SELECTIVE SYNTHESIS OF TRIOXAPROPELLANES USING MANGANESE(III) ACETATE

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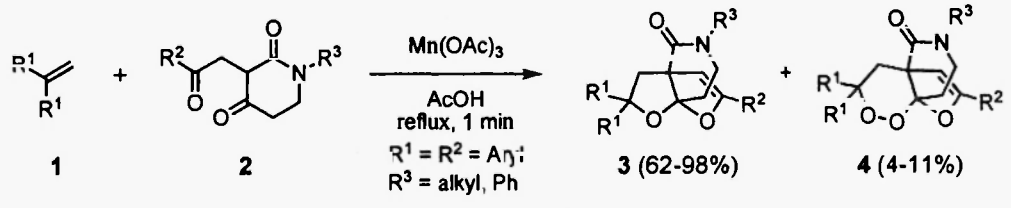
Abstract : The aerobic oxidation of 2-oxoethyl-substituted cyclic 1,3-dicarbonyl compounds **2**, **6**, **8** with diarylethenes **1** was carried out in the presence of a catalytic amount of manganese(III) acetate to produce the structurally unique trioxa[4.4.3]propellanes **4**, **7**, **9**, selectively, in good yields.

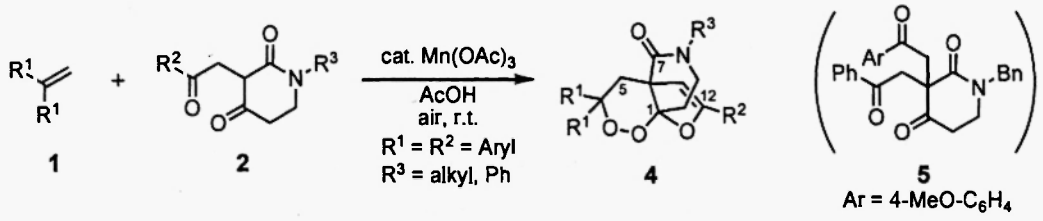
Propellanes containing a tricyclic system connected by a carbon-carbon single bond are found in many different categories of natural products.[1] Some of these propellanes exhibit antibacterial,[2] antibiotic,[3] anticancer,[2b] antifungal,[4] and platelet-activating factor antagonistic activities.[5] Due to not only these biological and pharmacological activities, but also to their challenging molecular framework, many synthetic chemists have investigated the total synthesis of these natural products and their derivatives.[6] Therefore, the synthesis of new propellanes has been gaining attention in terms of generating compounds with new biological activities. Recently, we reported that the oxidation of a mixture of 1,1-diarylethenes **1** and 3-(2-oxoethyl)piperidine-2,4-diones **2** with manganese(III) acetate in acetic acid at reflux temperature gave the azadioxa[4.3.3]propellanes **3** in high yields (Scheme 1).[7] Surprisingly, we found a small amount of the unique azaendoperoxypropellane **4** in the reaction mixture even under reflux reaction conditions.[8] Although the formation of **4** was avoided by removing the dissolved molecular oxygen in the reaction solvent, we were very interested in the endoperoxypropellanes **4** as an attractive synthetic target since the endoperoxide skeleton is found in metabolites and biologically active substances, for example, naturally occurring artemisinin, which is a well-known potent antimalarial agent.[9] In addition, a wide variety of natural nitrogen-containing propellanes has also been isolated and synthesized.[10] Therefore, we focused on the selective synthesis of trioxapropellanes, especially the azatrioxapropellanes.[11]



Scheme-1

First, we adopted the usual aerobic oxidation conditions[8] for the reaction of ethene **1** (R^1 = Ph) with 3-(2-oxoethyl)piperidine-2,4-dione **2** (R^2 = Ph, R^3 = Et). After chromatographic separation, the desired azatrioxa[4.4.3]propellane **4** was isolated in 47% yield (Scheme 2). However, a ring-opened hydroperoxide intermediate was also formed (19%). Therefore, to convert the hydroperoxide into **4**, the reaction mixture was heated at 100 °C for 30 min after the aerobic oxidation, giving only **4** in 66% yield (Table 1, entry 1).[12] A similar reaction of other combinations of the 1,1-diarylethenes **1** (R^1 = Ph, 4-Me-C_6H_4, 4-MeO-C_6H_4, 4-Cl-C_6H_4, and 4-F-C_6H_4) with the 3-(2-oxoethyl)piperidine-2,4-diones **2** (R^2 = Ph, 4-Me-C_6H_4, and 4-Cl-C_6H_4; R^3 = Bn, Me, Et, Pr, *i*-Pr, and Ph) was investigated and the corresponding azatrioxa[4.4.3]propellanes **4** were selectively produced in moderate to good yields except for entry 4 (Table 1). For the reaction of the alkene **1** having a 4-methoxyphenyl group at R^1, 3,3-bis(2-oxoethyl)piperidine-2,4-dione **5** (83%) was mainly isolated rather than **4** (11%) after the work-up (Scheme 2). It was considered that the cyclic peroxide **4** bearing the electron-donating group would be sensitive to the acidic solvent during heating, and therefore, easily rearranged to give the thermodynamically stable **5** and the corresponding

phenol.[8c 13] This problem was avoided by the reaction which was carried out at room temperature in air until the alkene **1** (R^1 = 4-MeO-C_6H_4) was completely consumed followed by rapid quenching with water (entry 4).



Scheme-2

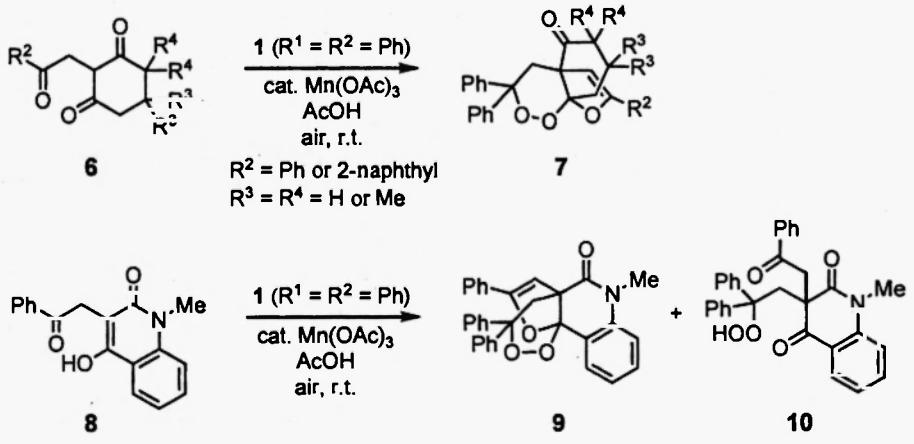
Table-1. Reaction of 1,1-Diarylethenes **1** with 3-(2-Oxoethyl)piperidine-2,4-diones **2** in the Presence of Manganese(III) Acetate[a]

Entry	1	2		1:2:Mn(III)[b]	4
	R^1	R^2	R^3		(%)[c]
1	Ph	Ph	Et	1:2:1	66
2	Ph	Ph	Bn	1:1.5:0.8	67
3	4-Me-C_6H_4	Ph	Bn	1:1.6:0.7	63
4[d]	4-MeO-C_6H_4	Ph	Bn	1:1.6:0.7	53[e]
5	4-Cl-C_6H_4	Ph	Bn	1:1.6:0.7	67
6	4-F-C_6H_4	Ph	Bn	1:1.4:0.7	58
7	Ph	4-Me-C_6H_4	Bn	1:2:0.7	68
8	Ph	4-Cl-C_6H_4	Bn	1:2:0.7	75
9	Ph	Ph	Me	1:2:1	58
10	Ph	Ph	Pr	1:2:1	67
11	Ph	Ph	*i*-Pr	1:2:0.8	67
12	Ph	Ph	Ph	1:2:0.7	62

[a] The reaction of **1** (0.25 mmol) with **2** was carried out in glacial acetic acid (10 mL) in air at room temperature for 7 h, and then the reaction mixture was heated at 100 °C for 30 min. [b] Molar ratio. [c] Isolated yield based on the amount of the alkene **1** used. [d] The reaction was carried out in air for 5 h at room temperature until the alkene **1** was completely consumed, followed by rapid quenching with water. [e] The hydroperoxide intermediate (38%) was also isolated.

The obtained azatrioxa[4.4.3]propellanes **4** were characterized by a spectroscopic method and elemental analysis. The ^{1}H NMR spectrum of **4** (R^1 = Ph, R^2 = Ph, R^3 = Bn) showed the presence of two sets of an AB quartet of benzyl protons and H-5 methylene protons at δ4.71 (1H, *d*, *J* = 14.9 Hz), 4.37 (1H, *d*, *J* = 14.9 Hz), 3.86 (1H, *d*, *J* = 14.3 Hz), and 2.69 ppm (1H, *d*, *J* – 14.3 Hz), respectively. One of the H-5 methylene protons (δ 2.69 ppm) seemed to be shielded by the anisotropic effect for the alkenic double bond of the dihydrofuran ring. The most characteristic peak of the sp^2 proton (H-13) appeared at δ 5.13 (1H, s). In the ^{13}C NMR spectrum, the characteristic downfield peak revealed at δ 111.8 ppm was assigned to the C-1 quaternary ketal carbon together with an amide carbonyl carbon (δ 169.3 ppm) and an sp^2 carbon (C-12) attached to the furan oxygen (δ 156.3). The quaternary carbon (C-4) connected to the endoperoxy oxygen and the quaternary carbon (C-6) at the ring junction also appeared at δ 86.0 and δ 54.7 ppm, respectively. In addition, all the peaks in the NMR spectra were correlated by the H-H COSY and H-C COSY spectra. Furthermore, the positive FAB mass spectrum and the elemental analysis agreed with the molecular formula.[14]

As we have established the optimum conditions, we applied the endoperoxypropellane formation to various cycloalkane-1,3-diones **6** and 4-hydroxy-1*H*-quinolin-2-ones **8**. The oxidation of 2-(2-oxo-2-phenylethyl)cyclohexane-1,3-dione (**6**)[15] with 1,1-diphenylethene (**1**) using a catalytic amount of manganese(III) acetate at room temperature gave the corresponding trioxa[4.4.3]propellane **7** (R^2 = Ph, R^3 = R^4 = H) in good yield after stirring for 30 min (Scheme 3 and Table 2, entry 1). In this case, a longer reaction time led to decomposition of the propellane **7** and decreased yield (entry 2). The reactions using other 2-(2-oxoethyl)cycloalkane-1,3-diones **6**[15] were carried out under similar aerobic oxidation conditions that successfully produced the desired propellanes **7** (entries 3-5).[16] For the reaction of 4,4-dimethylcyclohexane-1,3-dione **6** (R^2 = Ph, R^3 = H, R^4 = Me), only a single regioisomer was obtained (entry 4). The use of 2-(2-oxoethyl)cycloheptane-1,3-dione failed to produce the [5.4.3]propellane, and a complex mixture was obtained along with a large amount of the starting ethene **1**.



Scheme-3

Table 2. Reaction of 1,1-Diphenylethene (**1**) with Cycloalkane-1,3-diones **6** and 4-Hydroxy-1*H*-quinolin-2-one **8** in the Presence of Manganese(III) Acetate[a]

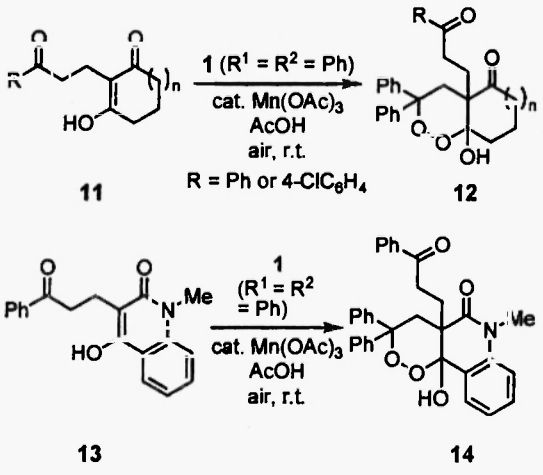
Entry	**6** or **8**	**1**:**6** or **8**:Mn(III)[b]	h	(%)[c]
1	**6**: R^2 = Ph, R^3 = R^4 = H	1:2:0.4	0.5	**7** (83)
2	**6**: R^2 = Ph, R^3 = R^4 = H	1:2:0.4	10	**7** (45)
3	**6**: R^2 = Ph, R^3 = Me, R^4 = H	1:2:0.4	0.5	**7** (75)
4	**6**: R^2 = Ph, R^3 = H, R^4 = Me	1:2:0.4	1.5	**7** (78)[d]
5	**6**: R^2 = 2-Naphthyl, R^3 = R^4 = H	1:2:0.4	1.5	**7** (75)
6	**8**	1:1.8:0.4	4.5	**9** (53) **10** (37)
7[e]	**8**	1:1.8:0.4	4.5	**9** (13) **10** (76)

[a] The reaction of **1** (0.25 mmol) with **6** or **8** was carried out in glacial acetic acid (10 mL) in air at room temperature for the period listed in the table, and then the reaction mixture was heated at 100 °C for 30 min. [b] Molar ratio. [c] Isolated yield based on the amount of the alkene **1** used. [d] A single regioisomer was obtained. [e] The reaction was quenched by adding water after 4.5 h.

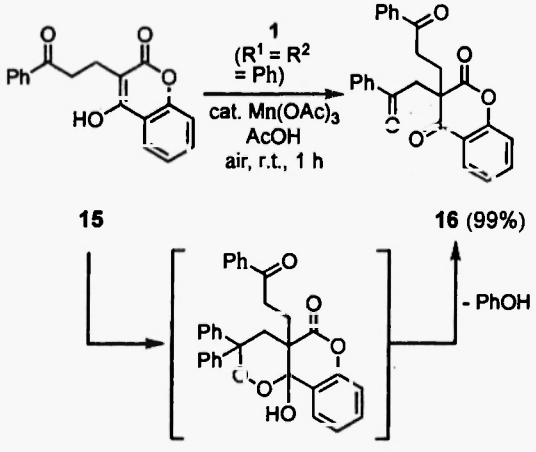
4-Hydroxy-3-(2-oxoethyl)-1*H*-quinolin-2-one **8** gave the azatrioxapropellane **9** together with a considerable amount of the hydroperoxide intermediate **10** (Scheme 3 and Table 2, entry 6).[17,18] When the reaction was quenched by adding water without heating, the hydroperoxide intermediate **10** was isolated in 76% yield (entry 7). The isolation of the stable hydroperoxide intermediate **10** could be explained by our previous studies.[8a,19] A similar reaction using quinolinone derivatives having no substituent at the 3 position yielded the stable 3,3-bis(2-hydroperoxyethyl)-1*H*-quinolin-2,4-diones.[8a] Barbituric acids and pyrazolidine-3,5-diones also provided the stable 5,5-bis(2-hydroperoxyethyl)barbituric acids[19a] and 4,4-bis(2-hydroperoxyethyl)pyrazolizine-3,5-diones,[19b,c] respectively. The unusual stability of the hydroperoxy group turned out to be the intramolecular hydrogen-bonding between the hydroperoxy group and the carbonyl oxygen based on the X-ray crystallographic analysis.[8a,19] In fact, the

absorption band of the amide carbonyl group of **10** appeared in an extremely low wavenumber (1636 cm^{-1}) in the IR spectrum.

A similar reaction of the 3-oxopropyl substituted cycloalkanediones **11** and quinolinone **13** was next investigated.[20] However, the oxopropylderivatives **11** and **13** failed to give any of the desired propellanes, only the intermediate 1,2-dioxan-3-ols **12** and **14**, respectively, in quantitative yields (Scheme 4, Table 3).[21,22] In order to convert **12** into the corresponding propellanes, the intermediates **12** were treated in acetic acid in the presence of manganese(II) acetate under various reaction conditions. However, the reaction became messy and the corresponding propellanes were not detected. The adoption of the 3-(4-chlorophenyl)-3-oxopropyl substituent in **11** had little influence on the reaction (entry 3). In marked contrast to these oxidations, 3-(3-oxopropyl)coumarin **15** quantitatively produced 3-(2-oxoethyl)-3-(3-oxopropyl)chroman-2,4-dione **16** (99%) after a 1-h stirring along with generating of phenol under similar conditions (Scheme 5).[8c,13,23,24]



Scheme-4



Scheme-5

Table 3. Reaction of 1,1-Diphenylethene (**1**) with Cycloalkane-1,3-diones **11** and 4-Hydroxy-1*H*-quinolin-2-one **13** in the Presence of Manganese(III) Acetate[a]

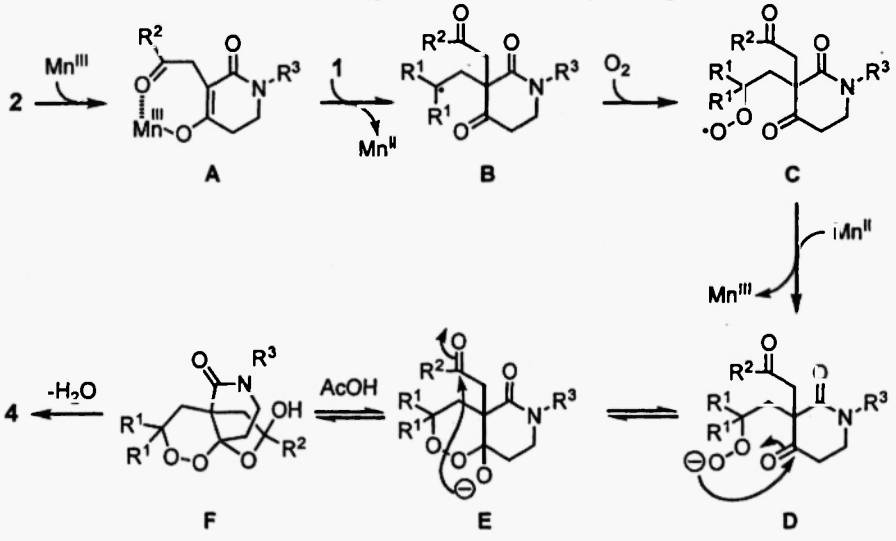
Entry	**11** or **13**	n	**1**:**11** or **13**:Mn(III)[b]	h	(%)[c]
1	**11**: R = Ph	0	1:2:0.5	1	**12** (94)
2	**11**: R = Ph	1	1:2:0.4	2	**12** (99)
3	**11**: R = 4-ClC_6H_4	1	1:2:0.4	3.5	**12** (98)
4	**13**	-	1:2:0.5	1	**14** (96)

[a] The reaction of **1** (0.25 mmol) with **11** or **13** was carried out in glacial acetic acid (10 mL) in air at room temperature for the period listed in the table, and then the reaction mixture was rapidely quenched with water. [b] Molar ratio. [c] Isolated yield based on the amount of the alkene **1** used.

We believe that the mechanism of these trioxapropellanes involves the initial formation of a manganese(III)-enolate complex **A** by ligand exchange of the cyclic triketones such as **2**, followed by electron transfer from the electron-rich aikene **1** to the manganese(III)–enolate complex to produce the carbon radical **B** (Scheme 6).[25] Trapping with the triplet molecular oxygen produced the peroxy radical **C**, which would be reduced by manganese(II) species in the reaction mixture to produce the peroxy anion **D**.[8b,c] Cyclization at the most favorable position of the carbonyl results in the equilibration of the endoperoxide anion **E**. Subsequent attack of the anion **E** on the terminal carbonyl gives the propellane **4** via dehydration.

In summary, we have accomplished the selective synthesis of the azatrioxa- **4**, **9**, and trioxa-[4.4.3]propellanes **7** by the manganese(III)-catalyzed autoxidation of the 1,1-diarylethenes with cyclic 1,3-dicarbonyl compounds having an oxoethyl substituent. The reaction is very simple and convenient, and done under mild reaction conditions.

Oxopropylsubstituted diketones did not afford the propellanes, but rather the dioxabicyclic intermediates. Conversion of the dioxabicyclic intermediates into the trioxa[4.4.4]propellanes is currently in progress.



Scheme-5

Acknowledgments

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References

1. A. J. Pihko and A. M. P. Koskinen, *Tetrahedron*, **61**, 8769-8807 (2005).
2. (a) J. J. Dugan, P. de Mayo, M. Nisbet, J. R. Robinson, and M. J. Anchel, *J. Am. Chem. Soc.*, **88**, 2838-2844 (1966). (b) M. Konishi, H. Ohkuma, T. Tsuno, and T. Oki, *J. Am. Chem. Soc.*, **112**, 3715-3716 (1990). (c) E. Haslam, *Shikimic Acid Metabolism and Metabolites*, John Wiley & Sons, New York, (1993).
3. G. A. Ellestad, M. P. Kunstmann, H. A. Whaley, and E. L. Patterson, *J. Am. Chem. Soc.*, **90**, 1325-1332 (1968).
4. J. Qian-Cutrone, Q. Gao, S. Huang, S. E. Klohr, and J. A. Veitch, Y.-Z. Shu, *J. Nat. Prod.*, **57**, 1656-1660 (1994).
5. (a) K. Okabe, K. Yamada, D. Yamamura, and S. Takeda, *J. Chem. Soc. C*, 1967, 2201-2206. (b) K. Nakanishi, *Pure Appl. Chem.*, **14**, 89-113 (1967).
6. (a) W. J. Greenlee and R. B. Woodward, *J. Am. Chem. Soc.*, 98, 6075-6076 (1976). (b) R. K. Boeckman and S. S. Ko, *J. Am. Chem. Soc.*, **102**, 7146-7149 (1980). (c) A. Ichihara, M. Ubukata, H. Oikawa, K. Murakami, and S. Sakamura, *Tetrahedron Lett.*, **21**, 4469-4472 (1980). (d) J. Taunton, J. L. Wood, and S. L. Schreiber, *J. Am. Chem. Soc.*, **115**, 10378-10379 (1993). (e) A. G. Myers, N. J. Tom, M. E. Fraley, S. B. Cohen, and D. J. Madar, *J. Am. Chem. Soc.*, **119**, 6072-6094 (1997). (f) M. D. Shair, T. Y. Yoon, K. K. Mosny, T. C. Chou, and S. J. Danishefsky, *J. Am. Chem. Soc.*, **118**, 9509-9525 (1996). (g) M. Uchiyama, Y. Kimura, and A. Ohta, *Tetrahedron Lett.*, **41**, 10013-10017 (2000). (h) E. J. Corey, M. Kang, M. C. Desai, A. K. Ghosh, and I. N. Houpis, *J. Am. Chem. Soc.*, **110**, 649-651 (1988). (i) M. T. Crimmins, J. M. Pace, P. G. Nantermet, A. S. Kim-Meade, J. B. Thomas, S. H. Watterson, and A. S. Wagman, *J. Am. Chem. Soc.*, **122**, 8453-8463 (2000).
7. K. Asahi and H. Nishino, *Tetrahedron Lett.*, **47**, 7259-7262 (2006).
8. (a) R. Kumabe and H. Nishino, *Tetrahedron Lett.*, **45**, 703-706 (2004). (b) K. Asahi and H.Nishino, *Heterocycl. Commun.*, **11**, 379-384 (2005). (c) K. Asahi and H. Nishino, *Tetrahedron*, **61**, 11107-11124 (2005).
9. (a) A. Rabert, O. Dechy-Cabaret, J. Cazelles, and B. Meunier, *Acc. Chem. Res.*, **35**, 167-174 (2002). (b) G. H. Posner and P. M. O'Neill, *Acc. Chem. Res.*, **37**, 397-404 (2004).
10. (a) A. Walser and C. Djerassi, *Helv. Chim. Acta*, **48**, 391-404 (1965). (b) K. Awang, T. Sevenet, A. H. A. Hadi, B. David, and M. Païs, *Tetrahedron Lett.*, **33**, 2493-2496 (1992). (c) K. Wiesner, I. Jirkowsky, M. Fishman, and C. A. J. Williams, *Tetrahedron Lett.*, **8**, 1523-1526 (1967). (d) T. Ibuka, K. Tanaka, and Y. Inubushi, *Tetrahedron Lett.*, **13**, 1393-1396 (1972). (e) M. Kurosu, L. R. Marcin, T. J. Grinsteiner, and Y. Kishi, *J. Am. Chem. Soc.*, **120**, 6627-6628 (1998).
11. H. Nishino, *Manganese(III)-Based Peroxidaton of Alkenes to Heterocycles* in S. Eguchi (Ed.), *Bioactive Heterocycles I*, Springer, Berlin, pp 39-76 (2006).
12. The typical aerobic oxidation was as follows. To a mixture of alkene **1** (0.25 mmol) and piperidinedione **2** (0.5 mmol) in glacial acetic acid (10 mL) was added manganese(III) acetate dihydrate (0.17-0.25 mmol). The mixture was stirred at room temperature in air until the alkene **1** was consumed (normally for 7 h), and then heated at 100 °C for 30 min. The solvent was removed *in vacuo*, and the residue was triturated with water followed by extraction with chloroform (10 mL x 3). The combined extract was dried over anhydrous magnesium sulfate, and then concentrated to dryness. The obtained endoperoxypropellane **4** was purified by TLC while eluting with chloroform.
13. C.-Y. Qian, J. Hirose, H. Nishino, and K. Kurosawa, *J. Heterocycl. Chem.*, **31**, 1219-1227 (1994).

14. 8-Benzyl-4,4,12-triphenyl-8-aza-2,3,11-trioxatricyclo[4.4.3.$0^{1,6}$]tridec-12-en-7-one (**4**: R^1 = R^2 = Ph, R^3 = Bn): R_f = 0.32 (chloroform); colorless microcrystals (from diethyl ether); mp 166.5 °C; IR (neat) ν 1639 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (1H, m, arom. H), 7.43-7.12 (18H, m, arom. H), 5.13 (1H, s, H-13), 4.71 (1H, d, J = 14.9 Hz, Ph-CH_2), 4.37 (1H, d, J = 14.9 Hz, Ph-CH_2), 3.86 (1H, d, J = 14.3 Hz, H-5), 3.38 (1H, ddd, J = 12.7, 11.8, 2.8 Hz, H-9), 3.11 (1H, ddd, J = 12.7, 4.6, 3.5 Hz, H-9), 2.69 (1H, d, J = 14.3 Hz, H-5), 2.23 (1H, ddd, J = 13.6, 3.5, 2.8 Hz, H-10), 1.95 (1H, ddd, J = 13.6, 11.8, 4.6 Hz, H-10); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3 (C=O), 156.3 (C-12), 146.8, 143.7, 136.3, 129.3 (arom. C), 129.1, 128.7, 128.28, 128.0, 127.7, 127.6, 127.1, 127.0, 125.42, 125.35, 125.2 (arom. CH), 111.8 (C-1), 100.5 and 100.4 (C-13), 86.0 (C-7), 54.7 (C-6), 50.6 (Ph-CH_2), 41.4 (C-9), 37.1 (C-5), 27.9 (C-10). Positive FAB MS (acetone-NBA) *m/z* 516 (M+1). Anal. calcd for $C_{34}H_{29}NO_4$: C, 79.20; H, 5.67; N, 2.72. Found: C, 79.33; H, 5.60; N, 2.74.
15. N. P. Maini and P. M. Sammes, *J. Chem. Soc., Perkin Trans. 1*, **1988**, 161-168.
16. 4,4,12-Triphenyl-2,3,11-trioxatricyclo[4.4.3.$0^{1,6}$]tridec-12-en-7-one (**7**: R^2 = Ph, R^3 = R^4 = H): R_f = 0.62 (chloroform); colorless oil; IR (KBr) ν 1703 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) 7.51-7.09 (15H, m, arom. H), 4.83 (1H, s, H-13), 3.46 (1H, d, J = 14.1 Hz, H-5), 2.61-2.53 (1H, m, H-10), 2.53 (1H, d, J = 14.1 Hz, H-5), 2.34-2.22 (2H, m, H-8, H-10), 1.90-1.83 (2H, m, H-9), 1.75 (1H, ddd, J = 13.4, 11.9, 4.4 Hz, H-8); ^{13}C NMR (75 MHz, $CDCl_3$) 207.7 (C=O), 156.7 (C-12), 146.9, 143.8 (2C, arom. C), 130.0 (2C, arom. CH), 129.3 (arom. C), 129.1, 128.3, 128.23, 128.20, 128.15, 127.9, 127.7, 127.1, 126.9, 125.4, 125.3, 125.2, 125.1 (13C, arom. CH), 113.7 (C-1), 98.6, 98.5 (1C, C-13), 85.8 (C-4), 59.8 (C-6), 36.4 (C-10), 35.9 (C-5), 28.2 (C-8), 16.3 (C-9). FAB HRMS (acetone-NBA) calcd for $C_{28}H_{25}O_4$ 425.1753 (M+1). Found 425.1784.
17. 8-Methyl-4,4,12-triphenyl-8-aza-2,3,11-trioxa-9,10-benzotricyclo[4.4.3.$0^{1,6}$]tridec-13-en-7-one (**9**): R_f = 0.38 (chloroform); colorless microcrystals (from diethyl ether/hexane); mp 174-175 °C; IR (KBr) 1666 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) 7.85-7.78 (2H, m, arom. H), 7.47-7.12 (15H, m, arom. H), 7.00-6.97 (2H, m, arom. H), 5.29 (1H, s, H-13), 3.61 (1H, d, J = 13.9 Hz, H-5), 3.32 (3H, s, N-CH_3), 2.81 (1H, d, J = 13.9 Hz, H-5); ^{13}C NMR (75 MHz, $CDCl_3$) 168.1 (C=O), 155.4 (C-12), 146.2, 143.5, 137.4 (3C, arom. C), 132.4, 131.7, 130.0 (arom. CH), 129.09 (arom. C), 129.06, 128.3, 128.2, 128.1, 127.1, 125.5, 125.4, 125.2, 123.8 (arom. CH), 117.6 (arom. C), 114.5 (arom. CH), 108.7 (C-1), 99.3 (C-13), 85.6 (C-4), 54.2 (C-6), 37.7 (C-5), 29.7 (N-CH_3). Anal. calcd for $C_{32}H_{25}NO_4$: C, 78.83; H, 5.17; N, 2.87. Found: C, 78.83; H, 5.20; N, 2.85.
18. 3-(2-Hydroperoxy-2,2-diphenylethyl)-1-methyl-3-(2-oxo-2-phenylethyl)-1*H*-quinoline-2,4-dione (**10**): R_f = 0.13 (chloroform); colorless microcrystals (from ethyl acetate/hexane); mp 174-175 °C; IR (KBr) 3500-3150 (OOH), 1682, 1636 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) 8.91 (1H, br. s, OOH), 7.85-7.83 (2H, m, arom. H), 7.59-6.90 (17H, m, arom. H), 4.24 (2H, s, CH_2), 3.58 (1H, d, J = 14.5 Hz, Bz-CH_2), 3.49 (1H, d, J = 14.5 Hz, Bz-CH_2), 3.26 (3H, s, N-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 197.6, 196.9, 174.5 (3C, C=O), 142.8, 141.7 (3C, arom. C), 135.4 (arom. CH), 135.2 (arom. C), 133.7, 130.8, 128.6, 128.4, 128.34, 128.28, 128.0, 127.6, 127.3, 127.2, 127.1, 125.8, 125.7, 125.5, 125.4, 123.6, 122.6 (arom. CH), 121.7 (arom. C), 114.6 (arom. CH), 86.5 (Ph_2>C), 55.0 (CH_2), 53.2 (C-3), 46.1 (Bz-CH_2), 29.9 (N-CH_3). Anal. calcd for $C_{32}H_{27}NO_5$: C, 76.02; H, 5.38; N, 2.77. Found: C, 76.04; H, 5.26; N, 2.83.
19. (a) C.-Y. Qian, H. Nishino, K. Kurosawa, and J. D. Korp, *J. Org. Chem.*, **58**, 4448-4451 (1993). (b) M. T. Rahman and H. Nishino, *Tetrahedron Lett.*, **44**, 5225-5228 (2003). (c) M. T. Rahman and H. Nishino, *Tetrahedron*, **59**, 8383-8392 (2003).
20. (a) S. Miyano, D.-L. L. Lu, M. S. Viti, and K. B. Sharpless, *J. Org. Chem.*, **50**, 4350-4360 (1985). (b) J.-C. Zhou and K. Schenk, *Helv. Chim. Acta*, **85**, 1276-1283 (2002).
21. 1-Hydroxy-6-(3-oxo-3-phenylpropyl)-4,4-diphenyl-2,3-dioxabicyclo[4.3.0]nonan-7-one (**12**: R = Ph, n = 0): R_f = 0.31 (chloroform-methanol 98:2 v/v); colorless microcrystals (from ethyl acetate); mp 137 °C; IR (KBr) 3600-3100 (OH), 1738, 1686 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) 7.95-7.92 (2H, m, arom. H), 7.53-7.16 (13H, m, arom. H), 4.79 (1H, br. s, OH), 3.34 (1H, d, J = 13.9 Hz, H-5), 3.18-3.05 (2H, m, Bz-CH_2CH_2), 2.40 (1H, d, J = 13.9 Hz, H-5), 2.32-1.67 (6H, m, H-8, H-9, Bz-CH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) 215.4, 199.7 (2C, C=O), 144.0, 140.0, 136.4 (3C, arom. C), 133.2, 128.5, 128.3, 128.1, 127.7, 127.6, 127.3, 127.1, 125.3 (15C, arom. CH), 106.4 (C-1), 85.1 (C-4), 50.7 (C-6), 35.2, 34.7, 31.7, 29.7, 28.2 (5C, C-5, C-8, C-9, Bz-CH_2CH_2). Anal. calcd for $C_{28}H_{26}O_5$: C, 76.00; H, 5.92. Found: C, 76.20; H, 6.03.
22. 4a-Hydroxy-9-methyl-10a-(3-oxo-3-phenylpropyl)-2,2-diphenyl-1,4a,9,10a-tetrahydro-2*H*-3,4-dioxa-9-azaphenanthren-10-one (**14**): R_f = 0.44 (chloroform-methanol 98:2 v/v); colorless microcrystals (from methanol); mp 161-164 °C; IR 3500-3000 (OH), 1686, 1651 (C=O); ^{1}H NMR (300 MHz, DMSO-d_6) 7.86-6.97 (19H, m, arom. H), 3.75 (1H, d, J = 13.4 Hz, H-1), 3.35 (1H, br. s, OH), 2.97-2.82 (2H, m, Bz-CH_2CH_2), 2.78 (1H, d, J = 13.4 Hz, H-1), 2.67 (3H, s, N-CH_3), 2.02-1.92 (1H, m, Bz-CH_2CH_2), 1.83-1.74 (1H, m, Bz-CH_2CH_2); ^{13}C NMR (75 MHz, DMSO-d_6) 198.9, 168.5 (2C, C=O), 144.6, 141.8, 138.5, 136.4 (4C, arom. C), 133.0, 130.9, 128.5, 128.1, 127.53, 127.45, 127.2, 126.6, 126.5, 125.9, 125.6, 122.6 (12C, arom. CH), 122.3 (arom. C), 114.1 (arom. CH), 97.8 (C-4a), 84.5 (C-2), 46.5 (C-10a), 35.1 (C-1), 32.4 (Bz-CH_2CH_2), 29.3 (Bz-CH_2CH_2), 29.2 (N-CH_3). Anal. calcd for $C_{33}H_{29}NO_5 \cdot 2/5H_2O$: C, 75.26; H, 5.66; N, 2.66. Found: C, 75.54; H, 5.72; N, 2.63.
23. (a) C.-Y. Qian, H. Nishino, and K. Kurosawa, *Bull. Chem. Soc. Jpn.*, **64**, 3557-3564 (1991). (b) C.-Y. Qian, T. Yamada, H. Nishino, and K. Kurosawa, *Bull. Chem. Soc. Jpn.*, **65**, 1371-1378 (1992). (c) V.-H. Nguyen, H. Nishino, and K. Kurosawa, *Tetrahedron Lett.*, **38**, 1773-1776 (1997). (d) V.-H. Nguyen, H. Nishino, and K. Kurosawa, *Heterocycles*, **48**, 465-480 (1998). (e) F. A. Chowdhury, H. Nishino, and K. Kurosawa, *Heterocycles*, **51**, 575-591 (1999).
24. 3-(2-Oxo-2-phenylethyl)-3-(3-oxo-3-phenylpropyl)chroman-2,4-dione (**16**): R_f = 0.56 (chloroform-methanol 98:2 v/v); colorless oil; IR (KBr) 1767, 1686 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$) 7.97-7.26 (14H, m, arom. H), 4.23 (1H, d, J = 17.8 Hz, Bz-CH_2), 4.05 (1H, d, J = 17.8 Hz, Bz-CH_2), 3.19-3.00 (2H, m, Bz-CH_2CH_2), 2.50-2.32 (2H, m, Bz-CH_2CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) 197.2 (2C, C=O), 193.0, 170.5 (2C, C=O), 154.6 (C-6), 136.9 (arom. CH), 136.0 (arom. C), 134.9 (arom. CH), 133.9 (arom. C), 133.3, 128.5, 128.3, 127.8, 127.33, 127.28, 125.0 (arom. CH), 118.1 (arom. C), 117.6 (arom. CH), 56.0 (C-3), 45.7 (Bz-CH_2), 32.8 (Bz-CH_2CH_2), 30.7 (Bz-CH_2CH_2). FAB HRMS (acetone-NBA) calcd for $C_{26}H_{21}O_5$ 413.1386 (M+1). Found 413.1376.
25. (a) B. B. Snider, *Chem. Rev.*, **96**, 339-363 (1996). (b) H. Nishino, V.-H. Nguyen, S. Yoshinaga, and K. Kurosawa, *J. Org. Chem.*, **61**, 8264-8271 (1996).

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