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Formic Acid Reduction. X.[1] Reductive Fission of Bridged Carbon-Carbon Bond of Bisdimedone Derivatives

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It has now been found that triethylammonium formate (TEAF), given by $5HCOOH \cdot 2N(C_2H_5)_3$ causes the reductive fission of the bridged carbon bonds of 2,2′-alkylidene- and 2,2′-arylidene-bisdimedones by heating. The reaction gave a number of products by the secondary reactions succeeding to the reductive fission. Routes of these reactions are also described.

In previous papers[1,3] from this laboratory, it has been shown with several compounds that the reductive fission of the carbon–carbon bond connecting to the active carbon adjacent to polar group such as carbonyl or imino group is caused by the reagent, triethylammonium formate (TEAF),[4] bp 95° (18 mmHg), given by $5HCOOH \cdot 2N(C_2H_5)_3$. That is, the reductive fission of the bridged methylene bonds of 5,5′-methylenebisbarbituric acid and of 5-(3-indolylmethylene)barbituric acid has been reported.[3] Furthermore, in the preceding paper on the formic acid reduction of 5,5-dimethyl-1,3-cyclohexanedione (dimedone) derivatives, the reductive fission of the bridged carbon bonds of 2,2′-methylenebisdimedone, 2,2′-benzylidenebisdimedone and 1,8-dioxo-3,3,6,6-tetramethyl-9-(2-dimedonyl)-1,2,3,4,5,6,7,8-octahydroxanthene was reported,[1] in that paper we made such a suggestion that the reductive fission of the analogous compounds, 2,2′-alkylidene- and 2,2′-benzylidene-bisdimedones might occur similarly. We now wish to describe the details of our work on this interesting reaction.

2,2′-Butylidene- (Ia), 2,2′-*β*-phenylethylidene- (Ib), 2,2′-cinnamylidene- (Ic), 2,2′-*p*-methoxybenzylidene- (Id), 2,2′-*m*-chlorobenzylidene- (Ie) and 2,2′-*p*-dimethylaminobenzylidenebisdimedone (If), which were prepared from the corresponding aldehydes and dimedone using boron trioxide as dehydrating agent in the same manner as previously reported[1] in the preparation of methylene- and benzylidene-bisdimedones, were used for the TEAF reaction. The TEAF reaction of these compounds was carried out under uniform conditions, *i.e.*, the substrate was heated along with TEAF (molar proportion of TEAF to substrate was 20:1 based on HCOOH) at 145—150°. Process of the reaction was indicated by considerable emission of carbon dioxide. In the runs with Ia, Ib and Ic, were isolated the products, 2-alkyl-substituted dimedone (IIa, $R=CH_3CH_2CH_2$-; IIb, $R=C_6H_5CH_2$-; IIc, $R=C_6H_5$-$CH=CH$-), 2-methyldimedone (III) and 1,8-dioxo-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8-octahydroxanthene (IV). In the runs with Id and Ie, 9-substituted 1,8-dioxo-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8-octahydroxanthene (Va, $R=p$-$CH_3OC_6H_4$-; Vb, $R=m$-ClC_6H_4-) was isolated in addition to the products mentioned in the above runs. In the run with If, IIf ($R=p$-$(CH_3)_2NC_6H_4$-), III, IV and N,N-dimethylaniline were isolated. The results are summerized in Table I.

The conversion of Ia, Ib and Ic into IIa—c, III and IV bears a close parallel to the conversion of 2,2′-methylenebisdimedone into III and IV in the TEAF reaction reported previously.[1] That is, as previously clarified in the reaction of 2,2′-methylenebisdimedone, these

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[1] Part IX: M. Sekiya and K. Suzuki, *Chem. Pharm. Bull.* (Tokyo), **19**, 1531 (1971).

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

[3] M. Sekiya and C. Yanaihara, *Chem. Pharm. Bull.* (Tokyo), **17**, 738 (1969); *idem, ibid.*, **17**, 810 (1969).

[4] K. Ito, *Yakugaku Zasshi*, **86**, 1166 (1966).

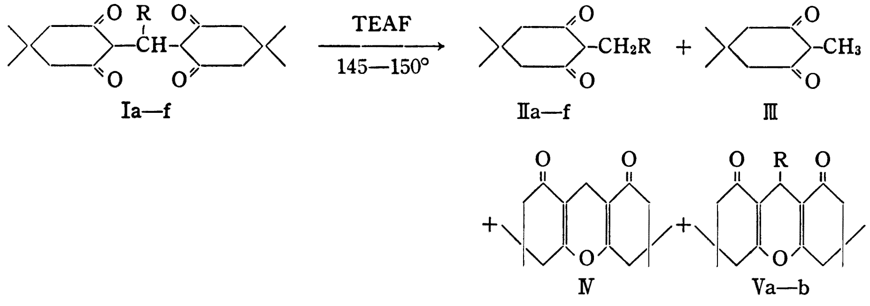
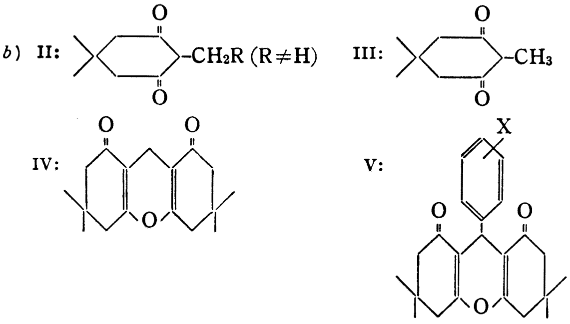


Table I. TEAF Reaction[a] of 2,2'-Alkylidene- and 2,2'-Arylidene-bisdimedones

Substrate No.	R	Reaction time (hr)	Products[b] and yields[c]			
			IIa—f	III	IV	Va—b
	H[d]	2.5	—	1.38	0.28	—
Ia	$CH_3CH_2CH_2$-	3.5	0.86	0.43	0.28	—
Ib	$C_6H_5CH_2$-	3.0	0.95	0.65	0.16	—
Ic	C_6H_5-CH=CH-	2.0	0.88	0.41	0.22	—
	C_6H_5-[d]	2.5	0.79[e]	0.47	0.18	0.17[f]
Id	p-$CH_3OC_6H_4$-	4.0	0.73	0.41	0.24	0.10
Ie	m-ClC_6H_4-	3.5	0.65	0.34	0.14	0.24
If	p-$(CH_3)_2NC_6H_4$-[g]	5.5	0.88	0.43	0.27	—

a) General procedure is given in experimental. In all runs, 0.03 mole of the substrate was used.

b)



c) Yields are given as molar equivalent from one mole of the substrate.

d) This data is quoted from previous paper.[1]

e) $R=C_6H_5$- in the II strucure

f) X=H in the V strucure

g) In this run, in addition to the products listed, N,N-dimethylaniline was also obtained.

reactions may be recognized to proceed by the reductive fission of the bridged carbon bond connecting to C_2 of dimedone grouping of Ia—c, giving IIa—c and dimedone, followed by the succeeding reaction, in which the later product, dimedone, reacts further with TEAF to give the products, III and IV (see Chart 1). The formation of IId—e, (IId, $R=p$-$CH_3OC_6H_4$-; IIe, $R=m$-ClC_6H_4-), III and IV from the substrate, Id—e, is also considered to take place similarly; the simultaneous formation of the product, Va—b (Va, $R=p$-$CH_3OC_6H_4$-; Vb, $R=m$-ClC_6H_4-) in these runs may be, however, recognized to be derived from direct dehydration of the substrate (see Chart 1). Such conversion mode of Id—e has a close parallel to the previously reported reaction of 2,2'-benzylidenebisdimedone.[1] No formation of

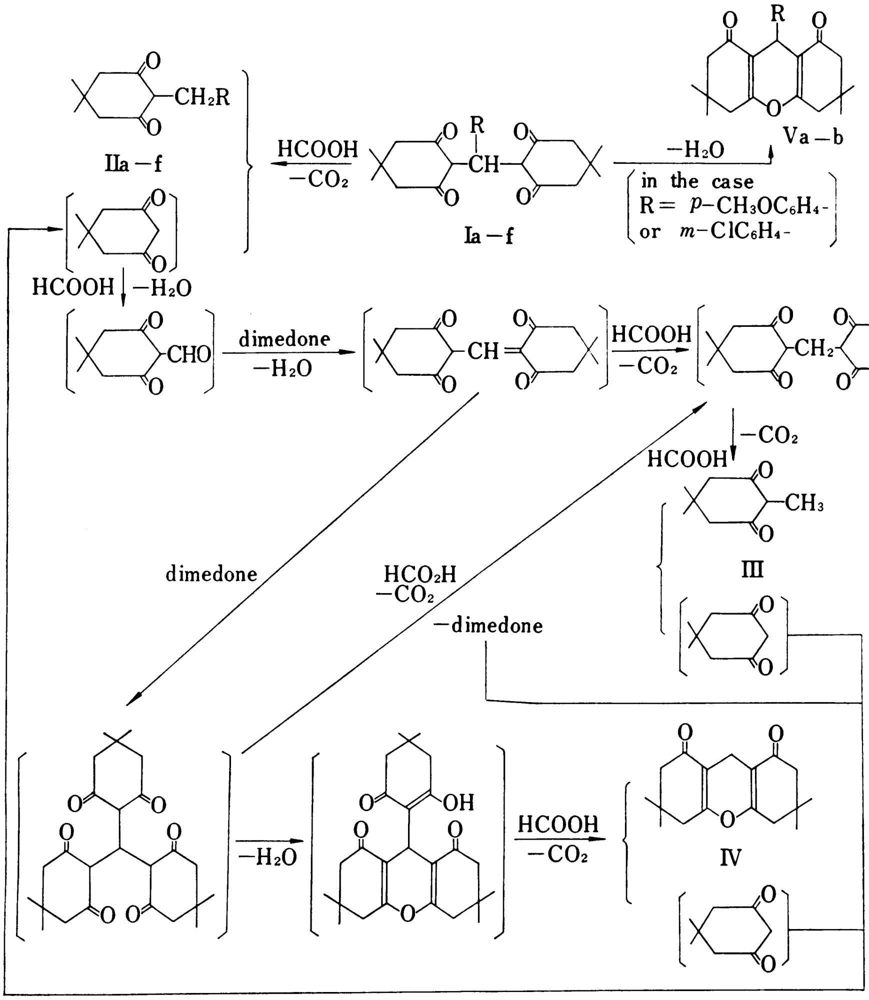
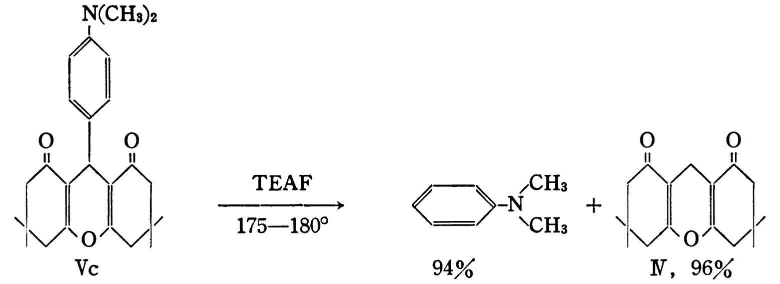


Chart 1. Route of TEAF Reaction of 2,2′-Alkylidene- and 2,2′-Arylidene-bisdimedones

the direct dehydration product from Ia, Ib and Ic was realized from the substantiation that these substrates were inert to the dehydration in TEAF medium, as 2,2′-methylenebisdimedone behaved similarly.[1]

Result of TEAF reaction with the substrate, If, showed no parallel to those with Id and Ie in no formation of direct dehydration product (see Table I). Occurrence of this difference was clarified by the following experiment. We prepared the dehydrating product, 1,8-dioxo-3,3,6,6-tetramethyl-9-(*p*-dimethylaminophenyl)-1,2,3,4,5,6,7,8-octahydroxanthene (Vc) from If using hydrochloric acid and this compound was heated with TEAF. It was noticeable that a reaction proceeded with emission of carbon dioxide to give dimethylaniline and IV.

This fact reveals an occurrence of reductive fission of the carbon bond of C_9 of such 9-*p*-dimethylaminophenyl substituted substrate, Vc. This reductive fission of Vc is considered to have occurred in the TEAF reaction of If, because in the reaction IV and N,N-dimethylani-



Vc 94% IV, 96%

line was formed instead of the direct dehydration product, Vc. The occurrence of the reductive fission is characteristic of Vc, because 1,8-dioxo-3,3,6,6-tetramethyl-9-phenyl-1,2,3,4,5,6,7,8-octahydroxanthene, Va and Vb were inert to this reaction even under drastic conditions.

Experimental

2,2′-Alkylidene- and 2,2′-Arylidene-bisdimedones. General Procedure——These compounds were best prepared from aldehyde and dimedone by the method using boron trioxide as dehydrating agent reported previously for the preparation of 2,2′-methylene- and 2,2′-benzylidene-bisdimedones.1) The procedures are entirely the same as those described, generally using 0.04 mole of dimedone, 0.02 mole of aldehyde, 0.012 mole of piperidine and 0.03 mole of boron trioxide. Reaction periods required and, yields and identities of the products are described in the following.

2,2′-Butylidenebisdimedone (Ia): Reacton time, 1.0 hr. Yield, 98%. Prisms (from MeOH), mp 133—135° (lit.,5) mp 134—135°). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1578, 1595 (C=O). UV$\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 260.5 (4.33).

2,2′-β-Phenylethylidenebisdimedone (Ib): Reaction time, 1.0 hr. Yield, 80%. Prisms (from MeOH), mp 164—166° (lit.,5a,6) mp 164—165°). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1588, 1592 (C=O). UV $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 218.5 (3.88), 261 (4.30).

2,2′-Cinnamylidenebisdimedone (Ic): Reaction time, 0.5 hr. Yield, 79%. Needles (from $CHCl_3$), mp 210—212° (lit.,5a) mp 215—217°). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1576, 1591 (C=O), 963 (*trans* -CH=CH-). UV $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 264 (4.45).

2,2′-*p*-Methoxybenzylidenebisdimedone (Id): Reaction time, 2.0 hr. Yield, 84%. Prisms (from MeOH), mp 140—142° (lit.,5a,7) mp 142—143°). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1549 (C=O). UV $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 228 (4.16), 261 (4.26).

2,2′-*m*-Chlorobenzylidenebisdimedone (Ie): Reaction time, 2.0 hr. Yield, 90%. Prisms (from MeOH), mp 190—192°. *Anal.* Calcd. for $C_{23}H_{27}O_4Cl$: C, 68.56; H, 6.76; Cl, 8.80. Found: C, 68.96; H, 6.67; Cl, 8.99. IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1594 (C=O). UV $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 220 (shoulder, 4.06), 260 (4.25).

2,2′-*p*-Dimethylaminobenzylidenebisdimedone (If): Reaction time, 1.5 hr. Yield, 88%. Prisms (from EtOH), mp 191—193° (lit.,5a,7a) mp 194.5—195.5°). IR $\nu_{\max}^{\mathrm{KBr}}$ cm^{-1}: 1594 (C=O). UV $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 258 (4.50), 301 (shoulder, 3.61).

TEAF Reaction of 2,2′-Alkylidene- and 2,2′-Arylidene-bisdimedones. General Procedure——The two 2,2′-alkylidene- and the four 2,2′-arylidene-bisdimedones obtained in the above were used as substrates for this reaction. In a flask provided with a thermometer, an inlet tube and an air condenser tube were placed 0.03 mole of the substrate and 51.9 g (0.60 mole based on HCOOH) of TEAF. The mixture was heated at 145—150° with constant stirring, while a constant stream of dry air free from CO_2 was introduced in order to check transfer of emission of CO_2 by Ba $(OH)_2$ solution. The reaction set in with vigorous emission of CO_2, but after several minutes the emission was weakened and continued. After emission of CO_2 was almost ceased, the reaction solution 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, washed and dried. Removal of the benzene gave crystals of IV, which was recrystallized from MeOH. When the substrate Id and Ie were used, removal of the benzene gave a crystalline mixture of IV and Va—b. Sepa-

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5) *a*) E.C. Horning and M.G. Horning, *J. Org. Chem.*, **11**, 95 (1946); *b*) A.A. Morton, F.D. Marsh, R.D. Coombs, A.L. Lyons, S.E. Penner, H.E. Ramsden, V.B. Backer, E.L. Little and R.L. Letsinger, *J. Am. Chem. Soc.*, **72**, 3785 (1950).

6) K.H. Lin and R. Robinson, *J. Chem. Soc.*, **1938**, 2005.

7) *a*) E.S. Padilla, *Anals. Fac. Farm. y Bioquim.*, **7**, 598 (1956) [*C.A.*, **53**, 7045 (1957)]; *b*) G.C. Chakravarti, H. Chattopadhyaya and P.C. Ghosh, *J. Indian Inst. Sci.*, **A14**, 141 (1932).

ration was carried out by silica gel column chromatography using benzene–AcOEt (4:1) as an eluent. Evaporation of the first eluent gave crystals of Va—b and of the second eluent gave crystals of IV. The foregoing alkaline extract combined with washings was acidified with 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 III. Recrystallization of the extraction residue from appropriate solvent gave crystals of II.

The run with Ia formed an exception of the above procedure, in which IIa and III were separated by silica gel column chromatography using $CHCl_3$–EtOH (95:5) as an eluent.

In the run with If, in addition, N,N-dimethylaniline was obtained by treatment of the TEAF distillate from the reaction mixture. To the distillate diluted with water, excess of KOH was added and the liberated triethylamine layer was separated and dried over K_2CO_3. After evaporation of the triethylamine, the residue was subjected to distillation under reduced pressure to give N,N-dimethylaniline, weighing 0.4 g, which was identified by noting exact correspondence of its infrared (IR) spectrum with that of the authentic sample.

Reaction periods and yields of products for all runs are shown in Table I. Of a series of the products, III and IV has been known in our previous paper.[1] Identities of these compounds were made by comparison of their IR and ultraviolet (UV) spectra with those of the authentic specimen and mixed melting point tests. Identities of the other products obtained in this work are described in the following.

2-*n*-Butyldimedone (IIa): Needles (from aqueous MeOH), 155—157° (lit.,[8] mp 155°). *Anal.* Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.60; H, 9.90. IR ν_{max}^{KBr} cm^{-1}: 1562 (C=O). UV λ_{max}^{MeOH} mμ (log ε): 266 (4.13). Mass Spectrum *m/e* (relative intensity): 196 (12), 167 (11), 154 (16), 153 (12), 141 (11), 140 (18), 125 (15), 112 (11), 111 (11), 98 (19), 97 (15), 85 (13), 84 (45), 83 (100), 70 (14), 69 (18), 57 (28), 56 (23), 55 (64), 43 (26), 42 (12), 41 (55), 39 (26). This material was converted to an oily material in the air.

2-*β*-Phenylethyldimedone (IIb): Scales (from aqueous MeOH), mp 129—131°. *Anal.* Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.65; H, 8.20. IR ν_{max}^{KBr} cm^{-1}: 1558 (C=O). Mass Spectrum *m/e* (relative intensity): 244 (55), 173 (20), 154 (14), 153 (68), 145 (20), 105 (54), 104 (100), 103 (14), 98 (14), 97 (89), 93 (14), 92 (67), 91 (71), 89 (11), 85 (12), 84 (35), 83 (54), 79 (14), 78 (16), 77 (20), 70 (16), 69 (43), 65 (32), 64 (10), 63 (14), 57 (14), 56 (13), 55 (89), 43 (25), 42 (14), 41 (47), 40 (15), 39 (36).

2-Cinnamyldimedone (IIc): Needles (from MeOH), mp 165—167°. *Anal.* Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.26; H, 7.87. IR ν_{max}^{KBr} cm^{-1}: 1552 (C=O), 961 (*trans* –CH=CH–). UV λ_{max}^{MeOH} mμ (logε): 215 (shoulder, 4.06), 257 (4.45), 293 (3.57). Mass Spectrum *m/e* (relative intensity): 256 (74), 249 (11), 185 (11), 173 (14), 172 (86), 171 (17), 166 (14), 165 (100), 157 (25), 129 (30), 128 (30), 117 (38), 116 (10), 115 (33), 104 (20), 103 (100), 97 (30), 92 (18), 91 (85), 84 (10), 83 (65), 70 (11), 69 (25), 57 (18), 56 (21), 55 (54), 42 (10), 41 (49).

2-*p*-Methoxybenzyldimedone (IId): Prisms (from MeOH), mp 177—178°. *Anal.* Calcd. for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 74.48; H, 7.71. IR ν_{max}^{KBr} cm^{-1}: 1551 (C=O). UV λ_{max}^{MeOH} mμ (logε): 226 (4.15), 266 (4.15), 285 (shoulder, 3.77). Mass Sepctrum *m/e* (relative intensity): 226 (36), 223 (10), 176 (33), 175 (13), 161 (14), 145 (23), 121 (64), 108 (100), 105 (13), 91 (10), 83 (17), 78 (11), 77 (23), 57 (25), 56 (15), 55 (21), 43 (11), 41 (28), 40 (11), 39 (13).

2-*m*-Chlorobenzyldimedone (IIe): Needles (from MeOH), mp 157—158°. *Anal.* Calcd. for $C_{15}H_{17}O_2Cl$: C, 68.05; H, 6.47; Cl, 13.39. Found: C, 67.86; H, 6.39; Cl, 13.24. IR ν_{max}^{KBr} cm^{-1}: 1556 (C=O). UV λ_{max}^{MeOH} mμ (log ε): 264 (4.15). Mass Spectrum *m/e* (relative intensity): 266 (13), 264 (38), 182 (13), 180 (39), 165 (15), 146 (11), 145 (100), 131 (11), 127 (14), 125 (24), 115 (10), 103 (17), 102 (11), 101 (11), 89 (10), 83 (58), 77 (15), 75 (12), 56 (13), 55 (41), 51 (13), 43 (20), 41 (34), 39 (26).

2-*p*-Dimethylaminobenzyldimedone (IIf): Prisms (from EtOH), mp 177—180°. *Anal.* Calcd. for $C_{17}H_{23}O_2N$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.53; H, 8.48; N, 5.20. IR ν_{max}^{KBr} cm^{-1}: 1564 (C=O). UV λ_{max}^{MeOH} mμ (log ε): 257 (4.57). Mass Spectrum *m/e* (relative intensity): 273 (29), 135 (11), 134 (100), 121 (68), 120 (13).

1,8-Dioxo-3,3,6,6-tetramethyl-9-(*p*-methoxyphenyl)-1,2,3,4,5,6,7,8-octahydroxathene (Va): Prisms (from MeOH), mp 237—241° (lit.,[6] mp 242°). *Anal.* Calcd. for $C_{24}H_{28}O_4$: C, 75.76; H, 7.42. Found: C, 75.52; H, 7.38. This product was identified by noting extract correspondence of its IR and UV spectra with those of an authentic specimen prepared by previously reported method.[6] IR ν_{max}^{KBr} cm^{-1}: 1661, 1673 (C=O). UV λ_{max}^{MeOH} mμ (log ε): 227 (4.34), 290 (3.80).

1,8-Dioxo-3,3,6,6-tetramethyl-9-(*m*-chlorophenyl)-1,2,3,4,5,6,7,8-octahydroxanthene (Vb): Prisms (from MeOH), mp 186—189°. *Anal.* Calcd. for $C_{23}H_{25}O_3Cl$: C, 71.77; H, 6.55; Cl, 9.21. Found: C, 71.47; H, 6.50; Cl, 9.11. IR ν_{max}^{KBr} cm^{-1}: 1658, 1668 (shoulder) (C=O). UV λ_{max}^{MeOH} mμ (log ε): 234 (4.11), 299 (3.81).

TEAF Reaction of 1,8-Dioxo-3,3,6,6-tetramethyl-9-(*p*-dimethylaminophenyl)-1,2,3,4,5,6,7,8-octahydroxathene (Vc)——A mixture of 11.8 g (0.03 mole) of Vc and 103.8 g (1.20 mole based on HCOOH) of TEAF was heated at 175—180° with constant stirring until no Vc was checked by TLC (silica gel, benzene–AcOEt) of the reaction mixture. After heating for 12 hr, the reaction solution was concentrated under reduced

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8) R.D. Desai, *J. Chem. Soc.*, **1932**, 1079.

pressure to remove triethylamine and excess of TEAF. The resulting residue was dissolved in benzene and the benzene solution was washed with 5% HCl and dried over $MgSO_4$. Removal of benzene and recrystallization of the resulting residue from MeOH gave prisms of IV, mp 168—169°. Yield, 7.9 g (96%). The product was identified by comparison of its IR and UV spectra with those of the authentic specimen. The foregoing TEAF distillate was diluted with water and excess of KOH was added. The liberated triethylamine layer was separated and dried over K_2CO_3. After evaporation of triethylamine, the residue was subjected to distillation under reduced pressure to give 3.4 g (94%) of an oily material, bp 84—87° (18 mmHg), which was identified as dimethylaniline by comparison of its IR spectrum with that of the authentic sample.

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