was poured into dilute hydrochloric acid and extracted with ether. The extracts were washed with saturated sodium bicarbonate and salt solutions, dried over magnesium sulfate and evaporated to give 1.8 g. of crude cyclization product XXIb (crude yield 94%) which could not be crystallized but was hydrolyzed directly to the amine by refluxing for 15 hours in a mixture of 11 ml. of glacial acetic acid, 5 ml. of water and 11 ml. of concentrated hydrochloric acid. The cooled solution was then poured into water and extracted well with ether. After washing the extracts with bicarbonate and saturated salt solutions and drying over magnesium sulfate, concentration gave 0.56 g. (52%) of a yellow crystalline compound; recrystallized from ether–heptane, m.p. 87–88°. Ether extraction of the original aqueous solution, after making it strongly basic, did not yield any further material.

Anal. Calcd. for $C_{13}H_{17}NO$: C, 76.80; H, 8.43; N, 6.89. Found: C, 77.09; H, 8.53; N, 7.14.

4-Ethyl-2,6-dimethyl-11H-indolo[3,2-c]quinoline (Ib).—A solution of 100 mg. of the aminophenylindole (IX) in 10 ml. of ethanol containing 1 ml. of an acetaldehyde solution (250 mg./ml.) was allowed to stand at room temperature for 5 minutes. Then 5 ml. of 20% hydrochloric acid was added. This resulted in an immediate red coloration, the precipitation of white crystals and the evolution of heat. After standing at room temperature for 30 minutes, the precipitate was filtered and recrystallized from ethanol yielding 92 mg. (73.5%), m.p. >300°.

Anal. Calcd. for $C_{19}H_{19}ClN_2$: C, 73.41; H, 6.16; N, 9.01. Found: C, 73.14; H, 6.36; N, 9.16.

The above hydrochloride was converted to the base by dissolving 75 mg. of material in about 3 ml. of hot ethanol and adding 10% ammonium hydroxide until the solution was basic. On concentration *in vacuo* crystals separated and these were removed by filtration. After recrystallization from ethanol 52 mg. (76%) of base was obtained, m.p. 194–195°.

Anal. Calcd. for $C_{19}H_{18}N_2$: C, 83.17; H, 6.61; N, 10.21. Found: C, 83.22; H, 6.56; N, 10.55.

A mixture of the above base with that from the selenium dehydrogenation of ibogamine[2] showed m.p. 195–196°. The infrared and ultraviolet absorption spectra of both bases and their hydrochlorides were identical.

SUMMIT, N. J.

[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

Diuretics. Organomercurials

BY CALVERT W. WHITEHEAD

RECEIVED OCTOBER 21, 1957

The alkoxymercuration of allylic compounds was carried out in fourteen different alcohols and in water. New alkoxy groups were thereby introduced into the basic mercurial diuretic structure. Mercuration of the *ortho*, *meta* and *para* isomers of N-allylcarbamylphenoxyacetic acid yielded anhydro N-(3-hydroxymercuri-2-alkoxypropyl)-carbamylphenoxyacetic acids in the case of the *ortho* and *meta* isomers, but did not give an anhydro derivative with the *para* isomer. The structures of these anhydro derivatives and of anhydro compounds prepared by the mercuration of α,β-unsaturated acids were established by infrared studies.

The presently known mercurial diuretics are all derivatives of β-alkoxyethylmercuric salts. They differ in the type of substituents on the β-carbon of the ethyl group and in the anion of the salt. The β-alkoxy group has, however, been limited in most examples to the methoxy group. In this investigation changes were made in the β-alkoxy group by the alkoxymercuration of olefins in a number of different alcohols.

The methoxymercuration of *o*-(N-allylcarbamyl)-phenoxyacetic acid (I) is reported[1] to yield *o*-(N-3 - acetoxymercuri - 2 - methoxypropylcarbamyl)-phenoxyacetic acid. In this present work when compound I was allowed to react with mercuric oxide in the presence of alcohols the products were not the expected *o*-(N-3-hydroxymercuri-2-alkoxypropylcarbamyl)-phenoxyacetic acids. They were instead dehydrated or anhydro forms of the expected products. Furthermore, the addition of mercuric acetate to the *m*- isomer II, under the conditions of the alkoxymercuration reaction, yielded anhydro *m*-(3-hydroxymercuri-2-alkoxypropylcarbamyl)-phenoxyacetic acids. An anhydro derivative, however was, not obtained from the *p*- isomer III. This latter isomer reacted with mercuric acetate in ethylene glycol to yield *p*-(N-3 - acetoxymercuric - 2 - β - hydroxyethoxypropylcarbamyl)-phenoxyacetic acid (VI). A few examples of the anhydro derivatives of mercurated carboxylic acids are given in the literature. Aliphatic α,β-unsaturated acids are reported to yield four-membered ring anhydrides of β-alkoxy-α-hydroxymercuripropionic acids.[2] The product obtained from the methoxymercuration of I is said to be converted to a 12-membered ring derivative.[3] The assigned structures of these reported anhydro compounds are not supported by findings other than elemental analysis. Since there was no firm basis for assigning these structures and consequently no reason to assign similar structures to the anhydro derivatives prepared here, they were further examined in order to establish the correct anhydro structure.

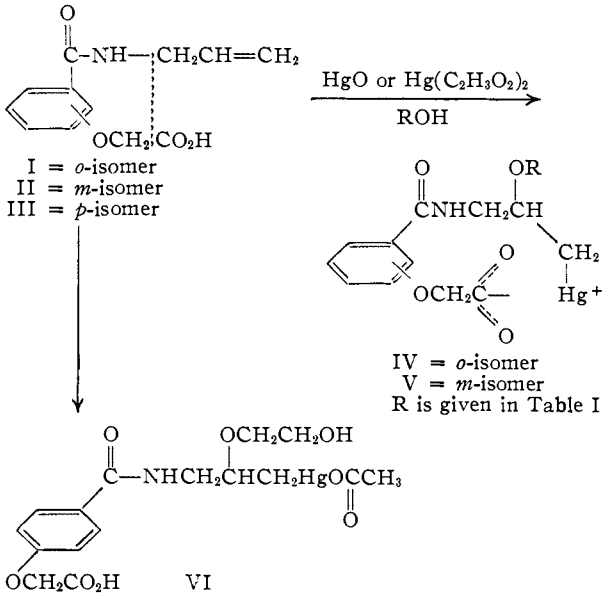
Evidence for the structures of the anhydro products was obtained by studying their infrared spectra. A moderately intense band for NH at 2.97 μ in the chloroform solution of the *o*-isomer IV (R = $(CH_2)_2OCH_3$) eliminates the possibility of the amide hydrogen having been replaced. Thus, an N–Hg bond is not present. Intense bands for amide at 6.10 and 6.53 μ also support the *mono*-substituted amide IV. Absence of a band for the carboxyl group suggests a zwitterion structure or internal salt between the carboxylate group and the positive mercury. The carboxylate absorption of mercuric acetate in chloroform solution consists primarily of two bands of medium intensity at 6.13 and 6.21 μ. Although a band at 6.20 μ

(1) M. Bockmühl and A. Schwarz, United States Patent 1,693,432; W. H. Feinstone, United States Patent 2,581,397.

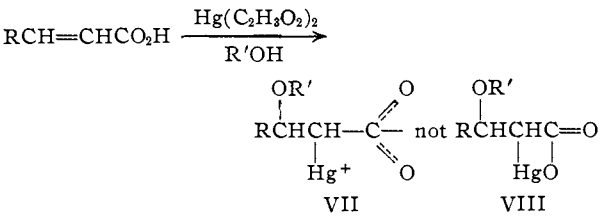
(2) F. C. Whitmore, "Organic Compounds of Mercury," The Chemical Catalog Co. (Reinhold Publ. Corp.), New York, 1922, pp. 137–153.

(3) K. O. Möller, *Arch. Exp. Path. Pharm.*, **153**, 111 (1930).

in the spectrum of IV (R = $(CH_2)_2OCH_3$) may arise, in part, from carboxylate, the carboxylate absorption is largely masked by an intense amide band at 6.10 μ. The infrared spectrum of a mineral oil mull of V (R = $(CH_2)OCH_3$) shows a band for carboxyl at 5.77 μ of comparatively low intensity. The carboxyl band at 5.77 μ in the spectrum of the unmercurated II is about as intense as the amide band at 6.0 μ. This is also true for the spectrum of I. Since the carboxyl band is altogether absent from the spectrum of IV (R = $(CH_2)_2OCH_3$), about 20% the intensity of the amide band in the spectrum of V (R = (CH_2)-OCH_3) and nearly equal in intensity with the amide band in the spectrum of the *p*-isomer VI it seems reasonable to propose that the *o*-isomer IV is entirely in the anhydro zwitterion form, the *m*-isomer V is largely in this form and the *p*-isomer VI is entirely in the non-zwitterion form. Titration of V (R = $(CH_2)_2OCH_3$) in aqueous 66% N,N-dimethylformamide indicates the approximate 20 mole per cent. of carboxyl observed in the infrared spectrum corresponds to the non-cyclic form and not to a form with a net positive charge. Six intense bands at 6.75, 7.70, 8.05, 8.60, 8.95 and 9.35 μ common to IV and I and the ethyl ester of I appear to be characteristic of the portion of the molecule to the left of the dotted line.



The results from the study of the above anhydro derivatives suggested mercurials obtained by the alkoxymercuration of α,β-unsaturated acids might also be in the anhydro zwitterion form VII rather than in the form of a four-membered ring (VIII). 2-Nonenoic and 5-phenyl-2-pentenoic acids were treated with mercuric acetate in 1-butanol and in methanol, respectively, to obtain anhydro 3-*n*-butoxy-2-hydroxymercurinonanoic acid (VII, R = $CH_3(CH_2)_5$, R′ = *n*-C_4H_9) and anhydro 3-methoxy-5-phenyl-2-hydroxymercuripentanoic acid (VII, R = $C_6H_5(CH_2)_2$, R′ = CH_3). The absence of carbonyl absorption in the infrared spectrum (mull) of the mercurated nonanoic acid eliminates the four-membered anhydride structure VIII. A four-membered ring of this type would be expected to contribute a short wave length carbonyl band. The presence of a 6.33 μ band similar to the carboxylate band present in the spectrum of mercuric acetate and asymmetric carboxylate bands at 7.33 and 7.60 μ confirm the anhydro zwitterion structure VII.



When *p*-allyloxy, *p*-allylcarbamylmethylene and *p*-allylsulfamyl derivatives of benzoic, phenylacetic, phenylmercaptoacetic and phenoxyacetic acids as well as succinylurea, *p*-crotonylaminobenzoic acid and *p*-crotonylaminophenylacetic acid, were mercurated, the products were believed to be the non-zwitterion type. They were insoluble in organic solvents and difficult to obtain pure. The preparations of only four representatives are therefore described. When esters of the above acids were treated with mercuric acetate in the various alcohols, readily soluble 2-acetoxymercuri-3-alkoxypropyl and 3-alkoxy-2-hydroxymercuripropyl derivatives (Tables II and III) resulted. Products of this type were also obtained from N-allylphthalimide and α-allylbenzhydrol. Methyl cinnamate yielded 2-acetoxymercuri-3-alkoxyhydrocinnamates. Two competitive reactions were in evidence during the alkoxymercuration of ethyl *m*-allyl-*p*-hydroxybenzoate. The product was ethyl *m*-(3-acetoxymercuri-2-β-hydroxyethoxypropyl)-*p*-hydroxybenzoate when mercurated in ethylene glycol and ethyl *m*-(3-acetoxymercuri-2-methoxypropyl)-*p*-hydroxybenzoate when mercurated in methanol, but was 2-acetoxymercuri-5-carbethoxy-2,3-dihydrobenzofurane when mercurated in benzyl alcohol or in ethanol. Adams[4] has previously described the formation of a 2,3-dihydrobenzofurane from *o*-allylphenol.

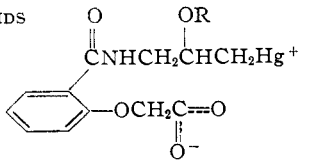
Anesthetized female dogs were injected intramuscularly with doses of the mercurials ranging from 0.75 to 3.0 mg. of mercury per kg. of body weight. The diuretic response was a measure of the increase in output of water and sodium chloride over normal urine output. The diuretic effect of the mercurials did not seem to be enhanced or depressed by changes made in the β-alkoxy group (OR in Tables I and III and OR′ in Table II). Some β-methoxyethoxy and β-hydroxyethoxy derivatives caused significantly less local irritation upon tissue when injected than did the corresponding β-methoxy derivatives. The pharmacological evaluation of the mercurials reported here was made by R. B. Robbins of this Laboratory.

Acknowledgment.—The author thanks Wm. Brown and H. L. Hunter for the microanalyses and H. Boaz for the infrared and titration data and the interpretation.

(4) R. Adams, F. L. Roman and W. N. Sperry, THIS JOURNAL, **44**, 1781 (1922).

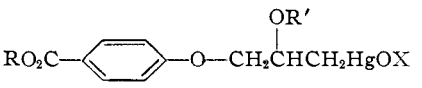
TABLE I

ANHYDRO *o*-[N-3-HYDROXYMERCURI 2-β-ALKOXYPROPYLCARBAMYL]-PHENOXYACETIC ACIDS



R	Formula	M.p., °C.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Mercury, % Calcd.	Mercury, % Found
$(CH_2)_2OH$	$C_{14}H_{17}HgNO_6$	Dec.	80	33.95	34.09	3.46	3.58		
$(CH_2)_2OCH_3$	$C_{15}H_{19}HgNO_6$	135	52	35.33	35.22	3.76	3.74	39.34	39.29
n-C_4H_9	$C_{16}H_{21}HgNO_5$	171	90	37.87	38.08	4.17	4.24		
$(CH_2)_2OC_2H_5$	$C_{16}H_{21}HgNO_6$	139	54	36.72	36.82	4.04	4.27	38.29	38.10
$(CH_2)_2O(CH_2)_2OH$	$C_{16}H_{21}HgNO_7$	162	55					37.12	37.61
$(CH_2)_2OC_4H_9$	$C_{18}H_{25}HgNO_6$	133	70					37.34	37.41
$(CH_2)_2OC_6H_5$	$C_{20}H_{21}HgNO_6$	197	88	42.05	42.05	3.69	3.87		
$(CH_2)_2OCH_2CH(C_2H_5)_2$	$C_{20}H_{29}HgNO_6$	124	70					33.40	33.14
n-$C_{10}H_{21}$	$C_{22}H_{33}HgNO_5$	164	39	44.10	43.74	5.56	5.81		

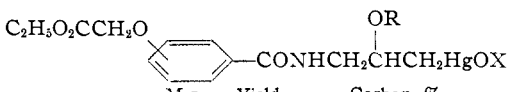
TABLE II



R	R′	X	Formula	M.p., °C.	Yield, %	Mercury, % Calcd.	Mercury, % Found
H	CH_3	H	$C_{11}H_{14}HgO_5$	Dec.	68	46.90	46.38
H	$(CH_2)_2OH$	H	$C_{12}H_{16}HgO_6$	Dec.	73	43.82	44.12
C_2H_5	CH_3	CH_3CO	$C_{15}H_{20}HgO_6$	78	70	40.30	40.33
C_2H_5	C_2H_5	CH_3CO	$C_{16}H_{22}HgO_6$	76	75	37.62[a]	37.53[a]
						4.34[b]	4.62[b]
C_2H_5	$(CH_2)_2OCH_3$	CH_3CO	$C_{17}H_{24}HgO_7$	52	78	37 05	37.20

[a] Values for carbon. [b] Values for hydrogen.

TABLE III



R	X	Formula	M.p., °C.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Mercury, % Calcd.	Mercury, % Found
$(CH_2)_2Cl$	H	$C_{16}H_{22}ClHgNO_6$[a]	145	98	34.29	33.99	3.95	4.06		
H	$OCCH_3$	$C_{16}H_{21}HgNO_8$[b,c]	149	60	34.30	34.38	4.16	3.94	35.68	35.65
$(CH_2)_2OCH_3$	$OCCH_3$	$C_{19}H_{27}HgNO_8$[a]	107	67					33.43	33.52
$CH_3CHCO_2C_2H_5$	H	$C_{19}H_{27}HgNO_8$[b]	110	55	37.09	36.61	4.29	4.10	34.30	34.55
$(CH_2)_2OC_2H_5$	$OCCH_3$	$C_{20}H_{29}HgNO_8$[a]	142	75	34.75	34.76	3.96	3.95		
$(CH_2)_2OC_4H_9$	$OCCH_3$	$C_{22}H_{33}HgNO_8$[a]	145	70					31.22	30.51

[a] *o*-Isomer. [b] *p*-Isomer. [c] Hydrate.

Experimental

N-Allylhydroxybenzamides and N-Allylcarbamylphenoxyacetic Acids.—A mixture of 152 g. (1.0 mole) of the appropriate methyl hydroxybenzoate and 124 g. (2.18 moles) of allylamine was heated in a sealed cylinder at 100–130° for 12 hours, cooled, diluted with cold water, acidified with hydrochloric acid and extracted with ether. The ether was washed several times with water, dried over anhydrous magnesium sulfate and filtered. Evaporation of the ether yielded the crude N-allyl hydroxybenzamides: **N-allyl-*m*-hydroxybenzamide**, m.p. 87°, yield 89%; **N-allyl-*o*-hydroxybenzamide**, yield 71%, an oil; **N-allyl-*p*-hydroxybenzamide**, yield 80%, melting point not recorded.

To a solution of 34 g. of sodium hydroxide in 2 l. of water was added 42 g. (0.236 mole) of the N-allylhydroxybenzamide and 26.5 g. (0.275 mole) of chloroacetic acid. The solution was heated to boiling for 2 hours. A second addition of 26.5 g. of chloroacetic acid was cautiously added with 17 g. of sodium hydroxide and the solution heated for another 1.5 hours. The solution was cooled and acidified with concd. HCl. The solid product was collected and recrystallized from ethanol. The following N-allylcarbamylphenoxyacetic acids were prepared.

***m*-(N-Allylcarbamyl)-phenoxyacetic acid**, yield 55 g. (99%), m.p. 120°. *Anal.* Calcd. for $C_{12}H_{13}NO_4$: N, 5.98. Found: N, 6.12.

***p*-(N-Allylcarbamyl)-phenoxyacetic acid**, yield 44%, m.p. 139°. *Anal.* Calcd. for $C_{12}H_{13}NO_4$: N, 5.98. Found: N, 6.00.

O-(N-Allylcarbamyl)-phenoxyacetic acid, yield 70%, m.p. 121.5° (lit. 120°).[5]

Anhydro *o*-(N-3-Hydroxymercuri-2-alkoxycarbamyl)-phenoxyacetic Acids, Table I.—One-tenth mole (23.5 g.) of *o*-(N-allylcarbamyl)-phenoxyacetic acid was added to 100–300 ml. of one of the alcohols represented by HOR in Table I. One-tenth mole (21.6 g.) of red mercuric oxide was added and the mixture was stirred mechanically and heated to 60°. After 2–4 hours the mercuric oxide was used and the warm solution was filtered. The filtrate was allowed to cool to room temperature and the product crystallized. The mercurial was then recrystallized from alcohol or a mixture of alcohol and N,N-dimethylformamide.

Anhydro *o*-(N-3-Hydroxymercuri-2-β-methoxyethoxypropylcarbamyl)-phenoxyacetic Acid Methyl Cellosolve Solvate.—The product obtained from methyl Cellosolve (yield 100 g. or 52%), as directed in the above paragraph, melted at 75°

(5) E. A. Tzofin and K. A. Chkhikvadze, *J. Gen. Chem.* (*U.S.S.R.*), **3**, 17 (1933); *C. A.*, **28**, 2343 (1934).

and its composition indicated it to be a methyl Cellosolve solvate. A sample was recrystallized from ethanol to yield the unsolvated product, m.p. 135° (Table I). The unsolvated compound was then recrystallized from methyl Cellosolve to yield the original methyl Cellosolve solvate, m.p. 75°.

Anal. Calcd. for $C_{18}H_{27}HgNO_8$: Hg, 34.24. Found: Hg, 34.02.

Anhydro *m*-(N-3-Hydroxymercuri-2-β-methoxypropylcarbamyl)-phenoxyacetic Acid.—Four and eight-tenths grams (0.02 mole) of *m*-(N-allylcarbamyl)-phenoxyacetic acid was added to 6.4 g. (0.02 mole) of mercuric acetate and 25 ml. of methyl Cellosolve. The solids dissolved and the solution was allowed to stand for three days. Petroleum ether was added and the mercurial separated as a flocculent precipitate. The precipitate was collected on a filter and washed with ethanol and then with ether, yield 7 g. (71%). The product was not crystalline and did not have an identifying melting point.

Anal. Calcd. for $C_{15}H_{19}HgNO_6$: Hg, 39.34. Found: Hg, 39.80.

Anhydro *m*-(N-3-Hydroxymercuri-2-β-hydroxyethoxypropylcarbamyl)-phenoxyacetic Acid.—A solution of 4.8 g. (0.02 mole) of *m*-(N-allylcarbamyl)-phenoxyacetic acid and 6.4 g. (0.02 mole) of mercuric acetate in 25 ml. of ethylene glycol was allowed to stand for 3 days. Water was added to precipitate the product as a gum. The gum was triturated with 25 ml. of ethanol and the mercurial solidified. The trituration was repeated several times with ethanol and finally with ether. The product was not crystalline; yield 7.5 g. (73%).

Anal. Calcd. for $C_{14}H_{17}HgNO_6$: Hg, 40.45. Found: Hg, 40.90.

***p*-(N-3-Acetoxymercuri-2-β-hydroxyethoxypropylcarbamyl)-phenoxyacetic Acid.**—A solution of 4.8 g. (0.02 mole) of *p*-(N-allylcarbamyl)-phenoxyacetic acid and 6.4 g. (0.02 mole) of mercuric acetate in 40 ml. of ethylene glycol was allowed to stand at room temperature. The product crystallized after several days, was collected and recrystallized from ethanol, m.p. 145°, yield 7 g. (63%).

Anal. Calcd. for $C_{16}H_{21}HgNO_8$: C, 34.55; H, 3.76. Found: C, 34.28; H, 3.39.

Anhydro 3-*n*-Butoxy-2-hydroxymercurinonanoic Acid.—To 75 ml. of dry 1-butanol was added 5.2 g. (0.033 mole) of 2-nonenoic acid[6] and 10.6 g. (0.033 mole) of mercuric acetate. The mixture was agitated until the solids dissolved. The resulting solution was allowed to stand for a few hours and the solid product separated from solution. This was thoroughly washed with hot methanol, yield 10 g. (72%), m.p. 186–188° dec. The product dissolved in dilute NaOH to give a clear solution.

Anal. Calcd. for $C_{13}H_{24}HgO_3$: Hg, 46.66. Found: Hg, 46.40.

Anhydro 2-Hydroxymercuri-3-methoxy-5-phenylpentanoic Acid.—To a solution of 8.8 g. (0.05 mole) of 5-phenyl-2-pentenoic acid[7] in 50 ml. of methanol was added 15.9 g. (0.05 mole) of mercuric acetate. The mixture was stirred until the mercuric acetate dissolved. After standing for 0.5 hour at room temperature, the product separated as an oil which crystallized. This was collected on a filter and washed with methanol; yield 15 g. (75%), m.p. 189–190°.

Anal. Calcd. for $C_{12}H_{14}HgO_3$: Hg, 49.20. Found: Hg, 48.69.

N-Allyl-*p*-hydroxyphenylacetamide.—A mixture of 97 g. (0.62 mole) of methyl *p*-hydroxyphenylacetate and 45 g. (0.79 mole) of allylamine was boiled under reflux for 24 hours. The excess allylamine was removed by reduced pressure distillation. The remaining sirup was dissolved in a minimum amount of warm ethyl acetate. Petroleum ether was added to incipient turbidity. The product crystallized from solution, was collected and again crystallized from a mixture of ethyl acetate and petroleum ether; yield 86 g. (74%), m.p. 84°. A sample was recrystallized twice from ethylene dichloride and the melting point remained unchanged.

Anal. Calcd. for $C_{11}H_{13}NO_2$: N, 7.34. Found: N, 7.30.

(6) V. J. Harding and C. Welzmann, *J. Chem. Soc.*, **97**, 301 (1910).

(7) E. H. Farmer and C. G. B. Hose, *ibid.*, **136**, 962 (1933).

***p*-(N-Allylcarbamylmethylene)-phenoxyacetic Acid.**—One-tenth mole of N-allyl-*p*-hydroxyphenylacetamide was treated with 18.8 g. (0.2 mole) of chloroacetic acid in sodium hydroxide solution in the manner described for the N-allylcarbamylphenoxyacetic acids; yield 29 g. (40%), m.p. 137–139°.

Anal. Calcd. for $C_{13}H_{15}NO_4$: N, 5.64. Found: N, 5.92, 5.52.

Ethyl *p*-(N-Allylcarbamylmethylene)-phenoxyacetate.—Fifty grams (0.26 mole) of N-allyl-*p*-hydroxyphenylacetamide, 32 g. (0.26 mole) of ethyl chloroacetate and 71 g. (0.51 mole) of anhydrous potassium carbonate were added to 500 ml. of anhydrous acetone and the mixture boiled under reflux for 48 hours. The solvent was removed by evaporation under reduced pressure and the residual sirup was crystallized from a mixture of ethyl acetate and petroleum ether; yield 51 g. (73%), m.p. 86°. The melting point was depressed when mixed with N-allyl-*p*-hydroxyphenylacetamide.

Anal. Calcd. for $C_{15}H_{19}NO_4$: N, 5.05. Found: N, 5.29.

Ethyl *m*-(N-Allylcarbamyl)-phenoxyacetate.—The procedure in the above paragraph was repeated with 48 g. (0.27 mole) of N-allyl-*m*-hydroxybenzamide, 33 g. (0.27 mole) of ethyl chloroacetate and 50 g. of anhydrous potassium carbonate in 300 ml. of acetone to yield 40 g. (56%), b.p. 204° at 1 mm.

Anal. Calcd. for $C_{14}H_{17}NO_4$: N, 5.32. Found: N, 5.26.

Ethyl *p*-(N-Allylcarbamyl)-phenoxyacetate.—Eighty-nine grams of *p*-(N-allylcarbamyl)-phenoxyacetic acid was added to 1 liter of absolute ethanol and 30 ml. of concentrated sulfuric acid and boiled under reflux for 12 hours. The alcohol was concentrated under reduced pressure and poured onto 1 kg. of ice. The solid was collected and recrystallized from a mixture of ethyl acetate and petroleum ether; yield 83 g. (82%), m.p. 104–105°.

Anal. Calcd. for $C_{14}H_{17}NO_4$: N, 5.32. Found: N, 5.33.

Ethyl *o*-(N-Allylcarbamyl)-phenoxyacetate.—Esterification of *o*-(N-allylcarbamyl)-phenoxyacetic acid gave a yield of 80% of the ethyl ester, m.p. 78°.

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.86; H, 6.51; N, 5.32. Found: C, 63.71; H, 6.45; N, 5.48.

***p*-(N-Allylsulfamyl)-phenylmercaptoacetic Acid.**—To a solution of 81 g. (2.02 moles) of sodium hydroxide in 500 ml. of water was added 128 g. (0.68 mole) of *p*-mercaptobenzenesulfonic acid and 64.6 g. (0.68 mole) of chloroacetic acid. The resulting solution was heated on the steam-bath for several hours and then allowed to cool. The white solid disodium salt of *p*-sulfophenylmercaptoacetic acid crystallized from solution. This was collected and dried (266 g. yield). The disodium salt was added to phosphorus oxychloride. A vigorous reaction occurred and the flask was placed in ice-water. After standing for 24 hours at room temperature, it was boiled under reflux for 2 hours. The excess phosphorus oxychloride was distilled under reduced pressure. The residual oil was stirred in cold water for one hour and the resulting *p*-chlorosulfonylphenylmercaptoacetic acid solidified, yield 106 g. Twenty-six and six-tenths grams (0.1 mole) of the crude *p*-chlorosulfonylphenylmercaptoacetic acid was allowed to react with 5.7 g. (0.1 mole) of allylamine in the conventional manner. The product was recrystallized from ethyl acetate to yield 16 g. (32% based on *p*-mercaptobenzenesulfonic acid) of *p*-N-allylsulfamylphenylmercaptoacetic acid, m.p. 129–130°.

Anal. Calcd. for $C_{11}H_{13}NO_4S_2$: N, 4.87. Found: N, 4.88.

***p*-(3-Hydroxymercuri-2-alkoxypropoxy)-benzoic Acids,** Table II.—To 17.8 g. (0.1 mole) of *p*-allyloxybenzoic acid in 75 ml. of the appropriate alcohol was added 31.8 g. (0.1 mole) of mercuric acetate. The solids dissolved and after standing at room temperature the solid product separated. The product was washed thoroughly with water, with ethanol, and then with ether.

***p*-(Crotonylamino)-phenylacetic Acid.**—Ten and one-half grams (0.07 mole) of *p*-aminophenylacetic acid was allowed to react with 8.3 g. (0.08 mole) of crotonyl chloride in aqueous bicarbonate solution in the usual manner to yield 9 g. (62%) of *p*-crotonylaminophenylacetic acid, m.p. 206°.

Anal. Calcd. for $C_{12}H_{13}NO_3$: N, 6.42. Found: N, 6.35.

***p*-(Crotonylamino)-benzoic Acid.**—The above procedure

was repeated with *p*-aminobenzoic acid; yield 70%, m.p. 268°.

Anal. Calcd. for $C_{11}H_{10}NO_3$: N, 6.85. Found: N, 6.76.

p-(2-β-Hydroxyethoxy-3-hydroxymercuributyrylamino)-phenylacetic Acid.—To 15 ml. of ethylene glycol was added 1 g. (0.01 mole) of *p*-crotonylaminophenylacetic acid and 1.5 g. (0.01 mole) of mercuric acetate. The resulting solution was allowed to stand for 5 days. The white solid that had separated was collected and washed with methanol and then with ether; yield 2 g. (50%), m.p. 205° dec.

Anal. Calcd. for $C_{14}H_{16}HgNO_6$: Hg, 40.53. Found: Hg, 40.23.

N-(3-Hydroxymercuri-2-β-hydroxyethoxypropyl)-N'-succinylurea Sodium Salt.—Twenty grams (0.1 mole) of N-allyl-N'-succinylurea[8] was dissolved in 40 ml. of ethylene glycol. Thirty-two grams (0.1 mole) of mercuric acetate was added and stirred. The reaction was exothermic and there was a strong odor of acetic acid. After standing for two days at room temperature, a sample was completely miscible in water and did not turn dark when made basic with sodium hydroxide. The excess ethylene glycol was distilled at 0.1 mm. and at a bath temperature of 120°. The remaining sirup was dissolved in methanol, clarified with carbon and filtered. Ether was added and the mercurial precipitated as an oil. The oil was separated, dissolved in a minimum amount of distilled water, and carefully neutralized with sodium hydroxide to a *p*H of 7.5. The water was evaporated under reduced pressure to give a 60% yield of white solid.

Anal. Calcd. for $C_{10}H_{17}HgN_2NaO_7$: Hg, 40.90. Found: Hg, 40.80.

General Method for the Mercuration of Ethyl *p*-Allyloxybenzoate,[9] Ethyl *p*-(N-Allylcarbamyl)-phenoxyacetate, Ethyl *o*-(N-Allylcarbamyl)-phenoxyacetate, N-Allylphthalimide,[10] α-Allylbenzhydrol[11] and Methyl Cinnamate.—A mixture of 6.4 g. (0.02 mole) of mercuric acetate and 0.02 mole of the allylic compound or of methyl cinnamate was stirred in 10–25 ml. of the appropriate alcohol (methyl Cellosolve, ethyl Cellosolve, butyl Cellosolve, β-chloroethanol, ethyl lactate, ethylene glycol, ethanol or methanol) or in 25 ml. of water. The mixture dissolved and after standing for 2–5 days at room temperature the product crystallized. This was collected and purified by recrystallization from ethyl acetate or a mixture of ethyl acetate and petroleum ether. The mercurials from ethyl *p*-allyloxybenzoate are listed in Table II, and from ethyl N-allylcarbamylphenoxyacetates in Table III. The other products are listed below.

N-(3-Acetoxymercuri-2-β-methoxyethoxypropyl)-phthalimide, yield 9 g. (88%), m.p. 109°. *Anal.* Calcd. for $C_{13}H_{19}HgNO_6$: C, 36.75; H, 3.72; N, 2.69. Found: C, 36.70; H, 3.85; N, 2.83.

N-(3-Acetoxymercuri-2-β-hydroxyethoxypropyl)-phthalimide, yield 9.5 g. (95%), m.p. 126°. *Anal.* Calcd. for $C_{15}H_{17}HgNO_6$: C, 35.50; H, 3.37; N, 2.77. Found: C, 35.57; H, 3.52; N, 2.92.

4-Acetoxymercuri-1,1-diphenyl-3-β-hydroxyethoxybutanol-1, yield 4.5 g. (41%), m.p. 114.5°. *Anal.* Calcd. for $C_{20}H_{24}HgO_5$: C, 44.07; H, 4.44. Found: C, 44.26; H, 4.48.

4-Acetoxymercuri-1,1-diphenyl-3-methoxybutanol-1, yield 7.2 g. (70%), m.p. 135.6–136°. *Anal.* Calcd. for $C_{19}H_{22}HgO_4$: Hg, 38.95. Found: Hg, 38.40.

Methyl 2-hydroxymercuri-3-β-hydroxyethoxyhydrocinnamate, yield 6.9 g. (78%), m.p. 216–218° dec. *Anal.* Calcd. for $C_{12}H_{16}HgO_5$: Hg, 45.40. Found: Hg, 45.70.

Methyl 2-acetoxymercuri-3-β-methoxyethoxyhydrocinnamate, yield 7.9 g. (80%), m.p. 97°. *Anal.* Calcd. for $C_{15}H_{20}HgO_6$: C, 36.30; H, 4.05. Found: C, 36.28; H, 3.97.

Methyl 2-acetoxymercuri-3-β-chloroethoxyhydrocinnamate, yield 7.5 g. (75%), recrystallized from ethanol, m.p. 124°. *Anal.* Calcd. for $C_{14}H_{17}ClHgO_5$: C, 33.48; H, 3.42. Found: C, 32.92; H, 3.34.

Ethyl *m*-(3-Acetoxymercuri-2-β-hydroxyethoxypropyl)-*p*-hydroxybenzoate.—Two grams (0.011 mole) of ethyl *m*-allyl-*p*-hydroxybenzoate[9] and 3.18 g. (0.01 mole) of mercuric acetate were dissolved in 5 ml. of ethylene glycol and allowed to stand at room temperature for three days. Ether was added and the product precipitated. The precipitate was crystallized from a mixture of ethyl acetate and petroleum ether; yield 4 g. (77%), m.p. 99–100°.

Anal. Calcd. for $C_{16}H_{22}HgO_7$: Hg, 38.03. Found: Hg, 37.82.

Ethyl *m*-(3-Acetoxymercuri-2-methoxy)-*p*-hydroxybenzoate.—The procedure in the above paragraph was repeated using methanol rather than ethylene glycol; yield 50%, m.p. 124–125°.

Anal. Calcd. for $C_{15}H_{20}HgO_6$: Hg, 40.25. Found: Hg, 40.22.

2-Acetoxymercuri-5-carbethoxy-2,3-dihydrobenzofurane.—The procedure described in the above paragraph was used with the exception that ethylene glycol was replaced with ethanol, methyl Cellosolve, or benzyl alcohol. The yields varied from 14–50%, m.p. 114–116°.

Anal. Calcd. for $C_{14}H_{16}HgO_5$: Hg, 43.01. Found: Hg, 42.95.

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[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

Diuretics. II. Alkoxymercuration by Mixed Anion Salts of Mercury

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RECEIVED OCTOBER 21, 1957

Alkoxymercuration of allylamides by means of mixed anion salts of mercury furnished a convenient and direct synthesis of twenty-one new mercurial diuretics.

Normal mercuric salts of mineral acids, with few exceptions, are not suitable for the alkoxymercuration of olefins. This is due to the insolubility of some mercuric salts and to the instability of the mercury–olefin adduct in the presence of mineral acid.[1] Mixed anion salts of $XHgOCOCH_3$, where X is a mineral acid anion, are moderately soluble in water and the common alcohols and yield predominantly HgX^+ and $CH_3CO_2^-$ ions in solution. Alkoxymercuration of allylic compounds by means of these mixed anion salts yielded the new mercurials $RCH_2CH(OR')CH_2HgX$ (III) reported here.

Mixed anion salts of mercury were prepared from mercuric acetate and each of the following normal salts: mercuric chloride, mercuric bromide, mercuric iodide, mercuric nitrate and mercuric thiocyanate. The mixed anion salts were established as discrete crystalline compounds by observing that their X-ray patterns were completely different from the patterns of the starting normal salts. The allylic compounds I employed

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