was observed between the 1-alkyl-3-carbethoxy-4-piperidylbenzoates and *p*-aminobenzoates.[10] In the above data there does not seem to be much correlation between the subcutaneous and absolute (intravenous) toxicities.

Summary

1. Several substituted piperidino-alkylbenzoates and *p*-aminobenzoates have been prepared and described.

2. The alkyl substituted piperidino compounds which contain three methylene groups between the piperidine nitrogen and the benzoyl group possess local anesthetic action, while the corresponding unsubstituted and carbethoxy substituted piperidino derivatives show no local anesthetic activity.

3. In general, the substituted piperidino derivatives are less toxic than the corresponding unsubstituted piperidino derivatives.

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THE MERCURATION OF *o*-NITROPHENOL

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Iodination of *o*-nitrophenol by the aid of yellow mercuric oxide was found by the author[1] to take place preferentially in the 4 as compared with the 6 position whether the medium employed was alcohol or glacial acetic acid, and in addition considerable di-iodination took place even when a deficiency of iodine was used. In consequence it became of interest to ascertain whether mercuration would exhibit a like preference.

Previous work on this subject by Hantzsch and Auld[2] established that when an alcoholic solution of *o*-nitrophenolate (1 mole) and aqueous mercuric acetate (1 mole) were boiled together, the mono-mercuri product formed yielded *p*-bromo-*o*-nitrophenol when brominated, thereby establishing mercuration in the 4 position. Later Raiziss and Proskouriakoff[3] proved that considerable dimercuration occurred under the above conditions and, although the various products were not orientated by them, tacit assumption of mercuration in the 4 position was made for the mono-mercuri products.

In the present investigation mercuration has been effected both by fusion of *o*-nitrophenol with mercuric acetate and also according to the directions of Raiziss and Proskouriakoff. In the former case marked

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[10] McElvain, THIS JOURNAL, **48**, 2184, 2241 (1926).

[1] Hodgson, *J. Chem. Soc.*, **1927**, 1141.

[2] Hantzsch and Auld, *Ber.*, **39**, 1105 (1906).

[3] Raiziss and Proskouriakoff, THIS JOURNAL, **44**, 787 (1922).

preference was shown for mercuration in the 6 position and practically no dimercuration occurred, whereas in aqueous alcoholic solution substitution in the 4 position accompanied by considerable dimercuration took place.

Orientations were established by conversion of the mercurated products into the corresponding iodonitrophenols.

The 6- and 4-acetoxymercuri-2-nitrophenols were readily converted into the 6- and 4-fluoro-, chloro-, bromo- and iodomercuri-2-nitrophenols, all of which were lighter in color than *o*-nitrophenol itself, the depths of shade increasing gradually from fluoro (almost colorless) to chloro (very pale brownish-yellow), bromo (pale yellow) and iodo (almost as deep a yellow as *o*-nitrophenol). Further, the 6-acetoxy- and 6-halogenomercuri-2-nitrophenols appear to be somewhat paler than the 4 substituted isomerides and, moreover, possess lower melting points and lesser solubilities in alcohol and acetic acid.

Experimental

6-Acetoxymercuri-2-nitrophenol.—An intimate mixture of *o*-nitrophenol (15 g.) and mercuric acetate (3 g.) was heated gradually to 150° during one hour, and kept at 140–150° for four hours with frequent shaking. The reaction product was mixed with a saturated solution of sodium chloride and steam distilled, when unchanged *o*-nitrophenol was recovered (12 g.) and a non-volatile residue (2 g.) obtained from which 6-chloromercuri-2-nitrophenol was removed by repeated extraction with boiling alcohol. The light brown almost colorless residue was dissolved as completely as possible in dilute sodium hydroxide, the solution filtered, reprecipitated by acetic acid and the product crystallized from glacial acetic acid, in which it is only moderately soluble, giving pale brownish-yellow, almost colorless micro clusters which do not appear to melt below 300°.

Anal. Calcd. for $C_8H_7O_5NHg$: N, 3.5. Found: 3.6.

When an aqueous suspension of 6-acetoxymercuri-2-nitrophenol is gently warmed for about 30 minutes with excess iodine dissolved in aqueous potassium iodide, almost the whole is converted into 6-iodo-2-nitrophenol (1 g. gives 0.62 g.; calcd. 0.71 g.), which is removed by steam distillation and crystallized from dilute alcohol, giving characteristic plates, m. p. 110°.

Anal. Calcd.: I, 47.9. Found: 47.7.

This product, when treated in glacial acetic acid solution with iodine and yellow mercuric oxide, was converted quantitatively into 4,6-di-iodo-2-nitrophenol. When the steam-volatile product was collected in small fractions, the first one had a melting point of 102° and appeared to contain a certain amount of 4-iodo-2-nitrophenol, recognized by microscopic examination. A negligible amount of 4,6-di-iodo-2-nitrophenol was detected in the iodination experiment above, which indicated that almost no dimercuration had taken place.

4-Acetoxymercuri-2-nitrophenol, prepared according to the directions of Raiziss and Proskouriakoff,[3] was treated with iodine as above and afforded a mixture of 4,6-di-iodo- and 4-iodo-2-nitrophenols, with a little 6-iodo-2-nitrophenol. The former, which was present in considerable amount, thus confirms Raiziss and Proskouriakoff's observation[3] with respect to the fairly extensive dimercuration which takes place under these conditions. The two latter products were separated by steam distillation, fractionally crystallized from alcohol and identified by microscopic examination, confirmation forthcoming by iodination of all the fractions to 4,6-di-iodo-2-nitrophenol, exclusively.

6- and 4-Halogenomercuri-2-nitrophenols.—These products were precipitated by the addition of the requisite halogen acid to solutions of the sodium 6- and 4-hydroxymercuri-2-nitrophenols prepared according to the directions of Raiziss and Proskouriakoff[8] except in the cases of the 6- and 4-iodomercuri-2-nitrophenols, which were precipitated by the addition of dilute sulfuric acid to solutions of the above sodium salts in which a large excess of potassium iodide had been dissolved. The 4-halogeno-mercuri compounds were all slightly deeper in color and more soluble in alcohol and acetic acid than the 6 isomerides and all possessed higher melting points where these existed.

For convenience and to abbreviate description the crystalline form, color and melting points of the 6 and 4 compounds are given in Table I below. Both sets were crystallized from alcohol.

Sodium-6-hydroxymercuri-2-nitrophenolate gives scarlet-red crystals, while the crystals of the 4 compound are a deeper red.

Anal. Calcd. for $C_6H_4O_4NNaHg$: N, 3.7. Found: 3.8.

TABLE I

HALOGENO-MERCURI-2-NITROPHENOLS

Name	6 Isomer			4 Isomer			Composition, %	
	M. p., °C.	Color	Crystal form	M. p., °C.	Color	Crystal form	Calcd.	Found
Fluoro	187	Pale yellow	Plates	195	. . .	Micro plates	N = 3.9	4.0
Chloro	185[a]	Pale yellowish-brown	Rect. plates	205	Creamy yellow	Micro clusters	Cl = 9.5	9.5
Bromo	177	Pale yellow	Plates	236	. . .	Needles	Br = 19.1	18.9
Iodo	215	Deep yellow	Needles	>300	Bright yellow	Micro needles	I = 27.3	27.0

[a] Crude product, m. p. 175°; contained some of the 4 isomer as shown by its reaction with iodine, etc. The pure product, m. p. 185°, gave only the 6 isomer.

Summary

Fusion of *o*-nitrophenol with mercuric acetate gives mainly 6-acetoxymercuri-2-nitrophenol. When solvent media are employed, 4-acetoxy-2-nitrophenol is formed preferentially, accompanied, however, by appreciable amounts of 4,6-diacetoxymercuri-2-nitrophenol.

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