A new domino autocatalytic reaction leading to polyfunctionalized spiro[5.5]undecanes and dispiro[4.2.5.2]pentadecanes†

Bo Jiang,[a,b] Wen-Juan Hao,[b] Jin-Peng Zhang,[c] Shu-Jiang Tu*[a,b] and Feng Shi[b]

Received 17th December 2008, Accepted 13th March 2009
First published as an Advance Article on the web 3rd April 2009
DOI: 10.1039/b822645h

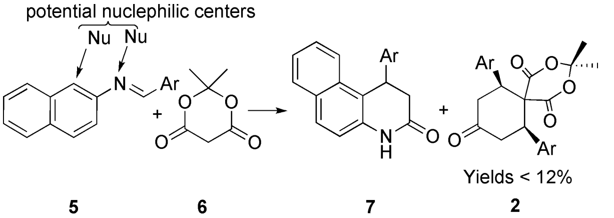
A new domino autocatalytic reaction of imines with Meldrum's acid was described. In this reaction, a series of polycyclic spiro[5.5]undecane-1,5,9-trione and dispiro[4.2.5.2]pentadecane-9,13-dione derivatives, with remarkable diastereoselectivity, were successfully synthesized in acidic condition, and up to six new bonds were formed accompanied by the C=N bond cleavage of the imines and the decomposition of Meldrum's acid, with by-product of acetohydrazide as a novel autocatalyst.

Introduction

The search for new avenues to molecular complexity from relatively simple substrates has been one of the major objectives of organic chemists for the last decade.[1] In this regard, the domino autocatalytic reaction as a unique and fascinating reaction type has played an important role.[2] In addition to the multiple formation of carbon–carbon bonds in one pot, the domino autocatalytic reaction intrinsically has the following advantages: automatic amplification of catalyst, high reaction efficiency, easy purification of the products, and consecutive reaction pattern. Therefore, autocatalysis combined with the domino reaction has made many contributions to modern organic chemistry, both from academic and industrial points of view. As a result, the continued development of new domino autocatalytic processes to create molecular complexity and diversity is becoming an interesting area for chemists.

Over the past few decades, Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione)[3] has been used as a versatile organic reagent[4,5] and its derivatives are very useful building blocks in synthetic organic chemistry.[6] Because of its high acidity (pK_a 4.83),[4] steric rigidness and notable tendency to regenerate acetone, Meldrum's acid is often employed in the design of reactions with multiple formation of carbon–carbon bonds.[7] Spirocyclic compounds including a Meldrum's acid unit are attractive intermediates in the synthesis of natural products and in medicinal chemistry, and are the starting materials for the synthesis of exotic amino acids which are used to modify the physical properties and biological activities of peptides, peptidomimetics, and proteins.[8] Thus, the synthesis of a new highly substituted spiro ring system with a Meldrum's acid unit has attracted widespread attention.[9] Barbas III *et al.* pioneered a new L-proline-catalyzed multi-component protocol of Meldrum's acid that provides one-pot domino synthesis of unsymmetrical spiro[5.5]undecanes **1**.[4] Recently, the Michael addition approach for the synthesis of symmetrical spiro[5.5]undecanes **2** has been described by Chande *et al.*[10] Although the diverse synthetic routes to spiro[5.5]undecanes have been developed, quite surprisingly, utilization of the domino autocatalytic reaction to build a symmetrical spiro[5.5]undecane framework and further realize protection of the carbonyl group to construct a dispiro[4.2.5.2]pentadecane skeleton (**3** and **4**) in one-pot has not stimulated much interest so far.

In the literature, Wang *et al.* have reported the treatment of imines **5** with Meldrum's acid **6** unexpectedly generating the spiro[5.5]undecanes **2** as by-products (Scheme 1).[11] This fact and the results of Barbas III *et al.* showed that a by-product amine from the reaction of Meldrum's acid to the imine C=N bond may have served as a self-catalyst to promote the formation of spirotriones **2**. The high reactivity of the two nucleophilic centers in imines **5** leads to the benzo[*f*]quinolin-3-one **7**. Therefore, our concern is whether the yield of spiro[5.5]undecanes **2** can be improved by using only one nucleophilic center of the imines.



Scheme 1 The reaction of imines with Meldrum's acid.

To our delight, we found that the one-pot reaction between *N*-arylidene-1-phenylethanamine **5′** with one nucleophilic center and Meldrum's acid **6** efficiently generated sprioheterocycles **2** with remarkable diastereoselectivity at elevated temperature in moderate yields (Scheme 2 and Table 1). Impressively, when the symmetric double imines **8** were employed to react with Meldrum's acid **6** under acidic conditions, sprioheterocycles **2** as single diastereomers were obtained in high yields as confirmed by ^{1}H NMR measurement, together with the acetohydrazide by-product, which serves as a novel self-catalyst in this reaction (Scheme 3). When the above reaction was performed in mixed solvent of HOAc and diol such as ethane-1,2-diol and

---

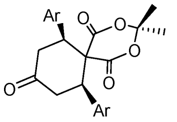
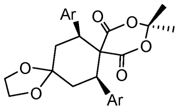
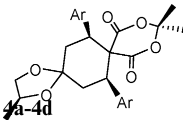
[a] College of Chemistry, Chemical Engineering, and Materials Science, Suzhou University, Suzhou, P. R. China. E-mail: laotu@xznu.edu.cn; Fax: +86(516) 83500065; Tel: +86(516) 83500065

[b] School of Chemistry and Chemical Engineering, Xuzhou Normal University, Xuzhou, Jiangsu, P. R. China

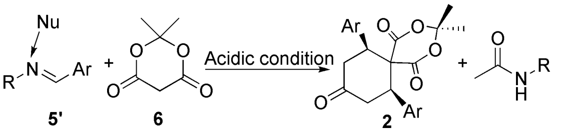
[c] Department of Public Health, Xuzhou Medical College, Xuzhou 221000, People's Republic of China

† Electronic supplementary information (ESI) available: Experimental data. CCDC reference numbers 658845, 658846, 658847 and 700773. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b822645h

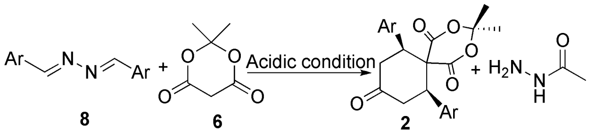
Table 1 The domino autocatalytic synthesis of products **2**, **3**, and **4**

Entry	Product	Ar =	Dialdimines	Time	Yield[a]/%
1		**2a**, 4-Chlorophenyl	**8a**	4 h	85 (40)[b]
2		**2b**, 4-Bromophenyl	**8b**	5 h	89 (38)[b]
3		**2c**, 4-Nitrophenyl	**8c**	18 h	58
4		**2d**, 3,4-Dichlorophenyl	**8d**	4 h	84
5		**2e**, Phenyl	**8e**	5 h	83 (42)[b]
6		**2f**, 4-Tolyl	**8f**	4 h	87
7		**2g**, 4-Methoxyphenyl	**8g**	5 h	89
8		**2h**, Benzo[*d*][1,3]dioxol-5-yl	**8h**	4 h	84 (36)[b]
9		**2i**, 4-Dimethylaminophenyl	**8i**	4 h	85
10	**2a-2k**	**2j**, 3,4,5-Trimethoxyphenyl	**8j**	3 h	81
11		**2k**, Thien-2-yl	**8k**	5 h	79
12		**3a**, 4-Chlorophenyl	**8a**	9 h	82
13		**3b**, 4-Bromophenyl	**8b**	8 h	84
14		**3c**, 4-Nitrophenyl	**8c**	24 h	50
15		**3d**, 3,4-Dichlorophenyl	**8d**	10 h	84
16		**3e**, 4-Methoxyphenyl	**8g**	7 h	85
17		**3f**, 2-Chlorophenyl	**8l**	9 h	70
18		**3g**, 4-Fluorophenyl	**8m**	8 h	82
19		**3h**, Phenyl	**8e**	8 h	83
20	**3a-3j**	**3i**, 3,4-Dimethoxyphenyl	**8n**	6 h	86
21		**3j**, Thien-2-yl	**8k**	8 h	78
22		**4a**, 4-Chlorophenyl	**8a**	8 h	79[c]
23		**4b**, 4-Bromophenyl	**8b**	8 h	81[c]
24		**4c**, Phenyl	**8e**	10 h	76[c]
25	**4a-4d**	**4d**, Thien-2-yl	**8k**	12 h	72[c]

[a] Reactions are performed with a dialdimines and Meldrum's acid in a ratio of 1:2.5; the yield is based on the starting dialdimines. [b] Reaction is performed with imines **5′** and Meldrum's acid in a ratio of 1:2.5; the yield is based on the starting imines. [c] The yield of two diastereomers.



Scheme 2 The reaction of *N*-arylidene-1-phenylethanamine with Meldrum's acid.



Scheme 3 The reaction of dialdimines with Meldrum's acid.

S-propane-1,2-diol, new dispiro[4.2.5.2]pentadecanes **3** and **4** were provided (Fig. 1).

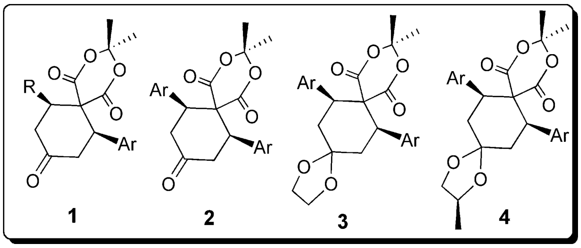


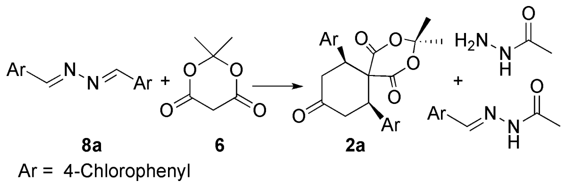
Fig. 1 The structure of spiro[5.5]undecane derivative.

Besides a high efficiency in the formation of multiple bonds as a domino process, this reaction has the following advantages: (1) the starting materials are readily available and the reagents are very cheap; (2) the reaction proceeds smoothly under very mild conditions without introducing strong acid, base or metal catalyst; (3) the workup is facile due to the fact that only by-product of acetohydrazide as an autocatalyst for the Diels–Alder reaction is released, which is easily isolated because of its water solubility; and (4) the dispiro[4.2.5.2]pentadecane-9,13-dione systems **3** and **4**, to our best knowledge, represent kind of new two-spiro heterocycles containing a 1,3-dioxane, a 1,3-dioxolane and a cyclohexane ring, with the 7,14-cis disposition of substituents. Indeed, the present protocol provides a novel, straightforward, and effective pathway to construct spiro heterotricycles of types **2**, **3** and **4**.

Results and discussion

Aldehydes and aldimines are both important electrophiles in organic synthesis, and addition reactions to these electrophiles constitute some of the most useful and fundamental organic transformations. It is generally accepted that aldimines are less reactive towards nucleophilic addition than their corresponding aldehydes owing to the difference in electronegativity between O and N,[12] and the steric hindrance present in the aldimines. Recently, however, an aldimine has been found to be more reactive than the corresponding aldehyde in many reactions.[13] In the present work, symmetric dialdimines **8** as starting materials were reacted with Meldrum's acid **6** in a molar ratio of 1:2.5 to yield polyfunctionalized spiro[5.5]undecanes **2** with high *syn*-selectivities.

Next, we devoted our efforts to the study of the reaction of symmetric dialdimines **8a** with Meldrum's acid **6** as a model reaction (Scheme 4). Experiments were carried out in various solvents such as toluene, THF and EtOH. Unfortunately, the reaction scarcely proceeded in toluene and THF, and an incomplete reaction was observed in the case of EtOH as solvent. In another case, when DMF was used as the solvent, the reaction proceeded better and product **2a** as a single diastereomer confirmed by ^{1}H NMR, was obtained in 46% isolated yield, accompanied with by-products of acetohydrazide and *N′*-(4-chlorophenylidene)acetohydrazide after purification of the reaction mixture by flash chromatography (Scheme 4). Subsequently, further optimization of the reaction conditions, including reaction temperature, reaction time and more solvents was investigated. Satisfyingly, after a series of experiments, glacial acetic acid was proved to be the best solvent and the yield of product **2a** reached 85% without the by-product of *N′*-(4-chlorophenylidene)acetohydrazide when the reaction was performed in HOAc at 80 °C for 4 h.

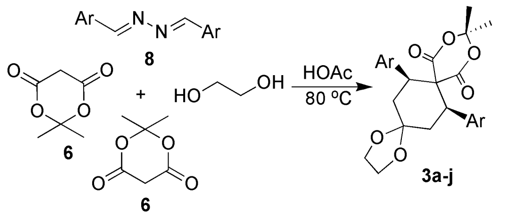


Scheme 4 Optimization of reaction conditions for product **2a**.

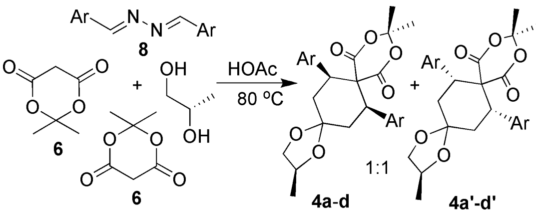
To extend the scope of this protocol for the synthesis of the fused spiroheterocycles, substrates **8b–k**, with electron-donating or electron-withdrawing groups on the phenyl rings, were then examined for their reactions with Meldrum's acid under the optimized conditions. As a result, a series of products **2b–k** were obtained in good yields of 79–89% except for the compound **2c** (Table 1, entries 1–11). The substrate **8k**, which contained the heteroaromatic group (2-thienyl), was also allowed to react with Meldrum's acid under identical conditions. Accordingly, thienyl-substituted spriocycle compound **2k** was generated.

To further investigate the synthetic potential of this process, reaction of Meldrum's acid with symmetric dialdimines **8a** was carried out in a mixed solvent of HOAc and ethylene glycol. Interestingly, new dispiro[4.2.5.2]pentadecane **3a** was furnished with ethylene glycol as a protection reagent of the carbonyl group under these mild reaction conditions. Subsequently, screening of the solvent ratio in the mixed solvents revealed that a mixture of glycol and HOAc (2:1, v/v) was the best solvent, affording the dispirodione **3a** as a single diastereomer in good yield. To test the reaction scope, various symmetric dialdimines **8** were treated with Meldrum's acid under the optimized conditions described above to yield a series of new dispirodiones **3a–j** with high syn-selectivities and concomitant formation of up to two quaternary carbon centers and six σ bonds including two C–O bonds. It is worth noting that to the best of our knowledge, there has not yet been any literature precedent for the synthesis of new polyfunctionalized dispiro[4.2.5.2]pentadecane-9,13-diones **3** *via* an autocatalytic reaction (Scheme 5).

To demonstrate the generality of this methodology, the replacement of ethylene glycol with chiral 1,2-propanediol (*S*-) was examined. To our delight, under the same conditions, the reaction proceeds stereoselectively also (mixtures of diastereomers **4a–d** and **4a′–d′** are obtained), with the generation of three new asymmetric carbons (Scheme 6). The ^{1}H NMR analysis of the products indicates the presence of a mixture of two diastereoisomers. The ratio of the isomers was close to 1:1 as demonstrated by ^{1}H NMR integration of the crude mixture (see the ESI†).



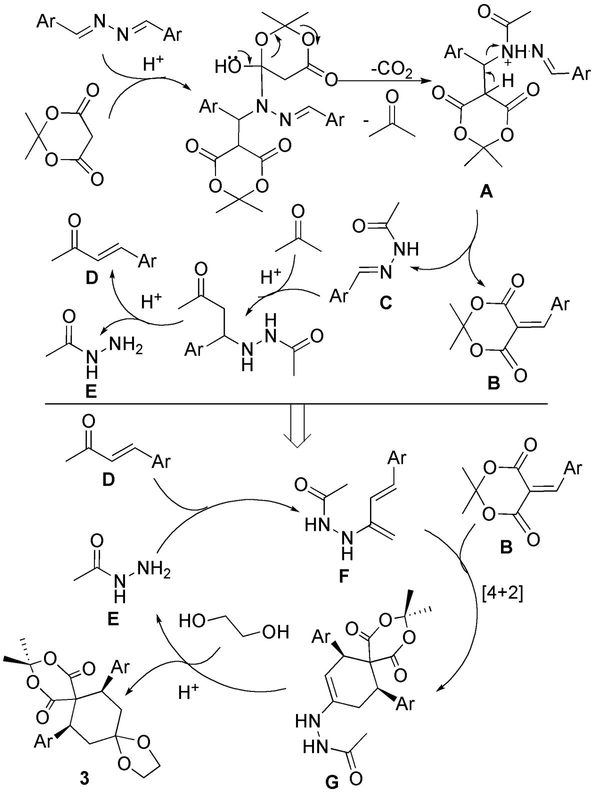
Scheme 5 The synthesis of dispiro[4.2.5.2]pentadecanes **3**.



Scheme 6 The synthesis of spiro[5.5]undecanes **4**.

Proposed reaction mechanism

A reasonable mechanism for the formation of the tricyclic dispiro[4.2.5.2]pentadecane-9,13-dione **3** was proposed and depicted in Scheme 7. First, due to the strong nucleophilicity of the nitrogen atom of dibenzylidenehydrazine, a Mannich-type reaction followed by a $\mathrm{S_NA}$ (nucleophilic acyl substitution) type reaction[14] occurs, leading to the fragmentation of the Meldrum's acid, release of acetone, and the formation of intermediate **A**



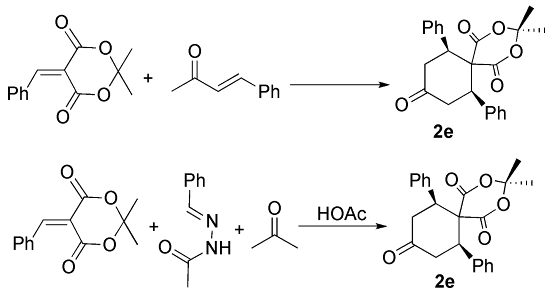
Scheme 7 The reaction mechanism of formation of product **3**.

Table 2 Investigation of reaction mechanism

Entry	Solvent	Catalyst	Time/h	Yield of **2e**
1	HOAc	Acetohydrazide	4	81
2	HOAc	—	6	trace
3	HCOOH	Acetohydrazide	7	trace

which undergoes retro-Mannich reaction to generate arylidene-Meldrum's acid **B** and intermediate **C**. The enones **D** and acetohydrazide **E** would be formed by a Mannich and retro-Mannich reaction of *N*-arylideneacetohydrazide C with acetone. The arylidene-Meldrum's acid **B** undergoes a Diels–Alder reaction with the soft nucleophilic Barbas dienamine (2-amine-1,3-butadiene)[15] **F**, generated in situ from enones **D** and the hydrazide **E**, to produce spirotriones **G**, which further react with diols in HOAc to dispiro[4.2.5.2]pentadecanes **3**. This hypothesis is supported by the mechanistic investigation of proline-catalyzed spirotriones' formation through the reaction of aldehyde and Meldrum's acid with enones reported by Barbas III *et al.*[4,9a]

In order to further clarify the mechanism for the formation of **2**, a model reaction between benzylidene-Meldrum's acid, for example, and 4-phenyl-but-3-en-2-one, was carried out in various reaction conditions (Table 2). In this reaction, the use of acetohydrazide as a catalyst in acetic acid leads to spiro[5.5]undecane **2e** in a yield of 81% (Table 2, entry 1) whereas the reaction scarcely proceeded in HOAc without acetohydrazide or using formic acid ($pK_a = 3.77$)[14] whose pK_a value was lower than that of acetic acid ($pK_a = 4.76$)[14] as reaction media in the presence of acetohydrazide (Table 2, entries 2 and 3). The results indicated that acetohydrazide might have formed ammonium salt by reacting with formic acid, losing the catalytic activity. In addition, the reaction of benzylidene-Meldrum's acid with *N*-benzylideneacetohydrazide (intermediate **C**) and acetone was performed in acetic acid to give the spiro[5.5]undecane **2e** in high yield (Scheme 8). Obviously, these experimental results further supported the mechanism for the products **2**. The key step to spiro[5.5]undecanes **2** was acetohydrazide catalyzed Diels–Alder reaction between compound **B** and enones **D**.



Scheme 8 The investigation of self-catalyst and reaction mechanism.

In most cases, the formation of a single product with concomitant formation of six σ bonds in these reactions illustrates the high efficiency of bond formation and the remarkable chemo-, regio-, and diastereoselectivity accompanying a remarkable increase in complexity starting from very simple and easily accessible achiral substrates. The structural elucidation and the attribution of the relative stereochemistry of the products rest upon NMR analysis and were unequivocally confirmed by X-ray diffraction of single crystals **2h**, **3g** and **4b** (see the ESI†) (Fig. 2–4).

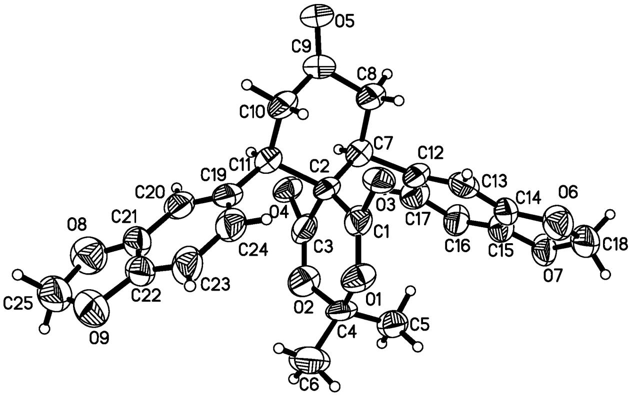


Fig. 2 The ORTEP drawing of **2h**.

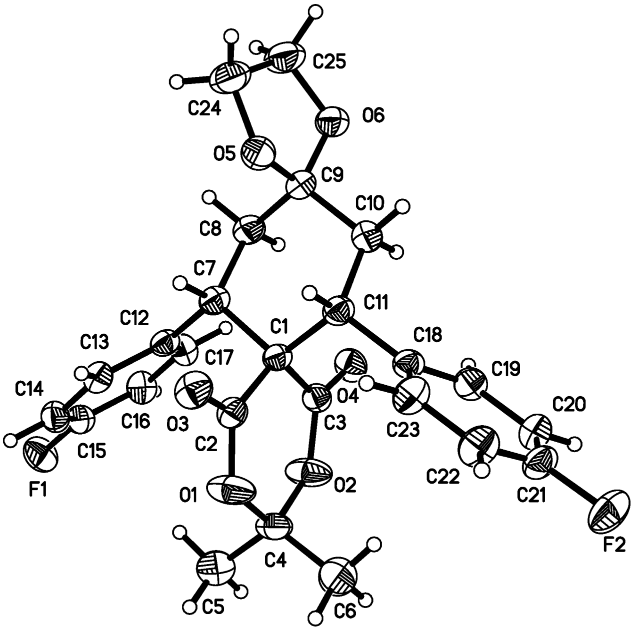


Fig. 3 The ORTEP drawing of **3g**.

Conclusion

In summary, a new and highly efficient autocatalytic domino reaction constitutes a good illustration of the potentiality of Meldrum's acid in stereocontrolled multiple σ bond forming reactions and provides a new route to polyfunctionalized spiro[5.5]undecane-1,5,9-triones and dispiro[4.2.5.2]pentadecane-9,13-diones for the first time. A reaction product, the acetohydrazide, plays a critical role in the success of the reaction by serving as a self-catalyst for the Diels–Alder reaction between arylidene-Meldrum's acid **B** and Barbas dienamine **F**. The simplicity of manipulation, ready availability of the substrates and reagents, and the easy access of a significant molecular complexity make this domino synthetic strategy attractive. An extension of this work is in progress.

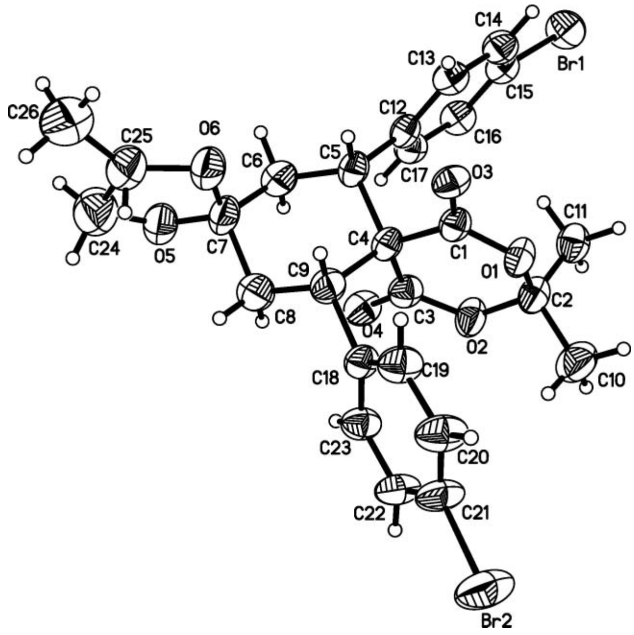


Fig. 4 The ORTEP drawing of **4b**.

Experimental

General

Melting points were determined in open capillaries and were uncorrected. ^{1}H NMR (^{13}C NMR) spectra were measured on a Bruker DPX 400 (100) MHz spectrometer in DMSO-d_6 with chemical shift (δ) given in ppm relative to TMS as internal standard. The exact mass measurements were obtained by a high resolution mass instrument (GCT-TOF instrument). X-Ray crystallographic analysis was performed with a Siemens SMART CCD and a Siemens P4 diffractometer.

General procedure for the synthesis of compounds 2a–2k

General procedure for the reaction of ethanamine 5′ with Meldrum's acid 6. In a 25-mL flask, *N*-arylidene-1-phenylethanamine **5′** (2 mmol), Meldrum's acid **6** (5 mmol), and HOAc (4.0 mL) were mixed and stirred at 80 °C until the disappearance of starting material was confirmed by TLC. Upon completion, the reaction mixture was cooled to room temperature, and introduced into water. The resulting suspension was neutralized with 10% NaOH. The solid was collected by washing with water. The aqueous layers were then extracted thoroughly with ethyl ether (3 × 10 mL), and organic phases were evaporated under reduced pressure to give solid. The combined solids were purified by flash column chromatography (silica gel, mixtures of petroleum ether/acetic ester, 10:1, v/v) to afford the desired pure spirotriones **2a** (**2b**, **2e**, and **2h**) and by-products acetamides.

General procedure for the reaction of diarylidenehydrazine 8 with Meldrum's acid 6. In a 25-mL flask, 1,2-diarylidenehydrazine **8** (2 mmol), Meldrum's acid **6** (5 mmol), and HOAc (4.0 mL) were mixed and stirred at 80 °C until the disappearance of starting material was confirmed by TLC. Upon completion, the reaction mixture was cooled to room temperature. The solid was collected by washing with water. The resulting suspension was neutralized with 10% NaOH. The aqueous layers were then extracted thoroughly with ethyl ether (3 × 10 mL), and organic phases were evaporated under reduced pressure to give solid. The combined solids were purified by flash column chromatography (silica gel, mixtures of petroleum ether/acetic ester, 10:1, v/v) to afford the desired pure spirotriones **2a**–**2k** and by-product acetohydrazide. All organic compounds except **2a**–**2e**, **2g**–**2h**, and **2k** are reported in the literature[4,9]and are fully characterized by spectral analysis.

General procedure for investigation of autocatalyst. In a 25-mL flask, benzylidene-Meldrum's acid (2 mmol), 4-phenyl-but-3-en-2-one (2 mmol), acetohydrazide(1 mmol), and HOAc (4 mL) (without HOAc or HCOOH) were mixed and then stirred at 80 °C until the disappearance of starting material was confirmed by TLC. Upon completion, the reaction mixture was cooled to room temperature. The subsequent work-up was the same as that of the above preparation of compounds **2e**.

General procedure for investigation of reaction mechanism. In a 25-mL flask, benzylidene-Meldrum's acid (2 mmol), *N*′-benzylideneacetohydrazide (2 mmol), acetone (5 mmol) and HOAc (4 mL) were mixed and then stirred at 80 °C until the disappearance of starting material was confirmed by TLC. Upon completion, the reaction mixture was cooled to room temperature. The subsequent work-up was the same as that of the above preparation of compounds **2e**.

General procedure for the synthesis of compounds 3a–3j and 4a–4d

In a 25-mL flask, 1,2-diarylidenehydrazine **8** (2 mmol), Meldrum's acid **6** (5 mmol), HOAc (4 mL) and ethane-1,2-diol (or *S*-1,2-propanediol, 8 mL) were mixed and then stirred at 80 °C until the disappearance of starting material was confirmed by TLC. Upon completion, the reaction mixture was cooled to room temperature, and introduced into water. The solid was collected by washing with water. The aqueous layers were extracted thoroughly with ethyl ether (3 × 10 mL), and organic phases were evaporated under reduced pressure to give solid. The combined solids were purified by flash column chromatography (silica gel, mixtures of petroleum ether/acetic ester, 10:1, v/v) to afford the desired pure dispiro[4.2.5.2]pentadecane-9,13-diones **3** and **4**.

7,11-Bis-(4-dimethylaminophenyl)-3,3-dimethyl-2,4-dioxaspiro-[5.5]undecane-1,5,9-trione (2i)

Pale yellow solid, mp: 229–231 °C.

^{1}H NMR (400 MHz) (δ, ppm): 6.94 (d, $J = 8.8$ Hz, 4H, ArH), 6.99 (d, $J = 8.8$ Hz, 4H, ArH), 3.87 (dd, $J_1 = 14.2$ Hz, $J_2 = 4.8$ Hz, 2H, CH$_2$), 3.48–3.37 (m, 2H, CH), 2.84 (s, 12H, NCH$_3$), 2.39 (dd, $J_1 = 15.4$ Hz, $J_2 = 4.8$ Hz, 2H, CH$_2$), 0.61 (s, 6H, CH$_3$). ^{13}C NMR (100 MHz) (δ, ppm): 207.3, 168.0, 156.1, 150.3, 128.6, 124.5, 112.4, 105.8, 60.7, 48.1, 42.8, 27.9. IR (KBr, ν, cm^{-1}): 3044, 2992, 2892, 1754, 1726, 1613, 1523, 1450, 1358, 1195, 1167, 1046, 946, 813, 716. ESI-MS: m/z 465.1 [M + H]$^+$ (100%), 497.2 [M + Na]$^+$.

7,14-Bis-(4-chlorophenyl)-11,11-dimethyl-1,4,10,12-tetraoxa-dispiro[4.2.5.2]pentadecane-9,13-dione (3a)

White solid, mp: 270–271 °C.

^{1}H NMR (400 MHz) (δ, ppm): 7.46 (d, J = 8.0 Hz, 4H, ArH), 7.13 (d, J = 8.0 Hz, 4H, ArH), 3.99-3.96 (m, 4H, CH_2), 3.86-3.81 (m, 2H, CH_2), 2.76 (t, J = 13.4 Hz, 2H, CH), 1.87-1.83 (m, 2H, CH_2), 0.56 (s, 6H, CH_3). ^{13}C NMR (100 MHz) (δ, ppm): 168.5, 164.3, 137.2, 133.2, 130.4, 129.2, 107.0, 105.9, 64.3, 60.2, 47.6, 35.5, 28.0. IR (KBr, ν, cm^{-1}): 3049, 2983, 1759, 1731, 1599, 1518, 1462, 1403, 1388, 1346, 1286, 1214, 1156, 1101, 1025, 968, 891, 769. Anal. calcd. for $C_{25}H_{24}Cl_2O_6$, C, 61.11; H, 4.92; found C, 61.09; H, 4.84.

2h. The single-crystal growth was carried out in ethanol at room temperature. Crystal data for $C_{25}H_{22}O_9$, M = 466.43, monoclinic, space group $P2(1)/c$, $a = 6.8061(8)$ Å, $b = 22.230(3)$ Å, $c = 14.9656(16)$ Å, $V = 2234.9(4)$ Å^3, $Z = 4$, $T = 298(2)$ K, $\mu = 0.106$ mm^{-1}, 10899 reflections measured, 3836 unique reflections, $R = 0.0943$, $R_w = 0.1917$. In the 1,3-dioxane ring, atoms C_7, C_8, C_{10}, and C_{11} are disordered over two positions. During the refinement process the disordered atoms C_7 and C_8 were both refined with occupancies of 0.58(2) and 0.42(2), respectively, and atoms C_{10} and C_{11} were both refined with occupancies of 0.56(2) and 0.44(2), respectively. In the cyclohexanone ring, atoms O_3 and O_4 are disordered over two positions, During the refinement process the disordered atom O_3 was refined with occupancies of 0.502(4) and 0.498(2) whereas atom O_4 was refined with occupancies of 0.414(4) and 0.586(2).

3g. The single-crystal growth was carried out in ethanol at room temperature. Crystal data for $C_{25}H_{24}F_2O_6$, M = 458.44, triclinic, space group $P\bar{1}$, $a = 8.146(4)$ Å, $b = 10.714(5)$ Å, $c = 13.580(7)$ Å, $V = 1104.6(9)$ Å^3, $Z = 2$, $T = 298(2)$ K, $\mu = 0.109$ mm^{-1}, 5811 reflections measured, 3845 unique reflections, $R = 0.0535$, $R_w = 0.1330$.

4b. The single-crystal growth was carried out in ethanol at room temperature. Crystal data for $C_{26}H_{26}Br_2O_6$, M = 594.29, triclinic, space group $P\bar{1}$, $a = 7.356(3)$ Å, $b = 12.590(5)$ Å, $c = 14.852(6)$ Å, $V = 1267.8(8)$ Å^3, $Z = 2$, $T = 193(2)$ K, $\mu = 3.236$ mm^{-1}, 6454 reflections measured, 4330 unique reflections, $R = 0.0728$, $R_w = 0.1245$. In the bromophenyl ring (C_{18}–C_{23}), atom Br_2 was disordered over two positions. During the refinement process the disordered atom Br_2 was refined with occupancies of 0.51(4) and 0.49(4). In the 1,3-dioxolane ring, atoms C_{25} and C_{26} are disordered over two positions. During the refinement process the disordered atoms C_{25} and C_{26} were refined with occupancies of 0.320(18) and 0.680(18), 0.320(18) and 0.680(18), respectively. During refinement, atoms C_{25} and C_{25}' are constrained to have the same x, y and z parameters and anisotropic displacement parameters. All of the atoms of C, O, Br closer than 3.8 Å are restrained with an s. u. value of 0.02 Å^2 to have the same Uij components. If (according to the connectivity table, *i.e.* ignoring attached hydrogens) one or both of the two atoms involved is terminal (or not bonded at all), 0.04 is used instead as 0.02. The distance between C_{24}, C_{26} and C_{24}, C_{26}' is restrained to 2.54 Å with an estimated standard deviation 0.02. The distances of C_{25}–C_{26}, C_{24}–C_{25} and C_{25}–C_{26}' are restrained to 1.53 Å with an estimated standard deviation 0.02. The distances of O_5–C_7, O_5–C_{24}, O_6–C_7, O_6–C_{25} are restrained to 1.43 Å with an estimated standard deviation 0.02.

Acknowledgements

We are grateful for financial support from the National Science Foundation of China (Nos. 20672090 and 20810102050), Natural Science Foundation of the Jiangsu Province (No. BK2006033), and Six Kinds of Professional Elite Foundation of the Jiangsu Province (No. 06-A-039).

References

1 (*a*) *New Avenues to Efficient Chemical Synthesis. Emerging Technologies*, Eds.: P. H. Seeberger, T. Blume, Springer, Heidelberg, 2007 (Ernst Schering Foundation Symposium Proceedings 2006-3); (*b*) K. C. Nicolaou, E. W. Yue, T. Oshima, in *The New Chemistry*, Ed.: N. Hall, Cambridge University Press, Cambridge, 2001, pp. 168–198; (*c*) L. F. Tietze, F. Hautner, in *Stimulating Concepts in Organic Chemistry*, Eds: F. Vgtle, J. F. Stoddart, M. Shibashaki, Wiley-VCH, Weinheim, 2000, pp. 38–64; (*d*) D. B. Ramachary, M. Kishor and G. Babul Reddy, *Org. Biomol. Chem.*, 2006, **4**, 1641–1646; (*e*) D. B. Ramachary and G. Babul Reddy, *Org. Biomol. Chem.*, 2006, **4**, 4463–4468; (*f*) D. B. Ramachary and M. Kishor, *J. Org. Chem.*, 2007, **72**, 5056–5068; (*g*) D. B. Ramachary, K. Ramakumar and V. V. Narayana, *J. Org. Chem.*, 2007, **72**, 1458–1463; (*h*) D. B. Ramachary and M. Kishor, *Org. Biomol. Chem.*, 2008, **6**, 4176–4187; (*i*) D. B. Ramachary, Y. V. Reddy and M. Kishor, *Org. Biomol. Chem.*, 2008, **6**, 4188–4197.

2 (*a*) H. Hagiwara, S. Endou, M. Fukushima, T. Hoshi and T. Suzuki, *Org. Lett.*, 2004, **6**, 1115–1118; (*b*) M. Fukushima, A. Morii, T. Hoshi, T. Suzuki and H. Hagiwara, *Tetrahedron*, 2007, **63**, 7154–7164; (*c*) M. Amedjkouh and M. Brandberg, *Chem. Commun.*, 2008, 3043–3045.

3 (*a*) L. F. Tietze and U. Beifuss, *Angew. Chem. Int. Ed. Engl.*, 1993, **32**, 131–163; (*b*) L. F. Tietze, T. H. Evers and E. Topken, *Angew. Chem. Int. Ed.*, 2001, **40**, 903–905; (*c*) S. Ikeda, *Angew. Chem. Int. Ed.*, 2003, **42**, 5120–5122; (*d*) R. J. Linderman, S. Binet and S. R. Petrich, *J. Org. Chem.*, 1999, **64**, 336–337; (*e*) P. Satymaheshwar, S. Jayakumar and J. J. Tepe, *Org. Lett.*, 2002, **4**, 3533–3535.

4 D. B. Ramachary, N. S. Chowdari and C. F. Barbas III, *Angew. Chem. Int. Ed.*, 2003, **42**, 4233–4237.

5 F. L. Muller, T. Constantieux and J. Rodriguez, *J. Am. Chem. Soc.*, 2005, **127**, 17176–17177.

6 (*a*) A. N. Meldrum, *J. Chem. Soc.*, 1908, **93**, 598–601; (*b*) D. Davidson and S. A. Bernhard, *J. Am. Chem. Soc.*, 1948, **70**, 3426–3428.

7 H. McNab, *Chem. Soc. Rev.*, 1978, **7**, 345–358.

8 (*a*) D. R. Zitsane, I. T. Ravinya, I. A. Riikure, Z. F. Tetere, E. Y. Gudrinietse and U. O. Kalei, *Russ. J. Org. Chem.*, 1999, **35**, 1457–1460; (*b*) D. R. Zitsane, I. T. Ravinya, I. A. Riikure, Z. F. Tetere, E. Y. Gudrinietse and U. O. Kalei, *Russ. J. Org. Chem.*, 2000, **36**, 496–501; (*c*) I. Bonnard, M. Rolland, C. Francisco and B. Banaigs, *Lett. Pept. Sci.*, 1997, **4**, 289–292; (*d*) S. M. Chande and R. R. Khanwelkar, *Tetrahedron Lett.*, 2005, **46**, 7787–7792; (*e*) A. S. Ivanov, *Chem. Soc. Rev.*, 2008, **37**, 789–811.

9 (*a*) D. B. Ramachary and C. F. Barbas III, *Chem. Eur. J.*, 2004, **10**, 5323–5231; (*b*) D. B. Ramachary and C. F. Barbas, III, *Org. Lett.*, 2005, **7**, 1577–1580; (*c*) E. E. Shults, E. A. Semenova, A. A. Johnson, S. P. Bondarenko, I. Y. Bagryanskaya, Y. V. Gatilov, G. A. Tolstikov and Y. Pommier, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 1362–1368; (*d*) S. Lu and H. Chen, *Huaxi Yaoxue Zazhi*, 1995, **10**, 29–31; (*e*) Q. Zhong, J. Shao and C. Liu, *Youji Huaxue*, 1988, **8**, 466–469.

10 M. S. Chande and R. R. Khanwelkar, *Tetrahedron Lett.*, 2005, **46**, 7787–7792.

11 X.-S. Wang, M.-M. Zhang, Z.-S. Zeng, D.-Q. Shi, S.-J. Tu, X.-Y. Wei and Z.-M. Zong, *Tetrahedron Lett.*, 2005, **46**, 7169–7173.

12 (*a*) N. B. Ambhaikar, J. P. Snyder and D. C. Liotta, *J. Am. Chem. Soc.*, 2003, **125**, 3690–3691; (*b*) M. Yamaguchi, in: *Comprehensive Organic Synthesis*, (Ed.: B. M. Trost, I. Flem-ing), Pergamon Press, Oxford, 1991, Vol. 1, p. 325.

13 (*a*) F. Chemla, V. Hebbe and J. Normant, *Synthesis*, 2000, 75–85; (*b*) Y. Hayashi, T. Urushima, M. Shoji, T. Uchimaru and I. Shiina, *Adv. Synth. Catal*, 2005, **347**, 1595–1604.

14 J. McMurry, *Fundamentals of Organic Chemistry*, 5th Ed. China Machine Press, 2003, p. 314.

15 (*a*) R. Thayumanavan, D. B. Ramachary, K. Sakthivel, F. Tanaka and C. F. Barbas III, *Tetrahedron Lett.*, 2002, **43**, 3817–3820; (*b*) D. B. Ramachary, N. S. Chowdari and C. F. Barbas III, *Tetrahedron Lett.*, 2002, **43**, 6743–4746; (*c*) D. B. Ramachary, N. S. Chowdari and C. F. Barbas III, *Synlett*, 2003, 1910–1914; (*d*) D. B. Ramachary, K. Anebouselvy, N. S. Chowdari and C. F. Barbas III, *J. Org. Chem.*, 2004, **69**, 5838–5849; (*e*) D. B. Ramachary, Y. V. Reddy and B. V. Prakash, *Org. Biomol. Chem.*, 2008, **6**, 719–726.