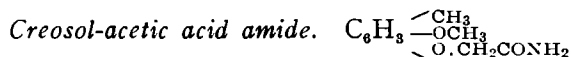


The amide is saponified by moderate heating with solutions of caustic alkalis.



This substance is prepared from creosol, just as the guaiacol-acetic acid amide is prepared from guaiacol, and crystallizes from warm water in fine white needles, which are odorless and tasteless. Its melting point is 127° and like the guaiacol-acetic acid amide it is saponified by caustic alkalis. Its solubilities are the same as those of guaiacol-acetic acid amide.

Below we append a tabular statement of some of the compounds of the various phenols with monochloroacetic acid and their melting or boiling points:

	M. P.	B. P.
Phenol acetic acid.....	96°	285°
Phenol acetic acid ethyl ester.....		251°
Phenol acetic acid amide.....	101.5°	
$\alpha$ -Naphthol-acetic acid.....	190°	
$\alpha$ -Naphthol-acetic acid ethyl ester.....	173°	
$\alpha$ -Naphthol-acetic acid amide.....	155°	
$\beta$ -Naphthol-acetic acid.....	151/152°	
$\beta$ -Naphthol-acetic acid ethyl ester.....	48/49°	
$\beta$ -Naphthol-acetic acid amide.....	147°	
Thymol-acetic acid.....	148°	
Thymol-acetic acid ethyl ester.....		290°
Thymol-acetic acid amide.....	96/97°	
Guaiacol-acetic acid.....	121°	
Guaiacol-acetic acid ethyl ester.....		270/271°
Guaiacol-acetic acid amide.....	138°	
Creosol-acetic acid.....	108°	
Creosol-acetic acid ethyl ester.....		276/277°
Creosol-acetic acid amide.....	127°	

We have also prepared the corresponding compounds of purified creosote from beechwood tar. We have made thus, creosote-acetic acid, its ethyl ester and its amide, all of which are mixtures and possess the same properties as those of the compounds which constitute them.

RESEARCH LABORATORIES OF SHARP & DOHME, Baltimore, June, 1912.

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### ESTIMATION OF IRON IN REDUCED IRON.

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O. E. WINTERS.

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Many methods for the determining of iron in reduced iron have been devised in recent years. In reviewing the various processes offered, opinion seems to be about equally divided as to whether the percentage of the total iron or of the metallic iron shall be taken as standard by which the value of reduced iron is to be gauged.

For estimating the total iron, the method which is described in the text of the Dutch, German and Italian Pharmacopœias stands out most prominently. In this process the iron is dissolved in acid, the resulting ferrous salt oxidized with potassium permanganate and the ferric salt estimated iodometrically in the usual way.

For the estimation of metallic iron only, the mercuric chloride method as given

in the Swiss, Belgian and Swedish Pharmacopœias and in Krauch-Merck, "Chemical Reagents, their Purity and Tests," 1907, page 116, and the iodometric method described in the United States, Austrian, and Japanese Pharmacopœias are applied. The French Codex gives a gasometric method; the British Pharmacopœia, one in which the iron is mixed with copper sulphate and the ferrous salt formed is titrated with standard bichromate solution; the Danish Pharmacopœia, one in which the iron is acted upon by ferric chloride in an atmosphere of  $\text{CO}_2$  in order to prevent oxidation, titrating the resulting ferrous salt with standard permanganate solution. The Hungarian Pharmacopœia simply directs to glow the iron in the air and weigh the oxide formed.

The requirements by the various Pharmacopœias are as follows:

Dutch .....	84.6% of metallic iron	Japanese .....	90% of pure iron
German .....	90% of metallic iron and 96.6% of total iron	British .....	Not less than 75% of metallic iron
Italian .....	98% of total iron	Danish .....	90% of metallic iron
Swiss .....	90% of metallic iron	Hungarian .....	80% of metallic iron
Swedish .....	90% of metallic iron	United States.....	90% of metallic iron

The methods in the different Pharmacopœias given in full are as follows:

*Dutch Pharmacopœia:* One hundred mgs. of iron are dissolved in 20 cc. of diluted sulphuric acid, then mixed with sufficient one-half percent potassium permanganate solution to produce a persistent pinkish color. After the excess of permanganate has been removed by a few drops of alcohol, 2 gm. of potassium iodide are dissolved in the solution and the mixture allowed to stand for one hour. The liberated iodine is then titrated with tenth-normal sodium thiosulphate solution, of which not less than 17.1 cc. should be used.

*German Pharmacopœia:* One gm. of reduced iron is dissolved in 50 cc. of diluted sulphuric acid, and the solution made up with water to measure 100 cc. Ten cc. of this solution are mixed with sufficient half percent potassium permanganate solution until a persistent pink color is produced. The excess of permanganate is removed by the addition of a few drops of tartaric acid solution. Two gms. of potassium iodide are then added and the mixture allowed to stand in a well-closed bottle for one hour. The iodine is then titrated with tenth-normal sodium thiosulphate solution, of which at least 17.3 cc. should be used.

*Italian Pharmacopœia:* One gm. of iron is dissolved in 25 cc. of diluted sulphuric acid and after solution has taken place the liquid is mixed with distilled water to measure 100 cc. To 10 cc. of this solution potassium permanganate solution is added until a pink color is obtained. The excess of permanganate is then removed by a few drops of alcohol, and after the addition of 1 gm. of potassium iodide in 5 cc. of water, the mixture is allowed to stand in a glass-stoppered bottle for half an hour at a temperature from  $35^\circ$  to  $40^\circ$  C. The liberated iodine is then titrated with tenth-normal sodium thiosulphate solution, of which not less than 17.5 cc. should be used.

*Swiss Pharmacopœia:* Five decigrams of reduced iron are added to the hot solution of 5 gm. of mercuric chloride in 50 cc. of water, the mixture heated for half an hour on a steam bath, shaking from time to time, and then allowed to

cool. The solution is made up with water to measure 100 cc. and filtered. Fifty cc. of the clear filtrate mixed with 10 cc. of diluted sulphuric acid should require at least 40.25 cc. of potassium permanganate solution to produce a persistent pink color.

*Belgian Pharmacopoeia*: A mixture of 1 gm. of iron and a solution of 5 gm. of mercuric chloride and 50 cc. of water in a 100 cc. graduated flask is heated for 20 minutes on a water bath, shaking occasionally. After cooling, sufficient water is added to make the volume measure 100 cc. and the mixture allowed to settle. Ten cc. of the clear liquid are then transferred to a glass-stoppered bottle, mixed with 20 cc. of diluted sulphuric acid and then drop by drop a one-half percent solution of potassium permanganate is added until a faint but persistent reddish color is obtained. The excess of permanganate is then removed by the addition of a few drops of alcohol. Two gm. of potassium iodide are then added and after having the bottle well stoppered the mixture is allowed to stand for one hour at ordinary temperature. The liberated iodine is then titrated with sodium thiosulphate solution, of which at least 14.3 cc. should be used.

*Swedish Pharmacopoeia*: Five-tenths gm. of reduced iron and 5 gm. of mercuric chloride are dissolved in 50 cc. of boiling water, the mixture heated for a few minutes on a water bath, shaking occasionally, and after cooling, sufficient water is added to make the solution measure 100 cc. The mixture is then filtered and 25 cc. of the clear filtrate, after the addition of 10 cc. of diluted sulphuric acid, is titrated with tenth-normal potassium permanganate, of which at least 20 cc. should be used.

*Krauch-Merck's Method*: "One gm. iron is brought into a 100 cc. measuring flask, 10 gm. of finely powdered mercuric chloride and 50 cc. of boiling water are added and the mixture kept boiling on wire gauze over a small flame for five minutes, shaking frequently. The flask is then filled up to mark at once with cold water. After cooling to 15° C. the flask is filled up again to mark, shaken well and left standing well stoppered for settling. The solution is filtered and 10 cc. of the filtrate are titrated with 1/10 normal permanganate of potash solution, under addition of 10 cc. diluted sulphuric acid. At least 16 cc. should be used of the permanganate solution. In order to control this test, dissolve in the titrated solution 2 gm. of potassium iodide, leave stand stoppered for one hour at a temperature of 20° C., and then titrate with 1/10 normal hyposulphite solution using starch solution as indicator. One cc. of 1/10 normal potassium permanganate or 1/10 hyposulphite solution is equal to 0.00559 gm. metallic iron."

*U. S. Pharmacopoeia*: (Text of this method well known.)

*Austrian Pharmacopoeia*: Three-tenths gm. of reduced iron are well mixed with 10 cc. of potassium iodide solution and 15 dgm. of iodine under cooling. When solution has taken place, the volume is made up with water to measure 100 cc. Fifty cc. of the solution should require not more than 10.3 cc. of 1/10 normal sodium thiosulphate solution to render the solution colorless.

*Japanese Pharmacopoeia*: Pour 10 cc. of potassium iodide solution on 0.3 gm. of reduced iron in finely powdered state and add gradually, under cooling and shaking, 1.5 gm. of coarsely powdered iodine; as soon as the iron and iodine have completely dissolved, dilute the solution to 100 cc. with water and set it

aside; titrate 50 cc. of the clear solution thus prepared with decinormal sodium thiosulphate solution, then not more than 10.3 cc. of the latter solution should be required for the complete decoloration.

*French Codex:* Five-tenths gm. of reduced iron is treated with diluted hydrochloric acid and the hydrogen is collected. In the case of pure iron, about 200 cc. of hydrogen should be obtained, measured under normal conditions of temperature and pressure.

*British Pharmacopoeia:* If 0.25 gm. of reduced iron be added to a hot solution of 1 gm. of copper sulphate in 15 cc. of water, in a flask that can immediately be well corked, and the whole be shaken occasionally during ten minutes, the liquid, after being rapidly filtered with the minimum of exposure to air, and acidulated with sulphuric acid, should not cease to yield a blue precipitate with solution of potassium ferricyanide until at least 33.7 cc. of N/10 volumetric solution of potassium bichromate have been added.

*Danish Pharmacopoeia:* Five-tenths gm. of the iron is heated in a 100 cc. graduated flask with 5 gm. of anhydrous ferric chloride in 50 cc. of boiled and cooled water. After cooling, the volume is made up with boiled and cooled water to measure 100 cc. and the mixture allowed to settle. Twenty cc. of the clear liquid, acidulated with 50 cc. of boiled and cooled diluted sulphuric acid, is titrated with tenth-normal potassium permanganate, of which at least 48 cc. should be used for every 0.1 gm. of reduced iron taken.

*Hungarian Pharmacopoeia:* One gm. of iron is heated in the presence of air for about fifteen minutes, when 1.34 gm. of iron oxide should be obtained.

In examining the above methods I found that those given for estimating the total iron work very satisfactorily, but that those described for determining metallic iron are open to criticism. In the iodometric method, the accurate weighing and transferring of iodine is a tedious operation, and the iron has to be powdered very fine in order to be completely dissolved. Even after prolonged standing, a coarsely powdered preparation will not be entirely converted into ferrous iodide. I found when working under the best possible conditions that results obtained varied as much as 1.5 percent.

With the mercuric chloride methods as described above, the results obtained agreed very closely. I may mention, however, that the time allowed for heating on a water-bath is insufficient to completely dissolve the iron. Even when the heating under these conditions is prolonged, it is difficult to distinguish between the undissolved iron and the deposited mercury. The modified method as given in Krauch-Merck, in which it is directed that the mixture be heated over an open flame, not only shortens the time of the estimation by about one-half hour, but also insures the complete solution of the iron.

The gasometric method gives good results, but has the disadvantage of being troublesome in manipulation, and besides this, depends too much on physical conditions, i. e., temperature and air pressure.

The method described in the British Pharmacopoeia, although giving results agreeing closely with those obtained by the mercuric chloride method, is, like all estimations in which the end point of the titration is found by spotting, subject to the personal equation.

The method as given in the Danish Pharmacopœia is not only a tedious operation, but gives low results. In no instance was I able to obtain a clear final filtrate.

These methods were applied to two samples of reduced iron, A and B, and the following results were obtained: Sample B contained sulphide in an excess of the amount allowed by the U. S. P. This sample was examined in order to ascertain whether or not sulphides had any influence on the results obtained by these processes.

As will be seen from the attached table, the presence of an excess of sulphide has no appreciable effect upon the results obtained with the method given for total iron or with the iodometric process. However, when the mercuric chloride method is used, a reaction seems to take place between the iron sulphide and mercuric chloride, as the result of which figures are obtained which are apparently too high.

Dutch		German		Italian			
A	B	A	B	A	B		
97.7%	97.8%	97.6%	97.8%	97.0%	97.8%		
97.9%	97.7%	97.5%	98.0%	96.9%	97.7%		
		97.6%	97.7%				
Swiss		Belgian		Swedish		Krauch-Merck	
A	B	A	B	A	B	A	B
91.4%	97.2%	91.2%	96.4%	91.3%	97.0%	91.6%	97.4%
91.2%	96.7%	91.7%	96.6%	91.7%	97.3%	91.7%	97.4%
						91.6%	97.5%
United States		Austrian		Japanese			
A	B	A	B	A	B		
91.0%	93.2%	89.0%	91.4%	88.6%	91.8%		
88.8%	93.8%	88.4%	89.9%	90.0%	90.1%		
89.3%	92.0%	90.0%	90.5%	89.1%			
French		British		Danish			
A	B	A	B	A	B		
90.3%	97.1%	89.6%	96.6%	81.6%	86.2%		
Hungarian		Heated 1 hr.					
Heated 15 min.							
A	B	A	B				
87.2%	85.4%	93.7%	92.3%				

In conclusion, I wish to say that the modified mercuric chloride method, when the sulphides are within the limit allowed by the U. S. P., is the most satisfactory. On account of its accuracy, simple manipulation, and shortness in carrying it out, this method cannot be too highly recommended.

While adding but little to the information already at hand, I trust that the results may be of some interest to the Revision Committee in selecting a method for the determination of iron in reduced iron to be inserted in the text of the U. S. P. Ninth Revision.

I wish to thank Dr. Herman Engelhardt, at whose initiative this work was undertaken, for advice and assistance in carrying it out.