# Sodium Acetate Catalyzed Multicomponent Cyclization of Aromatic Aldehydes, Acetone and Meldrum Acid

An, Lin<sup>a</sup>(安琳) Yang, Feng<sup>b</sup>(杨芬) Yao, Rong<sup>b</sup>(姚荣) Yan, Chaoguo<sup>\*,b</sup>(颜朝国)

<sup>a</sup> College of Pharmacy, Xuzhou Medical College, Xuzhou, 221004 Jiangsu, China

<sup>b</sup> College of Chemistry & Chemical Engineering, Yangzhou University, Yangzhou, Jiangsu 225002, China

The sodium acetate catalyzed three-component reaction of aromatic aldehyde, acetone and Meldrum acid or spirolactone at room temperature gave stereospecific 7,11-*cis*-diaryl-2,4-dioxaspiro[5,5]undecane-1,5,9-triones in a very efficient manner.

Keywords multicomponent reactions, meldrum acid, spiro compounds, stereospecificity, Knoevenagel condensation

## Introduction

Multicomponent reactions (MCRs) with at least three different substrates reacting in a well-defined manner to form a single compound have emerged as an effective tool for atom economic and benign organic synthesis.<sup>1,2</sup> Due to their convergence, productivity, facile execution and generation of highly diverse products from easily available starting materials, the design of multi-component reactions is an important field of research from the point of view of organic synthesis and combinatorial chemistry.<sup>3,4</sup> The domino Knoevenagel hetero-Diels-Alder reaction represents one of the most effective methods for the synthesis of heterocyclic compounds, especially for natural products synthesis.<sup>5,6</sup> In recent years, the hetero-Diels-Alder reactions have been used widely in numerous reactions of prominence in organic synthesis, because of their economical and stereo-controlled nature. These reactions allow the formation of two or more rings at once and avoid sequential chemical transformations.<sup>7,8</sup> However, only a few examples of domino carbon Knoevenagel/Diels-Alder reaction have been reported and the examples given in the literature are restricted to using organic amine and amino acid as organocatalyst for enantioselective synthesis.<sup>9-13</sup> In this paper, we wish to report using sodium acetate as catalyst for the stereospecific preparation of the spirocyclic compounds via the three component reactions of aromatic aldehydes, acetone and Meldrum acid or 1,5-dioxaspiro[5,5]undecane-2,4-dione.

### **Results and discussion**

Sodium acetate is a mild base catalyst and has been widely used in many condensation reactions and multi-component reactions.<sup>14,15</sup> Elinson *et al.* described a mul-

ticomponent reaction of aryl aldehydes, malononitrile and acetone in the presence of a catalytic amount of sodium acetate. which were stereoselectively cyclized into cis-4-dicyanomethylene-2,6-diarylcyclohexane-1,1-dicarbonitriles in 30%-60% yields.<sup>14</sup> This report promotes us to develop this methodology to the condensation reaction of other active methylene compounds such as Meldrum acid and dimedone. When a mixture of benzaldehyde (3.0 mmol), Meldrum acid (1.5 mmol) and acetone (15 mL) in the presence of anhydrous sodium acetate was stirred at room temperature for about 2 d, the spirocyclic compound 1a was obtained in 59% yield after workup. The reaction conditions were simple and briefly optimized. If the reaction was conducted in higher temperature  $(50-60 \ ^{\circ}C)$  the desired product is difficult to separate due to other byproducts formed. Adding more sodium acetate did not increase the yield of product because its solubility in acetone is very low. Under similar reaction conditions other aromatic aldehydes gave the expected spirocyclic compounds 1b-1f (Table 1) in 43%-85% yields. It should be pointed that a similar three-component pathway using the above mentioned starting materials or using aldehyde, benzalacetone and Meldrum acid in the presence of chiral pyrrolidine derivatives as catalyst had already been described by Ramachary and Barbas,<sup>10-12</sup> and such kind of spirocyclic compounds have been prepared by other synthetic methods.<sup>16-19</sup> It is interesting to find that the prepared siprocyclic compounds in this work were in very pure form because they gave high quality of analytical data only after crystallization in acetone. Aromatic aldehydes with p-chloro, p-bromo, p-methoxyl and p-t-butyl groups showed similar reactivity. When 1,5-dioxaspiro[5,5]undecane-2,4-dione was used in place of Meldrum acid, the desired dispiro-



 <sup>\*</sup> E-mail: cgyan@yzu.edu.cn
 Received January 21, 2010; revised August 16, 2010; accepted August 24, 2010.
 Project supported by the National Natural Science Foundation of China (No. 20972132).

cyclic compounds **1g**—**1j** were obtained in 57%—86% yields. The formation of the spirocyclic compounds **1a**—**1j** could be rationalized by domino Knoevenagel condensation, aldol condensation and Michael addition reaction.

Table 1Synthesis of 7,11-cis-diaryl-2,4-dioxaspiro[5.5]-un-decane-1,5,9-triones

2ArCHO	+ CH <sub>3</sub> COC	$H_3 + $	K <sup>R</sup> NaOAc R CH₃COCH₃ O≓	$ \begin{array}{c}                                     $
Entry	Compd.	R	Ar	Yield/%
1	1a	CH <sub>3</sub>	$C_6H_5$	59
2	1b	$CH_3$	p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	66
3	1c	$CH_3$	p-ClC <sub>6</sub> H <sub>4</sub>	48
4	1d	$CH_3$	p-BrC <sub>6</sub> H <sub>4</sub>	43
5	1e	$CH_3$	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	50
6	1f	$CH_3$	<i>p</i> -(CH <sub>3</sub> ) <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	85
7	1g	(CH <sub>2</sub> ) <sub>5</sub>	$C_6H_5$	57
8	1h	(CH <sub>2</sub> ) <sub>5</sub>	p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	58
9	1i	(CH <sub>2</sub> ) <sub>5</sub>	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	71
10	1j	(CH <sub>2</sub> ) <sub>5</sub>	<i>p</i> -(CH <sub>3</sub> ) <sub>3</sub> CC <sub>6</sub> H <sub>4</sub>	86

The structure of the prepared spirocyclic compounds 1a-1j were fully characterized by <sup>1</sup>H, <sup>13</sup>C NMR, MS, IR spectra and confirmed by X-ray diffraction determination of two single crystals of 1b and 1c. The <sup>1</sup>H NMR data clearly indicated all products **1a-1j** are in *cis*-spirane disastereomer. As for an example, <sup>1</sup>H NMR spectrum of 1i displays a singlet for two methoxyl groups at  $\delta$  3.76, which clearly show the two *p*-methoxyphenyl groups and two CH units in same environment. The two protons at CH units show a dd quartet peak at  $\delta$  3.94 due to the coupling of CH<sub>2</sub> groups at 8and 10-position. The two CH<sub>2</sub> groups at 8- and 10-positions also display two sets of mixed peaks for protons at axial and equatorial positions. The two axial protons show one triplet at  $\delta$  3.66 with J=14.4 Hz, while the two protons at equatorial position display another dd quartet at  $\delta$  2.60 (Figure 1). <sup>1</sup>H NMR spectra of other spiranes also show similar kind of peak pattern,



Figure 1 The partial <sup>1</sup>H NMR spectrum of compound 1i.

that is two sets of dd quartets and one triplet for two bridging CH groups and two CH<sub>2</sub> groups.

According to the carefully analysis of <sup>1</sup>H NMR data and comparison with the earlier reported results,<sup>9-13</sup> we could tentatively conclude that the two aryl groups in spiranes **1a—11** were in the *cis*-position, and this sodium acetate catalyzed multicomponent reaction is a diastereospecific catalytic reaction. The X-ray diffraction determination of single crystals **1b** and **1c** (Figure 2) further confirmed this conclusion. It is clearly seen that the cyclohexanone ring existed in chair conformation and the two *p*-chlorophenyl groups existed in *cis* equatorial orientation.



Figure 2 The molecular structure of compound 1c.

To explain the mechanism of this one-pot multicomponent reaction, we proposed a plausible reaction course, which is illustrated in Scheme 1. The first step is aldol condensation of aromatic aldehyde with acetone to give arylideneacetone (**A**) and Knoevenagel condensation of aromatic aldehyde with Meldrum acid to yield the arylidenemeldrum acid (**B**). The second step is Michael addition of remained methyl group of arylideneacetone (**A**) to intermediate (**B**) to give the addition intermediate (**C**). The third step is the intramolecular Michael addition in intermediate (**C**) to give the final cyclization product. In this straightforward mechanism sodium acetate acted as basic catalyst to

Scheme 1 Formation mechanism of spiro compound 1



accomplish the sequential aldol condensation, Knoevenagel condensation and Michael addition reaction.

The reactivity of other active methylene compounds such as cyclohexane-1,3-dione, dimedone, barbituric acid and 4-hydroxycoumarin in this reaction were also tested. It is pity to find that the reaction only stopped at the stage of Knoevenagel condensation and could went further to give cyclization products, even using previously prepared 1,3-dibenzalacetone to react with dimedone with sodium acetate as catalyst in acetone. After workup the condensation product of dimedone with two molar benzaldehyde was separated as main product, which clearly come from the transformation of benzalidene group from 1,3-dibenzalacetone. This result demonstrated that this multicomponent reaction is controlled by many complicated factors.

In summary we have developed a three component reaction involving aromatic aldehydes, acetone with Meldrum acid or 1,5-dioxaspiro[5,5]undecane-2,4-dione catalyzed by sodium acetate. This simple and practical approach can be used to prepare efficiently spiranes and dispiranes in a diastereospecific fashion.

#### Experimental

# General procedure for the three component reaction of aldehyde, acetone and Meldrum acid

A solution of aromatic aldehyde (3.0 mmol), Meldrum acid (1.5 mmol) or 1,5-dioxaspiro[5,5]undecane-2,4-dione (1.5 mmol) and anhydrous sodium acetate (0.30 g) in 15 mL of acetone was stirred at room temperature for about 48 h. The solvent was evaporated and the residue was washed with water to give the crude product, which was then recrystallized from acetone to yield pure product for analysis.

**3,3-Dimethyl-7,11-diphenyl-2,4-dioxaspiro[5.5]undecane-1,5,9-trione** (1a)<sup>10</sup> Light yellow solid, yield 59%; m.p. 203—206 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.35—7.28 (m, 6H, ArH), 7.24 (d, *J*=7.2 Hz, 4H, ArH), 4.03 (dd, <sup>2</sup>*J*<sub>HH</sub>=15.0 Hz, <sup>3</sup>*J*<sub>HH</sub>=4.2 Hz, 2H, 2CH), 3.73 (t, *J*=15.0 Hz, 2H, CH), 2.66 (dd, <sup>2</sup>*J*<sub>HH</sub>= 15.0 Hz, <sup>3</sup>*J*<sub>HH</sub>=4.2 Hz, 2H), 0.55 (s, 6H, 2CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 207.5, 168.1, 165.2, 137.1, 129.1, 128.6, 128.4, 106.3, 60.5, 50.1, 42.8, 28.3; IR (KBr) *v*: 3031 (w), 2926 (m), 1726 (vs), 1588 (w), 1491 (m), 1452 (m), 1369 (vs), 1118 (m), 853 (m), 703 (s) cm<sup>-1</sup>; MS *m/z* (%): 377.30 ([M-1]<sup>+</sup>, 100).

**3,3-Dimethyl-7,11-di**(*p*-methylphenyl)-2,4-dioxaspiro[5.5]undecane-1,5,9-trione (1b) White solid, yield 66%; m.p. 208—210 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.14—7.10 (m, 8H, ArH), 3.96 (dd, <sup>2</sup>J<sub>HH</sub>=14.4 Hz, <sup>3</sup>J<sub>HH</sub>=4.2 Hz, 2H, 2CH), 3.68 (t, J=14.4 Hz, 2H), 2.60 (dd, <sup>2</sup>J<sub>HH</sub>=15.0 Hz, <sup>3</sup>J<sub>HH</sub>=4.8 Hz, 2H), 2.28 (s, 6H, 2CH<sub>3</sub>), 0.59 (s, 6H, 2CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 207.9, 168.3, 165.4, 138.4, 134.1, 130.1, 129.7, 128.3, 106.2, 60.6, 49.7, 43.0, 28.2, 21.0; IR (KBr) *v*: 3003 (w) 2920 (m), 1753 (m), 1723 (vs), 1576 (s), 1512 (s), 1416 (w), 1289 (m), 1107 (w), 892 (w), 722 (m) cm<sup>-1</sup>; MS m/z (%): 405.46 ([M-1]<sup>+</sup>, 100).

**3,3-Dimethyl-7,11-di**(*p*-chlorophenyl)-2,4-dioxaspiro[5.5]undecane-1,5,9-trione (1c) White solid, yield 48%; m.p. 194—196 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.33 (d, J=2.4 Hz, 4H, ArH), 7.17 (d, J=8.4 Hz, 4H, ArH), 3.98 (dd, <sup>2</sup> $J_{HH}$ =14.4 Hz, <sup>3</sup> $J_{HH}$ =4.2 Hz, 2H, 2CH), 3.65 (t, J=15.0 Hz, 2H), 2.63 (dd, <sup>2</sup> $J_{HH}$ = 14.4 Hz, <sup>3</sup> $J_{HH}$ =4.2 Hz, 2H), 0.67 (s, 6H, 2CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 206.3, 167.9, 165.0, 135.4, 134.8, 129.3, 129.8, 129.4, 106.5, 60.3, 49.4, 42.7, 28.5; IR (KBr) *v*: 2999 (m), 2924 (w), 1918 (w), 1727 (vs), 1594 (m), 1492 (s), 1417 (m), 1388 (m), 1286 (s), 1019 (m), 984 (m), 839 (s), 680 (w) cm<sup>-1</sup>; MS *m*/z (%): 445.53 ([M-1]<sup>+</sup>, 100), 447.33 ([M+1]<sup>+</sup>, 95).

**3,3-Dimethyl-7,11-di**(*p*-bromophenyl)-2,4-dioxaspiro[5.5]undecane-1,5,9-trione (1d) White solid, yield 43%; m.p. 200—202 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.48 (d, *J*=8.4 Hz, 4H, ArH), 7.11 (d, *J*=8.4 Hz, 4H, ArH), 3.96 (dd, <sup>2</sup>*J*<sub>HH</sub>=14.4 Hz, <sup>3</sup>*J*<sub>HH</sub>=4.2 Hz, 2H, 2CH), 3.64 (t, *J*=15.0 Hz, 2H), 2.62 (dd, <sup>2</sup>*J*<sub>HH</sub>= 15.2 Hz, <sup>3</sup>*J*<sub>HH</sub>=4.2 Hz, 2H), 0.68 (s, 6H, 2CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 206.2, 167.9, 165.0, 135.9, 132.3, 130.1, 122.8, 106.5, 60.1, 49.5, 42.6, 28.5; IR (KBr) *v*: 3034 (w) 2996 (m), 2924 (w), 1726 (vs), 1586 (m), 1489 (s), 1371 (m), 1287 (s), 1070 (m), 984 (m), 839 (m), 833 (s), 722 (w) cm<sup>-1</sup>; MS *m*/*z* (%): 535.53 ([M-1]<sup>+</sup>, 100), 537.00 ([M+1]<sup>+</sup>, 65).

**3,3-Dimethyl-7,11-di**(*p*-methoxyphenyl)-2,4-dioxaspiro[5.5]undecane-1,5,9-trione (1e)<sup>10</sup> Light yellow solid, yield 50%; m.p.173—175 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.15 (d, *J*=8.4 Hz, 4H, ArH), 6.85 (d, *J*=8.4 Hz, 4H, ArH), 3.94 (dd, <sup>2</sup>*J*<sub>HH</sub>=14.4 Hz, <sup>3</sup>*J*<sub>HH</sub>=3.6 Hz, 2H, 2CH), 3.76 (s, 6H, 2OCH<sub>3</sub>), 3.65 (t, *J*=14.4 Hz, 2H), 2.60 (dd, <sup>2</sup>*J*<sub>HH</sub>=14.4 Hz, <sup>3</sup>*J*<sub>HH</sub>=3.6 Hz, 2H), 0.65 (s, 6H, 2CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 206.2, 166.8, 163.8, 158.9, 127.9, 127.6, 112.8, 104.7, 59.3, 53.7, 47.6, 41.5, 26.9; IR (KBr) *v*: 2949 (m), 2840 (w), 1725 (vs), 1610 (m), 1513 (s), 1456 (m), 1379 (m), 1285 (s), 1029 (m), 838 (m) cm<sup>-1</sup>; MS *m*/*z* (%): 437.27 ([M-1]<sup>+</sup>, 100).

**3,3-Dimethyl-7,11-di**(*p-tert*-butylphenyl)-2,4-dioxaspiro[5.5]undecane-1,5,9-trione (1f) White solid, yield 85%; m.p. 218—221 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.35 (d, J=8.4 Hz, 4H, ArH), 7.16 (d, J=8.4 Hz, 4H, ArH), 4.00 (dd, <sup>2</sup> $J_{HH}$ =14.4 Hz, <sup>3</sup> $J_{HH}$ =4.2 Hz, 2H, 2CH), 3.72 (t, J=15.0 Hz, 2H), 2.64 (dd, <sup>2</sup> $J_{HH}$ = 15.0 Hz, <sup>3</sup> $J_{HH}$ =4.2 Hz, 2H), 1.25 (s, 18H, 6CH<sub>3</sub>), 0.49 (s, 6H, 2CH<sub>3</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 208.1, 168.3, 165.2, 134.0, 128.0, 126.0, 106.2, 60.9, 49.5, 42.7, 34.4, 31.1, 28.0; IR (KBr) *v*: 2961 (s), 2871 (w), 1730 (vs), 1572 (w), 1467 (m), 1287 (s), 1180 (w), 838 (m), 572 (m) cm<sup>-1</sup>; MS *m*/*z* (%): 488.86 ([M-1]<sup>+</sup>, 100).

**11,5-Bis-phenyl-8,15-dioxadispiro**[**5.2.5.2**]hexadecane-**3,7,16-trione** (**1g**)<sup>10</sup> White solid, yield 57%; m.p. 210—212 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.35— 7.28 (m, 6H, ArH), 7.24 (d, *J*=7.2 Hz, 4H, ArH), 4.00 (dd, <sup>2</sup>*J*<sub>HH</sub>=14.4 Hz, <sup>3</sup>*J*<sub>HH</sub>=4.2 Hz, 2H, 2CH), 3.73 (t,

2453

J=14.4 Hz, 2H), 2.65 (d,  ${}^{2}J_{HH}=14.4$  Hz,  ${}^{3}J_{HH}=4.2$  Hz, 2H), 1.13—1.23 (m, 6H, 3CH<sub>2</sub>), 0.48 (s, 4H, 2CH<sub>2</sub>);  ${}^{13}$ C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 207.5, 168.4, 165.4, 137.2, 129.0, 128.5, 126.4, 106.7, 61.1, 50.1, 42.9, 37.2, 23.6, 21.6; IR (KBr) *v*: 2945 (m), 1758 (vs), 1578 (m), 1513 (m), 1420 (m), 1368 (m), 1259 (vs), 1183 (m), 1034 (m), 831 (m), 530 (m) cm<sup>-1</sup>; MS *m*/*z* (%): 417.40 ([M-1]<sup>+</sup>, 100).

**1,5-Bis**-*p*-methylphenyl-**8**,15-dioxadispiro[5.2.5.2]hexadecane-**3,7,16-trione** (**1h**) White solid, yield 58%; m.p. 178—180 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.12—7.09 (m, 8H, ArH), 3.96 (dd, <sup>2</sup>J<sub>HH</sub>=15.0 Hz, <sup>3</sup>J<sub>HH</sub>=4.2 Hz, 2H, 2CH), 3.69 (t, *J*=14.4 Hz, 2H), 2.61 (dd, <sup>2</sup>J<sub>HH</sub>=14.4 Hz, <sup>3</sup>J<sub>HH</sub>=4.2 Hz, 2H), 2.28 (s, 6H, 2CH<sub>3</sub>), 1.24—1.14 (m, 6H, 3CH<sub>2</sub>), 0.52 (s, 4H, 2CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 208.1, 168.6, 165.6, 138.4, 134.2, 129.6, 128.2, 106.7, 61.2, 49.7, 43.0, 37.2, 23.6, 21.7, 20.9; IR (KBr) *v*: 2930 (s), 2862 (w), 1726 (vs), 1576 (m), 1513 (w), 1411 (w), 1268 (m), 1074 (m), 825 (m), 722 (w), 523 (m) cm<sup>-1</sup>; MS *m*/*z* (%): 445.29 ([M-1]<sup>+</sup>, 100).

**1,5-Bis**-*p*-methoxyphenyl-8,15-dioxadispiro-[5.2.5.2]hexadecane-3,7,16-trione (1i)<sup>10</sup> White solid, yield 71%; m.p. 183—186 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.14 (d, *J*=4.8 Hz, 4H, ArH), 6.84 (d, *J*=8.4 Hz, 4H, ArH), 3.94 (dd, <sup>2</sup>*J*<sub>HH</sub>=14.4 Hz, <sup>3</sup>*J*<sub>HH</sub>=4.2 Hz, 2H, 2CH), 3.76 (s, 6H, 2OCH<sub>3</sub>), 3.66 (t, *J*=14.4 Hz, 2H), 2.60 (dd, <sup>2</sup>*J*<sub>HH</sub>=15.0 Hz, <sup>3</sup>*J*<sub>HH</sub>=4.2 Hz, 2H) 1.28—1.16 (m, 6H, 3CH<sub>2</sub>), 0.59 (s, 4H, 2CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 207.9, 168.7, 165.7, 159.6, 129.5, 129.3, 114.36, 106.8, 61.6, 55.4, 49.3, 43.2, 37.4, 23.7, 21.8; IR (KBr) *v*: 2940 (m), 1726 (vs), 1436 (m), 1301 (s), 1206 (s), 920 (m), 767 (w), 558 (m) cm<sup>-1</sup>; MS *m*/*z* (%): 477.53 ([M-1]<sup>+</sup>, 100).

**1,5-Bis**-*p*-tert-butylphenyl-8,15-dioxadispiro-[5.2.5.2]hexadecane-3,7,16-trione (1j) White solid, yield 86%; m.p. 254—256 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$ : 7.33 (d, J =8.4 Hz, 4H, ArH), 7.15 (d, J=8.4 Hz, 4H, ArH), 3.99 (dd, <sup>2</sup> $J_{HH}$ =14.4 Hz, <sup>3</sup> $J_{HH}$ =4.2 Hz, 2H, 2CH), 3.72 (t, J=14.4 Hz, 2H), 2.64 (dd, <sup>2</sup> $J_{HH}$ =14.4 Hz, <sup>3</sup> $J_{HH}$ =4.8 Hz, 2H), 1.24 (s, 18H, 6CH<sub>3</sub>), 1.27 —1.11 (m, 6H, 3CH<sub>2</sub>), 0.43—0.41 (m, 4H, 2CH<sub>2</sub>); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 150 MHz)  $\delta$ : 208.2, 168.4, 165.3, 151.8, 134.1, 128.0, 125.9, 106.6, 61.4, 49.4, 37.1, 34.5, 31.2, 23.6, 21.6; IR (KBr) *v*: 2959 (s) 2866 (w), 1762 (w), 1726 (vs), 1580 (m), 1512 (w), 1416 (w), 1280 (m), 836 (m), 712 (w) cm<sup>-1</sup>; MS m/z (%): 529.38 ([M-1]<sup>+</sup>, 100).

#### Supplement data

The single crystal data of compounds **1b** and **1c** have been deposited at the Cambridge Crystallographic Database Centre with CCDC 755442 (**1b**) and 755443 (**1c**).

#### References

- 1 Weber, L.; Illegen, K.; Almstetter, M. Synlett 1999, 366.
- Armstrong, R. W.; Combs, A. P.; Tempest, P. A.; Brown, S. D.; Keating, T. A. Acc. Chem. Res. 1996, 29, 123.
- 3 Domling, A.; Ugi, I. Angew. Chem., Int. Ed. 2000, 39, 3168.
- 4 Tietze, L. F. Chem. Rev. **1996**, 96, 115.
- 5 Tietze, L. F.; Kettschau, G. Top. Curr. Chem. 1997, 189, 1.
- 6 Behforouz, M.; Ahmadian, M. Tetrahedron 2000, 56, 5259.
- 7 Zhu, J. P.; Bienaymé, H. Multicomponent Reactions, Weinheim, Wiley-VCH, 2004.
- 8 Schmidt, R. R. Acc. Chem. Res. 1986, 19, 250.
- 9 List, B.; Castello, C. Synlett 2001, 1687.
- 10 Ramachary, D. B.; Barbas, C. F. III Chem. Eur. J. 2004, 10, 5323.
- 11 Ramachary D. B.; Anebouselvy, K.; Chowdari, N. S.; Barbas, C. F. III J. Org. Chem. 2004, 69, 5838.
- 12 Ramachary, D. B.; Chowdari, N. S.; Barbas, C. F. III Synlett 2003, 1910.
- Pizzirani, D.; Roberti, M.; Recanatini, M. *Tetrahedron Lett.* 2007, 48, 7120.
- 14 Elinson, M. N.; Vereshchagin, A. N.; Feducovich, S. K.; Zaimovskaya, T. A.; Starikova, Z. A.; Belyakova, P. A. *Tetrahedron Lett.* 2007, 48, 6614.
- 15 Liu, W. B.; Jiang, H. F.; Zhu, S. F.; Wang, W. *Tetrahedron* 2009, 65, 7985.
- 16 Chande, M. S.; Khanwelkar, R. R. Tetrahedron Lett. 2005, 46, 7787.
- 17 Shults, E.; Semenova, E.; Johnson, A.; Bondarenko, S.; Bagryanskaya, I.; Gatilov, Y.; Tolstikova, G.; Pomier, Y. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1362.
- 18 Jiang, B.; Hao, W. J.; Zhang, J. P.; Tu, S. J.; Shi, F. Org. Biomol. Chem. 2009, 7, 2195.
- 19 Hao, W. J.; Jiang, J.; Tu, S. J.; Wu, S. S.; Han, Z. G.; Cao, X. D.; Zhang, X. H.; Yan, Y.; Shi, F. J. Comb. Chem. 2009, 11, 310.

(E2001211 Zhao, C.)