Manganese(II) Acetate-Mediated Double 2-Hydroperoxyalkylations of Barbituric Acid and Its Derivatives

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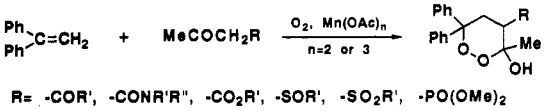
The reactions of 1,1-disubstituted ethenes with barbituric acid and its derivatives in the presence of manganese(II) acetate and air yielded 5,5-bis(2-hydroperoxyalkyl)barbituric acids **3aa-ac** and **3ba-ja** in 62–99% yields. The structure of **3ab** was determined by X-ray crystallography. The reaction of **1a** and **2a** was also effected by manganese(III) acetate (95%) and metallic manganese (92%), but in poor yield by cerium(IV) ammonium nitrate (50%). Treatment of 5,5-bis(2-hydroperoxy-2,2-diphenylethyl)-1,3-dimethylbarbituric acid (**3aa**) with perchloric acid gave 5,5-bis(benzoylmethyl)-1,3-dimethylbarbituric acid (**6**) and 5-(2-benzoylmethyl)-1,3-dimethyl-5-(2,2-diphenylethenyl)-barbituric acid (**7**), in which phenyl migration took place. Reduction of **3aa** with zinc powder in acetic acid or with triphenylphosphine in diethyl ether yielded 5,5-bis(2-hydroxy-2,2-diphenylethyl)-1,3-dimethylbarbituric acid (**10**), which was dehydrated to give a spirotetrahydropyran **11**.

Introduction

We recently reported that manganese(III) acetate-mediated free-radical cyclization of alkenes with active methylene compounds such as 1,3-diones,[1] acetoacetamides,[2] β-keto esters,[1a,3] a β-keto sulfoxide,[4] and β-keto sulfones[4] in the presence of air yielded 1,2-dioxan-3-ols in good yields (Scheme I). Manganese(II) acetate, on the other hand, gave better yields than manganese(III) acetate for the reaction of alkenes with 2-substituted 1,3-diketones and air. Acetoacetamides were converted to the corresponding 1,2-dioxan-3-ols with both manganese(II) and manganese(III) acetates in similar yields. We have further examined the reaction of alkenes with a cyclic diamide, barbituric acid, in the hope that products may have biological activities because some 1,2-dioxan-3-ols are known to inhibit root formation in adult tissue of *Eucalyptus grandis*[5] and barbituric acids have been known as hypnotic sedatives.[6] The reactions were investigated with particular attention being paid to the use of a combination of manganese(II) acetate and air. The results are described in this paper.

Scheme I[1-4]



Results

Reactions of 1,1-Diphenylethene (1a) with 1,3-Dimethylbarbituric Acid (2a) and Its Derivatives 2b and 2c in the Presence of Various Reagents and Air. When the reaction of 1,1-diphenylethene (**1a**) with 1,3-dimethylbarbituric acid (**2a**) in the presence of manganese(II) acetate was carried out in acetic acid at a molar ratio of 1:0.5:1 under a dry air stream at 23 °C for 12 h, the product ($C_{34}H_{32}N_2O_7$, elemental analysis and FAB mass) was found to be 5,5-bis(2-hydroperoxy-2,2-diphenylethyl)-1,3-dimethylbarbituric acid (**3aa**) (Table I, entry 1).

The structural assignment was based on the ^1H NMR, ^{13}C NMR, and IR spectra. The structure was finally confirmed by X-ray crystallography on compound **3ab** ($C_{32}H_{28}N_2O_7$, elemental analysis and FAB mass) which was obtained from the reaction of **1a** and barbituric acid (**2b**) (Table II). The ORTEP diagram of **3ab** is shown in Figure 1. The most characteristic feature of the structure was that two hydroperoxyl groups are both intramolecularly hydrogen-bonded to one of the carbonyl oxygens. One molecule of ethanol was contained in the lattice.[7]

The yield of **3aa** was improved to 96% by carrying out the reaction at a molar ratio of 1:1.5:0.05 (entry 4). However, the reaction using 0.001 molar manganese(II)

(1) (a) Tagegami, S.; Yamada, T.; Nishino, H.; Korp, J. D.; Kurosawa, K. *Tetrahedron Lett.* **1990**, *31*, 6371. (b) Nishino, H.; Tagegami, S.; Yamada, T.; Korp, J. D.; Kurosawa, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1810. (c) Qian, C.-Y.; Yamada, T.; Nishino, H.; Kurosawa, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1371.

(2) Qian, C.-Y.; Nishino, H.; Kurosawa, K. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3557.

(3) Yamada, T.; Iwahara, Y.; Nishino, H.; Kurosawa, K. *J. Chem. Soc., Perkin Trans. 1*, **1993**, 609.

(4) Qian, C.-Y.; Nishino, H.; Kurosawa, K. *J. Heterocycl. Chem.* **1993**, *30*, 209.

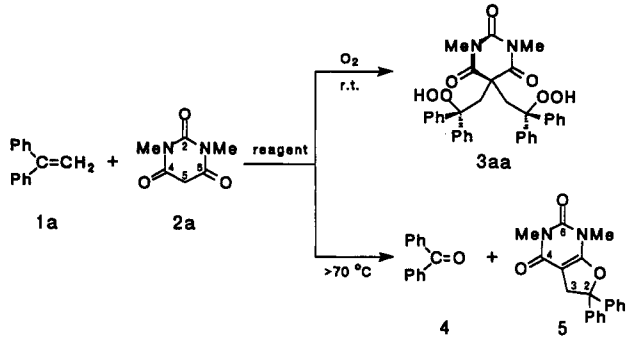
(5) (a) Paton, D. M.; Willing, R. R.; Nicholls, W.; Pryor, L. D. *Aust. J. Bot.* **1970**, *18*, 175. (b) Crow, W. D.; Nicholls, W.; Sterns, M. *Tetrahedron Lett.* **1971**, 1353. (c) Stern, M. J. *Cryst. Mol. Struct.* **1971**, *1*, 373.

(6) Guillen, S. R.; Guzman, C. M. *Pharmazie* **1988**, *43*, 827.

(7) X-ray data, analyses, and experimental details are available from the Cambridge Crystallographic Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

0022-3263/93/1958-4448$04.00/0

Table I. Reactions of 1,3-Dimethylbarbituric Acid with 1,1-Diphenylethene and Molecular Oxygen in Acetic Acid

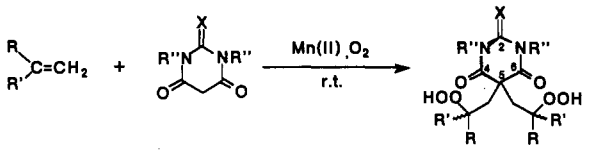


1a 2a 3aa 4 5

entry	reagent	molar ratio[a]	reaction condns (temp (°C), time (h))	composition of products (yield, %)[b]				
1	$Mn(OAc)_2$	1:0.5:1	23, 12	1a (28)		3aa (42)		
2	$Mn(OAc)_2$	1:1:1	23, 5	1a (19)		3aa (72)		
3	$Mn(OAc)_2$	1:1.5:1	25, 5			3aa (94)		
4	$Mn(OAc)_2$	1:1.5:0.05	25, 5			3aa (96)		
5	$Mn(OAc)_2$	1:1.5:0.001	25, 16	1a (64)	2a (42)	3aa (24)		
6	$Mn(OAc)_2$	1:1.5:1	70, 0.3				4 (98)	
7	$Mn(OAc)_3$	1:1.5:0.1	26, 5			3aa (95)		
8	$Mn(OAc)_3$	1:1.5:1	70, 0.3				4 (21)	5 (63)
9	Mn	1:1.5:1	24, 3			3aa (92)		
10	CAN[c]	1:1.5:1	23, 6			3aa (50)	4 (11)	

[a] 1a:2a:reagent. [b] Isolated yields based on the amount of 1a added. [c] $(NH_4)_2Ce(NO_3)_6$.

Table II. Synthesis of 5,5-Bis(2-hydroperoxyalkyl)barbituric Acids[a]



1a-j 2a-c 3ab,3ac,3ba-ja

product	R	R′	R″	X	time (h)	yield[b] (%)	racemic:meso
3ab	Ph	Ph	H	O	6	86	
3ac	Ph	Ph	Et	S	4	62	
3ba[c]	Me	Me	Me	O	5	81	
3ca	Et	Et	Me	O	3	88	
3da	4-MeC_6H_4	4-MeC_6H_4	Me	O	3	97	
3ea	4-ClC_6H_4	4-ClC_6H_4	Me	O	3	99	
3fa	4-FC_6H_4	4-FC_6H_4	Me	O	3	92	
3ga	Me	Ph	Me	O	2	73	29:71
3ha	Ph	4-ClC_6H_4	Me	O	3	97	41:59
3ia	Ph	4-BrC_6H_4	Me	O	3	84	44:56
3ja	Ph	1-naphthyl	Me	O	3	93	50:50

[a] The reactions were carried out in at a 1:1.5:0.1 molar ratio for 1:2:$Mn(OAc)_2 \cdot 4H_2O$ at 20–28 °C under a dry air stream. [b] Isolated yields after chromatography based on the amount of 1 used except for **3ba** for which yield was based on the amount of **2a**. [c] 2-Methylpropene (**1b**) was bubbled slowly through a mixture of **2a** (1.5 mmol) and $Mn(OAc)_2 \cdot 4H_2O$ (0.1 mmol) in acetic acid (25 mL).

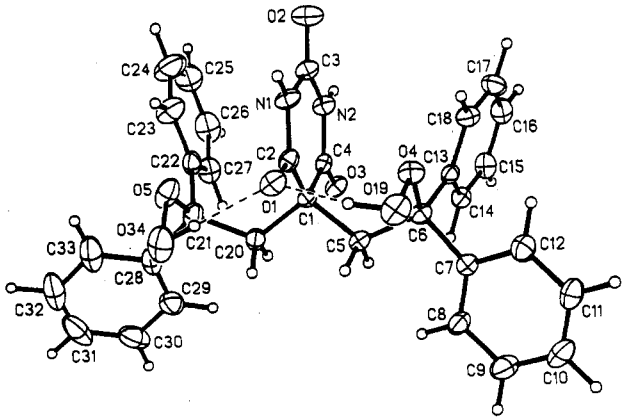


Figure 1. ORTEP Diagram of **3ab**.

acetate gave **3aa** in poor yield, and unchanged **1a** and **2a** were recovered (entry 5). The reaction at 70 °C yielded benzophenone (**4**) (entry 6). The reaction using manganese(III) acetate at room temperature also gave **3aa** in excellent yield (entry 7), but afforded **4** and 5,7-dimethyl-2,2-diphenyl-4,6-dioxo-5,7-diaza-2,3,4,5,6,7-hexahydrobenzo-[*b*]furan (**5**) at elevated temperature (entry 8). The reaction using metallic manganese yielded **3aa** (entry 9) and cerium(IV) ammonium nitrate (CAN) gave **3aa** and **4** (entry 10), but cobalt(II) and cobalt(III) acetates were not effective.

Reaction of **1a** and 1,3-diethyl-2-thiobarbituric acid (**2c**) was also examined and afforded 1,3-diethyl-5,5-bis(2-hydroperoxy-2,2-diphenylethyl)-2-thiobarbituric acid (**3ac**) (Table II).

Reactions of Various Alkenes 1b-j with 1,3-Dimethylbarbituric Acid (2a). The reactions using manganese(II) acetate were examined for 2-methylpropene (**1b**), 2-ethyl-1-butene (**1c**), 1,1-bis(4-methyphenyl)ethene (**1d**), 1,1-bis(4-chlorophenyl)ethene (**1e**), 1,1-bis(4-fluorophenyl)ethene (**1f**), 2-phenylpropene (**1g**), 1-(4-chlorophenyl)-1-phenylethene (**1h**), 1-(4-bromophenyl)-1-

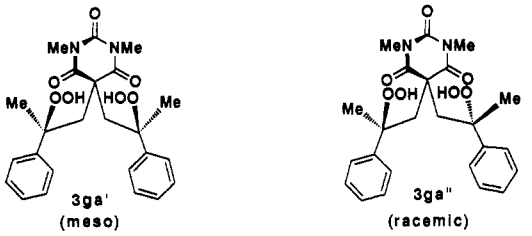
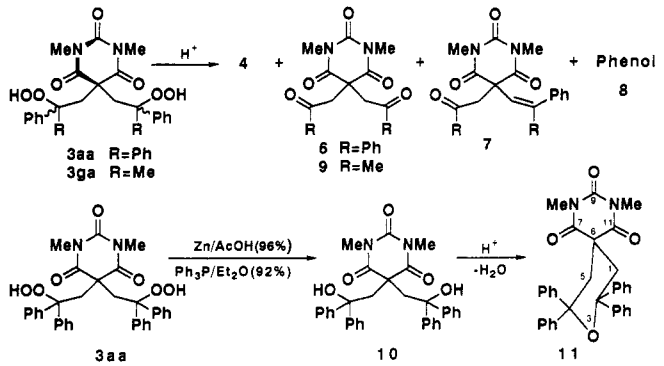


Figure 2. Structures of **3ga'** and **3ga''**.

Scheme II. Treatment of 3aa, 3ga, or 10 with Acid



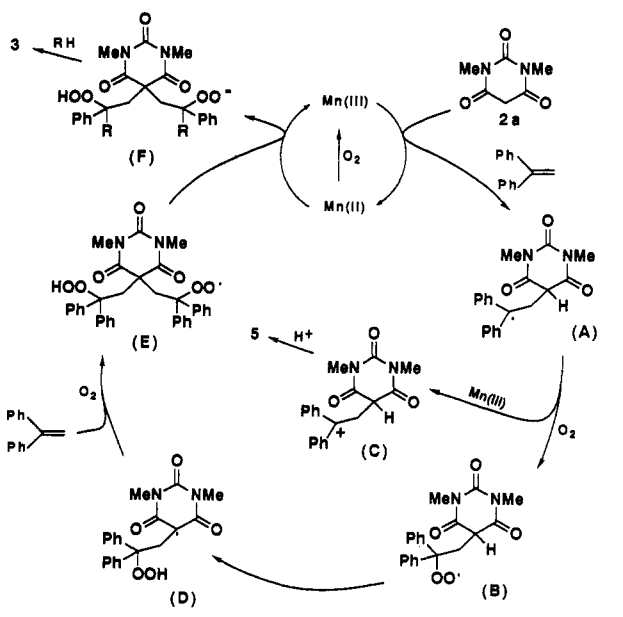
phenylethene (**1i**), and 1-(1-naphthyl)-1-phenylethene (**1j**). The reactions of 1,1-disubstituted ethenes **1b-j** with **2a** gave the corresponding 5,5-bis(2-hydroperoxyalkyl)-1,3-dimethylbarbituric acids **3ba-ja** in good yields (Table II). It was found that styrene, 1-octene, and *trans*-stilbene were not reactive in the reaction.

In previous studies on the formation of 1,2-dioxan-3-ols,[1-4] alkenes with different substituents at the C-1 position were not used so that the stereoisomers did not occur at the C-6 in the 1,2-dioxan-3-ols. 5,5-Bis(2-hydroperoxyalkyl)-1,3-dimethylbarbituric acids **3ga-ja** from 1,1-disubstituted alkenes **2g-j**, which have a phenyl group and methyl, 4-chlorophenyl, 4-bromophenyl, or 1-naphthyl group, consisted of two diastereomers. The diastereomers could not be separated into individual isomers. The ^{1}H NMR spectrum of 5,5-bis(2-hydroperoxy-2-phenylpropyl)-1,3-dimethylbarbituric acid (**3ga**) showed the presence of two singlets at δ 1.45 and 1.48 corresponding two C-methyl groups and three singlets at δ 1.93, 2.65, and 3.41 corresponding to two *N*-methyl groups. Assignments were based on an H,C-COSY spectrum. The spectral data indicated the presence of two diastereomers, that is, meso **3ga'** and racemic **3ga''** as shown in Figure 2. The meso **3ga'** has magnetically nonequivalent NMe groups and carbonyls (C-4 and C-6). On the other hand, the racemic **3ga''** has two equivalent NMe groups and carbonyls (C-4 and C-6). The isomer ratio was estimated on the basis of intensities of the CMe signals as shown in Table II; the meso isomer predominated.

Acid-Catalyzed Decomposition of 3aa and 3ga. In connection with the conversion of 1,2-dioxan-3-ols to substituted furans,[1c] the acid-catalyzed reactions of **3aa** and **3ga** were carried out. Upon treatment with perchloric acid in acetonitrile **3aa** gave **4**, 5,5-bis(benzoylmethyl)-1,3-dimethylbarbituric acid (**6**), 5-(benzoylmethyl)-1,3-dimethyl-5-(2,2-diphenylethenyl)barbituric acid (**7**), and phenol (**8**). The reaction of **3ga**, on the other hand, yielded 1,3-dimethyl-5,5-bis(2-oxopropyl)barbituric acid (**9**) and phenol (**8**). The methyl group in the side chains did not migrate in this reaction (Scheme II).

Reductions of 3aa with Zinc Powder in Acetic Acid and with Triphenylphosphine in Diethyl Ether.

Scheme III



When **3aa** was treated with zinc powder in acetic acid, it gave the corresponding diol **10**. A similar reaction with triphenylphosphine in diethyl ether also yielded the same diol. The diol **10** could be dehydrated to give a spirotetrahydropyran **11** upon treatment with perchloric acid.

Discussion

The formation of 5,5-bis(2-hydroperoxyalkyl)barbituric acids **3aa-ac** and **3ba-ja** could be accounted for in terms of radical reactions of alkene, 1,3-dimethylbarbituric acid (**2a**), and manganese(III) acetate producing radical **A** (Scheme III). Manganese(III) could be formed from manganese(II) acetate by air.[3] The radical **A** either trapped oxygen to form peroxyl radical **B** or was oxidized to the corresponding cation **C**. Under the present conditions, that is, in the presence of air and at room temperature, the former path should be favored. The peroxyl radical **B** can then be converted to radical **D** either by intramolecular hydrogen abstraction or by a series of reactions, that is, reduction of peroxyl radical, protonation, and abstraction of hydrogen at the C-5 position. A similar process from **D** to peroxyl anion **F** would yield **3**. In the reactions at an elevated temperature and in a higher concentration of manganese(III) acetate, the alternative path (**A** → **C**) became competitive; the carbocation **C** cyclized and were then deprotonated to yield **5**.

Formation of a ketone and a carbon–carbon double bond in decomposition of a hydroperoxide has precedence;[8] the acid-catalyzed reaction of 1-phenylcyclopentyl hydroperoxide gave cyclopentanone and 1-phenylcyclopentene, together with phenol and ring-opened compounds. Acid-catalyzed decomposition and elimination of hydrogen peroxide in **3aa** could account for the formation of **4**, **6**, **7**, and **8**.

Conclusion

Double 2-hydroperoxyalkylation of barbituric acid (**2b**) and its derivatives **2a** and **2c** at the C-5 position was achieved by the reaction of 1,1-disubstituted ethenes **1a-j** in the presence of manganese(II), manganese(III) acetate,

(8) Anderson, G. H.; Smith, J. G. *Can. J. Chem.* **1968**, *46*, 1561.

CAN, or metallic manganese and air. It was shown that compounds **3aa**, **3ba**, **3fa**, and **3ab** were not active for antifungal, insecticide, and weed killer tests.[9]

Experimental Section

Materials. Manganese(III) acetate [$Mn(OAc)_3 \cdot 2H_2O$] was prepared according to the method in the literature.[10] 1,1-Diphenylethenes **1a-j** were prepared by dehydration of the corresponding alcohols which were synthesized from substituted acetophenones and arylmagnesium bromides. 1,3-Dimethylbarbituric acid (**2a**), barbituric acid (**2b**), and manganese(II) acetate tetrahydrate were purchased from Tokyo-Kasei Co. Ltd. and used as received. 1,3-Diethyl-2-thiobarbituric acid (**2c**) was purchased from Aldrich Chemical Co. Inc.

Reactions of Alkenes 1a-j and Barbituric Acids 2a-c in the Presence of Manganese(II), Manganese(III) Acetate, Metallic Manganese, or Cerium(IV) Ammonium Nitrate and Air. The general procedure for the reaction of a barbituric acid with an alkene [except for 2-methylpropene (**1b**)] in the presence of the reagent and air was as follows. Manganese(II) acetate tetrahydrate (or other reagent) (0.001-1 mmol) was added to a stirred solution of an alkene (1 mmol) and a barbituric acid (0.5-1.5 mmol) in acetic acid (25 mL). In the case of **1b**, **1b** and dry air were bubbled slowly through a mixture of 1,3-dimethylbarbituric acid (**2a**) and manganese(II) acetate tetrahydrate (0.1 mmol) in acetic acid (25 mL). The mixture was stirred at the temperature shown in Tables I and II under a current of dry air for the period of time shown in the tables. The reaction was quenched by adding water (60 mL), and the mixture was extracted with benzene. After benzene was removed, the resulting products were separated on TLC (Wakogel B10) while eluting with a mixture of hexane and ethyl acetate (1:1 v/v). The yields are listed in Tables I and II. Analytical samples were further purified by recrystallization from a mixture of benzene and hexane except for **3ab**, which was recrystallized from ethanol.

5,5-Bis(2-hydroperoxy-2,2-diphenylethyl)-1,3-dimethylbarbituric acid (3aa): mp 124–126 °C; IR (KBr) 3356 (OOH), 1700–1640 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 2.68 (s, 6H, 2 × CH_3), 3.56 (s, 4H, 2 × CH_2), 7.36–7.60 (m, 20H, 4 × Ph), 8.78 (s, 2H, 2 × OOH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7 (C-4, C-6), 149.5 (C-2), 142.1 (arom C), 128.1, 127.6, 126.1 (arom CH), 86.6 (2 × C-O), 49.2 (C-5), 46.1 (2 × CH_2), 28.8 (2 × NCH_3); MS (FAB, positive ion) m/z 581 ($M^+ + H$). Anal. Calcd for $C_{34}H_{32}N_2O_7 \cdot 1/2C_6H_6$: C, 71.70; H, 5.69 N, 4.52. Found: C, 71.68; H, 5.60; N, 4.65.

5,5-Bis(2-hydroperoxy-2,2-diphenylethyl)barbituric acid (3ab): mp 234–235 °C; IR (KBr) 3400–3000 (NH, OOH), 1700–1640 cm^{-1} (C=O); ^1H NMR (400 MHz, acetone-d_6) δ 3.64 (s, 4H, 2 × CH_2), 7.15–7.36 (m, 20H, 4 × Ph), 9.19 (s, 2H, 2 × OOH); 9.65 (s, 2H, 2 × NH); ^{13}C NMR (22.5 MHz, DMSO-d_6) δ 175.2 (C-4, C-6), 149.2 (C-2), 144.3 (arom C), 129.0, 128.5, and 127.9 (arom CH), 87.9 (2 × CO), 50.2 (C-5), 47.3 (2 × CH_2); MS (FAB, negative ion) m/z 551 ($M^- - H$). Anal. Calcd for $C_{32}H_{28}N_2O_7 \cdot EtOH$: C, 68.23; H, 5.72; N, 4.67. Found: C, 68.22; H, 5.72; N, 4.76.

5,5-Bis(2-hydroperoxy-2-phenylpropyl)-1,3-dimethylbarbituric acid (3ga): mp 118–120 °C; IR ($CHCl_3$) 3394 (OOH), 1700–1640 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ 1.45 and 1.48 (s, s, 6H, 2 × CH_3), 1.93, 2.65, and 3.41 (s, s, s, 6H, 2 × NCH_3), 2.95, 2.91, 2.71, and 2.67 (d, d, d, d, 4H, J = 15.1 Hz, 2 × CH_2), 7.04–7.38 (m, 10H, 2 × Ph), 8.48 and 8.66 (s, s, 2H, 2 × OOH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 172.7, and 169.6 (C-4, C-6), 149.3 (C-2), 140.5, 140.2 (arom C), 127.9, 127.4, 127.3, 126.9, 124.9, and 124.8 (arom CH), 84.2 and 84.0 (2 × CO), 49.5 (C-5), 48.1 and 47.9 (2 × CH_2), 29.1, 28.5, and 28.0 (2 × NCH_3), 27.6 and 27.5 (2 × CH_3). Anal. Calcd for $C_{24}H_{28}N_2O_7$: C, 63.14; H, 6.18; N, 6.13. Found: C, 63.50; H, 6.23; N, 6.18.

4,6-Dioxo-5,7-diaza-5,7-dimethyl-2,2-diphenyl-2,3,4,5,6,7-hexahydrobenzo[*b*]furan (5): mp 190–191 °C; IR (KBr) 1703, 1662 cm^{-1} (C=O); ^1H NMR (60 MHz, $CDCl_3$) δ 3.40 (s, 3H, NCH_3), 3.55 (s, 3H, NCH_3), 3.90 (s, 2H, CH_2), 7.41 (s, 10H, 2 × Ph); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 160.3 and 160.2 (C-4, C-3a), 151.4 (C-6), 143.0 (arom C), 128.7, 128.4, 125.7 (arom CH), 97.7 (C-7a), 86.0 (C-2), 40.6 (C-3), 29.7 (CH_3) and 28.1 (CH_3). Anal. Calcd for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.76; H, 5.49; N, 8.17.

Acid-Catalyzed Decomposition of 3aa. Compound **3aa** (1 mmol) was dissolved in acetonitrile (10 mL) containing 60% perchloric acid (1 mmol), and the mixture was stirred at 50 °C for 30 min. After being diluted with water (20 mL), the reaction mixture was extracted with a mixture of benzene and diethyl ether (1:1 v/v, total 60 mL). The organic layer was separated and washed with water. After the solvent was removed, the resulting mixture was chromatographed on a silica gel plate while eluting with a mixture of benzene and diethyl ether (1:1 v/v). The products were further purified by recrystallization from 95% ethanol to obtain an analytical sample.

5,5-Bis(benzoylmethyl)-1,3-dimethylbarbituric acid (6): 56% yield; mp 238–239 °C; IR ($CHCl_3$) 1710–1640 cm^{-1} (C=O); ^1H NMR (60 MHz, $CDCl_3$) δ 3.47 (s, 6H, 2 × CH_3), 3.98 (s, 4H, 2 × CH_2), 7.23–8.07 (m, 10H, 2 × Ph); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 196.2 (2 × PhCO), 172.0 (C-4, C-6), 152.0 (C-2), 135.3 (arom C), 134.0, 128.8, and 128.1 (arom CH), 49.0 (2 × CH_2), 48.5 (C-5), 28.8 (2 × NCH_3). Anal. Calcd for $C_{22}H_{20}N_2O_6$: C, 67.33; H, 5.13; N, 7.14. Found: C, 67.63; H, 5.13; N, 7.16.

5-(Benzoylmethyl)-1,3-dimethyl-5-(2,2-diphenylethenyl)barbituric acid (7): 28% yield; mp 179–180 °C; IR (KBr) 1710–1640 cm^{-1} (C=O); ^1H NMR (60 MHz, $CDCl_3$) δ 3.12 (s, 6H, 2 × CH_3), 4.33 (s, 2H, CH_2), 6.27 (s, 1H, =CH–), 7.01–8.15 (m, 15H, 3 × Ph); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 197.0 (PhCO), 170.3 (C-4, C-6), 150.8 (C-2), 146.3 (=C<), 141.3, 135.3 (arom C), 133.9 (=CH–), 129.2, 128.7, 128.4, 128.3, 127.1, 126.0 (arom CH), 53.0 (C-5), 50.4 (CH_2), 28.6 (2 × CH_3). Anal. Calcd for $C_{28}H_{24}N_2O_4$: C, 74.25; H, 5.35; N, 6.19. Found: C, 74.12; H, 5.36; N, 6.16.

Reduction of 3aa. (a) With Zinc and Acetic Acid. Zinc powder (400 mg) was added to a mixture of **3aa** (1.16 g) and acetic acid (10 mL), and the mixture was stirred for 1 h at room temperature. The mixture was poured into water (50 mL), neutralized with sodium hydrogen carbonate, and filtered to remove the excess zinc. The filtrate was extracted with benzene (2 × 30 mL) and the benzene evaporated. The residue was purified on a silica gel plate with chloroform as a developing solvent, giving 5,5-bis(2-hydroxy-2,2-diphenylethyl)-1,3-dimethylbarbituric acid (**10**) (526 mg, 96%): mp 263–264 °C (from 95% ethanol).

(b) With Triphenylphosphine. A mixture of **3aa** (1.16 g) and triphenylphosphine (524 mg) in anhydrous diethyl ether (30 mL) was stirred at room temperature for 8 h. The reaction mixture was filtered, and the filtrate was poured into water (20 mL). Then the mixture was extracted with benzene (2 × 20 mL) and worked up in a manner similar to the above, giving **10** (504 mg, 92%).

Treatment of 10 with Perchloric Acid. Compound **10** (1 mmol) was dissolved in acetonitrile (10 mL) containing a 20% aqueous perchloric acid (1 mmol), and the mixture was stirred at 25 °C for 60 min. After being diluted with water (20 mL), the reaction mixture was extracted with a mixture of benzene and diethyl ether (1:1 v/v, total 60 mL), and the organic layer was washed with water. After the solvent was removed, the resulting mixture was chromatographed on a silica gel plate while eluting with a mixture of benzene and diethyl ether (1:1 v/v) to give 8,10-dimethyl-2,2,4,4-tetraphenyl-8,10-diaza-3-oxaspiro[5.5]undecane-7,9,11-trione (**11**): 99% yield; mp 170–171 °C (from 95% ethanol).

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Supplementary Material Available: Measurements and melting points, spectral data, and analytical data for compounds **3ac**, **3ba-fa**, **3ha-ja**, **9**, **10**, and **11**, the H,C-COSY spectrum of **3ga**, and a scheme for the mechanisms of the formation of **4**, **6**, **7**, and **8** from **3aa** (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(9) Biolgical activity tests were carried out at Agricultural Science Research Laboratory, Sumitomo Chemical Co. Ltd., Takarazuka, Hyogo 665, Japan.

(10) Andrulis, P. J., Jr.; Dewar, M. J. S.; Dietz, R.; Hunt, R. L. *J. Am. Chem. Soc.* **1966**, *88*, 5473.