Mn(III)-catalyzed Aerobic Oxidation of 3-Alkyl-4-hydroxy-1*H*-pyrrol-2(5*H*)-ones in the Presence of 1,1-Diarylethenes. Synthesis of Stable 8-Aza-1-hydroxy-2,3-dioxabicyclo[4.3.0]nonan-7-one Framework

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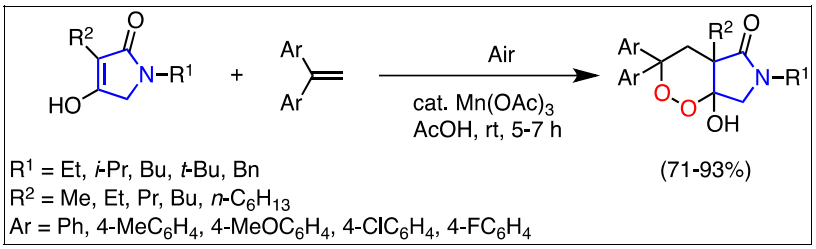

Twenty-two 3-alkyl-4-hydroxy-1*H*-pyrrol-2(5*H*)-ones were prepared and underwent Mn(III)-catalyzed aerobic oxidation in the presence of 1,1-diarylethenes to produce very stable crystalline 6-alkyl-8-aza-4,4-diaryl-1-hydroxy-2,3-dioxabicyclo[4.3.0]nonan-7-ones in high yields.

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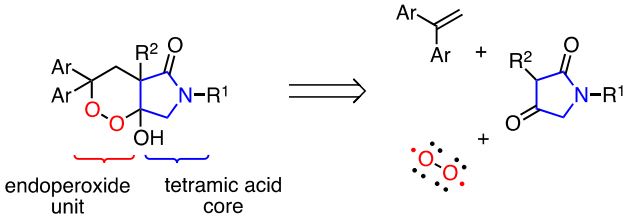
INTRODUCTION

Tetramic acids, that is, pyrrolidine-2,4-diones, are well known as a heterocyclic core of natural products [1–3] that have various biological activities such as antibacterial [4–6] and cytotoxic activities [7], endothelin [8] and glycine site *N*-methyl-D-aspartate receptor antagonists [9]. On the other hand, endoperoxides [10–12] and hydroperoxides [13,14] are an important oxidation intermediate, which also have various biological activities [15]. Therefore, it would be expected that 8-aza-2,3-dioxabicyclo[4.3.0]nonanes that have a fused tetramic acid core and an endoperoxide unit might be a candidate having stronger biological activities (Scheme 1). From this point of view, we reported the synthesis of an 8-aza-2,3-dioxabicyclo[4.3.0]nonane analog using the Mn(III)-based oxidation of 2,3-pyrrolidinedione-4-carboxylates [16] and 2,4-pyrrolidinedione-3-carboxylates [17] with various alkenes. In connection with our study, we found a very stable 8-aza-2,3-dioxabicyclo[4.3.0]nonan-7-one core that was obtained by the Mn(III)-catalyzed aerobic oxidation of 3-alkyl-substituted pyrrolidinediones with 1,1-diarylethenes [18]. In this article, the reaction details, characterization of the products, and reaction mechanism are described.

RESULTS AND DISCUSSION

Twenty-two different pyrrolidine-2,4-diones **1a–v** were synthesized by Dieckmann condensation of the corresponding alkanoyl-protected alkylaminoacetates that were prepared by the reaction of alkylaminoacetates with alkanoyl chlorides [19–25]. The prepared 2,4-pyrrolidinediones **1a–v** existed as an *enol* form, that is, 1,3-dialkyl-4-hydroxy-1*H*-pyrrol-2(5*H*)-ones, in solution [2,13,17]. With the pyrrolidine-2,4-diones in hand, we preliminarily examined the reaction of 1-benzyl-4-hydroxy-3-methyl-3-pyrrolin-2-one (**1a**) with 1,1-diphenylethene (**2a**) in the presence of $Mn(OAc)_3{\cdot}2H_2O$ according to Nguyen's procedure [16]. Surprisingly, the reaction proceeded under catalytic conditions and without a dry air stream, giving a single product. The best conditions were achieved at room temperature in air at the molar ratio of **1a**:**2a**:$Mn(OAc)_3$ = 1:0.5:0.1 (Table 1, entry 1). The crude product was purified by recrystallization from a mixture of ethyl acetate and hexane, giving stable colorless needles that melted at 210°C. The IR spectrum showed a broad absorption band at 3400–3000 cm^{-1} and a strong absorption band at 1656 cm^{-1} assigned to a hydroxyl and an amide carbonyl group, respectively. The ^1H NMR spectrum revealed the characteristic three pairs of geminal AB quartets at δ 4.76 and 3.72 ppm (J = 15.2 Hz), δ 3.55 and 2.29 ppm (J = 14.6 Hz), δ 3.30 and 2.92 ppm (J = 11.3 Hz), which were assigned to benzyl methylenes, dioxane ring methylenes at C-5, and pyrrolinone ring methylenes at C-9, respectively. These methylene protons correlated to the methylene carbons at δ 51.8, 45.4, and 36.6 ppm in the HMQC spectrum. The ^{13}C NMR spectrum revealed three quaternary carbons at δ 102.7 ppm assigned to the C-1 carbon attached to two oxygens, δ 85.7 ppm because of the C-4 carbon bearing one oxygen, and δ 44.7 ppm assigned to the C-6 ring junction. Their spectral data supported a typical *N*-benzyl-protected 1-hydroxy-2,3-dioxabicyclo[4.3.0]nonan-7-one core. Because the combustion analysis was consistent with the formula $C_{26}H_{25}NO_4$, the product was determined to be 8-aza-8-benzyl-1-hydroxy-6-methyl-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (Experimental section). Comparing the

Scheme 1



reaction using 3-methyl-2,4-pyrrolidinedione (**1a**) with that using 2,3-pyrrolidinedione-4-carboxylates [16] and 2,4-pyrrolidinedione-3-carboxylates [17], 3-alkyl-substituted 2,4-pyrrolidinediones such as **1a** must be the best candidate for the construction of the 8-aza-1-hydroxy-2,3-dioxabicyclo [4.3.0]nonan-7-one skeleton because the reaction proceeded in air using a strictly catalytic amount of the $Mn(OAc)_3$, without a dry air stream during the reaction, and the reaction time was quite shorter (only 4 h).

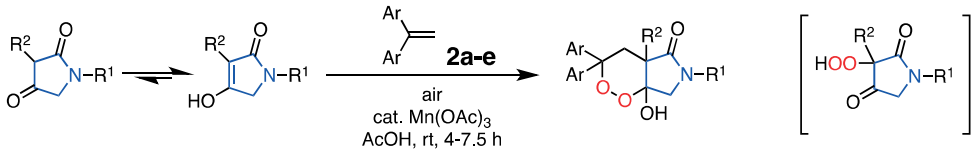
We were pleased to obtain a good result, so that we next investigated a similar aerobic oxidation of various 3-alkyl-2,4-pyrrolidinediones **1b–v** with 1,1-disubstituted ethenes **2a–e**. The reactions were carried out under the optimized conditions for the reaction of **1a** with **2a**. The results are shown in Table 1. All the reaction gave the corresponding 8-aza-1-hydroxy-2,3-dioxabicyclo[4.3.0]nonan-7-ones **3ba–ve** in acceptable yields.

In the case of 1-benzyl-3-propyl- **1c**, 1-*tert*-butyl-3-ethyl- **1o**, 1-*tert*-butyl-3-butyl- **1q**, and 1-*tert*-butyl-3-hexyl-pyrrolidinedione **1r**, 3-hydroperoxypyrrolidinediones **4ca**, **4oa**, **4qa**, and **4ra** were also isolated as a by-product (5–7% yields). In addition, the hydroperoxide **4ca** underwent Baeyer–Villiger rearrangement and recyclization with the release of carbon monoxide to afford 3-benzyl-5-hydroxy-5-propyloxazolidin-4-one [26].

The reaction did not proceed in the absence of $Mn(OAc)_3$ or molecular oxygen but only in the presence of a catalytic amount of $Mn(OAc)_3$ in air, even though the use of 0.03

Table 1

Reaction of 2,4-pyrrolidinediones **1** with alkenes **2** in the presence of $Mn(OAc)_3$.[a]



1a-v **3a-v** **4ca, 4oa, 4qa, 4ra**

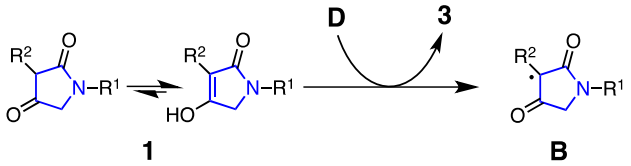
Entry	1		2		1:2:$Mn(OAc)_3$[b]	Time (h)	Product (%)[c]
1	**1a**	: R^1 = Bn, R^2 = Me	**2a**	: Ar = Ph	1:0.5:0.1	4	**3aa** (92)
2	**1b**	: R^1 = Bn, R^2 = Et	**2a**	: Ar = Ph	1:0.5:0.1	5	**3ba** (85)
3	**1c**	: R^1 = Bn, R^2 = Pr	**2a**	: Ar = Ph	1:0.5:0.2	7	**3ca** (89)[d]
4	**1d**	: R^1 = Bn, R^2 = Bu	**2a**	: Ar = Ph	1:0.5:0.1	5	**3da** (84)
5	**1e**	: R^1 = Et, R^2 = Me	**2a**	: Ar = Ph	1:0.5:0.2	6.5	**3ea** (89)
6	**1f**	: R^1 = *i*-Pr, R^2 = Me	**2a**	: Ar = Ph	1:0.5:0.1	7	**3fa** (78)
7	**1g**	: R^1 = *i*-Pr, R^2 = Et	**2a**	: Ar = Ph	1:0.5:0.1	7	**3ga** (81)
8	**1h**	: R^1 = *i*-Pr, R^2 = Pr	**2a**	: Ar = Ph	1:0.5:0.1	7	**3ha** (81)
9	**1i**	: R^1 = *i*-Pr, R^2 = Bu	**2a**	: Ar = Ph	1:0.5:0.1	7.5	**3ia** (77)
10	**1j**	: R^1 = Bu, R^2 = Me	**2a**	: Ar = Ph	1:0.5:0.1	5	**3ja** (91)
11	**1k**	: R^1 = Bu, R^2 = Et	**2a**	: Ar = Ph	1:0.5:0.2	5	**3ka** (88)
12	**1l**	: R^1 = Bu, R^2 = Pr	**2a**	: Ar = Ph	1:0.5:0.1	5.5	**3la** (85)
13	**1m**	: R^1 = Bu, R^2 = Bu	**2a**	: Ar = Ph	1:0.5:0.1	6	**3ma** (79)
14	**1n**	: R^1 = *t*-Bu, R^2 = Me	**2a**	: Ar = Ph	1:0.5:0.1	7.5	**3na** (93)
15	**1o**	: R^1 = *t*-Bu, R^2 = Et	**2a**	: Ar = Ph	1:0.5:0.1	7	**3oa** (76)[d]
16	**1p**	: R^1 = *t*-Bu, R^2 = Pr	**2a**	: Ar = Ph	1:0.5:0.1	5.5	**3pa** (85)
17	**1q**	: R^1 = *t*-Bu, R^2 = Bu	**2a**	: Ar = Ph	1:0.5:0.1	6.5	**3qa** (81)[d]
18	**1r**	: R^1 = *t*-Bu, R^2 = *n*-C_6H_{13}	**2a**	: Ar = Ph	1:0.5:0.1	6.5	**3ra** (78)[d]
19	**1s**	: R^1 = Bn, R^2 = Me	**2b**	: Ar = 4-Me-C_6H_4	1:0.5:0.1	5	**3sb** (85)
20	**1t**	: R^1 = Bn, R^2 = Me	**2c**	: Ar = 4-MeO-C_6H_4	1:0.5:0.1	4	**3tc** (82)
21	**1u**	: R^1 = Bn, R^2 = Me	**2d**	: Ar = 4-Cl-C_6H_4	1:0.5:0.1	4	**3ud** (75)
22	**1v**	: R^1 = Bn, R^2 = Me	**2e**	: Ar = 4-F-C_6H_4	1:0.5:0.1	6	**3ve** (71)

[a]The reaction of pyrrolidinedione **1** (1 mmol) with alkene **2** (0.5 mmol) was carried out in acetic acid (25 mL) at ambient temperature in air.
[b]Molar ratio.
[c]Isolated yield based on the alkene **2** used.
[d]A small amount of the corresponding 3-hydroperoxypyrrolidine-2,4-diones **4** (5–7%) was also isolated.

equivalents of $Mn(OAc)_3$ yielded the dioxabicyclo[4.3.0]nonan-7-ones **3**. Therefore, the mechanism for the formation of **3** would be explained as follows (Scheme 2); Mn(III)-enolate complex **A** produced *in situ* by the reaction of pyrrolidinedione **1** with $Mn(OAc)_3$ [27] underwent single-electron transfer oxidation to give pyrrolidinedione radical **B**. Because the pyrrolidinedione radical **B** is electron-poor, the radical **B** should inevitably be attacked by electron-rich alkene **2** via the electron donor-acceptor-like complex [28–30] to furnish tertiary radical **C**, which is easily trapped by dissolved molecular oxygen, giving peroxy radical **D**. The resulting peroxy radical intermediate **D** is reduced by the Mn(II) species to yield peroxy-Mn(III) complex **E**, which undergoes protonation with acetic acid and regeneration of the Mn(III) species to conclude the catalytic cycle and to provide hydroperoxide **F**. The γ-hydroperoxyketone **F** is then stabilized by cyclization, producing the final hemiacetal **3** [17,31].

The reduction of the peroxy radical **D** with the Mn(II) species deserves comments [32–35]. Although it might be possible to consider a radical-chain mechanism when the peroxy radical **D** directly abstracts hydrogen from pyrrolidinedione **1** to yield the final product **3** and regenerate the pyrrolidinedione radical **B** as shown in Scheme 3, it is obvious that the reaction occurs through the Mn(III)/Mn(II) redox system based on the following experiment. When a mixture of 2,4-pentanedione and $Mn(OAc)_2$ was stirred in AcOH at room temperature under oxygen, the solution turned from colorless to dark brown. This can be interpreted that $Mn(OAc)_2$ undergoes a ligand-exchange reaction with 2,4-pentanedione to afford the corresponding Mn(II)-enolate complex followed by oxidation with dissolved triplet molecular oxygen (biradical), producing the Mn(III) species. To put it the other way around, molecular oxygen should be reduced by the Mn(II) species, and the Mn(III) species could

Scheme 3



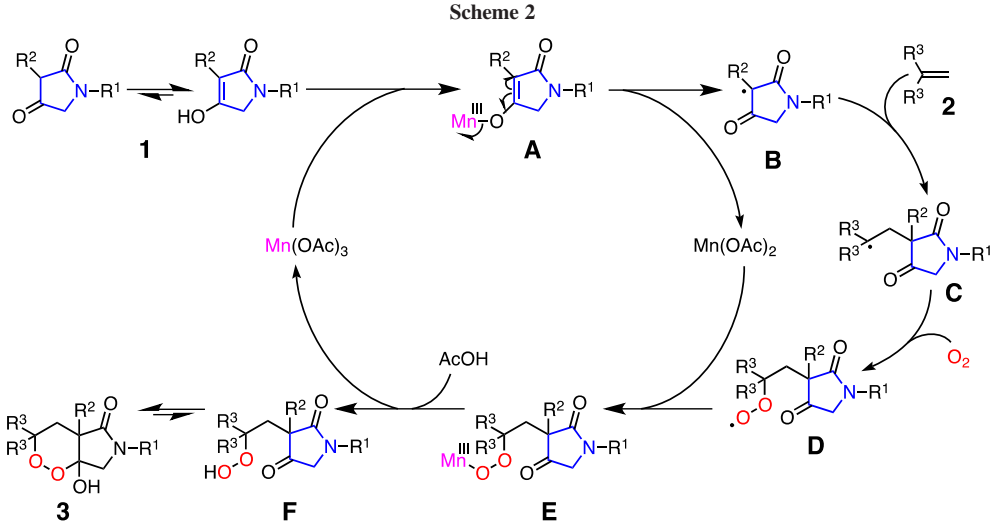
be generated in the solution, that is, the dark-brown color of the solution must be derived from the Mn(III) species. In fact, to the dark-brown colored solution, 1,1-diphenylethene was added, and the mixture was heated under reflux for 1 h to afford 3-acetyl-2-methyl-5,5-diphenyl-4,5-dihydrofuran. This is the well-known Mn(III)-based oxidative dihydrofuranation reaction [36,37]. Therefore, the peroxy radical **D** must be reduced by the Mn(II) species, and the Mn(III) species should be regenerated, and thus, the catalytic cycle is completed as shown in Scheme 2. In addition, it was also reported that the formation of 1,2-dioxan-3-ols could be possible using only $Mn(OAc)_2$ in air [31,38,39].

Isolation of the 3-hydroperoxypyrrolidinediones **4** might support the catalytic cycle in Scheme 2. Probably, the pyrrolidinedione radical **B** was somewhat trapped by dissolved molecular oxygen to afford **4** via a similar reduction pathway of the corresponding hydroperoxy radical with Mn(II) (Table 1, entries 3, 15, 17, and 18) [39,40].

CONCLUSION

Construction of the stable 8-aza-1-hydroxy-2,3-dioxabicyclo[4.3.0]nonan-7-one framework was achieved by the Mn(III)-catalyzed aerobic oxidation of alkyl-substituted tetramic acid derivatives **1** with 1,1-diarylethenes **2**. Because a peroxy bond of the hydroperoxides and endoperoxides

Scheme 2



tends to undergo homolytic cleavage *in vivo*, the 8-aza-1-hydroxy-2,3-dioxabicyclo[4.3.0]nonan-7-ones **3** may also have some biological activities such as antimalarial, insecticidal, bactericidal and cytotoxic activities, and an inhibitory effect toward mRNAs in cells [13,41].

EXPERIMENTAL

Measurements. Melting points were taken using a Yanako MP-J3 micromelting point apparatus and were not corrected. The NMR spectra were recorded using a JEOL JNM AL300 or ECX 500 FT-NMR spectrometer at 300 or 500 MHz for ^{1}H and 75 or 125 MHz for ^{13}C, with tetramethylsilane as the internal standard. The chemical shifts are reported in δ values (ppm) and the coupling constants in Hz. The IR spectra were measured in $CHCl_3$ or KBr using a Shimadzu 8400 FTIR spectrometer and expressed in cm^{-1}. The EI MS spectra were obtained by a Shimadzu QP-5050A gas chromatograph-mass spectrometer at an ionizing voltage of 70 eV. The high-resolution mass spectra and the elemental analysis were performed at the Instrumental Analysis Center, Kumamoto University, Kumamoto, Japan.

Materials. Manganese(II) acetate tetrahydrate, $Mn(OAc)_2{\cdot}4H_2O$, was purchased from Wako Pure Chemical Ind., Ltd. Manganese(III) acetate dihydrate, $Mn(OAc)_3{\cdot}2H_2O$, was prepared according to the method described in the literature [42,43]. 3-Alkyl-4-hydroxy-1*H*-pyrrol-2(5*H*)-ones **1a–v** were prepared by the reaction of the corresponding (alkylamino)acetates with acyl chlorides [13]. The prepared 2,4-pyrrolidinediones **1a–v** exist as an *enol* form (1,3-dialkyl-4-hydroxy-1*H*-pyrrol-2(5*H*)-ones) in an aprotic polar solvent, such as DMSO-d_6 [17].

Reaction of 1,3-dialkyl-4-hydroxy-1H-pyrrol-2(5H)-ones with alkenes in the presence of Mn(OAc)$_3$. To a solution of 1,3-dialkyl-4-hydroxy-1*H*-pyrrol-2(5*H*)-one **1** (1 mmol) and an alkene **2** (0.5 mmol) in glacial acetic acid (25 mL), $Mn(OAc)_3{\cdot}2H_2O$ (0.1 mmol) was added. The mixture was stirred at room temperature in air until the alkene was completely consumed, and then, the reaction was quenched by adding water (25 mL) to the mixture. The resulting aqueous mixture was extracted three times with dichloromethane (30 mL), and the combined extract was washed with water, a saturated aqueous solution of sodium hydrogen carbonate, dried over anhydrous magnesium sulfate, and then concentrated to dryness. The residue was purified by silica gel column chromatography using ethyl acetate and hexane (50:50 v/v), giving 6,8-dialkyl-4,4-diaryl-8-aza-1-hydroxy-2,3-dioxabicyclo[4.3.0] nonan-7-one **3**. The products **3a–v** were further purified by recrystallization from an appropriate solvent to obtain the analytical samples. The physical properties are listed in the following.

8-Aza-8-benzyl-1-hydroxy-6-methyl-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3aa). Yield (190.9 mg, 92%); R_f = 0.68 (EtOAc:hexane = 7:3 v/v); colorless needles (from EtOAc-hexane), mp 210°C; ir (KBr): ν 3400–3100 (OH), 1656 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.67–6.47 (15H, m, arom H), 4.76 (1H, d, *J* = 15.2 Hz, $PhCHH_a$), 3.72 (1H, d, *J* = 15.2 Hz, $PhCHH_b$), 3.66 (1H, s, OH), 3.55 (1H, d, *J* = 14.6 Hz, H_a-5), 3.30 (1H, d, *J* = 11.3 Hz, H_a-9), 2.92 (1H, d, *J* = 11.3 Hz, H_b-9), 2.29 (1H, d, *J* = 14.6 Hz, H_b-5), 1.60 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 174.4 (C═O), 145.1, 140.5, 135.2 (arom C), 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.6 (1C), 127.4 (2C), 127.3 (2C), 127.2 (1C), 124.8 (3C) (arom CH), 102.7 (C-1), 85.7 (C-4), 51.8, 45.4, 36.6 (CH_2), 44.7 (C-6), 22.6 (Me). *Anal.* Calcd for $C_{26}H_{25}NO_4$: C, 75.16; H, 6.06; N, 3.37. Found: C, 75.18; H, 6.12; N, 3.46.

8-Aza-8-benzyl-6-ethyl-1-hydroxy-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3ba). Yield (182.6 mg, 85%); R_f = 0.66 (EtOAc:hexane = 7:3 v/v); colorless needle (from EtOAc/hexane), mp 215–216°C; ir (KBr): ν 3500–3000 (OH), 1662 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.58–7.55 (2H, m, arom H), 7.34–7.07 (11H, m, arom H), 6.43–6.41 (2H, m, arom H), 4.63 (1H, d, *J* = 15.6 Hz, $PhCHH_a$), 3.71 (1H, d, *J* = 15.6 Hz, $PhCHH_b$), 3.44 (1H, d, *J* = 14.1 Hz, H_a-5), 3.40 (1H, s, OH), 3.20 (1H, d, *J* = 11.4 Hz, H_a-9), 2.69 (1H, d, *J* = 11.4 Hz, H_b-9), 2.12 (1H, d, *J* = 14.1 Hz, H_b-5), 1.71–1.56 (2H, m, CH_2), 0.87 (3H, t, *J* = 7.2 Hz, Me); ^{13}C NMR (DMSO-d_6): δ 172.9 (C═O), 145.9, 141.4, 135.9 (arom C), 128.4 (2C), 128.3 (2C), 127.6 (2C), 127.2 (1C), 127.1 (2C), 126.9 (1C), 126.9 (1C), 126.7 (1C), 124.8 (3C) (arom CH), 100.6 (C-1), 84.3 (C-4), 53.1, 44.1, 35.3, 29.7 (CH_2), 47.4 (C-6), 8.4 (Me). *Anal.* Calcd for $C_{27}H_{27}NO_4$: C, 75.50; H, 6.34; N, 3.26. Found: C, 75.50; H, 6.41; N, 3.24.

8-Aza-8-benzyl-1-hydroxy-6-propyl-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3ca). Yield (197.4 mg, 89%); R_f = 0.59 (EtOAc:hexane = 4:6 v/v); colorless needles (from EtOAc/hexane), mp 192°C; ir (KBr): ν 3392 (OH), 1674 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.67–7.64 (2H, m, arom H), 7.39–7.07 (11H, m, arom H), 6.45–6.42 (2H, m, arom H), 4.85 (1H, d, *J* = 15.3 Hz, $PhCHH_a$), 3.69 (1H, s, OH), 3.66 (1H, d, *J* = 15.3 Hz, $PhCHH_b$), 3.57 (1H, d, *J* = 14.7 Hz, H_a-5), 3.24 (1H, d, *J* = 11.4 Hz, H_a-9), 2.88 (1H, d, *J* = 11.4 Hz, H_b-9), 2.22 (1H, d, *J* = 14.7 Hz, H_b-5), 1.69–1.53 (4H, m, 2 × CH_2), 0.90 (3H, t, *J* = 6.9 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 172.3 (C═O), 145.4, 140.5, 135.2 (arom C), 128.6, 128.4, 127.9, 127.5, 127.4, 127.2, 127.2, 124.8 (arom CH), 102.5 (C-1), 85.6 (C-4), 52.7, 45.3, 40.1, 36.2, 16.9 (CH_2), 47.8 (C-6), 14.6 (Me). *Anal.* Calcd for $C_{28}H_{29}NO_4{\cdot}1/11H_2O$: C, 75.54; H, 6.61; N, 3.15. Found: C, 75.28; H, 6.59; N, 3.11.

8-Aza-8-benzyl-6-butyl-1-hydroxy-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3da). Yield (192.2 mg, 84%); R_f = 0.54 (EtOAc:hexane = 4:6 v/v); colorless needles (from Et_2O/hexane), mp 163°C; ir (KBr): ν 3500–3000 (OH), 1668 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.67–7.64 (2H, m, arom H), 7.40–7.06 (11H, m, arom H), 6.44–6.42 (2H, m, arom H), 4.81 (1H, d, *J* = 15.0 Hz, $PhCHH_a$), 4.34 (1H, br. s, OH), 3.67 (1H, d, *J* = 15.0 Hz, $PhCHH_b$), 3.56 (1H, d, *J* = 14.7 Hz, H_a-5), 3.24 (1H, d, *J* = 10.8 Hz, H_a-9), 2.88 (1H, d, *J* = 10.8 Hz, H_b-9), 2.23 (1H, d, *J* = 14.7 Hz, H_b-5), 1.74–1.50(2H, m, CH_2), 1.50–1.18 (4H, m, 2 × CH_2), 0.88 (3H, t, *J* = 7.5 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 1723.6 (C═O), 145.5, 140.6, 135.1 (arom C), 128.6 (2C), 128.3 (4C), 127.9 (2C), 127.5 (1C), 127.4 (1C), 127.2 (1C), 127.1 (1C), 124.9 (3C) (arom CH), 102.3 (C-1), 85.6 (C-4), 52.9, 45.3, 37.6, 36.2, 25.8, 23.3 (CH_2), 47.7 (C-6), 13.9 (Me). *Anal.* Calcd for $C_{29}H_{31}NO_4{\cdot}1/11H_2O$: C, 75.85; H, 6.84; N, 3.05. Found: C, 75.76; H, 6.70; N, 2.99.

8-Aza-8-ethyl-1-hydroxy-6-methyl-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3ea). Yield (157.3 mg, 89%); R_f = 0.54 (EtOAc:hexane = 7:3 v/v); colorless needles (from CH_2Cl_2/hexane), mp 223°C; ir (KBr): ν 3500–3000 (OH), 1668 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.58–7.55 (2H, m, arom H), 7.32–7.14 (8H, m, arom H), 3.70 (1H, br. s, OH), 3.42 (1H, d, *J* = 12.0 Hz, H_a-5), 3.37 (1H, d, *J* = 12.0 Hz, H_a-9), 3.34–3.20 (1H, m, NCHHa), 3.09 (1H, d, *J* = 12.0 Hz, H_b-9), 2.88–2.77 (1H, m, $NCHH_b$), 2.32 (1H, d, *J* = 11.0 Hz, H_b-5), 1.24 (3H, s, Me), 0.66 (3H, t, *J* = 9.0 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 173.7 (C═O), 145.0, 140.7 (arom C), 128.4, 127.7, 127.6, 127.1, 126.9, 124.9 (arom CH), 102.9 (C-1), 85.6 (C-4), 52.3, 36.9, 36.5, (CH_2), 44.7 (C-6), 22.0, 11.6 (Me). *Anal.* Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.08; H, 6.69; N, 3.87.

8-Aza-1-hydroxy-8-(isopropyl)-6-methyl-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (3fa). Yield (143.3 mg, 78%); R_f = 0.60 (EtOAc:hexane = 5:5 v/v); colorless needles (from EtOAc/hexane), mp 222°C; ir (KBr): ν 3500–3000 (OH), 1662 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.28–7.56 (2H, m, arom H), 7.32–7.16 (8H, m, arom H), 4.04 (1H, sep, *J* = 6.9 Hz, CH), 3.41 (1H, d, *J* = 14.7 Hz, H_a-5), 3.33 (1H, d, *J* = 11.1 Hz, H_a-9), 3.05 (1H, d, *J* = 11.1 Hz, H_b-9), 2.29 (1H, d, *J* = 14.7 Hz, H_b-5), 1.72 (1H, s, OH), 1.24 (3H, s, Me), 0.97 (3H, d, *J* = 6.9 Hz, Me), 0.53 (3H, d, *J* = 6.9 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 173.4 (C═O), 144.7, 140.4 (arom C), 128.4, 127.6, 127.5, 127.3, 126.8, 124.9 (arom CH), 102.8 (C-1), 85.6 (C-4), 48.2, 36.7 (CH_2), 44.9 (C-6), 42.0 (CH), 22.1, 19.3, 18.8 (Me). *Anal*. Calcd for $C_{22}H_{25}NO_4$: C, 71.91; H, 6.86; N, 3.81. Found: C, 71.76; H, 6.94; N, 3.75.

8-Aza-6-ethyl-1-hydroxy-8-(isopropyl)-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (3ga). Yield (143.1 mg, 75%); R_f = 0.69 (EtOAc:hexane = 5:5 v/v); colorless blocks (from EtOH/hexane), mp 239°C; ir (KBr): ν 3500–3000 (OH), 1666 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.58–7.55 (2H, m, arom H), 7.27–7.15 (8H, m, arom H), 4.09 (1H, sep, *J* = 6.6 Hz, , CH), 3.91 (1H, br. s, OH), 3.44 (1H, d, *J* = 14.4 Hz, H_a-5), 3.27 (1H, d, *J* = 11.4 Hz, H_a-9), 2.99 (1H, d, *J* = 11.4 Hz, H_b-9), 2.18 (1H, d, *J* = 14.4 Hz, H_b-5), 1.71 (2H, q, *J* = 6.0 Hz, CH_2), 0.98 (3H, t, *J* = 6.0 Hz, Me), 0.94 (3H, d, *J* = 6.6 Hz, Me), 0.49 (3H, d, *J* = 6.6 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 172.1 (C═O), 145.1, 140.4 (arom C), 128.4, 127.5, 127.3, 126.8, 124.9 (arom CH), 102.6 (C-1), 85.6 (C-4), 49.4, 36.3, 30.5 (CH_2), 48.1 (C-6), 41.9 (CH), 19.5, 18.7, 8.6 (Me). *Anal*. Calcd for $C_{23}H_{27}NO_4$: C, 72.42; H, 7.13; N, 3.67. Found: C, 72.29; H, 7.19; N, 3.67.

8-Aza-1-hydroxy-8-(isopropyl)-2,3-dioxa-4,4-diphenyl-6-propylbicyclo[4.3.0]nonan-7-one (3ha). Yield (160.2 mg, 81%); R_f = 0.75 (EtOAc:hexane = 5:5 v/v); colorless blocks (from $CHCl_3$/hexane), mp 209–210°C; ir (KBr): ν 3300–3000 (OH), 1654 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.58–7.55 (2H, m, arom H), 7.33–7.13 (8H, m, arom H), 4.17 (1H, br, OH), 4.09 (1H, sep, *J* = 6.9 Hz, CH), 3.44 (1H, d, *J* = 14.7 Hz, H_a-5), 3.27 (1H, d, *J* = 11.4 Hz, H_a-9), 2.99 (1H, d, *J* = 11.4 Hz, H_b-9), 2.19 (1H, d, *J* = 14.7 Hz, H_b-5), 1.79–1.23 (4H, m, 2 × CH_2), 0.96 (3H, d, *J* = 6.9 Hz, Me), 0.89 (3H, t, *J* = 6.9 Hz, Me), 0.48 (3H, d, *J* = 6.9 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 172.4 (C═O), 145.1, 140.4 (arom C), 128.4, 128.3, 127.5, 127.4, 126.8, 124.9 (arom CH), 102.6 (C-1), 85.6 (C-4), 49.4, 39.9, 36.6, 17.1 (CH_2), 48.0 (C-6), 42.0 (CH), 19.4, 18.6, 14.5 (Me). *Anal*. Calcd for $C_{24}H_{29}NO_4$: C, 72.89; H, 7.39; N, 3.54. Found: C, 72.92; H, 7.46; N, 3.62.

8-Aza-6-butyl-1-hydroxy-8-(isopropyl)-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (3ia). Yield (157.7 mg, 77%); R_f = 0.65 (EtOAc:hexane = 5:5 v/v); colorless needles (from CH_2Cl_2/hexane), mp 209°C; ir (KBr): ν 3500–3000 (OH), 1659 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.58–7.12 (10H, m, arom H), 4.08 (1H, sep, *J* = 6.9 Hz, CH), 3.70 (1H, br. s, OH), 3.45 (1H, d, *J* = 14.4 Hz, H_a-5), 3.28 (1H, d, *J* = 11.4 Hz, H_a-9), 2.99 (1H, d, *J* = 11.4 Hz, H_b-9), 2.18 (1H, d, *J* = 14.4 Hz, H_b-5), 1.65–1.61 (2H, m, CH_2), 1.47–1.22 (4H, m, 2 × CH_2), 0.97 (3H, d, *J* = 6.9 Hz, Me), 0.89 (3H, t, *J* = 7.2 Hz, Me), 0.48 (3H, d, *J* = 6.6 Hz, Me); ^{13}C NMR ($CDCl_3$) δ 172.3 (C═O), 145.1, 140.4 (arom C), 128.4, 127.5, 127.4, 126.8, 124.9 (arom CH), 102.7 (C-1), 85.6 (C-4), 49.2, 37.5, 36.5, 25.8, 23.3 (CH_2), 47.8 (C-6), 41.9 (CH), 19.5, 18.7, 13.9 (Me). *Anal*. Calcd for $C_{25}H_{31}NO_4$: C, 73.32; H, 7.63; N, 3.42. Found: C, 73.42; H, 7.67; N, 3.31.

8-Aza-8-butyl-1-hydroxy-6-methyl-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (3ja). Yield (173.6 mg, 91%); R_f = 0.55 (EtOAc:hexane = 5:5) v/v; colorless microcrystals (from EtOH/hexane), mp 222°C; ir (KBr): ν 3500–3000 (OH), 1664 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.50–7.46 (2H, m, arom H), 7.34–7.08 (8H, m, arom H), 3.49 (1H, br. s, OH), 3.30 (1H, d, *J* = 11.0 Hz, H_a-9), 3.28 (1H, d, *J* = 14.0 Hz, H_a-5), 3.12 (1H, t, *J* = 7.2 Hz, NCHHa), 2.98 (1H, d, *J* = 11.0 Hz, H_b-9), 2.62 (1H, t, *J* = 7.2 Hz, $NCHH_b$), 2.17 (1H, d, *J* = 14.0 Hz, H_b-5), 1.07 (3H, s, Me), 1.03–0.90 (2H, m, CH_2), 0.68–0.63 (2H, m, CH_2), 0.66 (3H, t, *J* = 7.9 Hz, Me); ^{13}C NMR (DMSO-d_6): δ 173.7 (C═O), 145.7, 141.4 (arom C), 128.2, 127.3, 127.3, 126.9, 126.4, 124.9 (arom CH), 102.1 (C-1), 84.3 (C-4), 52.7, 40.3, 35.9, 28.1, 18.6 (CH_2), 44.2 (C-6), 21.9, 13.8 (Me). *Anal*. Calcd for $C_{23}H_{27}NO_4$: C, 72.42; H, 7.13; N, 3.67. Found: C, 72.36; H, 7.18; N, 3.64.

8-Aza-8-butyl-6-ethyl-1-hydroxy-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (3ka). Yield (174.0 mg, 88%); R_f = 0.71 (EtOAc:hexane = 6:4 v/v); colorless needles (from EtOAc/hexane), mp 225°C; ir (KBr): ν 3500–3000 (OH), 1663 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.50–7.09 (10H, m, arom H), 3.40 (1H, s, OH), 3.31 (1H, d, *J* = 14.4 Hz, H_a-5), 3.22 (1H, d, *J* = 11.1 Hz, H_a-9), 3.12 (1H, t, *J* = 6.9 Hz, NCHHa), 2.97 (1H, d, *J* = 11.1 Hz, H_b-9), 2.66 (1H, t, *J* = 6.9 Hz, $NCHH_b$), 2.07 (1H, d, *J* = 14.4 Hz, H_b-5), 1.66–1.49 (2H, m, CH_2), 1.03–0.90 (2H, m, CH_2), 0.83 (3H, t, *J* = 7.5 Hz, Me), 0.65 (3H, br, Me); ^{13}C NMR (DMSO-d_6): δ 172.5 (C═O), 145.9, 141.4 (arom C), 128.2, 127.3, 127.2, 126.9, 126.3, 124.8 (arom CH), 101.9 (C-1), 84.2 (C-4), 53.9, 40.2, 35.4, 29.6, 28.1, 18.6 (CH_2), 47.4 (C-6), 13.7, 8.4 (Me). *Anal*. Calcd for $C_{24}H_{29}NO_4$: C, 72.89; H, 7.39; N, 3.54. Found: C, 72.96; H, 7.53; N, 3.56.

8-Aza-8-butyl-1-hydroxy-2,3-dioxa-4,4-diphenyl-6-propylbicyclo[4.3.0]nonan-7-one (3la). Yield (174.1 mg, 85%); R_f = 0.54 (EtOAc:hexane = 4:6 v/v); colorless needles (from $CHCl_3$/hexane), mp 172°C; ir (KBr): ν 3550–3150 (OH), 1693 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.58–7.56 (2H, m, arom H), 7.42–7.16 (8H, m, arom H), 4.26 (1H, br. s, OH), 3.45 (1H, d, *J* = 14.7 Hz, H_a-5), 3.34 (1H, d, *J* = 11.1 Hz, H_a-9), 3.27 (1H, m, NCHHa), 3.05 (1H, d, *J* = 11.1 Hz, H_b-9), 2.71 (1H, m, $NCHH_b$), 2.19 (1H, d, *J* = 14.7 Hz, H_b-5), 1.62–0.96 (6H, m, 3 × CH_2), 0.87 (3H, t, *J* = 7.2 Hz, Me), 0.79–0.71 (2H, m, CH_2), 0.72 (3H, t, *J* = 7.2 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 173.1 (C═O), 145.4, 140.5 (arom C), 128.3, 127.6, 127.4, 127.2, 126.9, 124.9 (arom CH), 102.5 (C-1), 85.5 (C-4), 53.7, 40.3, 39.9, 36.2, 28.6, 19.2, 16.9 (CH_2), 47.8 (C-6), 14.5, 13.7 (Me). *Anal*. Calcd for $C_{25}H_{31}NO_4$•1/11H_2O: C, 73.03; H, 7.64; N, 3.41. Found: C, 72.84; H, 7.70; N, 3.45.

8-Aza-6,8-dibutyl-1-hydroxy-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (3ma). Yield (163.1 mg, 77%); R_f = 0.74 (EtOAc:hexane = 4:6 v/v); colorless microcrystals (from EtOAc/hexane), mp 185–186°C; ir (KBr): ν 3500–3000 (OH), 1663 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.59–7.56 (2H, m, arom H), 7.29–7.14 (8H, m, arom H), 4.19 (1H, br. s, OH), 3.45 (1H, d, *J* = 14.7 Hz, H_a-5), 3.35 (1H, d, *J* = 11.4 Hz, H_a-9), 3.32–3.25 (1H, m, NCHHa), 3.05 (1H, d, *J* = 11.4 Hz, H_b-9), 2.77–2.68 (1H, m, $NCHH_b$), 2.19 (1H, d, *J* = 14.7 Hz, H_b-5), 1.66–0.94 (8H, m, 4 × CH_2), 0.88 (3H, t, *J* = 6.9 Hz, Me), 1.09–0.68 (2H, m, CH_2), 0.71 (3H, t, *J* = 7.8 Hz, Me); ^{13}C NMR ($CDCl_3$): δ ($CDCl_3$): 173.2 (C═O), 145.4, 140.5 (arom C), 128.4, 127.7, 127.5, 127.3, 126.9, 124.9 (arom CH), 102.6 (C-1), 85.6 (C-4), 53.7, 41.3, 37.5, 36.2, 28.6, 25.8, 23.3, 19.2 (CH_2), 47.7 (C-6), 13.9, 13.8 (Me). *Anal*. Calcd for $C_{27}H_{33}NO_4$•1/2H_2O: C, 72.19; H, 7.92; N, 3.24. Found: C, 72.08; H, 8.20; N, 3.29.

8-Aza-8-(t-butyl)-1-hydroxy-6-methyl-2,3-dioxa-4,4-diphenylbicyclo[4.3.0]nonan-7-one (3na). Yield (177.4 mg, 93%); R_f = 0.32 (EtOAc:hexane = 4:6 v/v); colorless needles (from EtOAc/hexane), mp 222–223°C; ir (KBr): ν 3600–3000 (OH),

1668 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.51–7.50 (2H, m, arom H), 7.48–7.10 (8H, m, arom H), 3.39 (1H, s, OH), 3.37 (1H, d, J = 10.8 Hz, H_a-9), 3.23 (1H, d, J = 14.1 Hz, H_a-5), 3.05 (1H, d, J = 10.8 Hz, H_b-9), 2.14 (1H, d, J = 14.1 Hz, H_b-5), 1.05 (3H, s, Me), 0.94 (9H, s, 3 × Me); ^{13}C NMR (DMSO-d_6): δ 173.5 (C═O), 145.5, 141.3 (arom C), 128.2, 127.2, 127.2, 127.1, 126.2, 124.9 (arom CH), 101.3 (C-1), 84.4 (C-4), 52.7 (quat. C), 51.2, 35.9 (CH_2), 44.8 (C-6), 26.7 (3 × Me), 21.8 (Me). *Anal*. Calcd for $C_{23}H_{27}NO_4$·1/11H_2O: C, 72.11; H, 7.15; N, 3.66. Found: C, 72.05; H, 7.43; N, 3.51.

8-Aza-8-(t-butyl)-6-ethyl-1-hydroxy-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3oa). Yield (150.0 mg, 76%); R_f = 0.43 (EtOAc:hexane = 2:8 v/v); colorless microcrystals (from EtOAc/hexane), mp 254°C; ir (KBr): ν 3300–3050 (OH), 1662 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.48–7.09 (10H, m, arom H), 3.44 (1H, s, OH), 3.29 (1H, d, J = 6.9 Hz, H_a-9), 3.25 (1H, d, J = 8.1 Hz, H_a-5), 3.05 (1H, d, J = 6.9 Hz, H_b-9), 2.03 (1H, d, J = 8.1 Hz, H_b-5), 1.64–1.47 (2H, m, CH_2), 0.95 (9H, s, 3 × Me), 0.85 (3H, t, J = 4.5 Hz, Me); ^{13}C NMR (DMSO-d_6): δ 177.5 (C═O), 150.8, 146.5 (arom C), 133.3, 132.4, 132.3, 131.3, 129.9 (arom CH), 106.1 (C-1), 89.4 (C-4), 58.1 (quat. C), 57.8, 40.9, 34.9 (CH_2), 53.1 (C-6), 31.9 (3 × Me), 13.6 (Me). *Anal*. Calcd for $C_{24}H_{29}NO_4$: C, 72.89; H, 7.39; N, 3.54. Found: C, 72.82; H, 7.42; N, 3.47.

8-Aza-8-(t-butyl)-1-hydroxy-2,3-dioxa-4,4-diphenyl-6-propylbicyclo[4.3.0]nonan-7-one (3pa). Yield (170.0 mg, 85%); R_f = 0.53 (EtOAc:hexane = 3:7 v/v); colorless needles (from EtOH/hexane), mp 253°C; ir (KBr): ν 3600–3100 (OH), 1655 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.48–7.07 (10H, m, arom H), 3.40 (1H, s, OH), 3.29 (1H, d, J = 11.0 Hz, H_a-9), 3.26 (1H, d, J = 14.0 Hz, H_a-5), 3.04 (1H, d, J = 11.0 Hz, H_b-9), 2.04 (1H, d, J = 14.0 Hz, H_b-5), 1.56–1.15 (4H, m, 2 × CH_2), 0.94 (9H, s, 3 × Me), 0.82 (3H, t, J = 7.2 Hz, Me); ^{13}C NMR (DMSO-d_6): δ 172.4 (C═O), 145.7, 141.3 (arom C), 128.2, 127.2, 127.1, 127.1, 126.1, 124.9 (arom CH), 101.0 (C-1), 84.2 (C-4), 52.9 (quat. C), 52.6, 39.3, 35.9, 16.5 (CH_2), 47.8 (C-6), 26.8 (3 × Me), 14.7 (Me). *Anal*. Calcd for $C_{25}H_{31}NO_4$: C, 73.32; H, 7.63; N, 3.42. Found: C, 73.49; H, 7.68; N, 3.41.

8-Aza-6-butyl-8-(t-butyl)-1-hydroxy-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3qa). Yield (171.5 mg, 81%); R_f = 0.70 (EtOAc: hexane = 3:7 v/v); colorless needles (from EtOH/hexane), mp 238°C; ir (KBr): ν 3600–3150 (OH), 1655 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.49–7.10 (10H, m, arom H), 3.38 (1H, s, OH), 3.29 (1H, d, J = 11.0 Hz, H_a-9), 3.26 (1H, d, J = 13.8 Hz, H_a-5), 3.04 (1H, d, J = 11.0 Hz, H_b-9), 2.04 (1H, d, J = 13.8 Hz, H_b-5), 1.60–1.15 (6H, m, 3 × CH_2), 0.94 (9H, s, 3 × Me), 0.84 (3H, t, J = 6.9 Hz, Me); ^{13}C NMR (DMSO-d_6): δ 172.5 (C═O), 145.7, 141.4 (arom C), 128.2, 127.1, 127.1, 126.2, 124.9 (arom CH), 101.1 (C-1), 84.3 (C-4), 52.9 (quat. C), 52.5, 36.7, 35.9, 25.2, 22.8 (CH_2), 47.8 (C-6), 26.8 (3 × Me), 14.8 (Me). *Anal*. Calcd for $C_{26}H_{33}NO_4$·1/2H_2O: C, 72.19; H, 7.92; N, 3.24. Found: C, 72.37; H, 8.01; N, 3.13.

8-Aza-8-(t-butyl)-6-hexyl-1-hydroxy-2,3-dioxa-4,4-diphenylbicyclo [4.3.0]nonan-7-one (3ra). Yield (176.2 mg, 78%); R_f = 0.67 (EtOAc:hexane = 2:8 v/v); colorless needles (from EtOAc/hexane), mp 225°C; ir (KBr): ν 3400–3100 (OH), 1657 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.58–7.56 (2H, m, arom H), 7.21–7.14 (8H, m, arom H), 3.60 (1H, s, OH), 3.41 (1H, d, J = 8.7 Hz, H_a-5), 3.38 (1H, d, J = 6.6 Hz, H_a-9), 3.14 (1H, d, J = 6.6 Hz, H_b-9), 2.12 (1H, d, J = 8.7 Hz, H_b-5), 1.59 (2H, t, J = 4.8 Hz, CH_2), 1.5–1.2 (8H, m, 4 × CH_2), 1.04 (9H, s, 3 × Me), 0.86 (3H, t, J = 4.8 Hz, Me); ^{13}C NMR ($CDCl_3$): δ 172.7 (C═O), 145.1, 140.4 (arom C), 128.4, 127.5, 127.4, 126.7, 124.9 (arom CH), 101.9 (C-1), 85.7 (C-4), 53.9 (quat. C), 52.3, 37.8, 36.3, 31.5, 29.8, 23.4, 22.5 (CH_2), 48.1 (C-6), 27.2 (3 × Me), 14.0 (Me). *Anal*. Calcd for $C_{28}H_{37}NO_4$: C, 74.47; H, 8.26; N, 3.10. Found: C, 74.29; H, 8.30; N, 2.93.

8-Aza-8-benzyl-1-hydroxy-4,4-bis(4-methylphenyl)-6-methyl-2,3-dioxabicyclo[4.3.0]-nonan-7-one (3sb). Yield (181.9 mg, 82%); R_f = 0.50 (EtOAc:hexane = 5:5 v/v); colorless needles (from EtOAc/$CHCl_3$), mp 213–214°C; ir (KBr): ν 3400–3150 (OH), 1656 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.54–7.51 (2H, m, arom H), 7.20–7.08 (7H, m, arom H), 7.05–7.02 (2H, m, arom H), 6.48–6.45 (2H, m, arom H), 4.81 (1H, d, J = 15.0 Hz, $PhCHH_a$), 3.85 (1H, s, OH), 3.68 (1H, d, J = 15.0 Hz, $PhCHH_b$), 3.50 (1H, d, J = 14.4 Hz, H_a-5), 3.30 (1H, d, J = 11.4 Hz, H_a-9), 2.92 (1H, d, J = 11.4 Hz, H_b-9), 2.31 (3H, s, Me), 2.27 (1H, d, J = 14.4 Hz, H_b-5), 2.25 (3H, s, Me), 1.29 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 174.6 (C═O), 142.4, 137.6, 137.3, 136.6, 135.2 (arom C), 129.0 (2C), 128.6 (2C), 128.5 (2C), 127.3 (3C), 127.2 (2C), 124.8 (2C), (arom CH), 102.6 (C-1), 85.6 (C-4), 51.8, 45.3, 36.6 (CH_2), 44.7 (C-6), 22.5, 21.0, 20.9 (Me). *Anal*. Calcd for $C_{28}H_{29}NO_4$: C, 75.82; H, 6.59; N, 3.16. Found: C, 75.69; H, 6.58; N, 3.25.

8-Aza-8-benzyl-1-hydroxy-4,4-bis(4-methoxyphenyl)-6-methyl-2,3-dioxabicyclo[4.3.0]-nonan-7-one (3tc). Yield (194.8 mg, 82%); R_f = 0.55 (EtOAc:hexane = 5:5 v/v); colorless needles (from CH_2Cl_2/hexane), mp 199°C; ir (KBr): ν 3500–3100 (OH), 1668 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.55–7.52 (2H, m, arom H), 7.18–7.10 (5H, m, arom H), 6.93–6.89 (2H, m, arom H), 6.79–6.76 (2H, m, arom H), 60.53–6.50 (2H, m, arom H), 4.81 (1H, d, J = 15.0 Hz, $PhCHH_a$), 3.77 (3H, s, OMe), 3.74 (3H, s, OMe), 3.72 (1H, d, J = 14.7 Hz, H_a-5), 3.61 (1H, s, OH), 3.45 (1H, d, J = 15.0 Hz, $PhCHH_b$), 3.32 (1H, d, J = 11.4 Hz, H_a-9), 2.94 (1H, d, J = 11.4 Hz, H_b-9), 2.27 (1H, d, J = 14.7 Hz, H_b-5), 1.30 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 174.6 (C═O), 158.9, 158.7, 137.5, 135.2, 132.5 (arom C), 128.7 (2C), 128.6 (2C), 127.3 (2C), 127.3 (2C), 126.7 (2C), 113.6 (2C), 113.2 (1C) (arom CH), 102.5 (C-1), 85.5 (C-4), 51.9, 45.5, 36.8 (CH_2), 44.7 (C-6), 55.2, 55.2 (OMe), 22.7 (Me). *Anal*. Calcd for $C_{28}H_{29}NO_6$: C, 70.72; H, 6.15; N, 2.95. Found: C, 70.65; H, 6.14; N, 3.05.

8-Aza-8-benzyl-4,4-bis(4-chlorophenyl)-1-hydroxy-6-methyl-2,3-dioxabicyclo[4.3.0]-nonan-7-one (3ud). Yield (181.6 mg, 75%); R_f = 0.44 (EtOAc:hexane = 5:5 v/v); colorless needles (from EtOAc/hexane), mp 217–218°C; ir (KBr): ν 3600–3000 (OH), 1657 (C═O); ^{1}H NMR ($CDCl_3$): δ 7.57–7.54 (2H, m, arom H), 7.35–7.31 (2H, m, arom H), 7.26–7.14 (7H, m, arom H), 6.51–6.49 (2H, m, arom H), 4.78 (1H, d, J = 15.0 Hz, $PhCHH_a$), 3.82 (1H, s, OH), 3.70 (1H, d, J = 15.0 Hz, $PhCHH_b$), 3.46 (1H, d, J = 14.7 Hz, H_a-5), 3.33 (1H, d, J = 11.4 Hz, H_a-9), 2.95 (1H, d, J = 11.4 Hz, H_b-9), 2.22 (1H, d, J = 14.7 Hz, H_b-5), 1.30 (3H, s, Me); ^{13}C NMR ($CDCl_3$): δ 174.2 (C═O), 142.9, 138.5, 134.9, 133.5, (arom C), 128.9 (2C), 128.7 (2C), 128.7 (2C), 128.3 (2C), 127.6 (1C), 127.3 (2C), 126.3 (2C), (arom CH), 102.6 (C-1), 84.9 (C-4), 51.9, 45.5, 36.3 (CH_2), 44.6 (C-6), 22.6 (Me). *Anal*. Calcd for $C_{26}H_{23}Cl_2NO_4$: C, 64.47; H, 4.79; N, 2.89. Found: C, 64.33; H, 4.78; N, 2.96.

8-Aza-8-benzyl-4,4-bis(4-fluorophenyl)-1-hydroxy-6-methyl-2,3-dioxabicyclo[4.3.0]-nonan-7-one (3ve). Yield (160.3 mg, 71%); R_f = 0.50 (EtOAc:hexane = 5:5 v/v); colorless needles (from CH_2Cl_2/hexane), mp 213°C; ir (KBr): ν 3600–3000 (OH), 1657 (C═O); ^{1}H NMR (DMSO-d_6): δ 7.62–7.58 (2H, m, arom H), 7.61 (1H, s, OH), 7.40–7.35 (2H, m, arom H), 7.23–7.10 (7H, m, arom H), 6.51–6.48 (2H, m, arom H), 4.62 (1H, d, J = 15.3 Hz, $PhCHH_a$), 3.73 (1H, d, J = 15.3 Hz, $PhCHH_b$), 3.41 (1H, d, J = 14.4 Hz, H_a-5), 3.34 (1H, d, J = 11.7 Hz, H_a-9), 2.75 (1H, d, J = 11.7 Hz, H_b-9), 2.22 (1H, d, J = 14.4 Hz, H_b-5), 1.17(3H, s,

Me); ^{13}C NMR (DMSO-d_6): δ 173.9 (C=O), 162.8, 159.6, 141.6, 137.1, 135.9, (arom C), 129.3 (1C), 129.2 (1C), 128.2 (2C), 127.3 (1C), 127.2 (1C), 126.9 (1C), 126.8 (2C), 115.2 (1C), 114.9 (1C), 114.5 (1C), 114.2 (1C) (arom CH), 101.9 (C-1), 83.9 (C-4), 51.9, 44.2, 35.9 (CH_2), 44.1 (C-6), 22.1 (Me). *Anal*. Calcd for $C_{26}H_{23}F_2NO_4 \cdot H_2O$: C, 66.52; H, 5.37; N, 2.98. Found: C, 66.52; H, 5.10; N, 2.97.

Reaction of 2,4-pentanedione with Mn(OAc)$_2$. To a solution of 2,4-pentanedione (12 mmol) and AcOH (20 mL), Mn $(OAc)_2 \cdot 4H_2O$ (2 mmol) was added. The mixture was stirred at room temperature under oxygen (5 atm) using an autoclave, and the color of the solution turned from colorless to dark brown within 48 h. To the dark-brown solution, 1,1-diphenylethene (1 mmol) was added, and then, the mixture was heated under reflux in air for 1 h. After removal of the solvent, the residue was treated with 2 M HCl, and the aqueous solution was extracted with $CHCl_3$. The resulting products were purified by silica gel TLC, giving 3-acetyl-2-methyl-5,5-diphenyl-4,5-dihydrofuran (12,4 mg, 4% yield) [36].

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