Acid-catalyzed Reactions of Cyclobutanones. II.[1] Generation of Acylium Ions from β,γ-Unsaturated Cyclobutanones

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Received October 5, 1971

Acid-catalyzed rearrangement of 3-methylene-2,2,4,4-tetramethylcyclobutanone (**1**) gave the γ-lactone of 2,2,3,4-tetramethyl-4-hydroxyvaleric acid. Reaction of 2,2,4,4-tetramethylcyclobutane-1,3-dione (**5**) with PPA gave diisopropylketone with evolution of carbon dioxide. Acylium ions are postulated as intermediates in both these reactions.

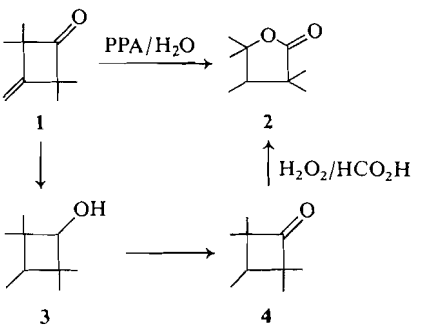
La transposition acido-catalysée du méthylène-3 tétraméthyl-2,2,4,4 cyclobutanone (**1**) conduit à la γ-lactone de l'acide tétraméthyl-2,2,3,4 hydroxy-4 valérique. La réaction de la tétraméthyl-2,2,4,4 cyclobutanedione-1,3 (**5**) avec le PPA conduit à la diisopropylcétone avec dégagement de dioxyde de carbone. Les ions acyliums sont postulés comme intermédiaires dans ces deux réactions.

Canadian Journal of Chemistry, **50**, 952 (1972)

The acid-catalyzed rearrangement of exocyclic α,β-unsaturated cyclobutanones has been shown to involve acylium ions as intermediates (1). The strain involved in having two sp^2 centers in an already strained cyclobutane ring (E_{strain} 26 kcal/mol) (2) would permit pathways of high activation energies in medium ring systems to operate in small rings. We wish to report some novel ring opening reactions of β,γ-unsaturated cyclobutanones in the presence of strong acid.

Rearrangement of 3-Methylene-2,2,4,4-tetramethylcyclobutanone (1) in Polyphosphoric Acid

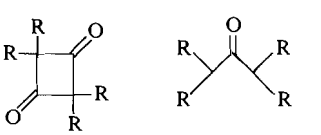
Ketone **1** was prepared according to Hannon (3). Reaction of ketone **1** in polyphosphoric acid (PPA) (50/50 mixture of P_2O_5 and H_3PO_4) at 100° for 1 h resulted in a smooth conversion to the lactone **2** (see Scheme 1). Its structure was deduced from analytical and spectroscopic data as well as independent synthesis. Atmospheric hydrogenation of **1** resulted in an 80/20 mixture of the over-reduced alcohol **3** and the saturated ketone **4**. Jones oxidation of this mixture gave a quantitative yield of **4** which under Baeyer–Villiger oxidation conditions resulted in the exclusive formation of lactone **2**, identical in all respects with the sample obtained from the acid reaction of ketone **1**.



SCHEME 1

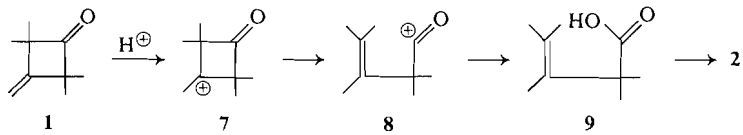
Reactions of 1,3-Cyclobutanediones in PPA

Commercial 2,2,4,4-tetramethylcyclobutane-1,3-dione (**5**) subjected to PPA at 100° for 1 h gave diisopropylketone (**6**) as the major product. Its structure was obtained from spectral data as well as comparison with an authentic sample.



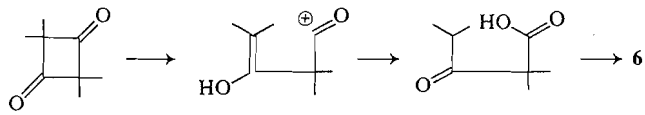
5 R = CH_3 **6** R = CH_3
5a R = C_6H_5 **6a** R = C_6H_5

[1]For paper I of this series see ref. 1.



1 7 8 9

SCHEME 2



5 10 11

SCHEME 3

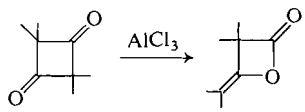
Evolution of carbon dioxide accompanied the acid reaction as evidenced by a positive test in passing the evolved gas through an aqueous solution of barium hydroxide under a stream of nitrogen. Under the same conditions 2,2,4,4-tetraphenylcyclobutane-1,3-dione (**5***a*) was inert.

Discussion

The formation of γ-lactone **2** from 3-methylene-2,2,4,4-tetramethylcyclobutanone (**1**) can be envisaged to proceed by Scheme 2. Although the carbonyl group in **1** would be preferentially protonated over the exo-methylene function, an equilibrium between the two species is established. Ring opening of **7** could compete over any other reaction pathway from the protonated ketone **1** to give acylium ion **8** which, upon reaction with water, gives rise to the β,γ-unsaturated carboxylic acid **9**. The cyclization of **9** to its lactone under the strong acid conditions is a common reaction.

A similar mechanism can be invoked for the formation of diisopropylketone from 2,2,4,4-tetramethylcyclobutane-1,3-dione (**5**). Protonation and ring opening could conceivably give rise to the acylium ion **10** (Scheme 3). Hydroxylation could result in the formation of 2,2,4-trimethyl-3-oxovaleric acid (**9**) which under these conditions could readily decarboxylate to diisopropylketone (**6**). The valeric acid derivative **9** was prepared from its methyl ester (4) which in turn is readily available from the alkali ring opening of 2,2,4,4-tetramethylcyclobutane-1,3-dione in methanol. Under the acid conditions it was shown that **9** gave a quantitative yield of ketone **6**.

Under completely anhydrous conditions 2,2,4,4-tetramethylcyclobutane-1,3-dione (**5**) has been reported to undergo an acid-catalyzed rearrangement to give lactone **12** (5) (eq. 1). In



[1] 5 12

this case the acylium ion (aluminum chloride complex) cyclizes by intramolecular addition of enolate ion. The inertness of 2,2,4,4-tetraphenylcyclobutane-1,3-dione (***4a***) to acid-catalyzed ring opening lies in the inherent stability of the phenyl substituents. A similar kind of rearrangement would disrupt the aromaticity of one of the phenyl substituents.

Experimental

Melting points are uncorrected. The i.r. spectra were recorded with a Unicam SP 1000 instrument. The n.m.r. spectra were measured with a Varian A-60 and a Varian HA-100 instrument. Samples were dissolved in CCl_4 solution using tetramethylsilane as the internal standard. Vapor phase chromatography was performed on a Varian Aerograph 90-P instrument using 3% SE-30 on a Varaport 30 column at an operating temperature of 100°.

3-Methylene-2,2,4,4-tetramethylcyclobutanone (1)

This ketone was prepared by the method of Hannon in a private communication (3) which is described below.

The monophenylimine of 2,2,4,4-tetramethylcyclobutane-1,3-dione (2.0 g) (6) in 10 ml ether was added in one lot to a stirred suspension of triphenylphosphonium methyl iodide (4.2 g) and potassium *t*-butoxide (1.2 g) in sodium dried ether (50 ml) under an atmosphere of nitrogen. The canary-yellow colored mixture was stirred overnight, diluted with water, and extracted with ether. The ether layer was then dried over anhydrous magnesium sulfate and the ether was evaporated under vacuum. The solid residue was taken up in petroleum ether (b.p. 40–60°) and the solution cooled in ice. The triphenylphosphine oxide which precipitated (2.5 g) was removed by filtration and the filtrate extracted with a solution of 80% methanol: water (2 × 100 ml). This solution was back-extracted with petroleum ether and the combined petroleum ether lots washed with water and dried over magnesium sulfate. Removal of the petroleum ether left an oil which could be crystallized by scratching (1.8 g) m.p. 45–47°. The solid was purified by evaporative distillation (60°/3 mm) m.p. 47–48°.

The imine of 3-methylene-2,2,4,4-tetramethylcyclobutanone (0.9 g) was stirred and refluxed with 50% acetic acid (50 ml). A solid collected in the reflux condenser in a few minutes. This was washed back into the solution and refluxing continued for 1 h. After cooling, the excess acetic acid was destroyed by addition of solid sodium bicarbonate. The mixture was then extracted with ether and the ether layer was washed with water until neutral, dried over anhydrous magnesium sulfate, and evaporated to give an oil. The oil mixture was sublimed at room temperature at 25 mm pressure to give a crystalline material, m.p. 43–44° (lit. 42–43° (3)).

Reaction of 3-Methylene-2,2,4,4-tetramethylcyclobutanone (1) with PPA

A mixture of 500 mg of **1** and 1 g of PPA (1:1 mixture of P_2O_5 and H_3PO_4 aged for 24 h at 100°) was heated at 100° for 1 h in a flask equipped with a condenser. Water (5.0 ml) was added to the cooled mixture and 50 ml of ether was added for extraction. The ether layer was washed neutral with water, dried over anhydrous magnesium sulfate, and the ether evaporated to give an oil which crystallized after scratching. The crystalline mixture was purified by preparative v.p.c. to give a crystalline material (**2**) m.p. 55–56°; i.r.: 1775 cm^{-1} (C=O stretch); n.m.r.: 0.94 (3H, d, J = 7.5 Hz), 1.03 (3H, s), 1.01 (3H, s), 1.22 (3H, s), 1.33 (3H, s), 2.00 p.p.m. (1H, q, J = 7.5 Hz); *m/e* 156, (base peak 42 *m/e*).

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.2; H, 10.3. Found: C, 69.0; H, 10.4.

Hydrogenation of 3-Methylene-2,2,4,4-tetramethylcyclobutanone (1)

Ketone **1** (500 mg) in 10 ml of ethyl acetate and 100 mg of PtO_2 was placed in an atmosphere of hydrogen overnight. The catalyst was filtered off and the ethyl acetate evaporated to give an oil which showed two peaks on v.p.c. in a ratio of 4:1. Both peaks were collected and had the following spectroscopic data. The major peak (**3**) was an oil, i.r.: 3420, 1120, 1065, 1015 (alcohol) cm^{-1}; *m/e*: 142. The minor peak (**4**) also was an oil, i.r.: 1786 cm^{-1} (C=O stretch, cyclobutanone); *m/e*: 140 (10 eV).

Jones Oxidation of the Hydrogenation Products of Ketone 1

The mixture (400 mg) obtained from the hydrogenation of ketone **1** was dissolved in 5.0 ml of acetone. To the cooled (0°) solution was added, dropwise, Jones reagent (7) until the yellow color persisted. Methanol was added dropwise until the yellow color disappeared. The solution was taken up in 50 ml ether, washed with water until neutral, dried over magnesium sulfate, and evaporated to give an oil **4** which had an identical i.r. spectrum with the minor component obtained from the hydrogenation of ketone **1**. The v.p.c. retention times were also identical.

Baeyer–Villiger Oxidation of Ketone 4

A mixture of 300 mg of ketone **4**, 1.0 ml of formic acid, and 0.5 ml of 30% H_2O_2 was stirred for 3 h. To this mixture was added 30 ml of ether. The ether extract was washed with 10% sodium bicarbonate solution and then 10% sodium sulfite solution, dried over anhydrous magnesium sulfate, and evaporated to give 270 mg of an oil which crystallized after scratching. This was further purified by preparative v.p.c. to give a crystalline product **2** m.p. 54–56°, which had identical i.r. and n.m.r. spectra with the material obtained from the acid reaction of ketone **1**, mixed m.p. 54–55°.

Reaction of 2,2,4,4-Tetramethylcyclobutane-1,3-dione (5) with PPA

A mixture of 1.0 g of **5** and 1.0 g of PPA was stirred at 100° for 1 h in a flask equipped with a condenser. Water (3.0 ml) was added to the cooled mixture. This was taken up in 50 ml of ether. The ether extract was washed with water until neutral, dried over anhydrous magnesium sulfate, and evaporated to give 800 mg of an oil which on v.p.c. showed two major peaks and one minor peak (<2% of mixture). The two major peaks were collected. The more polar one proved to be identical with 2,2,4,4-tetramethylcyclobutane-1,3-dione (**5**) by comparison of its i.r. spectrum and v.p.c. retention time. The less polar product showed i.r. and n.m.r. spectra identical with commercial sample of diisopropyl ketone. In a second run the gas evolved in the acid reaction was detected as CO_2 as evidenced by precipitation of $BaCO_3$ from an aqueous solution of barium hydroxide as the gas was passed through.

Reaction of 2,2,4,4-Tetraphenylcyclobutane-1,3-dione (4a) with PPA

The same procedure as for the PPA reaction with ketone **6** was repeated with 500 mg of ketone **6a**. After the usual work-up the starting material was recovered unchanged as shown by t.l.c., i.r., and n.m.r. spectra.

2,2,4-Trimethyl-3-oxovaleric Acid Methyl Ester

Dione **6** (2.0 g) in 10 ml of methanol containing 1.5 g of Na_2CO_3 and 5.0 ml of water was stirred at room temperature for 30 min. The mixture was taken up in 60 ml of ether, washed neutral with water, and evaporated to give 1.7 g of an oil, b.p. 92–93° (25 mm); i.r. 1720 (C=O, ketone), 1750 cm^{-1} (C=O stretch of ester); n.m.r.: 0.93 (6H, d, J = 7 Hz), 1.21 (6H, s), 2.71 (1H, q, J = 7 Hz), 3.55 p.p.m. (3H, s); *m/e*: 172.

2,2,4-Trimethyl-3-oxovaleric Acid (9)

A methanolic solution (5.0 ml) of 1.0 g of the methyl ester of **9** and 300 mg of sodium hydroxide was stirred at room temperature. Ether (25 ml) and water (5.0 ml) were added. The aqueous solution was separated and acidified with concentrated HCl solution. The acidified solution was re-extracted with 30 ml of ether. The ether layer was washed with water until neutral, dried over magnesium sulfate, and

evaporated to give 400 mg of an oil, b.p. 104° at 0.5 mm (lit. 105° at 0.5 mm (8)); i.r.: 3400–3100, 1720 cm^{-1} (carboxylic acid, broad peak): n.m.r.: 10.42 (1H, s, exchangeable with D_2O), 2.90 (1H, q, $J = 7$ Hz), 1.32 (6H, s), 1.03 p.p.m. (6H, d, $J = 7$ Hz).

*Reaction of 2,2,4-Trimethyl-3-oxovaleric Acid (**6**) with PPA*

The acid **6** (300 mg) was treated with PPA (0.5 g) using the identical procedure as described above for ketone **5**. Using the same work-up conditions 200 mg of an oil was obtained whose i.r. and n.m.r. spectra were identical with those of a commercial sample of diisopropyl ketone.

The author would like to thank the National Research Council of Canada for their financial support of this research.

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Erratum: Microwave Spectrum and Conformation of Tetrahydropyran

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(Ref.: Can. J. Chem. **47**, 1289 (1969))

AND

Erratum: Microwave Spectrum of Morpholine

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(Ref.: Can. J. Chem. **47**, 3453 (1969))
Received November 29, 1971

Canadian Journal of Chemistry, **50**, 955 (1972)

When recalibrating the Stark cell during the determination of the dipole moment of 1,3-dioxane, an error was discovered in the earlier calibration, which had been used in the calculations of the dipole moments of tetrahydropyran (1) and morpholine (2). Correcting this calculation error and using the same experimental data (1, 2) the corrected values are:

	μ_a(D)	μ_c(D)	μ(D)
Tetrahydropyran	1.39(0.02)	0.74(0.02)	1.58(0.03)
Morpholine	1.53(0.01)	0.27(0.01)	1.55(0.02)

The μ values agree well with those measured in benzene solution of 1.55 (3) and 1.52 D(4), respectively.

Also in Table IX of the morpholine publication (2), the transition given as 2_{12}–3_{22} is actually 2_{21}—3_{22}.

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