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One-pot synthesis of 2-oxa-7-azaspiro[4.4]nonane-8,9-diones using Mn(III)-based oxidation of 4-acylpyrrolidine-2,3-diones

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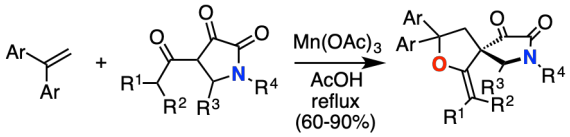
Thanh-Truc Huynh,[a] Van-Ha Nguyen,[b] Hiroshi Nishino[c]*



R^1, R^2 = alkyl and/or H; R^3 = H, Ph; R^4 = Bn, Me

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One-pot synthesis of 2-oxa-7-azaspiro[4.4]nonane-8,9-diones using Mn(III)-based oxidation of 4-acylpyrrolidine-2,3-diones†

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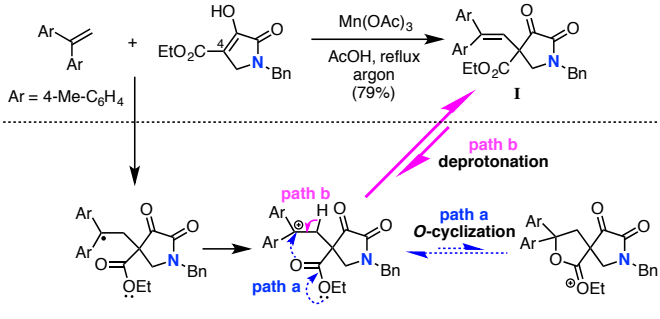
ABSTRACT

2-Oxa-7-azaspiro[4.4]nonane-8,9-diones were newly synthesized in good yields by the Mn(III)-based reaction of a mixture of 1,1-diarylethenes and 4-acylpyrrolidine-2,3-diones. Under the stated reaction conditions, the pyrrolidinedione ring remained intact and became one of the two rings of the 2-oxa-7-azaspiro[4.4]nonanedione scaffold. The procedure was simple and the product was easily separated. The structure determination and the mechanism for the formation of the 2-oxa-7-azaspiro[4.4]nonanediones were also discussed.

1. Introduction

The Mn(III)-based oxidation is a powerful tool in organic synthesis, and new applications and protocols have been continuously reported.[1,2] Tetrahydrofuran derivatives are found in many natural compounds, some of which derived from tetrose, pentose, hexose, and glycoside, have a significant biological importance.[3] Pyrrolidinediones have displayed an interesting biological activity and been used as an inhibitor of aldose reductase[4] and endothelin receptor antagonists.[5] Pyrrolidinediones[6] were also used as a versatile reagent for the preparation of β-lactams.[7] We previously reported a unique synthesis of spirodi-γ-lactones,[8a] spirodioxanes,[8b] trioxaspiro compounds,[8c] dioxatricyclic[8d] and oxa-aza-tricyclic compounds,[8e] spirofurans,[8f] and aza-spiro compounds[8g] using manganese(III) acetate dihydrate, $Mn(OAc)_3 \cdot 2H_2O$. In the course of our study, we found a simple and straightforward route based on the Mn(III) oxidation for the synthesis of new pyrrolidine-2,3-diones **I** with an ethenyl group substituted at the α-position of the carbonyl group (Scheme 1).[9,10] At that time, we anticipated producing a spiro compound (path a), but the deprotonation was fast under the stated conditions (path b). Based on these results, we postulated if the presence of a keto–carbonyl group at the C-4 position of the pyrrolidine-2,3-dione instead of an ester could allow the cyclization to produce a spiro bicyclic compound such as a furan connected through the α-carbon of the pyrrolidinediones. We then attempted to verify this idea using the Mn(III)-based oxidation of 1,1-diarylethenes with 4-acylpyrrolidine-2,3-diones as the starting material. As a result, the cyclization proceeded at the carbonyl oxygen and new 1-exomethylene-2-oxa-7-azaspiro[4.4]nonane-8,9-dione derivatives were produced in good yields as expected.



Scheme 1. Mn(III)-based reaction of alkene with 4-hydroxy-5-oxo-2,5-dihydropyrrole-3-carboxylate

2. Results and discussion

The pyrrolidine-2,3-diones **2a-e**[9,11] were prepared by the condensation of 2,4-dioxoalkanoates[12] with *N*-benzyl or *N*-methylmethanimines.[13] The pyrrolidinediones were purified by silica gel column chromatography, then recrystallization. With the starting material of the pyrrolidinediones **2a-e** in hand, we commenced the Mn(III)-based oxidation in the presence of 1,1-

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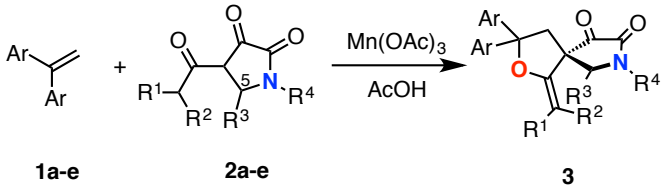
† Dedicated to Dr. Kazu Kurosawa, Professor Emeritus of Kumamoto University, on his 80th birthday



1a-e **2a-e** **3**

Scheme 2. Mn(III)-based reaction of alkenes **1a-e** with 4-acylpyrrolidine-2,3-diones **2a-e**

disubstituted alkenes. 1,1-Bis(4-methylphenyl)ethene (**1a**) and 1-benzyl-4-isobutyrylpyrrolidine-2,3-dione (**2a**) were first selected and the reaction using $Mn(OAc)_3 \bullet 2H_2O$ was carried out in glacial acetic acid at 70 °C. Since the oxidant was consumed in 16 min, the reaction was quenched and the mixture was worked up. Gratifyingly, the desired 2-oxa-7-azaspiro compound **3aa** was obtained in 38% isolated yield (Scheme 2 and Table 1, Entry 1).

When a similar reaction was performed at reflux temperature, the reaction was finished in 2 min and the yield of **3aa** was significantly improved (Entry 2). We then optimized the reaction and the maximum yield of **3aa** was 90% (Entry 4). The structure of **3aa** was determined by IR, ^{1}H NMR, ^{13}C NMR, and ^{13}C DEPT spectra, a 2D NMR study and elemental analysis. The presence of the dimethylmethylene group and C-5 spiro carbon was confirmed by the NMR spectrum, and the HMBC experiment was also in good agreement with the structure of 7-benzyl-3,3-bis(4-methylphenyl)-1-(propan-2-ylidene)-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (Fig. 1).[14]

Having succeeded in the synthesis of the anticipated spiro compound **3aa**, we turned our attention to a similar reaction using the other 1,1-diarylethenes **1b-e**. The reaction was conducted under similar conditions and the corresponding 2-oxa-7-azaspiro[4.4]-nonane-8,9-diones **3ba-ea** were obtained in good yields (Table 1, Entries 5-8). The use of 4-propionylpyrrolidine-2,3-dione **2b** instead of **2a** also gave the 2-oxa-7-azaspiro compound **3ab** in 81% yield (Entry 9). Although the reaction of 5-phenyl-4-propionyl- **2c** and the 4-butyryl-5-phenyl-pyrrolidine-2,3-diones **2d**, both bearing a phenyl group at the C-5 position of the pyrrolidinedione, led to a similar result (Entries 10 and 11), the reaction using 4-isobutyryl-1-methyl-5-phenylpyrrolidine-2,3-dione (**2e**) resulted in the decreased yield of the desired product (Entry 12). However, after a thorough chromatographic separation, 1-hydroxy-1-isopropyl-3,3-bis(4-methylphenyl)-7-methyl-6-phenyl-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (**4**) was also isolated in 22% yield probably due to the addition of water during the reaction (vide infra).[15] The ^{1}H NMR spectrum of the 6-phenyl-2-oxa-7-azaspiro[4.4]nonane-8,9-diones **3ac**, **3ad**, and **3ae** deserves comments.[16-18] The *ortho*-protons of the phenyl group appeared around δ 6.3 as a broad singlet because of the rotational barrier of the phenyl group by the C-1 exomethylene group (Fig. 2). Simultaneously, the H-4 proton (ca. δ 3.4) was deshielded by the ring current effect of one of the C-3 aryl groups. When the NMR spectrum of **3ae** was taken in $CDCl_3$ at 50 °C, the broad peak of the phenyl protons became sharp (See Supplementary data). In addition, the H-10 sp^2 proton (δ 3.37) of **3ac** and **3ad**, and the C-11 methyl group (δ 0.67) of **3ae** were shielded by the anisotropic effect of the C-9 carbonyl group. In the case of the by-product **4**, the anisotropic effect of the C-9 carbonyl group was extremely strong toward one of the methyl groups of the isopropyl group, showing δ 0.00 (3H, d, J = 6.7 Hz) (Fig. 3).[15] Fortunately, we got a single crystal of **3ae** from chloroform and finally established the structure by an X-ray crystallographic measurement (Fig. 4 and supplementary data).[19]

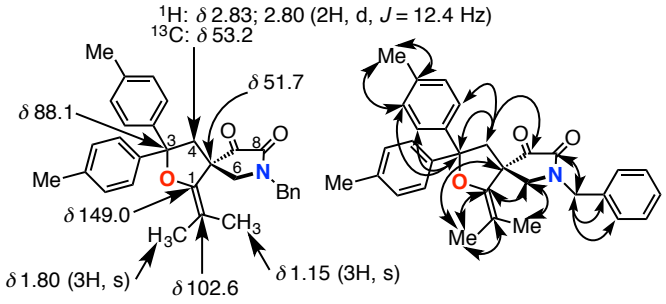


Fig. 1. Important ^{1}H and ^{13}C chemical shifts (left) and HMBC study of **3aa** (right)

Table 1. Mn(III)-based reaction of 1,1-diarylethenes **1a-e** with pyrrolidine-2,3-diones **2a-e**[a]

Entry	Ethene/**1**	Pyrrolidinedione/**2**	**1**:**2**:$Mn(OAc)_3$[b]	Temp/°C	Time/min	**3**/Yield/%[c]
1	**1a**: Ar = 4-Me-C_6H_4	**2a**: R^1 = R^2 = Me, R^3 = H, R^4 = Bn	1:1.5:3	70	16	**3aa** (38)
2	**1a**	**2a**	1:1.5:3	reflux	2	**3aa** (67)
3	**1a**	**2a**	1:2:3	reflux	3	**3aa** (87)
4	**1a**	**2a**	1:3:5	reflux	3	**3aa** (90)
5	**1b**: Ar = Ph	**2a**	1:3:5	reflux	3	**3ba** (87)
6	**1c**: Ar = 4-F-C_6H_4	**2a**	1:3:5	reflux	3	**3ca** (74)
7	**1d**: Ar = 4-Cl-C_6H_4	**2a**	1:2:3	reflux	3	**3da** (68)
8	**1e**: Ar = 4-MeO-C_6H_4	**2a**	1:2:3	reflux	3	**3ea** (60)
9	**1a**: Ar = 4-Me-C_6H_4	**2b**: R^1 = Me, R^2 = R^3 = H, R^4 = Bn	1:2:3	reflux	3	**3ab** (81)
10	**1a**	**2c**: R^1 = R^4 = Me, R^2 = H, R^3 = Ph	1:3:5	reflux	3	**3ac** (83)
11	**1a**	**2d**: R^1 = Et, R^2 = H, R^3 = Ph, R^4 = Me	1:3:5	reflux	3	**3ad** (80)
12	**1a**	**2e**: R^1 = R^2 = R^4 = Me, R^3 = Ph	1:3:5	reflux	3	**3ae** (60)[d]

[a] The reaction of ethene **1** (1 mmol) was carried out in acetic acid (15 mL).
[b] Molar ratio.
[c] Isolated yield based on the ethene **1**.
[d] 1-Hydroxy-1-isopropyl-3,3-bis(4-methylphenyl)-7-methyl-6-phenyl-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (**4**) was also isolated in 22% yield.

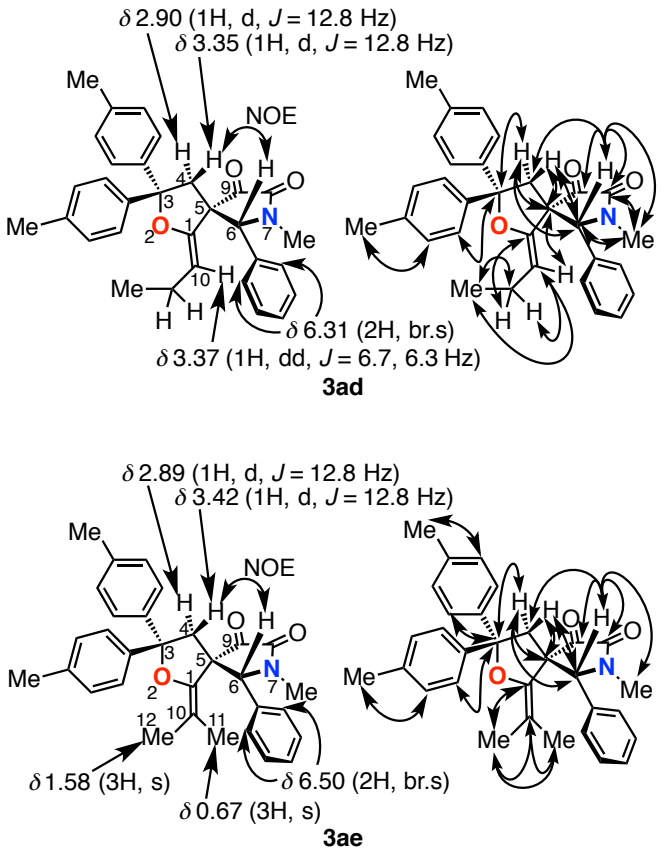
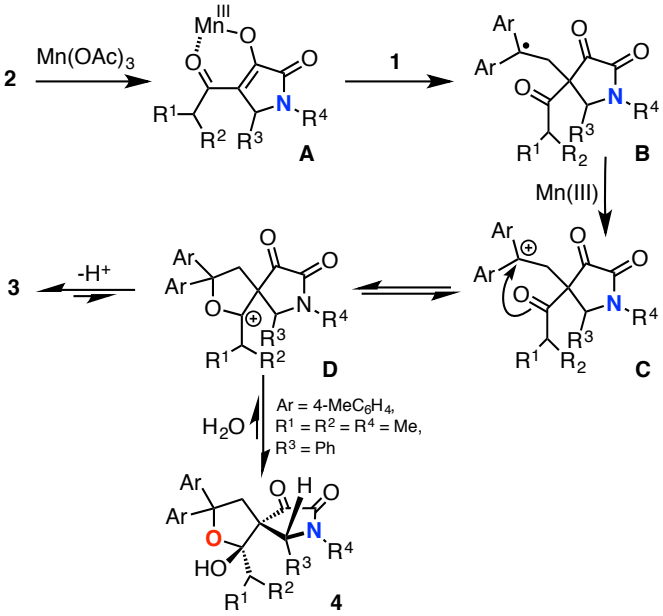


Fig. 2. Important ^{1}H chemical shifts, NOE (left) and HMBC study (right) of **3ad** (upper) and **3ae** (lower)

It was reported that the Mn(III)-enolate complex formation is the rate-determining step in the Mn(III)-based reaction of the α-alkyl-substituted 1,3-dicarbonyl compounds with alkenes.[1c,20] In this case, a similar enolization of **2** with $Mn(OAc)_3$ would occur during the first stage, producing complex **A** (Scheme 3). Complex **A** is electron deficient, thus an electron-rich alkene **2** should be easily oxidized to give radical **B**, which would be further oxidized to produce the carbocation **C**. The cation **C** would spontaneously cyclize with the carbonyl oxygen and undergo subsequent β-proton elimination that produces the 2-oxa-7-azaspiro compounds **3**. The formation of the stable tertiary carbocation **C** is crucial for the next *O*-cyclization to produce **3**. In fact, the reaction using styrene and terminal alkenes such as 1-hexene was complicated. When 4-isobutyryl-1-methyl-5-phenylpyrrolidine-2,3-dione (**2e**) was subjected to the oxidation, the desired 1-exomethylene-2-oxa-7-azaspiro compound **3ae** was mainly produced along with the hydroxy-2-oxa-7-azaspiro compound **4** formed by nucleophilic addition of water to the intermediate cation **D** due to relief of the steric hindrance.

In conclusion, our initial forecast was proved to be correct by the fact that the 2-oxa-7-azaspiro[4.4]nonane-8,9-dione derivatives **3** containing tetrahydrofuran and 2,3-pyrrolidinedione rings could be successfully synthesized in good yields by the Mn(III) oxidation of a mixture of 1,1-diarylethenes **1** and 4-acylpyrrolidine-2,3-diones **2**. The reaction was straightforward, the reaction time was significantly short, and the procedure was simple to obtain the desired product **3**. In addition, the structures of the products **3** and **4** were well characterized by spectroscopic methods including the X-ray single crystal analysis of **3ae**, and the mechanism for the formation of the products **3** and **4** was logically interpreted by the Mn(III)-based oxidation chemistry.[1,2,20,21] Further optimization of the reactions listed in Table 1, application of the reaction using the pyrrolidinediones **2** bearing other substituents, and bioassay of the pyrrolidinediones **2** and the products **3** for antibacterial, antiviral, bactericidal, insecticidal, herbicidal activities are currently underway.



Scheme 3. Plausible mechanism for the formation of **3** and **4**

Acknowledgments

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Supplementary data

Experimental detail, spectroscopic data of the products **3ba**, **3ca**, **3da**, **3ea**, **3ab**, and the copies of ^{1}H NMR, ^{13}C NMR, DEPT, COSY, NOESY, HMQC, and HMBC spectra for all the compounds **3** and **4**, and X-ray brief report of **3ae**.

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14. The structure of **3aa** was determined by spectroscopic methods, a 2D NMR study and elemental analysis.
7-Benzyl-3,3-bis(4-methylphenyl)-1-(propan-2-ylidene)-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (3aa): yellow needles (from chloroform/hexane); mp 182.0-182.5 °C; IR ($CHCl_3$) 1762.8 (–CO–), 1714.6 (–CON–); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.30 (3H, m, arom H), 7.22-7.20 (2H, m, arom H), 7.13-7.11 (4H, m, arom H), 7.07-7.03 (4H, m, arom H), 4.56 (1H, d, J = 14.4 Hz, H_a-CH), 4.52 (1H, d, J = 14.4 Hz, HC-H_b), 3.04 (1H, d, J = 11.8 Hz, H_a-6), 2.84 (1H, d, J = 11.8 Hz, H_b-6), 2.83 (1H, d, J = 12.4 Hz, H_a-4), 2.80 (1H, d, J = 12.4 Hz, H_b-4), 2.31 (3H, s, Me), 2.26 (3H, s, Me), 1.80 (3H, s, Me-12), 1.15 (3H, s, Me-11); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.5 (C-9), 158.4 (C-8), 149.0 (C-1), 140.6, 140.0, 137.3, 137.0, 134.1 (arom C), 129.1 (2C), 128.84 (2C), 128.82 (2C), 128.5 (2C), 128.3, 125.6 (2C), 125.4 (2C) (arom CH), 102.6 (C-10), 88.1 (C-3), 53.6 (C-6), 53.2 (C-4), 51.7 (C-5), 48.3 (CH_2), 20.93 (Me), 20.90 (Me), 18.9 (Me-12), 17.5 (Me-11) ; FAB HRMS (acetone/NBA): calcd for $C_{31}H_{32}NO_3$ 466.2382 (M+H); found 466.2365. Anal Calcd for $C_{31}H_{31}NO_3$•1/2H_2O: C, 78.45; H, 6.58; N, 2.95. Found: C, 78.57; H, 6.73; N, 2.92.
15. The structure of **4** was determined by spectroscopic methods, an HMQC study and elemental analysis (Fig. 3).

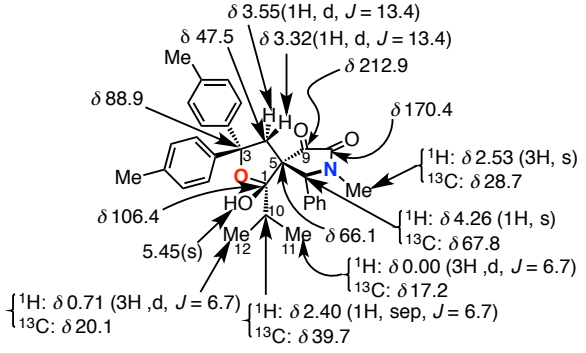


Fig. 3. Important ^{1}H and ^{13}C chemical shifts of **4**

1-Hydroxy-1-isopropyl-3,3-bis(4-methylphenyl)-7-methyl-6-phenyl-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (4): colorless cubes (from chloroform); mp 218.5-219.5 °C; IR (KBr) 3196 (OH), 1689.5 (C=O, N–C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (2H, d, J = 8.1 Hz, arom H), 7.40 (2H, d, J = 8.2 Hz, arom H), 7.31-7.26 (3H, m, arom H), 7.14 (2H, J = 8.2 Hz, arom H),7.12 (2H, m, arom H), 7.07 (2H, d, J = 8.1 Hz, arom H), 5.45 (1H, s, OH; exchanged by D_2O), 4.26 (1H, s, H-6), 3.55 (1H, d, J = 13.4 Hz, HC-H_a-4), 3.32 (1H, d, J = 13.4 Hz, HC-H_b-4), 2.53 (3H, s, Me-7), 2.40 (1H, sep, J = 6.7 Hz, H-10), 2.29 (3H, s, Me), 2.26 (3H, s, Me), 0.71 (3H, d, J = 6.7 Hz, Me-12), 0.00 (3H, d, J = 6.7 Hz, Me-11); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.9 (C-9), 170.4 (C-8), 143.2, 143.0, 137.0, 136.7, 134.7 (arom C), 129.2 (2C), 128.9 (3C), 128.8 (2C), 128.7 (2C), 125.6 (2C), 125.0 (2C) (arom CH), 106.4 (C-1), 88.9 (C-3), 67.8 (C-6), 66.1 (C-5), 47.5 (C-4), 39.7 (C-10), 28.7 (Me-7), 21.0 (Me), 20.9 (Me), 20.1 (Me-12), 17.2 (Me-11); FAB HRMS (acetone/NBA): calcd for $C_{31}H_{34}NO_4$ 484.2488 (M+H); found 484.2501. Anal Calcd for $C_{31}H_{33}NO_4$•1/4H_2O: C, 76.28; H, 6.92; N, 2.87. Found: C, 76.55; H, 7.03; N, 2.84.
16. The structure of **3ac** was determined by spectroscopic methods, a 2D NMR study and elemental analysis.
1-Ethylide-3,3-bis(4-methylphenyl)-7-methyl-6-phenyl-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (3ac): colorless needles (from chloroform/hexane); mp 182-183 °C; IR ($CHCl_3$) ν 1767 (C=O), 1715 (N–C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (2H, d, J = 8.2 Hz, ArH), 7.27 (2H, d, J = 8.2 Hz, ArH), 7.21 (2H, d, J = 8.0 Hz, ArH), 7.18 (3H, t, J = 7.4 Hz, ArH), 7.06 (2H, d, J = 8.0 Hz, ArH), 6.32 (2H, br. s, ArH), 4.40 (1H, s, H-6), 3.37 (1H, q, J = 6.9 Hz, H-10), 3.32 (1H, d, J = 12.7 Hz, H_a-4), 2.92 (1H, d, J = 12.7 Hz, H_b-4), 2.90 (3H, s, N–Me), 2.42 (3H, s, Me), 2.27 (3H, s, Me), 1.44 (3H, t, J = 6.9 Hz, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5 (C-9), 160.0 (C-8), 150.0 (C-1), 142.2, 140.8, 137.6, 137.1, 135.0 (arom C), 129.3 (2C), 128.9 (2C), 128.6, 128.3 (2C), 126.0 (2C), 125.2 (4C) (arom CH), 100.1 (C-10), 87.9 (C-3), 70.1 (C-6), 60.9 (C-5), 53.0 (C-4), 30.9 (N-Me), 21.1, 20.9 (Me), 10.7 (Me); FAB HRMS (acetone/NBA): calcd for $C_{30}H_{30}NO_3$ 452.2226 (M+H); found 452.2225. Anal Calcd for $C_{30}H_{29}NO_3$•4/5H_2O: C, 77.33; H, 6.62; N, 3.01. Found: C, 77.08; H, 6.37; N, 2.98.
17. The structure of **3ad** was determined by spectroscopic methods, a 2D NMR study and elemental analysis.
3,3-Bis(4-methylphenyl)-7-methyl-6-phenyl-1-propylidene-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (3ad): colorless needles (from chloroform/hexane); mp 188-189 °C; IR ($CHCl_3$) ν 1767 (C=O), 1717 (N–C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (2H, d, J = 8.2 Hz, ArH), 7.27 (2H, d, J = 8.2 Hz, ArH), 7.21 (2H, d, J = 8.3 Hz, ArH), 7.17 (3H, t, J = 7.5 Hz, ArH), 7.05 (2H, d, J = 8.3 Hz, ArH), 6.31 (2H, br. s, ArH), 4.42 (1H, s, H-6), 3.37 (1H, dd, J = 6.7, 6.3 Hz, H-10), 3.35 (1H, d, J = 12.8 Hz, H_a-4), 2.90 (1H, d, J = 12.8 Hz, H_b-4), 2.90 (3H, s, N–Me), 2.43 (3H, s, Me), 2.26 (3H, s, Me), 2.07 (1H, m, H–CH), 1.86 (1H, m, HC–H), 0.55 (3H, t, J = 7.5 Hz, Me); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5 (C-9), 160.0 (C-8), 149.1 (C-1), 142.2, 140.8, 137.5, 137.0, 134.9 (arom C), 129.3 (2C), 128.9 (2C), 128.5, 128.3 (2C), 126.0 (2C), 125.1 (4C) (arom CH), 107.5 (C-10), 87.9 (C-3), 70.1 (C-6), 60.1 (C-5), 52.8 (C-4), 30.8 (N-Me), 21.1, 20.8 (Me), 18.7 (CH_2), 13.7 (Me); FAB HRMS (acetone/NBA): calcd for $C_{31}H_{32}NO_3$ 466.2382 (M+H); found 466.2377.
18. The structure of **3ae** was determined by spectroscopic methods, a 2D NMR study and elemental analysis.
3,3-Bis(4-methylphenyl)-7-methyl-6-phenyl-1-(propan-2-ylidene)-2-oxa-7-azaspiro[4.4]nonane-8,9-dione (3ae): colorless microcrystals (from chloroform/hexane); mp 174-175 °C; IR ($CHCl_3$) ν 1765 (C=O), 1717 (N–C=O); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (2H, d, J = 8.3 Hz, ArH), 7.27 (2H, d, J = 8.5 Hz, ArH), 7.21 (2H, m, ArH), 7.19 (2H, d, J = 8.3 Hz, ArH), 7.15 (1H, t, J = 8.03 Hz, ArH), 7.05 (2H, d, J = 8.3 Hz, ArH), 6.50 (2H, br. s, ArH), 4.55 (1H, s, H-6), 3.42 (1H, d, J = 12.8 Hz, H_a-4), 3.00 (3H, s, N–Me), 2.89 (1H, d, J = 12.8 Hz, H_b-4), 2.39 (3H, s, Me), 2.26 (3H, s, Me), 1.58 (3H, s, Me-12), 0.67 (3H, s, Me-11); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4 (C-9), 160.0 (C-8), 143.9 (C-1), 143.7, 141.2, 137.6, 136.8, 135.0 (arom C), 129.3 (2C), 128.9 (4C), 128.3, 127.8 (2C), 126.1 (2C), 125.0 (2C) (arom CH), 107.0 (C-10), 86.8 (C-3), 69.5 (C-6), 60.2 (C-5), 54.7 (C-4), 31.2 (N-Me), 21.0, 20.9 (Me), 20.5 (Me-11), 17.5 (Me-12); Anal Calcd for $C_{31}H_{31}NO_3$: C, 79.97; H, 6.71; N, 3.01. Found: C, 79.73; H, 6.78; N, 3.07.
19. X-ray crystal data of **3ae** (Fig. 4): Empirical Formula $C_{31}H_{31}NO_3$; Formula Weight 465.59; Crystal Color, Habit colorless, block; Crystal Dimensions 0.370 × 0.327 × 0.187 mm; Crystal System triclinic; Lattice Type Primitive; Lattice Parameters a = 9.6559(4) Å, b =

9.9138(5) Å, c = 14.9614(8) Å, α = 75.345(2)°, β = 69.807(2)°, γ = 78.722(1)°, V = 1291.2(1) Å^3; Space Group P-1 (#2); Z value 2; D_{calc} 1.197 g/cm^3; F_{000} 496.00; μ(MoKα) 0.763 cm^{-1}; R_1 (I>2.00σ(I)) 0.0688; R (All reflections) 0.1444; wR_2 (All reflections) 0.2614; Goodness of Fit Indicator 1.131.

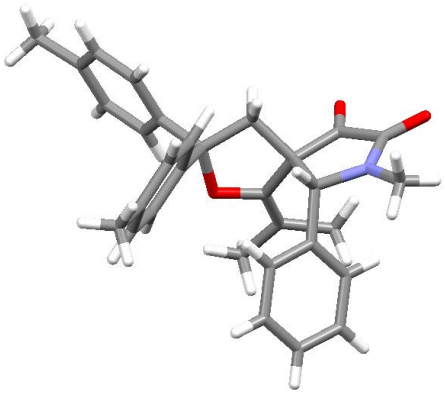
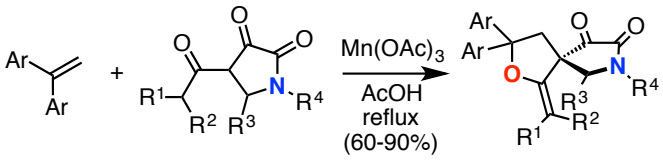


Fig. 4. Crystal structure of **3ae**

20. Snider, B. B. *Tetrahedron* **2009**, *65*, 10738-10744.
21. Cossy, J.; Bouzide, A.; Leblanc, C. *J. Org. Chem.* **2000**, *65*, 7258-7265.

Graphic abstract



R^1, R^2 = alkyl and/or H; R^3 = H, Ph; R^4 = Bn, Me