by 0.25LD_{50}, rat *p.o.* or i.p. in a 6-hr. period after treatment (six determinations). [g] Amount of reduction in temperature in degrees, compared with controls, caused by 0.25-LD_{50}, rat *p.o.* in a 6-hr. period after treatment (six determinations). [h] Per cent protection at 0.33LD_{50}, mouse i.p. [i] Per cent protection at 0.50LD_{50}, mouse i.p. [j] Approximate LD_{50}/168 hr. were determined by i.p. administration to groups of five NMRI mice. Observa-

pyrimidine analogs. The antiinflammatory action was most marked in the compounds where R = *o*-SO_2CH_3 (**1**), *p*-$SOCH_3$ (**3**), or *p*-SO_2CH_3 (**4**). Substitution in R′ with a 6-OCH_3 group did not markedly alter the activity (**4** *vs.* **5**). The introduction of a dialkylamino group in position R″ conferred significant activity in the otherwise inactive methylthio derivative (**7**, **8** *vs.* **2**).

Antipyretic and Hypothermal Activity.—A number of compounds in this series lowered body temperature in the yeast-fevered rat and, to some extent also, in the normal rat. Not only some of the 2-phenylimidazo[1,2-*a*]pyrimidine derivatives (**3**, **5**, **8**, **9**, and **11**) but also the imidazocyclohexenethiazole derivative (**17**) and the imidazopyridazine derivative (**21**) showed a high order of activity. It is of interest to note that the presence of the cyclohexene ring instead of the cyclopentene ring in the imidazole nucleus (**17** *vs.* **18**) or of the halogen atom in the pyridazine moiety (**21** *vs.* **20** and **22**) seemed to be responsible for increasing antipyretic and hypothermal activity. Of the 2-phenylimidazo[1,2-*a*]pyrimidine analogs, the most active compounds were those where R = *p*-$SOCH_3$ (**3**) and R = *p*-SO_2CH_3, R′ = 6-OCH_3 (**5**), as well as some of the Mannich bases (**8**, **9**, and **11**).

Anticonvulsant Activity.—Several compounds of this series were found to afford some protection against supramaximal electroshock and/or pentamethylenetetrazole seizures. Four compounds (**12**, **15**, **17**, and **22**) were found to give protection against the toxicity of strychnine. Although it is difficult to recognize any specific structure requirement for activity in these tests, it is interesting to note that even minimal changes in chemical structure resulted in significant changes in potency (**17** *vs.* **18**; **22** *vs.* **20**, **21**).

General Comments.—With the results of the earlier series[2] as background, the new compounds were screened in a variety of biological test systems. Examinations of the test data (Table III) show that some of the compounds prepared in this study exhibited interesting pharmacological properties; however, no clear-cut relationship could be recognized between pharmacological activities and chemical structure. No specific effect of a given substituent on the activity in a given test was detected.

None of the compounds prepared in this study showed a spectrum of activity comparable to that of the more interesting imidazo[1,2-*a*]pyridines described in the earlier paper, especially 2-(*p*-methylsulfonylphenyl)-imidazo[1,2-*a*]pyridine hydrochloride, which was found to be active in practically all tests performed.

Experimental Section[8]

2-(*o*-Methylsulfonylphenyl)imidazo[1,2-*a*]pyrimidine (1).—To a solution of 6.9 g. (0.073 mole) of 2-aminopyrimidine in 40 ml. of warm 95% ethanol was added 10 g. (0.036 mole) of *o*-methylsulfonyl-ω-bromoacetophenone. After warming at 60° for 3 hr.,

Antipyretic activity index[f] p.o.	Antipyretic activity index[f] i.p.	Hypothermal activity index[g]	Anticonvulsant activity: Electroshock[h] convulsions	Anticonvulsant activity: Pentylenetetrazol[h] Convulsions	Anticonvulsant activity: Pentylenetetrazol[h] Death	Anticonvulsant activity: Strychnine[i] Convulsions	Anticonvulsant activity: Strychnine[i] Death	Acute toxicity[j]: Estd. LD_{50}, mg./kg. mouse i.p.	Acute toxicity[j]: Gross behavioral changes
2.6	4.0	1.6	24	20	0	24	0	500	*k–q*
−1.0	5.8	2.2	0	50	30	0	0	>3000	*k, l, r, s*
...	6.6	13.4	90	80	0	0	0	800	*l, n–p, s*
3.4	3.8	1.1	0	40	40	0	0	700	*l, r–t*
5.5	9.7	11.3	10	0	0	0	0	>3000	*k, l, t*
1.4	−0.5	0.6	10	20	20	0	0	500	*o, p, t, u*
3.7	5.5	3.8	72	79	0	0	0	150	*k, l, n, p, q, s,*
1.0	7.2	7.7	14	19	14	4	0	400	*k, l, n, p–r, t*
4.8	7.5	5.3	80	100	20	0	0	400	*l, p–r, u–w*
1.1	−0.7	0.5	0	30	20	10	0	500	*l, m, o, s, u*
3.8	6.5	7.6	10	10	10	0	0	2500	*l, m, o, s, t*
3.8	2.8	3.4	60	40	30	20	20	2500	*k, o, r, s, u*
−1.5	0.9	1.0	0	40	50	0	0	500	*l, r, x*
−1.7	4.4	0.0	10	0	0	0	0	>3000	*k, l*
1.0	4.4	2.4	60	8	0	16	36	>3000	*l, r, u*
7.0	1.0	0.2	0	0	0	0	0	600	*k, t, u*
2.4	12.1	10.4	60	70	70	80	100	1800	*k, o, t*
1.2	3.2	0.2	0	0	0	0	0	>3000	*l, s, t*
2.0	4.6	5.4	0	0	0	0	0	1800	*k, l, n, s, t*
0.0	1.9	0.8	11	10	0	0	0	1500	*m, n, p, s, t*
1.9	11.8	6.0	0	20	11	0	0	2500	*k, q, r, t*
−0.1	3.0	1.1	0	10	11	65	88	2000	*k, l, t*
17.3	20.5	8.5	48	36	12	72	84	780	*k, q, w, z*
12.2	4.7	1.1	14	0	0	0	0	420	*l, p, u, aa*
12.5	10.5	4.4	52	40	20	4	4	308	*m, x*
6.4	6.1	1.1	8	20	20	0	0	355	*k, p*
23.4	43.7	10.1	36	76	12	41	32	1190	*k, r, s, u, v, z*

tions of the effects of these compounds on behavior were carried out simultaneously with the determination of toxicity. In all tests, the highest dose employed of a compound having low toxicity was 500 mg./kg. [k] Sedation, tranquilization. [l] Irritability. [m] Stimulation. [n] ↑ muscle tone. [o] Tremors. [p] Clonic convulsions. [q] Salivation. [r] Depression. [s] Respiratory irregularity. [t] Writhing. [u] ↓ Muscle tone. [v] Narcosis. [w] Hyperpnea. [z] Tonic convulsions. [y] S-488 = 2-(*p*-methylsulfonylphenyl)imidazo[1,2-*a*]pyridine hydrochloride. [z] Hypnosis. [aa] Hypothermia.

the mixture was cooled and the precipitate was filtered. Crystallization yielded 8.3 g. (85%) of product.

2-(*p*-Methylthiophenyl)imidazo[1,2-*a*]pyrimidine (2).—A suspension of 12.5 g. (0.132 mole) of 2-aminopyrimidine and 16 g. (0.065 mole) of *p*-methylthio-ω-bromoacetophenone in 100 ml. of 95% ethanol was warmed at 60° for 3 hr. The reagents dissolved completely. After chilling, a crystalline solid precipitated; it was filtered and recrystallized, yield 6.5 g. (41.5%).

Compounds **3** and **4** were prepared by the same method yielding 62 and 80%, respectively.

2-(*p*-Methylsulfonylphenyl)-6-methoxyimidazo[1,2-*a*]pyrimidine (5).—A solution of 12.5 g. (0.1 mole) of 2-amino-5-methoxypyrimidine[3] and of 13.85 g. (0.05 mole) of *p*-methylsulfonyl-ω-bromoacetophenone in 50 ml. of 95% ethanol was warmed at 60° for 3 hr. After chilling and filtering, the crystalline solid was recrystallized from 10% HCl and the free base was obtained by alkalinization. Recrystallization yielded 5 g. (33.5%) of product.

2-(*o*-Methylsulfonylphenyl)-3-[4-(2-hydroxyethyl)-1-piperazinylmethyl]imidazo[1,2-*a*]pyrimidine (6).—To a solution of 5 g. (0.0184 mole) of 2-(*o*-methylsulfonylphenyl)imidazo[1,2-*a*]pyrimidine in 50 ml. of glacial acetic acid were added 3.9 g. (0.03 mole) of 1-(2-hydroxyethyl)piperazine and 2.3 ml. (0.03 mole) of 40% formalin. After warming at 60° for 2 hr., the mixture was chilled, made alkaline, and extracted with methylene chloride. The solvent was removed *in vacuo* and the residue was triturated with hexane and recrystallized; yield 4.5 g. (60%).

Compounds **7** (50%), **8** (62%), **9** (60%), **10** (35%), **11** (70%), **12** (40%), and **13** (40%) were prepared by the same method.

(8) All melting points were taken in a Büchi melting point apparatus and are corrected.

5-(*p*-Methylsulfonylphenyl)-1H-imidazo[1,2-*d*]tetrazole Hydrochloride (14).—A suspension of 27.7 g. (0.1 mole) of *p*-methylsulfonyl-ω-bromoacetophenone and 20.6 g. (0.20 mole) of 5-amino-1H-tetrazole monohydrate in 200 ml. of 95% ethanol was warmed at 60° for 3 hr. The obtained solution was chilled and the crude product was filtered and crystallized; yield 18 g. (60%).

6-(*p*-Methylsulfonylphenyl)imidazo[2,1-*b*]thiazole (15).—This product was prepared as described above, starting from 2-aminothiazole and *p*-methylsulfonylphenyl-ω-bromoacetophenone; yield 80%.

5-Morpholinomethyl-6-(*p*-methylsulfonylphenyl)imidazo[2,1-*b*]thiazole (16).—To a solution of 13.9 g. (0.05 mole) of 6-(*p*-methylsulfonylphenyl)imidazo[2,1-*b*]thiazole in 100 ml. of glacial acetic acid were added 4.8 g. (0.055 mole) of morpholine and 4.25 ml. (0.055 mole) of 40% formalin. The mixture was warmed at 70° for 2 hr. After cooling and alkalinizing with 20% NaOH, the crude base was filtered and crystallized; yield 15.8 g. (85%).

2-(*p*-Methylsulfonylphenyl)-5,6,7,8-tetrahydroimidazo[2,1-*b*]benzothiazole Hydrochloride (17).—A solution of 15.4 g. (0.1 mole) of 2-amino-4,5,6,7-tetrahydrobenzothiazole[4] and 13.9 g. (0.05 mole) of *p*-methylsulfonyl-ω-bromoacetophenone in 120 ml. of 95% ethanol was warmed at 70° for 4 hr. After cooling, the crude product was filtered and crystallized; yield 11 g. (60%).

2-(*p*-Methylsulfonylphenyl)-6,7-dihydro-5H-imidazo[2,1-*b*]-cyclopentathiazole (18).—The product was prepared as described above, starting from 2-amino-5,6-dihydro-4H-cyclopentathiazole[4]; yield 50%.

5-(*p*-Methylsulfonylphenyl)-1H-imidazo[1,2-*b*]-*s*-triazole (19) was prepared as described above, starting from 3-amino-1,2,4-triazole; yield 35%.

Compounds **20** (50%), **21** (50%), and **22** (60%) were prepared by the same method.