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STUDIES ON THE ANTIVIRAL ACTIVITY OF
GUANYLHYDRAZONES ESPECIALLY AGAINST
ARBO- AND MYXOVIRUSES

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SUMMARY

265 chemical compounds, guanylhyazones, azlactones, hydrazones, phenols, carbonyl compounds, and miscellaneous ones were tested for in vitro antiviral activity against influenza virus. 104 out of 265 compounds were completely inhibitory by the screening test.

Selected 89 compounds were qualitatively analyzed for the antiviral and toxic activities. 14 out of 89 compounds were found to be inhibitory with the ratio of 4 or more of non-toxic concentration versus minimal inhibitory concentration.

One compound, serial No. 212, synthesis No. 178 inhibited HA production with a final concentration of 1.6 μ cc and was toxic with a final concentration of 25 μ cc.

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INTRODUCTION

It has been reported that poliovirus multiplication was inhibited by guanidine in vitro (Lwoff, 1963). Guanidine derivatives were inhibitory against polio, coxakie, measles, influenza and parainfluenza viruses (Crowther and Melnick, 1961; Tamm and Eggers et al., 1962; Ueda, 1961, 1962; Lodde, 1962).

It was recently reported that amantadine hydrochloride inhibited influenza virus penetration into the host cells (Hoffmann et al., 1965).

This paper reports the screening results of guanylhydrazones, azlactones, hydrazones, phenols and carbonyl compounds with the method of chorio-allantoic membrane culture. All chemical compounds used were synthesized at the Department of Organic Chemistry, Kitasato University College of Hygienic Sciences.

MATERIALS and METHODS

Influenza A virus Adachi strain : Infected allantoic fluid of 80th and 81st egg-passages was ampuled in amount of 1 ml each and stored in a dry-ice box until use. One-tenth ml of serial ten-fold dilution of the stock virus was inoculated into test tube containing a piece chorio-allantoic membrane and egg-shell in Hanks's solution (Iwasaki et al., 1955).

After shaking culture of 4 tubes each dilution for 48 hours at 36°C, hemagglutination titer of each culture fluid was determined by the standard hemagglutination test with chicken red cells. The maximal dilution showing positive hemagglutination in all four tubes was detected.

Serial dilution of the stock virus between this maximal dilution showing positive hemagglutination in all four tubes and the next ten-fold dilution were retested to estimate exact titer of inducing dilution of the stock virus was determined and named 1 MID₁₀₀. Ten MID₁₀₀ was used as inoculum in the experiments.

2. Chemical compounds

All chemical compounds were synthesized at the Department of Organic Chemistry, Kitasato University college of Hygienic Sciences and dissolved in distilled water or 50 % glycerin. Dissolved compound solutions were autoclaved at 121°C for 20 minutes prior to use. The abbreviations W and G were adopted for distilled water and 50 % glycerin used as solvent, respectively.

3. Hemagglutination test

An equal volume of culture fluid from a group of 4 tubes was mixed and two-fold serial dilutions were made in an amount of 0.4 ml of PBS on plastic-plate. Same amount of 0.5 % chicken red cell suspension was added and allowed to hemagglutinate for 60 minutes at room temperature.

4. A) Screening test of antiviral effect of chemical compounds.

All chemical compounds tested were selected first as inhibitory, partially inhibitory, and non-inhibitory ones by the application of only one concentration as indicated in text.

The content of culture tube was as follows:

chorio-allantoic membrane	Ca. 5 X 10 mm	1	piece
egg-shell	Ca. 5 X 5 mm	1	piece
Hanks' BSS (pH 7.2-7.4)		0.8	ml
virus 10 MID ₁₀₀ / 0.1 ml		0.1	ml
Test sample solution		0.1	ml
	Total	1.0	ml.

An equal volume of chemical solution and 10 MID₁₀₀ / 0.1 ml of virus were mixed and allowed to react at room temperature for 30 minutes and two-tenth ml of the mixture was inoculated into four culture tubes for each group containing 0.8 ml of Hanks' BSS, a piece of chorio-allantoic membrane and egg-shell, and appropriate controls were made. The fluid was cultivated in rubber-stoppered test tube (14 X 120 mm) by shaking machine (stroke distance 120 mm : 110 strokes per minute) for 48 hours at 36°C incubating room.

B) Determination of antiviral concentration of chemical compounds.

All chemical compounds could be divided into three groups of inhibitory, partially inhibitory, and non-inhibitory ones by the screening test. Only inhibitory compounds were selected and determined for the minimal inhibitory concentration and non-toxic concentration against virus by the limiting dilution of compounds.

The method of determining minimal concentration of each compound was same as described above and the final concentration of compound which inhibited completely hemagglutinin production was taken as minimal inhibitory concentration.

5. Toxicity test of compounds.

The test tubes containing chorio-allantoic membrane in 0.9 ml of Hanks' BSS was incubated with 0.1 ml of appropriately diluted compound solution for 18 hours at 37°C on shaking machine. The incubated membrane was washed twice with 5 ml of PBS, respectively. The washed membrane was inoculated with 10 MID₁₀₀ / 0.1 ml virus in 1 ml of Hanks' BSS. After 48 hour incubation at 36°C, hemagglutinin titer of culture fluid was determined by the standard hemagglutination test technique. The maximal concentration of each compound which produced hemagglutinin was taken as non-toxic concentration.

RESULTS

1. Screening test of antiviral effect of chemical compounds.

A total of 265 chemical compounds listed in Table I were tested for antiviral activity by the application of only one concentration as indicated in text. Compounds were autoclaved prior to use after about 18 hour storage at room temperature. Antiviral activity of each compound was noted in Table II. As shown in Table III, the tested compounds were distributed into such three groups as inhibitory, partially inhibitory, and non-inhibitory ones among each group. The numbers of the inhibitory compounds in each group are as follows :

44 compounds (49.5 %) in group A--guanyldhydrazones.

7 compounds (38.8 %) in group B-----carbonyls,

22 compounds (30.1 %) in group D-----azlactones,

17 compounds (53.1 %) in group E-----phenols,

14 compounds (31.8 %) in group F-----miscellaneous.

As summarized in Table IV, a total of 104 compounds (39.2 %) were completely inhibitory, 67 compounds (25.2 %) were partially inhibitory and 94 compounds (35.4 %) were non-inhibitory.

bv

2. Determinations of antiviral and toxic concentrations of chemical compounds.

Quantitative analysis of antiviral and toxic activities of selected compounds showing negative hemagglutinin production by the screening test was performed. Compounds were dissolved and autoclaved prior to use. The procedures used were fully described in Materials and Methods. The minimal concentration of each compound which inhibited completely hemagglutinin production was taken as the minimal inhibitory end point by the inhibition test. The maximal concentration of each compound which produced hemagglutinin was taken as the non-toxic end point by the toxicity test. Two relative concentrations each compounds were listed in Table V. The non-toxic end point and the minimal inhibitory end point were compared for each compounds. The ratio of two final concentrations was listed at the right column in Table V.

As can be seen in Table VI, one compound of group A--guanyldhydrazones, three compounds of group D--hydrazones, four compounds of group E--phenols, and six compounds of group F--miscellaneous ones were found to be inhibitory against virus with the effective ratio of 4 or more.

The compound, serial number 212 inhibited completely hemagglutinin production with the final concentration of 1.6 μ /cc and was found to be toxic at the final concentration of 25 μ /cc, therefore the ratio of this compound number 212 was 16.

As summarized in Table VII, a total of 14 compounds were found to be inhibitory with the ratio of 4 or more.

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TABLE I List of chemical compounds

Serial No. of compound	Synthesis No. of compound	Molecular weight	Melting point (°C)	Concentration of 0.1% solution in solvent	Chemical structure	Chemical name
1	Group A 115	283.5	270	1000		p-nitro benzaldehyde guanyldiazene hydrochloride
2	117	362.4	247	1000		p-bromo-p-nitro benzaldehyde guanyldiazene hydrochloride
3	273	278.0	237	1000		p-dimethylamino benzaldehyde guanyldiazene hydrochloride
4	276	233.0	170 ~ 171	1000		p-chloro benzaldehyde guanyldiazene hydrochloride
5	277	243.5	244 ~ 246	1000		p-nitro benzaldehyde guanyldiazene hydrochloride
6	278	212.5	202 ~ 203	1000		acetophenone guanyldiazene hydrochloride
7	279	255.5	257 ~ 260	1000		p-acetyl amino benzaldehyde guanyldiazene hydrochloride
8	280	238.5	237	1000		benzaldehyde guanyldiazene hydrochloride
9	281	162.0	178	1000		benzaldehyde guanyldiazene
10	282	360.5	178	500		p-bromo-p-dimethylamino benzaldehyde guanyldiazene hydrochloride
11	283	257.5	280	1000		p-nitro-acetophenone guanyldiazene hydrochloride

12	284	374.5	230	1000	g		p-bromo-N-(p-acetylaminophenyl)benzylacetamide quanylhydrazine hydrochloride
13	285	295.5	213	1000	g		p-acetylaminobenzylacetamide quanylhydrazine hydrochloride
14	290	293.0	226	1000	w		p-chlorobenzylacetamide quanylhydrazine hydrochloride
15	292	269.5	271	1000	g		N-(p-acetylaminophenyl)benzylacetamide quanylhydrazine hydrochloride
16	293	352.0	213 ~ 214	500	g		p-chloro-N-(p-bromobenzylacetamide) quanylhydrazine hydrochloride
17	296	245.0	210 ~ 211	500	g		N-(p-dimethylaminophenyl)benzylacetamide quanylhydrazine hydrochloride
18	298	243.5	250 ~ 1	1000	g		m-nitrobenzylacetamide quanylhydrazine hydrochloride
19	302	242.5	205 ~ 7	1000	g		p-methoxyacetophenone quanylhydrazine hydrochloride
20	304	267.0	246 ~ 7	1000	w		p-chloroacetophenone quanylhydrazine hydrochloride
21	327	283.5	213 ~ 4	1000	g		m-nitrobenzylacetamide quanylhydrazine hydrochloride
22	406	252.5	181 ~ 2	1000	g		p-methylbenzylacetamide quanylhydrazine hydrochloride
23	418	319.5	214 ~ 5	1000	g		p-bromobenzylacetamide quanylhydrazine hydrochloride

24	644	362.5	243~4	1000	g		α -methyl-2-phenylacetone quanyldiazonium hydrochloride
25	622	297.5	244	500	g		α -methyl-2-phenylacetone quanyldiazonium hydrochloride
26	906	272.0	190~1	1000	W		N,N'-anhydrobis(3-hydroxyethyl)- N'-aminoguanidide hydrochloride
27	902	184.0	60~64	1000	W		Acetone N,N'-anhydrobis(3-hydroxy- ethyl) quanyldiazonium
28	903	312.0	169~171	1000	W		Acetone N,N'-anhydrobis(3-hydroxy- ethyl) quanyldiazonium hydrochloride
29	904	359.0	53~55	1000	W		Acetone S-ethyl isothiosemi- carbazone
30	907	360.0	210.5~213	1000	W		Benzaldehyde N,N'-anhydrobis(3- hydroxyethyl) quanyldiazonium hydrochloride
31	909	233.0	114~6	1000	W		2-methyl isothiosemicarba- zide hydrochloride
32	931	400.0	197~9	500	g		Benzaldehyde N,N'-anhydrobis(3- hydroxyethyl) quanyldiazonium hydrochloride
33	932	414.0	151	1000	W		2-methyl benzaldehyde N,N'-anhy- drobis(3-hydroxyethyl) quanyldiazonium hydrochloride
34	934	370.0	197~9	1000	W		Acetophenone N,N'-anhydrobis(3- hydroxyethyl) quanyldiazonium hydrochloride
35	960	465.0	160~5	1000	W		4-bromo cinnamalddehyde N,N'-anhy- drobis(3-hydroxyethyl) quanyldiazonium hydrochloride

36	983	282.5	197.5-198	1000	W	$\text{CH}_3\text{O}-\text{C}_6\text{H}_4-\text{CH}=\text{C}(\text{CH}_3)-\text{C}(=\text{NH})-\text{NH}-\text{C}(=\text{NH})-\text{NH}_2$	α -methyl anisol acetone guanyldiazene hydrochloride
37	987	207.0	116~7	1000	A	$\text{NH}=\text{C}(\text{NH}_2)-\text{NH}-\text{NH}_2$	N,N' -anhydrous β -hydroxyethyl N -aminoguanidine nitrate
38	988	180.5	245~6	1000	A	$\text{NH}=\text{C}(\text{NH}_2)-\text{NH}-\text{NH}_2$	N,N' -anhydrous β -hydroxyethyl N -aminoguanidine hydrochloride
39	990	292.0	141.5~2	1000	A	$\text{C}_6\text{H}_5-\text{CH}=\text{NHC}(\text{NH}_2)=\text{NH}$	Benzaldehyde N,N' -anhydrous β -hydroxyethyl guanylhydrazine
40	991	268.5	203.5-212.5	1000	A	$\text{C}_6\text{H}_5-\text{CH}=\text{NHC}(\text{NH}_2)=\text{NH}$	Benzaldehyde N,N' -anhydrous β -hydroxyethyl guanylhydrazine hydrochloride
41	992	231.0	112~112.5	1000	A	$\text{C}_6\text{H}_5-\text{C}(\text{CH}_3)=\text{NHC}(\text{NH}_2)=\text{NH}$	Acetophenone N,N' -anhydrous β -hydroxyethyl guanylhydrazine
42	993	282.5	211~212	1000	A	$\text{C}_6\text{H}_5-\text{C}(\text{CH}_3)=\text{NHC}(\text{NH}_2)=\text{NH}$	Acetophenone N,N' -anhydrous β -hydroxyethyl guanylhydrazine hydrochloride
43	994	220.5	79~81	1000	A	$\text{CH}_3\text{C}(\text{CH}_3)=\text{NHC}(\text{NH}_2)=\text{NH}$	Acetone N,N' -anhydrous β -hydroxyethyl guanylhydrazine hydrochloride
44	997	273.0	172.3-173	1000	W	$\text{CH}_3\text{C}(\text{CH}_3)=\text{NHC}(\text{NH}_2)=\text{NH}$	Acetone N -methyl methanesulfonyl carbazone hydrochloride
45	1030	297.5	242~3	1000	G	$\text{CH}_3\text{C}(\text{CH}_3)=\text{NHC}(\text{NH}_2)=\text{NH}$	α -methyl-m-nitro benzalacetone guanylhydrazine hydrochloride
46	1046	309.5	232	1000	G	$\text{CH}_3\text{C}(\text{CH}_3)=\text{NHC}(\text{NH}_2)=\text{NH}$	α -methyl-p-acetaminobenzalacetone guanylhydrazine hydrochloride
47	1050	312.0	203~210	1000	W	$\text{CH}_3\text{C}(\text{CH}_3)=\text{NHC}(\text{NH}_2)=\text{NH}$	α -methyl-p-dimethylaminobenzal- acetone guanylhydrazine hydrochloride

48	1051	326.0	188-190	1000	W	$\text{CH}_3\text{CH}_2\text{C}(\text{CH}_3)=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	Methyl ethyl ketone N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
49	1052	417.0	259-260	1000	W	$\text{CH}_3\text{CONH}-\text{C}_6\text{H}_4-\text{CH}=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Acetaminobenzaldehyde N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
50	1053	405.0	221	1000	W	$\text{NO}_2-\text{C}_6\text{H}_4-\text{CH}=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Nitrobenzaldehyde N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
51	1054	459.0	197.2	1000	W	$\text{NO}_2-\text{C}_6\text{H}_4-\text{CH}=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Nitro-m-nitrobenzaldehyde N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
52	1055	403.0	206-208	1000	W	$\text{CH}_3\text{CH}_2\text{N}(\text{C}_6\text{H}_5)_2-\text{CH}=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Dimethylaniline benzaldehyde N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
53	1056	376.0	189-192	1000	W	$\text{OH}-\text{C}_6\text{H}_4-\text{CH}=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	Salicylaldehyde N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
54	1057	386.0	210-211	1000	W	$\text{C}_6\text{H}_5-\text{CH}=\text{CH}-\text{CH}=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	Cinnamaldehyde N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
55	1058	479.0	145-7	1000	W	$\text{C}_6\text{H}_5-\text{CH}=\text{C}(\text{CH}_3)-\text{CH}=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	N-Transbenzoinacetone N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
56	1059	445.0	242	500	G	$\text{NO}_2-\text{C}_6\text{H}_4-\text{CH}=\text{CH}-\text{C}(\text{CH}_3)=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Nitrobenzoinacetone N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
57	1062	431.0	202-3	1000	G	$\text{NO}_2-\text{C}_6\text{H}_4-\text{CH}=\text{CH}-\text{C}(\text{CH}_3)=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Nitro-cinnamaldehyde N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
58	1063	408.5	214-5	1000	W	$\text{Cl}-\text{C}_6\text{H}_4-\text{C}(\text{CH}_3)=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Chloroacetophenone N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride
59	1064	434.5	222	1000	W	$\text{Cl}-\text{C}_6\text{H}_4-\text{CH}=\text{CH}-\text{C}(\text{CH}_3)=\text{N}(\text{N}(\text{H})\text{C}_6\text{H}_5)_2$	p-Chlorobenzoinacetone N,N'-anhydrobis(p-benzoyl)guanethydrone hydrochloride

50	1065	513.5	169	500	♀		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-chloro-N-methylbenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
61	1066	443.0	194~5	1000	W		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-dimethylaminobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
62	1067	457.0	213	1000	W		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-acetaminobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
63	1068	457.0	176	1000	♀		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-dimethylaminobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
64	1069	471.0	219	1000	W		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-acetaminobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
65	1070	419.0	194~5	1000	W		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-nitroacetophenone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
66	1071	394.5	230~1	1000	W		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-chlorobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
67	1072	510.0	148~9	1000	♀		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-nitro-N-benzylcinnamalddehyde N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
68	1073	524.0	30~53.9	1000	♀		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-nitro-N-benzylcinnamalddehyde N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
69	1074	429	196	1000	♀		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-dimethylaminobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
70	1075	508.0	178	1000	♀		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-dimethylaminobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide
71	1076	431.0	246~7	1000	W		CH_3 $\text{CH}_2-\text{C}(=\text{O})-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2$ (N)	p-acetaminobenzylacetone N,N'-anhydride (p-hydroxyethyl)quanyldiacylhydrazine hydrate diolide

72	1077	443.0	272.5	1000	1000	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{CH}=\text{CH}-\text{CH}=\text{NNHC}=\text{NH}$ N^{O} I II $\text{bis}(p\text{-hydroxyethyl})\text{guanylethyrosine hydrochloride}$ $p\text{-acetaminophenylsuccinylaldehyde-N,N'-anhydride}$
73	1078	448.5	89~91	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4-\text{CH}=\text{C}(\text{CH}_3)-\text{C}(\text{CH}_3)=\text{NNHC}=\text{NH}$ N^{O} I II $p\text{-chloro-}\alpha\text{-methylbenzalacetone N,N'-anhydride}$ $\text{bis}(p\text{-hydroxyethyl})\text{guanylethyrosine hydrochloride}$
74	1079	287.0	213.5	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4-\text{CH}=\text{C}(\text{CH}_3)-\text{C}(\text{CH}_3)=\text{NNHC}(\text{NH}_2)=\text{NH}$ $\alpha\text{-methyl-}p\text{-chlorobenzalacetone}$ $\text{guanylethyrosine hydrochloride}$
75	1081	522.0	156	500	500	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{CH}=\text{C}(\text{CH}_3)-\text{C}(\text{CH}_3)=\text{NNHC}=\text{NH}$ N^{O} I II $p\text{-dimethylamino-}\alpha\text{-bromobenzalacetone N,N'-anhydride}$ $\text{bis}(p\text{-hydroxyethyl})\text{guanylethyrosine hydrochloride}$
76	1093	419.0	183~5	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{C}(\text{CH}_3)=\text{NNHC}=\text{NH}$ N^{O} I II $p\text{-dimethylamino acetophenone N,N'-anhydride}$ $\text{bis}(p\text{-hydroxyethyl})\text{guanylethyrosine hydrochloride}$
77	1094	536.0	196~7	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{CH}=\text{C}(\text{CH}_3)-\text{C}(\text{CH}_3)=\text{NNHC}(\text{NH}_2)=\text{NH}$ $\alpha\text{-bromo-}p\text{-methylacetophenone N,N'-anhydride}$ $\text{bis}(p\text{-hydroxyethyl})\text{guanylethyrosine hydrochloride}$
78	1096	257.5	230~1	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{C}(\text{CH}_3)=\text{NNHC}(\text{NH}_2)=\text{NH}$ $m\text{-methylacetophenone}$ $\text{guanylethyrosine hydrochloride}$
79	1097	292.0	223~230	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{C}(\text{CH}_3)=\text{NNHC}(\text{NH}_2)=\text{NH}$ $p\text{-dimethylamino acetophenone}$ $\text{guanylethyrosine hydrochloride}$
80	1098	192.0	185	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{CH}=\text{NNHC}(\text{NH}_2)=\text{NH}$ $p\text{-methylbenzaldehyde}$ guanylethyrosine
81	1099	347.5	196	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{CH}=\text{C}(\text{CH}_3)=\text{NNHC}(\text{NH}_2)=\text{NH}$ $\alpha\text{-bromo-}p\text{-methoxybenzalacetone}$ $\text{guanylethyrosine hydrochloride}$
82	1100	273.0	217.5~218	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{C}(\text{CH}_3)=\text{NNHC}(\text{NH}_2)=\text{NH}$ $\alpha\text{-chloro benzalacetone}$ $\text{guanylethyrosine hydrochloride}$
83	1101	307.5	231~2	1001	1001	$\text{CH}_3\text{C}_6\text{H}_4\text{NH}-\text{CH}=\text{C}(\text{CH}_3)=\text{NNHC}(\text{NH}_2)=\text{NH}$ $\alpha\text{-chloro-}p\text{-chlorobenzalacetone}$ $\text{guanylethyrosine hydrochloride}$

84	1102	318.0	251~2	1000	G		α -chloro-p-nitro benzalacetone glyoxal hydrone hydrochloride
85	1103	318.0	253	1000	G		α -chloro-m-nitro benzalacetone glyoxal hydrone hydrochloride
86	1104	316.0	175~6	500	G		α -chloro-p-dimethylamino benzal- acetone glyoxal hydrone hydrochloride
87	1105	330.0	236	1000	G		α -chloro-p-acetylaminobenzal- acetone glyoxal hydrone hydrochloride
88	1106	266.5	183	500	G		α -chloro-p-methoxy benzalacetone glyoxal hydrone hydrochloride
89	1107	232.0	201.5~212	500	G		p-methoxy benzalacetone glyoxal hydrone hydrochloride

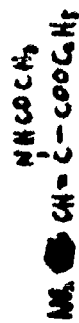
Note: Solvent, G = 50% glycerin, W = distilled water.

Group B - carbonyl

90	1	191	109- 110	1000	G	<chem>NO2-C6H4-CH=CH-CO-CH3</chem>	p-Nitro benzalacetone
91	2	177	141- 142	1000	G	<chem>NO2-C6H4-CH=CH-CNO</chem>	p-Nitrocinnamaldehyde
92	5	191	155- 158	1000	G	<chem>NO2-C6H4-NH-CO-CH(OH)-C(CH3)2</chem>	o-(3,β-dimethylacrylylanino) phenol
93	6	226	55-6	1000	G	<chem>NO2-C6H4-CH=CH-CH2-OCOCH3</chem>	p-Nitro cinnamyl acetate
94	9	256	137.5 -133	1000	G	<chem>NO2-C6H4-CH=CH-CHO</chem>	p-Nitro- -bromocinnamaldehyde
95	23	163	156-7	1000	G	<chem>CH3-CONH-C6H4-CHO</chem>	p-Acetylaminobenzaldehyde
96	29	253	128	1000	G	<chem>Cc1cc(ccc1C(=O)OC)C(=O)OC</chem>	p-Nitrobenzal diacetate

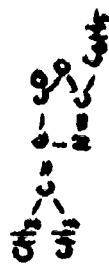
97	30	151	106- 107.5	1000	G	NO_2  CHO	p-Nitrobenzaldehyde
98	34	139	177	1000	G	CH_3 CO  CH=CHCHO	p-Acetylamino cinnamaldehyde
99	69	256	136.5 -137	1000	G	NO_2  CH=CHCHO 8r	p-Nitro-4-bromo cinnamaldehyde
100	71	270	120	1000	G	NO_2  CH=CHCOCH ₃ 8r	p-Nitro-4-bromobenzalacetone
101	73	551	128	1000	G	NO_2  CH=CHCOCH ₃ 8r 8r	p-Nitrobenzalacetone, -A dibromide
102	120	1777	165- 170	1000	G	CH_3 CONH  COCH ₃	p-Acetylaminoacetophenone
103	121	198	52-53	1000	G	 CH (CH, CO ₂) ₂	Furfurylidene diacetate
104	125	165	82- 82.5	1000	G	NO_2 -  COCH ₃	p-Nitroacetophenone
105	137	253	112-3	1000	G	 CH=CHCOCH ₃	Distyrylketone

106	148	135	105.5 -6.5	1000	G	NH_2  COCH_3	p-Amino acetophenone
107	198	306	125	1000	G	 $\text{CH}=\text{C}(\text{Br})\text{COCH}_3$	d-β-Dibromo benzalacetone
Group C-azlactone							
108	7	294	238	1000	G	NO_2  $\text{CH}=\text{C}(\text{CO})\text{NHCOCH}_3$	2-phenyl-4-(p-nitrobenzal) azlactone
109	8	326	192	1000	G	NO_2  $\text{CH}=\text{C}(\text{COCH}_3)\text{NHCOCH}_3$	Methyl d-(p-nitro) benzalhippurate
110	10	232	184-5	1000	G	NO_2  $\text{CH}=\text{C}(\text{CO})\text{NHCOCH}_3$	4-p-Nitrobenzal-2-methyl-5-oxazolone
111	17	250	210	1000	G	NO_2  $\text{CH}=\text{C}(\text{COOH})\text{NHCOCH}_3$	d-Acetylamino-p-nitro cinnamic acid
112	165	321	167-8	1000	G	NO_2  $\text{CH}=\text{C}(\text{COCH}_3)\text{NHCOCH}_3$	Ethyl-d-benzalamino p-nitro-cinnamate
113	166	264	175-6	1000	G	NO_2  $\text{CH}=\text{C}(\text{COCH}_3)\text{NHCOCH}_3$	Methyl-d-acetylamino p-nitro cinnamate
114	167	303	243-4	1000	G	NO_2  $\text{CH}=\text{C}(\text{CONHMe})\text{NHCOCH}_3$	d-Benzoylamino-p-nitrocinnamic acid hydrazide



Ethyl-d-acethylamino-p-nitro cinnamate

115 194 278 178 1000 G



4-Isopropylidene-2-phenyl-5-omazolone

116 196 201 99 1000 G

Group D-hydrazone



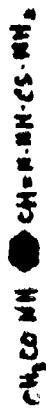
p-Nitrocl-namaldehyde semicarbazone

117 12 234 223 1000 G



p-Phenylacetamido-cinnamaldehyde thio-semicarbazone

118 15 338 202 1000 G



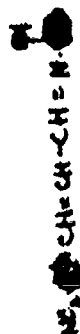
Sibion

119 18 236 207 1000 G



p-Nitro cinnamaldehyde thiosemicarbazone

120 19 250 207 1000 G



p-Nitrocinnamaldehyde-o-hydroxyanil

121 20 268 152-153 1000 G



Thiourea

122 22 76 169-170 1000 G



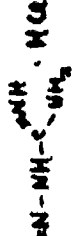
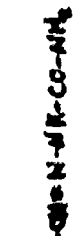
p-Aminocinnamaldehyde thiosemicarbazone

123 24 220 205 1000 G

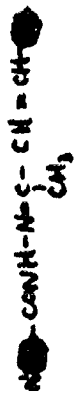
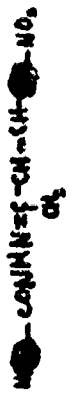
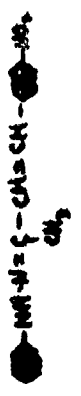
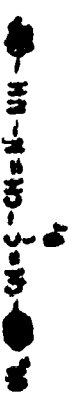
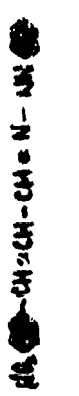
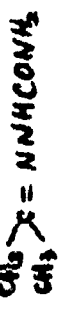
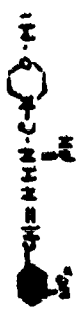
124	26	262	222-5	1000	G	<chem>CC(=O)Nc1ccc(cc1)/C=C/C(=O)Nc2ccc(cc2)S(=O)(=O)c3ccccc3</chem>	p-Acetylamino-cinnamaldehyde thiosemicarbazone
125	27	296	139- 142	1000	G	<chem>CC(=O)Nc1ccc(cc1)/C=C/C(=O)Nc2ccc(cc2)S(=O)(=O)c3ccccc3</chem>	p-Nitrocinnamaldehyde p-ethoxyanil
126	31	329	207	1000	G	<chem>CC(=O)Nc1ccc(cc1)/C=C/C(=O)Nc2ccc(cc2)S(=O)(=O)c3ccccc3</chem>	4-Bromo-p-nitrocinnamaldehyde thiosemicarbazone
127	32	261	225	1000	G	<chem>CC(=O)Nc1ccc(cc1)/C=C/C(=O)Nc2ccc(cc2)S(=O)(=O)c3ccccc3</chem>	p-Acetylamino-cinnamaldehyde thiosemicarbazone
128	33	117	147- 147.5	1000	G	<chem>CC(=O)Nc1ccc(cc1)/C=C/C(=O)Nc2ccc(cc2)S(=O)(=O)c3ccccc3</chem>	Acetaldehyde thiosemicarbazone
129							
130							
131	37	264	240	1000	G	<chem>CC(=O)Nc1ccc(cc1)/C=C/C(=O)Nc2ccc(cc2)S(=O)(=O)c3ccccc3</chem>	p-Nitrobenzalacetone thiosemicarbazone
132	39	290	223	1000	G	<chem>CC(=O)Nc1ccc(cc1)/C=C/C(=O)Nc2ccc(cc2)S(=O)(=O)c3ccccc3</chem>	p-1-methylbutylaminocinnamaldehyde thiosemicarbazone

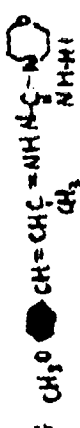
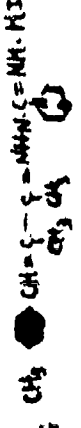
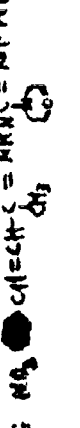
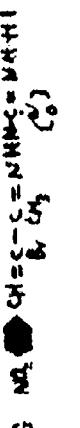
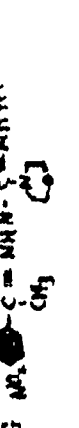
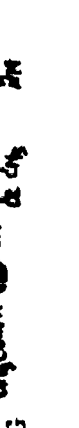
133	43	351	229	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-Cinnamoylaminocinnamaldehyde thiosemicarbazone
134	44	324	218	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-Benzoylaminocinnamaldehyde thiosemicarbazone
135	45	374	216- 218	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-Tosylaminocinnamaldehyde thiosemicarbazone
136	46	302		1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-(3-Methyl-2-butenyl) amino cinnamaldehyde thiosemicarbazone
137	48	224	234	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-Nitrobenzaldehyde thiosemicarbazone
138	49	271	220	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-(3-methy-2-butenyl) amino benzaldehyde thiosemicarbazone
139	51	319	212- 213	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-Phenylacetylaminocinnamaldehyde thiosemicarbazone
140	54	293	201	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-Hexanoylaminobenzaldehyde thiosemicarbazone
141	55	318	198-9	1000	G	<chem>NC(=O)C1=CC=C(C=C1)C(=O)N</chem>	p-Hexanoylaminocinnamaldehyde thiosemicarbazone

142	57	194	197-198	1000	G	$\text{NH}_2 \text{---} \text{CH}=\text{N} \text{---} \text{HCSNH}_2$	p-Aminobenzaldehyde thiosemicarbazone
143	59	357.5	205	1000	G	$\text{NO}_2 \text{---} \text{CH}=\text{CH} \text{---} \text{CH}_2 \text{---} \text{CH}_2 \text{---} \text{N} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix} \text{---} \text{HCSNH}_2$	1-p-Nitrophenyl-5-dimethylamino pentene-1-one-3-thiosemicarbazone hydrochloride
144	61	236	230	1000	G	$\text{CH}_3 \text{---} \text{CONH} \text{---} \text{CH}=\text{N} \text{---} \text{NH} \text{---} \text{CS} \text{---} \text{NH}_2$	p-Acetylamino benzaldehyde thiosemicarbazone
145	62	294	216	1000	G	$\text{HOOC} \text{---} \text{CH}_2 \text{---} \text{CH}_2 \text{---} \text{CONH} \text{---} \text{CH}=\text{N} \text{---} \text{HCSNH}_2$	pp-Succinoylamino benzaldehyde thiosemicarbazone
146	63	262	236	1000	G	$\text{CH}_3 \text{---} \text{CH}=\text{CH} \text{---} \text{CONH} \text{---} \text{CH}=\text{N} \text{---} \text{HCSNH}_2$	p-Crotonylaminobenzaldehyde thiosemicarbazone
147	64	288	235	1000	G	$\text{CH}_3 \text{---} \text{CH}=\text{CH} \text{---} \text{CONH} \text{---} \text{CH}=\text{CH} \text{---} \text{CH} \text{---} \text{N} \text{---} \text{HCSNH}_2$	p-Crotonylaminocinnamaldehyde thiosemicarbazone
148	65	262	214	1000	G	$\text{CH}_3 \text{---} \text{C} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix} \text{---} \text{CONH} \text{---} \text{CH}=\text{N} \text{---} \text{HCSNH}_2$	p-Methacrylamino benzaldehyde thiosemicarbazone
149	66	234	190	1000	G	$\text{NH}_2 \text{---} \text{CH}=\text{CH} \text{---} \text{C} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix} \text{---} \text{N} \text{---} \text{HCSNH}_2$	p-Aminobenzalacetone thiosemicarbazone
150	67	276	220-227	1000	G	$\text{CH}_3 \text{---} \text{CONH} \text{---} \text{CH}=\text{CH} \text{---} \text{N} \text{---} \text{HCSNH}_2$	p-Acetylamino benzalacetone thiosemicarbazone

151	74	408	191 d. 1000	G	NO_2 	p-Nitro-4-bromobenzaldehyde Thiosemicarbazone
152	77	103	244 d. 1000	G	$\text{NH}_2\text{C}(\text{NH})\text{NNO}_2$	Nitroguanidine Nitroguanidine
153	78	136	172-173 1000	G	$\text{H}_2\text{N}\cdot\text{C}(\text{=NH})\text{NHNH}_2\cdot\text{H}_2\text{CO}_2$	Aminoguanidine bicarbonate
154	97	421	221-222 1000	G	NO_2 	Pyridinium-nitro benzal acetone 3-hydroxy phenylhydrazine-4-carboxylate
155	107	269.5	238 1000	G	NO_2 	p-Nitro-2-nitro-4-bromobenzaldehyde hydrochloride
156	111	348	265 d. 1000	G	NO_2 	p-Nitro-2-nitro-4-bromobenzaldehyde guanyldichloride
157	113	313	223 d. 1000	G	NO_2 	p-Nitro-2-nitro-4-bromobenzaldehyde semicarbasone
158	1115	283	270 d. 1000	G	NO_2 	p-Nitro-2-nitro-4-bromobenzaldehyde hydrochloride
159	116	248	235 d. 1000	G	NO_2 	p-Nitro-2-nitro-4-bromobenzaldehyde semicarbasone

160	117	362.5	249-50	1000	G	NO_2	CH_3	CH_3	p-Nitro-d-bromobenzalacetone guanyl hydrazine hydrochloride
161	118	327	229	1000	G	NO_2	CH_3	CH_3	p-Nitro-d-bromobenzalacetone semicarbazone
162	123	250	225	1000	G	CH_3	CH_3	CH_3	p-Acetylaminacetophenone thiosemicarbazone
163	124	208	185	1000	G	N_2N	CH_3	CH_3	p-Aminoacetophenone thiosemicarbazone
164	126	238	240 d.	1000	G	NO_2	CH_3	CH_3	p-Nitroacetophenone thiosemicarbazone
165	127	218	215-216	1000	G				Furfural isonicotinoyl hydrazone
166	128	296	246 d.	1000	G	NO_2	CH_3	CH_3	p-Nitrocinnamaldehyde isonicotinoyl hydrazone
167	129	260	250 d.	1000	G	NO_2	CH_3	CH_3	5-Nitrofurfural isonicotinoyl hydrazone
168	133	157	148-149	1000	G	CH_3	CH_3	CH_3	4-Ethylpentene 3-one-2 thiosemicarbazone

169	149	265	186-187	1000	G		Benzalacetone isonicotinoyl hydrazone
170	150	310	256-257	1000	G		p-Nitrobenzalacetone isonicotinoyl hydrazone
171	152	281	193-196	1000	G		p-Nitro benzalacetone phenyl hydrazone
172	158	379	155 d.	1000	G		p-Nitro-d-bromocinnamaldehyde phenyl hydrazide
173	159	267	181-181.5	1000	G		p-Nitrocinnamaldehyde phenylhydrazide
174	185	113	187-188	1000	G		Acetone semicarbazone
175	1112	403	216-219	1000	G		m-nitrobenzaldehyde N,N'-anhydrobis(p-hydroxyethyl)-guanyldiazide
176	1115	390	116-117	1000	G		p-methoxybenzaldehyde N,N'-anhydrobis(p-hydroxyethyl)-guanyldiazide
177	1119	405	172-173	1000	G		p-methoxyacetophenone N,N'-anhydrobis(p-hydroxyethyl)-guanyldiazide

178	1120	430	206- 207.5	1000	G		p-methoxybenzalacetone N:N'-anhydrobis (beta-hydroxyethyl)guanyldiazone hydroiodide
179	1121	428	152-153	1000	G		- methylanisalacetone-N:N'-anhydrobis(beta-hydroxyethyl)-guanyldiazone-hydroiodide
180	1123	445	230	1000	G		m-nitrobenzalacetone N:N'-anhydrobis-(beta-hydroxyethyl)-guanyl diazone hydroiodide
181	1124	524	181.5	1000	G		m-nitro-d-brombenzalacetone N:N'-anhydrobis (beta-hydroxyethyl)-guanyldiazonehydroiodide
182	1156	419	203-205	1000	G		m-nitroacetophenone N:N'-anhydrobis(beta-hydroxyethyl)-guanyl diazone hydrochloride
183	1157	3888	202-203	1000	G		d - chloro-m-nitrobenzalacetone N:N'-anhydrobis(beta-hydroxyethyl)guanyl diazone hydrochloride
184	1165	400	252	1000	G		d - chloro-p-acetylamino benzalacetone N:N'-anhydrobis(beta-hydroxyethyl) guanyldiazone hydrochloride
185	1167	373	188-190	1000	G		p-methoxy- -chlorobenalacetone N:N'-anhydrobis(beta-hydroxyethyl)guanyl diazone hydrochloride
186	1168	378	193-194	1000	G		p-chloro- -chlorobenalacetone N:N'-anhydrobis(beta-hydroxyethyl) guanyl diazone hydrochloride
187	1169	364	167	1000	G		d-chloro-p-nitrobenzalacetone N:N'-anhydrobis(beta-hydroxyethyl) guanyldiazone

189	1172	343	208-209	1000	G		2-chloro-4-hydroxybenzaldehyde
190	Group B-phenol 52	109	173	1000	G		2-aminophenol
191	53	151	192	1000	G		2-methoxyphenol
192	56	273	104.5-5	1000	G		2,4-dihydroxybenzoic acid
193	60	145	75	1000	G		2-hydroxyquinoline
194	76	154	213	1000	G		3,4-dihydroxybenzoic acid
195	91	270	190-199	1000	G		Sodium 3-hydroxy-4-carboxyphenyl sulfonate
196	92	168	148-149	1000	G		p-Hydroxy-4-hydrazinobenzoic acid
197	93	301	228-229	1000	G		p-Nitrobenzaldehyde 3-hydroxy-4-carboxyphenyl hydrazone
198	94	302	195	1000	G		Vanillin 3-hydroxy-4-carboxyphenyl hydrazone
199	95	208	198-199	1000	G		Acetone 3-hydroxy-4-carboxyphenyl phenylhydrazone
200	96	204.5	177	1000	G		3-hydroxy-4-carboxyphenyl hydrazone hydrochloride
201	99	341	221-222	1000	G		p-Nitrobenzaldehyde 3-hydroxy-4-carboxyphenyl hydrazone
202	103	248	173	1000	G		4-Methylpentene-3-one-2-m-hydroxy-p-carboxyphenyl hydrazone
203	110	313	213	1000	G		p-Acetylaminobenzaldehyde-3-hydroxy-4-carboxyphenyl hydrazone

204	168	137	46	1000	3		p-methyl-m-amino-anisol -
205	169	154	77	1000	G		p-Nitro-ortho-aminophenol
206	170	168	135-140	1000	G		5-Nitro-2-aminoanisol
207	171	155	201-202	1000	G		5-Nitro-2-aminophenol
208	172	319	280	1000	G		3-Amino-1-naphthol-3,6-disulfonic acid
209	173	188.5	274	1000	G		5-Nitro-4-chloro-2-amino phenol
210	175	239	290	1000	G		6-Amino-1-naphthol-3-sulfonic acid
211	176	154	1000	1000	G		4-Nitro-2-amino phenol
212	178	214.5	235-240	1000	G		4,5-dichloro-2-aminophenol hydrochloride
213	180	168	1000	1000	G		p-Nitro-o-anisidine
214	182	239	293	1000	G		2-Amino-8-naphthol-6-sulfonic acid
215	184	244	290(d)	1000	G		Dianisidine-HCl salt
216	185	199	158-168.2	1000	G		Dicromic acid
217	186	154	200	1000	G		5-Nitro-2-aminophenol
218	187	235	260	1000	G		Mono methyl-p-aminophenol sulfate
219	189	108	285	1000	G		3-Amino-4-hydroxybenesulfonic acid



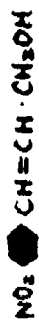
4-Chloro-2-aminophenol



1-Amino-2-naphthol

Group F - Miscellaneous

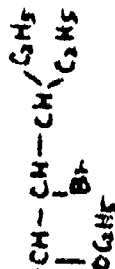
p-Nitrocinnamyl alcohol



o-bromo-B-(p-nitrophenyl)-B-methoxypropionaldehyde dimethyl acetal



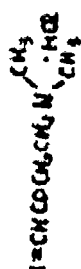
o-Bromo-B-ethoxy-p-Nitro hydrocinnamaldehyde diethylacetal



5-(p-Tolylamino)-8-hydroxy quinoline



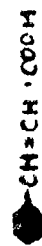
1-p-Nitrophenyl-5-dimethyl aminopentene-1-one-3 hydrochloride



Isonicotinoylaminoguanidine hydrochloride



p-acetylaminocinnamic acid



p-Hydrazinocinnamic acid



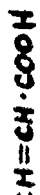
p-Nitrobenzoic acid



p-Aminobenzoic acid



p-Aminocinnamic acid



p-Nitrocinnamic acid



2-amino-4-nitro toluene



220	192	143.5	136.2-.5	1000	G	
221	193	159	160	1000	G	
Group F - Miscellaneous						
222	3	179	125+127	1000	G	
223	4	334	59-63	1000	G	
224	33	344	149-150	1000	G	
225	50	263	190	1000	G	
226	58	284.5	186-187	1000	G	
227	72	215.5	300	1000	G	
228	79	205	250-251	1000	G	
229	81	178	218	1000	G	
230	84	167	232-239	1000	G	
231	85	137	185-186.5	1000	G	
232	86	163	167	1000	G	
233	87	193	285	1000	G	
234	88	152	108.5-109	1000	G	

235	102	205	103-105 100-101 d.	1000	G		3-Methyl-5-p-nitrophenyl pyrazolino
236	106	191	145-147	1000	G		p-nitrocinnamaldehyde hydrazone
237	108	194	203-204 d.	1000	G		4,β-dinitrostyrene
238	109	220	200-201 d.	1000	G		1-p-Nitrophenyl-4-nitrobutadiene-1,3
239	114	299	182-182.5	1000	G		1-p-Nitrophenyl-2-bromo-4-nitro-1,3-butadiene
240	130	171	235-235	1000	G		p-Nitrobenzoic acid
241	131	195	54-56	1000	G		Ethyl p-nitrobenzoate
242	134	247	103-104	1000	G		1-Phenylthiocarbamoyl-3-methyl-5,5-dimethylpyrazoline
243	135	203	191-192	1000	G		3-Methyl-5-p-nitrophenyl pyrazole
244	141	256	146-147	1000	G		d-Benzoyl-β-phenyl thiourea
245	142	152	155-156	1000	G		Phenylthiourea
246	143	322	185-5.5 d.	1000	G		1-Benzoylthiocarbamoyl-3-methyl-5-phenyl pyrazoline
247	144	367	199-200	1000	G		1-Benzoylthiocarbamoyl-3-methyl-5-p-nitrophenyl pyrazoline
248	145	194	170-171	1000	G		d-Acetyl-β-phenylthiourea
249	146	218	230-231	1000	G		1-Thiocarbamoyl-3-methyl-5-phenylpyrazoline
250	147	263	271	1000	G		1-Thiocarbamoyl-3-methyl-5-p-nitrophenyl pyrazoline

251	153	236	112-113	1000	G		3-methyl-1,5-diphenyl pyrazoline
252	154	280	113-3.5	1000	G		1-phenyl-3-methyl-5-p-nitro-phenyl pyrazoline
253	160	217	160-161	1000	G		1-phenyl-3-thiocarbamoyl-3-methyl-5-phenyl pyrazoline
254	161	233	171-122	1000	G		1,3-methyl-5-nitro-formyl phenylpyrazoline
255	162	188	88.5-90	1000	G		1-formyl-3-methyl-5-phenyl pyrazoline
256	163	179	90-91	1000	G		4-bromo-3-methyl-crotonic acid
257	164	202	77.5-73	1000	G		1-acetyl-3-methyl-5-phenylpyrazoline
258	174	223	290	1000	G		1-naphthylamino-6-sulfonic acid
259	177	143	169.5-170.5	1000	G		1-naphthyl amine
260	179	303	293	1000	G		1-aminonaphthyl-3,8-di-sulfonic acid-mono Na salt.
261	181	303	293	1000	G		2-aminonaphthalene-5,7 di-sulfonic acid
262	183	303	300	1000	G		1-aminonaphthalene-4,8-disulfonic acid mono sodium salt
263	183	360	3000	1000	G		2-(4-aminonaphthyl)azo-naphthalene-4,8-disulfonic acid
264	190	223	285	1000	G		1-Naphthylamine-7-sulfonic acid
265	191	123	1000	1000	G		p-amino diphenylamine diazonium salt

Table 11. Screening test of chemical compounds in chick
chorioallantoic membrane culture

Serial No.	Synthesis No.	Concen- tration	\$ HA \$ percent	Serial No.	Synthesis No.	Concen- tration	\$ HA \$ percent
1	115	100	0	39	990	100	50
2	117	100	0	40	991	100	50
3	273	100	0	41	992	100	25
4	276	100	0	42	993	100	50
5	277	100	0	43	994	100	100
6	278	100	0	44	997	100	50
7	279	100	50	45	1030	100	0
8	280	100	100	46	1046	100	0
9	281	100	0	47	1050	100	0
10	282	50	12.5	48	1051	100	50
11	283	100	0	49	1052	1000	100
12	284	100	0	50	1053	100	50
13	285	100	25	51	1054	100	0
14	290	100	0	52	1055	100	6.3
15	292	100	50	53	1056	100	100
16	293	50	0	54	1057	100	12.5
17	296	50	12.5	55	1058	100	0
18	298	100	0	56	1059	50	0
19	302	100	0	57	1062	100	0
20	304	100	0	58	1063	100	6.3
21	327	100	0	59	1064	100	0
22	406	100	0	60	1065	50	100
23	418	100	0	61	1066	100	50
24	444	100	0	62	1067	100	100
25	622	50	0	63	1068	100	100
26	901	100	50	64	1069	100	50
27	902	100	50	65	1070	100	50
28	903	100	12.5	66	1071	100	25
29	904	100	50	67	1072	100	0
30	907	100	100	68	1073	100	12.5
31	909	100	50	69	1074	100	0
32	931	50	50	70	1075	100	50
33	932	100	12.5	71	1076	100	50
34	954	100	50	72	1077	100	100
35	960	100	0	73	1078	100	0
36	983	100	0	74	1079	100	0
37	987	100	50	75	1081	50	12.5
38	988	100	100	76	1083	100	50

Serial No.	Synthesis No.	Concentration	HA percent	Serial No.	Synthesis No.	Concentration	HA percent
77	1094	100	0	115	194	100	100
78	1096	100	0	116	196	100	100
79	1097	100	12.5	Group D			
80	1098	100	0	117	12	100	100
81	1099	100	0	118	15	100	50
82	1100	100	0	119	18	100	100
83	1101	100	0	120	19	100	100
84	1102	100	0	121	20	100	100
85	1103	100	0	122	22	100	0
86	1104	50	0	123	24	100	100
87	1105	100	0	124	26	100	50
88	1106	50	6.3	125	27	100	50
89	1107	50	0	126	31	100	12.5
Group B				127	32	100	100
90	1	100	0	128	33	100	25
91	2	100	0	129	35	100	0
92	5	100	100	130	36	100	0
93	6	100	100	131	37	100	100
94	9	100	0	132	39	100	12.5
95	23	100	100	133	43	100	100
96	29	100	100	134	44	100	100
97	30	100	25	135	45	100	50
98	34	100	0	136	46	100	50
99	69	100	6.3	137	48	100	100
100	71	100	0	138	49	100	100
101	73	100	0	139	51	100	100
102	120	100	100	140	54	100	100
103	121	100	100	141	55	100	100
104	125	100	100	142	57	100	25
105	137	100	25	143	59	100	0
106	148	100	100	144	61	100	100
107	198	100	0	145	62	100	50
Group C				146	63	100	100
108	7	100	100	147	64	100	100
109	8	100	100	148	65	100	50
110	10	100	100	149	66	100	0
111	17	100	100	150	67	100	100
112	165	100	100	151	74	100	0
113	166	100	100	152	77	100	100
114	167	100	100	153	78	100	100

Serial No.	Synthesis No.	Concentration	HA percent	Serial No.	Synthesis No.	Concentration	HA percent
154	97	100	0	192	56	100	25
155	107	100	0	193	60	100	0
156	111	100	0	194	76	100	100
157	113	50	0	195	91	100	100
158	115	100	0	196	92	100	0
159	116	100	100	197	93	100	100
160	117	100	0	198	94	100	0
161	118	100	100	199	95	100	0
162	123	100	100	200	96	100	100
163	124	100	100	201	99	50	0
164	126	100	100	202	103	100	100
165	127	100	100	203	110	50	0
166	128	100	100	204	162	100	100
167	129	50	0	205	169	100	25
168	133	100	100	206	170	100	50
169	149	100	0	207	171	100	25
170	150	100	100	208	172	100	100
171	152	100	100	209	173	50	0
172	158	50	0	210	175	100	0
173	159	100	100	211	176	100	50
174	195	100	100	212	178	100	0
175	1112	100	50	213	180	100	100
176	1115	100	100	214	182	100	0
177	1119	100	100	215	184	100	0
178	1120	100	0	216	185	100	0
179	1121	100	12.5	217	186	100	12.5
180	1123	100	50	218	187	100	0
181	1124	100	25	219	189	100	0
182	1156	100	100	220	192	100	0
183	1157	100	0	221	193	100	0
184	1165	100	0	Group F			
185	1167	100	25	222	3	100	100
186	1168	50	0	223	4	100	50
187	1169	50	0	224	38	100	0
189	1172	100	0	225	50	100	50
Group E				226	58	50	0
190	52	100	0	227	72	100	100
191	53	100	50	228	81	100	100

Serial No.	Synthesis No.	Concentration	HA percent	Serial No.	Synthesis No.	Concentration	HA percent
229	79	100	100	248	145	100	100
230	84	100	100	249	146	100	100
231	85	100	100	250	147	100	100
232	86	100	100	251	153	50	0
233	87	100	100	252	154	50	12.5
234	88	100	50	253	160	100	100
235	102	100	100	254	161	100	100
236	106	100	100	255	162	100	50
237	108	50	0	256	163	100	0
238	109	50	0	257	164	100	100
239	114	50	0	258	174	100	0
240	130	100	50	259	177	100	0
241	131	100	100	260	179	100	0
242	134	100	100	261	181	100	0
243	135	100	100	262	183	100	0
244	141	100	100	263	188	100	100
245	142	100	100	264	190	100	0
246	143	100	100	265	191	100	0
247	144	100	100				

S: Final concentration of compound solution, %/cc

3S: HA percent of control.

TABLE III Result of Screening test of 265 compounds

Inhibitory	Partially inhibitory	Non-inhibitory
Group A		
1, 2, 3, 4, 5, 6, 9, 11, 12, 14, 15, 18, 19, 20, 21, 22, 23, 24, 25, 35, 36, 45, 46, 47, 51, 55, 56, 57, 59, 67, 69, 73, 74, 77, 78, 80, 81, 82, 83, 84, 85, 86, 87, 88, Total 44	7, 10, 13, 15, 17, 26, 27, 28, 29, 31, 32, 33, 34, 37, 39, 40, 41, 42, 44, 48, 50, 52, 54, 58, 61, 64, 65, 66, 68, 70, 71, 75, 76, 79, 88, Total 35	8, 30, 38, 43, 49, 53, 60, 62, 64, 72, Total 10
Group B		
90, 91, 94, 98, 100, 101, 107, Total 7	97, 99, 105, Total 3	92, 93, 95, 96, 102, 103, 104, 106, Total 8
Group C		
-	-	108, 109, 110, 111, 112, 113, 114, 115, 116, Total 9
Group D		
122, 129, 130, 143, 140, 151, 154, 155, 156, 157, 158, 160, 167, 169, 172, 178, 183, 184, 186, 187, 189, Total 22	118, 124, 125, 126, 128, 132, 135, 136, 142, 145, 148, 175, 179, 180, 181, 185, Total 16	117, 119, 120, 121, 123, 127, 131, 133, 134, 137, 138, 139, 140, 141, 144, 146, 147, 150, 152, 153, 159, 161, 162, 163, 164, 165, 166, 168, 170, 171, 173, 174, 176, 177, 182, Total 35
Group E		
190, 193, 196, 198, 199, 201, 203, 209, 210, 212, 214, 215, 216, 218, 219, 220, Total 17	191, 192, 205, 206, 207, 211, 217, Total 7	194, 195, 197, 200, 202, 204, 208, 213, Total 8

Group F		
224, 226, 237, 238, 239, 251, 256, 258, 259, 260, 261, 262, 264, 265.	223, 225, 234, 240, 252, 255.	222, 227, 228, 229, 230, 231, 232, 233, 235, 236, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 253, 254, 257, 263.
Total 14	Total 6	Total 24

TABLE IV Summary of screening test.

Group of compound	Inhibitory		Partially inhibitory		Non-inhibitory		Total
	No.*	%	No.*	%	No.*	%	
A	44	49.4	35	39.3	10	11.2	89
B	7	38.8	3	16.6	8	44.6	18
C	0	0	0	0	9	100	9
D	22	30.1	16	21.9	35	47.9	73
E	17	53.1	7	21.8	8	25	32
F	14	31.8	6	13.6	24	54.5	44
Total	104	39.2	67	25.2	94	35.4	265

No.* : Numbers of chemical compounds.

TABLE V Quantitative analysis of antiviral and cytotoxicity tests in membrane culture

Serial No.	Synthesis No.	Antiviral activity				Cytotoxic activity				Ratio ³
		100 ¹⁾	50	25	12.5	100 ¹⁾	50	25	12.5	
Group A										
1	115	0	0	6.3	50	0	6.3	50	100	1
2	117	0	0	0	12.5	0	0	100	100	1
3	273	0	0	0	100	0	100	100	100	2
4	276	0	0	6.3	25	0	25	100	100	1
5	277	0	0	25	50	50	100	100	100	22
11	283	0	0	0	12.5	50	100	100	100	24
12	284	0	0	6.3	50	0	25	100	100	1
14	290	0	0	0	6.3	0	0	12.5	100	1
16	293	-	0	0	6.3	-	0	12.5	100	1
18	298	0	50	50	100	100	-	-	-	22
19	302	0	0	12.5	50	12.5	100	100	-	22
20	304	0	0	12.5	50	6.3	50	100	100	22
21	327	0	0	0	25	0	0	12.5	50	2
22	406	d 0	0	0	50	d 0	0	12.5	-	1
23	418	0	0	6.3	12.5	0	0	100	100	1/2
24	444	0	0	0	100	0	6.3	100	100	2
25	622	-	0	0	25	-	25	100	100	22
36	983	0	0	0	6.3	0	0	0	100	1/2
45	1030	0	0	0	25	0	0	0	50	1/2
46	1046	0	0	6.3	12.5	12.5	100	100	-	22
47	1050	0	6.3	50	100	100	100	100	-	-
51	1054	0	0	25	50	50	100	100	-	22
56	1059	0	50	100	100	-	100	100	100	2 1/2
57	1062	0	25	100	50	100	100	100	-	2 1/2
59	1064	0	6.3	25	50	100	100	100	-	2 1/2

67	1072	0	0	50	50	50	100	100	-	≥ 2			
69	1074	0	0	25	25	25	100	100	-	≥ 2			
73	1078	0	0	0	100	0	100	100	100	2			
74	1079	0	0	50	100	0	0	-	-	-			
77	1094	0	25	50	100	100	100	100	-	≥ 1			
78	1096	0	0	25	100	50	100	100	-	≥ 2			
80	1098	0	0	0	100	0	100	100	-	2			
81	1099	0	0	0	12.5	0	0	100	-	1			
82	1100	0	0	6.3	50	0	0	0	6.3	1/4			
83	1101	0	0	0	6.3	0	0	0	100	1/2			
84	1102	0	0	6.3	50	0	0	100	100	1/2			
85	1103	0	0	0	12.5	0	0	12.5	100	1			
86	1104	d	0	0	50	100	d	-	0	100	100	1/2	
87	1105	0	0	0	50	0	0	12.5	100	1			
Group E	89	d	0	6.3	50	100	d	-	50	100	100	≥ 1/2	
	90	1	0	25	100	100	0	50	100	100	1/2		
	91	2	0	0	12.5	50	0	0	50	100	1/2		
	94	9	0	0	0	25	0	0	0	25	1/2		
	98	34	0	0	25	200	0	200	200	50	1		
	100	71	0	0	50	50	0	0	25	100	1/2		
	101	73	0	0	0	25	0	0	0	25	1/2		
	107	198	0	0	0	25	0	12.5	50	100	2		
Group D													
	129	35	0	0	0	25	25	50	50	50	≥ 4		
	130	36	0	0	0	12.5	25	100	100	100	≥ 4		
	149	66	c	0	50	50	100	c	0	50	100	100	1/2
	151	74	d	0	0	25	100	d	0	25	50	100	1
	155	107	0	0	0	100	0	0	0	100	1/2		
	156	111	0	0	0	0	0	0	0	100	1		
	158	115	0	0	0	100	0	0	0	50	1/2		

160	117	0	0	0	0	0	0	50	100	2
167	129	d 0	0	50	100	d 25	100	200	200	≥ 2
169	149	0	0	25	50	0	0	0	12.5	1/4
172	158	d 0	25	100	100	d 100	200	200	200	≥ 1
178	1120	0	0	12.5	50	b 0	100	100	100	4
179	1121	e 0	0	0	50	e 0	25	50	50	2
183	1157	0	0	0	25	0	0	25	100	1
186	1168	c 0	0	0	25	c 0	100	100	100	2
187	1169	c 0	0	0	50	c 0	100	100	100	2

Group E

190	52	0	0	25	25	a 0	0	0	25	2
196	92	e 0	0	50	50	e 0	100	100	100	1
198	94	g 0	100	100	100	0	0	50	100	4
199	95	e 0	50	200	200	e 0	100	100	100	1/2
201	99	d 0	25	100	100	d 200	200	200	200	≥ 1/2
209	173	d 0	50	100	200	d 200	200	200	200	≥ 1/2
210	175	c 0	0	12.5	25	c 25	25	50	25	≥ 2
212	178	g 0	0	0	25	0	0	25	50	16
214	182	b 0	0	0	50	b 25	50	100	100	≥ 4
215	184	b 0	0	0	12.5	b 100	100	100	100	≥ 4
218	187	h 0	0	25	100	f 0	0	0	12.5	2
219	189	b 0	0	100	100	b 6.3	6.3	6.3	25	≥ 2
220	192	0	0	0	25	0	0	100	25	2
221	193	0	0	0	12.5	0	0	50	100	1

Group F

226	58	e 0	0	50	100	e 0	0	50	100	2
237	108	d 0	0	100	100	e 0	100	100	100	1
238	109	d 0	0	25	100	d 0	0	50	50	1/2
239	114	d 0	0	0	100	d 25	50	100	100	≥ 4
251	153	d 0	100	100	100	d 200	200	200	200	≥ 1

256	163	b	0	0	0	12.5	b	25	25	25	50	24
258	174	b	0	0	0	50	b	0	12.5	12.5	50	2
259	177		0	0	100	100		0	50	100	100	4
260	179	b	0	0	0	100	b	0	50	25	50	2
261	181	b	0	0	12.5	100	b	25	25	50	100	22
262	183	b	0	0	0	25	b	50	50	100	100	24
264	190	b	0	0	0	25	b	25	25	100	100	24
265	191	f	0	0	0	100	f	50	100	100	50	24

Legend : 1) Final concentration μ /cc.

2) Non-toxic concentration. / Inhibitory maximal concentration.

Following Letters, a ~ h, in column of Antiviral activity and Cytotoxic activity indicate starting concentrations as follows

a : 800	e : 25
b : 400	f : 12.5
c : 200	g : 6.3
d : 50	h : 3.2

TABLE VI Result of antiviral test of 89 compounds.

Group of compound	Ratio*									
	1 or less				2			4	16	
A	1, 14, 36, 57, 82, 86,	2, 16, 45, 59, 83, 87,	4, 22, 47, 77, 84, 89.	12, 23, 56, 81, 85,	3, 19, 24, 51, 73,	5, 20, 25, 67, 78,	18, 21, 46, 69, 80.	11.		
	Total 23				Total 15			Total 3		
B	90, 100,	91, 101.	94, 98,	93,	107.					
	Total 6				Total 1					
D	149, 158,	150, 169,	155, 172,	156, 173.	160, 186,	167, 179, 187.		129, 130, 178.		
	Total 8				Total 5			Total 3		
E	196, 221.	199, 201,	209, 209,		190, 219,	210, 218, 220.		198, 214, 215.	212.	
	Total 5				Total 5			Total 3		
F	237, 238,	251.			226, 261.	258, 260,		239, 262,	256, 264,	259, 265.
	Total 3				Total 4			Total 6		

Ratio* : Non-toxic concentration / Inhibitory maximal concentration

TABLE VII Summary of antiviral test.

Group of compound	Ratio*								Total
	1 or less		2		4		16		
	Nov**	%	Nov**	%	Nov**	%	Nov**	%	
A	23	59	15	38.5	1	25	-	0	39
B	6	86	1	14	-	0	-	0	7
C	-	0	-	0	-	0	-	0	0
D	8	50	5	31.2	3	18.8	-	0	16
E	5	35.7	5	35.7	3	21.4	1	7.2	14
F	3	23	4	30.8	6	46.2	-	0	13
Total	45	50.1	30	33.7	13	14.6	1	1.1	89

Ratio* : Non-toxic concentration / Inhibitory maximal concentration

Nov* : Numbers of chemical compounds.

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3. REPORT TITLE STUDIES ON THE ANTIVIRAL ACTIVITY OF GUANYLHYDRAZONES ESPECIALLY AGAINST ARBO- AND MYXOVIRUSES (U)		
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13. ABSTRACT Two hundred and sixty-five chemical compounds, guanylhyaazones, azlactones, hydrazones, phenols, carbonyl compounds and miscellaneous ones were tested for in vitro antiviral activity against influenza virus. 104 out of 265 compounds were completely inhibitory by the screening test. Selected 89 compounds were qualitatively analyzed for the antiviral and toxic activities. 14 out of 89 compounds were found to be inhibitory with the ratio of 4 or more of non-toxic concentration versus minimal inhibitory concentration. One compound, serial No. 212, synthesis No. 178 inhibited HA production with a final concentration of 1.6 μ /cc and was toxic with a final concentration of 25 μ /cc. (Author)		

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14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Viruses Issue Culture Drug Synthesis Antiviral Activity Hemagglutination Test Screening Test Toxicity Test Japan						

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