These data also indicate why certain practices in the handling of chloroacetic acid have been beneficial. For example, in many preparations in the literature, the use of sodium carbonate has been specified for the neutralization of chloroacetic acid. This has served to prevent excessively high alkalinities during the neutralization and thus reduced the amount of hydrolysis. The same result can be achieved by careful neutralization with sodium hydroxide with good stirring and cooling. It further indicates the inadvisability of adding the acid to the alkali in neutralization.

As already mentioned, plots of log concentration against time indicated that most of the runs were of the first order. The exception was the run at pH 12.5; this plot shows a deviation from a straight line, in the direction of a more rapid reaction. This deviation started when about 65% had reacted and may have been due to a slight increase in pH.

LITERATURE CITED

(1) Buchanan, *Ber.*, 4, 340 (1871).
(2) *Ibid.*, 4, 863 (1871).
(3) Dawson and Pycock, *J. Chem. Soc.*, 1934, 778.
(4) *Ibid.*, 1936, 153.
(5) Dawson, Pycock, and Smith, *Ibid.*, 1943, 517.
(6) Drushel and Simpson, *J. Am. Chem. Soc.*, 39, 2455 (1917).
(7) Guggenheim, *Phil. Mag.*, [7] 2, 538 (1926).
(8) Kastle and Keiser, *Am. Chem. J.*, 15, 471 (1893).
(9) Lassen and Eichloff, *Ann.*, 342, 115 (1905).
(10) Senter, *J. Chem. Soc.*, 91, 460 (1907).

Cyclization of Pseudoionone by Acidic Reagents

E. EARL ROYALS

Georgia School of Technology, Atlanta, Ga.

A study has been made of the cyclization of pseudoionone by various acidic reagents to yield mixtures of α- and β-ionones. Particular attention has been given to the influence of the cyclizing agent on the composition of the resulting ionone mixture. The mechanism of the reaction is discussed, and suitable preparative procedures for α- and β-ionone are recommended.

PSEUDOIONONE (I) under the influence of acidic reagents is converted into a mixture of α-ionone (II) and β-ionone (III), the artificial violet odor of commerce (3, 10, 11). Because of the great technical importance of the ionones, a number of methods have been developed for the cyclization of pseudoionone. These are described mainly in the patent literature (4, 6, 7).
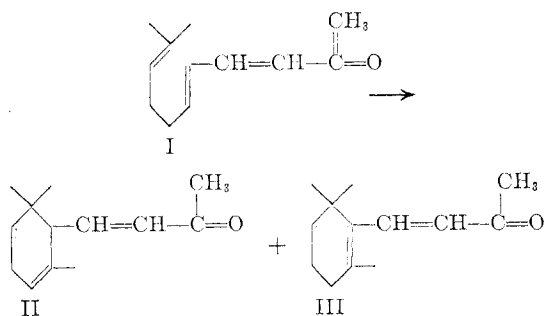
Although the relative proportions of α- and β-ionones obtained on cyclization of pseudoionone are dependent on the cyclizing agent used, little attention has been given to this phase of the problem beyond the general statements that concentrated sulfuric acid gives mainly β-ionone (9), whereas phosphoric, formic (9), acetic, and benzoic acids (8) produce mainly the alpha isomer. Hibbert and Cannon developed laboratory procedures for the preparation of an ionone said to be essentially the alpha isomer (4). Ito studied in some detail the cyclization of pseudoionone by sulfuric and phosphoric acids, and showed that the proportion of isomeric ionones obtained is dependent on the concentration of the cyclizing acid (5). The present investigation was undertaken to extend existing knowledge as to the effect of the cyclizing agent on the relative proportions of α- and β-ionones obtained on cyclizing pseudoionone, to throw light on the mechanism of the cyclization reaction, and to develop practical methods for the production of α- and β-ionones.

CYCLIZATION PROCEDURES

Citral was obtained from Fritzsche Brothers, Inc., and was used without further purification. The acetone and various acidic reagents were of c.p. grade. Phosphoric acid of strength greater than 85% was prepared by adding the calculated quantity of phosphorus pentoxide to the ordinary sirupy acid. Pseudoionone was prepared according to the following procedure (11): A mixture of 200 grams (1.31 moles) of citral, 200 grams (3.44 moles) of acetone, and 200 cc. of a saturated solution of barium hydroxide was vigorously stirred for 3–4 days at room temperature (about 28° C.). The organic material was taken up in ether and washed successively with water, 5% tartaric acid solution, and again with water. The ether solution was dried over sodium sulfate, the ether was removed by distillation, and the residue was distilled under reduced pressure. The fraction boiling around 150–165° C. (15 mm.) was collected. This material was freed of citral and condensation products of acetone by steam distilling until about one liter of distillate was collected. The residue was dried over anhydrous sodium sulfate and fractionated under reduced pressure through an 8-inch column packed with glass helices and externally heated. The portion boiling at 144–149° C. (10–11 mm.) and showing n_D^{20} of 1.5230–1.5280 (successive fractions) was taken for use as pseudoionone. The literature reports for pseudoionone prepared by this method (11), 143–145° C. (12 mm.) and 1.5275, respectively.

The cyclizations of pseudoionone (Table I) were carried out in the following general manner: The cyclizing agent was placed in a 200-cc. three-necked flask fitted with a mechanical stirrer, a dropping funnel, and a thermometer reaching into the reaction mixture. The flask was cooled in an ice bath, and the cyclizing agent was vigorously stirred while 20 grams of pseudoionone were added dropwise during 15–30 minutes; the rate of addition was adjusted so that the temperature of the reaction mixture did not exceed 10–15° C. When the pseudoionone had all been added, the cooling bath was removed, and stirring was continued for a period considered sufficient to permit complete reaction. The reaction mixture was poured into 500 cc. of ice water and ex-
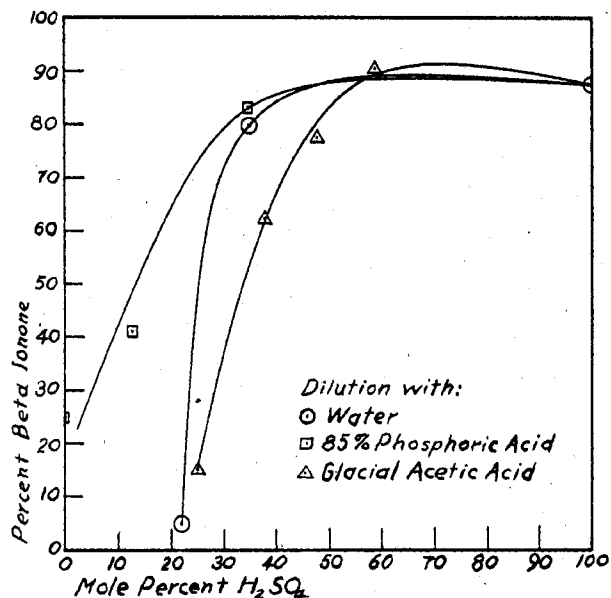
Figure 1. Effect of Dilution on Cyclization of Pseudoionone with Sulfuric Acid

tracted with ether. The ether solution was thoroughly washed with water and dried over anhydrous sodium sulfate, and the ether was removed by distillation. The residue was subjected to steam distillation for 5–6 hours; the ionone passed over in the distillate, and resinification products were left behind. The aqueous distillate was extracted with ether, the extract was dried over anhydrous sodium sulfate, and the ether was removed by distillation. The residue was distilled under reduced pressure from a small Claisen flask. Details of the vacuum distillations are recorded in Table I. In no case did more than 1–2 grams of residue and holdup remain from the final distillation; low yields were always accounted for on the basis of polymerized material nonvolatile with steam.

This general procedure was followed in all cases except those involving cyclization with aluminum chloride and with the solid acids, chloroacetic and trichloroacetic. The former were carried out by adding the required quantity of c.p. aluminum chloride (small pellets) in small portions during 30 minutes to a stirred solution of pseudoionone in a suitable solvent (petroleum ether or carbon disulfide). In cyclizations with the solid acids, the reaction vessel was heated in a water bath to about 55° C. to maintain the cyclizing agent in the molten state during the addition of the pseudoionone and the subsequent stirring period. These reaction mixtures were worked up by the procedure described above. Further details are given in Table I.

The compositions of the ionone mixtures obtained were estimated from the refractive index at 20° C. on the assumption of a linear relation between composition and index. The following values were taken for use in the calculation: α-ionone, $n_D^{20} = 1.4980$; β-ionone, $n_D^{17} = 1.521$ (1). The compositions given in Table I were calculated by this method and were not checked by any gravimetric procedure.

INFLUENCE OF CYCLIZING AGENT

Table I shows the experimental results obtained in this research. Consideration of experiments 1, 4, 7, and 9 demonstrates a definite relation between the strength of the cyclizing acid, as measured by its dissociation constant in water, and the composition of the ionone mixture obtained on cyclization of pseudoionone. The pertinent data are summarized in Table II. The proportion of β-ionone in the cyclized product increases

with the strength of the cyclizing acid. Indeed, the data may be fitted to the relation,

$$\% \ \beta\text{-ionone} \ = \ 15 \log K_a \ + \ 87.7 \tag{1}$$

with a fair degree of accuracy. The maximum deviation from this relation occurs with trichloroacetic acid; the observed proportion of β-ionone is 11% lower than the calculated value. This deviation may be due in part to an experimental error. In the final distillation of the ionone mixture obtained by cyclization with trichloroacetic acid, a small forerun of an unidentified material of lower refractive index than the ionones was obtained. Contamination of the ionone fraction with small amounts of this material would have led to a low value for the fraction of β-ionone in this mixture. In no other case was a forerun obtained in the final distillation of the ionone mixtures.

Brønsted (2) showed that for an acid-catalyzed reaction in a given solvent, the following relation should exist

$$\log k \ = \ A \log K_a \ + \ B \tag{2}$$

where k = catalytic rate constant
     K_a = acid dissociation constant of catalyst
     A, B = constants

Equation 1 follows directly from this relation on the assumption that the percentage β-ionone in the cyclized product is proportional to the catalytic rate constant for its formation. Equation 1 holds only when applied to the cyclization of pseudoionone by very concentrated acids. With more dilute acids as cyclizing agents the relation breaks down, an indication that another complicating factor is here concerned. This factor will be discussed later in the paper.

The use of the acid salts, zinc and aluminum chlorides, as cyclizing agents produced mixtures rich in α-ionone; aluminum chloride gave relatively more of the beta isomer. This is in accord with generally accepted ideas of the relative acidity of these two salts, the more acid (electrophilic) aluminum chloride yielding a higher percentage of β-ionone. Zinc chloride in glacial acetic acid gave an excellent yield of α-ionone almost free of the beta isomer. Generally poor results were obtained with aluminum chloride; this reagent proved to be a powerful catalyst for the polymerization of pseudoionone and thus led to low over-all yields of ionone.

Dilution had a marked effect on the relative proportion of α- and β-ionones obtained on cyclizing pseudoionone with a given acidic reagent. Although it is usually stated in the literature (9) that phosphoric acid gives mainly the alpha isomer, experiments 4, 5, and 6 show that the proportion of isomers actually obtained is dependent on the concentration of the acid in accordance with the observations of Ito (5). Thus, whereas 100% phosphoric acid gives an ionone containing 61% of the beta isomer, the use of 85% phosphoric acid reduces this figure to 23%. A similar situation exists with sulfuric acid as cyclizing agent, although a relatively greater dilution is necessary to change the proportion of isomers from principally β- to α-ionone. Concentrated sulfuric acid cyclizes pseudoionone to an ionone which contains about 87% of the beta isomer. The effect of diluting sulfuric acid with 85% phosphoric acid, glacial acetic acid, or water is shown in Figure 1. The curve for dilution with 85% phosphoric acid demonstrates the relatively greater cyclizing activity of sulfuric acid over phosphoric. As the mole percentage of sulfuric acid increases, the proportion of β-ionone increases sharply until at 35 mole % sulfuric acid the ionone produced contains 83% of the beta isomer. Water and acetic acid, on the other hand, have little or no cyclizing activity as compared to sulfuric acid, and so act merely as diluents for this reagent. As concentrated sulfuric acid is progressively diluted with water, little change occurs at first in the proportion of ionones; at about 30–40 mole % sulfuric acid, however, the curve breaks sharply downward, and thereafter the ionone produced is almost entirely

TABLE I. CYCLIZATION OF PSEUDOIONONE BY ACIDIC REAGENTS

Expt. No.	Reagent	Time[a], Min.	Temp.[a], °C.	B.P. of Product °C.	Mm.	n_D^{20}	β-Ionone[b]	Yield, %
1	60 g. concd. sulfuric acid	5	25	127–34	10–9	1.5180	87	34.0
2	100 g. 75% sulfuric acid	25	25	129–35	11–9	1.5160	79	66.5
3	100 g. 60% sulfuric acid	60	20	125–38	10	1.4990	5	29.0
4	100 g. 100% phosphoric acid	10	20	117–31	11–9	1.5119	61	40.5
5	100 g. 94% phosphoric acid	25	25	118–25	7–6	1.5038	26	70.5
6	150 g. 85% phosphoric acid	25	30	117–22	6	1.5032	23	60.0
7	80 g. molten trichloroacetic acid	30[c]	40–50[c]	121–38	9–8	1.5130	66	38.0
8	100 g. chloroacetic acid	60[c]	50[c][d]	137–50	11–9[d]	1.5195[d]	..	58.5[d]
9	100 cc. formic acid	120	100	107–17	5–4	1.5060	..	40.0
10	50 g. anhydrous ZnCl2 in 100 cc. glacial acetic acid	120	34	123–38	10–9	1.4995	7	61.5
11	13.5 g. AlCl3 in 75 cc. petroleum ether[e]	30	30	144–48	11–8[d]	1.5250[d]	..	67.0[d]
12	20 g. AlCl3 in 100 cc. carbon disulfide[e]	300	25	Extensive polymerization				
13	13.5 g. AlCl3 in 75 cc. carbon disulfide[e]	60	28	122–40	9–8	1.5084	46	26.0[f]
14	50 g. concd. sulfuric acid, 50 g. 85% phosphoric acid	15	25	129–38	12–11	1.5170	83	66.0
15	20 g. concd. sulfuric acid, 80 g. 85% phosphoric acid	20	25	121–7	8–7	1.5072	41	71.0
16	50 g. 20% oleum, 50 g. 85% phosphoric acid	10	25	125–34	11–9	1.5175	85	63.5
17	70 g. concd. sulfuric acid, 30 g. glacial acetic acid	20	25	118–21	6–5	1.5184	90	71.5
18	60 g. concd. sulfuric acid, 40 g. glacial acetic acid	30	28	133–40	12	1.5155	77	65.0
19	50 g. concd. sulfuric acid, 50 g. glacial acetic acid	30	25	124–35	10	1.5121	62	68.5
20	35 g. concd. sulfuric acid, 65 g. glacial acetic acid	45	30	113–30	8–7	1.5014	15	55.0
21	20 g. concd. sulfuric acid, 80 g. glacial acetic acid	60	30	120–35	13–11	1.4960	0	42.0

[a] Pseudoionone, 20 grams, was added dropwise to the vigorously stirred cyclizing agent at 5–15° C. during 15–30 minutes. The mixture was then stirred for the time and at the temperature indicated.
[b] Calculated from refractive index.
[c] Pseudoionone was added to the reagent during 15 minutes at about 55° C.
[d] Recovered pseudoionone.
[e] Aluminum chloride was added in small portions during 30 minutes to a cooled solution of pseudoionone in the indicated solvent.
[f] 16% pseudoionone was recovered: b.p., 144–50° C. at 9 mm.; n_D^{20} 1.5226.

of the alpha structure. A similar situation exists when sulfuric acid is diluted with glacial acetic acid, except that the break in the dilution curve comes at a somewhat higher concentration of sulfuric acid (about 60 mole %), and the change in cyclizing activity is somewhat more gradual than with water–sulfuric acid mixtures.
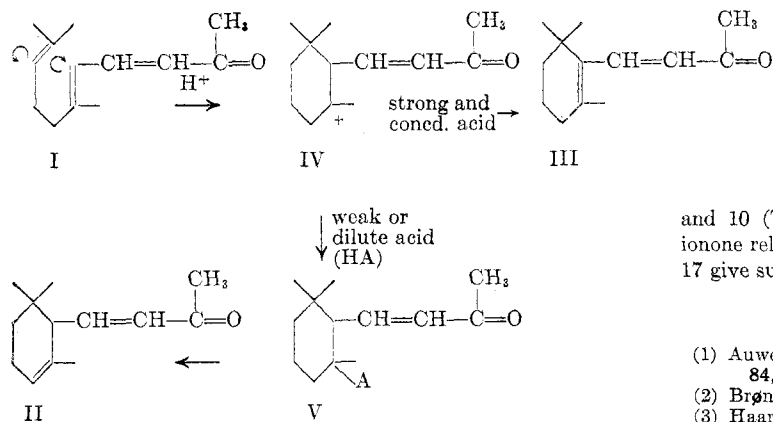
MECHANISM OF THE REACTION

The preceding relations existing between the composition of the ionone mixtures obtained on cyclizing pseudoionone with

TABLE II. CYCLIZATION OF PSEUDOIONONE BY CONCENTRATED ACIDS

Cyclizing Acid	−Log K_a	β-Ionone in Cyclized Product, % Obsvd.	Calcd.
Sulfuric (concd.)	0.40	87	81.7
Trichloroacetic (molten)	0.70	66	77.2
Phosphoric (100%)	1.96	61	58.3
Formic (88%)	3.67	36	32.6

acid reagents, the acid strength, and the dilution of the cyclizing acid suggest the following mechanism for the reaction. Under the influence of an acidic reagent, pseudoionone is converted into the carbonium ion structure (IV). Undoubtedly the conjugated system, including the carbonyl group of I, exerts its anionic activity in strongly acid solutions; but since the cyclization is dependent on the development of an anionic center at the α-carbon of this system, only the latter polarization is shown in the diagram. In concentrated solutions of strong acids, the reaction is completed by eliminating a proton from the labile carbonium ion in such a manner that the ring double bond of the resulting ionone is in conjugation with the side chain—that is, to produce β-ionone (III). In weakly acidic media or in dilute solutions of any acid, however, the carbonium ion (IV) is rapidly removed from the field of action by combination with an anion to give structure V. This intermediate, in contrast to the labile carbonium ion, is relatively nonreactive and can yield ionone only by a subsequent reaction step involving the elimination of a molecule of the acid (HA) and requiring a definite activation energy. The particular ionone produced from intermediate V then becomes a matter of relative reaction rates rather than thermodynamic stability of the resulting ionone. Presumably α-ionone is formed from this intermediate at a considerably more rapid rate than is β-ionone.

Several of the procedures here described for the cyclization of pseudoionone seem satisfactory as laboratory methods for the synthesis of reasonably pure α- and β-ionones. Procedures 6 and 10 (Table I) are recommended for the preparation of α-ionone relatively free of the beta isomer; experiments 2, 16, and 17 give suitable preparative procedures for β-ionone.

LITERATURE CITED

(1) Auwers, K., and Eisenlohr, F., J. prakt. Chem., 82, 126 (1910); 84, 68 (1911).
(2) Brønsted, J. N., Chem. Rev., 5, 231 (1928).
(3) Haarmann and Reimer, Ber., 27, 319, 768 (1894).
(4) Hibbert, H., and Cannon, L. T., J. Am. Chem. Soc., 46, 122 (1924).
(5) Ito, S., Rept. Osaka Ind. Research Lab. (Japan), 5, No. 10 1–22 (1924); 6, No. 12, 1–42 (1925).
(6) Loshakov, P. V., and Shumeiko, A. K., Russian Patent 56,732 (March 31, 1940).
(7) Meuly, W. C. (to Du Pont Co.), U. S. Patents 1,996,116 (April 2, 1935) and 2,080,497 (May 18, 1937).
(8) Schultz, G., and Goettelmann, E., German Patent 288,688 (July 21, 1914).
(9) Simonsen, J. L., "The Terpenes", Vol. I, p. 105, Cambridge Univ. Press, 1931.
(10) Tiemann, F., Ber., 31, 808, 867, 1736, 2313 (1898); 32, 827 (1899); 33, 3708 (1900).
(11) Tiemann, F., and Krueger, P., Ibid., 26, 2692 (1893).