Tetrahedron. Vol. 23, pp. 3757 to 3762. Pergamon Press Ltd. 1967. Printed in Great Britain

ON THE MECHANISM OF THE CYCLIZATION OF ψ-IONONE WITH DEUTERATED ACIDS*

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(*Received* 6 *January* 1967; *accepted for publication* 19 *January* 1967)

Abstract—The cyclization of ψ-ionone with deuterated sulphuric acid and deuterated phosphoric acid to α- and β-ionone is discussed. β-ionone is formed predominantly via α-ionone.

INTRODUCTION

IN AN earlier report[2] on the cyclization of ψ-ionone under the influence of deuterated sulphuric acid we discussed the validity of the mechanism of this reaction as given by Smit, *et al.*[3-5] These authors assumed that in the cyclization of ψ-ionone to α- and β-ionone with sulphuric acid *primarily* α- and β-ionone are formed in a ratio of 9:1. Owing to the irreversible isomerization of α-ionone to β-ionone under these conditions the latter compound can be obtained almost exclusively.

The purpose of the present investigation[1] is to test the assumption of the Russian authors unequivocally by the cyclization of ψ-ionone in deuterated acids and studying the deuterium content in the reaction products. For this purpose deuterium

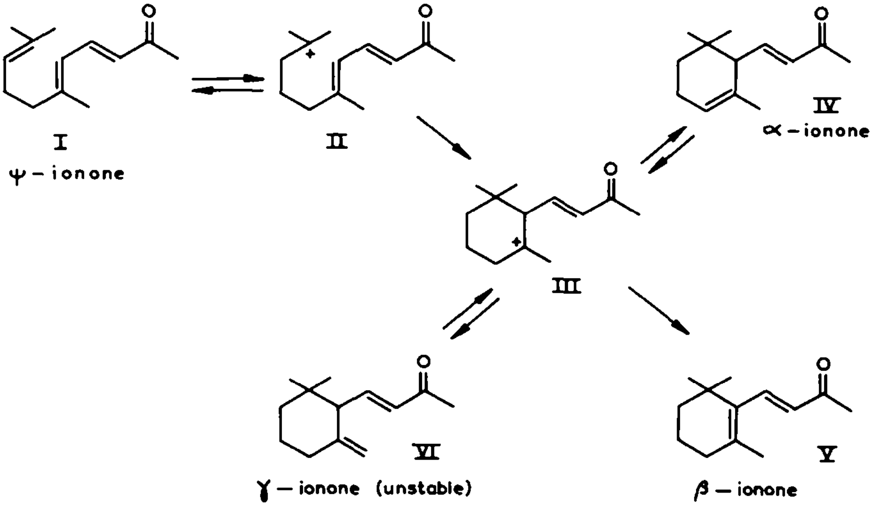

FIG. 1 Mechanism of the cyclization of ψ-ionone with sulphuric acid.

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* Taken in part from the Thesis of H. A. van 't Hof, Amsterdam (1966).[1]

[1] Thesis, H. A. van 't Hof, Amsterdam (1966).

[2] Th. J. de Boer, H. A. van 't Hof and J. U. Veenland, *Rec. Trav. Chim.* **83**, 689 (1964).

[3] V. A. Smit and V. F. Kucherov, *Uspekhi Khim* **28**, 272 (1959); *Chem. Abstr.* **53**, 14915f (1959).

[4] A. V. Semenovsky, V. A. Smit and V. F. Kucherov, *Proc. Acad. Sci. USSR* (Engl. ed.) **132**, 687 (1960).

[5] V. A. Smit, A. V. Semenovsky, V. M. Medveda and V. F. Kucherov, *Proc. Acad. Sci. USSR* (Engl. ed.) **124**, 141 (1959).

analyses of α-ionone and β-ionone were performed by a mass-spectrometric determination of the average number of deuterium atoms and location of the deuterium atoms by NMR spectrometry.[1,2] Our experiments support the mechanism depicted in Fig. 1 for the cyclization of ψ-ionone with sulphuric acid.

Results of cyclization of ψ-ionone and isomerizations of α- and γ-ionone with deuterosulphuric acid

Cyclizations of ψ-ionone in mixtures of deuterosulphuric acid, heavy water and nitromethane were carried out under various conditions[5] as indicated in Table 1. This Table also lists the isomerization of α- and γ-ionone.

TABLE 1. DEPENDENCE OF PRODUCT RATIOS (α-:β-IONONE) ON REACTANT RATIOS (ψ-, α- OR γ-IONONE): D_2SO_4:D_2O

Exp.	g of ionone ψ-, α- or γ-		g of D_2SO_4 (100%)	g of D_2O	g of nitromethane	Temp	Reaction time in min	Ratio α-:β-ionone
1	3·60	ψ-	11·30	—	9·00	10°	11	0:100
2	3·60	α-	11·30	—	9·00	10°	11	0:100
3	5·00	ψ-	13·80	—	11·30	−14°	15	17:83
4	5·00	ψ-	13·11	0·125	11·52	−14°	15	23:77
5	5·00	ψ-	12·42	0·25	11·85	−14°	15	41:59
6	5·00	ψ-	11·73	0·375	12·14	−14°	15	47:53
7	5·00	ψ-	11·04	0·50	12·42	−14°	15	68:32
8	5·00	ψ-	10·35	0·625	12·71	−14°	15	77:23
9	5·00	ψ-	9·66	0·75	13·00	−14°	15	76:24
10	5·00	α-	9·66	0·75	13·00	−14°	15	89:11
11	3·00	γ-	6·20	0·39	7·63	−10°	15	59:41
12	5·00	ψ-	10·35	0·625	12·71	−10°	15	59:41

When mixtures of α- and β-ionone were obtained in these reactions the components were separated by preparative gas chromatography. The deuterium content of the components is given in Table 2 for α-ionone and in Table 3 for β-ionone. Under the reaction conditions β-ionone does not exchange deuterium.

DISCUSSION

In Fig. 2 the results of experiments 1 and 2 are depicted.

For β-ionone from reaction 1 (ψ-ionone → β-ionone, molar ratio D_2SO_4: ψ-ionone = 6) the deuterium content can be easily explained. The cyclization starts with deuteration of the double bond at the *gem*-dimethyl group (Fig. 1), therefore carbon-5 of β-ionone is deuterated. The intermediate carbonium ions II and III (Fig. 1) exchange hydrogen at the α-positions[6-10] (equilibria with alkenes). This

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[6] D. N. Kursanov, E. V. Bykova and V. N. Setkina, *Bull. Acad. Sci. USSR* (transl.) 790 (1958).

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Table 2. Deuterium distribution in α-ionone obtained in the cyclization of ψ-ionone and in the isomerisation of γ-ionone

	Exp. 3	Exp. 4*	Exp. 5	Exp. 6	Exp. 7	Exp. 8	Exp. 9	Exp. 11
Relative amount of deuterosulphuric acid (Exp. 3–9) arbitrary units	100	95	90	85	80	75	70	
% of α-ionone formed in α/β mixture	17	23	41	47	68	77	76	
D-content at								
C-1	—	—	—	0·1	0·1	—	—	—
Methyl at C-2	0·5	0·8	0·4	0·5	0·2	0·5	0·3	0·9
C-3	0·6	0·6	0·4	0·4	0·4	0·1	0·1	0·3
C-4	—	—	—	—	—	—	—	—
C-5†	0·5	0·3	0·7	0·2	0·8	0·4	0·9	—
gem-Dimethyl†	0·4	—	0·2	0·5	0·1	0·6	0·3	0·1
C-1′	0·2	0·3	0·4	0·1	0·1	0·3	0·3	0·2
C-3′	0·1	0·2	—	0·1	—	—	—	—
C-4′	—	0·2	—	—	—	—	—	—
Total	2·3	2·4*	2·1	1·9	1·7	1·9	1·9	1·5

* Errors due to NMR measurements in a more diluted sample.

† It is not clear why the deuterium content at C-5 and in the *gem*-dimethyl group is not reproducible. We expected ca. 1·0 deuterium atom at C-5.

Table 3. Deuterium distribution in β-ionone obtained in the cyclization of ψ-ionone (exp. 1, 3–9), the isomerizations of α-ionone (exp. 2) and of γ-ionone (exp. 11)

	Exp. 1	Exp. 2	Exp. 3	Exp. 4	Exp. 5	Exp. 6	Exp. 7	Exp. 8	Exp. 9	Exp. 11†
Relative amount of deuterosulphuric acid (Exp. 3–9) arbitrary units			100	95	90	85	80	75	70	
% of β-ionone formed in α/β mixture	100	100	83	77	59	53	32	23	24	
D-content at Methyl at C-2	0·4	0·5	0·4	0·4	0·6	0·4	0·5	0·3	0·5	1·0
C-3	0·9	1·1	1·1	0·9	0·8	0·7	0·6	0·1	0·2	0·5
C-4 } * C-5 }	1·1*	0·5	0·9	1·1	0·7	0·9	0·6	1·0	0·7	—
gem-Dimethyl	0·7	0·2	0·1	0·1	0·1	0·2	0·1	0·5	0·3	—
C-1′	0·1	0·2	0·1	—	0·1	0·1	0·1	—	—	—
C-3′	—	—	—	0·1	0·1	—	—	—	0·1	—
C-4′	—	—	—	—	—	—	—	—	0·1	—
Total	3·2	2·5	2·6	2·6	2·4	2·3	1·9	1·9	1·9	1·5

* Separate determination not possible.

† Corrected for an error due to deformed multiplets.

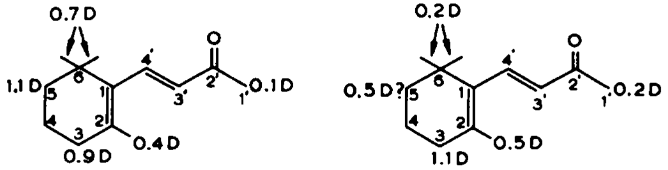

FIG. 2 Deuterium content of β-ionone obtained from ψ- and α-ionone (Exp. 1 and 2).

"carbonium ion exchange" accounts for the deuterium content at the *gem*-dimethyl group and in the Me group at C-2 in β-ionone. It also explains the presence of deuterium at C-3. The amount of deuterium at this position is much greater than that in the Me groups. This means that the equilibrium of carbonium ion III with α-ionone is very important or in other words that β-ionone is formed predominantly from α-ionone. Because deuterium incorporation proceeds via carbonium ions no deuterium is present at C-4. Although in the NMR spectrum hydrogens at C-4 and C-5 are not recorded separately any decrease of the corresponding peak by deuteration must essentially be due to incorporation at C-5. The small deuterium content at C-1′ may be due to an enolization process but is not certain because of the experimental error in the deuterium determination.[1]

For β-ionone from reaction 2 (α-ionone → β-ionone) the deuterium content can be explained analogically. The deuterium content at C-4 + C-5 is not certain because of integration of overlapping and deformed signals[1] but might be due to an equilibrium between carbonium ions II and III. Exchange of II can also explain the presence of deuterium in the *gem*-dimethyl group, but an equilibrium between II and III seems unlikely. When the cyclization of ψ-ionone is carried out under less rigorous conditions (lower temp, relatively smaller amount of sulphuric acid (100%) than in Exp. 1) mixtures of α- and β-ionone are formed (Exp. 3–9). In the α-ionone obtained (Table 2) the amount of deuterium at C-1 is negligible. This means that β-ionone is formed irreversibly from carbonium ion III. At C-3 a smaller amount of deuterium is found at low acid concentrations although the same total amount of deuterium is used: α-ionone is more stable at low than at high acid concentration and is hence not attacked by D^+ so readily.

The deuterium content at C-3 in β-ionone (Table 3, Exp. 3–9) is most interesting. When smaller amounts of acid are used (again the total amount of deuterium was kept constant), C-3 contains smaller amounts of deuterium: at high acid concentration (e.g. Exp. 3) much β-ionone is formed, but a predominant part of this β-ionone must be formed via α-ionone thus by deuteration at C-3. At low acid concentration (e.g. Exp. 9) little β-ionone is formed, but much of this is formed in a direct way from ψ-ionone and hence without deuteration at C-3.

Comparison of reaction 9 and 10 learns that about 13% of β-ionone is formed in a direct way. This means that α-ionone is formed about 7 times as fast from carbonium ion II as β-ionone. This corresponds with a difference in energy of activation of about 1·0 kcal/mol at −14°. This difference probably originates from a steric effect in the abstraction of a proton from carbon atom-1 in the carbonium ion III as compared with proton abstraction from carbon atom-3. As α-ionone is in equilibrium with III and β-ionone is not, all α-ionone isomerizes to β-ionone;

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[11] G. Ohloff and G. Schade, *Angew. Chem.* **74**, 944 (1962).

ψ- and γ-ionone give with about the same rate (contrary to α-ionone) the cyclic carbonium ion III since they give the same α-/β-ratio: 59/41 under the same reaction conditions (Exp. 11 and 12). For γ-ionone (VI) there is an equilibrium with III, but γ-ionone* is unstable under the reaction conditions.

Cyclization of ψ-ionone with deuterophosphoric acid

In the cyclization of ψ-ionone with phosphoric acid (85 %) α-ionone is formed as the main product.[12] With more concentrated phosphoric acid it is possible to prepare approximately equimolar mixtures of α- and β-ionone. The cyclization of ψ-ionone (Exp. 13) and the isomerization of α-ionone (Exp. 14) were carried out with deuterophosphoric acid (93·6 %). In these reactions more drastic conditions (much more acid, no solvent, higher temp and longer reaction time) are necessary than in the reactions with sulphuric acid. Cyclization of ψ-ionone yields 40 % α- and 60 % β-ionone, isomerization of α-ionone yields 47 % α- and 53 % β-ionone. This suggests that in the cyclization about 7 % β-ionone is formed in a direct way.

Table 4 lists the deuterium content of α- and β-ionone obtained by cyclization of ψ-ionone (Exp. 13) and isomerization of α-ionone (Exp. 14) with deuterophosphoric acid.

TABLE 4. DEUTERIUM DISTRIBUTION IN α- AND β-IONONE OBTAINED BY CYCLIZATION OF ψ-IONONE (EXP. 13) AND ISOMERIZATION OF α-IONONE (EXP. 14) WITH DEUTEROPHOSPHORIC ACID

	Number of deuterium atoms per molecule of α-ionone		Number of deuterium atoms per molecule of β-ionone	
	Exp. 13	Exp. 14	Exp. 13	Exp. 14
D-content at				
C-1	0·8	0·6	—	—
Methyl at C-2	1·5	1·2	1·8	1·6
C-3	0·6	0·7	1·1	1·3
C-4	—	—	1·2	—
C-5	1·5	0·3		
gem-Dimethyl	2·1	—	2·3	—
C-1′	0·6	0·8	0·8	1·2
C-3′	—	—	0·1	—
C-4′	—	—	—	—
Total	7·1	3·6	7·3	4·1

The amounts of deuterophosphoric acid (93·6 %) were chosen so that per molecule of ψ- resp. α-ionone about 50 deuterium atoms were available. The abundance of deuterated acid and the other rigorous conditions result in stronger deuteration than in the reactions described for deuterosulphuric acid. Especially "carbonium ion exchange" is more important. In α-ionone also deuterium is found at C-1. This means that β-ionone is in equilibrium with carbonium ion III (Fig. 1).

There is considerable deuterium in the acetyl group (C-1′) due to enolization.

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* We thank Mr. Schade of the Max Planck Institut für Kohlenforschung at Mülheim/Ruhr for a sample of γ-ionone.[11]

[12] E. E. Royals, *Ind. Eng. Chem.* **38**, 546 (1946).

Qualitatively, for the remainder, the same results were obtained as in the reactions with deuterosulphuric acid. Under the conditions of the cyclization β-ionone isomerizes for 19% to α-ionone. In the β-ionone from this reaction 0·5 deuterium atom was found in the acetyl group (C-1') and 0·6 deuterium atom at C-3. This is in agreement with an equilibrium with α-ionone.

EXPERIMENTAL

Deuterosulphuric acid (100%) was prepared from heavy water and SO_3 as described.[13] Deuterophosphoric acid was prepared from $POCl_3$ and D_2O according to directions given[14] for phosphoric acid. During the course of the investigation it was found that the ratio α-/β-ionone is somewhat smaller in cyclization with a proton acid than with a corresponding—somewhat weaker—deutero acid. Phosphoric acid and deuterophosphoric acid of the same Ho (Do) gave α- and β-ionone in considerably different ratios.[1]

Experiments 1 and 2 (cyclization of ψ-ionone and isomerization of α-ionone to β-ionone) were carried out as follows: to a stirred soln of 11·30 g deuterosulphuric acid (100%) in 9·00 g freshly distilled nitromethane, 3·60 g of ψ- resp. α-ionone was added in 5 min. Per molecule of ψ- resp. α-ionone 12 atoms of deuterium are available. During addition—especially the addition of ψ-ionone—much heat was evolved. The reaction temp was held at about 10° by cooling. The total reaction time was 11 min. The reaction mixture was poured into a mixture of ice, water and ether. The ethereal layer was separated and the water layer extracted with ether. The ethereal layers were washed with $NaHCO_3$ aq and water and dried with $MgSO_4$. Distillation *in vacuo* yielded the desired product.

Experiments 3–12 were carried out similarly, the conditions being given in Table 1. Deuterium atoms (10·6) per molecule of ψ-ionone were available.

Experiments 13 and 14 (cyclization of ψ-ionone and isomerization of α-ionone with deuterophosphoric acid) were carried out according to Hibbert and Cannon,[15] 50 atoms of deuterium always being available per molecule ψ-ionone.

In all these experiments the b.p. of the reaction product varied from 65°/0·2 mm (α-ionone) to 70°/0·2 mm (β-ionone). The yield in cyclization was 60% and in isomerization 70%.

Under the conditions of the cyclization β-ionone was treated for 15 min with deuterosulphuric acid. Mass-spectrometrically no deuterium could be detected (no change in the $M + 1/M$ ratio) in the β-ionone recovered. The same holds for nitromethane, when treated for 4 hr with deuterosulphuric acid under the cyclization conditions.

GLC was used on an analytical or preparative scale. Analytical columns (length 2 m) had an inner diameter of 5 mm, preparative columns (length 3·5 m) an inner diameter of 8 mm. For analytical work 15% stationnary phase on "Kieselguhr", for preparative work 25% stationnary phase on "Kieselguhr" was used. As stationnary phase silicone oil[16] was used for mixtures of α- and β-ionone.

In experiment 11 Emulphor-0[17] was used to show that γ-ionone was completely converted. Column temps: analytical 170°, preparative 190°, Exp. 11: 210°. Carrier gas: He. Isomer ratios were calculated from peak areas.

Mass spectra were taken on an A.E.I.-type MS-2-H instrument. The bombarding energy for deuterium analyses was: α-ionone 9·6 eV, β-ionone 9·2 eV.

NMR spectra were obtained with a Varian HR-60 and a Varian A-60 spectrometer (solvent CCl_4, internal standard TMS).

Acknowledgements—The authors are indebted to Drs. B. C. Roest for valuable assistance in the experimental work and his interest in the subject. They wish also to express their thanks to Drs. P. J. van der Haak, Dr. H. J. Hofman, Dr. P. K. Korver and Mr. C. Kruk for valuable assistance with the NMR and mass-spectra and to Chemische Fabriek "Naarden" for generous gifts of ionones.

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