

PERIODATE-PERMANGANATE OXIDATIONS

III. DETERMINATION OF ISOPROPYLIDENE GROUPS¹

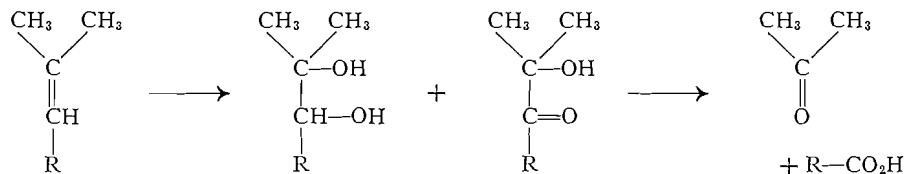
BY E. VON RUDLOFF

ABSTRACT

The reaction of the periodate-permanganate reagent with olefinic double bonds was applied to the determination of isopropylidene groups. The oxidation of compounds containing such groups gave a quantitative yield of acetone which could be readily determined by known iodometric and colorimetric procedures. Use of aqueous solutions of pyridine or dioxane as solvent permitted analysis of water-insoluble compounds. The colorimetric determination of acetone was then preferred. This method also allowed a simultaneous estimation of terminal methylene groups. The content of isopropylidene groups of commercial samples of three terpenes of the geraniol type was determined.

INTRODUCTION

The oxidation of olefinic double bonds with the periodate-permanganate reagent was described in part I of this series (2). From the general characteristics of this reaction the oxidation of an isopropylidene group would be expected to proceed as follows at pH 7-8:



each isopropylidene group yielding one molecule of acetone. At neutrality the acetone formed by the oxidation of mesityl oxide did not appear to react further with the reagent (2). The yield of acetone could, therefore, be used as a convenient measure of isopropylidene groups in general. In conjunction with the semiquantitative estimation of terminal methylene groups, described in part II (3), such a procedure should also make it possible to distinguish readily between these two positions of unsaturation, which would be of special interest in the study of terpenes and resin acids.

RESULTS AND DISCUSSION

In preliminary experiments the effect of pH on the stability of acetone in the oxidation mixture was determined. Table I shows the amount of oxidant consumed when acetone was oxidized at varying pH values with five times the amount of oxidant used in the standard procedure (2).

Since the hydroxylation and cleavage steps are relatively fast reactions (2), it is safe to assume that the amount of acetone lost owing to oxidation will be insignificant at a pH below 8.0.

Acetone can be conveniently determined both iodometrically (5) and colori-

¹Manuscript received August 9, 1955.

Contribution from the National Research Council of Canada, Prairie Regional Laboratory, Saskatoon, Saskatchewan. Issued as Paper No. 204 on the Uses of Plant Products and as N.R.C. No. 3744.

TABLE I
OXIDANT CONSUMED BY ACETONE
Atoms oxygen/mole of acetone

	pH					
	5.4	6.6	6.9	7.3	7.7	8.0
After 70 hr.	0	0.03	0.04	0.05	0.10	0.40
After 142 hr.	0	0.06	0.07	0.10	0.19	0.78

metrically (7). In the former method the acetone was distilled from an alkaline solution after the excess oxidant had been destroyed with sodium arsenite solution. This method could not, however, be used when volatile compounds were present which react with iodine or alkaline iodine solution, unless these were removed by prior oxidation. The colorimetric method proved to be less accurate (the error was $\pm 2\%$), but it had the advantage that aliquots could be used directly from the reduced reaction mixture. In addition, the color reaction is more specific and no interference was obtained when formaldehyde was present in concentrations more than twice that of acetone.

Water-soluble Compounds

From experiments using mesityl oxide as test substance the following conclusions were drawn:

- (1) The amount of oxidant should be at least twice the theoretical amount required for complete oxidation as deduced from the above reaction scheme.
- (2) Increasing the amount of permanganate in the periodate-permanganate reagent increases the rate of reaction (2), but too high a permanganate concentration results in a more rapid oxidation of the acetone formed.
- (3) If other volatile compounds, such as aldehydes, are formed during the oxidation, these may be removed from the distillate by dichromate oxidation (4) in acidic medium at room temperature. Acetone itself is not oxidized under these conditions, but a second distillation step is then introduced into the procedure. As an alternative, the more convenient, though slightly less accurate, colorimetric determination of acetone may be used.

Under optimum conditions the yield of acetone was 95 to 96% of the theoretical. This represented a practically quantitative result, since the sample of mesityl oxide used gave after oxidation a yield of about 2% formaldehyde, indicating the presence of 2 to 3% of the isomer having the double bond in the 4,5-position. The presence of this isomer in mesityl oxide has been reported before (1).

Because of the possible interference with the iodometric determination by volatile reaction products or unreacted starting material from the oxidation of mesityl oxide, 3-methyl-2-butenoic acid appeared to be a more satisfactory test substance and was consequently prepared by hypochlorite oxidation of mesityl oxide (6). On oxidation this acid would be expected to yield acetone, oxalic acid, and carbonic acid, with glyoxylic acid and formic acid as intermediates. The only distillable product at any stage of the periodate-permanganate oxidation from an alkaline reaction mixture would therefore be acetone.

The rate of oxidation of 3-methyl-2-butenic acid was similar to that of mesityl oxide, e.g. at pH 7 the amount of oxidant consumed was equivalent to 2.08, 3.09, 3.65, and 3.88 oxygen atoms after 0.05, 0.5, 3, and 70 hr. respectively. A formaldehyde determination indicated the presence of up to 2% of the Δ^3 -isomer. The yield of acetone was determined iodometrically after different reaction times (from 5 to 360 min. at 5 to 10 min. intervals) with the reagent containing the normal and twice and four times the normal amount of potassium permanganate. A practically quantitative yield was obtained (98.8, 98.8, and $98.4 \pm 0.4\%$ respectively) within one hour of reaction time, and this yield did not appear to drop during a further period of two hours.

Water-insoluble Compounds

When the above procedure was applied to terpenes of the geraniol group, difficulty was encountered because of their insolubility. A study was therefore made of certain organic solvents which, when added to the aqueous reaction mixture, would increase the solubility sufficiently without interfering with the periodate-permanganate oxidation. Of the solvents tested only pyridine and dioxane proved suitable. Reagent blanks containing these solvents, especially dioxane, consumed appreciable amounts of iodine in excess of the aqueous reagent blank (Table II), but the oxidation of mesityl oxide appeared to be little altered in rate and degree by their presence (Table III). When pyridine

TABLE II
TITRATION OF REAGENT BLANKS CONTAINING 25% ORGANIC SOLVENTS
TAKING COMPARATIVE AQUEOUS BLANKS AS 0
Ml. 0.025 *N* iodine solution

Medium	Time (hr.)				
	$\frac{1}{4}$	$\frac{1}{2}$	1	3	24
25% Pyridine solution	0.10	0.15	0.22	0.36	0.72
25% Dioxane solution	1.34	1.36	1.39	1.54	3.58

TABLE III
OXIDANT CONSUMED (ATOMS OXYGEN/MOLE) BY MESITYL OXIDE IN VARIOUS
MEDIA UNDER STANDARD CONDITIONS

Medium	pH	Time (hr.)							
		$\frac{1}{12}$	$\frac{1}{6}$	$\frac{1}{2}$	1	3	22	46	72
Aqueous	7.2	3.0	3.05	3.20	3.50	3.75	3.97	4.00	4.04
Aqueous	7.7	3.05	—	3.28	3.56	3.82	3.98	4.02	4.06
25% Pyridine	8.4	3.12	—	3.24	—	3.48	3.90	4.05	4.11
25% Dioxane	7.3	2.94	3.22	3.44	—	3.84	—	—	—

was used the pH of the reaction mixture was 8.4 and the addition of potassium carbonate was therefore omitted. The reaction mixture containing 25% dioxane decolorized overnight and the reaction stopped. This may have been due to the regeneration of permanganate by periodate being slowed down to a critical value. When 30% or more solvent was used, this phenomenon was

noticed at an earlier stage. However, the early part of the reaction involving the formation of acetone is relatively fast and a quantitative yield of acetone could still be obtained.

Difficulties were experienced when the iodometric method for determining acetone was used since most of the solvent distilled over with the acetone. With dioxane the error introduced was not large, but when pyridine was used the procedure had to be modified by introducing a second distillation step. After the acetone and pyridine from the first distillation was collected, excess 10% sulphuric acid (20-25 ml.) was added and the acetone was redistilled. Although the results obtained by this modification were satisfactory, the procedure was cumbersome and the colorimetric method was preferred. The latter method gave results similar to those with aqueous solutions as long as the reagent blank and reference samples contained the same amount of solvent.

3-Methyl-2-butenic acid was oxidized in the different solvent systems under the usual conditions, and aliquots were analyzed colorimetrically after various reaction times. The time required to reach a maximum yield of acetone was different for each medium, but the maximum values were maintained for 5 to 10 min. After this period the yield dropped somewhat faster than would be expected from the rate of oxidation of the acetone (in an aqueous medium) alone. The results obtained were:

- (1) in aqueous solution = 99% of theoretical (maximum after 10 min.),
- (2) solution containing 25% pyridine = 100% (maximum after 30 min.),
- (3) solution containing 25% dioxane = 99% (maximum after 20 min.).

The foregoing results show that the procedures outlined should be of value in both structure determination and routine analysis, especially since as little as 0.01 mM. of a substance was sufficient for quantitative results. The use of the reagent for determining the position of double bonds in unsaturated fatty acids and related compounds will be the subject of a future communication.

Application to Terpenes

The method was applied to the analysis of three commercial samples of terpenes. Each compound gave the maximum yield of acetone (see Table IV)

TABLE IV
YIELDS OF ACETONE* FROM TERPENES
Per cent of the theoretical

Medium	Terpene		
	Geraniol	Citronellol	Citronellal
Solution containing 25% pyridine	88	79	77
Solution containing 30% dioxane	89	81	79

*Colorimetric procedure.

already after 5 to 10 min. These results show that in each of the terpenes the isomer having the isopropylidene grouping is the major component. The same

reaction mixtures were also analyzed for their content of formaldehyde resulting from the presence of terminal methylene groups. The maximum yields for geraniol, citronellol, and citronellal were 43%, 4%, and 8.5% respectively.

EXPERIMENTAL

Apparatus

The condenser was constructed of capillary glass-tubing surrounded by an ordinary cooling jacket. The tubing extended into the receiver so that the distillate was collected under 10 to 15 ml. of water. The receiver was surrounded by ice water. The connection to the distillation flask was through a standard glass joint.

The colorimetric measurements were carried out with a Coleman electro-photometer (Junior 6A).

Reagents

Analytical grade reagents and solvents were used. Mesityl oxide (Eastman Kodak) was redistilled through a Podbielniak fractionating column. Pyridine and dioxane were further purified by treating with weak alkaline permanganate solution for 16 hr. at room temperature and redistilling over solid potassium hydroxide after the excess permanganate had been reduced.

3-Methyl-2-butenic acid was synthesized by hypochlorite oxidation of mesityl oxide (6) and was purified by recrystallization from water and light petroleum, m.p. 67–68°C. (reported m.p. 66–67.5°C.); neutralization equivalent found 100.7, calc. 100.1. The terpenes were of technical or practical grade (Eastman Kodak) and were not purified further.

Periodate-Permanganate Oxidant

The stock solution of the oxidant contained 20.980 gm. (98.33 mM.) sodium *meta*-periodate and 167 ml. 0.01 *M* (1.67 mM.) potassium permanganate per liter. In experiments using two or four times the concentration of permanganate, the amount of periodate was reduced in order to maintain the total concentration of oxidant at 100 mM. per liter.

Standard Procedure of Oxidation

The substance to be oxidized, 0.5 mM., was dissolved in distilled water, or where necessary, in the required amount of organic solvent, and the solution was made up to 100 ml. with distilled water. To 50 ml. of this solution sufficient potassium carbonate was added (about 25 mgm. for a neutral substance) to give the final reaction mixture a pH of 7.2 to 7.5. To this solution 20 ml. stock oxidant solution was added with shaking, the time of addition being noted, and the solution was quickly made up to 100 ml. Aliquots of 10 ml. were analyzed at the desired time intervals by the method described in part I (2).

Periodate-Permanganate Oxidation and Iodometric Acetone Determination

Aliquots of 10 ml. of the oxidation mixture were placed in 100 ml. flasks having ground glass joints. At the required time interval the oxidation was stopped by adding to each aliquot 1 ml. 1 *M* sodium arsenite, 1 ml. 2 *N* NaOH, and 10 to 15 ml. water. About half the volume of this solution was distilled,

the distillate being collected in 10 to 15 ml. ice-cooled water. Five milliliters 2 *N* sodium hydroxide and 5.0 ml. 0.1 *N* iodine solution were added to the distillate and this solution was allowed to stand out of contact with direct sunlight for 10 to 15 min. Five milliliters 10% sulphuric acid was then added and the liberated iodine was titrated with 0.025 *N* sodium thiosulphate to the starch end point. When dioxane was present 10–15 ml. sulphuric acid had to be added. When pyridine was present the distillate was treated with excess 10% sulphuric acid (approx. 20 ml.) and redistilled. In this way the iodometric determination could be carried out without interference from the pyridine.

Periodate-Permanganate Oxidation and Colorimetric Acetone Determination

The solution of the compound to be oxidized, 2.0 ml., was pipetted into a 25 ml. volumetric flask and 2.0 ml. 0.1 *N* potassium carbonate, 10 ml. water, and 8.0 ml. stock oxidant solution were added. The solution was made up to 25 ml. after noting the time when the oxidant was added. Aliquots of 5.0 ml. of this reaction mixture were pipetted into 10 ml. volumetric flasks and after 5, 10, 20, or 30 min. reaction time 2.0 ml. 1 *M* sodium arsenite and 2.0 ml. 2 *N* sulphuric acid were added. The solutions were allowed to stand for 15 to 30 min., when 0.4 ml. 10 *N* sodium hydroxide (enough to neutralize the solution) was added to each sample, and these were then made up to 10 ml. These solutions could be kept for several hours before colorimetric analysis. Aliquots of 2.0 ml. of each sample were pipetted into a 25 × 200 mm. test tube and 3.0 ml. distilled water was added. When all samples, reagent blanks, and reference standards were thus prepared, 4.0 ml. 10 *N* sodium hydroxide was added with a syringe and finally, with mixing, 1.0 ml. of salicylic aldehyde solution. The salicylic aldehyde solution (1 volume of the aldehyde and 4 volumes ethanol) was used within five to six hours after preparation. The test tubes were immediately placed in a water-bath at 50°C., kept at 45–50°C. for 20 min. and then at room temperature for 30 min. The contents were transferred to 19 mm. cuvettes for immediate measurement of the percentage transmission at 530 $m\mu$ as compared to a reagent blank.

Formaldehyde Determinations

Aliquots of 1.0 ml. from the reaction mixture in the 10 ml. volumetric flasks could be used directly and these were analyzed as described in part II (3).

ACKNOWLEDGMENT

The author wishes to express his thanks to Drs. A. C. Neish and A. S. Perlin for helpful advice.

REFERENCES

1. DUPONT, G. and MENUT, M. Bull. soc. chim. France [V], 6: 1215. 1939.
2. LEMIEUX, R. U. and RUDLOFF, E. VON. Can. J. Chem. 33: 1701. 1955.
3. LEMIEUX, R. U. and RUDLOFF, E. VON. Can. J. Chem. 33: 1710. 1955.
4. NEISH, A. C. Nat. Research Council of Can. Rept. No. 46-8-3. 2nd revision, 1952.
5. PREGI, F. and GRANT, J. Quantitative organic microanalysis. The Blakiston Co., Philadelphia. 1946. p. 170.
6. SMITH, L. I., PRICHARD, W. W., and SPILLANE, L. J. Organic synthesis. Vol. 23. John Wiley & Sons, Inc., New York. 1946. p. 27.
7. SNELL, F. D. and SNELL, C. T. Colorimetric methods of analysis. Vol. III. D. Van Nostrand Company Inc., New York. 1953. p. 285.