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PAPER

A novel synthesis of oxazolidine-2,4-diones *via* an efficient fixation of CO_2 with 3-aryl-2-alkynamides†

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A very mild protocol for fixation of carbon dioxide with 2-alkynamides in DMSO at 30 °C using a CO_2 balloon in the presence of K_2CO_3 has been developed, which leads to an efficient assembly of oxazolidine-2,4-diones. It is observed that the regioselectivity was controlled by the aryl group.

Introduction

Recently much attention has been paid to the chemistry of carbon dioxide as an attractive carbon resource in organic synthesis. More and more methods for transformations of CO_2 into useful organic compounds have been reported.[1] In this area, the reaction of propargyl alcohols and amines with CO_2 yielding cyclic carbonates and urethanes has already been well described in the literature.[2] However, due to the low nucleophilicity of amide, the fixation of CO_2 with amide has seldom been reported.[3] On the other hand, we noticed that oxazolidine-2,4-diones are widely used in medicine and agriculture as antiepileptic agents,[4a] anti-inflammatory agents,[4b–c] herbicides,[4f–g] and the synthesis of oxazolidine-2,4-diones is usually lengthy (Fig. 1).[4] Besides transformations from heterocyclic intermediates, the most general methods are the cyclizations of α-hydroxy esters with urea or isocyanates and α-hydroxy amides with chloroformates or carbonates (Scheme 1).[4a,5] However, the most efficient route to oxazolidine-2,4-diones would be from the reactions of 2-alkenamide or 2-alkynamide with CO_2. Recently, we have reported the fixation of CO_2 with 2,3-allenamides under mild conditions to synthesize 1,3-oxazine-2,4-diones (eqn (1)).[6] Herein, we wish to report a simple chemical fixation of CO_2 with 3-aryl-2-alkynamides for unexpected synthesis of oxazolidine-2,4-diones.

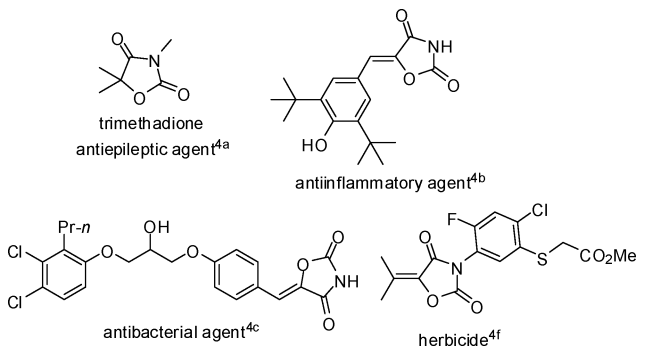
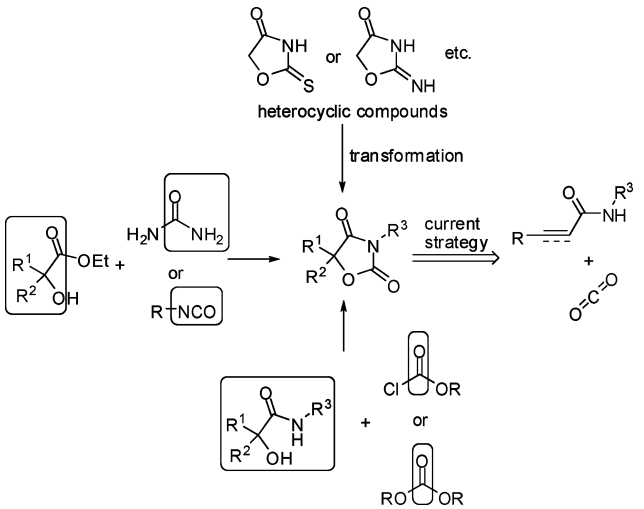
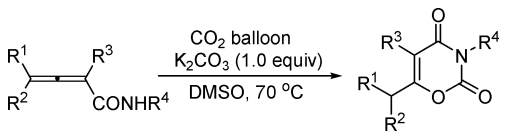


Fig. 1 Some biologically active oxazolidine-2,4-diones.



Scheme 1 Synthesis of oxazolidine-2,4-diones.



(1)

Results and discussion

We used *N*-benzyl-3-phenylpropiolamide **1a** as the substrate to test the reaction under the CO_2 transformation conditions for the reaction of 2,3-allenamides with CO_2.[6] Fortunately, we observed the formation of a new solid compound in 16% yield determined by ^{1}H NMR spectroscopy (entry 1, Table 1). With the X-ray diffraction study, we learned that the solid compound was

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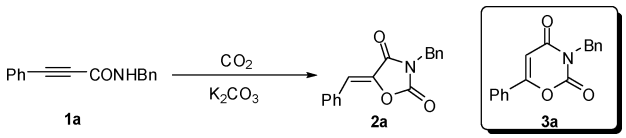
Table 1 Optimization of reaction conditions for the reaction of *N*-benzyl-3-phenylpropiolamide **1a** with carbon dioxide[a]



entry	solvent	base (equiv)	temp. (°C)	time (h)	yield (%) of **2a**	recovery of **1a**
1	DMSO	1.0	70	3	16	0
2	DMSO	1.0	30	11	75	9
3[b]	DMSO	1.0	30	11	0	100
4	DMF	2.0	30	11	65	22
5	DMA	2.0	30	11	40	30
6	**DMSO**	**2.0**	**30**	**11**	**75**	**0**
7	DMSO	3.0	30	11	77	0
8[c]	DMSO	2.0	30	11	66	0
9[d]	DMSO	2.0	30	11	0	93

[a] The reaction was carried out using 0.2 mmol of **1a** in dried solvent with a CO_2 balloon, and the yields were determined by ^1H NMR analysis with CH_2Br_2 as the internal standard. [b] DMSO was commercially available and used without treatment. [c] The reaction was carried out under CO_2 atmosphere. [d] The reaction was carried out under N_2 atmosphere.

oxazolidine-2,4-dione **2a** with a single *Z* configuration but not 1,3-oxazine-2,4-dione **3a** as we were expecting (Fig. 2).[7] Encouraged by this result, we optimized the reaction conditions for the chemical fixation of CO_2 with **1a**. Some typical reaction conditions are summarized in Table 1. Due to the possible instability of product **2a**, we lowered the reaction temperature to 30 °C, and **2a** was formed in 75% yield determined by ^1H NMR spectroscopy with 9% recovery of starting material **1a** within 11 h (entry 2, Table 1). No reaction occurred with 100% recovery of starting material **1a** when commercial DMSO was used, which shows that a trace amount of water in DMSO may stop this transformation in the deprotonation step (entry 3, Table 1). When 2.0 equiv of K_2CO_3 were used, **2a** was obtained in 75% yield determined by ^1H NMR spectroscopy with complete conversion of the starting material **1a** within 11 h (entry 6, Table 1). Increasing the concentration of K_2CO_3 to 3.0 equiv did not improve the yield of **2a** very much (entry 7, Table 1). Without the CO_2 balloon, the yield of **2a** dropped to 66% determined by ^1H NMR spectroscopy under the CO_2 atmosphere (entry 8, Table 1). When the reaction was carried out in the presence of K_2CO_3 under N_2 atmosphere, the formation of oxazolidine-2,4-dione **2a** was not observed with 93% recovery of the starting material **1a**, which indicated that the CO_2 unit in the product **2a** was from the CO_2 gas, not the carbonate base K_2CO_3 (entry 9, Table 1).

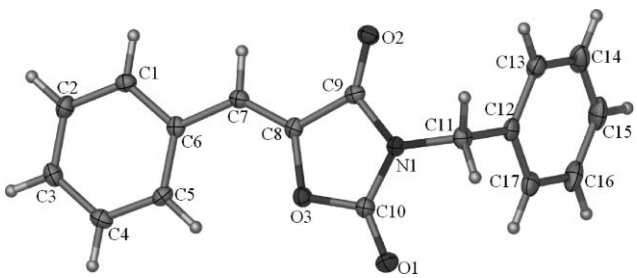
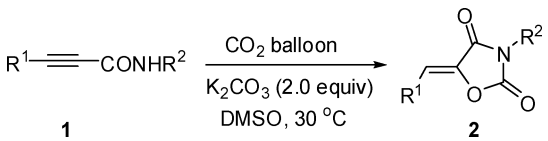


Fig. 2 ORTEP representation of **2a**.

Some typical results of different 3-aryl-2-alkynamides under the optimized conditions are listed in Table 2. The substituent R^2 on

Table 2 Reaction of different 2-alkynamides with carbon dioxide[a]



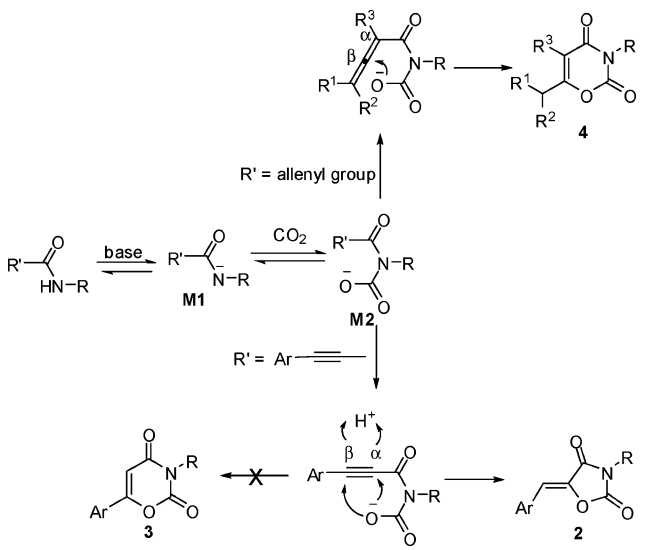
entry	R^1	R^2	time (h)	isolated yield (%) of **2**
1	Ph	Bn (**1a**)	11	62 (**2a**)
2	Ph	*n*-Bu (**1b**)	11	80 (**2b**)
3	Ph	Et (**1c**)	11	66 (**2c**)
4	Ph	allyl (**1d**)	11	72 (**2d**)
5[b,c]	Ph	*i*-Pr (**1e**)	11	68 (**2e**)
6[d]	Ph	*i*-Pr (**1e**)	11	46 (**2e**)
7[e]	Ph	H (**1f**)	11	0
8	4-PrC_6H_4	*n*-Bu (**1g**)	12	69 (**2g**)
9	4-MeC_6H_4	*n*-Bu (**1h**)	16	69 (**2h**)
10	4-MeOC_6H_4	*n*-Bu (**1i**)	11	67 (**2i**)
11	4-MeOC_6H_4	Bn (**1j**)	11	68 (**2j**)
12	4-FC_6H_4	*n*-Bu (**1k**)	11	72 (**2k**)
13	3-thienyl	Bn (**1l**)	11	61 (**2l**)
14[b]	2-thienyl	Bn (**1m**)	11	55 (**2m**)
15[f]	cyclohexenyl	Bn (**1n**)	11	0
16[g]	*n*-Bu	Bn (**1o**)	11	0

[a] The reaction was carried out using 0.2 mmol of **1** and 2.0 equiv of K_2CO_3 in DMSO (distilled from CaH_2) with a CO_2 balloon at 30 °C unless otherwise stated. [b] K_2CO_3 (3.0 equiv) was used. [c] Compound **1e** was recovered in 16% yield. [d] Cs_2CO_3 (2.0 equiv) was used. [e] Compound **1f** was recovered in 64% yield. [f] Compound **1n** was recovered in 92% yield. [g] Compound **1o** was recovered in 100% yield.

the nitrogen atom of 2-alkynamides can be alkyl, benzyl and allyl groups (entries 1–4, Table 2). When the *i*-propyl group substituted 2-alkynamide **1e** was applied, the product **2e** was afforded in 68% yield with 16% recovery of **1e** even using 3.0 equiv of K_2CO_3 due to the steric effect (entry 5, Table 2). Using a stronger base such as Cs_2CO_3, the yield of **2e** was 46% though the starting material **1e** was consumed completely (entry 6, Table 2). However, when 3-phenylpropiolamide **1f** was applied, no reaction occurred with 64% recovery of the starting material (entry 7, Table 2).

The substituent R^1 can be phenyl groups bearing both electron-donating and electron-withdrawing groups (entries 8–12, Table 2). Heterocyclic aryl groups such as 2- or 3-thienyl group substituted 2-alkynamides could also be applied to the reaction with slightly lower yields (entries 13 and 14, Table 2). It should be noted that the reaction of cyclohexenyl substituted propiolamides **1n** and *n*-butyl substituted propiolamides **1o** under the same reaction conditions did not occur with recovery of starting materials, which shows the importance of the aryl group moiety for this transformation (entries 15–16, Table 2).

Based on these facts, a rational mechanism for the formation of **2** is depicted in Scheme 2. The amide **1** would lose a proton under the basic conditions with K_2CO_3 to form anionic intermediate **M1**, which may attack the carbon atom in carbon dioxide to form the intermediate **M2**. There is an issue of regioselectivity (α *vs.* β). When the R′ is an allenyl group, the oxygen anion would attack the central carbon atom in the allene moiety (β carbon atom) to form six-membered product **4**, which was controlled by the carbonyl group. However, when the amide was changed to 3-aryl-2-alkynamide, although both 5-exo-dig and 6-endo-dig are favored according to the Baldwin's rule, the oxygen anion in the intermediate **M2** would attack α carbon atom in the C–C triple bond to form five-membered product **2**, which was obviously directed by the aryl group. This also explains why the aryl group is so important in this reaction and why the alkyl substituted 2-alkynamides fail for this reaction.



Scheme 2 Reaction mechanism.

Conclusions

In conclusion, we have developed a very mild protocol for fixation of carbon dioxide with 2-alkynamides in DMSO at 30 °C using a CO_2 balloon in the presence of K_2CO_3, which leads to an efficient assembly of oxazolidine-2,4-diones. The regioselectivity of this reaction was controlled by the aryl group which is different from the reaction of 2,3-allenamides with carbon dioxide. As a result of the easy availability of starting materials, the usefulness of the products and the efficient fixation of carbon dioxide, this reaction may have potentials in organic synthesis. Further studies including expanding the substrate scope in this area are being pursued in our laboratory.

Experimental

Materials

DMSO was distilled from CaH_2. THF was distilled from Na/benzophenone. Et_3N was distilled from KOH. The other commercially available chemicals were purchased and used without additional purification unless noted otherwise.

Synthesis of starting materials

Known compounds **1a**,[8a] **1b**,[8b] **1c**,[8c] **1d**,[8d] **1e**,[8c] **1f**,[8a] **1j**,[8e] **1o**[8f] and new compounds **1g–1i**, **1k–1n** were prepared following the known procedure.[8a]

***N*-(*n*-Butyl)-3-(4-*n*-propylphenyl)propiolamide (1g).** To the reaction vessel containing ethyl 3-(4-*n*-propylphenyl)propiolate (1.0808 g, 5.00 mmol) were added 2 mL of H_2O and 2 mL of *n*-$BuNH_2$ sequentially, Then the resulting solution was stirred at room temperature. After 15 h, the reaction was diluted with 25 mL of CH_2Cl_2, washed with water twice, and dried over anhydrous Na_2SO_4. After filtration and evaporation, chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5/1) of the crude product afforded **1g** (1.1213 g, 92%) as a solid, m.p.: 48.0–49.0 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51–7.39 (m, 2H, Ar-*H*), 7.22–7.10 (m, 2H, Ar-*H*), [5.92 (bs), 5.76 (bs), 1H, N*H*], [3.49 (q, *J* = 6.8 Hz), 3.35 (q, *J* = 6.7 Hz), 2H, N-CH_2], 2.70–2.50 (m, 2H, Ar-CH_2), 1.71–1.47 (m, 4H, 2×MeCH_2), 1.46–1.30 (m, 2H, CH_2), 1.01–0.83 (m, 6H, 2×Me); MS (*m*/*z*): 244 (M^+ + 1, 2.47), 243 (M^+, 14.26), 171 (100); IR (KBr, cm^{-1}): 3285, 2959, 2931, 2866, 2226, 1629, 1537, 1464, 1433, 1410, 1375, 1307, 1223, 1179, 1151, 1112; Anal. Calcd. for $C_{16}H_{21}NO$: C 78.97, H 8.70, N 5.76; Found: C 79.16, H 8.72, N 6.08%.

***N*-(*n*-Butyl)-3-(*p*-tolyl)propiolamide (1h).** Following the procedure for the preparation of **1g**, the reaction of 1.0657 g (5.67 mmol) of ethyl 3-(*p*-tolyl)propiolate, 2 mL of H_2O and 2 mL of *n*-$BuNH_2$ afforded 1.0541 g (86%) of **1h** (eluent: petroleum ether/ethyl acetate = 10/1–5/1) as a solid, m.p.: 56.9–57.4 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47–7.37 (m, 2H, Ar-*H*), 7.22–7.10 (m, 2H, Ar-*H*), [5.95 (bs), 5.81 (bs), 1H, N*H*], [3.48 (q, *J* = 6.7 Hz), 3.35 (q, *J* = 6.7 Hz), 2H, N-CH_2], [2.38 (s), 2.36 (s), 3H, Ar-CH_3], 1.63–1.48 (m, 2H, CH_2), 1.48–1.30 (m, 2H, MeCH_2), 1.01–0.88 (m, 3H, Me); MS (*m*/*z*): 216 (M^+ + 1, 1.61), 215 (M^+, 10.30), 143 (100); IR (KBr, cm^{-1}): 3271, 2961, 2932, 2872, 2216, 1630, 1534, 1464, 1377, 1353, 1303, 1222, 1209, 1182, 1023; Anal. Calcd. for $C_{14}H_{17}NO$: C 78.10, H 7.96, N 6.51; Found: C 77.99, H 7.81, N 6.63%.

***N*-(*n*-Butyl)-3-(4-methoxyphenyl)propiolamide (1i).** Following the procedure for the preparation of **1g**, the reaction of 1.0130 g (4.97 mmol) of ethyl 3-(4-methoxyphenyl)propiolate, 2 mL of H_2O and 2 mL of *n*-$BuNH_2$ afforded 1.1276 g (98%) of **1i** as a solid, m.p.: 66.2–67.0 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.42 (m, 2H, Ar-*H*), 6.92–6.80 (m, 2H, Ar-*H*), 6.02 (bs, 1H, N*H*), [3.82 (s), 3.81 (s), 3H, OMe], [3.47 (q, *J* = 7.0 Hz), 3.34 (q, *J* = 6.8 Hz), 2H, N-CH_2], 1.65–1.48 (m, 2H, CH_2), 1.48–1.27 (m, 2H, MeCH_2), 1.00–0.87 (m, 3H, Me); MS (*m*/*z*): 232 (M^+ + 1, 2.02),

231 (M^+, 13.76), 159 (100); IR (KBr, cm^{-1}): 3269, 3051, 2959, 2925, 2871, 2210, 1630, 1605, 1537, 1510, 1465, 1438, 1287, 1252, 1224, 1172, 1107, 1031; Anal. Calcd. for $C_{14}H_{17}NO_2$: C 72.70, H 7.41, N 6.06; Found: C 72.69, H 7.41, N 6.07%.

***N*-(*n*-Butyl)-3-(4-fluorophenyl)propiolamide (1k).** Following the procedure for the preparation of **1g**, the reaction of 0.9706 g (5.06 mmol) of ethyl 3-(4-fluorophenyl)propiolate, 2 mL of H_2O and 2 mL of *n*-$BuNH_2$ afforded **1k** with some minor impurity after purification by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5/1). This product was further purified by recrystallization to afford 0.9623 g (87%) of **1k** (*n*-hexane/CH_2Cl_2) as a solid, m.p.: 59.1–59.5 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.45 (m, 2H, Ar-*H*), 7.15–6.98 (m, 2H, Ar-*H*), [5.97 (bs), 5.85 (s), 1H, N*H*], [3.48 (q, *J* = 6.7 Hz), 3.35 (q, *J* = 6.6 Hz), 2H, N-CH_2], 1.65–1.46 (m, 2H, CH_2), 1.46–1.29 (m, 2H, MeCH_2), 1.00–0.81 (m, 3H, Me); ^{19}F NMR (282 MHz, $CDCl_3$) δ −107.15, −107.61 (standard by frequency conversion of $CDCl_3$); MS (*m*/*z*): 220 (M^+ + 1, 1.17), 219 (M^+, 7.79), 147 (100); IR (KBr, cm^{-1}): 3304, 2964, 2935, 2868, 2229, 1624, 1598, 1538, 1505, 1471, 1400, 1375, 1351, 1307, 1231, 1157, 1095; Anal. Calcd. for $C_{13}H_{14}FNO$: C 71.21, H 6.44, N 6.39; Found: C 71.15, H 6.45, N 6.35%.

***N*-Benzyl-3-(3-thienyl)propiolamide (1l).** Following the procedure for the preparation of **1g**, the reaction of 1.1863 g (6.59 mmol) of ethyl 3-(3-thienyl)propiolate, 2.5 mL of H_2O and 2.5 mL of $BnNH_2$ afforded **1l** with some minor impurity after purification by chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5/1–3/1). This product was further purified by recrystallization to afford 0.8678 g (54%) of **1l** (*n*-hexane/CH_2Cl_2) as a solid, m.p.: 111.4–112.0 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68–7.62 (m, 1H, Ar-*H*), 7.42–7.27 (m, 6H, Ar-*H*), 7.20–7.14 (m, 1H, Ar-*H*), 6.16 (bs, 1H, N*H*), [4.69 (d, *J* = 7.2 Hz), 4.54 (d, *J* = 5.7 Hz), 2H, N-CH_2]; MS (*m*/*z*): 242 (M^+ + 1, 12.00), 241 (M^+, 64.86), 135 (100); IR (KBr, cm^{-1}): 3215, 3105, 3036, 2847, 2218, 1625, 1558, 1494, 1452, 1420, 1359, 1294, 1225, 1172, 1089, 1030; Anal. Calcd. for $C_{14}H_{11}NOS$: C 69.68, H 4.59, N 5.80; Found: C 69.79, H 4.72, N 6.03%.

***N*-Benzyl-3-(2-thienyl)propiolamide (1m).** Following the procedure for the preparation of **1g**, the reaction of 0.4535 g (2.52 mmol) of ethyl 3-(2-thienyl)propiolate, 1 mL of H_2O and 1 mL of $BnNH_2$ afforded 0.2171 g (36%) of **1m** (eluent: petroleum ether/ethyl acetate = 5/1–3/1) as a solid, m.p.: 107.3–107.6 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47–7.21 (m, 7H, Ar-*H*), 7.07–6.95 (m, 1H, Ar-*H*), [6.22 (bs), 6.05 (bs), 1H, N*H*], [4.67 (d, *J* = 6.3 Hz), 4.54 (d, *J* = 5.7 Hz), 2H, N-CH_2]; MS (*m*/*z*): 242 (M^+ + 1, 9.74), 241 (M^+, 50.45), 135 (100); IR (KBr, cm^{-1}): 3273, 3088, 2207, 1625, 1583, 1552, 1496, 1453, 1425, 1366, 1277, 1231, 1180, 1061, 1029, 1009; Anal. Calcd. for $C_{14}H_{11}NOS$: C 69.68, H 4.59, N 5.80; Found: C 69.74, H 4.60, N 6.12%.

***N*-(*n*-Butyl)-3-cyclohexenylpropiolamide (1n).** Following the procedure for the preparation of **1g**, the reaction of 0.9073 g (5.10 mmol) of ethyl 3-cyclohexenylpropiolate, 2 mL of H_2O and 2 mL of *n*-$BuNH_2$ afforded 0.9200 g (88%) of **1n** (eluent: petroleum ether/ethyl acetate = 3/1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.41–6.27 (m, 1H, ═C*H*), 5.80 (bs, 1H, N*H*), [3.38 (q, *J* = 6.7 Hz), 3.29 (q, *J* = 6.7 Hz), 2H, N-CH_2], 2.21–2.02 (m, 4H, CH_2-C═C-CH_2), 1.69–1.45 (m, 6H, 3×CH_2), 1.44–1.25 (m, 2H, MeCH_2), 1.00–0.83 (m, 3H, Me); MS (*m*/*z*): 206 (M^+ + 1, 1.98), 205 (M^+, 8.93), 133 (100); IR (neat, cm^{-1}): 3263, 3054, 2931, 2862, 2207, 1633, 1538, 1435, 1360, 1348, 1290, 1265, 1226, 1184, 1137, 1077; Anal. Calcd. for $C_{13}H_{19}NO$: C 76.06, H 9.33, N 6.82; Found: C 76.03, H 9.27, N 6.73%.

Reactions of 2-alkynamides with CO_2

(*Z*)-3-Benzyl-5-benzylideneoxazolidine-2,4-dione (2a). To the reaction vessel containing K_2CO_3 (54.5 mg, 0.39 mmol) were charged **1a** (46.2 mg, 0.20 mmol) and 2 mL of DMSO sequentially under CO_2 atmosphere. The CO_2 gas from a CO_2 balloon was dried by passing through a gas washing bottle with conc. H_2SO_4 and directed through a relief needle fixed with the rubber stopper to the reaction mixture. The resulting solution was heated at 30 °C with stirring. After 11 h, the reaction was quenched with 10 mL of H_2O, extracted with ether (15 mL × 3), washed with brine, and dried over anhydrous Na_2SO_4. After filtration and evaporation, chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20/1) of the crude product afforded **2a** (34.0 mg, 62%) as a solid, m.p.: 158.2–159.2 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79–7.70 (m, 2H, Ar-*H*), 7.50–7.29 (m, 8H, Ar-*H*), 6.78 (s, 1H, ═C*H*), 4.80 (s, 2H, N-CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.0, 152.0, 137.4, 134.3, 131.1, 130.6, 130.5, 129.0, 128.9, 128.8, 128.5, 113.8, 43.8; MS (*m*/*z*): 280 (M^+ + 1, 14.65), 279 (M^+, 78.90), 118 (100); IR (KBr, cm^{-1}): 1807, 1733, 1674, 1495, 1451, 1433, 1398, 1340, 1309, 1291, 1235, 1170, 1081, 1067; Anal. Calcd. for $C_{17}H_{13}NO_3$: C 73.11, H 4.69, N 5.02; Found: C 73.20, H 4.72, N 4.96%.

(*Z*)-5-Benzylidene-3-(*n*-butyl)oxazolidine-2,4-dione (2b). Following the procedure for the preparation of **2a**, the reaction of 40.1 mg (0.20 mmol) of **1b** and 55.8 mg (0.40 mmol) of K_2CO_3 in DMSO (2 mL) afforded 39.0 mg (80%) of **2b** (eluent: petroleum ether/ethyl acetate = 25/1) as a solid, m.p.: 82.7–83.4 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80–7.71 (m, 2H, Ar-*H*), 7.50–7.36 (m, 3H, Ar-*H*), 6.76 (s, 1H, ═C*H*), 3.65 (t, *J* = 7.4 Hz, 2H, N-CH_2), 1.78–1.62 (m, 2H, CH_2), 1.46–1.30 (m, 2H, MeCH_2), 0.96 (t, *J* = 7.4 Hz, 3H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.4, 152.3, 137.5, 131.0, 130.7, 130.4, 129.0, 113.3, 40.0, 29.6, 19.8, 13.5; MS (*m*/*z*): 246 (M^+ + 1, 4.12), 245 (M^+, 25.65), 118 (100); IR (KBr, cm^{-1}): 1816, 1721, 1666, 1495, 1449, 1413, 1354, 1315, 1264, 1236, 1187, 1082, 1006; Anal. Calcd. for $C_{14}H_{15}NO_3$: C 68.56, H 6.16, N 5.71; Found: C 68.88, H 6.40, N 5.72%.

(*Z*)-5-Benzylidene-3-ethyloxazolidine-2,4-dione (2c). Following the procedure for the preparation of **2a**, the reaction of 34.2 mg (0.20 mmol) of **1c** and 55.4 mg (0.40 mmol) of K_2CO_3 in DMSO (2 mL) afforded 28.4 mg (66%) of **2c** (eluent: petroleum ether/ethyl acetate = 25/1) as a solid, m.p.: 123.6–124.3 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85–7.68 (m, 2H, Ar-*H*), 7.52–7.35 (m, 3H, Ar-*H*), 6.75 (s, 1H, ═C*H*), 3.71 (q, *J* = 7.2 Hz, 2H, N-CH_2), 1.32 (t, *J* = 7.2 Hz, 3H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.1, 152.0, 137.5, 131.0, 130.7, 130.4, 129.0, 113.2, 35.3, 13.0; MS (*m*/*z*): 218 (M^+ + 1, 5.78), 217 (M^+, 43.70), 118 (100); IR (KBr, cm^{-1}): 1813, 1735, 1682, 1496, 1452, 1441, 1415, 1372, 1347, 1320, 1246, 1211, 1169, 1115, 1080, 1045; Anal. Calcd. for $C_{12}H_{11}NO_3$: C 66.35, H 5.10, N 6.45; Found: C 66.31, H 5.33, N 6.46%.

(*Z*)-3-Allyl-5-benzylideneoxazolidine-2,4-dione (2d). Following the procedure for the preparation of **2a**, the reaction of 36.7 mg (0.20 mmol) of **1d** and 56.2 mg (0.41 mmol) of K_2CO_3 in DMSO (2 mL) afforded 32.6 mg (72%) of **2d** (eluent: petroleum ether/ethyl acetate = 15/1) as a solid, m.p.: 79.7–80.5 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84–7.68 (m, 2H, Ar-*H*), 7.50–7.36 (m, 3H, Ar-*H*), 6.78 (s, 1H, ═C*H*-Ar), 6.00–5.78 (m, 1H, ═C*H*-CH_2), 5.45–5.25 (m, 2H, ═CH_2), 4.25 (d, J = 5.7 Hz, 2H, N-CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.8, 151.8, 137.4, 131.1, 130.6, 130.5, 129.5, 129.0, 119.6, 113.6, 42.2; MS (*m*/*z*): 230 (M^+ + 1, 6.03), 229 (M^+, 41.47), 118 (100); IR (KBr, cm^{-1}): 1816, 1740, 1682, 1452, 1433, 1403, 1351, 1238, 1176, 1101; Anal. Calcd. for $C_{13}H_{11}NO_3$: C 68.11, H 4.84, N 6.11; Found: C 68.47, H 5.01, N 5.99%.

(*Z*)-5-Benzylidene-3-isopropyloxazolidine-2,4-dione (2e). Following the procedure for the preparation of **2a**, the reaction of 37.6 mg (0.20 mmol) of **1e** and 82.9 mg (0.60 mmol) of K_2CO_3 in DMSO (2 mL) afforded 31.5 mg (68%) of **2e** (eluent: petroleum ether/ethyl acetate = 25/1) as a solid, m.p.: 123.8–125.0 °C (*n*-hexane/CH_2Cl_2). The reaction of 37.0 mg (0.20 mmol) of **1e** and 132.7 mg (0.41 mmol) of Cs_2CO_3 in DMSO (2 mL) afforded 20.8 mg (46%) of **2e**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80–7.69 (m, 2H, Ar-*H*), 7.50–7.36 (m, 3H, Ar-*H*), 6.72 (s, 1H, ═C*H*), 4.44 (heptet, J = 7.0 Hz, 1H, N-C*H*), 1.49 (d, J = 7.0 Hz, 6H, 2×Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.2, 151.5, 137.2, 131.0, 130.8, 130.3, 129.0, 112.9, 45.3, 19.4; MS (*m*/*z*): 232 (M^+ + 1, 5.15), 231 (M^+, 34.78), 118 (100); IR (KBr, cm^{-1}): 1815, 1738, 1686, 1666, 1496, 1452, 1403, 1388, 1371, 1347, 1249, 1207, 1181, 1071, 1021, 1002; Anal. Calcd. for $C_{13}H_{13}NO_3$: C 67.52, H 5.67, N 6.06; Found: C 67.48, H 5.73, N 6.11%.

(*Z*)-3-(*n*-Butyl)-5-(4-*n*-propylbenzylidene)oxazolidine-2,4-dione (2g). Following the procedure for the preparation of **2a**, the reaction of 48.2 mg (0.20 mmol) of **1g** and 56.0 mg (0.41 mmol) of K_2CO_3 in DMSO (2 mL) afforded 39.3 mg (69%) of **2g** (eluent: petroleum ether/ethyl acetate = 25/1) as a liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 8.4 Hz, 2H, Ar-*H*), 7.23 (d, J = 8.4 Hz, 2H, Ar-*H*), 6.74 (s, 1H, ═C*H*), 3.64 (t, J = 7.4 Hz, 2H, N-CH_2), 2.61 (t, J = 7.7 Hz, 2H, Ar-CH_2), 1.78–1.57 (m, 4H, 2×MeCH_2), 1.46–1.30 (m, 2H, CH_2), 1.02–0.89 (m, 6H, 2×Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.4, 152.3, 145.8, 136.9, 131.1, 129.1, 128.2, 113.5, 40.0, 37.9, 29.6, 24.2, 19.8, 13.7, 13.5; MS (*m*/*z*): 288 (M^+ + 1, 6.70), 287 (M^+, 34.43), 160 (100); IR (neat, cm^{-1}): 2960, 2925, 2873, 1822, 1738, 1674, 1608, 1511, 1442, 1404, 1371, 1345, 1301, 1246, 1192, 1162, 1092, 1042; HRMS Calcd for $C_{17}H_{21}NO_3$ (M^+): 287.1521, Found: 287.1521.

(*Z*)-3-(*n*-Butyl)-5-(4-methylbenzylidene)oxazolidine-2,4-dione (2h). Following the procedure for the preparation of **2a**, the reaction of 43.3 mg (0.20 mmol) of **1h** and 56.6 mg (0.41 mmol) of K_2CO_3 in DMSO (2 mL) afforded 35.8 mg (69%) of **2h** (eluent: petroleum ether/ethyl acetate = 25/1) as a solid, m.p.: 87.0–88.4 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, J = 8.1 Hz, 2H, Ar-*H*), 7.23 (d, J = 8.1 Hz, 2H, Ar-*H*), 6.73 (s, 1H, ═C*H*), 3.64 (t, J = 7.4 Hz, 2H, N-CH_2), 2.38 (s, 3H, Ar-Me), 1.77–1.61 (m, 2H, CH_2), 1.46–1.25 (m, 2H, MeCH_2), 0.95 (t, J = 7.2 Hz, 3H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.4, 152.3, 141.0, 136.9, 131.0, 129.7, 127.9, 113.4, 39.9, 29.6, 21.5, 19.8, 13.5; MS (*m*/*z*): 260 (M^+ + 1, 4.24), 259 (M^+, 25.13), 132 (100); IR (KBr, cm^{-1}): 2959, 2877, 1817, 1735, 1675, 1608, 1514, 1440, 1404, 1362, 1345, 1318, 1288, 1239, 1161, 1094, 1065, 1042; Anal. Calcd. for $C_{15}H_{17}NO_3$: C 69.48, H 6.61, N 5.40; Found: C 69.43, H 6.66, N 5.35%.

(*Z*)-3-(*n*-Butyl)-5-(4-methoxybenzylidene)oxazolidine-2,4-dione (2i). Following the procedure for the preparation of **2a**, the reaction of 45.7 mg (0.20 mmol) of **1i** and 55.1 mg (0.40 mmol) of K_2CO_3 in DMSO (2 mL) afforded 36.7 mg (67%) of **2i** (eluent: petroleum ether/ethyl acetate = 25/1–15/1) as a solid, m.p.: 106.0–106.6 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73–7.65 (m, 2H, Ar-*H*), 6.98–6.88 (m, 2H, Ar-*H*), 6.70 (s, 1H, ═C*H*), 3.84 (s, 3H, OMe), 3.63 (t, J = 7.4 Hz, 2H, N-CH_2), 1.75–1.61 (m, 2H, CH_2), 1.45–1.27 (m, 2H, MeCH_2), 0.95 (t, J = 7.5 Hz, 3H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.5, 161.3, 152.4, 136.0, 132.9, 123.4, 114.4, 113.3, 55.3, 39.9, 29.6, 19.8, 13.5; MS (*m*/*z*): 276 (M^+ + 1, 6.32), 275 (M^+, 36.31), 148 (100); IR (KBr, cm^{-1}): 2979, 2952, 2867, 2835, 1814, 1740, 1678, 1603, 1514, 1447, 1408, 1345, 1307, 1257, 1163, 1095, 1064, 1027; Anal. Calcd. for $C_{15}H_{17}NO_4$: C 65.44, H 6.22, N 5.09; Found: C 65.38, H 6.30, N 5.03%.

(*Z*)-3-Benzyl-5-(4-methoxybenzylidene)oxazolidine-2,4-dione (2j). Following the procedure for the preparation of **2a**, the reaction of 53.3 mg (0.20 mmol) of **1j** and 55.6 mg (0.41 mmol) of K_2CO_3 in DMSO (2 mL) afforded 42.2 mg (68%) of **2j** (eluent: petroleum ether/ethyl acetate = 20/1–10/1) as a solid, m.p.: 117.8–118.7 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75–7.65 (m, 2H, Ar-*H*), 7.50–7.40 (m, 2H, Ar-*H*), 7.40–7.27 (m, 3H, Ar-*H*), 6.98–6.88 (m, 2H, Ar-*H*), 6.73 (s, 1H, ═C*H*), 4.78 (s, 2H, N-CH_2), 3.84 (s, 3H, OMe); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.1, 161.3, 152.1, 135.9, 134.5, 133.0, 128.81, 128.77, 128.4, 123.3, 114.5, 113.8, 55.3, 43.6; MS (*m*/*z*): 310 (M^++1, 13.88), 309 (M^+, 68.64), 148 (100); IR (KBr, cm^{-1}): 1805, 1735, 1666, 1601, 1572, 1512, 1455, 1443, 1430, 1401, 1348, 1312, 1259, 1174, 1091, 1070, 1025; Anal. Calcd. for $C_{18}H_{15}NO_4$: C 68.89, H 4.89, N 4.53; Found: C 69.75, H 5.01, N 4.64%.

(*Z*)-3-(*n*-Butyl)-5-(4-fluorobenzylidene)oxazolidine-2,4-dione (2k). Following the procedure for the preparation of **2a**, the reaction of 43.2 mg (0.20 mmol) of **1k** and 56.2 mg (0.41 mmol) of K_2CO_3 in DMSO (2 mL) afforded 37.2 mg (72%) of **2k** (eluent: petroleum ether/ethyl acetate = 25/1) as a solid, m.p.: 102.6–103.8 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81–7.69 (m, 2H, Ar-*H*), 7.18–7.05 (m, 2H, Ar-*H*), 6.71 (s, 1H, ═C*H*), 3.65 (t, J = 7.4 Hz, 2H, N-CH_2), 1.78–1.60 (m, 2H, CH_2), 1.46–1.28 (m, 2H, MeCH_2), 0.95 (t, J = 7.4 Hz, 3H, Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 163.6 (d, J = 251.4 Hz), 162.3, 152.2, 137.2 (d, J = 2.7 Hz), 133.1 (d, J = 8.4 Hz), 127.0 (d, J = 3.2 Hz), 116.2 (d, J = 22.7 Hz), 112.0, 40.1, 29.6, 19.8, 13.5; ^{19}F NMR (282 MHz, $CDCl_3$): δ −108.0 (standard by frequency conversion of $CDCl_3$); MS (*m*/*z*): 264 (M^+ + 1, 3.56), 263 (M^+, 21.57), 136 (100); IR (KBr, cm^{-1}): 2959, 2873, 1819, 1728, 1674, 1602, 1511, 1447, 1416, 1373, 1356, 1310, 1292, 1239, 1186, 1163, 1085, 1058, 1010; Anal. Calcd. for $C_{14}H_{14}FNO_3$: C 63.87, H 5.36, N 5.32; Found: C 63.98, H 5.41, N 5.23%.

(*Z*)-3-Benzyl-5-(thiophen-3-ylmethylene)oxazolidine-2,4-dione (2l). Following the procedure for the preparation of **2a**, the reaction of 47.9 mg (0.20 mmol) of **1l** and 55.1 mg (0.40 mmol) of K_2CO_3 in DMSO (2 mL) afforded 34.8 mg (61%) of **2l**

(eluent: petroleum ether/ethyl acetate = 15/1) as a solid, m.p.: 155.9–156.4 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83–7.75 (m, 1H, Ar-*H*), 7.52–7.41 (m, 3H, Ar-*H*), 7.40–7.28 (m, 4H, Ar-*H*), 6.84 (s, 1H, =C*H*), 4.78 (s, 2H, N-CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.9, 151.9, 136.6, 134.4, 132.0, 130.7, 128.9, 128.8, 128.6, 128.5, 126.7, 107.8, 43.8; MS (*m*/*z*): 286 (M^+ + 1, 16.21), 285 (M^+, 100); IR (KBr, cm^{-1}): 3102, 3031, 2947, 1808, 1735, 1674, 1518, 1495, 1456, 1438, 1406, 1354, 1343, 1322, 1249, 1212, 1156, 1090, 1069; Anal. Calcd. for $C_{15}H_{11}NO_3S$: C 63.14, H 3.89, N 4.91; Found: C 63.18, H 4.09, N 4.99%.

(*Z*)-3-Benzyl-5-(thiophen-2-ylmethylene)oxazolidine-2,4-dione (2m). Following the procedure for the preparation of **2a**, the reaction of 47.1 mg (0.20 mmol) of **1m** and 81.6 mg (0.59 mmol) of K_2CO_3 in DMSO (2 mL) afforded 30.7 mg (55%) of **2m** (eluent: petroleum ether/ethyl acetate = 15/1) as a solid, m.p.: 177.2–178.0 °C (*n*-hexane/CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 4.8 Hz, 1H, Ar-*H*), 7.53–7.40 (m, 3H, Ar-*H*), 7.40–7.28 (m, 3H, Ar-*H*), 7.12 (t, *J* = 4.4 Hz, 1H, Ar-*H*), 7.01 (s, 1H, =C*H*), 4.78 (s, 2H, N-CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.5, 151.6, 135.6, 134.4, 133.5, 133.1, 132.0, 128.9, 128.8, 128.5, 128.1, 107.4, 43.8; MS (*m*/*z*): 286 (M^+ + 1, 13.07), 285 (M^+, 74.61), 124 (100); IR (KBr, cm^{-1}): 3104, 1810, 1728, 1668, 1495, 1457, 1435, 1398, 1344, 1318, 1247, 1231, 1167, 1071, 1051; Anal. Calcd. for $C_{15}H_{11}NO_3S$: C 63.14, H 3.89, N 4.91; Found: C 63.11, H 3.97, N 5.01%.

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Notes and references

1 For a most recent review, see: T. Sakakura, J.-C. Choi and H. Yasuda, *Chem. Rev.*, 2007, **107**, 2365.

2 For recent reports, see: (*a*) M. Yoshida and M. Ihara, *Angew. Chem., Int. Ed.*, 2001, **40**, 616; (*b*) M. Shi and Y.-M. Shen, *J. Org. Chem.*, 2002, **67**, 16; (*c*) M. Yoshida, M. Fujita, T. Ishii and M. Ihara, *J. Am. Chem. Soc.*, 2003, **125**, 4874; (*d*) M. Yoshida, M. Fujita and M. Ihara, *Org. Lett.*, 2003, **5**, 3325; (*e*) Y. Gu, F. Shi and Y. Deng, *J. Org. Chem.*, 2004, **69**, 391; (*f*) Y. Kayaki, M. Yamamoto, T. Suzuki and T. Ikariya, *Green Chem.*, 2006, **8**, 1019; (*g*) W. Yamada, Y. Sugawara, H. M. Cheng, T. Ikeno and T. Yamada, *Eur. J. Org. Chem.*, 2007, 2604; (*h*) M. Yoshida, T. Murao, K. Sugimoto and M. Ihara, *Synlett*, 2007, 575; (*i*) Y. Kayaki, M. Yamamoto and T. Ikariya, *J. Org. Chem.*, 2007, **72**, 647; (*j*) M. Yoshida, Y. Komatsuzaki and M. Ihara, *Org. Lett.*, 2008, **10**, 2083; (*k*) Y. Kayaki, M. Yamamoto and T. Ikariya, *Angew. Chem., Int. Ed.*, 2009, **48**, 4194; (*l*) S. Yoshida, K. Fukui, S. Kikuchi and T. Yamada, *J. Am. Chem. Soc.*, 2010, **132**, 4072.

3 Using electrochemical method, see: (*a*) L. Rossi, M. Feroci, M. Verdecchia and A. Inesi, *Lett. Org. Chem.*, 2005, **2**, 731; (*b*) M. A. Casadei, F. M. Moracci, G. Zappia, A. Inesi and L. Rossi, *J. Org. Chem.*, 1997, **62**, 6754; (*c*) M. A. Casadei, S. Cesa, F. M. Moracci, A. Inesi and M. Feroci, *J. Org. Chem.*, 1996, **61**, 380; (*d*) M. A. Casadei, S. Cesa and A. Inesi, *Tetrahedron*, 1995, **51**, 5891; (*e*) Using strong bases LDA or *n*-BuLi, see: G. M. Coppola and R. E. Damon, *J. Heterocycl. Chem.*, 1995, **32**, 1133; (*f*) A. R. Katritzky, W.-Q. Fan, A. E. Koziol and G. J. Palenik, *Tetrahedron*, 1987, **43**, 2343; (*g*) A. R. Katritzky and W.-Q. Fan, *Org. Prep. Proced. Int.*, 1987, **19**, 263; (*h*) G. M. Coppola and R. E. Damon, *J. Heterocycl. Chem.*, 1995, **32**, 1133.

4 (*a*) J. W. Clark-Lewis, *Chem. Rev.*, 1958, **58**, 63; (*b*) P. C. Unangst, D. T. Connor, W. A. Cetenko, R. J. Sorenson, C. R. Kostlan, J. C. Sircar, C. D. Wright, D. J. Schrier and R. D. Dyer, *J. Med. Chem.*, 1994, **37**, 322; (*c*) D. A Heerding, L. T. Christmann, T. J. Clark, D. J. Holmes, S. F. Rittenhouse, D. T. Takata and J. W. Venslavsky, *Bioorg. Med. Chem. Lett.*, 2003, **13**, 3771; (*d*) R. L. Dow, B. M. Bechle, T. T. Chou, D. A. Clark, B. Hulin and R. W. Stevenson, *J. Med. Chem.*, 1991, **34**, 1538; (*e*) Y. Momose, T. Maekawa, T. Yamano, M. Kawada, H. Odaka, H. Ikeda and T. Sohda, *J. Med. Chem.*, 2002, **45**, 1518; (*f*) Y.-L. Li, Y.-X. Song and T.-J. Guo, *Cont. Chem. Indu.*, 2003, **32**, 18; (*g*) Y.-L. Li, W.-R. Miao and Y.-H. Zhou, *Chin. J. Pest.*, 2005, **44**, 503.

5 (*a*) T. L. Patton, *J. Org. Chem.*, 1967, **32**, 383; (*b*) A. Oku, S. Nakaoji, T. Kadono and H. Imai, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 2966; (*c*) A. Zask, *J. Org. Chem.*, 1992, **57**, 4558; (*d*) A. Benavides, R. Martínez, H. A. Jiménez-Vázquez, F. Delgado and J. Tamariz, *Heterocycles*, 2001, **55**, 469.

6 G. Chen, C. Fu and S. Ma, *Org. Lett.*, 2009, **11**, 2900.

7 Crystal data for compound **2a**: $C_{17}H_{13}NO_3$, *MW* = 279.28, monoclinic, space group P2(1)/c, final *R* indices [$I > 2\sigma(I)$], *R*1 = 0.0411, *wR*2 = 0.0979, *R* indices (all data) *R*1 = 0.0487, *wR*2 = 0.1027, *a* = 6.4285(4) Å, *b* = 31.4664(18) Å, *c* = 7.0702(4) Å, α = 90°, β = 106.517(2)°, γ = 90°, *V* = 1371.16(14) Å^3, *T* = 173(2) K, *Z* = 4, reflections collected/unique 15862/2426 (*R*int = 0.0299), number of observations [$I > 2\sigma(I)$] 2086, parameters: 190. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC 779363.

8 (*a*) S. A. Jr. Lang and E. Cohen, *J. Med. Chem.*, 1975, **18**, 441; (*b*) Y. Iwanami, *Nippon Kagaku Zasshi*, 1962, **83**, 600; (*c*) A. Yokoyama, K. Ashida and H. Tanaka, *Chem. Pharm. Bull.*, 1964, **12**, 690; (*d*) H. Jiang, S. Ma, G. Zhu and X. Lu, *Tetrahedron*, 1996, **52**, 10945; (*e*) H. Imase, K. Noguchi, M. Hirano and K. Tanaka, *Org. Lett.*, 2008, **10**, 3563; (*f*) G. T. Crisp and M. J. Millan, *Tetrahedron*, 1998, **54**, 637.

