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Formic Acid Reduction. IX.[1] Reactions of 5,5-Dimethyl-1,3-cyclohexanedione with TEAF[2] and Their Reaction Routes

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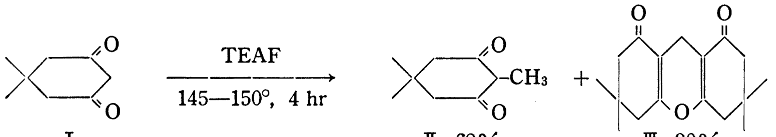
On heating 5,5-dimethyl-1,3-cyclohexanedione with a reagent, triethyl ammonium formate, given by 5HCOOH·2N $(C_2H_5)_3$, methylation at its 2-position was induced. This reaction appears refered to as a methylation of active methylene compound as is previously realized in 5-methylation of barbituric acids. Route of the reaction was revealed and found to involve some characteristic intermediate reduction steps induced by formic acid, that is, hydrogenation of carbon–carbon double bond and reductive fission of carbon–carbon single bond of intermediate compounds.

In the previous paper[4] of this series, it has been reported that the triethylammonium formate, (TEAF)[2] given by 5HCOOH·2N $(C_2H_5)_3$, induces the 5-methylation of barbituric acids by heating with this reagent. Our interest in this reaction prompts us to extend our investigation to some active methylene compounds. In the present paper, we wish to report the reactions of 5,5-dimethyl-1,3-cyclohexanedione (dimedone) (I) with TEAF, which involve its 2-methylation reaction, and their reaction routes.

When dimedone, I, was heated along with TEAF at 145—150°, a reaction proceeded with emission of carbon dioxide to give 2-methyldimedone (II) and 1,8-dioxo-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8-octahydroxanthene (III) in 68% and 30% yield respectively. The melting points of these compounds corresponded well with those reported for the substances prepared by entirely different methods.[5,6] The infrared (IR) and mass (MS) spectra of II, and the IR and nuclear magnetic resonance (NMR) spectra of III were also consistent with their formulations.



I

II, 68%

III, 30%

The formation of II in the TEAF reaction of I has a close parallel to the conversion of barbituric acids to 5-methylbarbituric acids in its TEAF reaction reported previously.[3] Regarded from the paper just mentioned, the route of methylation of I may appear similar to that reported for the 5-methylation of barbituric acids. That is, as can be seen in Chart 1, the reaction proceeds *via* formylation to 2-formyldimedone (IV), coupling with I to 2,2′-methyl-

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[1] Part VIII: M. Sekiya and S. Takayawa, *Chem. Pharm. Bull.* (Tokyo), **18**, 2146 (1970).

[2] Constant boiling-liquid, bp 95° (15 mmHg), [K. Ito, *Yakugaku Zasshi*, **86**, 1166 (1966)].

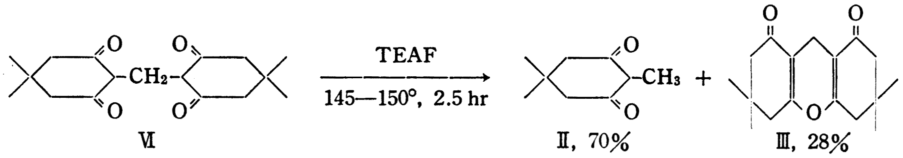
[3] Location: *2-2-1 Oshika, Shizuoka.*

[4] M. Sekiya and C. Yanaihara, *Chem. Pharm. Bull.* (Tokyo), **17**, 738 (1969).

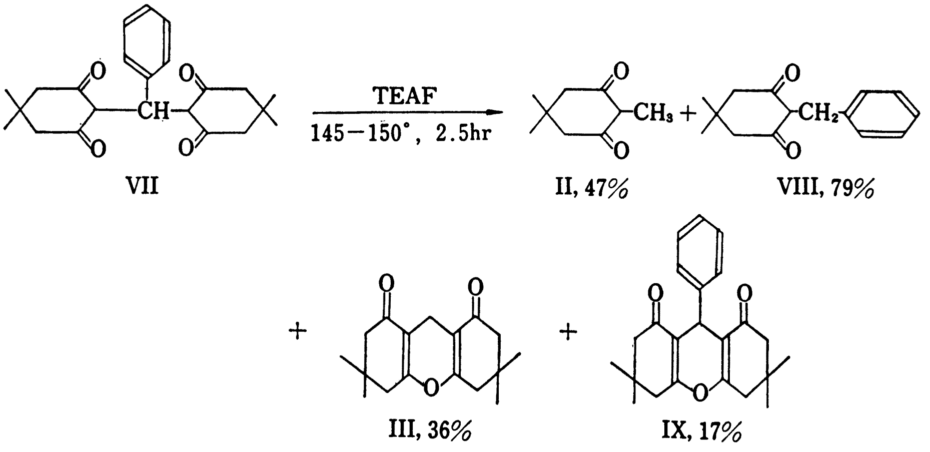
[5] *a*) R.D. Desai, *J. Chem. Soc.*, **1932**, 1079; *b*) H.E. Zaugg and A.D. Schaefer, *J. Am. Chem. Soc.*, **87**, 1857 (1965); W.E. Siberman and T. Henshall, *ibid.*, **79**, 4107 (1957); P. Hirsjarvi, *Ann. Acad. Sci. Fennicae*, Ser. A II. Chem., **23**, 108 (1946); J. Voitila, *ibid.*, **A49**, 110 (1938); P.S. Mayuranathan, *J. Indian Inst. Sci.*, **16A**, 113 (1933).

[6] *a*) E.S. Padilla, *Anales. Fac. Farm. y Bio-Quim.*, **7**, 598 (1956); *b*) M.V. Kowjalgi and B. H. Iyer, *J. Indian Inst. Sci.*, **34**, 5 (1952).

idynebisdimedone (V), reduction to 2,2'-methylene compound (VI), successively, and then followed by reductive fission to give II and I, and the resulting I retraces the former route. The intermediate reduction step to VI from V with TEAF is very likely in view of the previous report[7] on the TEAF reduction of 2-arylidene-1,3-diketones, although it is impossible to demonstrate the reaction because of failure in preparation[8] of V. The intermediate, VI, was prepared from I and paraform by using boron trioxide as a dehydrating agent (see Experimental) and was subjected to the TEAF reaction under the same conditions to expect the same route as described before. A reaction proceeded to give the same products, II and III in 70% and 28% yield, respectively, as those in the TEAF reaction of I.



The same type of the compound, 2,2'-benzylidenebisdimedone (VII), which was prepared by the same method as in the preparation of VI, suffered the same mode of reaction with TEAF to give II, 2-benzyldimedone (VIII), III and 1,8-dioxo-3,3,6,6-tetramethyl-9-phenyl-1,2,3,4,5,6,7,8-octahydroxanthene (IX). The melting point of VIII corresponded well with that reported previously,[5a,9] however, the melting point of IX differed somewhat from those repoted previously.[6a,10,11] Identification of these compounds was made by noting well agreement with the assigned structures in the NMR, IR and MS spectra.



As in the same route foresaid, the formation of II in the reactions of VI and VII is considered to be formed by the retracing route from I, which is initially formed by the reductive fission of the bridged carbon bond connecting to C_2 of dimedone grouping of VI or VII. Se-

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7) M. Sekiya and K. Suzuki, *Chem. Pharm. Bull.* (Tokyo), **18**, 1530 (1970).

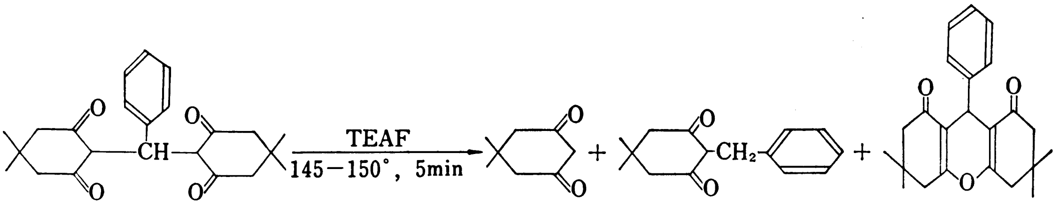
8) Attempts to prepare V from I and IV were unsuccessful. All the time, a reaction proceeded to give 1,8-dioxo-3,3,6,6-tetramethyl-9-(2-hydroxy-6-oxo-4,4-dimethylcyclohex-1-enyl)-1,2,3,4,5,6,7,8-octahydroxanthene, X (see Chart 1).

9) *a*) H. Stetter, H. Kesseler, and H. Meisel, *Chem. Ber.*, **87**, 1617 (1954); *b*) H. A.P. Dejongh and H. Wynberg, *Tetrahedron*, **21**, 515 (1965).

10) *a*) E.C. Horning and M.G. Horning, *J. Org. Chem.*, **11**, 95 (1946); *b*) G.C. Chakravarti, H. Chattopadhyaya, and P.C. Ghosh, *J. Indian Inst. Sci.*, **A14**, 141 (1932).

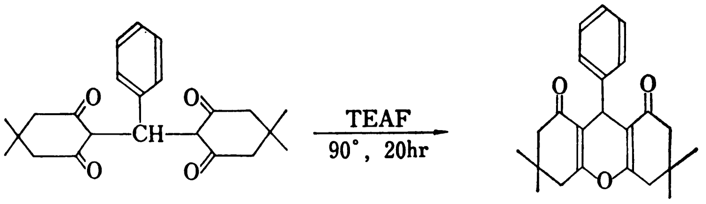
11) G. Swoda and P. Schuster, *Monatsh.*, **95**, 398 (1964).

lected VII as a substrate, this was substantiated by the fact that, when VII was heated with TEAF for few minutes at 145—150°, I, VIII and IX were obtained.



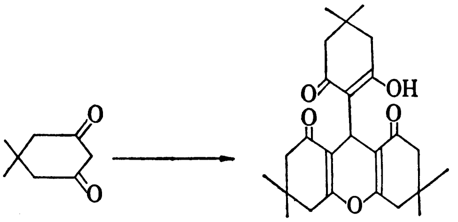
VII I, 79% VIII, 78% IX, 13%

In view of the facts described hitherto, as for the formation of II from I in the TEAF reaction, the foresaid route involving the reduction of methylidyne double bond and the reductive fission of carbon–carbon bond, which has been previously[3] introduced in the 5-methylation of barbituric acids, appears pertinent. However, routes of side formations of 1,8-dioxo-1,2,3,4,5,6,7,8-octahydroxanthenes (III from I, VI and VII; IX from VII) in the above TEAF reactions are drawn to a further subject to be solved. Formation of IX directly from VII by dehydration, which was considered to be in competition with the formation of I and VIII, was demonstrated under the conditions of heating longer with TEAF at 90°, at which emission of carbon dioxide was not observed and accordingly, formic acid reduction was to be avoided.



VII IX, 43%

On the other hand, under the same conditions, no formation of III from VI was observed and thus the direct formation of III from VI was excluded. We then heated I with TEAF at 90°, at which no emission of carbon dioxide was checked, for longer period. Under these conditions 1,8-dioxo-3,3,6,6-tetramethyl-9-(2-hydroxy-6-oxo-4,4-dimethylcyclohex-1-enyl)-1,2,3,4,5,6,7,8-octahydroxanthene (X) was obtained exclusively. The same formation was also brought about by heating at 145—150° in the same way as in the foresaid reaction but for a period of several minutes. Identity of the compound, X, was made by well correspondence of the melting point and the IR spectrum with those of the substance prepared from I and ethyl orthoformate.[12]



I X

1) 90°, 5hr; yield of X, 96%
2) 145—150°, 20 min; yield of X, 62%; recovery of I, 28%

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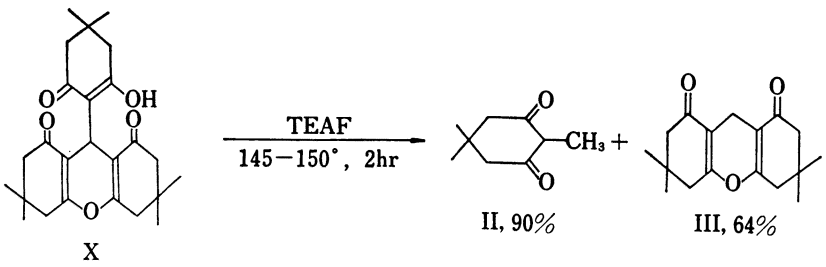
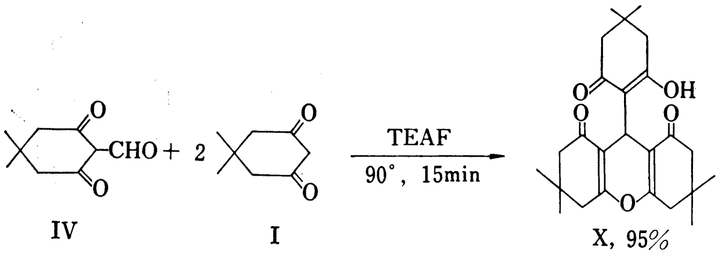
[12] *a*) B.D. Akehurst and J.R. Bartels-Keith, *J. Chem. Soc.*, **1957**, 4798; *b*) E.G. Meek, J.H. Turnbull and W. Wilson, *ibid.*, **1953**, 811.

It was noticeable that, when the compound, X, was resubjected to TEAF reaction at 145—150° for 2 hours, II and III were obtained in fair yields. Thus, the compound, X, was realized as an intermediate in the formation of III from I.



This reaction of X appears to indicate a reductive fission of the carbon–carbon bond of C_9 of the octahydroxanthene converting to III and I, followed by the succeeding reaction, in which the later product, I, reacts further with TEAF to give II and III as described in the foregoing. This route was supported by a fact that, when this reaction was interrupted within several minutes, the product, I, though it was a small amount, could be isolated from the reaction mixture in addition to the formation of II and III.

In order to gain information pertinent to the route of the formation of X from I, we prepared[12a)] a probable intermediate, IV, and a mixture of this compound and I in 1:2 molar proportion was allowed to react with TEAF at 90° for several minutes. A reaction proceeded smoothly resulting in the formation of X in fair yield.



Since that the compound, IV, may be formed from I by interaction of TEAF is very likely, IV is considered as an intermediate in the formation of X from I in its TEAF reaction. A likely route of the formation of X from I and IV appears to follow *via* formation of methylidyne compound, V, successively Michael addition of I to give tri(2-hydroxy-6-oxo-4,4-dimethylcyclohex-1-enyl)methane (XI) by influence of triethylamine base, followed by dehydration, as shown in Chart 1.

From the above discussion, the whole pathway for the formation of II and III from I can be described as shown in Chart 1. It can be said that the TEAF reaction of I may proceed in two ways, that is, the formation of II through the intermediate methylene compound, VI, and the formation of III through the intermediate X. As described in the foregoing, the formation of VI is brought about by the reduction of V, however, there is also considered another possibility of the formation from XI by a reductive fission of the carbon–carbon bond of its central methine-carbon. In our unpublished data, a variety of 2,2′-arylidene- and 2,2′-alkylidene-bisdimedones undergo a reductive fission of the methine carbon bond connecting to C_2 of the dimedonyl grouping on heating with TEAF, although this work will be described in the succeeding paper of this series. Thus, the formation of II and III would be in competition diverging from intermediates, V and XI.

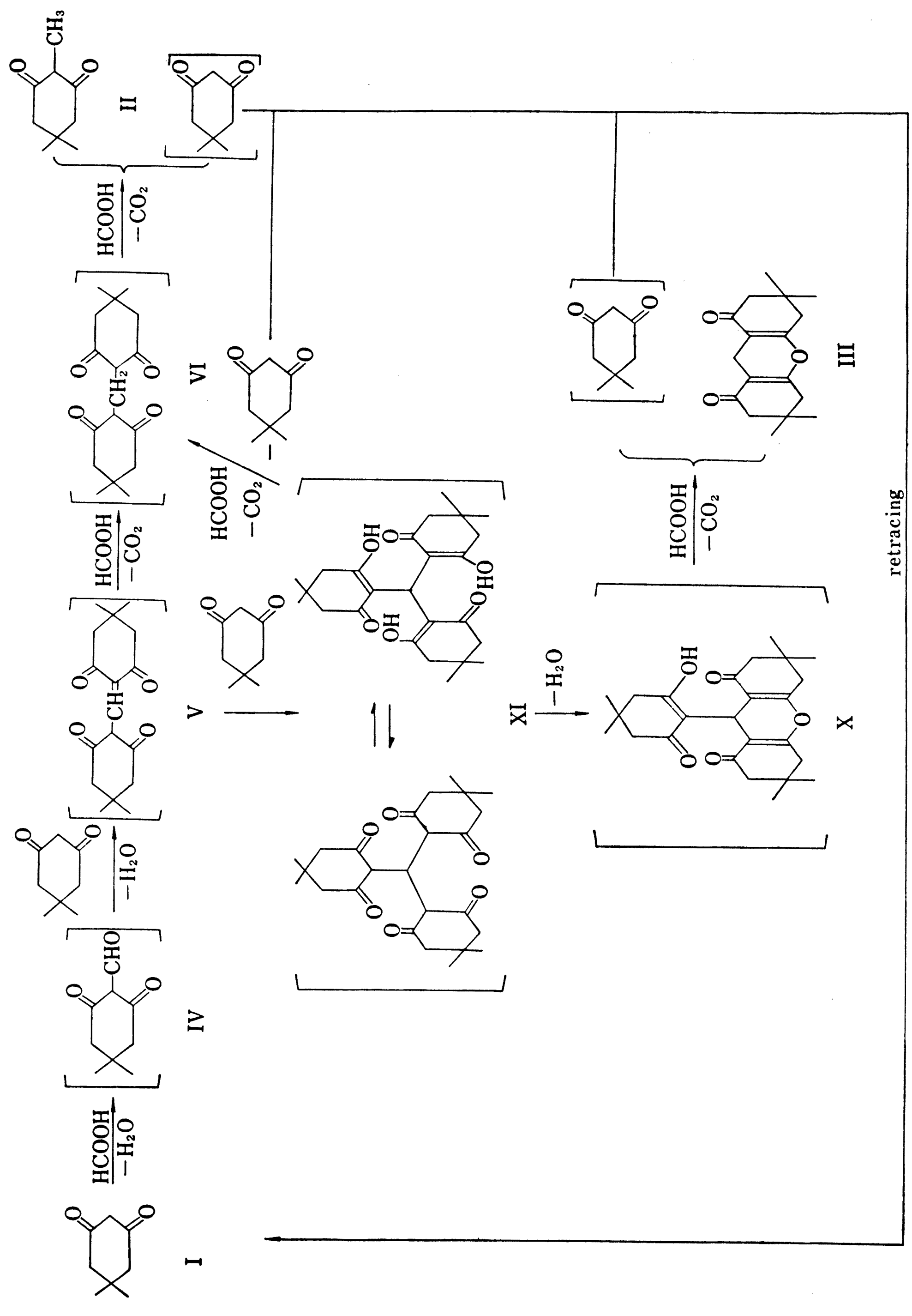


Chart 1. Reaction Route for the 2-Methylation of Dimedone

In the TEAF reaction of I at 145—150°, increase of triethylamine proportion to formic acid led to increased yield of II. Increasing by 0.5-fold of triethylamine, the yield of II was raised to 92%. On the other hand, when heated with 99% formic acid alone at 145—150° in a zirconium-lining autoclave, no formation of II was observed, but III and VI was obtained in 66% and 5% yield, respectively, in addition to a formation of resinous material. The conversion to II from VI was not affected by formic acid even at 145—150°. Higher yield of III from I in the above formic acid reaction appears to be caused by acceleration of dehydrating steps, X from XI and III from VI, by catalytic behavior of high formic acid concentration. By heating with 99% formic acid, conversion of X to III and I at 145—150° and of VI to III even at low temperature, 90° was demonstrated. The later conversion was not affected by TEAF as described in the foregoing.

Experimental

2,2′-Methylenebisdimedone (VI) and 2,2′-Benzylidenebisdimedone (VII)——To a benzene solution of dimedone (I) (0.04 mole) and piperidine (0.012 mole), suspended with boron trioxide (0.03 mole), paraform or benzaldehyde (0.02 mole) was added in small portions. The mixture was refluxed with stirring until no I was detected by TLC (silica gel, $CHCl_3$–EtOH=9–1) of the reaction mixture. After filtration of the warm mixture, the filtrate was concentrated under reduced pressure. Recrystallization of the residual crystalline material gave almost pure crystals.

The product VI was obtained by the reaction of 0.5 hours' refluxing. Prisms (from MeOH), mp 190—191° (lit.,6a,10a,13) 191—191.5°). Yield, 97%. IR ν_{max}^{KBr} cm^{-1}: 1589, 1611 (C=O). UV ν_{max}^{MeOH} mμ (log ε): 257 (4.37). NMR (10% solution in $CDCl_3$) τ14): 8.94 (12H, singlet, 4-C$\underline{H}_3$), 7.72 (8H, singlet, 4 ring –C$\underline{H}_2$-), 6.85 (2H, singlet, bridged -C$\underline{H}_2$-), −0.99 (2H, singlet, 2 enolic -O$\underline{H}$).

The product VII was obtained by the reaction of 2 hours' refluxing. Prisms (from MeOH), mp 190—192° (lit., 6a,10a,15) mp 196°). Yield, 81%. *Anal.* Calcd. for $C_{23}H_{28}O_4$: C, 74.97; H, 7.66. Found: C, C, 75.06; H, 7.30. IR ν_{max}^{KBr} cm^{-1}: 1578 (C=O). UV λ_{max}^{MeOH} mμ (log ε): 242 (shoulder, 4.01); 260.5 (4.12).

TEAF Reaction of Dimedone (I)——a) In a flask provided with a thermometer, an inlet tube and an air condenser tube were placed 14.0 g (0.1 mole) of I and 173 g (2.0 mole based on HCOOH) of TEAF. The mixture was heated at 145—150° with stirring. The reaction solution took on orange color soon after and this color disappeared after 4 hours' heating. During the course of the reaction, emission of CO_2 was observed, transfer of which was checked by $Ba(OH)_2$ solution by means of introduction of dry air free from CO_2. After standing overnight, 1,8-dioxo-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8-octahydroxanthene (III) was deposited in the reaction mixture and collected by filtration. Plates (from MeOH), mp 168—169° (lit.,6) mp 171°). Yield, 4.1 g (30%). *Anal.* Calcd. for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.26; H, 8.04. IR ν_{max}^{KBr} cm^{-1}: 1658, 1685 (shoulder) (C=O). UV λ_{max}^{MeOH} mμ (log ε): 231 (4.19), 306 (3.70). NMR (10% solution in $CDCl_3$) τ: 8.88 (12H, singlet, 4 -C$\underline{H}_3$), 7.72 (4H, singlet, C_4 -$\underline{H}_2$ and C_5-$\underline{H}_2$), 7.62 (4H, singlet, C_2 -$\underline{H}_2$ and C_7 -$\underline{H}_2$), 7.15 (2H, singlt, C_9 -$\underline{H}_2$). The foregoing filtrate was concentrated under reduced pressure to remove triethylamine and excess of TEAF. Recrystallization of the resulting crystalline redisue from H_2O gave 2-methyldimedone (II), prisms, mp 159—162° (lit., 5) mp 163—163.5°). Yield, 10.5 g (68%). *Anal.* Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.99; H, 9.15. IR ν_{max}^{KBr} cm^{-1}: 1569 (C=O). UV λ_{max}^{MeOH} mμ (log ε): 265 (4.11) [lit.,16) UV λ_{max} mμ (log ε): 264 (4.13), 265 (4.16)]. Mass Spectrum *m/e* (relative intensity): 155 (15), 154 (74), 99 (13), 98 (95), 97 (10), 84 (14), 83 (100), 71 (10), 70 (72), 69 (18), 57 (18), 56 (79), 55 (76), 54 (15), 53 (20), 52 (10), 51 (14), 50 (10), 45 (10), 44 (12), 43 (42), 42 (25), 41 (59), 40 (15), 39 (48), 38 (12). (lit.,17) Mass Spectrum *m/e*: 154, 98, 83, 70, 56, 55, 41).

When, by further addition of 40.5 g (0.4 mole) of triethylamine, a reaction was carried out in a zirconium-lining autoclave under the same conditions as those described in the above reaction, yield of II was raised to 92% and yield of III was 7%.

b) A reaction was processed in the same way as in a), but suspended after about 20 min when the reaction solution colored deeply. After immediate cooling, 1,8-dioxo-3,3,6,6-tetramethyl-9-(2-hydroxy-6-oxo-4,4-dimethylcyclohex-1-enyl)-1,2,3,4,5,6,7,8-octahydroxanthene (X) was deposited in the reaction mixture and collected by filtration. Colorless needles (from MeOH), mp 226—228° (lit.,12) mp 223—226°).

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13) P. Brenneisen, C.A. Grob, R.A. Jackson, and M. Ohta, *Helv. Chim. Acta*, **48**, 146 (1965); M. Winter and E. Demole, *ibid.*, **44**, 271 (1961); F.M. Beringer, P.S. Forgione, and M.D. Yudes, *Tetrahedron*, **8**, 49 (1960); K. Schmid, P. Fahrni, and H. Schmid, *Helv. Chim. Acta*, **39**, 708 (1956); D. Spenser and T. Henshall, *J. Am. Chem. Soc.*, **77**, 1943 (1955); D.D. Phillips, *ibid.*, **76**, 5385 (1954); J.G. Smith and G.F. Wright, *Can. J. Chem.*, **32**, 729 (1954); S.B. Baker, *J. Am. Chem. Soc.*, **74**, 827 (1952); S.V. Liberman and E.C. Wagner, *J. Org. Chem.*, **14**, 1001 (1949); D.J. Bell, *J. Chem. Soc.*, **1948**, 992.

14) TMS was used as internal standard.

15) M.V. Ionescu, *Bull. Soc. Stiinte Cluj.*, **3**, 54 (1926).

16) E.G. Meek, J.H. Turnbull, and W. Wilson, *J. Chem. Soc.*, **1953**, 2891; B. Eistert and W. Reiss, *Chem. Ber.*, **87**, 108 (1954).

17) M. Vandewalle, N. Schamp, and H. Dewilde, *Bull. Soc. Chim. Belgs.*, **76**, 111 (1967).

Yield, 6.2 g. Solution of X in TEAF takes orange color. *Anal.* Calcd. for $C_{25}H_{32}O_5$: C, 72.79; H, 7.82. Found: C, 72.11; H, 7.63. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 3402 (OH), 1646 (C=O), 1608 (>C=C<). UV $\lambda_{\max}^{\mathrm{KBr}}$ mμ (log ε): 235.5 (4.30), 275 (shoulder, 3.88), 305 (shoulder, 3.68). The IR and UV spectra of this product are consistent with those of an authentic sample prepared by the previously reported method.[12] When the foregoing TEAF filtrate was poured into water, an additional amount of X was deposited as crystals and collected by filtration. Yield, 2.0 g, total yield, 8.2 g (62%). To the filtrate KOH was added so as to neutralize the formic acid portion and triethylamine was evaporated under reduced pressure. After acidification with HCl, the solution was subjected to extraction with benzene. Removal of benzene gave a recovery of I, weighing 4 g (28%).

c) The same mixture of I and TEAF as that in a) was heated at about 90° at which almost no emission of CO_2 was observed. The heating was continued for 20 hr until no I was detected by TLC (silica gel, $CHCl_3$–EtOH=9–1) of the reaction mixture. The product, X was deposited in the colored reaction mixture and collected by filtration. Yield, 10.2 g. The product was identified by noting exact correspondence of its IR and UV spectra with those of the specimen obtained in the foregoing. By concentration of the foregoing filtrate under reduced pressure followed by recrystallization of the crystalline residue from MeOH, an additional amount of X was obtained, weighing 3.0 g. Total yield, 13.2 g (96%).

Formic Acid Reaction of Dimedone (I)——A mixture of 14.0 g (0.1 mole) of I and 93 g (2.0 mole) of 99% formic acid was heated at 145—150° in a zirconium-lining autoclave for 4 hr. The reaction mixture was concentrated under reduced pressure and the resulting residue was dissolved in benzene. The benzene solution was extracted with 10% NaOH solution, washed and dried. Removal of benzene gave III. Yield, 9.1 g (66%). The product was identified by comparison of its IR and UV spectra with those of the specimen obtained in the foregoing. The alkaline extract combined with washings was acidified with HCl. Resinous material liberated was collected by decantation and extracted several times with boiling water. The extract was concentrated under reduced pressure and the resulting residue was recrystallized from MeOH to give recovery of I, weighing 0.4 g (3%). The extraction residue was triturated with MeOH and the resulting solid material was recrystallized frm MeOH to prisms, mp 190—191°. Yield, 0.7 g (5%). This material was identical with VI by noting exact correspondence of its IR and UV spectra with those of an authentic sample.

TEAF Reaction of 2,2′-Methylenebisdimdone (VI)——A mixture of 8.8 g (0.03 mole) of VI and 51.9 g (0.60 mole based on HCOOH) of TEAF was heated at 145—150° with constant stirring, while considerable emission of CO_2 was observed. The reaction solution took on orange color gradually and after 2.5 hours' heating this color disappeared, when emission of CO_2 almost ceased. Crystals of III, mp 168—169°, were deposited in the reaction mixture and collected by filtration. Yield, 2.3 g (28%). The product was identified by comparison of its IR and UV spectra with those of an authentic specimen obtained in the above. The foregoing filtrate was concentrated under reduced pressure to remove triethylamine and excess of TEAF. The resulting residue was recrystallized from H_2O to prisms, mp 159—162°, which were identified as II by noting exact correspondence of its IR and UV spectra with those of the specimen obtained above. Yield, 6.4 g (70%).

Formic Acid Reaction of 2,2′-Methylenebisdimedone (VI)——A mixture of 2.9 g (0.01 mole) of VI and 9.3 g (0.20 mole) of 99% formic acid was heated at about 90° for one hr. The reaction mixture was concentrated under reduced pressure and the resulting residue was dissolved in benzene. The benzene solution was extracted with 10% NaOH solution, washed and dried. Removal of benzene gave crystals of III. Yield, 1.7 g (59%). The product was identified by comparison of its IR and UV spectra with those of an authentic specimen obtained above.

TEAF Reaction of 2,2′-Benzylidenebisdimedone (VII)——a) A mixture of 11.1 g (0.03 mole) of VII and 51.9 g (0.60 mole based on HCOOH) of TEAF was heated at 145—150° with constant stirring. The reaction set in with vigorous emission of CO_2, but after several minutes the emission was weakened and continued. After heating for 2.5 hr, the emission of CO_2 almost ceased and the reaction solution was concentrated under reduced pressure to remove triethylamine and excess of TEAF. The resulting residue was dissolved in benzene and the benzene solution was washed with 10% NaOH solution, and dried over $MgSO_4$. Removal of benzene gave a crystalline mixture of III and 1,8-dioxo-3,3,6,6-tetramethyl-9-phenyl-1,2,3,4,5,6,7,8-octahydroxanthene (IX). Separation of these was carried out by silica gel column chromatography using benzene–AcOEt (4:1) as an eluent. Evaporation of first eluent gave crystals of IX. Prisms (from MeOH), mp 217—218° (lit., mp 204—204.5°,[6a,10] 256—257°[11]). Yield, 1.8 g (17%). *Anal.* Calcd. for $C_{25}H_{26}O_3$: C, 78.82; H, 7.48. Found: C, 78.45; H, 7.44. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1661, 1678 (shoulder) (C=O) [lit.,[11] IR $\nu_{\max}$ cm^{-1}: 1655 (C=O)]. UV $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 235 (4.16), 297 (3.70). NMR (10% solution in $CDCl_3$) τ: 9.00 (6H, singlet, 2-$C\underline{H}_3$), 8.90 (6H, singlet, 2 -$C\underline{H}_3$), 7.80 (4H, singlet, C_4 -$\underline{H}_2$ and C_5 -$\underline{H}_2$), 7.52 (4H, singlet, C_2 -$\underline{H}_2$ and C_7 -$\underline{H}_2$), 5.23 (1H, singlet, C_9 -$\underline{H}$), 2.97—2.60 (5H, multiplet, aromatic protons). Removal of second eluent gave crystals of III. Yield, 1.5 g (36 %). The product was identified by noting exact correspondence of its IR and UV spectra with those of an authentic specimen obtained in the foregoing.

The foregoing alkaline extract combined with washings was acidified with aqueous HCl and crystals deposited were collected by filtration. The crystals were extracted several times with boiling water. Concentration of the extract and recrystallization of the resulting residue from aqueous MeOH gave prisms of

II, which was identified by comparison of its IR and UV spectra with those of an authentic specimen obtained in the foregoing. Yield, 2.2 g (47%). The above extraction residue was recrystallized from MeOH to give 2-benzyldimedone (VIII). Needles, mp 154—155° (lit.,[5a,9] mp 154—155°). Yield, 5.5 g (79%). *Anal.* Calcd. for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.13; H, 7.85. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1553 (C=O) [lit.,[9b] IR $\nu_{\max}^{\mathrm{Nujol}}$ cm^{-1}: 1550 (C=O)]. UV $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 265 (4.04) [lit.,[9b] UV $\lambda_{\max}$ mμ (log ε): 265 (4.18)]. NMR (5% solution in $CDCl_3$)τ: 9.06 (3H, singlet, -C$\underline{H}_3$), 8.83 (3H, singlet, -C$\underline{H}_3$), 7.34 (4H, singlet, 2 ring -C$\underline{H}_2$-), 6.80 (2H, singlet, benzyl -C$\underline{H}_2$-), 2.98—2.50 (5H, multiplet, aromatic protons), 0.87 (1H, singlet, enolic -O$\underline{H}$). Mass Spectrum *m/e* (relative intensity): 230 (89), 202 (12), 174 (23), 173 (13), 159 (11), 147 (20), 146 (100), 145 (50), 132 (17), 131 (54), 129 (15), 128 (20), 127 (19), 118 (25), 117 (22), 116 (20), 115 (12), 105 (15), 104 (23), 103 (26), 92 (13), 91 (65), 83 (60), 78 (25), 77 (25), 70 (11), 69 (15), 65 (20), 57 (22), 56 (29), 55 (39), 53 (10). 50 (11), 43 (35), 42 (11), 41 (45), 39 (31).

b) A mixture of 11.1 g (0.03 mole) of VII and 51.9 g (0.60 mole based on HCOOH) of TEAF was heated at 145—150° with constant stirring. When vigorous emission of CO_2 was weakened after heating for about several min, the reaction was suspended by cooling. On cool, 0.4 g (4%) of VII, which was deposited in the reaction mixture, was recovered. The filtrate was concentrated under reduced pressure to remove triethylamine and excess of TEAF. The resulting residue was dissolved in benzene and the benzene solution was extracted with 10% NaOH solution, washed and dried. Removal of benzene gave crystals, mp 216—218°, which were identified as IX by comparison of its IR and UV spectra with those of the specimen obtained in the foregoing. Yield, 1.4 g (13%). The foregoing alkaline extract combined with washings was acidified with HCl, when crystals were deposited. The crystals collected by filtration were extracted several times with boiling water. Concentration of the aqueous extract gave prisms of I, mp 146—148°. Yield, 3.3 g (79%). The product was identified by noting exact correspondence of its IR and UV spectra with those of the authentic sample. The solid insoluble in boiling water was recrystallized from MeOH to needles of VIII, mp 154—155°. Yield, 5.4 g (78%). The product was identified by comparison of its IR and UV spectra with those of the specimen obtained above.

c) The same mixture of VII and TEAF as that described in a) was heated at about 90° so as to avoid the emission of CO_2. After 20 hours' heating with constant stirring, the reaction mixture was cooled, when IX was deposited in the reaction mixture and collected by filtration. Yield, 3.5 g. The product was identified by noting exact correspondence of its IR and UV spectra with those of the specimen obtained in a). The foregoing filtrate was concentrated under reduced pressure to remove triethylamine and excess of TEAF. The resulting residue was dissolved in benzene and extracted with 10% NaOH solution. The benzene layer was washed and dried. Evaporation of benzene gave an additional amount of IX, weighing 1.0 g. Total yield, 4.5 g (43%).

TEAF Reaction of 1,8-Dioxo-3,3,6,6-tetramethyl-9-(2-hydroxy-6-oxo-4,4-dimethylcyclohex-1-enyl)-1,2,3,4,5,6,7,8-octahydroxanthene (X)——a) A mixture of 13.8 g (1/30 mole) of X and 173 g (2.0 mole based on HCOOH) of TEAF was heated at 145—150° with constant stirring, while considerable emission of CO_2 was observed. At the beginning of the reaction, the solution took on orange color and after 2 hour's heating this color disappeared. On cool, crystals of III were deposited in the reaction mixture and collected by filtration. Yield, 8.7 g (0.0317 mole, 64%[18]). This product was identified by comparison of its IR and UV spectra with those of an authentic specimen obtained in the TEAF reaction of I. The foregoing filtrate was concentrated under reduced pressure to remove triethylamine and excess of TEAF. Recrystallization of the resulting crystalline residue gave prisms of II, mp 159—162°. Yield, 4.6 g (0.0298 mole, 90%[19]). The product was identified by noting exact correspondence of its IR and UV spectra with those of the specimen obtained in the foregoing.

b) A reaction was processed in the same way as described in a) but suspended by cooling after about 20 minutes' heating when vigorous emission of CO_2 was weakened. Crystals, which were composed of III and unreacted X, were deposited in the reaction mixture. The crystals collected were dissolved in benzene and the benzene solution was extracted with 10% NaOH solution. Evaporation of the dry benzene solution gave crystals of III. Yield, 3.4 g. The product was identified by comparison of its IR and UV spectra with those of the specimen obtained above. Acidification of the aqueous extract with HCl gave a recovery of X, weighing 3.5 g (25%).

The foregoing filtrate was concentrated under reduced pressure to remove triethylamine and excess of TEAF. The resulting residue was dissolved in benzene and the benzene solution was extracted with 10% NaOH solution.. By the same way as described above, evaporation of benzene gave an additional amount of III, weighing 1.7 g. Total yield, 5.1 g (0.0186 mole, 37%[18]). The aqueous extract was acidified with HCl,

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18) This calculation involves the formation of III from I, which is produced as an intermediate from the reductive fission reaction of X, in addition to the formation of III directly from the reductive fission of X. Taking account of this route, theoretical molar amount of the product III is 1.5 mole from one mole of X.

19) This calculation is based on the formation of II from I, which is produced as an intermediate from the reductive fission reaction of X.

when crystals deposited. The crystals collected were extracted several times with boiling water. Recrystallization of the extraction residue from MeOH gave an additional amount of unreacted X, weighing 2.9 g (21%). The aqueous extract was concentrated under reduced pressure and the resulting residue was submitted to column chromatography on silica gel using benzene–AcOEt (1:1) as an eluent. Evaporation of the fractions gave II, weighing 1.5 g (0.0097 mole, 29%[19]) and I, weighing 0.2 g (4%). Both the products were identified by noting exact correspondence of their IR and UV spectra with those of the specimen obtained in the foregoing.

Formic Acid Reaction of 1,8-Dioxo-3,3,6,6-tetramethyl-9-(2-hydroxy-6-oxo-4,4-dimethylcyclohex-1-enyl)-1,2,3,4,5,6,7,8-octahydroxanthene (X)——A mixture of 13.8 g (1/30 mole) of X and 93.9 g (2.0 mole) of 99% formic acid was heated at 145—150° in a zirconium-lining autoclave for 4 hr. The reaction mixture was concentrated under reduced pressure and the resulting residue was dissolved in benzene. The benzene solution was extracted with 10% NaOH solution, washed and dried. Removal of benzene gave crystals of III, mp 168—169°. Yield, 12.1 g (0.0441 mole, 88%[18]). The product was identified by comparison of its IR and UV spectra with those of the specimen obtained above. Acidification of the alkaline extract combined with washings with HCl gave crystals of VI, mp 190—191°, which were collected by filtration. Yield, 1.3 g (0.0044 mole, 27%[20]). The product was identified by noting exact correspondence of its IR and UV spectra with those of an authentic specimen.

Reaction of 2-Formyldimedone (IV) and Dimedone (I) in TEAF——A solution of 0.84 g (0.005 mole) of IV and 1.4 g (0.010 mole) of I dissolved in 26.0 g (0.30 mole based on HCOOH) of TEAF was heated at about 90° with constant stirring for 20 min, while crystals were deposited. After cooling the reaction mixture, the crystals were collected by filtration, which were identified as X by noting exact correspondence of its IR and UV spectra with those of the specimen obtained in the foregoing. Yield, 1.8 g. After concentration of the foregoing filtrate, recrystallization of the resulting residue from MeOH gave an additional amount of X. Total yield, 1.95 g (95%).

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20) This calculation is based on the formation of VI from I, which is produced as an intermediate from the reductive fission reaction of X.