I. The Isomeric 2,3-Epoxypentanes and 2-Pentanes. The Extent to which Mixtures of Diastereomers are Formed in Reactions of Some Pentane Compounds.

II. The Preparation of Cyclopropene.

III. The Thermal Decomposition of Trans-1,2-cyclobutane-bis-(trimethylammonium) Hydroxide.

Thesis by

Maurice Jay Schlatter

In Partial Fulfilment of the Requirements for the Degree of Doctor of Philosophy

California Institute of Technology

Pasadena, California

1941

Table of Contents

Page

I. The Isomeric 2,3-Epoxypentanes and 2-Pentenes. The Extent to which Mixtures of Diastereomers are Formed in Reactions of Some Pentane Compounds - 1

Experimental - 4

Summary - 7

II. The Preparation of Cyclopropene - - - - - - - - - - - - - - - - - - 8

Experimental - 11

Acknowledgment - 22

Summary - 23

Bibliography - 24

III. The Thermal Decomposition of Trans-1,2-cyclobutane bis-(trimethylammonium) Hydroxide - - - - - - - - - - - - - - - - - - 25

Experimental - 27

Acknowledgment - 37

Summary - 38

Bibliography - 39

Propositions - 40

The Isomeric 2,3-Epoxypentanes and 2-Pentenes. The Extent to which Mixtures of Diastereomers are Formed in Reactions of Some Pentane Compounds.

[Reprinted from the Journal of the American Chemical Society, 63, 22 (1941).]

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, NO. 782]

The Isomeric 2,3-Epoxypentanes and 2-Pentenes. The Extent to which Mixtures of Diastereomers Are Formed in Reactions of Some Pentane Compounds

BY H. J. LUCAS, M. J. SCHLATTER AND R. C. JONES

The isomeric *cis* and *trans*-2-pentenes have been the subject of numerous investigations.[1-6] Their preparation from the isomeric 2,3-epoxypentanes analogous to the preparation of *cis* and *trans*-2-butene from *trans* and *cis*-2,3-epoxybutane,[7] and from *cis* and *trans*-2,3-epoxybutane[8] has been accomplished. In addition, a study has been made of the extent to which a single reaction only takes place during a given chemical change, that is to say, if the change takes place with complete retention of configuration or with complete inversion of configuration, whichever the case may be. This could not be done for any single chemical change, however, but only for a group of two or more changes.

The changes investigated are shown in Fig. 1. Here only one of the two antipodes of *dl*-mixtures is shown. The configurations have been assigned on the basis that they are analogous to the configurations of the corresponding butane derivatives, for no evidence is available from these reactions or from the physical properties of the pentane derivatives themselves. This assignment of configuration to the pentenes, however, agrees in general with those made previously.[1,3,4,5b,6c,9] Walden inversions are indicated by the conventional arrow and circled shaft. The dotted arrows indicate that the reaction was not tried, but is predicted.

Figure 1 shows how each isomeric 2,3-epoxypentane can be converted into *cis* and *trans*-2-pentene by two different paths. One path involves the following steps: oxide $\xrightarrow{-O-}$ glycol $\longrightarrow$ diacetate $\xrightarrow{-O-}$ dibromide $\xrightarrow{-O-}$ 2-pentene. The other path is: oxide $\xrightarrow{-O-}$ bromohydrin $\longrightarrow$ dibromide $\xrightarrow{-O-}$ 2-pentene. In the first case three inversions are involved and in the second, two inversions. It is possible to pass from any one compound shown to any other compound (for this purpose each bromohydrin mixture is regarded as a compound) if it can be assumed that hypobromous acid adds to 2-pentene with one inversion, as it does to 2-butene.[8] The step involved here, *viz.*, 2-pentene $\xrightarrow{-O-}$ bromohydrin, was not investigated. Although it would be possible to prepare the *cis* oxide from the *trans* oxide, and *vice versa*, and also the *cis*-2-pentene from the *trans*-2-pentene, and *vice versa*, no product would be entirely free of its isomer, as discussed later.

The starting materials for the cycle were the *cis*- and *trans*-2,3-epoxypentanes, which were obtained as 100% and 98% pure products, respectively, by fractional distillation at 200 mm. of a mixture of the two isomers.[10] This mixture was obtained from a mixture of the isomeric 2-pentenes[11] through the chlorohydrins by the procedure employed with the corresponding C_4 compounds.[7] The much greater separation of the boiling points of the oxides (4.9 at 200 mm. and 5.2° at 748 mm., Table II) as compared to 0.6° in the case of the 2-pentenes, shows the advantage of fractionating the oxides.

The lower boiling oxide, approximately 75% of the total, was assigned the *trans* configuration and the higher boiling oxide the *cis* configuration, analogous with the butene oxides.[7,12]

The stereochemical relationship between *trans*-2-pentene, *trans*-2,3-epoxypentane, and the intermediate chlorohydrin presumably is correctly

(1) (a) Bourguel, *Bull. soc. chim.* [4] **41**, 1475 (1927); (b) Bourguel, Grédy and Piaux, *Compt. rend.*, **195**, 129 (1932); (c) Grédy, *Bull. soc. chim.*, [5] **2**, 1029 (1935).

(2) Clark and Hollonquist, *Trans. Roy. Soc. Can.*, [3] **24**, Sect. 3, 1115 (1930).

(3) Kharasch, Walling and Mayo, THIS JOURNAL, **61**, 1559 (1939).

(4) Lauer and Stodola, *ibid.*, **56**, 1215 (1934).

(5) (a) Lucas and Moyse, *ibid.*, **47**, 1459 (1925); (b) Lucas and Prater, *ibid.*, **59**, 1682 (1937).

(6) (a) Sherrill, Otto and Pickett, *ibid.*, **51**, 3023 (1929); (b) Sherrill, Baldwin and Haas, *ibid.*, **51**, 3034 (1929); (c) Sherrill and Matlock, *ibid.*, **59**, 2134 (1937); (d) Sherrill and Launspach, *ibid.*, **60**, 2562 (1938).

(7) Wilson and Lucas, *ibid.*, **58**, 2396 (1936).

(8) Winstein and Lucas, *ibid.*, **61**, 1576 (1939).

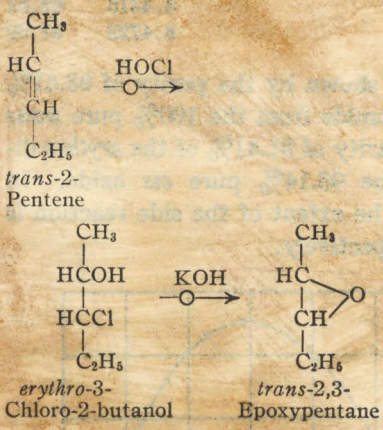
(9) Carr and Stücklen, *ibid.*, **59**, 2138 (1937).

(10) The authors are indebted to Mr. Herbert Sargent for his assistance in carrying out this separation.

(11) From secondary amyl alcohol, by the method of Norris and Reuter, THIS JOURNAL, **49**, 2624 (1927).

(12) Brockway and Cross, *ibid.*, **59**, 1147 (1937).

represented by the scheme, Fig. 1, analogous with the C_4 compounds, for it has been shown that *trans*-2-butene yields *trans*-2,3-epoxybutane,[7] and that one inversion accompanies the formation of *cis*-2,3-epoxybutane from the corresponding bromohydrin.[8]



Presumably a similar relationship holds for *cis*-2-pentene and *cis*-2,3-epoxypentane.

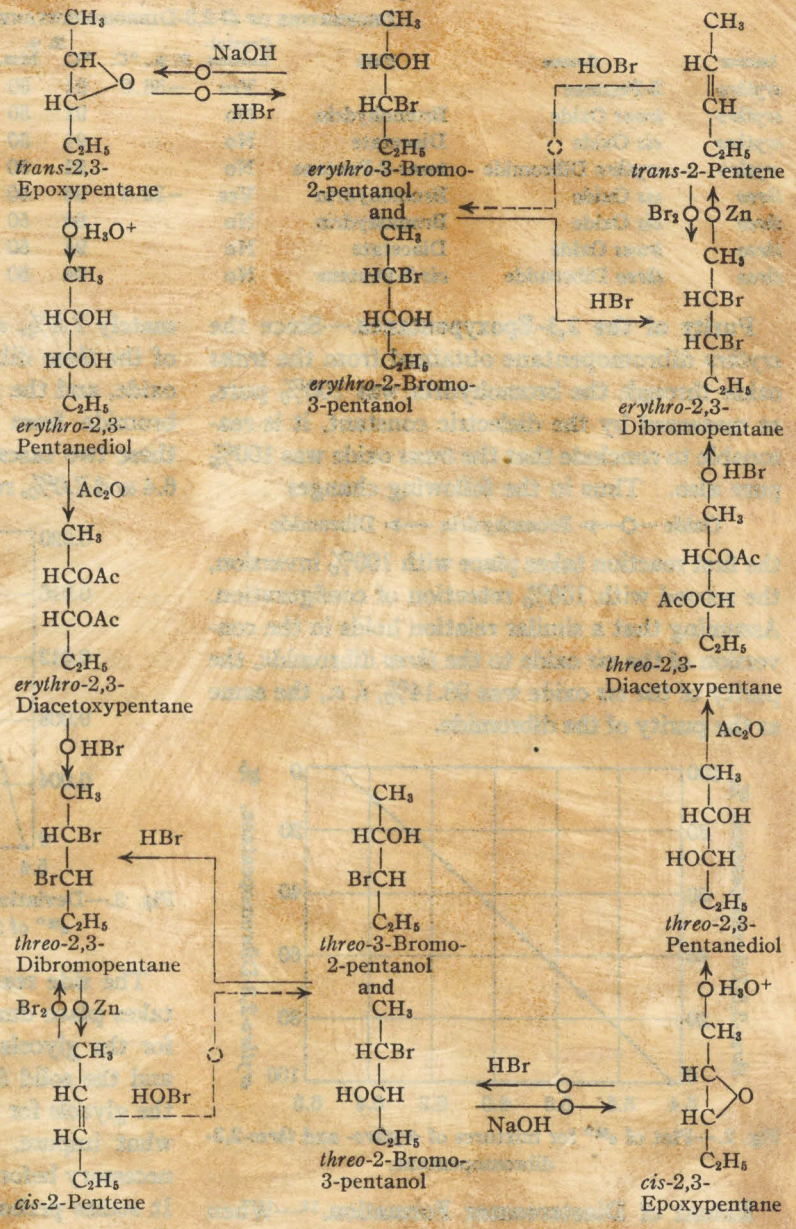
The composition of the original crude 2-pentene mixture therefore is approximately 75% *trans* and 25% *cis*, on the basis of the oxide composition. This agrees with conclusions drawn previously.[5b,6c,d]

The conversion of the epoxypentanes to dibromopentanes by both methods (Fig. 1) presented no particular difficulty, for all the reactions proceed at room temperature, although slowly in the case of hydrobromic acid with bromohydrins and diacetates, and all the products can be purified by distillation at 50 mm. without alteration. In order to obtain the two dibromides in a high state of purity each was purified by a systematic process of crystallization at −80° from aqueous methanol. Kharasch, Walling and Mayo[3] have used this solvent for purifying the higher melting (*threo*) isomer.

The purity of different specimens of the diastereomeric 2,3-dibromopentanes can be ascertained by comparing their properties with the properties of the specimens purified by crystallization. As in the case of the 2,3-dibromobutanes,[8,13] the property most useful for this purpose is the dielectric constant, ϵ, which differs markedly for the two *dl* forms. On the other hand, the refractive index and specific gravity values differ by only small amounts (Table I).

The dielectric constant of mixtures of the dibromides deviates slightly from linearity, as shown in Fig. 2. The corrections to be applied, as shown in Fig. 3, reach a maximum at a composition of 50%. This correction, although small, must be taken into account. The error of the method is less than 0.1%.

Fig. 1.



(13) Wood and Winstein, THIS JOURNAL, **62**, 548 (1940).

TABLE I

PROPERTIES OF *dl*-2,3-DIBROMOPENTANES

Isomer	Source	Path	Crystallization	F. p., °C.	B. p. °C.	B. p. Mm.	$n^{20}D$	d^{25}_4	ϵ_2	Purity, %
erythro	2-Pentene		Yes	−56.0	91	50	1.5087	1.6724	5.4288	100.00
erythro	*trans* Oxide	Bromohydrin	No		91	50			5.4288	100.00
erythro	*cis* Oxide	Diacetate	No		91	50			5.5151	91.41
erythro	*erythro* Dibromide	*trans*-2-Pentene	No		91	50			5.4476	98.13
threo	*cis* Oxide	Bromohydrin	Yes	−32.4	94	50	1.5089	1.6745	6.5072	100.00
threo	*cis* Oxide	Bromohydrin	No		94	50			6.4857	98.14
threo	*trans* Oxide	Diacetate	No		94	50			6.4316	93.61
threo	*threo* Dibromide	*cis*-2-Pentene	No		94	50			6.4723	97.09

Purity of the 2,3-Epoxypentanes.—Since the *erythro* dibromopentane obtained from the *trans* oxide through the bromohydrin was 100% pure, as measured by the dielectric constant, it is reasonable to conclude that the *trans* oxide was 100% pure also. Thus in the following changes

Oxide —O→ Bromohydrin ⟶ Dibromide

the first reaction takes place with 100% inversion, the second with 100% retention of configuration. Assuming that a similar relation holds in the conversion of the *cis* oxide to the *threo* dibromide, the purity of the *cis* oxide was 98.14%, *i. e.*, the same as the purity of the dibromide.

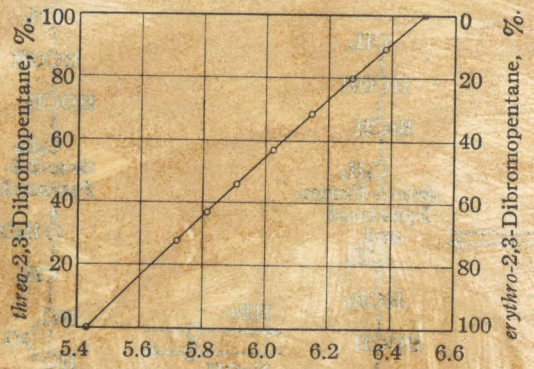


Fig. 2.—Plot of $\epsilon^{25°}$ for mixtures of *erythro*- and *threo*-2,3-dibromopentane.

Extent of Diastereomer Formation.[14]—When the 2,3-epoxypentanes are converted into bromohydrins with hydrobromic acid, and the latter to 2,3-dibromopentanes with hydrobromic acid, only one product results, as pointed out above. However, when the dibromide is made from the oxide through the steps

Oxide —O→ Glycol ⟶ Diacetate —O→ Dibromide

the extent of diastereomer formation is approximately 7.5%, as shown by the purity of 93.61% of the *threo* dibromide from the 100% pure *trans* oxide, and the purity of 91.41% of the *erythro* dibromide from the 98.14% pure *cis* oxide. In these two cases the extent of the side reaction is 6.4 and 7.0%, respectively.

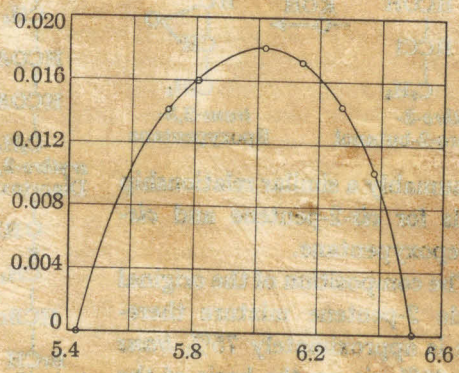


Fig. 3.—Deviation of $\epsilon^{25°}$ from linearity plotted against $\epsilon^{25°}$ of 2,3-dibromopentane mixtures.

The side reaction in the cycle above probably takes place during the opening of the oxide ring, for the glycols themselves did not melt sharply and the solid 3,5-dinitrobenzoates prepared from the glycols for identification purposes were somewhat impure. Five or six crystallizations were necessary before the melting points were constant. It seems probable therefore that the glycols and diacetates were not better than 93% pure.

The extent of the side reaction in the cycle of changes involved in preparing the pentene from the pure dibromide and then reconverting the hydrocarbon to dibromide is 2 or 3%:

2,3-Dibromopentane —O→ 2-Pentene —O→ 2,3-Dibromopentane

From Table I it can be seen that the purity of the final dibromide from the initially pure *erythro* and *threo* dibromide is 98.13 and 97.09% respectively. Although it is not possible from the data available to decide at which step the side reaction comes in, it seems reasonable to believe that it accompanies

(14) The expression diastereomer formation is used to indicate that the replacement at one of the two asymmetric carbon atoms is less than 100% retention or inversion of configuration, whichever the case may be, *i. e.*, a second reaction accompanies the main reaction. Essentially this is equivalent to racemization, but since these compounds are optically inactive, no change in rotatory power is observable.

the addition of bromine to the hydrocarbon. In any case, the hydrocarbons are better than 97% pure.

The extent of the side reaction in the following cycle is zero, within experimental error:

2,3-Epoxypentane —O→ Bromohydrin —O→ 2,3-Epoxypentane

The refractive index of each of the final epoxypentanes was identical with the initial value. Although from the refractive index values alone (1.3867 and 1.3941; see also Table II) a contamination up to 2% might not be detected, the constancy of the refractive index in the different fractions obtained by fractional distillation of each oxide indicates that the products were essentially 100% pure.

cis- and *trans*-2-Pentenes.—These were obtained from the corresponding 2,3-dibromopentanes by the action of metallic zinc. They were distilled in an all glass apparatus in an atmosphere of nitrogen. The physical constants of the hydrocarbons are shown in Table VI.

There is a difference of 0.6° in the boiling points of the two hydrocarbons. Compared to the values observed by others, the boiling points recorded here are slightly lower. The refractive index of the *trans* isomer agrees well with the values of others,[3,4,5] but that of the *cis* isomer is higher than any other value.[3,5b,6c,6d] Hydrogenation of 2-pentyne[1c,3,6d] does not appear to give as pure *cis*-2-pentene as does debromination of the *threo* dibromide.[3]

Experimental

2-Pentene.—Secondary amyl alcohol was fractionally distilled and the fraction distilling at 115–120° was dehydrated according to the method of J. F. Norris and Reuter.[11] 520 g. (5.9 mole) of the alcohol was added slowly to a cold mixture of 600 ml. water, 600 ml. concentrated sulfuric acid and 3 g. diatomaceous earth in a liter 3-necked flask equipped with safety tube and short Hempel column attached to a long condenser, the latter attached to a 1-liter flask surrounded by ice. The mixture was heated at 90–110° for about three hours, or until no more pentene distilled; crude yield 398 g. (5.7 moles). This was shaken with dilute sodium hydroxide, dried with calcium chloride and combined with several other batches. This was subjected to careful fractional distillation so as to obtain a fraction over the range, 35.5–35.8° at 742 mm.; yield, 55%.

2-Pentene Chlorohydrin.—The mixture of isomeric 2-pentenes (4.5 kg.) was converted into the mixed chlorohydrins in the usual manner.[7] Working in batches of 250 g. (3.57 moles) of 2-pentene, 392 g. of H. T. H. (65% available chlorine),[15] 600–700 g. of a mixture of water and ice, and 240 g. (4.0 moles) of glacial acetic acid, a 47.5% yield of mixed chlorohydrin, b. p. 64–71° at 30 mm., was realized. The total amount was about 3900 g.

2,3-Epoxypentane.—A total of 3850 g. (31.4 moles) of the mixed chlorohydrins was converted into the oxide[7] in batches as follows: In a 3-liter 3-necked flask provided with a mercury seal stirrer, a bent tube leading to a condenser for downward distillation, a dropping funnel, and a thermometer extending nearly to the bottom of the flask, 1350 g. (24 moles) of technical potassium hydroxide flakes was dissolved with stirring in 675 ml. of water. With the temperature in the flask at about 125°, 625 g. (5.10 moles) of 2-pentene chlorohydrin was added slowly with agitation over a period of three hours. Wet 2,3-epoxypentane distilled and was partially dried with potassium carbonate. The rest of the water was removed by cooling the oxide to −80° in a carbon dioxide–alcohol freezing mixture and drawing off the dry oxide from the ice crystals through a filter stick while the mixture was still in the cooling-bath. The yield of mixed 2,3-epoxypentane was 2612 g. (30.4 moles) or 96%.

The Isomeric 2,3-Epoxypentanes.—The mixture was fractionally distilled through a four-foot, total reflux column filled with glass helices and equipped with a manostat which maintained the pressure within ±0.5 mm. Fractionation was carried out at 200 mm. because of the possibility that some rearrangement might take place if the mixture were subjected to extended heating at higher temperature. Four fractionations resulted in almost complete separation of the two isomers.

The lower boiling oxide was obtained over a range of less than 0.1°, the higher boiling over a range of about 0.2°. There was a loss of about 50% during the fractionations which were conducted intermittently over a period of more than a year. The approximate weight of pure *trans* isomer obtained was 900 g. and of the *cis* isomer, 200 g. These oxides are pleasant smelling liquids, slightly soluble in water, readily soluble in the usual organic solvents.

TABLE II

2,3-Epoxypentane	B. p., °C., at mm. 748	200	$n^{20}D$	$n^{25}D$	d^{25}_4
cis	85.4	48.6	1.3941	1.3915	0.8195
trans	80.2	43.7	1.3867	1.3840	0.8031

From the form of the distillation curve, it was determined that the original oxide mixture was approximately 75% *trans*. This indicates that the pentene mixture obtained from secondary amyl alcohol is about 75% *trans*-2-pentene.

The Isomeric 2,3-Pentanediols.—240 g. (2.78 moles) of *trans*-2,3-epoxypentane, 1500 ml. of water and 0.2 ml. of concentrated sulfuric acid were stirred vigorously at room temperature for eight hours in a 2-liter flask equipped with a reflux condenser and mechanical stirrer. The initially heterogeneous system became homogeneous after three hours. The acid was neutralized with sodium hydroxide and the water distilled off on a water pump, keeping the bath temperature below 70°. On distilling the residue at 10 mm. from a Claisen flask, *erythro*-2,3-pentanediol distilled as a viscous liquid; yield, 236 g. (81%). A like yield was obtained with the *threo* isomer, from the *cis* oxide.

Both compounds are viscous liquids, readily soluble in

(15) Calcium hypochlorite, Mathieson Alkali Works, Inc.

water, alcohol and isopropyl ether. Attempts to crystallize them were unsuccessful. Each reacted readily when heated with 3,5-dinitrobenzoyl chloride to yield a solid di-3,5-dinitrobenzoate, which required five or six crystallizations from pyridine before the melting point was constant.

TABLE III

dl-2,3-Pentanediol	B. p., °C., 10 mm.	$n^{20}D$	d^{25}_4	M. p. (cor.) of di-3,5-dinitrobenzoate, °C.
erythro	89	1.4431	0.9782	207
threo	83	1.4320	0.9654	160.5

The Isomeric 2,3-Diacetoxypentanes.—Fifty-two grams (0.50 mole) of *erythro*-2,3-pentanediol and 117 g. (1.15 mole) of freshly distilled acetic anhydride were mixed in a 500-ml. flask equipped with reflux condenser and drying tube, and two drops of concentrated sulfuric acid added.[7] The mixture began to reflux spontaneously and was kept under control by cooling with an ice-bath when necessary. The mixture was allowed to stand overnight, the acetic acid and excess acetic anhydride distilled off using a water pump and the residue fractionally distilled through a short Vigreux column at 10 mm., yielding 83 g. of *erythro*-2,3-diacetoxypentane (88%). A like yield was obtained with the *threo* isomer.

Both compounds are liquids less viscous than the diols, but more viscous than the dibromides made from them. They are insoluble in water, readily soluble in the usual organic solvents. The dielectric constant ϵ, has been reported previously.[13]

TABLE IV

dl-2,3-Diacetoxypentane	B. p., °C. at 10 mm.	$n^{20}D$	d^{25}_4	ϵ^{25}
erythro	85	1.4167	1.0022	6.734
threo	89	1.4195	1.0073	5.228

The 2,3-Dibromopentanes from the 2,3-Diacetoxypentanes.—In 350 ml. of hydrobromic acid saturated with hydrogen bromide[16] at 0° was dissolved 125.5 g. (0.67 mole) of *erythro*-2,3-diacetoxypentane. The liquid was sealed in an ampoule made from a 500-ml. round bottom flask, allowed to warm to room temperature and shaken occasionally for two days. After two or three hours the liquid turned cloudy, due to the separation of dibromopentane, and later a distinct second phase was visible. In some preparations of dibromide, from diacetates, bromohydrins or oxides, the dibromide phase was lighter, in others heavier, than the aqueous phase, depending upon the degree of saturation with hydrogen bromide. The ampoule was opened, resaturated with hydrogen bromide at 0°, sealed and shaken occasionally for four days, at which time both phases were clear and the reaction was over. The organic phase was always the lighter. The ampoule was chilled, opened and the phases separated without dilution in a separatory funnel. The organic phase after washing with water and dilute sodium carbonate and drying with calcium chloride, was fractionated at reduced pressure through a 60-cm. total reflux column packed with glass helices to yield 138 g. (0.60 mole) of *threo*-2,3-dibromopentane, 90% of theory. A like yield was obtained with the *erythro* isomer. The physical constants are given in Table I and the purity is discussed in the first part of this paper.

(16) From bromine and tetralin.

The 2-Pentene Bromohydrins.—In a 500-ml. 3-necked flask fitted with a mechanical stirrer, dropping funnel and thermometer dipping into the reaction mixture was placed 200 ml. of 48% hydrobromic acid. Into the flask surrounded by an ice-bath, 86 g. (1 mole) of *trans*-2,3-epoxypentane was run in over a period of three hours, the temperature of the reaction mixture never rising above 5°. The mixture was stirred one hour longer and separated. The aqueous phase was diluted with 200 ml. of water and extracted with two 50-ml. portions of ether. A little anhydrous potassium carbonate was added to the extracts. After standing overnight, the ether phase was concentrated on a water-bath. The bromohydrin was distilled through a short Vigreux column at 10 mm., yielding 151 g. of *erythro* bromohydrin, 90% of theory. A like yield was obtained with the *threo* isomer. These compounds are liquids only slightly soluble in water, soluble in organic solvents. On standing for some time specimens of the bromohydrins became colored, some samples more quickly than others. The *erythro* isomer became blue-violet, the *threo*, wine red. When redistilled at 10 mm., the distillate was colorless, and the small undistilled residue was dark colored, almost black. On high dilution the characteristic color developed.

The physical constants, Table V, may have little significance for each preparation probably is a mixture of two compounds (Fig. 1). However, each acts as a pure substance to give a single oxide when heated with aqueous potassium hydroxide.

TABLE V

dl-2-Pentene bromohydrin	B. p., 10 mm., °C.	$n^{20}D$	d^{25}_4
erythro	59	1.4717	1.3654
threo	53	1.4758	1.3636

The 2,3-Dibromopentanes from the 2-Pentene Bromohydrins.—One hundred eighty ml. of 48% hydrobromic acid in a 300-ml. ampoule was sautrated with hydrogen bromide[16] at 0°, and 50 g. (0.30 mole) of *erythro*-2-pentene bromohydrin added. The ampoule was sealed and allowed to come to room temperature. Cloudiness developed in about one hour. The mixture was shaken occasionally for seven days. By this time both phases were clear. The product was worked up as described above, yielding 65 g. (0.28 mole) of *erythro*-2,3-dibromopentane, 94%. A like yield was obtained with the *threo* isomer. The physical constants are given in Table I, and the purity is discussed in the first part of this paper.

The 2,3-Dibromopentanes from the 2,3-Epoxypentanes.—The dibromides may be prepared directly from the epoxides without isolating the bromohydrins. To 500 g. of 48% hydrobromic acid in a 1-liter 3-necked flask equipped with dropping funnel, thermometer and mechanical stirrer and surrounded by an ice-bath, was added 172 g. (2 moles) of *trans*-2,3-epoxypentane over a period of three hours, the temperature never rising above +5°. The mixture was transferred to an ampoule made from a 1-liter round-bottom flask, enough 48% hydrobromic acid added to make the volume about 750 ml. and the mixture saturated with hydrogen bromide.[16] The ampoule was sealed, then allowed to warm to room temperature. Cloudiness

appeared in one to three hours. The mixture was shaken occasionally over a period of three days. The ampoule was opened, again saturated with hydrogen bromide, sealed, allowed to warm to room temperature and shaken occasionally. At the end of three more days both phases were clear. The organic phase was worked up as before, and fractionally distilled through a 40-cm. Vigreux total-reflux column at 10 mm., to yield 428 g. of *erythro*-2,3-dibromopentane, 93%. A like yield was obtained with the *threo* isomer. The physical constants are given in Table I, and the purity is discussed in the first part of this paper.

Crystallization of Dibromides.—The dibromides were diluted with one-half to two times their volume of methanol[3] in 250 ml. centrifuge bottles, and then cooled to −78° in carbon dioxide–isopropyl ether freezing mixtures. The liquids were seeded with crystals obtained by cooling small samples of the mixtures in liquid air until they were frozen solid and then placing them in the carbon dioxide–isopropyl ether mixtures. The chilled methanol solutions were stirred frequently to hasten crystallization and to prevent the formation of cakes. *threo*-2,3-Dibromopentane crystallized easily in a coarse, loose form, but the *erythro* isomer crystallized with more difficulty in leaflets which were harder to centrifuge. The more impure the dibromide, the longer the time required for complete crystallization. This varied from eight to ten hours for the 75% *erythro*-2,3-dibromopentane diluted with one-half volume of methanol to ten or fifteen minutes for the pure *threo*-2,3-dibromopentane diluted with one volume of methanol. The *erythro* isomer, because of its greater solubility (necessitating the use of more concentrated and therefore more viscous solutions) and lower melting point, was much more difficult to purify in good yield by crystallization than was the *threo* isomer. With both isomers, it was sometimes found advantageous to use methanol containing a small amount of water in place of pure methanol as a solvent.

When crystallization was thought to be complete, the crystals were loosened from the sides of the centrifuge bottle with a stirring rod and the mixture centrifuged rapidly for 2 to 5 min. in a centrifuge chilled with "dry ice." The supernatant liquid was poured off, the crystals washed with a small portion of methanol at −78°, the mixture centrifuged and the washings combined with the mother liquor. In this way a network of crystallizations was carried out, using the mother liquor from one crystallization for a less pure batch of dibromide. From time to time the dibromide crystals (after melting) were diluted with an equal volume of water, separated, washed with water, dried with calcium chloride and distilled at 50 mm. The dielectric constants were then determined and in this way the progress of the purification was followed. A network of about 35 or 40 crystallizations in all was made in the purification of each isomer.

The centrifuge used in this work was heat insulated and chilled by keeping the floor of the shield covered with a considerable amount of powdered "dry ice." In addition, the heavy bronze centrifuge cups were cooled in carbon dioxide–isopropyl ether before placing the chilled centrifuge bottles in them.

In order to obtain a large amount of the pure *erythro* dibromide, crude 2-pentene, from *s*-amyl alcohol and sulfuric acid,[11] was converted into the dibromide and this was subjected to fractional crystallization. The crystallization of the *erythro* isomer was difficult at first. The method probably would work better if the dibromide mixture were subjected beforehand to fractional distillation so as to remove some of the *threo* isomer.

The Dielectric Constants.—These were determined according to the procedure described by Wood and Winstein, using the same apparatus.[13] It was found that the dielectric constant of mixtures is not strictly additive (Fig. 2) but that correction must be made. The maximum deviation from a straight line is about 1.5% for a 50–50 mixture (Fig. 3). There is less than 0.1% error in the analysis of mixtures of the two *dl*-2,3-dibromopentanes by means of the dielectric constant, when the proper correction is made. This method of analysis is superior to any others because of accuracy and rapidity, and also because the material can be recovered.

***cis* and *trans*-2-Pentene.**—In a 500-ml. flask equipped with a dropping funnel and a 15-cm. Vigreux column with a cold finger condenser cooled by ice water, was placed 75 g. (1.15 mole) of 10 mesh zinc shot and 250 ml. of absolute alcohol. The mixture was held at 70° by means of a water-bath while 230 g. (1.0 mole) of *erythro*-2,3-dibromopentane was added over a period of one and one-half hours. The pentene distilled out as formed along with some alcohol, and was collected in a receiver at −80°. The condensate was washed with three 100-ml. portions of ice water and allowed to stand overnight with magnesium perchlorate. The pentene was fractionated in an atmosphere of nitrogen without removing the solid, through a 60-cm. total reflux column packed with glass helices. The *trans*-2-pentene which distilled completely with no range, weighed 52 g., 74% of theory. For preparing *cis*-2-pentene, 140 g. (0.61 mole) of the *threo* dibromide was taken. A like yield resulted. The thermometer used was calibrated against a thermometer having a Bureau of Standards calibration. The constants are shown in Table VI.

TABLE VI

2-Pentene	B. p. °C.	Mm.	$n^{20}D$	d^{20}_4	d^{25}_4
cis	36.08	744	1.3828	0.6554	0.6504
trans	35.48	744	1.3798	0.6475	0.6426

The 2,3-Dibromopentanes from the *cis*- and *trans*-2-Pentenes.—Into a 50-ml. 3-necked flask surrounded by an ice-bath and equipped with a mechanical stirrer and two dropping funnels, was run in simultaneously 13.0 g. (0.186 mole) of *trans*-2-pentene and sufficient bromine to maintain at all times a slight excess of bromine.[17] The addition required about one and one-half hours. A small amount of hydrogen bromide was given off. The dibromide was shaken with sodium bisulfite solution, water and dilute sodium carbonate, separated, dried with calcium chloride and distilled. The product, *erythro*-2,3-dibromopentane, weighed 37.0 g., 87%. A like yield was obtained with the *threo* isomer. The properties of these dibromides are given in Table I. The purity is discussed in the first part of this paper.

(17) In order to minimize the coupled reaction of addition and substitution, which is aided by excess of pentene and by rapidity of addition, the bromine should be in slight excess and the reaction should be carried out slowly in diffused light.

The 2,3-Epoxypentenes from the 2-Pentene Bromohydrins.—The procedure is similar to that described for preparing the epoxide from the chlorohydrin. When 33.4 g. (0.2 mole) of *erythro*-2-pentene bromohydrin was added slowly with agitation to a solution of 56 g. (1 mole) of potassium hydroxide pellets in 25 ml. of water at 100–110° in a 100-ml. 3-necked flask equipped with mercury sealed stirrer, thermometer, dropping funnel and condenser arranged for distillation, wet epoxypentane distilled over. This was dried with magnesium sulfate and distilled through a 30 cm. Vigreux column with finger condenser at a reflux ratio of ten, yielding 12 g. (70% yield) of *trans*-2,3-epoxypentane, 80% of which distilled between 80.0 and 80.2° at 746 mm. Nothing came over above 80.2°. The refractive index of the last 2 ml. of distillate was $n^{25}D$ 1.3840, identical with the value for pure *trans*-2,3-epoxypentane (Table II). Thus the reaction product was pure *trans*-2,3-epoxypentane, for any *cis* isomer, had it been present, would have become concentrated in the last 2 ml. of distillate.

Similarly 18 g. (0.108 mole) of *threo*-2-pentene bromohydrin with 35 g. (0.6 mole) of potassium hydroxide in 20 ml. of water gave 7 g. (0.08 mole) of *cis*-2,3-epoxypentane, distilling 85.2–85.4° at 750 mm. As soon as the water was removed, the rest of the distillate (90% of the total) was collected in two approximately equal fractions. The refractive index of these two was $n^{25}D$ 1.3915, identical with the value for pure *cis*-2,3-epoxypentane.

Summary

The oxide of 2-pentene has been separated into the *cis* and *trans*-2,3-epoxypentanes by fractional distillation.

cis-2-Pentene and *trans*-2-pentene have been synthesized from the isomeric 2,3-epoxypentanes.

With hydrobromic acid, *trans*-2,3-epoxypentane is converted into 100% pure *erythro*-2,3-dibromopentane and *cis*-2,3-epoxypentane into *threo*-2,3-dibromopentane.

Through the steps, 2,3-pentanediol, 2,3-diacetoxypentane and 2,3-dibromopentane the *cis* oxide yields the *dl-erythro* dibromide, and the *trans* oxide the *dl-threo* dibromide mainly. The formation of the other isomer takes place to the extent of about 7%.

When a pure *dl*-2,3-dibromopentane is converted into the corresponding 2-pentene, and this is allowed to react with bromine, the resulting dibromide contains 2 or 3% of the other isomer.

When a pure *cis* or *trans*-2,3-epoxypentane is converted into the bromohydrin and the oxide regenerated from this, the resulting oxide is pure.

Measurement of the dielectric constant is an accurate method of analysis of mixtures of the diastereomeric *dl*-2,3-dibromopentanes.

PASADENA, CALIFORNIA RECEIVED JUNE 5, 1940

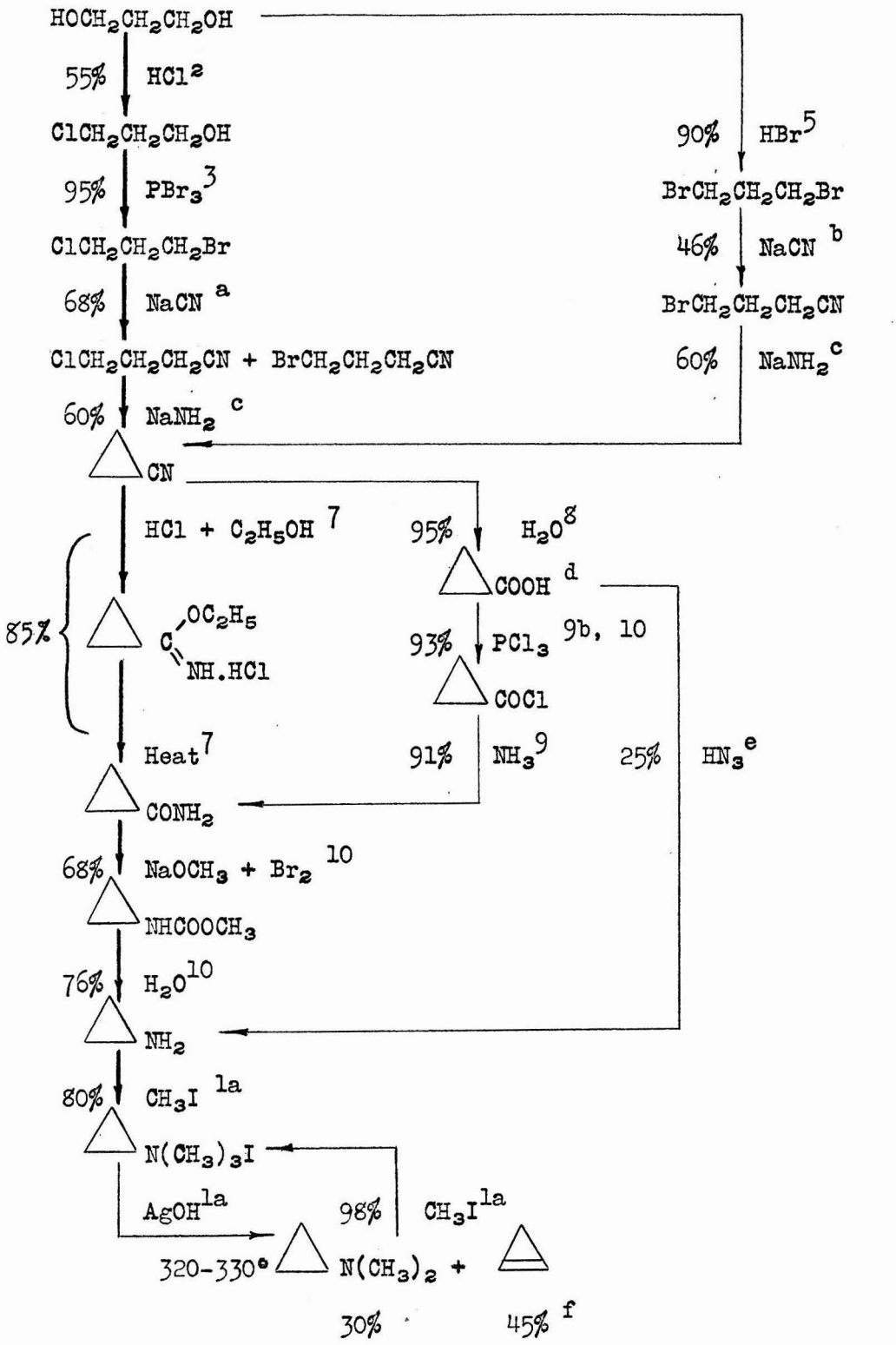
The Preparation of Cyclopropene

Cyclopropene was synthesized in 1922 by Demjanow and Dojarenko[1a] and our entire knowledge regarding this interesting compound is due to the researches[1] carried out by these Russian scientists. In order to make it available in amounts sufficient for an extended investigation of its physical and chemical properties, the conditions attending its formation were studied in some detail. The steps employed in the synthesis are outlined in the accompanying chart.

The yields indicated are conservative, reproducible values obtained on a preparative scale as the result of four to thirty runs at each step. The overall yield based on these figures and choosing the path (bold-faced arrows) found to be most convenient is 3.3%. Taking into account the quaternary iodide recovered from the dimethylcyclopropylamine formed in the last step, this value becomes 4.7%.

From a detailed study of the decomposition of the quaternary base on platinized asbestos it was shown that the optimum temperature for cyclopropene formation is 320-330°. Dimethylcyclopropylamine and methylacetylene which had previously been reported[1a] were also obtained. A more detailed discussion of the thermal decomposition is given in the experimental part.

Pure cyclopropene was obtained by distilling the hydrocarbons through a Podbielniak column. It distilled at -36° to -35° at 744 mm. and analyzed for C_3H_4. In confirmation of Demjanow and Dojarenko[1] it was found that the olefine reacts energetically with bromine and polymerizes readily. It could not be conveniently stored, even at -78°.



---

a The method of Allen[4] gives γ-chlorobutyronitrile in the yield indicated. A modification giving a similar yield of a mixture of

γ-chloro and γ-bromobutyronitrile (which is equally useful in this synthesis) was employed to facilitate the handling of large batches.

b The method used was a modification of the procedure of Gabriel.[6]

c The method used was essentially a large scale modification of the method of Cloke et al.[3] This procedure was equally satisfactory with the pure γ-halogen nitriles or mixtures of them.

d The yields of this acid by decarboxylation of cyclopropane-1, 1-dicarboxylic acid are unsatisfactory. The reaction is being investigated.

e This step has not been previously described in the literature. The conversion of cyclobutanecarboxylic acid directly to the corresponding amine has been reported recently by Heisig.[11]

f This yield is based on dibromocyclopropane isolated.

The[1a] statement that cyclopropene can be regenerated from dibromocyclopropane by treatment with zinc and alcohol was not confirmed. This procedure gave a product consisting to a large extent of cyclopropane. The problem of the reconversion of the stable dibromide to cyclopropene is of importance in connection with the handling of large amounts of the latter and is the subject of further studies.

Experimental*

Trimethylene Chlorohydrin was prepared by the methods of Marvel and Calvery[2] and of Hultman, Davis and Clarke[12]. The treatment of trimethylene glycol with the theoretical amount of phosphorus trichloride gave the less satisfactory yield of 40%. An attempt to use thionyl chloride, either alone or in conjunction with pyridine, gave, in addition to chlorohydrin, other products not easily separated by fractional distillation. These interfered with subsequent steps.

Trimethylene Chlorobromide was prepared in twenty mole batches by the method of Cloke et al[3] and was used without purifying by distillation.

γ-Chloro and γ-Bromobutyronitrile from Trimethylene Chlorobromide.--To 765 g. (15.6 moles) of technical sodium cyanide eggs in 1350 ml. of warm water in a 12-liter round bottom flask surrounded by a water bath and equipped with a large capacity reflux condenser, was added 3500 ml. of 96% alcohol and 2360 g. (15 moles) of trimethylene chlorobromide. The mixture was warmed and the ensuing vigorous reaction controlled by addition of ice to the bath and by playing a stream of

* Melting points reported in this paper are corrected.

water on the upper part of the flask. After the reaction had subsided, refluxing was continued for an additional hour and then 3-1/2 liters of alcohol rapidly distilled off. The oil was decanted from the aqueous and solid phases in the flask, these latter extracted thoroughly with chloroform and the extract combined with the oil. The resulting solution was washed with half saturated calcium chloride and with water, the solvent removed and the residue fractionated at reduced pressure; 1193 g. of product (b.p. 89-115°/26 mm.) was obtained. Analysis of the mixture by fractionation showed it to consist of 67.5% of γ-chlorobutyronitrile (b.p. 94°/26 mm.) and 32.5% of γ-bromobutyronitrile (b.p. 108°/26 mm.). This corresponds to a combined yield of 69%.

γ-Bromobutyronitrile from Trimethylene Dibromide.*--To 808 g. (4 moles) of trimethylene dibromide in 3200 ml. of 96% alcohol was added 160 g. (3.14 moles) of sodium cyanide in 300 ml. of water. The mixture was shaken thoroughly for five minutes, permitted to react at room temperature for one hour and then refluxed for 45 minutes. After cooling, the mixture was poured into 9 liters of water, and extracted repeatedly with chloroform. Fractionation at reduced pressure gave 268 g. of recovered trimethylene dibromide and 188 g. of γ-bromobutyronitrile (b.p. 104-107°/23 mm.)(47% on the basis of trimethylene dibromide consumed).

---

* The following procedure was worked out in this laboratory by Messrs. Raymond Clinton and Thurston Skei.

Cyclopropyl Cyanide from the γ-Halogenbutyronitrile Mixture.--
One liter of liquid ammonia and 0.5 g. of hydrated ferric nitrate were placed in a two-liter three-neck flask equipped with mechanical stirrer and dry ice reflux condenser protected by a soda lime tower; 92 g. (4 moles) of sodium shavings was added over a period of three quarters of an hour. The mixture was stirred until the blue color had disappeared (one or two hours). In a similarly equipped three-liter three-neck flask (reaction flask) were placed 1-1/2 liters of liquid ammonia and 4.25 moles of γ-halogenbutyronitrile mixture (pure γ-chloro- or γ-bromobutyronitrile can be substituted for the mixture). The flasks were connected by a 10 mm. glass tube reaching to the bottom of the sodamide flask and extending 1 cm. through a stopper in one neck of the other. By means of positive air pressure, controlled by a finger over an air by-pass, the sodamide suspension was forced over into the reaction flask at such a rate that about one hour was required for the addition; constant stirring was maintained in both flasks. The sodamide flask was rinsed out with 300 ml. of liquid ammonia, and the washing added to the reaction mixture. Stirring was continued for four hours*, during the first two hours of which the mixture refluxed gently. During the second two hours no more dry ice was added to the traps and slow evaporation of ammonia took place. The sodamide addition tube was replaced with a dropping funnel and one liter of anhydrous ether slowly added to the solution. The reaction mixture

* With pure γ-chlorobutyronitrile and γ-bromobutyronitrile, the time of stirring should be two and six hours respectively (time of refluxing zero and 4 hours).

was rapidly filtered through a sintered glass funnel and the filter cake washed with anhydrous ether. The ammonia and ether were removed on a water bath*, the residue filtered** and then fractionated at 80 mm.; 149 g. of cyclopropyl cyanide (b.p. 69-70°/80 mm.) (61% yield on the basis of γ-halogenbutyronitrile actually used) and 0.6 mole of γ-halogenbutyronitrile were obtained. A rosin-like residue was left in the distilling flask.

Cyclopropanecarboxylic Acid.--To 336 g. (6 moles) of potassium hydroxide in 1200 ml. of water, was added 268 g. (4 moles) of cyclopropyl cyanide and the mixture refluxed. After initiation of the reaction it was found necessary to cool until the vigorous refluxing subsided. The solution was heated for six hours, cooled in an ice bath and 1500 ml. (4.5 moles) of 6 N sulfuric acid slowly added. Continuous extraction with ether and fractionation of the ether extract yielded 332 g. (96%) of cyclopropanecarboxylic acid (b.p. 80-81°/13 mm.).

Cyclopropanecarboxamide from the Acid Chloride.--The acid chloride*** was prepared by the method described by Lipp et al[10]. The amide was prepared by saturating a solution of 171 g. (1.64 moles) of the acid

---

* In one experiment using pure bromonitrile, crystals of organic material separated out at this point. These crystals were filtered off and recrystallized from absolute alcohol, m.p. 134°C.
Anal. Calcd. for $C_4H_9N_2Br$: C, 29.11; H, 5.50; N, 16.98. Found: C, 29.39; H, 5.79; N, 16.23.
This compound dissolved readily in water and gave an immediate test for bromide ion. The substance is probably cyclopropylcarbamidine hydrobromide, $\Delta C(NH_2)^+Br^-$.

** With pure γ-chlorobutyronitrile, no solid separates at this point.

*** Commercial thionyl chloride gave none of the desired product; cf. Skraup and Binder.[13]

chloride in 1500 ml. of anhydrous ether with ammonia at 0° under anhydrous conditions. Solvent was removed in vacuo and the residual fine white powder extracted with chloroform in a Soxhlet extractor. Large colorless prisms separated out; yield 126.5 g. (91%) m.p. 125°.

Cyclopropanecarboxamide from Cyclopropyl Cyanide.--Ethyl imidocyclopropane carboxylate hydrochloride was prepared from 67 g. (1 mole) of cyclopropyl cyanide by the method[7] of Cloke and coworkers. Without isolation of the imido ester salt, volatile materials were removed at reduced pressure, and the solid residue heated in the same vessel in an oil bath at 130-150°; a stream of ethyl chloride was smoothly given off. To complete the decomposition, the temperature was raised to 165° and the pressure reduced to 20 mm. A small amount of ethyl cyclopropane carboxylate was trapped out. The crystalline residue on recrystallization from ethanol gave 75 g. (87%) of cyclopropanecarboxamide.

Cyclopropylamine from Cyclopropanecarboxamide.--The urethane was prepared in 68% yield according to Lipp et al[10]. It is important that the material be completely worked up within a short time after the methanol has been distilled off.* From this, cyclopropylamine was

---

* Distillation of the residue at 2 mm. yielded two solids boiling at 120-125°/2 mm. and 155-160°/2 mm. The low boiling material proved to be unchanged cyclopropanecarboxamide (analysis, mixed m.p.). Recrystallization from alcohol of the higher boiling material gave a compound melting at 100°.

Anal. Calcd. for C_4H_6CN: C, 57.12; H, 7.19; N, 16.66. Found: C, 57.16; H, 7.17; N, 16.63.

The compound is probably N-cyclopropyl-N-carboxycyclopropyl urea $\triangle NHCONHCO\triangle$; cf. Hofmann, Ber., 14, 2725 (1881); 15, 754 (1882).

obtained[10] in 76% yield.

Cyclopropylamine from Cyclopropanecarboxylic Acid.--In a one-liter three-neck flask equipped with dropping funnel, mechanical stirrer, gas evolution indicator, and thermometer dipping into the liquid was placed 130 ml. of concentrated sulfuric acid. First 62 g. (0.72 mole) of cyclopropanecarboxylic acid was slowly added, keeping the temperature below 40°; then a solution of hydrazoic acid[14] in chloroform (from 75 g. of sodium azide and found by titration to contain 34.4 g. (0.80 mole) of hydrazoic acid) was added over a period of two hours, maintaining the temperature between 35-40°. Stirring and heating were continued another five hours, at the end of which time gas evolution had almost stopped. The reaction mixture was poured on 200 g. of ice and the resulting mixture steam distilled to remove chloroform and excess hydrazoic acid. Then 250 g. of sodium hydroxide dissolved in a small amount of water was added slowly while the liberated base distilled over into 250 ml. of 3 N C.P. hydrochloric acid. Evaporation of the hydrochloric acid solution gave 21.6 g. of solid containing ammonium chloride in addition to cyclopropylamine hydrochloride.

This solid was dissolved in the minimum amount of water and added through a dropping funnel to 30 g. of potassium hydroxide and 5 ml. of water in a distilling flask. The amine which distilled was dried over barium oxide and fractionated; 10.3 g. (25% of theory) of cyclopropylamine (b.p. 49-50°/750 mm.) was obtained.* The following derivatives were prepared: phenyl thiourea[9], colorless plates from aqueous ethanol,

* A similar experiment with 20 g. of isobutyric acid yielded 80% of the theoretical amount of isopropylamine.

m.p. 125.5°; benzamide[9], white needles from aqueous methanol, m.p. 99°; picrate, orange needles from ethanol and petroleum ether, m.p. 149°. Identical derivatives were prepared from the amine obtained from the urethane.

Trimethylcyclopropylammonium Iodide from Cyclopropylamine.--To 68 g. (0.73 moles) of cyclopropylamine hydrochloride in 150 ml. of methanol and 400 g. (2.82 moles) of methyl iodide was added 160 g. of potassium hydroxide in 800 ml. of methanol with stirring over a period of three hours, keeping the temperature at 30-40° C. The mixture was refluxed for an additional two hours; evaporation to dryness in vacuo at 40° C. gave 551 g. of solid. This yielded 165 g. (83%) of trimethylcyclopropylammonium iodide on extraction with chloroform for ninety-six hours in a Soxhlet extractor.

Trimethylcyclopropylammonium Iodide from Dimethylcyclopropylamine.--To 40 g. (0.47 mole) of dimethylcyclopropylamine (see below) in 400 ml. of absolute alcohol was added 100 g. (0.704 mole) of freshly distilled methyl iodide with stirring over a period of fifteen minutes. The mixture was allowed to stand overnight. A large crop of white crystals separated out; yield 104 g. (96%) m.p. 274°.

Anal. Calcd. for $C_6H_{14}NI$: C, 31.71; H, 6.23; N, 6.17; I, 55.90. Found: C, 31.79; H, 6.24; N, 6.20; I, 55.99.

Thermal Decomposition of the Quaternary Base.--Trimethylcyclopropylammonium hydroxide was prepared from 22.7 g. (0.1 mole) of quaternary iodide by Demjanow's[1a] procedure. The solution was concentrated in vacuo at 40°, taking care to avoid carbonate formation by

the use of nitrogen-filled apparatus. The concentrated base (approx. 20 ml.) was brownish and cloudy, and was used in this form. The pyrolysis tube was made by blowing a test tube bottom on a piece of 30 mm. pyrex tubing 12 cm. in length with neck constricted to hold a small two-hole rubber stopper. A condenser made from 8 mm. tubing was sealed to the tube 8 cm. from the bottom. The rubber stopper carried a gas inlet tube (for sweeping the system with carbon dioxide) and a short stem dropping funnel which projected 1/2 cm. through the stopper.* A hydrostatic head was maintained on the liquid to be added by connecting the sidearm of a filter flask to the top of the dropping funnel. The filter flask was fitted with a rubber stopper carrying a funnel with a 30 cm. stem; this reached the bottom of the flask and was filled with water. The bulb of the pyrolysis tube was lined with a layer of 20% platinized asbestos, 3 mm. thick. The condenser attached to the pyrolysis tube was connected to a 100 ml. receiver which was followed by a 100 ml. spiral gas wash bottle containing 3 N hydrochloric acid (to absorb trimethylamine and any dimethylcyclopropylamine which did not condense in the receiver). This, in turn, was connected to a gasometer containing saturated sodium chloride.** After sweeping the

---

* It is important that this dropping tube does not project into the hot zone of the pyrolysis tube.

** The gasometer was made from two 2-1/2 liter bottles. The rubber stopper of the first carried a gas inlet tube and differential pressure manometer flush with the stopper and a 12 mm. tube reaching to the bottom of the bottle. This was connected by rubber tubing to a similar tube reaching to the bottom of the second bottle. The gasometer was calibrated. Gas could be drawn into or displaced from the first bottle by lowering or raising the second bottle.

air from the apparatus with carbon dioxide, the pyrolysis tube was heated to the desired temperature by a metal bath and the concentrated solution of base added over a period of 10-12 min. This yielded 1600-1800 ml. of gas at the optimum temperature (320-330°). The apparatus was flushed out with 800 ml. of carbon dioxide which was combined with gas in the gasometer. Bromination (see below) of gas obtained under optimum conditions gave 8-9.5 g. of 1,2-dibromocyclopropane (material boiling below 50°/25 mm.) and 1.5-2 g. of higher boiling residue.

The contents of the hydrochloric acid wash bottle were poured into the receiver and the combined solutions evaporated to dryness in vacuo. The mixed amine hydrochlorides were treated with alkali and steam distilled. Drying of the amines over potassium hydroxide and subsequent fractionation gave dimethylcyclopropylamine, b.p. 60.1°/748 mm.; n_D^{20} 1.3999; d_4^{25} 0.7607; picrate, yellow needles (from ethanol), m.p. 196.5° d.

A series of more than twenty decompositions, each of one-tenth mole of quaternary iodide, was carried out at temperature intervals within the range 250° to 450°. It was found that of temperatures below 320° the ratio of hydrocarbons to dimethylcyclopropylamine formed decreased rapidly while there was very little change in the ratio of cyclopropene to methylacetylene. At 250° the total hydrocarbon formed was less than one-third that obtained at the optimum temperature. As the temperature of the decomposition was increased above 330°, the total volume of hydrocarbon obtained decreased somewhat and

the ratio of cyclopropene to methylacetylene obtained fell off rapidly. At the optimum temperature (320° to 330°) this ratio was bout 10 : 1, while at 450° it dropped to 1 : 1.5. The condition of the catalyst improved with use for the first three or four times, but after this was somewhat erratic in its behavior. From this it is seen that the ratio of hydrocarbons to amine appears to be affected by the condition of the catalyst, though the ratio of cyclopropene to methylacetylene depends primarily on the temperature. A variation in the ratio of hydrocarbon to amine is not seriously disadvantageous as the amine may be quantitatively reconverted[1a] to the quaternary salt. In some experiments, products isolated from decomposition of the quaternary base account for 85 to 90% of the quaternary iodide.

Examination of Hydrocarbon Pyrolysis Products.--The presence of an acetylenic hydrocarbon was confirmed by testing samples of gas with cuprous chloride dissolved in ethanolamine; a yellow precipitate was obtained. The relative amounts of cyclopropene and methylacetylene in the mixture were determined by passing further samples from the gasometer (corresponding to 0.1 mole quaternary iodide) into excess bromine at 0° over a period of one and one-half hours. The bromine and bromide were then treated with sodium bisulfite to remove excess bromine, washed with water, dried with calcium chloride and distilled. The portion boiling to 50°/25 mm. was collected and found to be nearly pure dibromocyclopropane; the weight of the residue was taken as an index of the amount of methylacetylene present.

One hundred and fifty g. of the combined bromination product from a series of pyrolyses at various temperatures, on careful fractionation, yielded 117 g. of 1,2-dibromocyclopropane (b.p. 57-58°/50 mm.; m.p. -1 to +1°; $n^{20}D$ 1.5360; d_4^{25} 2.0838), 11.9 g. of 1,1,2,2-tetrabromopropane (b.p. 110-112°/10 mm., $n^{20}D$ 1.6162; d_4^{25} 2.668), 6.1 g. of 1,1,3,3-tetrabromopropane (b.p. 122-123°/10 mm.; $n^{20}D$ 1.6198; d_4^{25} 2.683), and small intermediate fractions.

Isolation of Cyclopropene.--Three liters of hydrocarbon pyrolysis products, dried with magnesium perchlorate and freed of carbon dioxide with ascarite was fractionated at atmospheric pressure (744 mm.) in a small Podbielniak column.* Approximately 700 ml. of gas distilled over at -36 to -35°; the residue, 3 to 4 ml. of slightly yellow somewhat viscous oil gave no further distillate on warming to room temperature. As the original sample contained methylacetylene as well as cyclopropene, this seems to indicate that cyclopropene can combine with methylacetylene as well as with itself. The ratio of hydrogen to carbon was determined on three 10 ml. samples of pure hydrocarbon gas by burning in a semi-micro combustion furnace.

Anal. Calcd. for C_3H_4: H/C ratio, 1.33. Found: 1.332, 1.346, 1.320.

---

* The author wishes to acknowledge the assistance of Dr. B. H. Sage and Mr. Robert Dourson, of the American Petroleum Institute Laboratories at this Institute, in carrying out this distillation.

Acknowledgment

The author wishes to acknowledge his indebtedness to Dr. E. R. Buchman for suggesting the problem and to him and Professor H. J. Lucas for guidance during the course of the investigation. Thanks are also due to Professor J. B. Cloke for suggestions relating to the preparation of cyclopropyl cyanide and to Mr. Alf O. Reims and to Mr. Herbert Sargent for aid with some of the preparations.

Summary

The preparation of cyclopropene by the thermal decomposition of trimethylcyclopropylammonium hydroxide on a platinum catalyst was studied in detail. The optimum temperature for cyclopropene formation was found to be 330°.

Pure cyclopropene was obtained by fractional distillation of the hydrocarbons obtained by pyrolysis of the quaternary base. It boils at -36° at 744 mm.

Cyclopropylamine was prepared from trimethylene glycol by several paths. The individual steps were investigated from a preparative point of view.

Bibliography

1. a. Demjanow and Dojarenko, Ber. 56, 2200 (1923); Bull. acad. sci. Russ., [6] 297 (1922); b. Bull. acad. sci. U.S.S.R., [7] 653 (1929); [C.A., 24, 1848 (1930)].

2. Marvel and Calvery in "Organic Syntheses", Coll. Vol. I, John Wiley and Sons, Inc., New York, New York, 1932, p. 519.

3. Cloke , Anderson, Lachmann and Smith, J. Am. Chem. Soc., 53, 2794 (1931).

4. Allen, "Organic Syntheses", Coll. Vol. I, John Wiley and Sons, Inc., New York, N.Y., 1932, p. 150.

5. Kamm and Marvel in "Organic Syntheses", Coll. Vol. I, John Wiley and Sons, Inc., New York, N.Y., 1932, p. 28.

6. Gabriel, Ber., 22, 3336 (1889); see Derick and Hess, J.Am. Chem. Soc., 40, 546 (1918).

7. Cloke, Knowles and Anderson, J. Am. Chem. Soc., 58, 2547 (1936).

8. Henry, Bull. classe sci. Acad. roy. Belg., [3] 37, 17 (1899) [Chem. Zentr. 70, I, 975 (1899)].

9. Kishner, a.) J. Russ. phys. chem. Soc., 33, 377 (1901); b.) ibid. 37, 304 (1905) [Chem. Zentr., 72, II, 579 (1901); 76, I, 1704 (1905)].

10. Lipp, Buchkremer and Seeles, Ann., 499, 13 (1932).

11. Heisig, J. Phys. Chem., 43, 1210 (1939).

12. Hultman, Davis and Clarke, J. Am. Chem. Soc., 43, 369 (1921).

13. Skraup and Binder, Ber., 62, 1130 (1929).

14. von Braun, Ann., 490, 125 (1931).

The Thermal Decomposition of Trans-1,2-cyclobutane-bis-(trimethylammonium) Hydroxide

The possibility of synthesizing cyclobutadiene is being investigated on a broad basis in this laboratory under the direction of Dr. E. R. Buchman. One line of attack on this problem is a study of the thermal decomposition of the four possible cyclobutane di-quaternary ammonium bases. The results obtained from the pyrolysis of the most easily obtained member of the series, trans-1,2-cyclobutane-bis-(trimethyl-ammonium) hydroxide, are reported in this paper.

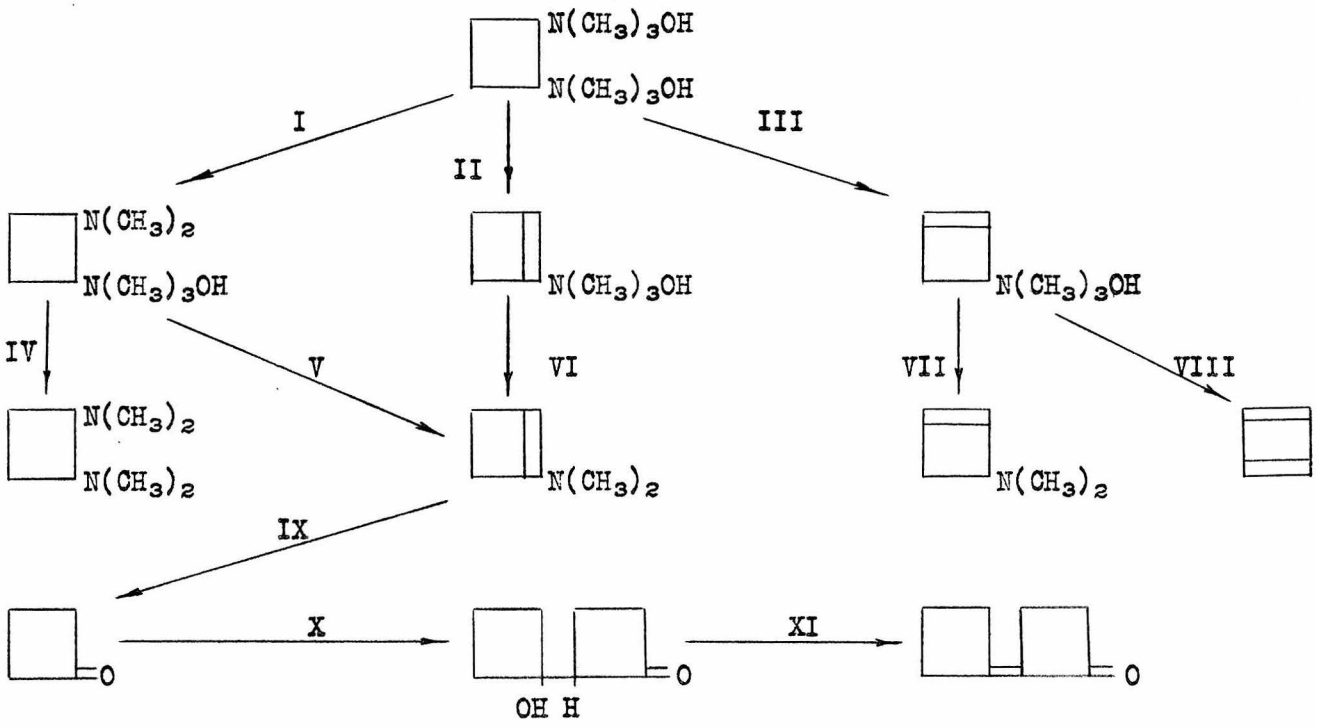


Chart: Reactions which might occur during the thermal decomposition of trans-1,2-cyclobutane-bis-(trimethylammonium) hydroxide without breaking the four-ring.

The first step of the thermal decomposition would be - by analogy with the pyrolysis of trimethylcyclopropylammonium hydroxide - one or more of the reactions, I, II or III, shown on the chart. This is assuming retention of the four-ring structure. Hurd and Drake[1] found that the pyrolysis of 1,2-butane-bis-(trimethylammonium) hydroxide gave 44% of ethylacetylene and 56% of methylallene. Pyrolysis of 2,3-butane-bis-(trimethylammonium) hydroxide gave approximately 45% of 1,3-butadiene and 55% of methylallene or a mixture of methylallene and dimethylacetylene. On the basis of these data, both reactions II and III might be expected.

In the case of trans-1,2-cyclobutane-bis-(trimethylammonium) hydroxide, reaction III, if it takes place at all, occurs to a very small extent. This conclusion is based on the probability that 1-dimethylaminocyclobutene-2 would be stable by analogy with other β-γ-unsaturated tertiary amines[2] and therefore would have been isolated in the scheme given in the experimental part if it had been present in any considerable amount.

It is not possible to say definitely that reactions I and II both take place, as the α,β-unsaturated dimethylamine might be formed by either path. That reaction I occurs, however, is shown definitely by the isolation and characterization of trans-1,2-bis-(dimethylamine) cyclobutane as the picrate and methiodide. Although the fact that 1-dimethylaminocyclobutene-1 (V, VI) is formed as an intermediate was not shown by its isolation or by the isolation of additive derivatives formed from it, it is clear that this must be the case from the

isolation of considerable amounts of cyclobutanone (IX) (characterized as the semicarbazone, phenylhydrazone and 2,4-dinitrophenylhydrazone), the condensation products X and XI (characterized as the 2,4-dinitrophenylhydrazones) and dimethylamine formed in reaction IX (characterized as the benzenesulfonamide). The tendency of vinyl tertiary amines to give the corresponding aldehyde or ketone and corresponding secondary amine, in the presence of water, has been reported by Sou[2]. The polymerization product (X) resulted from the well known aldol condensation, not previously reported for cyclobutanone, and the compound (XI) by loss of one molecule of water from X.

Experimental

Thermal Decomposition of the Di-quaternary Base.--Trans-1,2-cyclobutane-bis-(trimethylammonium) hydroxide was prepared from 42.6 g. (0.1 mole) of the di-quaternary iodide by shaking it in aqueous solution with an excess of freshly prepared silver oxide* until the colloidal particles in the supernatant liquid had coagulated. The mixture was then filtered rapidly with suction and the filter cake washed with distilled water. The filtrate and washings were concentrated in vacuo at 40°, taking care to avoid carbonate formation by the use of nitrogen filled apparatus. The evaporation was stopped when the volume had been reduced to about 40 ml. and the gray to brownish, cloudy solution used for pyrolysis in this form.

---

* The silver oxide was prepared from 68 g. (0.4 mole) of silver nitrate and 26 g. (0.465 mole) of potassium hydroxide. It was washed with ten changes of distilled water by decantation in order to remove free alkali.

The apparatus for the thermal decomposition was the same as that described for the pyrolysis of trimethylcyclopropylammonium hydroxide.* The spiral gas wash bottle contained 100 ml. of 3 N hydrochloric acid. The air was displaced from the apparatus with carbon dioxide and the concentrated solution of base pyrolyzed by dropping it on platinized asbestos at 350-360° over a period of 15 minutes. No gas collected in the gasometer and very little went into the hydrochloric acid wash bottle.**

The pyrolysis distillate was made acid with a small excess (25 ml.) of 6 N hydrochloric acid and the organic phase collected in ether. The aqueous phase was shaken with several portions of ether; the extracts combined, dried with sodium sulfate and most of the ether removed through an efficient total reflux column. The residue will be referred to as the "neutral fraction".

The above aqueous solution was made basic by the addition of 30 ml. of 6 N sodium hydroxide solution and continuously extracted with ether for four hours (further extraction gave a negligible amount of basic material). Most of the ether was removed from the extract through an efficient total reflux column. The residue will be referred to as the "higher amine" fraction. The volatile amines were lost in this case but were investigated in another experiment.

---

* This thesis, "The Preparation of Cyclopropene", pg. 18

** In one pyrolysis carried out at 410-420°, about 300 ml. of gas was collected in the gasometer. Fifty ml. of this condensed in a dry ice trap to give a mobile liquid with pleasant, unsaturated odor. This analyzed for an H/C molal ratio of 1.94 when burned in a semimicro combustion apparatus.

Investigation of the Neutral Fraction.--The concentrate from the ether extraction of the acidic solution was transferred to a small distilling flask with a capillary and surrounded by a water bath. The flask was connected to a Dry Ice trap and everything which would distill below a bath temperature of 100° and pressure of 2 mm. was taken over into the trap. The material from the trap was distilled at atmospheric pressure through a small Young-type column made from a 10 cm. section of 7 mm. glass tubing. This gave 1.84 g. of material boiling from 80-100° and a small amount (0.23 g.) of an intermediate fraction boiling from 100°/760 mm.-57°/18 mm. The residue was combined with the residue from the first distillation giving 2.15 g. of higher boiling neutral fraction.

The material boiling from 80-100° (I) had an odor similar to that of cyclopentanone (on standing it acquired a different, very penetrating odor). Two drops of (I) in one ml. of CCl_4 rapidly decolorized 20 drops of 3% bromine in carbon tetrachloride with evolution of hydrogen bromide (fumes and acid reaction to moist litmus), further decolorization occurred very slowly. (In a parallel experiment, 2 drops of allyl alcohol decolorized 120 drops of 3% bromine). (I) gave derivatives characteristic of the carbonyl group. The semicarbazone of (I) was prepared by adding just enough alcohol to 0.3 ml. of water and 0.10 ml. of (I), in a centrifuge tube, to give a solution and then stirring in 0.10 g. of semicarbazide hydrochloride and 0.12 g. of hydrated sodium acetate. In a few minutes white crystals began to separate and in 30 minutes the mixture was centrifuged. After two recrystallizations from water the semicarbazone was obtained as rosettes of white needles,

M.P. 212-212.5°.

Anal. Calcd. for $C_5H_9N_3O$: C, 47.23; H, 7.14; N, 33.05.
Found: C, 47.36; H, 7.25; N, 32.61.

Curtius[3] reported the semicarbazone of cyclobutanone, M.P. 211-212° (dec).

The phenylhydrazone of (I) was prepared by adding just enough alcohol to 1 ml. of water and 0.10 ml. of (I) to give a solution and then adding 0.2 ml. of phenylhydrazine. An oil separated in 2-3 minutes. The oil was induced to crystallize by removing all of the aqueous phase, adding a few drops of absolute alcohol and scratching. On recrystallizing three times from water-alcohol mixtures pale yellow needles were obtained, M.P. 98-98.5°. The phenylhydrazone decomposed after standing for three days. Curtius reported the phenylhydrazone of cyclobutanone, M.P. 95-96°.

The 2,4-dinitrophenylhydrazone of (I) was prepared by adding 0.1 ml. of (I) to a boiling mixture of 0.2 g. 2,4-dinitrophenylhydrazine, 5 ml. of 50% alcohol and 1 drop of concentrated hydrochloric acid. An immediate color change was obtained, the mixture was heated at 80° for 10 minutes, enough alcohol added to cause complete solution of the derivative and the mixture set aside to crystallize. Two recrystallizations from absolute alcohol gave orange-red needles, M.P. 147.1-147.3°.

Anal. Calcd. for $C_{10}H_{10}N_4O_4$: C, 48.00; H, 4.03; N, 22.40.
Found: C, 48.49; H, 4.29; N, 22.53.

Lipp, Buchkremer and Seeles[4] reported the 2,4-dinitrophenylhydrazone of cyclobutanone as orange-red needles, M.P. 132.3° and an acceptable nitrogen analysis for the derivative. On the basis of the C, H and N analysis of our derivative and the agreement between the melting points

of the semicarbazone and phenylhydrazone with those reported by Curtius, it seems reasonable to believe that the melting point of the 2,4-dinitrophenylhydrazone of cyclobutanone is 147°. Kishner[5] reported that cyclobutanone forms an addition compound with sodium bisulfite and has a b.p. 98.5-99°. (I) formed such an addition compound (somewhat less readily than cyclopentanone) and had a b.p. approximating that reported by Kishner for cyclobutanone (the amounts available to us were too small for convenient fractionation).

The higher boiling neutral fraction was transferred to a special micro still having a very short vapor path. On distillation, 1.36 g. of material boiling at 60-70°/5 mm. (II) was obtained. A forerun of 0.29 g. was collected and a small residue left in the still. The material boiling from 60-70°/5 mm. had a very aromatic terpene-like odor similar to that of green hemlock. (II) gave a phenylhydrazone which could not be induced to crystallize. The semicabazone formed very slowly in low yield, and was not investigated further. (II) formed an addition compound with saturated sodium bisulfite. On re-crystallization from saturated sodium bisulfite solution it separated in white needles.

Chromatography of the 2,4-Dinitrophenylhydrazones Prepared from (II).--The 2,4-dinitrophenylhydrazone mixture was prepared by adding 0.1 ml. of (II) to a hot mixture of 0.2 g. of 2,4-dinitrophenylhydrazine and 3 ml. of glacial acetic acid. The color changed slightly and the hydrazine went into solution. The mixture was heated 20 minutes at 80° and then the acetic acid evaporated in a stream of nitrogen. The last

traces of acetic acid were removed from the red gummy residue at 1 mm. and 80°. The residue was taken up in benzene and chromatographed on alumina* ** . Three bands appeared on the column, a thin dark brown very strongly absorbed band on the top of the column (III), a moderately strongly absorbed yellow band (IV) and a very weakly absorbed orange band which was generally washed completely into the filtrate (V). The top band (III) was eluted with alcohol and evaporated to dryness in a stream of nitrogen (10-20 mg.). The residue was very dark and had a reddish brown cast. It dissolved very readily in alcohol and was precipitated by the addition of benzene or isopropyl ether, in which it was insoluble. It was not investigated further.

The yellow band (IV), which corresponds to the main constituent in the mixture, was eluted with 2% acetic acid in benzene. The filtrate from the elution was evaporated to dryness (230 mg.) in an inert atmosphere and the residue crystallized from benzene. This gave clusters of orange needles, M.P. 186-187°.***

Anal. Calcd. for $C_{14}H_{16}N_4O_5$: C, 52.49; H, 5.04; N, 17.50. Found: C, 52.96; H, 5.30; N, 17.93.

---

* For a description of the methods of chromatography see Zechmeister and Cholnoky[6].

** Chromatographic absorption on talc, alumina, aluminum phosphate and other absorbents from benzene, ligroin and chlorinated hydrocarbon solvents has been applied to the separation of 2,4-dinitrophenylhydrazones by Strain[7].

*** This is the temperature at which a fresh sample will melt when placed in the bath for 10 seconds.

The column filtrate containing the orange band (V) which was washed through the column was evaporated to dryness (40 mg.) in an inert atmosphere. The residue crystallized from benzene and isopropyl ether in clusters of scarlet blades, M.P. 184-187° (Sinters)*. Sample deepens in color several degrees below this.

Anal. calcd. for $C_{14}H_{14}N_4O_4$: C, 55.62; H, 4.67; N, 18.54. Found: C, 55.99; H, 5.01; N, 18.93.

Investigation of the Higher Amine Fraction.--The "higher amine" concentrate was obtained from the ether extract of the alkaline pyrolysis distillate after removal of the neutral components from the acidified mixture. It was transferred to a small distilling flask equipped with a capillary. This was connected to a Dry Ice trap and everything that would distill below a bath temperature of 90° and a pressure of 2 mm. was taken into the trap. This was distilled through a small Young-type column; 0.2 ml. of material boiling from 90-110°/760 mm. (VI) and 0.3 ml. of material which would distill below a bath temperature of 150° at 25 mm. (VII). A small residue remained in the flask.

One ml. of methyl iodide was added to (VI). White crystals immediately separated, but turned to a milky oil in about 30 seconds. Absolute ether was added and the methyl iodide-ether solution poured off. This was shaken with semicarbazide hydrochloride and sodium acetate in a small amount of water. A small amount of semicarbazone was obtained which was found by a mixed melting point to be identical with the cyclobutanone derivative.

---

* This is the temperature at which a fresh sample will melt when placed in the bath for 10 seconds.

The oily material was taken up in a small amount of water and treated with saturated sodium picrate. A precipitate was obtained which crystallized in yellow needles from alcohol and water, M.P. 269-272° (dec).

Anal. Calcd. for $C_{22}H_{28}N_8O_{14}$: C, 42.05; H, 4.50; N, 17.83. Found: C, 41.83; H, 4.73; N, 16.74.

In spite of the low nitrogen analysis, consideration of the possibilities leads to the conclusion that the compound is probably trans-1,2-cyclobutane-bis-(trimethylammonium) picrate. This compound would be formed if (VI) should contain any trans-1,2-bis-(dimethylamino) cyclobutane.

Treatment of a few drops of (VII) with an ethanol solution of picric acid gave a precipitate. This crystallized from alcohol and water in yellow needles; M.P., dec. sharply at 239°. The identity of this compound was established by an approximate agreement of the decomposition point and exact similarity of crystal form as seen by microscopic comparison with an authentic sample of the picrate of trans-1,2-bis-(dimethylamino) cyclobutane.

In one pyrolysis carried out at 350-400°, the contents of the hydrochloric acid wash bottle were combined with the pyrolysis distillate and the neutral material removed with ether. The acid solution was then evaporated to dryness in vacuo, taken up in a small amount of water and slowly added to potassium hydroxide pellets in an apparatus arranged for the absorption of volatile amines in hydrochloric acid. All of the amines which would distill from saturated potassium hydroxide solution below a bath temperature of 60° were carried over. An oily layer remained in

the distilling flask. This changed to a brownish amorphous solid on standing over concentrated base for 24 hours. Steam distillation removed no more basic material from the residue. It was thoroughly washed with water and dried in a vacuum desiccator; weight of residue, 1.7 g.

The amorphous chocolate-brown residue (VIII) was very slightly soluble in water, very soluble in dilute hydrochloric acid, insoluble in dilute base, soluble in alcohol, pyridine and nitrobenzene; insoluble in ether and isopropyl ether. Fractional precipitation from hydrochloric acid with dilute base, showed that the solid was not homogeneous--the last flocculent precipitate obtained was a pale yellow color.

Chromatographic absorption of (VIII) from alcohol on alumina showed it to contain at least three components. One component was strongly absorbed at the top of the column as a brown layer with a weak orange fluorescence under ultraviolet light. Another more weakly absorbed orange yellow band with a lemon yellow fluorescence under ultraviolet light and a filtrate having a pale yellow color and greenish fluorescence under ultraviolet light were also obtained. The mixture was not investigated further.

Investigation of the Volatile Amines.--The acid solution containing the volatile amines was evaporated to dryness in vacuo at 100°, giving 12.5 g. of a mixture of volatile amine hydrochlorides. These were dissolved in water and the volume made up to 100 ml. One fourth of the solution was added slowly with shaking to 40 ml. of 20% potassium hydroxide in an ampoule chilled in an ice salt freezing mixture.

Then 2.4 ml. of benzenesulfonyl chloride was added and the ampoule sealed. It was allowed to warm to room temperature while shaking--large white crystals separated. The ampoule was heated on a water bath at 60° for 20 minutes (the crystals turned to an oil), cooled, opened and extracted with three 20 ml. portions of ether. On evaporation of the ether 0.81 g. of solid was obtained, M.P. 47° after recrystallization from isopropyl ether. This is the melting point reported for the dimethylbenzenesulfonamide[8]. Identical control experiments carried out with dimethylamine and trimethylamine hydrochloride mixtures of known composition indicate that the original mixture contained approximately one-fifth dimethylamine.

The presence of trimethylamine was established by elimination, from the fact that the volatile amine mixture distilled completely between 0° and 10°. The presence of other amines which might form benzenesulfonamides is excluded from the fact that the low melting dimethylamine derivative was obtained as a solid without recrystallization.

Acknowledgment

I wish to thank Dr. E. R. Buchman for suggesting the problem and Mr. Alf O. Reims for preparing the starting material for the research.

Summary

The thermal decomposition of trans-1,2-cyclobutane-bis-(trimethylammonium) hydroxide on a platinum catalyst at 350-360° was studied in detail.

No evidence was obtained which would indicate that any cyclobutadiene or 1-dimethylaminocyclobutene-2 were formed during the pyrolysis.

Trans-1,2-bis-(dimethylamino) cyclobutane, cyclobutanone, aldol condensation products of cyclobutanone, dimethylamine and trimethylamine were shown to be present in the pyrolysis distillate.

1-Dimethylaminocyclobutene-1 was postulated as an unstable intermediate, reacting with water under the conditions of the experiment to give cyclobutanone and dimethylamine.

Bibliography

1. Hurd and Drake, J. Am. Chem. Soc., 61, 1943 (1939).

2. Sou, Bull. faculte sci. univ. franco-chinoise Peiping, 5, 1 (1935); C.A., 30, 4463 (1936).

3. Curtius, J. prakt. Chem., [2] 94, 262 (1916).

4. Lipp, Buchkremer and Seeles, Ann., 499, 20 (1932).

5. Kishner, J. Russ. Phys. Chem. Soc., 39, 924 (1907); Chem. Zentr., 1908 I, 123.

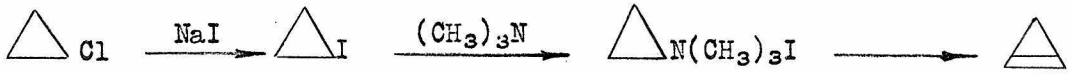
6. Zechmeister and Cholnoky, "Principles and Practice of Chromatography" Translation by Bacharach and Robinson, Chapman and Hall, Ltd., London. 1941

7. Strain, J. Am. Chem. Soc., 57, 758 (1935).

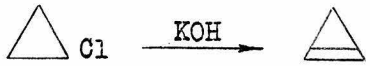
8. Shriner and Fuson, "Identification of Organic Compounds", John Wiley and Sons, Inc., New York, 1935, p. 119.

Propositions

1. The series of reactions:



is less likely to give cyclopropene than the reaction



2. An explanation is offered for the following data obtained when 10 g. of 1,2-dibromocyclopropane was treated with zinc dust and 80% alcohol at 80°.

Time (min.)	Volume of gas evolved (cc.)
0	0
16	200
20	1100
25	1200
55	1250

3. Another mechanism is proposed to explain the following configurational changes - (1) retention with $SOCl_2$; (2) partial inversion with $SOCl_2$ and pyridine; (3) partial inversion with PCl_3; (4) complete inversion with PCl_3 and pyridine - in the halogenation of optically active phenylmethylcarbinol. (Kenyon, Phillips and Taylor, J. Chem. Soc. 1931, 382).

4. Ethyl carbonate is proposed for use as a solvent in many sodio malonic ester and similar types of condensations in order to avoid some of the difficulties which arise when ether, benzene or alcohol are used in this way.

5. Mereshkowski's claim (Zent. 1914, I, 2161) to have synthesized methylcyclopropene is doubtful.

6. The strong tendency for the following reaction to take place, even in the presence of very small amounts of alcohol (Cope and McElvain, J.Am.Chem.Soc. 54, 4311 (1932)),

$$BrCH{=}CHC(Et)(COOEt)_2 + EtOH \longrightarrow BrCH_2CH{=}C(Et)COOEt + Et_2CO_3$$

7. The use of camphor-wire in the Rast method for determining molecular weights is a useful refinement.

8. A modification of the method for carrying out sodio malonic ester and similar condensations is proposed for use in the following cases.

   i) Preparation of 1,1-dicarbethoxy-ring compounds from dihalides,

   ii) Preparation of the monocondensation products with compounds possessing two active groups,

   iii) Preparation of mono-substituted malonic esters from compounds having a high tendency toward di-substitution.

9. The following method is proposed for preparing certain difficultly obtainable substituted malonic esters. The cyanacetic ester is treated with hydrogen chloride and alcohol to give the imino-ether hydrochloride and then hydrolyzed to the substituted malonic ester.

10. The freezing point depression and analysis for certain inorganic constituents in the blood serum of cambarus clarkii (crayfish) reported by Lienemann (J. Cell. and Comp. Physiol. 11, 149 (1938)) is self-contradictory.

11. The inhibition of the skeletal muscles of the crustaceans is not closely related to inhibition in the vertebrates.

12. A semimicro analytical laboratory should be set up to supplement the micro analytical department.

13. A scheme of research direction involving the following points is suggested.

   1) Course work for the first year includes a paper on some limited field within the sphere of interest of one of the professors in the department. Later a seminar is given by the new student on some phase of the same subject, with emphasis on unsolved

problems in the field and projected schemes for attack of these problems.

2) A new man, on arrival at the school, is assigned to a senior graduate student and, after careful discussion with the professor and senior student, begins work on some little problem of immediate interest both to the professor and to the student with whom the new man is to work.