

the same experimental conditions, deteriorated only 4.9% as compared to 96% for the thiosalicylate compound.

Inhibition of Catalytic Oxidation by 2-Ethylmercurithiopyridine-5-Carboxylic Acid.—Since 2-ethylmercurithiopyridine-5-carboxylic acid resisted substantial catalytic oxidation for long periods of time at room and elevated temperatures it might be assumed that this compound forms a coördination complex, catalytically inert in character, with copper. If a catalytically inactive complex is formed between copper salts or ions and the mercapto pyridine compound then the latter should inhibit the catalytic oxidation of a mercapto compound susceptible to such action. To test this hypothesis a series of solutions, the compositions of which are indicated below, was prepared, placed in vials and heated at 60° C. At hourly intervals 5-cc. samples were withdrawn, chilled immediately and titrated with *N*/200 iodine solution.

Solution *A*—100 cc. contain:

Sodium ethylmercurithiosalicylate	0.05 Gm.
Sodium borate	0.14 Gm.
Sodium chloride	0.10 Gm.
Cu	0.10 mg.

Solution *B*—100 cc. contain:

Sodium ethylmercurithiosalicylate	0.05 Gm.
Sodium 2-ethylmercurithiopyridine-5-carboxylate	0.05 Gm.
Cu	0.10 mg.
Sodium borate	0.14 Gm.
Sodium chloride	0.10 Gm.

Solution *C*—100 cc. contain:

Sodium ethylmercurithiosalicylate	0.05 Gm.
Sodium 2-ethylmercurithiopyridine-5-carboxylate	0.05 Gm.
Sodium borate	0.14 Gm.
Sodium chloride	0.10 Gm.

Table IV.—Inhibition of Oxidation of Sodium Ethylmercurithiosalicylate by Sodium 2-Ethylmercurithiopyridine-5-Carboxylate. *t* = 60° C.

Hours Heated	Per Cent Oxidation		
	Solution <i>A</i>	Solution <i>B</i>	Solution <i>C</i>
1	28.7	2.1	0.6
2	33.4	0.0	0.0
3	41.6	0.0	0.0
4	46.7	0.9	0.0
5	51.4	4.8	0.0

From the results it is seen, at least for the interval of time indicated, that 2-ethylmercurithiopyridine-5-carboxylic acid effectively prevented the catalytic oxidation of ethylmercurithiosalicylate, and therefore the copper ions must have been bound by complex formation with the thiopyridine compound. It should be observed that the complex formed in this instance is not of the type formed by other sulphydryl compounds such as cysteine (9), glutathione, etc., with metal ion oxidation catalysts.

Sodium 2-thiopyridine-5-carboxylate does not form a catalytically inactive complex with metal

ion catalysts for in the presence of Cu 1:1,000,000 a 1:1000 solution of this salt, heated at 60° C. for 1 hour, was oxidized 20%, and when heated at 60° C. for 237 hours over 96% was oxidized. In the absence of added copper this compound, similarly treated for 237 hours, deteriorated 85% and was therefore susceptible to autocatalytic action in the presence of atmospheric oxygen.

The addition of a number of pyridine compounds to solutions of sodium ethylmercurithiosalicylate containing Cu 1:1,000,000 exerted no action in inhibiting the oxidation of the compound. In these experiments pyridine, 2-aminopyridine, 2-pyridone and 2-mercaptopyridine were studied.

SUMMARY

1. The preparation of some new organic mercurials has been described.
2. Oxidation tests carried out on one of the compounds indicate that they are substantially resistant to catalytic oxidation.

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Note on the U. S. P. XI (Supplement II) Monograph on Cyclopropane*

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This Department has been studying the standards of purity for Cyclopropane for a year or more but did not make rapid progress until the Research Division of the Ohio Chemical Company kindly provided us with small cylinders of a specially purified cyclopropane, of methyl acetylene, propylene and allene. Our thanks are due to them for making this study possible.

In the preparation of cyclopropane several unsaturated gases might be formed, and indeed in various commercial samples as much as 2% or over of unsaturated com-

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pounds have been found, as will be reported below. The unsaturated compound usually considered to be present is propylene. The boiling point of cyclopropane according to the International Critical Tables 1927, is -34.5° C. at 760 mm. Ashdown (1) gives -32.89° C. The boiling point of propylene is -47.67° C. and might be removed by fractional distillation. A sample of cyclopropane prepared in this laboratory when fractionated by expert low-temperature distillation contained mere traces of propylene. The anesthetic value of propylene has been adequately studied (2, 3, 4). Secondly allene, $\text{CH}_2=\text{CH}=\text{CH}_2$, might occur as an impurity. Beilstein gives its boiling point as -32° C. and it might have been present in the sample of cyclopropane referred to, as it would not have been detected in the fractionation. Its anesthetic action has been studied by Ferguson (5). The third compound which certain organic chemists expected would occur is methyl acetylene, $\text{CH}_3\equiv\text{C}-\text{CH}$, which has a boiling point of -23.5° C. The method of Illosvay van Nagy Illosva (6) for the detection of acetylene yields with methyl acetylene a yellowish precipitate. When a large volume of commercial cyclopropane was slowly bubbled through this reagent no trace of yellow precipitate occurred. Henderson (7) has recently studied the anesthetic properties of this gas. It is further possible that hexenes might be produced, but owing to their high boiling point these would probably be removed by fractionation. We are therefore chiefly concerned with allene and propylene.

EXPERIMENTAL

Definition and Assay.—The definition of cyclopropane in the U. S. P. XI, Second Supplement, states that "Cyclopropane contains not less than 99% $\text{CH}_2-\text{CH}_2-\text{CH}_2$ " *i. e.*, 99% cyclopropane. Yet in the method of assay, namely, absorption of the gas from the cylinder in sulfuric acid, propylene and allene, as well as the cyclopropane, will dissolve if they are present.

According to this method of assay "the residual gas . . . does not exceed 1% of the volume of the original gas taken for assay." That is, according to the assay one per cent of the original gas may consist of other impurities than unsaturated hydrocarbons, namely air, carbon dioxide and carbon monoxide, all of which would not be absorbed by sulfuric acid. Furthermore, the method does not say whether

the gas for analysis is to be taken from the liquid or the gaseous phase, which is likely to contain more air than the liquid one. Our samples have been drawn from the gaseous phase and in some cases commercial samples, as shown below, contain as much as 1% of gas unabsorbable in sulfuric acid; in one or two cases slightly more was present. It is possible that all these gases would have qualified if the sample for analysis had been drawn from the liquid phase.

In addition to the assay with sulfuric acid which will allow the presence of 1% of unabsorbable gas, the monograph sets a limit for the amount of unsaturated impurity, allene and propylene, and as will be shown below this may amount to another 1% or more. Consequently the requirement that the gas must be 99% cyclopropane seems hard to justify.

Tests for Identity and Impurity.—The one test to which we wish to refer is that for unsaturated hydrocarbons, *i. e.*, propylene and allene. A liter of cyclopropane is passed through a column 12–14 cm. deep and containing 50 cc. of *N*/100 potassium permanganate in 15 minutes. The orifice from which the bubbles arise is defined and the solution kept during the process at 3° C. ± 2 . In order to pass this test "the volume of hundredth-normal potassium permanganate reduced by the gas is not more than 10 cc. (propylene, allene and other unsaturated hydrocarbons)."

We soon found much difficulty in obtaining satisfactory duplicate results in applying this method, using either samples of commercial gas or percentage mixtures made up from propylene and practically pure cyclopropane furnished us by the Ohio Chemical Company. The first experiments were performed by aspirating a liter of gas through the permanganate by means of a suction pump. The irregularities in results were attributed to the difficulty of performing this test in exactly 15 minutes. It was also observed that the bubbles were not uniform in size. Consequently a flask was filled with a saturated solution of calcium chloride which had been saturated with cyclopropane, and this solution was displaced by the gas to be examined; in turn the gas was displaced from the flask by the same saturated solution which entered the flask from a funnel fixed above to give a constant pressure head. The level of the funnel was maintained almost constant by an inverted Mariotte flask, the oblique orifice of which just entered the fluid in the funnel.

With the addition of this method of securing a more uniform rate of bubbling, all conditions were strictly adhered to in the experiments reported in detail, though approximately the same quantitative results were obtained in many other experiments where the bubbling was not so closely controlled, and are not reported in detail. Constancy of rate of bubbling becomes particularly important when the amount of the impurity is large, but even more important is the constancy of size of bubbles which one fails to obtain in such a crude apparatus. During the bubbling operation one can observe the for-

mation of large and small bubbles. Large bubbles appear to break at times when the tip of the bubbler is above a certain point in the cylinder containing the permanganate. Moving the tip very little results in giving bubbles of different sizes, with consequent different titration of permanganate. A spiral of glass about the bubbling tube was tried in order to break up the bubbles, but even with this small and large bubbles were present and results were not uniform.

According to specifications, commercial gases must contain 99% of cyclopropane. If no gas unabsorbable in sulfuric acid is present, then the 1% may be propylene. In order to discover if the disappearance of 10 cc. of permanganate corresponded to the presence of 1% of propylene in a liter of gas, samples of gas prepared by adding 10 cc. of propylene to 990 cc. of special cyclopropane were bubbled through permanganate. The special cyclopropane used up about 1.8 cc. of permanganate. In Table I, which gives the results of these analyses, this amount has been deducted.

Table I.—Cubic Centimeters of *N*/100 Potassium Permanganate Used up by 1 Liter 11% Propylene in Cyclopropane

Date	Time in Minutes	Cc. of <i>N</i> /100 <chem>KMnO4</chem> Soln.
Feb. 2	14	11.9
Feb. 2	15	9.3
Feb. 2	16	12.9
Feb. 6	15	9.4
Feb. 7	15	9.1
Feb. 10	18	10.9
Feb. 27	16	11.9
Feb. 27	16	10.3
Feb. 27	15 ¹ / ₂	14.1
Mar. 2	15 ¹ / ₄	9.2
Mar. 2	16 ¹ / ₂	11.2
Mar. 2	16	11.9
		Av. 10.9

When a 2% propylene in cyclopropane was passed, the figures were in all cases less than was to be expected from those found for a 1% propylene, for example, 17.2, 16.4, 12.3, 15.8.

We would conclude from our experiments that the reduction of 10 cc. of permanganate would correspond approximately to 10 cc. of propylene in a liter, *i. e.*, 1%, and that the method becomes quantitatively less accurate as the content of propylene increases beyond 1%. To demonstrate that bubbling a liter of 2% propylene through permanganate did not remove all the propylene, a liter flask was fitted with a 2-hole stopper. Through one hole a short glass tube was passed, the outer end holding a small balloon. Through the other hole a capillary tube was passed until it almost touched the bottom of the flask. Fifty cubic centimeters of permanganate were placed in the flask and 20 cc. of propylene were passed in, requiring about 2 minutes, the flask being well agitated during this interval. By this means the propylene was brought into intimate contact with the permanganate and subsequent titration showed that on two such trials 25.7 and 25.5 cc. of permanganate disappeared, as compared with 17.2, 16.4, etc., as cited above.

When a liter of 1% allene in cyclopropane was tested, so much of the permanganate was reduced that reproducible results could not be attained. Consequently, a mixture containing 0.1% in the purified Ohio cyclopropane was used. The average result of several runs was 7.9 cc. of permanganate reduced (spread from 7.7 to 8.1). A 0.2% mixture reduced only 14.6 cc. (instead of 15.8 cc.), while a 0.58% mixture reduced only 25.4 cc. and 1.3% only 30.2 cc.

Here, again, and even more strikingly than with propylene, the permanganate method does not give quantitative results and is only approximately quantitative when 10 cc. or less of permanganate are reduced.

It is also obvious that the standard set, namely, the reduction of not more than 10 cc. of permanganate, would not allow the presence in cyclopropane of more than a little over 0.1% of allene, while it would allow about 1% of propylene. Turning to the results of applying this method to commercial samples, it is very obvious that very low percentages of allene in a gas would condemn it, although it might contain 99.8% cyclopropane.

Owing to a suggestion from the Imperial Chemical Company in Great Britain prior to the publication of the Supplement, we had been testing Wijs solution as a method of estimating the amount of unsaturated impurity. We had used various methods of absorbing in the Wijs solution and finally found that the use of 25 cc. of Wijs solution in the small bubbler described in *Industrial and Engineering Chemistry* (9) gave very satisfactory results when a liter of gas was passed in half an hour.

When a liter of the specially purified Ohio gas was passed through Wijs solution, 0.4 cc. of *N*/10 thiosulfate solution was the equivalent of the Wijs solution attacked. This calculated in terms of propylene is 0.05%. The permanganate method on the same gas showed that 1.8 cc. of *N*/100 were reduced. This again means a small amount of propylene but seems to be substantially higher than the amount revealed by the Wijs method. Again, this amount has been deducted from the results with prepared mixtures.

Using a 1% mixture of propylene in cyclopropane, approximately theoretical results were obtained, the average result being that 8.8 cc. of thiosulfate were the equivalent of the Wijs solution disappearing. In terms of propylene this would be 10.47 cc. instead of the 10 cc. actually employed.

When several analyses of 1% of allene in cyclopropane were made, the results were always higher than calculated for the breaking of one double bond; namely, Wijs solution equivalent to 13.9 cc. of thiosulfate disappeared, which is equivalent to 16.2 cc. calculated as propylene instead of 10. For the saturation of both double bonds the calculation of 10 cc. of allene should equal 20 cc. of propylene.

A twenty-five cc. sample of Wijs solution may be employed to measure mixtures up to 2% of propylene and will give approximately quantitative results,

From the figures reported it is evident that Wijs solution will give a more accurate measure of the amount of propylene present than the permanganate method and this is true of allene as well.

Our very early tests on commercial gases with the Wijs solution convinced us that the unsaturated hydrocarbons varied considerably. Tests with the permanganate method, both by aspirating the gases through permanganate or forcing them through as indicated above, showed similar variation. Five analyses made on a tank purchased March 1, 1940, showed that 13.2, 13.9, 11.9, 10.4, 12.4 cc. of *N*/100 permanganate were reduced. When unsaturated impurities are present in small amounts, less variation was obtained, another tank showing 1.8, 1.9, 2.0, 2.0, on the four occasions tested. The amount of gas unabsorbable in sulfuric acid was estimated in some samples and again some variation was apparent. Table II gives some results obtained by the permanganate and Wijs methods, together with the amount of unabsorbable gas in some commercial samples tested.

Table II.—Absorbable Gas and Results with the KMnO_4 and Wijs Methods

Manufacturer	Per Cent of Gas Unabsorbable by Sulfuric Acid	Cc. of <i>N</i> /100 Reduced by 1 L. of Gas	Wijs Method, Cc. of <i>N</i> /10 $\text{Na}_2\text{S}_2\text{O}_8$ Soln. per L. of Gas	Unsaturated Hydrocarbons, % Calculated as Propylene	
				KMnO_4 Method	Wijs Method
X	...	15.8	...	2 (?)	...
X	...	18.1	...	2.5 (?)	...
X	...	13.2	...	1.5 + (?)	...
X	...	15.2	18.1	2% + (?)	2.15
X	...	9.8	8.5	1%	1.01
X	0.5	9.9	12.6	1% + (?)	1.5
X	0.75	25.04	28.4	3% + (?)	3.4
Y	1.1	5.2	2.6	0.4	0.31
Y	1.0	2.0	1.4	0.1	0.16
Y	...	17.1	15.5	2% + (?)	1.84

(?) Doubtful maximal values owing to inaccuracy of method.

CONCLUSIONS

The question now arises as to whether the standard for the unsaturated impurity should be altered so as to meet the commercial variations found or enforced so that manufacturers are forced to provide a more uniform product. It is obvious that cyclopropane can be made with less of the unsaturated impurity than occurs frequently. It is a manufacturer's problem whether this can be achieved regularly.

The dangers arising from the inclusion of even 2.5% of propylene do not seem to be great. It is true that propylene was condemned on account of the occurrence of cardiac irregularities, but at that time it was not known that these occurred even with ether, and the purest cyclopropane obtainable will also produce irregularities, as experiments in animals have shown. Cardiac deaths under cyclopropane, properly administered, do not seem to have been re-

corded. There seems no good reason for making the standard so rigid.

Allene is a less desirable impurity than propylene because of the lung damage it produces in anesthetic concentrations. Ferguson's experiments suggest that this would probably not occur in low concentrations such as 2%. It also produces cardiac irregularities in anesthetic concentrations.

The Supplement allows for the presence of up to 1% of gas not absorbed by sulfuric acid and this amount frequently occurs in manufacturers' samples and seems to be a fair standard. But from the above, it is evident that the estimation of unsaturated impurity, if propylene alone were present, would allow of the presence of 1% of this gas. Consequently the definition which

states that "Cyclopropane contains not less than 99% of $\text{CH}_2-\text{CH}_2-\text{CH}_2$ " should be altered to read "not less than 98%," and as commercial samples frequently contain, as the Wijs method clearly shows, more than 1%, often 2%, of unsaturated impurity, the requirement of even 98% cyclopropane would be very rigid.

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