Cyclopentadienone Ethylene Ketal[1]

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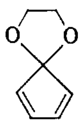
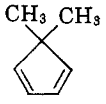
The cyclic ethylene ketal of cyclopentadienone has been generated and isolated as its dimer. Attempts to prepare the monomeric ketal failed. Routes have been developed for the synthesis of 5-bromo and 4-dimethylaminocyclopentenone as well as other cyclopentane derivatives.

In the preceding paper, some experiments on the generation and trapping of cyclopentadienones have been reported.[4] When it was discovered that this ketone was too reactive to be isolated and that its synthetic applications were severely limited by its reluctance to enter into Diels–Alder reaction as a diene, we began a study of methods for the synthesis of a ketal of cyclopentadienone, reasoning that the masking of the carbonyl group might reduce the reactivity of this interesting molecule sufficiently to allow isolation. This approach appeared especially promising since both 1,1-dimethylcyclopentadiene[5] (II) and 1,1-dimethylenecyclopentadiene[6] (III) are apparently quite stable in the monomeric state, the former, indeed, requiring heat before any reaction takes place with maleic anhydride. It is also true that the ketal of tetrachlorocyclopentadienone (IV) is a stable monomer and reacts normally in the Diels–Alder reaction.[7]


I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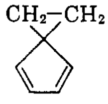
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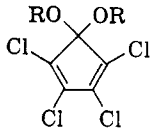
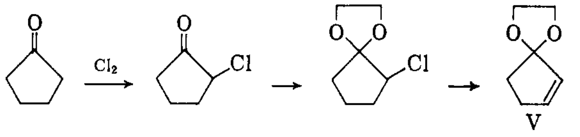

IV

Wanzlick and co-workers[8] had previously prepared the ethylene ketal of cyclopentenone (V) by the steps shown in eq. 1, and we adopted this useful molecule as a starting point for our experiments. An examination was made of the reaction of this olefin with N-bromosuccinimide (NBS) in an attempt to introduce an allylic halogen atom. The results of the reactions were quite erratic until it was recognized that the bromination could be induced to take two different courses depending upon the reaction conditions. If the halogenation was carried out in very dry carbon tetrachloride and heavily initiated with AIBN and light, then allylic bromination proceeded normally to form 4-bromocyclopentenone ketal (VI). If, on the other hand, free-radical bromination was inhibited and a small amount of gaseous hydrogen bromide was introduced as a catalyst, an isomeric bromide was formed. This new bromide was assigned to the structure 5-bromocyclopentenone ketal (VII) on the basis of its n.m.r. spectrum and further transformations described below. It presumably arises by an elimination–addition mechanism.[9]



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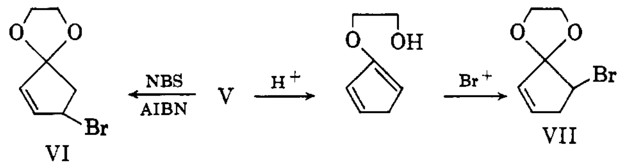
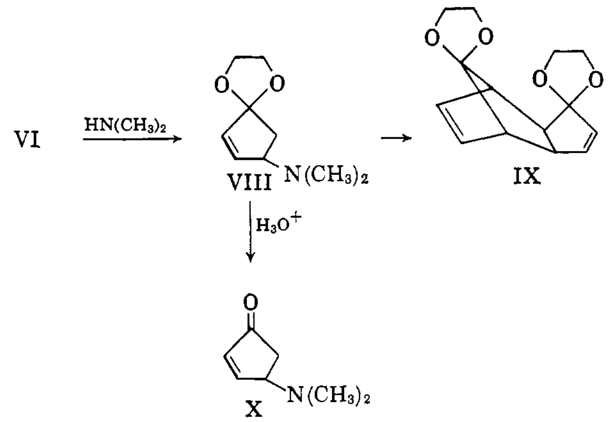


4-Bromocyclopentenone ketal (but not its 5-bromo isomer) reacts readily with dimethyl amine in carbon tetrachloride solution to form a tertiary amine, 4-dimethylaminocyclopentenone ketal (VIII). This amine may be oxidized to its amine oxide, and attempts were made to eliminate the elements of dimethylhydroxylamine pyrolytically. This elimination was unsuccessful, and only small amounts of cyclopentadiene ketal dimer were formed.



Amine VIII readily forms a crystalline quaternary ammonium salt when treated with methyl iodide, and elimination of the elements of trimethylamine occurred under the conditions of the Hofmann elimination. In spite of numerous attempts, no monomeric cyclopentadienone ketal could be isolated. Instead, in every case the dimer IX was the product. Because of the very strongly basic reaction mixture needed for the generation of the ketal, it was not possible to carry out the reaction in the presence of good dienophiles, but attempts to sweep the monomer, as formed, into solutions of dienophiles were unsuccessful. All indications from our experiments were that the ketal was very reactive and dimerized as soon as it formed. In this regard it resembles the ketone itself, which also could

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[2] Alfred P. Sloan Foundation Fellow, 1960–1964.

[3] Shell Oil Co. Fellow, 1962.

[4] C. H. DePuy, M. Isaks, K. L. Eilers, and G. F. Morris, *J. Org. Chem.*, **29**, 3503 (1964).

[5] C. F. Wilcox and M. Mesirov, *ibid.*, **27**, 1841 (1960); R. S. Rouse and W. E. Tyler, *ibid.*, **26**, 3525 (1961).

[6] K. Alder, H. Ache, and F. Flock, *Ber.*, **93**, 1888 (1960).

[7] J. A. Krynitsky and R. W. Bost, *J. Am. Chem. Soc.*, **69**, 1918 (1947).

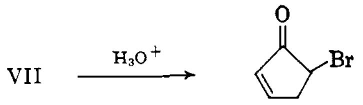
[8] H. W. Wanzlick, G. Gollman, and H. Metz, *Ber.*, **88**, 69 (1955).

[9] A. Marquet, H. B. Kagan, M. Dvolaitzky, C. Mamlok, C. Weidmann, and J. Jacques, *Compt. rend.*, **248**, 984 (1959).

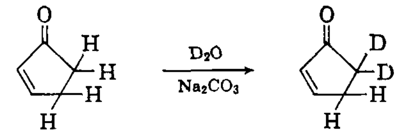
not be obtained monomeric. A number of attempts were made to regenerate the monomer by cracking the dimeric ketal. These attempts were also unsuccessful. At temperatures well above those required to induce cracking of dicyclopentadiene, the dimeric ketal was stable. Still higher temperatures led to charring, but no monomer could be observed.[10]

Mild acid hydrolysis of 4-dimethylaminocyclopentenone ketal converts it into the free keto amine X. This compound is quite unstable, polymerizing at room temperature in a few hours, but it may be stored over Dry Ice. Its quaternary salt, formed on treatment with methyl iodide, or its hydrobromide is more stable. Hofmann elimination of the quaternary ammonium salt gives the dimer of cyclopentadienone,[4] as does attempted formation of the amine oxide by oxidation of the amine.

We next turned our attention to 5-bromocyclopentenone ketal (VII). The halogen in this molecule is quite inert and does not react with dimethylamine or with silver nitrate in ethanol. Prolonged heating (5 days' reflux) of a sample with sodium ethoxide in ethanol gave a 17% conversion to the ketal dimer IX and a 50% recovery of the starting bromide. Hydrolysis of the bromo ketal with dilute, aqueous acid gave a 62% yield of a bromo ketone, 5-bromocyclopentenone (XI). This compound was of interest because Hafner and Goliasch[11] had assigned this structure to the reaction product of cyclopentenone with N-bromosuccinimide. The compound isolated by Hafner and Goliasch[11] has been shown to be 4-bromocyclopentenone by the comparison of its infrared spectrum with that obtained in these laboratories.[4] In the presence of bases bromo ketone XI polymerizes but does not form any cyclopentadienone dimer. This dimer is formed in almost quantitative yield from the isomeric 4-bromocyclopentenone. The great difference in ease of elimination of the two bromo ketones is understandable in terms of a carbanionic mechanism for the eliminations. The hydrogens adjacent to the carbonyl group in cyclopentenone are much more acidic than those in the β-position, despite the fact that the latter are vinylogs of the former. If cyclopentenone is dissolved in D_2O and a trace of sodium carbonate is added, the α- but not the β-hydrogens are rapidly exchanged for deuterium, as shown by the n.m.r. spectrum.



XI



Experimental

2-Chlorocyclopentanone.[8]—In a 3-l. three-necked flask equipped with a stirrer, gas inlet tube extending to the bottom of the flask, and efficient stirrer, was placed a mixture of cyclopentanone (500 g. 5.94 moles), 290 g. (2.90 moles) of calcium carbonate, 320 ml. of water, and 290 g. of a 40% solution of calcium chloride. A stream of chlorine gas was passed rapidly into the flask while the solution was stirred vigorously. After about 15 min. of chlorine addition, a pale, yellow-green color had built up in the cyclopentanone layer. At this point an ultraviolet lamp was held on the reaction for about 10 min. The reaction started suddenly, the color vanished, and cooling by means of an external ice bath was necessary. After this momentary display of exothermicity, the reaction proceeded smoothly and maintained its own reaction temperature with moderate external cooling. After the reaction was over, as evidenced by the disappearance of the calcium carbonate slurry and the termination of CO_2 evolution (test with lime water), the layers were separated, the aqueous layer was extracted once with chloroform, and the extract was combined with the organic layer. The solution was distilled under aspirator pressure through a 29-in. asbestos-wrapped column packed with glass helices. The first fraction gave 130 g. of recovered cyclopentanone. 2-Chlorocyclopentane, 370 g. (71% yield based on unrecovered cyclopentanone), distilled at 80–83° (15 min.).

Ethylene Ketal of 2-Chlorocyclopentenone.—A mixture of 370 g. (3.12 moles) of 2-chlorocyclopentanone, 815 ml. of benzene, and 0.1 g. of *p*-toluenesulfonic acid was placed in a 2-l. three-necked flask equipped with addition funnel, stirrer, and Dean–Stark water separator. The solution was heated to reflux and 138 ml. (3.33 moles) of ethylene glycol added slowly over a period of 90 min. while stirring. After 5 hr. of reflux, water separation was complete (59 ml. collected), and the reaction mixture was cooled, washed twice with 2 *N* NaOH solution and once with water, and distilled through a 29-in. glass helices column to give 400 g. (81% yield) of 2-chlorocyclopentanone ketal, b.p. 87–89° (15 min.).

Ethylene Ketal of Cyclopentenone (V).[8]—A mixture of 425 g. (7.6 moles) of KOH pellets and 835 ml. of diethylene glycol was heated at 170° in a three-necked flask equipped with stirrer, addition funnel, and condenser, until dissolved. Ammonium chloride (4 g.) was added and as the temperature was raised to 200° chloro ketal, 400 g. (2.53 moles), was added over a period of 1 hr. Heating was continued for an additional 1.5 hr., the mixture cooled somewhat, a distilling head was attached, and the distillate boiling below 110° at 15 mm. was collected in one fraction. The distillate was washed with water, the organic layer was separated, and the aqueous layer was extracted with ether. The ether extract and organic layer were combined, dried, and distilled to give 220 g. (69% yield) of olefin, b.p. 65–67° (15 mm.).

4-Bromocyclopentenone Ketal (VI).—Into a previously dried 300-ml. three-necked flask equipped with a stirrer, condenser, and addition funnel was placed 14.2 g. (0.08 mole) of N-bromosuccinimide and 200 ml. of CCl_4. Approximately 0.1 g. of azobis(isobutyronitrile) was added, and with stirring the contents of the flask were heated to reflux. A solution of 10.0 g. (0.08 mole) of cyclopentenone ketal (V) in 50 ml. of CCl_4 was added over a period of 20 min., with constant irradiation with an ultraviolet lamp, and the mixture was then stirred while heating for an additional 10 min. The solution was cooled and filtered with suction to remove succinimide, which was formed in quantitative yield. The bromoenone ketal was ordinarily used as a solution in CCl_4. It could be concentrated by removal of the CCl_4 *in vacuo*, but it decomposed on attempted distillation.

4-(N,N-Dimethylamino)cyclopent-2-enone Ketal (VIII).—A solution of 40 g. (0.317 mole) of cyclopentenone ketal (V) was brominated according to the above procedure and the solution of the bromoenone ketal in 800 ml. of CCl_4 was placed in a 1-l. three-necked flask equipped with a stirrer, a reflux condenser, and a gas inlet tube extending to the bottom of the flask. The solution was cooled to 5° in an ice bath and 100 ml. (1.58 moles) of anhydrous dimethylamine was bubbled in. A flocculent precipitate formed as addition proceeded. After 18 hr. at room temperature, the brown solution was washed with 2 *N* NaOH and water and dried. The product, isolated by distillation, weighed 35.0 g. (67% from ene ketal), was a deep wine-red color, and had b.p. 65° (1.5 mm.).

Anal. Calcd. for $C_9H_{15}NO_2$: N, 8.28. Found: N, 8.24.

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(10) The dimer of cyclopentadienone ketal has also been synthesized by E. Vogel and E.-G. Wyes [*Angew. Chem.*, **74**, 489 (1962)] by a reverse Diels–Alder reaction in which diethyl phthalate is formed simultaneously. This method has the advantage that the ketal can be generated in the absence of base, although higher temperatures are required than for the Hofmann elimination. Generated in this way, cyclopentadienone ketal can be trapped with maleic anhydride. The ketal dimers formed by the two different routes are identical, as shown by their spectra and mixture melting point. We are grateful to Professor Vogel for stimulating discussions and information prior to publication.

(11) K. Hafner and K. Goliasch, *Ber.*, **94**, 2909 (1961).

Cyclopentenone Ketal 4-Trimethylammonium Iodide.—A solution of 35.0 g. (0.212 mole) of the tertiary amine in 100 ml. of anhydrous ether was cooled to 0° and 31.0 g. (0.218 mole) of methyl iodide was added with vigorous stirring. After stirring for 2 hr. the salt was removed by filtration to give 45.5 g. (70% yield) of crystalline quaternary iodide.

Anal. Calcd. for $C_{10}H_{16}INO_2$: C, 38.55; H, 5.80; N, 4.50. Found: C, 38.31; H, 5.89; N, 4.60.

Cyclopentadienone Ketal Dimer (IX).—This dimer was obtained by the base-promoted elimination of the quaternary salt under a wide variety of conditions. A mixture of 45.5 g. (0.148 mole) of the 4-trimethylammonium iodide was treated with 2 equiv. of silver oxide in aqueous solution. The silver salts were removed by filtration and the quaternary hydroxide solution was concentrated under reduced pressure. This sirup was stored over Dry Ice and portions pyrolyzed in flasks in which the products were swept into cold traps with and without dienophiles, as films under vacuum, and in sublimers with large, Dry Ice cooled cold fingers. The traps and cold fingers were uniformly free of monomeric ketal, and practically free from dimer. In each case, extraction of the pyrolysate with ether and removal of the ether gave, after sublimation, crystalline dimer IX, m.p. 91–92°, identical with an authentic specimen.[10]

Anal. Calcd. for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.58, 67.36; H, 6.63, 6.59.

4-(N,N-Dimethylamino)cyclopent-2-enone Ketal N-Oxide.—The procedure was essentially that of Meinwald.[12] A solution of 3.83 g. (0.023 mole) of amine in 10 ml. of methanol was cooled to −10° and 7.7 g. (0.068 mole) of 30% hydrogen peroxide was added over a period of 20 min. After standing overnight, the reaction mixture was cooled to 0°, a methanolic suspension of 50 mg. of platinum[13] was added, and the solution was stirred an additional 5 hr. The decomposition of excess hydrogen peroxide was complete at this time, as indicated by lead sulfide test paper. The platinum was removed by filtration and the methanol was removed at 40° to give the N-oxide (17 g.) as a clear tan oil. A small portion of dry ethanol was added and again removed at 40° to dry the oxide. A sample gave a good crop of picrate crystals, m.p. 132–133°, from 95% ethanol.

Anal. Calcd. for $C_{15}H_{12}N_4O_{10}$: C, 43.48; H, 4.38; N, 13.52. Found: C, 43.95; H, 4.58; N, 13.31.

4-(N,N-Dimethylamino)cyclopent-2-enone (X).—Into a 300-ml. flask was placed 60 ml. of 2 *N* hydrochloric acid; while vigorous stirring was maintained, 4-(N,N-dimethylamino)cyclopent-2-enone ketal (VIII) was added slowly. The resulting solution was stirred at room temperature for 30 min.; 20 ml. of methylene chloride was added and then, with caution, solid sodium bicarbonate. When the aqueous layer was saturated with sodium bicarbonate, the mixture was filtered and the organic layer was separated. The aqueous layer was extracted with two 20-ml. portions of methylene chloride and twice with ether. The organic layers were combined, dried over anhydrous sodium sulfate, and subjected to fractional distillation, yielding 4-(N,N-dimethylamino)cyclopent-2-enone, 4.85-g. (64%) yield, b.p. 57° (1 mm.). The amine is stable at Dry Ice temperatures, but decomposes upon standing at room temperature. Methyl iodide was added to a portion of the amine dissolved in ether to give the methiodide, recrystallized from ethanol as a white, slightly hygroscopic solid, m.p. 176–177° dec.

Anal. Calcd. for $C_8H_{14}INO$: C, 35.97; H, 5.28; I, 47.51; N, 5.24. Found: C, 35.98; H, 5.24; I, 47.28; N, 5.41.

5-Bromocyclopent-2-enone Ethylene Ketal (VII).—Into a 300-ml. three-necked flask equipped with a stirrer, condenser, and addition funnel and wrapped with aluminum foil so as to exclude all light was placed N-bromosuccinimide (14.2 g., 0.08 mole) and 150 ml. of carbon tetrachloride. The contents of the flask were heated to reflux and dry hydrogen bromide gas was passed through the solution for 20–30 sec. The addition funnel was replaced and cyclopent-2-enone ketal (10 g., 0.09 mole) in 50 ml. of carbon tetrachloride was added over a period of 1 hr. Hydrogen bromide gas was charged twice more to the reaction mixture in the next 0.5 hr., and heating was continued for an additional hour. The reaction mixture was cooled in an ice bath, the succinimide was removed by filtration, and the resulting clear, pale yellow solution was placed in a 500-ml. flask. Anhydrous methylamine (approximately 3 equiv.) was added to the solution and the solution was stirred for 18 hr. at room temperature to remove all 4-bromo compound. The solution was washed twice with 2 *N* sodium hydroxide solution and once with water and dried over sodium sulfate. The carbon tetrachloride was removed under reduced pressure and the residue was subjected to vacuum distillation to give 5-bromo compound (8 g., 57% yield), b.p. 60° (1 mm.).

Base Elimination of 5-Bromocyclopent-2-enone Ketal.—Into a 50-ml. flask equipped with a condenser and drying tube was placed 5.1 g. (0.024 mole) of 5-bromocyclopent-2-enone ketal and 25 ml. of 1 *N* sodium ethoxide in ethanol. The resulting solution was heated under reflux for 5 days. The solution was diluted with 75 ml. of water and extracted with ether, and the extracts were combined, dried, and removed by distillation to give an oil. Trituration of the oil with hexane left crystalline dicyclopentadienone ketal (IX, 0.53 g., 17% yield). Evaporation of the hexane and distillation gave unreacted bromo ketal (2.56 g., 50% yield) and a small amount of residue.

5-Bromocyclopent-2-enone (XI).—5-Bromocyclopent-2-enone ketal was hydrolyzed with 1 *N* hydrochloric acid for 4 hr. at room temperature. The aqueous layer was extracted with methylene chloride, the extracts were combined and dried, the solvent was removed under aspirator vacuum, and the resulting concentrate was distilled to give 5-bromocyclopent-2-enone, b.p. 56° (1 mm.), 62% yield.

Anal. Calcd. for C_5H_5BrO: C, 37.58; H, 3.13; Br, 49.55. Found: C, 37.79; H, 3.20; Br, 49.42.

Catalytic hydrogenation of the bromoenone over Adams catalyst resulted in the uptake of 2 molar equiv. of hydrogen without a break and yielded cyclopentanone, identified as its 2,4-dinitrophenylhydrazone.

5-*p*-Nitrobenzoyloxycyclopent-2-enone.—This derivative was prepared according to the procedure described in Shriner, Fuson, and Curtin,[14] m.p. 145–146°.

Anal. Calcd. for $C_{12}H_9NO_4$: C, 58.30; H, 3.67; N, 5.67. Found: C, 58.31; H, 3.69; N, 5.53.

Acknowledgment.—We are indebted to the National Science Foundation through Grant G-14916 for the purchase of the ultraviolet spectrophotometer used in this work.

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[13] R. Feulgen, *Ber.*, **54**, 360 (1931).

[14] R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 200.