thoroughly before submitting for analysis; yield, 7.8 g. (94.7%); m.p. 340–344° dec.; lit.[2] 320–330° dec.

Anal. Calcd. for $C_5H_{11}NO_3S$: C, 36.34; H, 6.71; N, 8.48. Found: C, 36.53; H, 6.82; N, 8.29.[6]

Infrared and ultraviolet spectra[8] showed that no starting material was present. When reduction in aqueous ammonia was attempted in the presence of rhodium on a carrier, complete uptake of hydrogen was never achieved even when a 60% ratio of catalyst to compound was used.

Attempted Hydrogenation of VII.—A solution of 6.3 g. (0.033 mole) of VII[4] in 100 ml. of water and 3 ml. of concentrated ammonium hydroxide was subjected to reduction under 3 atm. pressure in the presence of 2.0 g. of 5% rhodium on alumina. No uptake occurred. The solution was filtered and rehydrogenated with fresh catalyst. This operation was repeated several times. No uptake of hydrogen was ever observed. Attempted reduction in the absence of ammonia with the same catalyst or with platinum oxide also failed.

(8) Infrared examination was carried out by Mr. A. Kammer and ultraviolet work by Mr. V. Papendick, both of this laboratory.

The Synthesis of N-Hydroxycarbanilides and Their Evaluation as Germicides

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Previous workers have shown that substituted carbanilides are a biocidally active group of compounds, but none have investigated the activity of the N-hydroxycarbanilides. The introduction of a hydroxyl group on the nitrogen atom of a carbanilide should give the resulting compound chelating properties and thereby perhaps increase the germicidal activity.

Although the reaction of phenylhydroxylamine and phenylisocyanate to give N-hydroxycarbanilide is known,[1] only a very few N-hydroxycarbanilides are reported in the literature[2] and there are no examples where dihalo- and polyhalo-substituted phenylhydroxylamines are used.

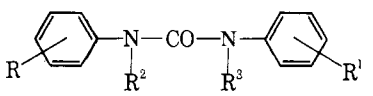
The preparation of dihalo- and polyhalo-substituted phenylhydroxylamines, by reduction with zinc dust in the presence of ammonium chloride, proceeds quite smoothly. However, the isolation of the product is difficult since it will oxidize rapidly in air in a matter of seconds to the azoxybenzene derivative. It was found that the phenylhydroxylamine could be used without isolation; care had to be taken however to remove all alcohol and water used in the reduction step before proceeding to the reaction with the isocyanate.

The monohalo phenylhydroxylamines having a methyl group in the *ortho* position were found to be more stable than the monohalo phenylhydroxylamines and could be isolated and recrystallized in good yields without undue oxidation.

The N-hydroxycarbanilides were screened, by the agar dilution method,[3] and were found to be a biocidally active class of compounds. In general, they were more active than the corresponding carbanilides. Table I compares the relative activity of several carbanilides with that of the corresponding N-hydroxycarbanilides.

TABLE I

COMPARISON OF ACTIVITY OF CARBANILIDES AND N-HYDROXYCARBANILIDES AGAINST *Staphylococcus aureus*



R	R¹	Minimum inhibitory concentration (p.p.m.) R^2 = R^3 = H	R^2 = OH, R^3 = H	R^2 = H, R^3 = OH
3-Cl	3-CF_3	125	31	31
4-Cl	4-Cl	...	15	
4-Cl	3-CF_3-4-Cl	31	2	
3,4-Cl_2	3,4-Cl_2	...	4	
3,5-Cl_2	3-NO_2	...	8	
3,5-Cl_2	3-CF_3-4-Cl	8	0.5	
3,4,5-Cl_3	3-CF_3	31	0.5	8

The physical data and germicidal activity against *Staphylococcus aureus* of the N-hydroxycarbanilides are shown in Table II.

Experimental

The N-hydroxycarbanilides isolated were found to be white or off-white solids which could be recrystallized from aqueous methanol. They melted with decomposition, readily formed sodium salts, and gave blue or green colorations with ferric chloride solution indicative of chelate formation. They were soluble in alcohol, dimethylformamide, and ether; partially soluble in benzene and chloroform; and insoluble in water and petroleum ether. Exposure to sunlight for 2–3 days gave changes in the melting points and additional peaks in the infrared curves of the compounds, indicating instability under these conditions.

Method A.—This procedure was suitable for the fairly stable monohalo phenylhydroxylamines which were isolated and purified before reacting with the isocyanates.

Method B.—Procedure A was modified by not isolating the freshly prepared phenylhydroxylamine. This method was used for the very unstable dihalo and polyhalo phenylhydroxylamines. Any oxidized phenylhydroxylamine that was formed could be removed readily by washing the N-hydroxycarbanilide with petroleum ether (b.p. 40–60°). The isocyanates used, with the exception of the monohalo derivatives which were commercially available, were prepared by the phosgenation of the amine.[4]

3′,4,5′-Trichloro-N-hydroxycarbanilide (Method A).—To a solution of 1.91 g. (0.0133 mole) of 4-chlorophenylhydroxylamine in 50 ml. of chloroform was added a solution of 2.5 g. (0.0133 mole) of 3,5-dichlorophenyl isocyanate in 50 ml. of chloroform. After stirring for a few min. a white precipitate was formed. The mixture was stirred for 1 hr., then filtered, the white solid vacuum dried, and then recrystallized from aqueous methanol to give white crystals, m.p. 155–156°, in 75% yield.

3,3′,4,4′-Tetrachloro-N-hydroxycarbanilide (Method B).—A mixture of 21.9 g. (0.114 mole) of 3,4-dichloronitrobenzene in 240 ml. of 2B alcohol and 4.8 g. of ammonium chloride in 60 ml. of water was stirred well and heated to reflux. At reflux small portions of pure zinc dust were carefully added over approximately a 1-hr. period until the mixture became colorless. Approximately 43 g. of zinc dust were necessary. The mixture was then cooled slightly, quickly vacuum stripped to dryness, then slurried with 500 ml. of chloroform, filtered, the filtrate quickly was dried with anhydrous sodium sulfate and then filtered into a solution of 12.68 g. (0.068 mole) of 3,4-dichlorophenyl isocyanate in 100 ml. of chloroform. The mixture was stirred for 1–2 hr. The white precipitate, which formed almost immediately, was removed by filtration and washed with a little petroleum ether (to remove oxidized

(1) E. Beckmann, *J. prakt. Chem.*, [2]**56**, 71 (1897).

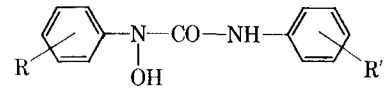
(2) B. Hirsch, *ibid.*, **284**, 264 (1961).

(3) S. A. Waksman and H. C. Reilley, *Ind. Eng. Chem. Anal. Ed.*, **17**, 556 (1945).

(4) D. J. Beaver, D. P. Roman, and P. J. Stoffel, *J. Am. Chem. Soc.*, **79**, 1236 (1957).

TABLE II

N-HYDROXYCARBANILIDES



R	R'	Method[a]	M.p., °C. dec.	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found	Min. inhibitory concn. (p.p.m.)[b]
H	2-Cl	A	115–117	$C_{13}H_{11}ClN_2O_2$	59.44	59.08	4.22	4.17	10.67	10.74	13.50	13.20	125 p
H	3-Cl	A	148–149	$C_{13}H_{11}ClN_2O_2$	59.44	59.67	4.22	4.45	10.67	10.75	13.50	13.52	...
H	4-Cl	A	162–163	$C_{13}H_{11}ClN_2O_2$	59.44	59.84	4.22	4.05	10.67	10.71	13.50	13.45	...
H	2,3-Cl_2	A	153–154	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.67	3.39	3.40	9.43	9.42	23.87	23.40	...
H	2,5-Cl_2	A	169–170	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.66	3.39	3.62	9.43	9.20	23.87	23.55	...
H	3,4-Cl_2	A	162–164	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.31	3.39	3.41	9.43	9.51	23.87	23.87	...
H	3,5-Cl_2	A	151–152	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.70	3.39	3.50	9.43	9.69	23.87	23.62	62
H	3-CF_3	A	144	$C_{14}H_{11}F_3N_2O_2$	56.75	56.77	3.74	3.44	9.46	9.20	...	...	250
3-Cl	H	A	148–150	$C_{13}H_{11}ClN_2O_2$	59.44	59.59	4.22	4.41	10.67	10.73	13.50	13.69	...
3-Cl	2-Cl	A	144	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.68	3.39	3.71	9.43	9.64	23.87	22.95	...
3-Cl	3-Cl	A	150–151	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.44	3.39	3.64	9.43	9.40	23.87	23.79	31
3-Cl	4-Cl	A	153–154	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.83	3.39	3.27	9.43	9.45	23.87	23.62	125
3-Cl	2,3-Cl_2	A	161–162	$C_{13}H_9Cl_3N_2O_2$	...	...	...	...	8.45	8.52	32.09	32.15	15
3-Cl	2,5-Cl_2	A	158–159	$C_{13}H_9Cl_3N_2O_2$	47.10	47.25	2.74	2.64	8.45	8.41	32.09	32.12	31
3-Cl	3,4-Cl_2	A	148–149	$C_{13}H_9Cl_3N_2O_2$	47.10	47.25	2.74	2.60	8.45	8.60	32.09	32.34	31
3-Cl	3,5-Cl_2	A	172	$C_{13}H_9Cl_3N_2O_2$	...	...	...	...	8.45	8.55	32.09	31.97	15
3-Cl	3-CF_3	A	125–126	$C_{14}H_{10}ClF_3N_2O_2$	50.85	50.96	3.05	2.93	8.48	8.16	10.72	10.81	31
4-Cl	H	A	159	$C_{13}H_{11}ClN_2O_2$	59.44	59.52	4.22	4.11	10.67	10.87	13.50	13.42	...
4-Cl	2-Cl	A	158–159	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.59	3.39	3.20	9.43	9.67	23.87	23.81	...
4-Cl	3-Cl	A	133–134	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.66	3.39	3.13	9.43	9.41	23.87	23.81	31
4-Cl	4-Cl	A	166	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.56	3.39	3.58	9.43	9.32	23.87	23.86	15
4-Cl	2,3-Cl_2	A	174	$C_{13}H_9Cl_3N_2O_2$	47.10	46.99	2.74	2.63	8.45	8.44	32.09	31.96	...
4-Cl	2,5-Cl_2	A	196	$C_{13}H_9Cl_3N_2O_2$	47.10	47.28	2.74	2.63	8.45	8.35	32.09	31.78	...
4-Cl	3,4-Cl_2	A	150–151	$C_{13}H_9Cl_3N_2O_2$	47.10	46.93	2.74	2.70	8.45	8.57	32.09	31.91	8
4-Cl	3,5-Cl_2	A	155–156	$C_{13}H_9Cl_3N_2O_2$	47.10	47.35	2.74	2.50	8.45	8.43	32.09	31.92	15
4-Cl	3-CF_3	A	125	$C_{14}H_{10}ClF_3N_2O_2$	50.85	51.13	...	...	8.48	8.39	10.72	10.73	15
4-Cl	3-CF_3-4-Br	B	148	$C_{14}H_9BrClF_3N_2O_2$	41.06	41.95	2.22	2.55	6.84	7.11	8.66	8.98	15
4-Cl	3-CF_3-4-Cl	B	142–144	$C_{14}H_9Cl_2F_3N_2O_2$	...	...	...	...	...	...	19.43	19.40	2
4-Cl	3,4,5-Cl_3	B	168–169	$C_{13}H_8Cl_4N_2O_2$	42.66	42.53	2.20	2.20	7.66	8.01	38.74	38.73	15
3-CF_3	H	B	145	$C_{14}H_{11}F_3N_2O_2$	56.75	56.80	3.74	3.68	9.46	9.56	...	...	125
3-CF_3	2-Cl	B	161	$C_{14}H_{10}ClF_3N_2O_2$	50.85	51.05	3.05	3.01	8.48	8.40	10.72	10.71	125
3-CF_3	3-Cl	B	128–129	$C_{14}H_{10}ClF_3N_2O_2$	50.85	51.07	3.05	2.94	8.48	8.48	10.72	10.63	31
3-CF_3	4-Cl	B	155	$C_{14}H_{10}ClF_3N_2O_2$	50.85	50.93	3.05	3.12	8.48	8.48	10.72	10.67	31
3-CF_3	2,3-Cl_2	B	167	$C_{14}H_9Cl_2F_3N_2O_2$	46.06	46.01	2.49	2.32	7.68	7.43	19.43	19.13	62
3-CF_3	2,5-Cl_2	B	160–161	$C_{14}H_9Cl_2F_3N_2O_2$	46.06	45.94	2.49	2.46	7.68	7.75	19.43	19.41	62
3-CF_3	3,4-Cl_2	B	148–149	$C_{14}H_9Cl_2F_3N_2O_2$	46.06	45.97	2.49	2.66	7.68	7.87	19.43	19.43	31
3-CF_3	3,5-Cl_2	B	165	$C_{14}H_9Cl_2F_3N_2O_2$	46.06	46.25	2.49	2.45	7.68	7.88	19.43	19.11	31
3-CF_3	3-CF_3	B	127	$C_{15}H_9F_6N_2O_2$	49.45	49.58	2.77	3.01	7.69	7.84	...	...	8
3-CF_3	3-CF_3-4-Cl	B	147–148	$C_{14}H_9ClF_6N_2O_2$	45.17	45.04	2.28	2.32	7.03	7.24	8.89	8.76	0.5

3-CF_3	3-CF_3-4-Br	B	146	$C_{15}H_9BrF_6N_2O_2$	40.65	40.62	2.05	1.96	6.32	6.22	...	...	0.5
3-CF_3	3,4,5-Cl_3	B	170–172	$C_{14}H_8Cl_3F_3N_2O_2$	42.08	42.12	2.02	2.12	7.01	6.89	26.62	26.52	...
2,5-Cl_2	H	B	160–161	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.67	3.39	2.98	9.43	9.40	23.87	24.00	...
2,5-Cl_2	3-Cl	B	171–172	$C_{13}H_9Cl_3N_2O_2$	47.10	47.39	2.74	3.06	8.45	8.55	32.09	31.95	125
2,5-Cl_2	3,4-Cl_2	B	175	$C_{13}H_8Cl_4N_2O_2$	42.66	42.50	2.20	2.38	7.66	7.68	38.74	38.64	...
2,5-Cl_2	3,5-Cl_2	B	174–175	$C_{13}H_8Cl_4N_2O_2$	42.66	42.39	2.20	2.08	7.66	7.54	38.74	38.81	...
2,5-Cl_2	3-CF_3	B	160–161	$C_{14}H_9Cl_2F_3N_2O_2$	46.06	46.02	2.49	2.49	7.68	7.47	19.43	19.41	...
3,4-Cl_2	H	B	150	$C_{13}H_{10}Cl_2N_2O_2$	52.55	52.44	3.39	3.47	9.43	9.38	23.87	24.10	62
3,4-Cl_2	2-Cl	B	156–157	$C_{13}H_9Cl_3N_2O_2$	47.10	46.98	2.74	2.85	8.45	8.56	32.09	32.12	8
3,4-Cl_2	3-Cl	B	151–152	$C_{13}H_9Cl_3N_2O_2$	47.10	47.39	2.74	3.06	8.45	8.47	32.09	32.08	15
3,4-Cl_2	4-Cl	B	167	$C_{13}H_9Cl_3N_2O_2$	47.10	47.38	2.74	2.83	8.45	8.42	32.09	32.19	31
3,4-Cl_2	2,3-Cl_2	B	181	$C_{13}H_8Cl_4N_2O_2$	42.66	42.78	2.20	2.28	7.66	7.58	38.74	39.13	...
3,4-Cl_2	2,5-Cl_2	B	166–167	$C_{13}H_8Cl_4N_2O_2$	42.66	42.42	2.20	2.25	7.66	7.72	38.74	38.80	62
3,4-Cl_2	3,4-Cl_2	B	140–141	$C_{13}H_8Cl_4N_2O_2$	42.66	42.68	2.20	2.60	7.66	7.87	38.74	38.69	4
3,4-Cl_2	3,5-Cl_2	B	179–180	$C_{13}H_8Cl_4N_2O_2$	42.66	42.62	2.20	2.26	7.66	7.74	38.74	38.82	4
3,4-Cl_2	3-CF_3	B	149–150	$C_{14}H_9Cl_2F_3N_2O_2$	46.06	46.14	2.49	2.15	7.68	7.78	19.43	19.40	15
3,4-Cl_2	3-CF_3-4-Cl	B	161–162	$C_{14}H_8Cl_3F_3N_2O_2$	42.08	42.02	2.02	1.96	7.01	6.92	26.62	27.04	15
3,4-Cl_2	3-CF_3-4-Br	B	167	$C_{14}H_8BrCl_2F_3N_2O_2$	37.86	38.01	1.82	1.81	6.31	6.44	15.97	15.84	125
3,4-Cl_2	3,4,5-Cl_3	B	178	$C_{13}H_7Cl_5N_2O_2$	38.99	39.45	1.76	1.75	7.00	7.06	44.27	44.23	1
3,5-Cl_2	2-Cl	B	179	$C_{13}H_9Cl_3N_2O_2$	47.10	46.98	2.74	2.75	8.45	8.68	32.09	32.02	15
3,5-Cl_2	3-Cl	B	179	$C_{13}H_9Cl_3N_2O_2$	47.10	47.34	2.74	2.75	8.45	8.53	32.09	32.48	15
3,5-Cl_2	4-Cl	B	179–180	$C_{13}H_9Cl_3N_2O_2$	47.10	47.48	2.74	2.32	8.45	8.65	32.09	32.37	8
3,5-Cl_2	3,4-Cl_2	B	186–187	$C_{13}H_8Cl_4N_2O_2$	42.66	42.85	2.20	2.13	7.66	7.88	38.74	38.82	4
3,5-Cl_2	3,5-Cl_2	B	184	$C_{13}H_8Cl_4N_2O_2$	42.66	42.32	2.20	2.18	7.66	7.61	38.74	38.66	1
3,5-Cl_2	3-CF_3	B	185–186	$C_{14}H_9Cl_2F_3N_2O_2$	46.06	46.10	2.49	2.58	7.68	7.87	19.43	19.43	31
3,5-Cl_2	3,5-$(CF_3)_2$	B	188–189	$C_{15}H_8Cl_2F_6N_2O_2$	41.60	41.37	1.86	1.79	6.47	6.57	16.37	16.25	4
3,5-Cl_2	3-CF_3-4-Cl	B	172–173	$C_{14}H_8Cl_3F_3N_2O_2$	42.08	41.97	2.02	1.68	7.01	7.09	26.62	26.58	0.5
3,5-Cl_2	3-CF_3-4-Br	B	175–176	$C_{14}H_8BrCl_2F_3N_2O_2$	37.86	37.71	1.82	1.98	6.31	6.47	15.97	15.88	15
3,5-Cl_2	3,4,5-Cl_3	B	200	$C_{13}H_7Cl_5N_2O_2$	38.99	39.12	1.76	1.64	7.00	7.18	44.27	44.32	62
3,5-Cl_2	3-NO_2	B	189	$C_{13}H_9Cl_2N_3O_4$	45.64	45.68	2.65	2.74	12.29	12.30	20.73	20.81	8
3,5-Cl_2	4-NO_2	B	182–183	$C_{13}H_9Cl_2N_3O_4$	45.64	45.68	2.65	2.60	12.29	12.38	20.73	20.84	1
3,5-Cl_2	3-CH_3	B	169–170	$C_{13}H_{12}Cl_2N_2O_2$	54.00	54.25	3.89	3.80	9.0	9.03	22.78	22.75	62
3,5-Cl_2	4-CH_3	B	165	$C_{14}H_{12}Cl_2N_2O_2$	54.00	54.12	3.89	3.86	9.0	8.94	22.78	22.88	...
3,5-Cl_2	4-CH_3O	B	170-171	$C_{14}H_{12}Cl_2N_2O_3$	51.39	51.25	3.70	3.75	8.56	8.51	21.67	21.82	...
2-CH_3-3-Cl	3-Cl	A	164–165	$C_{14}H_{12}Cl_2N_2O_2$	54.02	54.11	3.89	3.91	9.01	8.91	22.79	22.90	...
2-CH_3-3-Cl	4-Cl	A	170	$C_{14}H_{12}Cl_2N_2O_2$	54.02	54.04	3.89	4.05	9.01	8.91	22.79	22.65	...
2-CH_3-3-Cl	3,4-Cl_2	A	179	$C_{14}H_{11}Cl_3N_2O_2$	48.66	48.72	3.21	3.37	8.11	8.24	30.78	30.86	...
2-CH_3-3-Cl	3,5-Cl_2	A	176–177	$C_{14}H_{11}Cl_3N_2O_2$	48.66	48.73	3.21	3.34	8.11	8.08	30.78	30.77	...
2-CH_3-3-Cl	3-CF_3	A	168–169	$C_{15}H_{12}ClF_3N_2O_2$	52.25	52.36	3.51	3.46	8.13	8.25	10.29	10.21	...
2-CH_3-5-Cl	3-Cl	A	175–176	$C_{14}H_{12}Cl_2N_2O_2$	54.02	54.12	3.89	3.83	9.01	8.85	22.79	22.91	...
2-CH_3-5-Cl	4-Cl	A	162–163	$C_{14}H_{12}Cl_2N_2O_2$	54.02	54.05	3.89	3.85	9.01	9.00	22.79	22.78	...
2-CH_3-5-Cl	3-CF_3	A	156–157	$C_{15}H_{12}ClF_3N_2O_2$	52.25	52.37	3.51	3.41	8.13	8.00	10.29	10.31	125
2-CH_3-4,5-Cl_2	3-CF_3	B	154–155	$C_{15}H_{11}Cl_2F_3N_2O_2$	47.50	47.71	2.93	2.95	7.39	7.35	18.70	18.71	15
3,4,5-Cl_3	4-Cl	B	198	$C_{13}H_8Cl_4N_2O_2$	42.66	42.51	2.20	2.00	7.66	7.59	38.75	38.74	2
3,4,5-Cl_3	3,5-Cl_2	B	207	$C_{13}H_7Cl_5N_2O_2$	38.99	38.95	1.76	1.77	7.00	7.08	44.32	44.36	2
3,4,5-Cl_3	3,4,5-Cl_3	B	200–210	$C_{13}H_6Cl_6N_2O_2$	35.90	36.03	1.39	1.49	6.44	6.53	48.90	48.87	1
3,4,5-Cl_3	3-CF_3	B	164	$C_{14}H_8Cl_3F_3N_2O_2$	42.08	42.08	2.02	1.98	7.01	7.08	26.61	26.42	0.5
3,4,5-Cl_3	3-CF_3-4-Br	B	190	$C_{14}H_7BrCl_3F_3N_2O_2$	35.14	35.23	1.48	1.58	5.86	5.92	22.22	22.11	4

[a] Methods A and B are described in the Experimental section. [b] Against *S. aureus;* dilute agar.

3,4-dichlorophenylhydroxylamine). Work-up of the mother liquor yielded more product. Recrystallization from aqueous methanol gave off-white crystals, m.p. 149–150° dec., in 89% yield (based on weight of isocyanate).

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A Simple Method for Predicting the Carcinogenic Properties of Polycyclic Aromatic Molecules[1]

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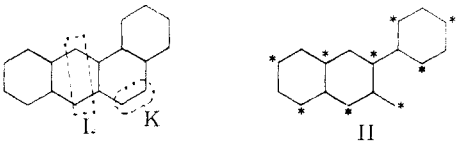
There have been numerous attempts to predict theoretically the carcinogenic activity of aromatic, substituted aromatic, and heteroaromatic compounds. As early as 1938 it was postulated that the electron density in the mesophenanthrenic bond (the K region) of such molecules could be correlated with carcinogenic activity.[2] Later work has employed calculations of free valence, localization energies,[3,4] energies of the various molecular orbitals of the carcinogen,[5,6] and other theoretical quantities. All of these workers have been more or less successful in finding a usable correlation between the theoretical property under consideration and carcinogenic activity. The complexity of these methods, however, has prevented their use by those who are not experienced in the application of molecular orbital (MO) theory.

It is the purpose of the present work to illustrate the application of one of the simplest MO approximations, the Dewar localization energy approximation,[7] to the prediction of the carcinogenic activity of aromatic systems.

Method.—It has been shown that in many polycyclic aromatic systems the presence of a highly reactive K region is favorable for carcinogenic activity[8] while the presence of a reactive L region is unfavorable.[9]

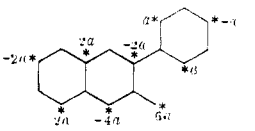
One of the theoretical indices which has been used successfully to approximate the reactivity of a π-electronic system is the localization energy, the energy required to localize the appropriate number of π-electrons in the area undergoing attack.[10] The localization energies for the K region and the L region should thus lead to a prediction of the carcinogenic activity of various compounds. Dewar's implementation[7] of the Coulson, Longuet-Higgins perturbation theory[11,12] leads to an extremely simple method which involves no matrix diagonalization or other matrix manipulation for calculating the required localization energies.

As an example of the application of the method, consider 1,2-benzanthracene (I), a molecule which has both an active K region and an active L region.



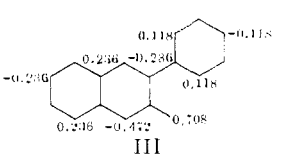
I II

If a single position is removed from conjugation in an alternant aromatic hydrocarbon, an odd-alternant system results. For example, if position 3 in I is removed, the remaining system, II, has 17 centers which may be designated as active (starred) and inactive (unstarred). These are assigned such that more centers are starred than not, and no two adjacent centers are either starred or unstarred. The highest occupied MO in an odd-alternant system with n centers and n or $n + 1$ electrons is a nonbonding molecular orbital (NBMO). Coulson and Rushbrooke[11] have shown that such a NBMO has nodes (*i.e.*, no electron density) at the unstarred centers. They have further shown that the algebraic sums of the MO coefficients around a given unstarred center must be equal to zero. This, coupled with the normalizing condition that the sum of the squares of the coefficients for any given MO must equal unity allows a simple calculation of the MO coefficients for the starred centers. For example, by arbitrarily assigning the value of a to the coefficient at position 1′ in II, the following values fulfill the first criterion. The second criterion leads to eq. 1.

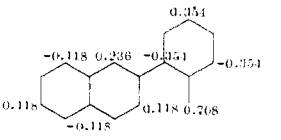


$$a^2 + (-a)^2 + (a)^2 + (-2a)^2 + (2a)^2 + (-2a)^2 + (2a)^2 + (-4a)^2 + (6a)^2 = 1 \quad (1)$$

or $71a^2 = 1$ and $a = 1/\sqrt{71} = 0.118$. This gives the following NBMO coefficients for II. For isolation of

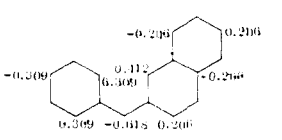


III

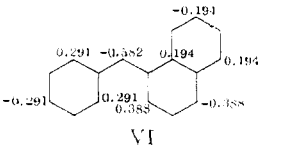


IV

the 4 position in I, the NBMO coefficients are shown in IV. For isolation of the 9 and 10 positions, the NBMO coefficients are shown in V and VI, respectively.



V



VI

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