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Reaction of Oxymercurials.
Synthesis of 6,6-Dimethyl-spiro[2,5]octan-4,8-dione[*1]

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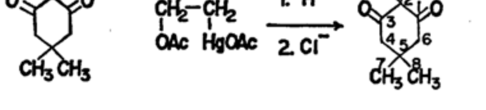
The reaction of oxymercurial of ethylene with dimedone in acetic acid containing perchloric acid, followed by treatment with sodium chloride, gave 2-(β-chloromercuriethyl)-5,5-dimethylcyclohexan-1,3-dione. Upon treating this mercurial with an equimolar amount of aqueous potassium hydroxide, 6,6-dimethyl-spiro[2,5]octan-4,8-dione was obtained. Oxymercurial of propylene reacted with dimedone to form a mixture of 4-oxo-2,6,6-trimethyl-2,3,4,5,6,7-hexahydrobenzofuran and 4-oxo-3,6,6-trimethyl-2,3,4,5,6,7-hexahydrobenzofuran under simultaneous demercuration; the mercurial corresponding to that in the case of ethylene could not be isolated.

In a previous paper,[1] it has been demonstrated that alkyl groups containing mercury can be introduced into active methylene by the reaction of acyclic β-diketones with oxymercurials of olefins. This paper will report that the same reaction takes place between dimedone (a cyclic β-diketone) and the oxymercurial of ethylene, and that the resulting mercurial, which is isolated as a chloromercury derivative, reacts with aqueous potassium hydroxide at room temperature to form 6,6-dimethyl-spiro[2,5]-octan-4,8-dione, which might be an interesting compound for UV absorption and NMR spectroscopy. The same attempt will also be applied to the oxymercurial of propylene.

Into a solution of β-acetoxyethylmercuric acetate (1,8 molar) which had been prepared by introducing ethylene to acetic acid containing mercuric acetate, perchloric acid (1 molar) and dimedone (a slight excess over the oxymercurial) were added.



(I)

The reaction product was isolated as a crystalline chloromercury derivative for experimental convenience. After a reaction at 10—20°C for one day, 2-(β-chloromercuriethyl)-5,5-dimethylcycohexane-1,3-dione (I), mp 199—201°C, was obtained in a 25%

[*1] A part of this paper was presented at the 19th Annual Meeting of the Chemical Society of Japan, Yokohama, April, 1966.

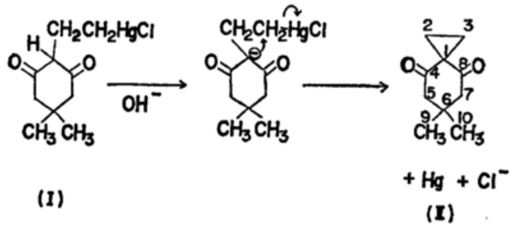
1) K. Ichikawa, O. Itoh, T. Kawamura, M. Fujiwara and T. Ueno, *J. Org. Chem.*, **31**, 447 (1966).

yield. By prolonging the reaction time to 7 days, the yield was increased to 35%. At temperatures above 25°C, metallic mercury was formed and the yield of I decreased. For example, the yields of I were 22% (accompanied by 11% demercuration) and 18% (accompanied by 22% demercuration) in the reactions at 25—30°C for 2 days and at 40°C for 5 hr respectively.

The results of the experiments with purified β-acetoxyethylmercuric acetate, which had been isolated and recrystallized, were the same as those with the oxymercurials prepared *in situ*.

The structure of I was assigned by analogy with the results obtained with acyclic β-diketones and on the basis of the spectral data. The UV spectra (λ_{max} 262 mμ, $\varepsilon = 3600$ in chloroform and λ_{max} 269 mμ, $\varepsilon = 12200$ with a shoulder at λ_{max} 300 mμ, $\varepsilon = 5800$ in ethanol) showed the presence of an enolizable β-diketo group. The IR spectrum also supported this structure, since absorptions observed at 2300—2700 (w, broad), 1730 (w), 1700 (s), and 1630 (w) cm^{-1} can be assigned to $\nu_{O-H\cdots O=C}$, $\nu_{C=O}$, $\nu_{C=O}$, and $\nu_{C=C}$ respectively. The NMR spectrum obtained at 60 Mc, using tetramethylsilane as an internal standard, in pyridine can be explained reasonably in terms of the enol form of I. The signals observed at τ −1.43 (singlet), 6.84 (triplet), 7.57 (singlet) 7.75 (triplet), and 9.00 (singlet), with relative intensities of 1 : 2 : 4 : 2 : 6, can be assigned to those due to the protons at O, C_9, C_4 and C_6, C_{10}, and C_7 and C_8 respectively (Fig. 1).

When I was treated with an equimolar amount of potassium hydroxide (10% aqueous) at 40°C for 3 hr, demercuration proceeded and 6,6-dimethyl-spiro-[2,5]octan-4,8-dione (II), bp 86.2—86.5°C/3 mmHg, n_D^{25} 1.4808, was obtained in a 90% yield on the basis of demercuration (75%). The mechanism is considered to be the same as that of 1,1-diacetylcyclopropane formation from 3,3-diacetylpropylmercuric chloride,[1] since the reaction conditions and scheme are the same. In the latter case, it has been suggested that the demercuration was assisted by the chelation of the β-diketo group with mercury. However, this cannot be applied to the present case, since the diketo group of dimedone cannot form a chelate compound. This demercuration mechanism, however, appears to require further investigation, because the purification of the mercurials is a necessary condition for the demercuration. Unknown impurities appear to inhibit the reaction.



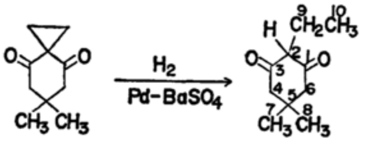
(I)

(II)

The structure of II was identified on the basis of the results of elementary analysis and the spectral data. Analysis showed that II has a formula of $C_{10}H_{14}O_2$ (Found: C, 72.53; H, 8.74%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%). The IR spectrum showed absorptions at 1705 and 1678 cm^{-1} due to $\nu_{C=O}$, and at 3020 cm^{-1} due to the ν_{C-H} of the cyclopropane ring.

The NMR spectrum clearly proved that the assigned structure is correct. In deuterochloroform, using tetramethylsilane as an internal standard, signals were observed at τ 7.44, 8.25, and 8.87, with relative intensities of 4 : 4 : 6; these signals can be assigned to those due to the protons at C_5 and C_7, C_2 and C_3, and C_9 and C_{10} respectively (Fig. 2).

As further evidence, when II was hydrogenated over Pd-BaSO$_4$ catalyst in methanol at room temperature, the product was crystalline ethyldimedone.



Since this product is unstable, it was identified by means of the NMR spectrum. In a pyridine solvent, signals were observed at τ 7.18 (quartet, $J=7.3$ cps), 7.63 (singlet), 8.73 (triplet, $J=7.3$ cps) and 8.98 (singlet), with relative intensities of 2 : 4 : 3 : 6. These signals may be assigned to the protons at C_9, C_4 and C_6, C_{10}, and C_7 and C_8 (Fig. 3).

When the reaction mixture of oxymercurial of ethylene and dimedone mentioned above was kept at the higher temperature of 40°C for 10 hr, the formation of metallic mercury (29% of the total amount) was observed. A work-up of the mixture gave 0.7 g of a liquid product, bp 109—113°C/4 mmHg. Gas chromatographical analysis showed that this product consisted of II (2%) and another product (96%). Spectral data disclosed that the latter was 4-oxo-6,6-dimethyl-2,3,4,5,6,7-hexahydrobenzofuran (III). The infrared spectrum showd a characteristic absorption of the 3-acetyl-4,5-dihydrofuran skeleton at 1635 cm^{-1}.[2-4]

The NMR spectrum is also consistent with this structure. Two singlets at τ 8.90 and 7.75 and three triplets at 7.70 ($J=1.5$ cps), 7.15 (broad, $J=9.2$ cps), and 5.39 ($J=9.2$ cps), with relative intensities of 6 : 2 : 2 : 2 : 2, can be assigned to the protons at C_{10} and C_{11}, C_5, C_7, C_3, and C_2 respectively.[2,5] The broading of the triplet at τ 7.15 is due to a long-range

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[2] F. H. Greenberg, *J. Org. Chem.*, **30**, 1251 (1965).

[3] K. Ichikawa, S. Uemura and T. Sugita, *Tetrahedron*, **22**, 407 (1966).

[4] K. Ichikawa and S. Uemura, *J. Org. Chem.*, **32**, 493 (1967).

[5] O. H. Mattson and C. A. Wachtmeister, *Tetrahedron Letters*, **1967**, 1855.

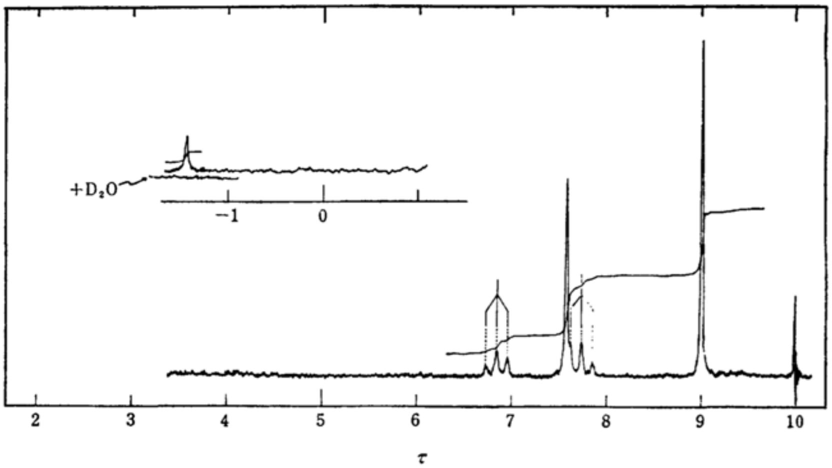


Fig. 1. NMR spectrum of β-chloromercuriethyldimedone (I) in $CDCl_3$ (60 Mc).

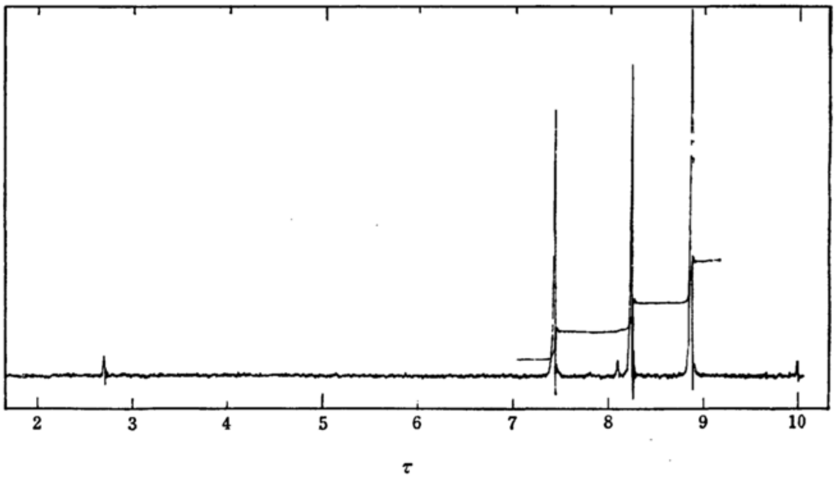


Fig. 2. NMR spectrum of 6,6-dimethyl-spiro[2,5]octan-4,8-dione in $CDCl_3$ (60 Mc).

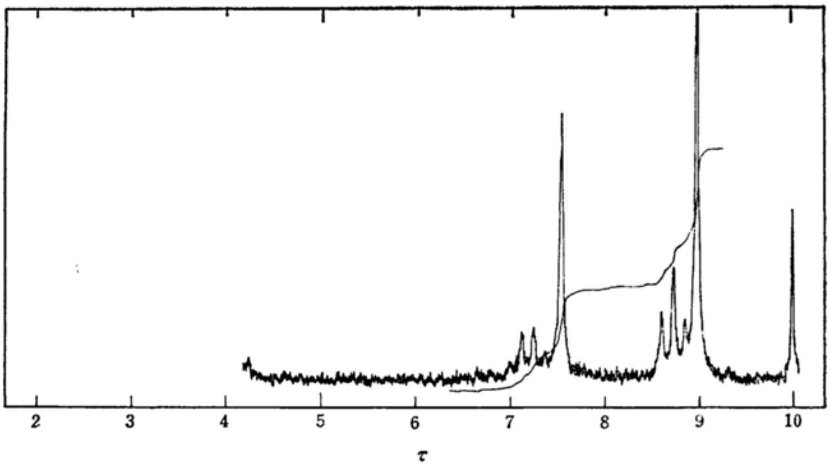


Fig. 3. NMR spectrum of ethyldimedone in pyridine (60 Mc).

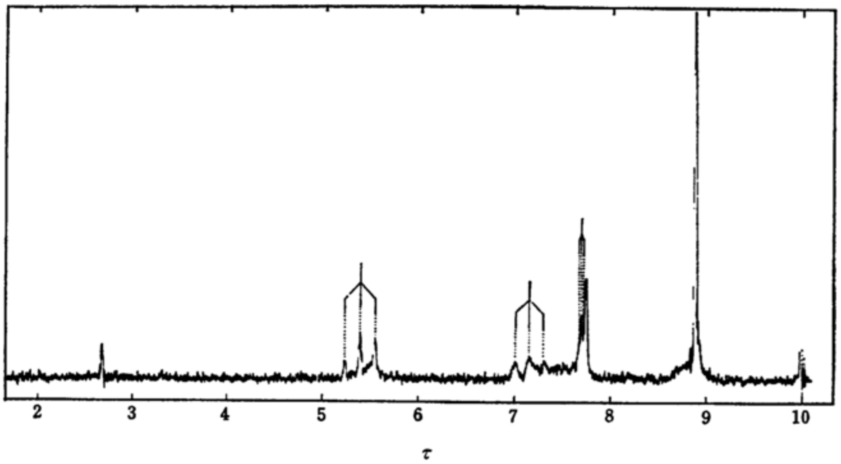


Fig. 4. NMR spectrum 4-oxo-6,6-dimethyl-2,3,4,5,6,7-hexahydrobenzofuran (III) in $CDCl_3$ (60 Mc).

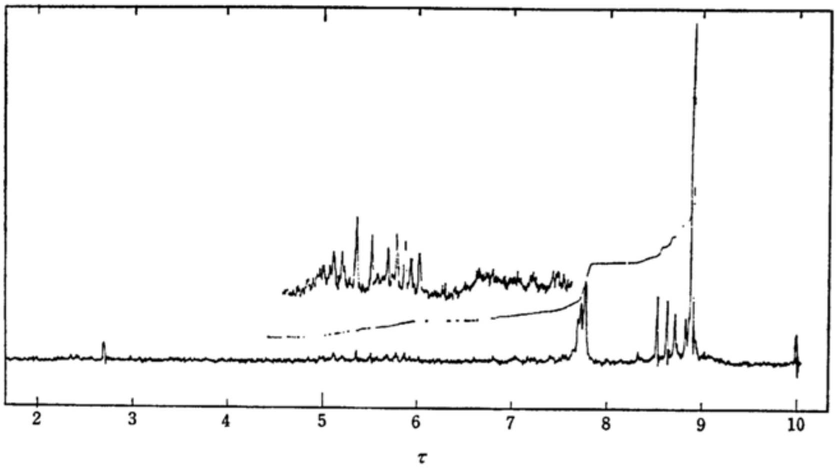
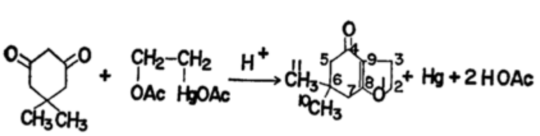


Fig. 5. NMR spectrum of a mixture of 4-oxo-2,6,6-trimethyl- (IV) and 4-oxo-3,6,6-trimethyl-2,3,4,5,6,7-hexahydrobenzofuran (V) in $CDCl_3$ (60 Mc).



(III)

coupling ($J=1.5$ cps) between 7-methylene and 3-methylene protons, this coupling is generally observed in this system and will be discussed in a separate paper.

This result of dihydrofuran formation is similar to those of the reactions between the oxythallate[3] and oxyplumbate[4] of ethylene and acetylacetone, and the mechanism also appears to be similar. However, the possibility of the formation of the same product through the isomerization of the cyclopropane (II) by acid cannot be excluded, because an attempt to obtain dinitrophenylhydrazone of II in ethanol containing sulfuric acid gave the hydrazone of III instead of II, and the same type of isomerization has been demonstrated to proceed in concentrated sulfuric acid.[6]

In the case of oxymercurial of propylene, 2-acetoxypropylmercuric acetate, the reaction with dimedone was slower than that of ethylene. Even after a reaction at 5—15°C for 5 days, the presence of unreacted oxymercurial was detected, and the formation of metallic mercury was also observed. The expected mercurial appears to be unstable and to be subject to demercuration under these conditions. Several attempts to isolate the mercurial corresponding to I in an earlier stage of the reaction were unsuccessful. After a reaction at 5—15°C for 5 days, 58% of the total mercury in the reaction mixture precipitated as metal.

Gas chromatographical analysis of the organic products showed that the main product (more than

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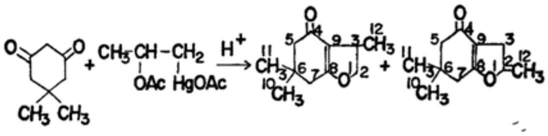
[6] O. Itoh, T. Kawamura and K. Ichikawa, *Bull. Inst. Chem. Res., Kyoto Univ.*, **44**, 207 (1966).

96%) is a mixture of two compounds (55 : 45), with close retention times. Because of the difficulty of purification and separation, the structures were estimated on the basis of the spectral data and the results of analogous reactions.[3,4]

The NMR spectrum was explained reasonably by assuming that the product is a mixture of 4-oxo-2,6,6-trimethyl-2,3,4,5,6,7-hexahydrobenzofuran (IV) and 4-oxo-3,6,6-trimethyl-2,3,4,5,6,7-hexahydrobenzofuran (V). The signals observed at τ 8.90 (singlet), 7.77 (singlet) and 7.71 (triplet), with relative intensities of 6 : 2 : 2, can be assigned to those due to the protons of the C_{10} and C_{11}, C_5, and C_7 of both IV and V. The broad complicated signals observed at τ 6.4—7.6 and 4.8—6.1, with relative intensities of *ca.* 1.5 : 1.5, are those due to protons of the C_2 and C_3 of IV and V respectively. The two doublets centered at τ 8.59 (J=6.2 cps) and 8.77 (J=6.8 cps) can be reasonably assigned to the protons of methyl groups attached to the C_2 of IV and the C_3 of V on the basis of the results observed in the NMR spectra of 3-acetyl-2,5-dimethyl-4,5-dihydrofuran[6] and 3-acetyl-2,4-dimethyl-4,5-dihydrofuran.[7]



(V) (IV)

Experimental

2-(β-Chloromercuriethyl)-5,5-dimethylcyclohexan-1,3-dione (I). The following is an example of a typical experimental procedure. Into an acetic acid solution of β-acetoxyethylmercuric acetate which had been prepared by introducing ethylene into a mixture of mercuric acetate (0.6 mol) and acetic acid (180 g), dimedone (100 g, 0.6 mol) was added. The reaction mixture (heterogeneous) was kept at 0°C, and then 70% perchloric acid (48 g) was slowly added. Throughout the procedure, the mixture was stirred mechanically; it became homogeneous after the addition of the acid. After the mixture had stood at 5—15°C for 24 hr, a grey slurry was formed. This reaction mixture was then added to an aqueous sodium chloride solution to precipitate white crystals, which were dried and recrystallized from ethanol. Seventy-three g of I (18% yield), mp 199—201°C, were thus obtained. The results of mercury content analysis (49.3%)[8] agreed with the calculated value (49.7%). IR (KBr): 3300 (w), 2930 (m), 2700—2300 (broad, w), 1730 (m), 1700 (m), 1630 (w). 1570 (m), 1547 (s), 1415 (m), 1377 (sh., w), 1366 (s), 1355 (s), 1311 (m), 1246 (s), 1136 (s), 1015 (w), 820 (w), 800 (w), 690 (w), 645 (w), 595 (m), 575 (w), 490 (w), 455 (w) cm^{-1}.

6,6-Dimethyl-spiro [2,5] octan-4,8-dione (II). Into 50 m*l* of a 10% aqueous solution of potassium hydroxide, 40.3 g of I was added, and the mixture was stirred at room temperature (15—20°C) for 3 hr. When the reaction temperature was raised to 25—30°C, the formation of metallic mercury was observed. After a reaction at 25—30°C for 3 hr, the metallic mercury (14 g, 70% of the theoretical amount) was removed, and the mixture was acidified with 1 m*l* of 1 N hydrochloric acid and extracted twice with 100 m*l* portions of ether. By evaporating the solvent, 11.5 g of II (90% yield, on the basis of demercuration) was obtained. Gas chromatographical analysis showed that the product consisted only of II, bp 86.2—86.5°C/3 mmHg, n_D^{25} 1.4804. UV: $\lambda_{max}^{n\text{-Hexane}}$ 196 mμ (ε=4700) and 267 mμ (ε=35); $\lambda_{max}^{\text{EtOH}}$ 203 mμ (broad, ε=4050) and 276 mμ (ε=60). IR (liquid film): 3020 (w), 2960 (m), 2880 (w), 1705 (s), 1678 (s), 1465 (m), 1405 (m), 1390 (w), 1370 (m), 1335 (s), 1320 (s), 1290 (m), 1265 (w), 1175 (m), 1140 (m), 1120 (w), 1080 (m), 1035 (w), 1015 (w), 985 (m), 915 (m), 610 (w), 585 (w) cm^{-1}.

Found: C, 72.53; H, 8.74%. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49%.

II was added to an excess 2,4-dinitrophenylhydrazine solution (ethanol-sulfuric acid) to prepare the hydrazone in the usual way.[9] The red crystals thus obtained were recrystallized from ethanol, mp 165—168°C. This hydrazone was not of II, but of III. A mixed melting point determination with that of III showed no depression.

Found: C, 54.68; H, 5.20%. Calcd for $C_{16}H_{18}N_4O_5$; C, 55.48; H, 5.24%.

This shows that II was converted to III during the preparation of hydrazone.

Hydrogenation of II to Ethyldimedone. With a palladium - barium sulfate catalyst (1.0 g), II (0.213 g, 1.05 mmol) was hydrogenated in methanol (30 m*l*) at room temperature. In 5 min, 23 m*l* of hydrogen were absorbed. After filtering off the catalyst, the solvent was distilled to give crystalline ethyldimedone. The IR spectrum disclosed the presence of two carbonyls (1690 and 1665 cm^{-1}), a carbon-carbon double bond (1620 cm^{-1}) and intermolecular hydrogen-bonded carbonyl (1550 cm^{-1}).

4-Oxo-6,6-dimethyl-2,3,4,5,6,7-hexahydrobenzofuran (III). To an acetic acid (15 g) solution of β-acetoxyethylmercuric acetate prepared from 0.05 mol of mercuric acetate and ethylene, dimedone (0.05 mol) and then 70% perchloric acid (4 g) were added. The reaction was continued at 40°C for 10 hr under stirring. After the metallic mercury formed (2.9 g, 29%) had been removed, the reaction mixture was added to an aqueous sodium chloride solution. The crystals formed (3 g, 15% yield) were filtered off and the remaining solution was extracted three times with 100-m*l* portions of ether. The ether extract was washed with a 5% sodium bicarbonate solution and then with water. After drying over sodium sulfate, the solvent was distilled off. Distillation gave 0.7 g of III (29% yield on the basis of demercuration), bp 109—113°C/4 mmHg. 2,4-Dinitrophenylhydrazone melted at 167—169°C.

Found: C, 55.55; H, 5.40%. Calcd for $C_{16}H_{18}N_4O_5$: C, 55.48; H, 5.40%.

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[7] S. Uemura, T. Nakano and K. Ichikawa, *Nippon Kagaku Zasshi* (*J. Chem. Soc. Japan, Pure Chem. Sect.*), **89**, 203 (1968).

[8] I. A. Koten and R. Adams, *J. Am. Chem. Soc.*, **46**, 2764 (1924).

[9] R. L. Shriner, R. C. Fuson and D. Y. Curtin, " The Systematic Identification of Organic Compounds," Wiley, New York (1956), p. 219.

4-Oxo-2,6,6-trimethyl-2,3,4,5,6,7-hexahydrobenzofuran (IV) and 4-Oxo-3,6,6-trimethyl-2,3,4,5,6,7-hexahydrobenzofuran (V). By the same method as has been described in the case of I, a reaction mixture of β-acetoxypropylmercuric acetate (0.5 mol), dimedone (0.68 mol), and perchloric acid (70%, 45 g) in acetic acid (150 g) was prepared. By a reaction at 5—15°C for 5 days, 58% of the total mercury was precipitated as metal. The reaction mixture was then filtered, water (twice the volume) was added, neutralized with a sodium hydroxide solution, and extracted with ether. After the ether had been removed, 80 g of an oily product were obtained. This contained unidentified mercury compounds, the oil was extracted with petroleum ether repeatedly (10 times with 100 m*l* portions). After the oil had been dried over anhydrous sodium sulfate and the solvent removed, a liquid product (15 g), bp 110—115°C/6 mmHg, was obtained. Gas chromatographic analysis showed that the main product (more than 96%) was a mixture of two components with close retention times. The two components could not be separated into pure components either by distillation or by column chromatography. IR (liquid film): 2950 (s), 2875 (s), 1718 (m), 1625 (s), 1460 (m), 1445 (m), 1398 (s), 1365 (m), 1335 (w), 1285 (w), 1240 (m), 1215 (s), 1165 (m), 1140 (m), 1100 (m), 1010 (m), 945 (m), 890 (m), 820 (w), 610 (m) cm^{-1}. UV: $\lambda_{max}^{\text{Hexane}}$ 262 mμ (ε=12500), $\lambda_{max}^{\text{Ethanol}}$ 272 mμ (ε=13300).

Spectral Measurements. IR, UV, and NMR spectra were recorded by JASCO IR-S, Hitachi EPS 2, and Varian 60A apparatuses respectively.

Reagents. The commercial ethylene and propylene were used without further purification. The dimedone was also a commercial one, mp 144—146°C. All the other reagents were commercial products of an analytical grade.