whose pmr spectrum showed 85–87% exchange of methylene protium for deuterium.

**E. 24, $D_2O$, and $Et_3N$.**—A mixture of **24** (0.20 g, 0.00141 mol), deuterium oxide (0.80 ml), dry tetrahydrofuran (10 ml), and triethylamine (*ca.* 0.01 ml) resulted in some decomposition of **24** in 6 hr. Sublimation led to **24**, yield 0.12 g, whose pmr spectrum revealed complete disappearance of the 2.95-ppm signal for methylene protium.

**F. 24, $D_2O$, and HCl.**—Sublimed **24** (0.19 g), obtained from a mixture of **24** (0.22 g, 0.00157 mol), deuterium oxide (0.80 ml), and hydrochloric acid (*ca.* 0.01 ml) in tetrahydrofuran (10 ml) for 10 hr, contained only 10% methylene protium.

**G. 25, $D_2O$, and $Et_3N$.**—Diketone **25** is extensively decomposed in less than 15 min in deuterium oxide–tetrahydrofuran containing small amounts of triethylamine.

**H. 25, $D_2O$, and HCl.**—In neat deuterium oxide containing a trace of hydrochloric acid, **25** undergoes 90% exchange of its methylene protium for deuterium in 20 hr.

**I. 29a, $D_2O$, and Sodium Acetate.**—A suspension of **29a** (0.30 g, 0.00175 mol) in deuterium oxide (1.2 ml) containing sodium acetate (10 mg) was stirred for 12 hr. Examination of **29a** after removal of solvent showed no decomposition to have occurred. The infrared spectrum and melting point of the **29a** recovered were the same as of initial **29a**. The pmr spectrum of the recovered **29a** showed that 40% of its methylene protium, $\tau$ 6.6, has been exchanged.

**J. 29a, $D_2O$, and HCl.**—A solution of **29a** (0.25 g, 0.0145 mol), deuterium oxide (1.0 ml), and concentrated hydrochloric acid (0.01 ml) in deuterioacetic acid (4.0 ml) was refluxed for 2 hr and then kept at 50° for 9 hr.

**Registry No.**—**6**, 22837-57-6; **10a**, 22837-58-7; **10b**, 22837-59-8; **10c**, 22837-60-1; **10d**, 22837-61-2; **12a**, 22837-62-3; **12b**, 20142-93-2; **12d**, 22837-64-5; **12e**, 22837-65-6; **13**, 22837-66-7; 5,6-dihydro adduct of **13**, 22837-67-8; **14**, 22837-68-9; **18**, 22837-69-0; **24**, 7180-62-3; **25**, 22837-71-4; **34**, 22837-73-6; 1-oximino-3,4-diphenyl-3-cyclopentene-1,2-dione, 22837-72-5; 2-bromo-1,3,4-cyclopentanetrione, 22922-42-5.

# A New Synthesis of 2-Hydroxy-3-methylcyclopent-2-en-1-one. II[1]

KIKUMASA SATO, YASUHIKO KOJIMA, AND HARUHITO SATO

*Department of Applied Chemistry, Faculty of Engineering, Yokohama National University, Yokohama, Japan*

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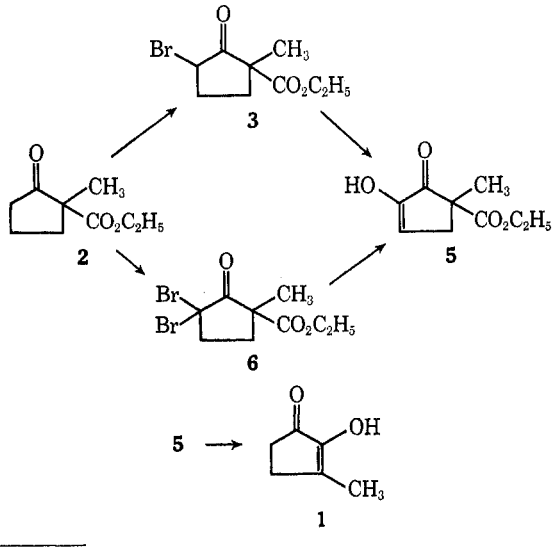
The synthesis of 2-hydroxy-3-methylcyclopent-2-en-1-one (**1**) was accomplished by the DMSO oxidation of 5-bromo-2-carbethoxy-2-methylcyclopentanone (**3**), the side reaction of which was prevented by the addition of epichlorohydrin (**7**). The two-step hydrolysis of 5,5-dibromo-2-carbethoxy-2-methylcyclopentanone (**6**) using morpholine gave **1** in a pure state. On the other hand, the reaction of 2,5-dibromocyclopentanone (**9**) with morpholine gave 2-morpholino-2-cyclopentenone (**10**), while 2,6-dibromocyclohexanone (**11**), when subjected to similar conditions, was converted into 1-cyclopentene-1-carboxymorpholide (**12**).

An earlier paper in this series[1] described a synthesis of 2-hydroxy-3-methylcyclopent-2-en-1-one (**1**) following two synthetic routes from 2-carbethoxy-2-methylcyclopentanone (**2**). Both procedures involved the oxidation of **2** with selenium dioxide and the nitrosation of **2** with *n*-butyl nitrite, respectively. In addition, it has been found[1] that the dimethyl sulfoxide (DMSO) oxidation of 5-bromo-2-carbethoxy-2-methylcyclopentanone (**3**) gave 3-bromo-5-carbethoxy-2-hydroxy-5-methylcyclopent-2-en-1-one (**4**).

In this paper, we aim to elucidate such an abnormal oxidation of cyclic $\alpha$-bromo ketones as described above,




and accomplish the preparation of **1** from the intermediate **2**, *via* two routes containing 5-carbethoxy-2-hydroxy-5-methylcyclopent-2-en-1-one (**5**) as the key precursor: the DMSO oxidation of **3** and the hydrolysis of 5,5-dibromo-2-carbethoxy-2-methylcyclopentanone (**6**).

The DMSO oxidation of 2-bromocyclopentanone and 2-bromocyclohexanone gave 3-bromo-2-hydroxycyclopent-2-en-1-one and 3-bromo-2-hydroxycyclohex-2-en-1-one, respectively. Accordingly, this series of reactions was confirmed to be a characteristic one of cyclic $\alpha$-bromo ketones. Since Hunsberger and Tien[2] have reported that dimethyl sulfoxide oxidizes hydrogen bromide to bromine, it appeared that a normal reaction could occur when hydrogen bromide liberated in the reaction was captured by such a neutral base as an epoxide. The DMSO oxidation of **3** in the presence of epichlorohydrin (**7**) gave a normal product **5** (58.5%) along with 1-bromo-3-chloro-2-propanol (**8**). Expected $\alpha$ diketone was also obtained by the DMSO oxidation of 2-bromocyclohexanone using phenyl glycidyl ether as the epoxide. From these results, the extraordinary reaction mentioned above is interpreted as follows. The existence of **7** prevents the produced $\alpha$-diketone from subsequent bromination, because epoxides react with hydrogen bromide formed in the reaction. This process of the DMSO oxidation gave **1** in an overall yield of 29% based upon the diethyl adipate. This is a satisfactory result, compared with the two procedures[1] already described.

The bromination of ketone **2** gave **6** in 85% yield. Compound **1** could be prepared merely by the hydrolysis

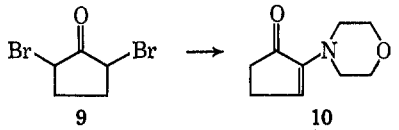
(1) For previous paper, see K. Sato, S. Suzuki, and Y. Kojima, *J. Org. Chem.*, **32**, 339 (1967).

(2) I. M. Hunsberger and J. M. Tien, *Chem. Ind.* (London), 88 (1967).

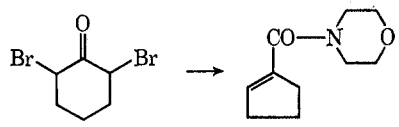
of **6** in aqueous potassium hydroxide. However, the basic hydrolysis of **6** brought about a ring fission mainly and gave crystals (mp 108–109°) which seemed to be 2,2-dibromo-5-carbethoxycaproic acid. When the hydrolysis of **6** was carried out in dilute basic solution, the cleavage was predominant even at a suitable temperature in which **1** was obtainable.

On the other hand, the treatment of **6** with morpholine, followed by the acid hydrolysis, afforded **5** in 49% yield. Compound **1** was synthesized from **6** without the isolation of **5**. This process utilizing morpholine not only gave **1** in a total yield of 30% equal to that of the DMSO oxidation, but also had the advantage of being easy to work with.

In addition, we have examined the reaction of cyclic $\alpha,\alpha'$-dibromo ketones with morpholine. The bromination of cyclopentanone with 2 mol of bromine has been shown[3,4] to give 2,5-dibromocyclopentanone (**9**). The reaction of **9** with morpholine at 20° afforded a new typified compound, 2-morpholino-2-cyclopentenone (**10**) together with morpholine hydrobromide. The structure of **10** was assigned on the basis of its ir and uv spectra. The ir spectrum showed conjugated carbonyl absorption at 1690 $cm^{-1}$, and the uv spectrum indicated that **10** possessed a 2-cyclopentenone containing a 2-substituent [uv max (EtOH) 285 m$\mu$ ($\epsilon$ 20,000)].



**9** **10**



**11** **12**

The inference concerning the present reaction mechanism was based on facts that, although the treatment of **9** with silver acetate gives a monoacetoxy derivative,[3] diacetoxide cannot be obtained from **9**.[4] It is supposed that morpholine may remove hydrogen bromide from molecule after the monodisplacement of **9** by 1,4 elimination through enolization. Consequently, **9** affords **10** without producing a dimorpholino derivative.

On the other hand, it was found out that the reaction of 2,6-dibromocyclohexanone (**11**) with morpholine was different from that of **9**. Compound **11** afforded 1-cyclopentene-1-carboxymorpholide (**12**), which was converted to 1-cyclopentenecarboxylic acid on acid hydrolysis. However, when 2-bromocyclohexanone was produced in the same way, only a substitution occurred without suffering from a ring contraction. These results of the two reactions show a new fact that the Favorskii rearrangement depends on the basicity and nucleophilicity of the basic reagent and may be considerably influenced by the steric effect of the reactants.

The above-stated results have revealed an interesting relationship between product and ring size. It is supported that each bromo derivative of five- and six-membered cyclic ketones takes a quite different action in the reaction with morpholine possessing both a strong basicity and nucleophilicity.

(3) P. Y. Yeh, H. C. Hsiu, and P. K. Chang, *Chemistry* (Taiwan), 315 (1955).

(4) I. V. Machinskaya and A. S. Podberezina, *Zh. Obshch. Khim.*, **28**, 1501 (1958).

## Experimental Section[5]

**Reaction of 2-Bromocyclopentanone with DMSO.**—Freshly distilled 2-bromocyclopentanone (8.2 g, 0.05 mol) was dissolved in 50 ml of DMSO and stirred at 70° for 2 hr. After cooling, the reaction mixture was poured into 100 ml of ice water and extracted with ether. Removal of the ether and recrystallization from benzene gave 2.9 g (32%) of 3-bromo-2-hydroxycyclopent-2-en-1-one, mp 152.5–154.0°, lit.[6] mp 152.0–154.0°.

**5-Carbethoxy-2-hydroxy-5-methylcyclopent-2-en-1-one (5) from 5-Bromo-2-carbethoxy-2-methylcyclopentanone (3).**—A solution of 8.5 g (0.034 mol) of **3** and 3.2 g (0.034 mol) of epichlorohydrin in 100 ml of DMSO was stirred at 70° for 7 hr. The reaction mixture was cooled, poured into water, and extracted with chloroform. After drying, the chloroform was evaporated and the residual oil was distilled to yield 1.3 g (20.7%) of **5**.

Alternatively, DMSO was removed at reduced pressure from the reaction mixture, and the reulting oil was distilled to give 4.8 g (80%) of 1-bromo-3-chloro-2-propanol [bp 66–70° (1 mm), lit.[7] bp 92° (20 mm)] and 5.6 g of the crude oil [bp 98–103° (1 mm)]. Redistillation of the latter oil gave 3.7 g (58.5%) of **5**, bp 97–99° (1 mm), lit.[1] bp 97–99° (1 mm).

**Basic Hydrolysis of 5-Carbethoxy-2-hydroxy-5-methylcyclopent-2-en-1-one (5).**—A mixture of 3.7 g (0.02 mol) of **5** and 20 ml of 2 *N* potassium hydroxide was stirred for 30 min at room temperature. The resulting mixture was acidified and extracted with chloroform. The chloroform was distilled off and crude solids were then obtained. Recrystallization from water gave 1.4 g (63%) of 2-hydroxy-3-methylcyclopent-2-en-1-one (**1**), mp 104–106° [a mixture melting point with an authentic sample from natural sources (mp 106–107°) showed no depression].

**2-Hydroxycyclohex-2-en-1-one.**—A solution of 28.3 g (0.16 mol) of freshly distilled 2-bromocyclohexanone and 24.0 g (0.16 mole) of phenyl glycidyl ether in 150 ml of DMSO was stirred at 80° for 4 hr. After cooling, the reaction mixture was poured into ice water and repeated by extracting with chloroform. The extract was dried and concentrated yielding 33.3 g of dark oil. Distillation of this oil gave 8.1 g (45%) of 2-hydroxycyclohex-2-en-1-one [bp 75–76° (23 mm), lit.[8] bp 83° (20 mm)], which was identified on gas chromatography by comparing the retention times of peaks with those of an authentic sample obtained by selenium dioxide oxidation[8] of cyclohexanone.

**2-Carbethoxy-5,5-dibromo-2-methylcyclopentanone (6).**—To a solution of 10.0 g (0.055 mol) of 2-carbethoxy-2-methylcyclopentanone (**2**) in 150 ml of carbon tetrachloride was added 20.0 g (0.125 mol) of bromine at room temperature, dropwise and with stirring. After stirring and refluxing for 20 hr, the reaction mixture was poured into water and the organic layer was separated. After drying and removal of the solvent, distillation of the residual oil gave 16.3 g (85%) of **6**: bp 115–117° (2 mm); $n^{20}D$ 1.4909; $d^{20}_4$ 1.0260; ir (film) 1735 (ester C=O), 1710 $cm^{-1}$ (C=O).

*Anal.* Calcd for $C_9H_{12}Br_2O_3$: C, 32.95; H, 3.65. Found: C, 32.88; H, 3.98.

**Basic Hydrolysis of 2-Carbethoxy-5,5-dibromo-2-methylcyclopentanone (6).**—A mixture of 6.6 g (0.02 mol) of **6** and 50 ml of 2*N* potassium hydroxide was stirred at 100° for 1 hr. The resulting mixture was acidified and extracted with chloroform. The chloroform was evaporated and the residue was poured onto a column of silica gel; the column was eluted with 20:1 benzene–ethanol mixture. After removal of solvents, there remained 0.5 g (24%) of **1**, mp 100–103°, and 2.5 g of crystal, mp 108–109°.

**2-Hydroxy-3-methylcyclopent-2-en-1-one (1) from 2-Carbethoxy-5,5-dibromo-2-methylcyclopentanone (6).**—To 17.4 g (0.2 mol) of morpholine was added 6.6 g (0.02 mol) of **6**, dropwise and with stirring. The reaction mixture was stirred at 35° for

(5) Melting points are corrected and boiling points are uncorrected. Infrared spectra were determined with a Hitachi Model EPI-S2 spectrophotometer fitted with a sodium chloride prism. Ultraviolet spectra were recorded with a Hitachi Model EPS-3T spectrophotometer. The nmr spectra were determined with a JEOL Model C-60H spectrometer.

(6) J. D. Knight and D. J. Cram, *J. Amer. Chem. Soc.*, **73**, 4136 (1951).

(7) L. Blanchard, *Bull. Soc. Chim. Fr.*, **41**, 824 (1927).

(8) C. C. Hach, C. V. Banks, and H. Diehl, *Org. Syn.*, **4**, 229 (1963).

2.5 hr. The removal of morpholine under reduced pressure gave white crystals and 5.4 g of red oils. The crystals were filtered, and recrystallization from ethanol gave 6.1 g (91%) of morpholine hydrobromide, mp 202°, lit.[9] mp 202°.

The filtrate was stirred with 2 *N* potassium hydroxide solution for 1 hr at room temperature. The solution was then acidified with hydrochloric acid and extracted with chloroform. After drying, the chloroform was evaporated to dryness and the residue was recrystallized from water to yield 1.1 g (49%) of **1**, mp 104–105.5°.

**Reaction of 2,5-Dibromocyclopentaone (9) with Morpholine.**—To a stirred solution of 21.7 g (0.25 mol) of morpholine in 100 ml of dry ether, 12.1 g (0.05 mol) of **9** was added dropwise with an ice–water bath cooling. The mixture was stirred for several hours at room temperature. The precipitated morpholine hydrobromide was filtered and the removal of ether and surplus morpholine under reduced pressure gave 8.1 g of viscous oils. The oils were crystallized after standing for a few days at −70°. The crystals that formed were recrystallized from a small amount of methanol, affording 4.8 g (57.5%) of 2-morpholino-2-cyclopentenone (**10**): mp 63°; uv max (*n*-hexane) 285 mμ (ε 20,000); ir (KBr) 1690 (C=O), 1613 (C=C), 1110 cm$^{-1}$ (C–O–C); nmr ($CDCl_3$) δ 6.42 (broad s, 1), 3.81 (m, 4), 3.09 (m, 4), 2.47 (almost s, 1).

*Anal.* Calcd for $C_9H_{13}O_2N$: C, 64.65; H, 7.84. Found: C, 64.61; H, 8.02.

**Reaction of 2,6-Dibromocyclohexanone (11) with Morpholine.**—To a solution containing 28.0 g (0.11 mol) of **11** in 100 ml of absolute ether, 47.6 g (0.55 mol) of morpholine was added at room temperature, dropwise and with stirring. After standing overnight, the deposited morpholine hydrobromide was filtered off, and the resulting oil was distilled to yield 5.1 g (25.5%) of 1-cyclopentene-1-carboxymorpholide (**12**): bp 113–114° (0.07 mol); $n^{20}D$ 1.5254; $d^{20}_4$ 1.1326; uv max (EtOH) 213 mμ (ε 10,000); ir (film) 1620 (C=O), 1120 cm$^{-1}$ (C–O–C); nmr ($CCl_4$) δ 5.80 (broad s, 1), 3.57 (sharp s, 8), 2.48 (m, 4), 1.86 (m, 2).

*Anal.* Calcd for $C_{10}H_{15}O_2N$: C, 66.27; H, 7.73. Found: C, 66.04; H, 7.58.

A solution of 1.4 g (0.0077 mol) of **12** in 12 ml of 2 *N* hydrogen chloride was stirred at 80° for 2 hr. The reaction mixture was then cooled and filtered, affording 0.4 g (80%) of 1-cyclopentene-1-carboxylic acid, mp 124°, lit.[10] mp 120–121°.

**Reaction of 2-Bromocyclohexanone with Morpholine.**—To a solution of 9.8 g (0.055 mol) of 2-bromocyclohexanone in 50 ml of dry ether, 14.7 g (0.17 mol) of morpholine was added with an ice–water bath cooling. After standing overnight at room temperature, the reaction mixture was then filtered and the resulting oil was distilled to yield 5.1 g (50.5%) of 2-morpholinocyclohexanone, bp 114–115° (3 mm), lit.[11] bp 148° (20 mm).

*Anal.* Calcd for $C_{10}H_{17}O_2N$: C, 65.54; H, 9.39; N, 7.64. Found: C, 65.40; H, 9.49; N, 7.53.

**Registry No.**—**1**, 80-71-7; **6**, 24454-32-8; **10**, 24454-33-9; **12**, 24454-34-0.

(9) J. Gilbert and H. Gault, *Bull. Soc. Chim. Fr.*, 2975 (1965).

(10) H. Sletter and K. Kiehs, *Ber.*, **98**, 2099 (1965).

(11) M. Mousseron, J. Jullien, and Y. Jolchine, *Bull. Soc. Chim. Fr.*, 757 (1952).

# Mechanism of the Cationic Addition-π,π-Transannular Cyclization of Disubstituted Methanes with 1,5-Cyclooctadiene

IWAO TABUSHI, KAHEE FUJITA, AND RYOHEI ODA

*Department of Synthetic Chemistry, Kyoto University, Sakyo-Ku Kyoto, Japan*

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The reaction of 1,5-cyclooctadiene with methoxymethyl acetate, dimethoxymethane, or chloromethyl methyl ether (Lewis acid catalysis) afforded mainly addition-π,π-transannular cyclization products, *cis*-bicyclo[3.3.0]-octane derivatives which exclusively consisted of *endo*-2-methoxymethyl isomers, and bicyclo[3.2.1]octane derivatives. The stereochemistry of the products and the high tendency of cyclization showed that attack of methoxymethyl cation was from the outside of the boat 1,5-cyclooctadiene with a simultaneous nucleophilic attack of the $\Delta^5$ double bond on the transient carbonium ion, which was followed by a partially concerted attack of an anion moiety (Scheme VII).

The well-documented double-bond participation in carbonium ion solvolyses[1] suggests that unconjugated dienes of appropriate configuration and conformation should form cyclized products upon reaction with cationic species.[2] A suitable system for investigating this cationic addition-π,π-transannular cyclization is *cis,cis*-1,5-cyclooctadiene [1,5-COD]. A model indicates that its boat form, shown to be the stable conformer by dipole measurements,[3] affords the close proximity necessary for orbital overlap. In addition, double-bond participation has previously been shown to be important in the solvolysis of the related compounds, $\Delta^4$-cyclooctenyl tosylate and brosylate.[4,5]

In the present paper, reactions of several disubstituted methane–Lewis acid combinations and 1,5-COD are described which afford predominately cyclic products.[6] This high proportion of cyclic products agrees with the previously reported results from the reaction of 1,5-COD with formic acid[7] and acetyl chloride.[8]

However, the stereochemistry of the product reported from the latter reaction is quite contrary to our findings. Results more similar to ours were reported for the reaction of *cis,cis*-1,6-cyclodecadiene with $Br_2$ in methanol[9] although even these results differ in a significant manner.

The following paper describes the reaction of 1,5-COD with methoxymethylacetate, dimethoxymethane, and chloromethyl methyl ether (Lewis acid catalysis). From careful analysis of the stereochemistry of the products, a mechanism for the cationic addition–cyclization reaction is presented. The discussion of this mechanism includes a comparison with results on similar

(1) P. D. Bartlett, "Nonclassical Ions," W. A. Benjamin, Inc., New York, N. Y., 1965.

(2) Cationic addition cyclizations are also known in some instances [*e.g.*, H. F. Tiemann and F. W. Seemler, *Chem. Ber.*, **26**, 2708 (1893); L. Ruzicka, *Helv. Chim. Acta*, **6**, 483 (1923)], but detailed mechanistic investigations are rather scarce [*e.g.*, W. S. Jonnson, A. van der Gen, and J. J. Swoboda, *J. Amer. Chem. Soc.*, **89**, 171 (1967)].

(3) J. D. Roberts, *ibid.*, **72**, 3300 (1950).

(4) W. D. Closson and G. T. Kwiatkowski, *Tetrahedron Lett.*, 6435 (1966).

(5) A. C. Cope, J. M. Crisar, and P. E. Peterson, *J. Amer. Chem. Soc.*, **82**, 4299 (1960).

(6) Preliminary reports have been presented on the subject: I. Tabushi, K. Fujita, and R. Oda, *Tetrahedron Lett.*, 3815, 3755 (1967).

(7) A. C. Cope and P. E. Peterson, *J. Amer. Chem. Soc.*, **81**, 1643 (1959).

(8) T. S. Cantrell, *J. Org. Chem.*, **32**, 1669 (1967); only formation of the cyclized product was described.

(9) F. M. Gipson, H. W. Guin, S. H. Simonsen, C. G. Skinner, and W. Shive, *J. Amer. Chem. Soc.*, **88**, 5366 (1966).