



Cite this: *RSC Adv.*, 2021, **11**, 31395

Received 9th July 2021  
Accepted 11th September 2021

DOI: 10.1039/d1ra05305a

rsc.li/rsc-advances

# Furan oxidation by Mn(III)/Co(II) catalysts – application to benzofuran synthesis†

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Furans containing a  $\beta$ -ketoester group at 2-position undergo oxidative ring-opening by Mn(III)/Co(II) catalysts under an O<sub>2</sub> atmosphere to produce 1,4-dicarbonyl moieties through an endoperoxide intermediate, which consecutively cyclized with the  $\beta$ -ketoester unit to afford 4-hydroxy-2-cyclohexen-1-ones. This oxidation/cyclization products were efficiently transformed into versatile benzofuran derivatives after consecutive aromatization and Paal–Knorr reaction.

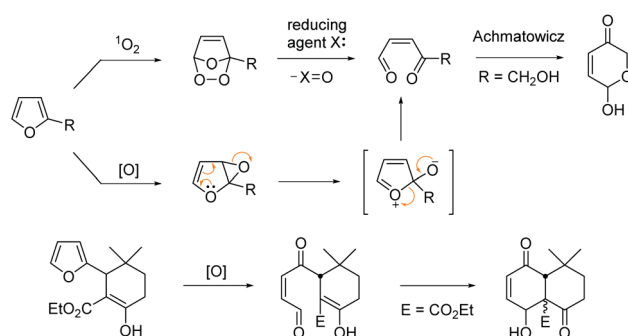
Furan is a hetero-aromatic compound, ready to react with various oxidants or reactive electrophiles to serve as versatile C<sub>4</sub> building blocks in organic synthesis.<sup>1</sup> Furan can produce a conjugated 1,4-dicarbonyl unit by singlet oxygen through an endoperoxide intermediate,<sup>2</sup> which may be trapped by a nearby internal hydroxy group to generate a pyranose structure as was reported by Achmatowicz.<sup>3</sup> This oxidative conversion may also be attained through the epoxide intermediate by other oxidants including dioxiranes, metal oxides, *N*-bromosuccinimide, H<sub>2</sub>O<sub>2</sub>, peroxy acids *etc.*<sup>4</sup> Lallemand *et al.* demonstrated that the furan oxidation product by MCPBA would be trapped by a nearby enolic carbon of  $\beta$ -ketoester leading to a polyoxygenated decalin system (Scheme 1).<sup>5</sup>

We recently reported that the Mn<sup>III</sup>-mediated peroxy radical in  $\beta$ -ketoester **A** induced oxidation of the acetyl group to  $\alpha$ -ketoester **C** through the dioxetane intermediate **B**, which was eventually transformed into bichalcophen **D** by hetero-aromatization (Paal–Knorr reaction).<sup>6a</sup> In the present work, we want to report that  $\beta$ -ketoester **2a** containing a proximal furan moiety undergoes the furan oxidation to the conjugated 1,4-dicarbonyl intermediate **E** under the same reaction conditions, and is trapped by the active  $\alpha$ -methinyl carbon radical of  $\beta$ -ketoester to produce 4-hydroxy-2-cyclohexen-1-ones **3a-1** and **3a-2** (Scheme 2). Whereas the distal electron-deficient furan ring in **A** was not affected, the proximal furan ring in **2a** was smoothly oxidized by Mn<sup>III</sup>/Co<sup>II</sup> catalysts under aerobic condition. Cyclohexenones **3a-1** and **3a-2**, stereoisomers at the  $\alpha$ -carbon of  $\beta$ -ketoester with both hydroxy and benzoyl substituents in equatorial positions (*vide infra*), were produced in equal amounts, which would be perfect substates for the conversion into versatile benzofuran derivative **4a** after decarbonylative aromatization and Paal–Knorr reaction.

We herein delineated the optimal condition for the furan oxidation of  $\beta$ -ketoester **2a** to produce 4-hydroxy-2-cyclohexen-1-ones **3a-(1/2)**. Generality of the furan oxidation was demonstrated for  $\beta$ -ketoesters **2** with various aryl substituents. Finally, the transformation of the above oxidative cyclization products **3** into versatile benzofuran derivatives **4** was described.

The substrate **2a** for furan oxidation was prepared by conjugate addition of ethyl acetoacetate to chalcone derivative **1a** containing a furan-2-yl group at  $\beta$ -position. Ethyl acetoacetate was utilized as reagent and solvent at 60 °C under CeCl<sub>3</sub> and NaI catalysts (10 mol% each).<sup>7</sup> The Michael adduct **2a** was

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Scheme 1 Furan as versatile C<sub>4</sub> building blocks for pyranose and cyclohexenone by oxidation.

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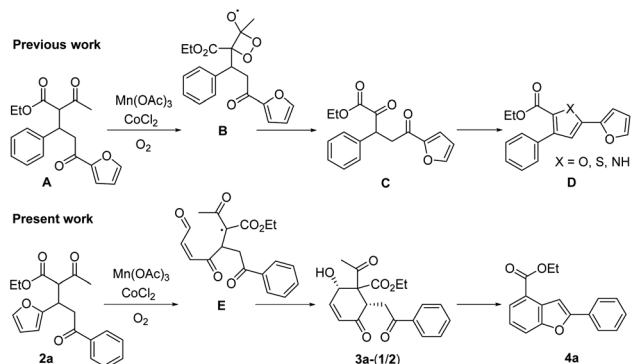
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† Electronic supplementary information (ESI) available: Experimental section, <sup>1</sup>H/<sup>13</sup>C-NMR spectra, ORTEP diagrams for **3j-1**, **3a-2**, and **5-2**, UV/FL spectra for **4a**. CCDC 2076252–2076254. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d1ra05305a

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Scheme 2 Disparate reactivity of  $\beta$ -ketoesters **A** and **2a** under the  $\text{Mn}^{\text{III}}/\text{Co}^{\text{II}}$  catalyzed oxidation.

obtained in 58% yield as a 1 : 1 diastereomeric mixture, which was utilized for the oxidation reaction without separation. The typical condition for the previous oxidative deacetylation of chalcone derivative **A** under  $\text{Mn}(\text{OAc})_3$  and  $\text{CoCl}_2$  catalysts (10 mol% each) in AcOH was utilized as a standard condition for the optimization study of the furan oxidation of **2a** (Table 1).<sup>6a</sup>

The furan oxidation/cyclization product, 4-hydroxy-2-cyclohexen-1-ones **3a-(1/2)**, was obtained in 44% yield at 25 °C under the above standard condition in 48 h (entry 1). UV irradiation at 365 nm wavelength not only speed up the rate (13 h), but also increase the yield of the reaction (57%, entry 2). Similar improvement on the yield (55%) and the reaction time (18 h) was observed under  $\text{O}_2$  atmosphere, supplied by a balloon filled with  $\text{O}_2$  (entry 3). These two effects can be combined to further speed up the oxidation reaction (5 h), but the yield remained

almost the same (63%) within experimental errors (entry 4). The positive  $\text{O}_2$  effect was obvious in the  $\text{Mn}^{\text{III}}$  catalyst regeneration as well as in the peroxy radical formation.<sup>8</sup> UV irradiation would generate singlet oxygen for the furan oxidation in the presence of metal catalysts just as in organic dye sensitizer.<sup>9</sup> In the absence of  $\text{Mn}^{\text{III}}$  catalyst (only in the presence of  $\text{Co}^{\text{II}}$  catalyst), normal illumination was not enough to generate singlet oxygen (entry 5), and UV irradiation was necessary to produce the oxidation products **3a-(1/2)** in 44% yield (entry 6). The reactions under argon<sup>8b</sup> atmosphere as well as in the presence of TEMPO<sup>10</sup> (1 equiv.) were unable to generate the peroxy radical or singlet oxygen as was expected (entries 7 and 8).

Temperature and solvent effects on the furan oxidation by peroxy radical were then studied (entries 9–12). Low temperature would be beneficial to the reaction utilizing a gaseous reagent because of the increased solubility of gas in solution. When the reaction was proceeded at 0 °C (15% volume of  $\text{CF}_3\text{CO}_2\text{H}$  was added to lower the m.p. of AcOH solution),<sup>11</sup> however, only 20% yield of products **3a-(1/2)** was obtained presumably due to insufficient activation energy for the reaction. Higher temperature reaction (at 40 °C) produced even lower 16% product yield, presumably because of lower solubility of  $\text{O}_2$  in solution. AcOH was superior to  $\text{Ac}_2\text{O}$  as solvent, but only a trace amount of the product was obtained in EtOH even for a prolonged reaction time. Therefore, we determined the optimal condition for the furan oxidation utilizing  $\text{Mn}(\text{OAc})_3$  and  $\text{CoCl}_2$  (10 mol% each) as that of entry 4 in Table 1 (in AcOH at 25 °C under  $\text{O}_2$  with 365 nm UV irradiation).

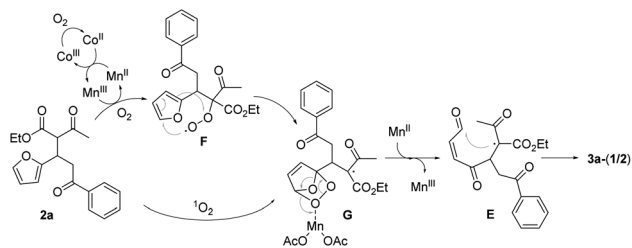
Singlet oxygen mechanism would partly explain the oxidation of **2a** to **3a-(1/2)**.<sup>2</sup> We were also inclined to suggest the peroxy radical mechanism based on the optimization study as well as our previous work (Scheme 3).<sup>8a</sup> The initially formed  $\alpha$ -

Table 1 Optimization study for the oxidation of **2a** to **3a-(1/2)** under  $\text{Mn}^{\text{III}}/\text{Co}^{\text{II}}$  catalysts<sup>a</sup>

Entry	Solvent	Temp. (°C)	Time (h)	Atmosphere	Light	Yield (%) <b>3a-(1/2)</b>
1	AcOH	25	48	Air	Normal	44
2	AcOH	25	13	Air	UV <sup>b</sup>	57
3	AcOH	25	18	$\text{O}_2$	Normal	55
4	AcOH	25	5	$\text{O}_2$	UV <sup>b</sup>	63
5 <sup>c</sup>	AcOH	25	24	$\text{O}_2$	Normal	0
6 <sup>c</sup>	AcOH	25	24	$\text{O}_2$	UV <sup>b</sup>	44
7	AcOH	25	24	Argon	Normal	0
8 <sup>d</sup>	AcOH	25	48	$\text{O}_2$	UV <sup>b</sup>	0
9 <sup>e</sup>	AcOH	0	24	Air	Normal	20
10	AcOH	40	24	Air	Normal	16
11	$\text{Ac}_2\text{O}$	25	43	Air	Normal	30
12	EtOH	25	120	Air	Normal	Trace

<sup>a</sup> The catalytic oxidation reactions were carried out in 0.5–1.0 g scale (1.5–3.0 mmol) of the Michael adduct **2a**. <sup>b</sup> UV at 365 nm was irradiated to the reaction flask in a darkroom lamp. <sup>c</sup> The reaction was carried out only with  $\text{Co}^{\text{II}}$  (without  $\text{Mn}^{\text{III}}$ ). <sup>d</sup> The reaction was carried out in the presence of TEMPO (1 equiv.). <sup>e</sup>  $\text{CF}_3\text{CO}_2\text{H}$  (15% of total volume) was added to lower the melting point of the solution.



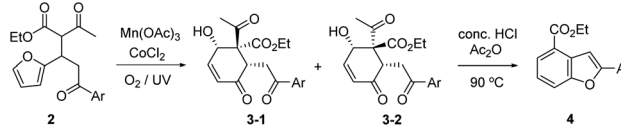


**Scheme 3** Mechanism of the oxidation of **2a** to **3a-(1/2)** by  $\text{Mn}^{\text{III}}/\text{Co}^{\text{II}}$  catalysts.

carbon radical of  $\beta$ -ketoester unit in **2a** by  $\text{Mn}(\text{OAc})_3$  captured  $\text{O}_2$  to afford the peroxy radical **F**, which would oxidize the proximal furan moiety by peroxy radical transfer. The endoperoxide **G** would be a common intermediate in both mechanisms, which would be reductively ring-opened by the assistance of  $\text{Mn}(\text{OAc})_2$ .  $\text{Mn}(\text{OAc})_3$  can be regenerated in this way together with the general oxidation by  $\text{CoCl}_2$  catalyst and  $\text{O}_2$ . Cyclization between methinyl carbon radical and the formyl group in **E** produced 4-hydroxy-2-cyclohexen-1-ones **3a-(1/2)**.

Generality of the furan oxidation under  $\text{Mn}^{\text{III}}/\text{Co}^{\text{II}}$  catalysts was demonstrated for various  $\beta$ -ketoesters **2**, prepared in 58–94% yields by conjugate addition of ethyl acetoacetate to  $\beta$ -furyl- $\alpha,\beta$ -unsaturated aryl ketones **1** of diverse aromatic moieties (Table 2). Two diastereomeric 4-hydroxy-2-cyclohexen-1-ones **3**-

**Table 2** Generality of furan oxidation by  $\text{Mn}^{\text{III}}/\text{Co}^{\text{II}}$  catalysts and application to benzofuran synthesis<sup>a</sup>



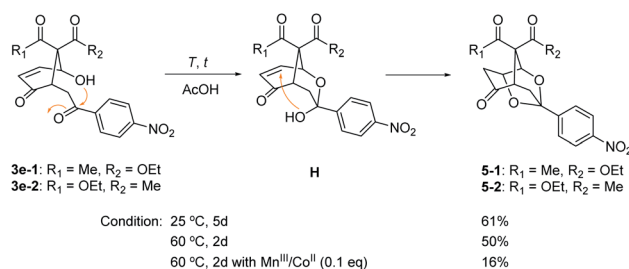
Entry	Compd.	Ar-	Yield (%) 3-1 <sup>b</sup>	Yield (%) 3-2 <sup>c</sup>	Yield (%) 4
1	<b>a</b>	$\text{C}_6\text{H}_5-$	30	33	41
2	<b>b</b>	$p\text{-F-C}_6\text{H}_4-$	25	23	38
3	<b>c</b>	$p\text{-Cl-C}_6\text{H}_4-$	22	24	56
4	<b>d</b>	$p\text{-Br-C}_6\text{H}_4-$	19	18	46
5 <sup>d</sup>	<b>e</b>	$p\text{-NO}_2\text{-C}_6\text{H}_4-$	31	31	11
6	<b>f</b>	$p\text{-MeO-C}_6\text{H}_4-$	27	36	52
7	<b>g</b>	$m\text{-MeO-C}_6\text{H}_4-$	35	9	43
8	<b>h</b>	$o\text{-MeO-C}_6\text{H}_4-$	21	21	42
9	<b>i</b>	$p\text{-Me-C}_6\text{H}_4-$	31	23	45
10	<b>j</b>	2-Naphthyl-	24	21	56
11	<b>k</b>	2-Furyl-	20	16	33
12	<b>l</b>	2-Thiophenyl-	19	20	47
13	<b>m</b>		44	—	44

<sup>a</sup> The catalytic oxidation reactions were carried out in 0.5–1.0 g scale (1.5–3.0 mmol) of the Michael adducts **2a-m**. <sup>b</sup> The stereochemistry of **3-1** was assigned by X-ray diffraction analysis of compound **j**. <sup>c</sup> The stereochemistry of **3-2** was assigned by X-ray diffraction analysis of compound **a**. <sup>d</sup> Compounds **5-1** and **5-2** (1 : 1) were also obtained in 20% yield. See Scheme 4 for the structure and the mechanism of formation.

**1** and **3-2** were obtained in most cases at the quaternary carbon center, while the substituents at the other two chiral centers were fixed as *syn* in equatorial positions. The structures of both racemates were identified by X-ray diffraction experiments on **3j-1** (Ar = 2-naphthalene) and **3a-2** (Ar = Ph).<sup>12</sup> The ORTEP diagrams of both structures were included in the ESI.† The <sup>1</sup>H-NMR spectra of diastereomers were very similar in each group, and the stereochemistry of the other products was decided unambiguously by comparison of the <sup>1</sup>H-NMR with that of the above authentic.

Furan oxidation and subsequent cyclization under the above optimized condition were progressed smoothly for  $\beta$ -ketoesters **2** with various aryl substituents to produce 4-hydroxy-2-cyclohexen-1-ones **3-1** and **3-2** in total 36–63% yields. The furan oxidation/cyclization seems to be insensitive to the identity of distal aromatic moiety. Highest yields (total 62–63%) of **3** were obtained for 4-nitrophenyl (**2e**) and 4-methoxyphenyl (**2f**) as well as the parent phenyl (**2a**) cases. It is interesting to note that further cyclization to 1,3-dioxolanes **5-1** and **5-2** (20% yield, 1 : 1 diastereomers, see Scheme 4) was observed for the electron-withdrawing 4-nitrophenyl case (*vide infra*). The structure of **5-2** was also identified by X-ray analysis (see ORTEP diagram in ESI†).<sup>12</sup> Halogen substituents survived during this radical reaction even though somewhat lower yields of **3** (total 37–48%) were obtained (entries 2–4). Furan oxidation also progressed smoothly for the phenyl group with *ortho*- and *meta*-alkoxy substitutions with a little diminished yield, in which diastereomer **3-1** was obtained as the major isomer in *meta* cases (entries 7 and 13). Diversity of the aromatic substituents included 2-naphthalene, 2-furan, 2-thiophene, and 2-benzodioxolane (entries 10–13). It was noteworthy that the proximal furan in **2k** was readily oxidized, while the remote electron-deficient (less reactive) furan survived under this condition (entry 11).

The benzofuran structure is widely distributed in biologically active nature products and regarded as a core skeleton for the drug discovery.<sup>13</sup> Fluorescent 2-arylbenzofurans might be important as labelling and optoelectrical materials (see ESI† for UV/FL spectra of **4a**), for which efficient synthetic methods have been studies.<sup>14</sup> The above furan oxidation/cyclization product, 4-hydroxy-2-cyclohexen-1-ones **3** with 6-aryl substituent, provided versatile 2-arylbenzofuran derivatives **4** after decarbonylative aromatization and Paal-Knorr reaction (Table 2). Various conditions for Paal-Knorr reaction of 4-hydroxy-2-



**Scheme 4** 1,3-Dioxolanes **5** by further cyclization of furan oxidation product **3e**.

cyclohexen-1-ones **3-1** and **3-2** were tried, among which the one using concentrated HCl in acetic anhydride at 90 °C produced highest yields of the desired 2-arylbenzofuran derivatives **4**. The conversion requires a strong acid at high temperature for decarbonylative aromatization as well as Paal-Knorr reaction. An appreciable amount of tar formation seemed to be indispensable under the condition using benzene solvent, which was significantly reduced in acetic anhydride solvent. The corresponding benzofuran derivatives **4** were obtained in 33–56% yield ranges except the electron-withdrawing 4-nitrophenyl case (entry 5), where the Paal-Knorr reaction might be slowed down to produce **4e** in only 11% yield presumably due to the competition to form 1,3-dioxolane **5**.

The caged 1,3-dioxolanes **5-1** and **5-2** (1 : 1 stereoisomers) were obtained in 20% yield as by-product from  $\beta$ -ketoester **2e** with *p*-nitrophenyl substituent (*vide supra*). It was presumed to be formed by intramolecular Michael addition of the hemiacetal **H**, which was derived from the nucleophilic addition of *syn* 4-hydroxyl group onto the electron-deficient carbonyl group in **3e** (Scheme 4). Further cyclization to 1,3-dioxolane **5** was observed only for **3e** with *p*-nitrophenyl group. This structure is similar to anticonvulsant paeonimetabolin I, a metabolite from paeoniflorin, which is an important ingredient of traditional Chinese medicine curing for abdominal pain.<sup>15</sup> An optimal condition for intramolecular cyclic acetalization of **3e** (a 1 : 1 mixture of stereoisomers) has been screened. 1,3-Dioxolane **5** (a 1 : 1 mixture of stereoisomers) was produced in 61% yield at 25 °C for 5 days and in 50% yield at 60 °C for 2 days in AcOH. The presence of Mn<sup>III</sup>/Co<sup>II</sup> catalysts at 60 °C deteriorated the acetalization reaction to give **5** in only 16% yield.

In conclusion,  $\beta$ -ketoesters **2**, easily prepared from chalcones **1** containing a  $\beta$ -furan-2-yl substituent by conjugate addition of ethyl acetoacetate, undergo facile furan oxidation by Mn<sup>III</sup>/Co<sup>II</sup> catalyst under O<sub>2</sub> atmosphere. The resulting 1,4-dicarbonyl moiety participates in consecutive intramolecular cyclization with the  $\beta$ -ketoester unit to produce 4-hydroxy-2-cyclohexen-1-ones **3**. The furan oxidation may proceed through the endoperoxide intermediate formed by the  $\alpha$ -peroxy radical of the  $\beta$ -ketoesters and partly by singlet oxygen. Generality of the furan oxidation by Mn<sup>III</sup>/Co<sup>II</sup> catalyst was demonstrated for  $\beta$ -ketoesters **2** with various aroyl substituents. 4-Hydroxy-2-cyclohexen-1-one **3e** with 4-nitrophenyl substituent underwent further intramolecular acetalization to produce caged 1,5-dioxolane **5**. 4-Hydroxy-2-cyclohexen-1-ones **3** were smoothly converted into versatile 4'-carboethoxy-5-arylbenzofurans **4** after simultaneous decarbonylative aromatization and Paal-Knorr reaction under conc. HCl in acetic anhydride at 90 °C. The new inventions described in this paper undoubtedly contribute to the valuable addition to the repertoires of furan oxidation in organic synthesis.

## Author contributions

T. Wang: synthesis (lead), analysis (supporting); M. Zhang: synthesis (equal), analysis (supporting); Y. Zheng: synthesis (supporting); J. Seong: data curation (supporting), M.-S. Lah: data curation (lead), S. Koo: project administration (lead),

funding acquisition (lead), investigation (lead), formal analysis (lead), writing manuscript (lead).

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

This work was supported by the National Research Foundation of Korea (NRF) through the grant funded by the Korean government, Ministry of Science and ICT (NRF-2020R1A2C1010724) and partly by Basic Science Research Program funded by the Ministry of Education (NRF-2020R1A6A1A03038817). This paper is dedicated to my dear Professor Lanny S. Liebeskind.

## Notes and references

- (a) P. Merino, *Org. React.*, 2015, **87**, 1–256; (b) P. Merino, T. Tejero, J. I. Delso and R. Matute, *Curr. Org. Chem.*, 2007, **11**, 1076–1091; (c) G. Piancatelli, M. D'Auria and F. D'Onofrio, *Synthesis*, 1994, 867–889; (d) B. H. Lipshutz, *Chem. Rev.*, 1986, **86**, 795–819.
- (a) W. Adam and K. Takayama, *J. Org. Chem.*, 1979, **44**, 1727–1728; (b) B. L. Feringa, *Recl. Trav. Chim. Pays-Bas*, 1987, **106**, 469–488.
- O. Achmatowicz, Jr, P. Bukowski, B. Szechner, Z. Zwierzchowska and A. Zamojski, *Tetrahedron*, 1971, **27**, 1973–1996.
- (a) L. Zhang, Y. Zhang, W. Li and X. Qi, *Angew. Chem.*, 2019, **131**, 5042–5045; (b) Y. Kobayashi, G. B. Kumar, T. Kurachi, H. P. Acharya, T. Yamazaki and T. Kitazume, *J. Org. Chem.*, 2001, **66**, 2011–2018; (c) A. Massa, M. R. Acocella, M. De Rosa, A. Soriente, R. Villano and A. Scettri, *Tetrahedron Lett.*, 2003, **44**, 835–837; (d) J. Finlay, M. A. Mckerverey and H. Q. N. Gunaratne, *Tetrahedron Lett.*, 1998, **39**, 5651–5654; (e) L. A. Badovskaya, V. V. Poskonin and L. V. Povarova, *Russ. Chem. Bull.*, 2017, **66**, 593–599.
- (a) P.-Y. Renard and J.-Y. Lallemand, *Synlett*, 1993, 163–164; (b) C. Descoins, Jr, G. V. Thanh, F.-D. Boyer, P.-H. Ducrot, C. Descoins and J.-Y. Lallemand, *Synlett*, 1999, 240–242.
- (a) X. Jiang, H. Jin, T. Wang, H. Yoo and S. Koo, *Synthesis*, 2019, **51**, 3259–3268; (b) H. Jin, X. Jiang, H. Yoo, T. Wang, C. G. Sung, U. Choi, C.-R. Lee, H. Yu and S. Koo, *ChemistrySelect*, 2020, **5**, 12421–12424.
- G. Bartoli, M. Bosco, M. C. Bellucci, E. Marcantoni, L. Sambri and E. Torregiani, *Eur. J. Org. Chem.*, 1999, 617–620.
- (a) Y. Ju, D. Miao, J. G. Seo and S. Koo, *Adv. Synth. Catal.*, 2014, **356**, 3059–3066; (b) Z. Li, H. Jung, M. Park, M. S. Lah and S. Koo, *Adv. Synth. Catal.*, 2011, **353**, 1913–1917.
- (a) K. Gollnick and A. Griesbeck, *Angew. Chem., Int. Ed.*, 1983, **22**, 726–727; (b) M. R. Iesce, F. Cermola, A. Guitto, R. Scarpato and M. L. Graziano, *J. Org. Chem.*, 1995, **60**, 5324–5327; (c) T. Montagnon, M. Tofi and G. Vassilikogiannakis, *Acc. Chem. Res.*, 2008, **41**, 1001–1011.



- 10 M. V. Baldovi, M. Mohtat and J. C. Scaiano, *Macromolecules*, 1996, **29**, 5497–5499.
- 11 Y. Ju, D. Miao, R. Yu and S. Koo, *Org. Biomol. Chem.*, 2015, **13**, 2588–2599.
- 12 CCDC deposition numbers: 2076252 for **3j-1**, 2076253 for **3a-2**, and 2076254 for **5-2**.†
- 13 (a) Y.-h. Miao, Y.-h. Hu, J. Yang, T. Liu, J. Sun and X.-j. Wang, *RSC Adv.*, 2019, **9**, 27510–27540; (b) H. Khanam and Shamsuzzam, *Eur. J. Med. Chem.*, 2015, **97**, 483–504; (c) R. Naik, D. S. Harmalkar, X. Xu, K. Jang and K. Lee, *Eur. J. Med. Chem.*, 2015, **90**, 379–393.
- 14 L.-Y. Liao, G. Shen, X. Zhang and X.-F. Duan, *Green Chem.*, 2012, **14**, 695–701.
- 15 (a) S. Hatakeyama, M. Kawamura, E. Shimanuki and S. Takano, *Tetrahedron Lett.*, 1992, **33**, 333–336; (b) O. A. Heikal, T. Akao, S. Takeda and M. Hattori, *Biol. Pharm. Bull.*, 1997, **20**, 517–521.

