Note

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.5b01845 • Publication Date (Web): 16 Nov 2015

Downloaded from <http://pubs.acs.org> on November 30, 2015

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N-Heterocyclic Carbene-Catalysed Diastereoselective Vinylogous Michael Addition Reaction of γ -Substituted Deconjugated Butenolides

Hao Guo,^a Fen Xing,^a Guang-Fen Du,^{a*} Kuo-Wei Huang,^b Bin Dai,^{a*} Lin He^{a*}

^aSchool of Chemistry and Chemical Engineering, Shihezi University, Xinjiang Uygur Autonomous Region 832000, People's Republic of China

E-mail: duguangfen@shzu.edu.cn; helin@shzu.edu.cn; db_tea@shzu.edu.cn

^bDivision of Chemical and Life Sciences & Engineering, and Catalysis Center, King Abdullah University of Science and Technology (KAUST), Thuwal 23955-6900, Saudi Arabia

Abstract: An efficient N-heterocyclic carbene (NHC)-catalysed vinylogous Michael addition of deconjugated butenolides was developed. In the presence of 5 mol% of the NHC catalyst, both γ -alkyl and aryl-substituted deconjugated butenolides undergo vinylogous Michael addition with various α , β -unsaturated ketones, esters, or nitriles to afford γ,γ -disubstituted butenolides containing adjacent quaternary and tertiary carbon centers in good to excellent yields with excellent diastereoselectivities. In this process, the free carbene is assumed to act as a strong Brønsted base to promote the conjugate addition.

Keywords: N-heterocyclic carbene, vinylogous Michael addition, deconjugated butenolide, Brønsted base

The γ,γ -disubstituted butenolide unit is one of the most ubiquitous structural motif in a myriad of natural products and pharmaceutically active compounds.¹ In the past decade, continuous efforts have been exerted to develop highly efficient methods for the synthesis of these significant building blocks.² Based on the transformation of performed silyloxyfurans, vinylogous Mukaiyama aldol, Mannich and Michael reactions have been extensively studied, which provide facile access to γ,γ -disubstituted butenolide derivatives.³ However, in view of economy and efficiency, the direct stereoselective γ -functionalization of deconjugated butenolide itself is more attractive.⁴ Particularly, the application of γ -monosubstituted deconjugated butenolides (e.g. α -angelica lactone) is more interesting, which can lead to γ,γ -disubstituted butenolide with adjacent quaternary and tertiary stereocenters. The first breakthrough was documented by Chen and co-workers.⁵ The functionalized γ,γ -disubstituted butenolides were constructed stereoselectively via direct allylic alkylation of deconjugated butenolides with Morita-Baylis-Hillman carbonates. Followed by this excellent work, several groups developed the direct vinylogous Michael-type addition of γ -substituted deconjugated butenolides with different Michael acceptors.⁶ Using a similar strategy, vinylogous Mannich-type reaction of α -angelica lactone was also reported by Feng and co-workers.⁷ Recently, using *L*-tert-leucine-derived amine-thiourea as catalyst, we⁸ developed vinylogous conjugate addition of γ -substituted deconjugated butenolides, which provide optically active γ,γ -butenolide-substituted amides efficiently. Despite remarkable progress made in this research field, the direct functionalization of γ -substituted deconjugated

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4 butenolides remain far less examined and some challenges still unresolved, such as
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6 the usage of transition metals, γ -alkyl and aryl-substituted butenolides can not be well
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8 tolerated. Therefore, the development of more general and efficient protocol for this
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10 transformation is still highly desirable.
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14 The last decade has witnessed an explosive growth in the field of N-heterocyclic
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16 carbenes (NHCs)-catalysis.⁹ As powerful Lewis base catalysts, NHCs have been
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18 utilized broadly in various transformations. Except for benzoin reaction¹⁰ and Stetter
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20 reaction,¹¹ NHCs-catalysed homoenolate reaction of enals,¹² redox reaction of
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22 functional aldehydes,¹³ cycloaddition of ketenes¹⁴ and other reactions¹⁵ based on the
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24 strong nucleophilicity of this organocatalysts have been developed. However,
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26 compared to the intensive studies of Lewis basic properties of NHCs, the exploration
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28 of Brønsted basic properties of NHCs is still in its infancy. Based on this important
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30 Brønsted base characteristic, NHCs-catalysed transesterification was developed by
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32 Nolan and Hedrick independently,¹⁶ while NHCs-mediated amidation of esters was
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34 also documented by Movassaghi and our group.¹⁷ Recently Coquerel and co-workers
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36 reported an interesting NHCs-promoted carba-Michael addition.¹⁸ Subsequently,
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38 NHCs-catalysed oxo-, aza- and sulpha-Michael additions were also developed by
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40 Scheidt, Zhang, Huang and our group.¹⁹ These work further promote us to explore the
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42 more interesting vinylogous Michael addition. Herein, we report an efficient
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44 NHCs-catalysed diastereoselective vinylogous Michael addition of γ -substituted
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46 deconjugated butenolides to different Michael acceptors.
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56 We began our study with the commercially available chalcone **1a** and α -angelica
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lactone **2a**. To our delight, under the catalysis of 10 mol% stable NHC (1,3-bis(2,6-diisopropylphenyl)imidazole-2-ylidene, IPr),²⁰ the vinylogous Michael addition smoothly proceeded in THF at room temperature to furnish the desired γ,γ -disubstituted butenolide **3a** in 92% yield with good diastereoselectivities (Table 1, entry 1). Encouraged by this result, several other NHCs were subsequently investigated for the addition. NHCs generated *in situ* from imidazolium and imidazolinium can promote the reaction efficiently with different diastereoselectivities (Table 1, entries 2-5). Whereas NHCs derived from triazolium or thiazolium did not catalyze the reaction (Table 1, entries 6 and 7). A brief screening of the reaction media indicated that solvents have obvious effect on the reaction, and dichloromethane was proved to be the best choice with respect to both yields and selectivities (Table 1, entries 8-12). Reduction of catalyst loading to 5 mol% led to improved diastereoselectivities without sacrificing reaction yield (Table 1, entry 13). However, further reduction of the catalyst loading to 1 mol% led to dramatic decrease of catalytic efficiency (Table 1, entry 14). Other Brønsted bases were also tested for the reaction. As shown in Table 1, only trace of product **3a** was generated under the catalysis of 5 mol% DBU or Et₃N (Table 1, entries 15-16). Further increasing DBU loading to 10 mol% led to the desired product in good yield, but only with low diastereoselectivities (Table 1, entry 17).

Table 1. Screening of the reaction conditions^a

Entry	NHC	solvent	T (h)	Yield (%) ^b	d.r. ^c
1	4 (10 mol%)	THF	3h	92	6:1
2	5a, DBU (10 mol%)	THF	3h	94	4:1
3	5b, DBU (10 mol%)	THF	3h	80	1:1
4	5c, DBU (10 mol%)	THF	3h	95	3:1
5	6, DBU (10 mol%)	THF	13h	90	5:1
6	7, DBU (10 mol%)	THF	12h	trace	/
7	8, DBU (10 mol%)	THF	12h	trace	/
8	4 (10 mol%)	toluene	3h	93	< 2:1
9	4 (10 mol%)	DCM	3h	93	> 20:1
10	4 (10 mol%)	CH ₃ CN	3h	42	5:1
11	4 (10 mol%)	DMF	3h	59	12:1
12	4 (10 mol%)	DMSO	3h	64	> 20:1
13	4 (5 mol%)	DCM	2h	92	> 20:1
14	4 (1 mol%)	DCM	7h	6	/
15	DBU (5 mol%)	DCM	24h	trace	/

16	Et ₃ N (5 mol%)	DCM	24h	trace	/
17	DBU (10 mol%)	DCM	12h	72	3.7:1

^a **1a** (1 equiv., 0.5 mmol), **2a** (1.5 equiv., 0.75 mmol), NHC (10 mol%), solvent (2 mL); ^b Isolated total yield of two diastereomers; ^c Determined by ¹H NMR analysis of the crude products.

With the optimal reaction conditions in hand (Table 1, entry 13), the scope of Michael acceptors was next investigated. A great variety of differently substituted chalcones underwent the vinylogous Michael addition with α -angelica lactone smoothly to produce the corresponding products in high yields with excellent diastereoselectivities (Scheme 1). Meanwhile, the electronic properties and different positions of the substituents have no obvious effect on the reaction yields and selectivities (Scheme 1, **3a-3o**). Both Naphthyl enones and heteroaryl analogues performed the direct vinylogous reaction smoothly, producing the corresponding products efficiently with excellent diastereoselectivities (Scheme 1, **3p-3s**). Gratifyingly, alkyl substituted enones were also proved to be the suitable reactants for the reaction. In the presence of 20 mol% NHC, alkyl derived enone **1t** coupled with α -angelica lactone efficiently to produce **3t** in 77% yield, albeit with low diastereoselectivities (Scheme 1, **3t**). Intriguingly, cyclic enone furnished the desired product with excellent *anti/syn*-selectivities (Scheme 1, **3u**). Vinyl ethyl ketone **1v** could also participate the addition, but with low yield owing to the oligomerization of the active terminal enone (Scheme 1, **3v**). Notably, the relatively unreactive acrylates and acrylonitrile performed very well, affording the corresponding disubstituted

butenolides in moderate to good yields (Scheme 1, **3w-3y**). To the best of our knowledge, this is the first example for direct vinylogous Michael reaction of deconjugated butenolide with α , β -unsaturated esters and nitrile.

Scheme 1. Evaluation of Michael Acceptors^a

^a Reaction conditions: Same as in Table 1, entry 13; d.r. was determined by ¹H NMR analysis of the crude reaction mixture; isolated total yield of two diastereomers ^b The relative configuration of the major diastereomer of **3j** was determined by X-ray diffraction analysis. ^c Using 10 mol% of NHC **4**. ^d Using 20 mol% of NHC **4**.

Subsequently, different γ -substituted deconjugated butenolides were explored for the reaction. As shown in scheme 2, both γ -alkyl and γ -aryl substituted deconjugated butenolides underwent the reaction smoothly, producing the desired adducts in excellent diastereoselectivities with moderate to high yields (Scheme 2, **3z-3ag**).

Scheme 2. Vinylogous Michael Addition of γ -Substituted Deconjugated Butenolides^a

^a Reaction conditions: Same as in Table 1, entry 13; d.r. was determined by ¹H NMR analysis of the crude reaction mixture; isolated total yield of two diastereomers ^b Using 10 mol% of NHC **4**.

Based on the experimental results and the pioneering studies,^{18, 19} a plausible mechanism was proposed as depicted in Scheme 3. The NHC perform as a Brønsted

base to attack the α -H of deconjugated butenolide to form complex **I**, and after enolization to form dienolate intermediate **II**, which might trigger the following conjugate addition to chalcone and lead to the formation of the final product.

Scheme 3. Proposed Mechanism

A proposed transition state model that account for the diastereoselectivity is demonstrated in Fig. 1.²¹ In order to minimize the van der Waals repulsion between the phenyl group and the bulky NHC, the nucleophilic addition proceed via **TS1** preferentially to afford *anti*-product.

Fig. 1. Proposed Transition State models

On the other hand, NHC might act as a Lewis base to attack chalcone in a 1, 4-fashion and initiate the addition. However, the results of control experiment indicate that the *in situ* generated dienolate **9** can not react with the 1, 4-adduct **10** to produce the desired product. Therefore, this possible mechanism can be ruled out (Scheme 4).

Scheme 4. Control Experiment

In summary, we have developed a novel diastereoselective vinylogous Michael-type addition of deconjugated butenolide that capitalize on the Brønsted basicities of NHCs, both γ -alkyl and γ -aryl-substituted deconjugated butenolides are well tolerated for the reaction. The extremely mild conditions, simple procedure and broad substrates scope provide an efficient protocol for the synthesis of γ , γ -disubstituted butenolides.

Experimental Section

All reactions were conducted under nitrogen atmosphere in an oven-dried glassware with magnetic stirring bar. ^1H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded using deuterated chloroform as solvent, with tetramethylsilane as an internal standard and reported in ppm (δ). α -Angelica lactone and chalcones were obtained from Adamas-beta and used without purification. γ -Substituted deconjugated butenolides²²⁻²⁴ and compound **10**²⁵ were synthesized according to literature procedure. Anhydrous THF and toluene were distilled from sodium and benzophenone. CH_2Cl_2 and CH_3CN were distilled from calcium hydride.

General procedure for NHCs-catalyzed vinylogous Mukaiyama Michael reaction of γ -substituted deconjugated butenolides: IPr **4** (0.015 mmol, 6 mg) was dissolved in anhydrous dichloromethane (1.0 mL), then chalcone **1a** (0.3 mmol, 62.4 mg) and α -angelica lactone **2a** (0.45 mmol, 41 μL) were added under N_2 . Subsequently the reaction solution was stirred at ambient temperature until full

consume of the starting chalcone as indicated TLC. The crude mixture was concentrated under vacuum. The crude product was purified by flash silica gel column chromatography to give the desired product **3a**.

5-methyl-5-(3-oxo-1,3-diphenylpropyl)furan-2(5H)-one (3a)^{6d}

Purified with ethyl acetate/petroleum ether (1/3) to give **3a** as white solid (84.5mg, 92% yield); mp 93.8-95.4 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.84 (dd, *J* = 8.2, 1.0 Hz, 2H), 7.55 - 7.51 (m, 1H), 7.46 - 7.38 (m, 5H), 7.35 - 7.25 (m, 3H), 5.98 (d, *J* = 5.6 Hz, 1H), 3.82 (t, *J* = 6.3 Hz, 1H), 3.31 (qd, *J* = 18.0, 6.6 Hz, 2H), 1.32 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.7, 172.6, 163.4, 139.4, 136.6, 133.4, 129.4, 128.6, 127.5, 120.4, 90.4, 46.7, 39.4, 22.9; FTIR (film): 3059, 3029, 2904, 1746, 1685, 1595, 1449, 1237, 1105, 956, 816, 748, 702, 685, 535 cm⁻¹; HRMS (MALDI -TOF): *m/z* calcd for C₂₀H₁₈O₃ [M+Na]⁺ 329.1148, found: 329.1153.

anti: 5-methyl-5-(3-oxo-3-phenyl-1-(p-tolyl)propyl)furan-2(5H)-one (3b)

Purified with ethyl acetate/petroleum ether (1/5) to give **3b** as white solid (71.1 mg, 74% yield); mp 110.2-112.7 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.84 (dd, *J* = 8.3, 1.2 Hz, 2H), 7.52 (t, *J* = 6.8 Hz, 1H), 7.43 - 7.38 (m, 3H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 5.97 (d, *J* = 5.6 Hz, 1H), 3.76 (d, *J* = 6.6 Hz, 1H), 3.31 (qd, *J* = 17.9, 6.4 Hz, 2H), 2.31 (s, 3H), 1.32 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.7, 172.6, 161.5, 137.0, 136.6, 136.3, 133.3, 129.3, 129.2, 128.6, 128.0, 120.3, 90.5, 46.4, 39.4, 22.7, 21.1; FTIR (film): 3074, 2979, 2920, 2360, 2343, 1737, 1694, 1450, 1369, 1231, 1113, 955, 814, 763, 691, 578 cm⁻¹; HRMS (MALDI -TOF): *m/z* calcd for C₂₁H₂₀O₃ [M+Na]⁺ 343.1305, found: 343.1310.

anti: 5-(1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)-5-methylfuran-2(5H)-one (3c)

Purified with ethyl acetate/petroleum ether (1/3) to give **3c** as white solid (85.7 mg, 84% yield); mp 153.2-155.5 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.83 (dd, *J* = 8.3, 1.1 Hz, 2H), 7.54 (d, *J* = 17.3 Hz, 1H), 7.42 (t, *J* = 6.7 Hz, 3H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H), 6.00 (d, *J* = 5.6 Hz, 1H), 3.83 - 3.77 (m, 1H), 3.26 (qd, *J* = 18.0, 6.3 Hz, 2H), 1.31 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.4, 172.4, 170.0, 137.9, 136.4, 133.5, 133.4, 130.8, 128.8, 128.7, 127.9, 120.6, 90.1, 46.1, 39.3, 23.0; FTIR (film): 3422, 3075, 2930, 1741, 1686, 1491, 1459, 1420, 1365, 1232, 1112, 989, 902, 829, 754, 693, 670, 578 cm⁻¹; HRMS (MALDI -TOF): *m/z* calcd for C₂₀H₁₇ClO₃ [M+Na]⁺ 363.0758, found: 363.0762.

anti: 5-methyl-5-(1-(4-nitrophenyl)-3-oxo-3-phenylpropyl)furan-2(5H)-one (3d)

Purified with ethyl acetate/petroleum ether (1/3) to give **3d** as yellow solid (94.8 mg, 90% yield); mp 157.1-159.9 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 8.23 - 8.17 (m, 2H), 7.86 - 7.80 (m, 2H), 7.67 - 7.61 (m, 2H), 7.59 - 7.54 (m, 1H), 7.45 - 7.41 (m, 3H), 6.06 (d, *J* = 5.6 Hz, 1H), 3.97 (t, *J* = 6.3 Hz, 1H), 3.29 (qd, *J* = 18.2, 6.4 Hz, 2H), 1.32 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 196.8, 172.0, 160.4, 147.3, 147.1, 136.1, 133.8, 130.5, 128.8, 127.9, 123.8, 121.1, 89.5, 46.4, 39.2, 23.4; FTIR (film): 3080, 2930, 2855, 2361, 2344, 1753, 1678, 1597, 1518, 1448, 1345, 1217, 951, 824, 691 cm⁻¹; HRMS (MALDI-TOF): *m/z* calcd for C₂₀H₁₇NO₅ [M+Na]⁺ 374.0999, found: 374.0993.

anti: 5-(1-(2-methoxyphenyl)-3-oxo-3-phenylpropyl)-5-methylfuran-2(5H)-one (3e)

Purified with ethyl acetate/petroleum ether (1/3) to give **3e** as colorless liquid (67.6 mg, 67% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.92 - 7.81 (m, 2H), 7.56 - 7.51 (m, 1H), 7.49 - 7.38 (m, 4H), 7.28 - 7.21 (m, 1H), 6.96 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 8.3 Hz, 1H), 5.93 (d, J = 5.6 Hz, 1H), 4.58 - 4.54 (m, 1H), 3.85 (s, 3H), 3.36 - 3.24 (m, 2H), 1.33 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.9, 172.8, 161.9, 157.2, 136.7, 133.2, 128.6, 128.4, 127.9, 121.0, 119.7, 110.7, 90.8, 55.6, 39.1, 22.1; FTIR (film): 3361, 2922, 2839, 2359, 1667, 1606, 742, 690, 543, 513 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{21}\text{H}_{20}\text{O}_4$ $[\text{M}+\text{Na}]^+$ 359.1254, found: 359.1258.

anti: 5-methyl-5-(3-oxo-3-phenyl-1-(*m*-tolyl)propyl)furan-2(5H)-one (3f)

Purified with ethyl acetate/petroleum ether (1/5) to give **3f** as colorless liquid (85.5 mg, 89% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.86 (dd, J = 8.4, 1.3 Hz, 2H), 7.56 - 7.52 (m, 1H), 7.44 - 7.39 (m, 3H), 7.27 - 7.21 (m, 1H), 7.04 - 6.92 (m, 2H), 6.81 (ddd, J = 8.3, 2.6, 0.9 Hz, 1H), 5.98 (d, J = 5.6 Hz, 1H), 3.81 (s, 4H), 3.32 (qd, J = 18.0, 6.3 Hz, 2H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.6, 172.6, 161.4, 159.6, 141.0, 136.6, 133.4, 129.6, 128.6, 128.0, 121.8, 120.3, 115.4, 112.5, 90.3, 55.2, 46.7, 39.3, 22.8; FTIR (film): 3498, 3354, 3086, 2934, 2836, 1770, 1683, 1582, 1489, 1102, 1043, 953, 820, 785, 690, 639, 550, 513, 466 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{21}\text{H}_{20}\text{O}_3$ $[\text{M}+\text{K}]^+$ 359.1044, found: 359.1041.

anti: 5-(1-(2-chlorophenyl)-3-oxo-3-phenylpropyl)-5-methylfuran-2(5H)-one (3g)

Purified with ethyl acetate/petroleum ether (1/5) to give **3g** as white solid (76.5 mg, 75% yield); mp 189.9-192.5 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.86 - 7.81 (m, 2H), 7.61 (dd, J = 7.8, 1.7 Hz, 1H), 7.55 - 7.48 (m, 2H), 7.42 - 7.38 (m, 3H), 7.27

(td, $J = 7.6, 1.4$ Hz, 1H), 7.22 - 7.16 (m, 1H), 5.99 (d, $J = 5.6$ Hz, 1H), 4.62 (t, $J = 6.4$ Hz, 1H), 3.30 (qd, $J = 18.1, 6.3$ Hz, 2H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.1, 172.5, 161.4, 137.4, 136.4, 135.0, 133.4, 130.0, 129.6, 128.7, 128.6, 128.0, 127.4, 120.4, 90.3, 41.0, 39.3, 22.5; FTIR (film): 3082, 2990, 2895, 1759, 1678, 1448, 1374, 1296, 1261, 1146, 1103, 952, 824, 754, 694 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{20}\text{H}_{17}\text{ClO}_3$ $[\text{M}+\text{Na}]^+$ 363.0758, found: 363.0757.

anti: 5-(1-(3-bromophenyl)-3-oxo-3-phenylpropyl)-5-methylfuran-2(5H)-one (3h)

Purified with ethyl acetate/petroleum ether (1/5) to give **3h** as colorless liquid (95.6 mg, 83% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.89 - 7.81 (m, 2H), 7.60 - 7.53 (m, 2H), 7.46 - 7.35 (m, 5H), 7.21 (t, $J = 7.8$ Hz, 1H), 6.01 (d, $J = 5.6$ Hz, 1H), 3.81 (t, $J = 6.3$ Hz, 1H), 3.27 (qd, $J = 18.1, 6.2$ Hz, 2H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.2, 172.4, 161.0, 141.9, 136.4, 133.5, 132.3, 130.7, 130.2, 128.7, 128.2, 128.0, 122.7, 120.6, 90.0, 46.3, 39.3, 23.1; FTIR (film): 3062, 2981, 2932, 2360, 2342, 1755, 1683, 1595, 1567, 1475, 1448, 1103, 953, 820, 755, 691 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{20}\text{H}_{17}\text{BrO}_3$ $[\text{M}+\text{Na}]^+$ 407.0253, found: 407.0252.

anti: 5-(3-(4-bromophenyl)-3-oxo-1-phenylpropyl)-5-methylfuran-2(5H)-one (3i)

Purified with ethyl acetate/petroleum ether (1/5) to give **3i** as white solid (85.3 mg, 74% yield); mp 149.9-151.2 $^\circ\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ 7.75 - 7.70 (m, 2H), 7.60 - 7.55 (m, 2H), 7.44 - 7.38 (m, 3H), 7.37 - 7.31 (m, 2H), 7.29 (dt, $J = 4.6, 2.1$ Hz, 1H), 6.01 (d, $J = 5.6$ Hz, 1H), 3.83 - 3.76 (m, 1H), 3.29 (qd, $J = 17.9, 6.9$ Hz, 2H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 196.7, 172.5, 161.3, 139.1, 135.3,

132.0, 129.5, 129.4, 128.6, 128.6, 127.6, 120.5, 90.3, 46.8, 39.3, 22.8; FTIR (film): 3104, 3078, 3031, 2893, 1746, 1682, 1586, 1492, 1232, 1099, 1068, 922, 824, 735, 701, 644, 537, 459 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{20}\text{H}_{17}\text{BrO}_3$ $[\text{M}+\text{Na}]^+$ 407.0253, found: 407.0249.

anti: 5-(3-(4-chlorophenyl)-3-oxo-1-phenylpropyl)-5-methylfuran-2(5H)-one (3j)

Purified with ethyl acetate/petroleum ether (1/4) to give **3j** as white solid (83.7mg, 82% yield); mp 121.1-123.5 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ = 7.81-7.79 (m, 2H), 7.39 - 7.43 (m, 5H), 7.37 -7.32 (m, 2H), 7.30 - 7.27 (m, 1H), 6.01 (d, J = 5.6 Hz, 1H), 3.82 - 3.76 (m, 1H), 3.30 (qd, J = 17.9, 6.4 Hz, 2H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 196.5, 172.5, 161.3, 139.9, 139.2, 134.9, 129.4, 129.4, 129.0, 128.6, 127.6, 120.4, 90.3, 46.8, 39.3, 22.8; FTIR (film): 2994, 2360, 2343, 1750, 1672, 1585, 1284, 1099, 846, 707, 528 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{20}\text{H}_{17}\text{ClO}_3$ $[\text{M}+\text{Na}]^+$ 363.0758, Found: 363.0756.

anti: 5-(3-(3-methoxyphenyl)-3-oxo-1-phenylpropyl)-5-methylfuran-2(5H)-one (3k)

Purified with ethyl acetate/petroleum ether (1/5) to give **3k** as colorless liquid (91.8mg, 91% yield); ^1H NMR (400 MHz, CDCl_3) δ = 7.46 - 7.23 (m, 10H), 7.11 - 7.04 (m, 1H), 5.99 (d, J = 5.6 Hz, 1H), 3.83 - 3.78 (m, 4H), 3.32 (qd, J = 17.9, 6.4 Hz, 2H), 1.33 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.5, 172.5, 161.3, 159.8, 139.3, 137.9, 129.7, 129.4, 128.5, 127.4, 120.5, 120.4, 119.7, 112.2, 90.35, 55.4, 46.8, 39.4, 22.7; FTIR (film): 3361, 2922, 2839, 2359, 1667, 1606, 742, 690, 543, 513 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{21}\text{H}_{20}\text{O}_4$ $[\text{M}+\text{Na}]^+$ 359.1254, found:

359.1261.

anti: 5-(3-(3-bromophenyl)-3-oxo-1-phenylpropyl)-5-methylfuran-2(5H)-one (3l)

Purified with ethyl acetate/petroleum ether (1/3) to give **3l** as yellow solid (93.3 mg, 81% yield); mp 79.3-81.2 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.97 (t, *J* = 1.8 Hz, 1H), 7.80 -7.72 (m, 1H), 7.66 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.45- 7.37 (m, 3H), 7.36 - 7.26 (m, 4H), 6.02 (d, *J* = 5.6 Hz, 1H), 3.79 (t, *J* = 6.3 Hz, 1H), 3.30 (qd, *J* = 18.0, 7.1 Hz, 2H), 1.34 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 196.3, 172.45, 161.3, 139.1, 138.2, 136.2, 131.0, 130.3, 129.4, 128.6, 127.6, 126.5, 123.0, 120.5, 90.3, 46.8, 39.5, 22.8; FTIR (film): 3062, 2905, 1742, 1697, 1566, 1453, 1413, 1375, 1297, 1235, 1105, 997, 953, 813, 704, 677, 537 cm⁻¹; HRMS (MALDI -TOF): *m/z* calcd for C₂₀H₁₇BrO₃ [M+Na]⁺ 407.0253, found: 407.0251.

anti:5-(1-(2-chlorophenyl)-3-(4-methoxyphenyl)-3-oxopropyl)-5-methylfuran-2(5H)-one (3m)

Purified with ethyl acetate/petroleum ether (1/5) to give **3m** as white solid (85.5 mg, 77% yield); mp 114.5-116.8 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.83 (d, *J* = 8.9 Hz, 2H), 7.61 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.49 (d, *J* = 5.6 Hz, 1H), 7.39 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.26 (dd, *J* = 7.6, 6.3 Hz, 1H), 7.20 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 2H), 5.97 (d, *J* = 5.6 Hz, 1H), 4.62 (t, *J* = 6.4 Hz, 1H), 3.83 (s, 3H), 3.20 (qd, *J* = 17.9, 6.3 Hz, 2H), 1.34 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 195.5, 172.6, 163.7, 161.5, 137.5, 135.0, 130.3, 130.1, 129.6, 129.4, 128.5, 127.3, 120.3, 113.8, 90.4, 555, 41.0, 38.9, 22.5; FTIR (film): 3422, 3075, 2930, 1741, 1686, 1491, 1459, 1420, 1365, 1232, 1112, 989, 902, 829, 754, 693, 670, 578 cm⁻¹; HRMS

(MALDI -TOF): m/z calcd for $C_{21}H_{19}ClO_4$ $[M+Na]^+$ 393.0868, found: 393.0864.

anti:5-(1-(2,4-dichlorophenyl)-3-(4-methoxyphenyl)-3-oxopropyl)-5-methylfuran-2(5H)-one (3n)

Purified with ethyl acetate/petroleum ether (1/5) to give **3n** as white solid (93.3 mg, 77% yield); mp 121.1-123.5 °C; 1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.83 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 8.5 Hz, 1H), 7.49 (d, J = 5.6 Hz, 1H), 7.44 (d, J = 2.2 Hz, 1H), 7.27 (dd, J = 8.7, 2.4 Hz, 1H), 6.90 (d, J = 9.0 Hz, 2H), 6.00 (d, J = 5.6 Hz, 1H), 4.57 (t, J = 6.4 Hz, 1H), 3.86 (s, 3H), 3.18 (qd, J = 17.9, 6.4 Hz, 2H), 1.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 195.2, 172.4, 163.8, 161.1, 136.2, 135.7, 133.6, 130.9, 130.3, 129.3, 129.3, 127.7, 120.5, 113.9, 90.1, 55.5, 40.7, 38.8, 22.6; FTIR (film): 3091, 2936, 2838, 1757, 1664, 1599, 1474, 1376, 1252, 1214, 1172, 1103, 1032, 945, 812 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $C_{21}H_{18}Cl_2O_4$ $[M+Na]^+$ 427.0479, found: 427.0474.

anti:5-(3-(4-bromophenyl)-1-(2-chlorophenyl)-3-oxopropyl)-5-methylfuran-2(5H)-one(3o)

Purified with ethyl acetate/petroleum ether (1/5) to give **3o** as white solid (90.3mg, 72% yield) mp 189.6-192.5 °C; 1H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.71 (d, J = 8.5 Hz, 2H), 7.63 - 7.53 (m, 3H), 7.49 (d, J = 5.6 Hz, 1H), 7.41 (dd, J = 7.9, 1.2 Hz, 1H), 7.30 - 7.21 (m, 1H), 7.23 - 7.21 (m, 1H), 6.01 (d, J = 5.6 Hz, 1H), 4.60 (t, J = 6.4 Hz, 1H), 3.23 (d, J = 6.4 Hz, 2H), 1.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) = 196.2, 172.4, 161.3, 137.2, 135.0, 135.0, 132.0, 129.9, 129.7, 129.5, 128.7, 128.7, 127.4, 120.5, 90.2, 41.0, 39.3, 22.4; FTIR (film): 3091, 2983, 1756, 1672, 1586, 1568,

1474, 1396, 1474, 1396, 1298, 1264, 1104, 1071, 967, 947, 822, 764, 744, 541, 477
cm⁻¹; HRMS (MALDI -TOF): m/z calcd for C₂₀H₁₆BrClO₃ [M+Na]⁺ 440.9863, found:
440.9866.

anti: 5-methyl-5-(1-(naphthalen-1-yl)-3-oxo-3-phenylpropyl)furan-2(5H)-one (3p)

Purified with ethyl acetate/petroleum ether (1/5) to give **3p** as white solid (105.8 mg, 99% yield); mp 56.3-57.8 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 8.29 (d, *J* = 8.5 Hz, 1H), 7.91 - 7.80 (m, 5H), 7.63 - 7.50 (m, 4H), 7.46 - 7.41 (m, 3H), 6.00 (d, *J* = 5.6 Hz, 1H), 4.94 (t, *J* = 6.1 Hz, 1H), 3.48 (qd, *J* = 18.3, 6.2 Hz, 2H), 1.35 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.8, 172.7, 161.9, 136.4, 136.1, 133.9, 133.4, 132.3, 129.2, 128.7, 128.0, 126.6, 126.5, 125.6, 125.6, 123.1, 120.1, 90.8, 40.4, 39.1, 22.7; FTIR (film): 3056, 2979, 1751, 1683, 1597, 1511, 1284, 1230, 1101, 951, 820, 781, 760, 689 cm⁻¹; HRMS (MALDI -TOF): m/z calcd for C₂₄H₂₀O₃ [M+Na]⁺ 379.1311, found: 379.1305.

anti:5-methyl-5-(1-(naphthalen-2-yl)-3-oxo-3-phenylpropyl)furan-2(5H)-one (3q)

Purified with ethyl acetate/petroleum ether (1/3) to give **3q** as white solid (85.5 mg, 80% yield); mp 44.5-47.2 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.89 - 7.83 (m, 6H), 7.61 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.56 - 7.47 (m, 4H), 7.45 - 7.40 (m, 2H), 6.04 (d, *J* = 5.6 Hz, 1H), 4.03 (t, *J* = 6.3 Hz, 1H), 3.43 (qd, *J* = 18.0, 6.8 Hz, 2H), 1.38 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.6, 172.7, 161.4, 137.0, 136.5, 133.4, 133.3, 132.7, 128.7, 128.4, 128.0, 127.9, 127.6, 127.3, 126.2, 126.0, 120.5, 90.5, 46.8, 39.5, 23.0; FTIR (film): 2361, 1752, 1685, 1449, 1101, 817, 752, 688, 431, 425, 416

cm⁻¹; HRMS (MALDI-TOF): m/z calcd for C₂₄H₂₀O₃ [M+Na]⁺ 379.1308, found: 379.1305.

anti: 5-(1-(furan-2-yl)-3-oxo-3-phenylpropyl)-5-methylfuran-2(5H)-one (3r)

Purified with ethyl acetate/petroleum ether (1/4) to give **3r** as yellow solid (83.5 mg, 94% yield); mp 41.3-43.5 °C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.94 -7.88 (m, 2H), 7.58 - 7.54 (m, 1H), 7.47 - 7.43 (m, 3H), 7.34-7.33 (m, 1H), 6.32-6.30 (m, 1H), 6.23 (d, *J* = 3.2 Hz, 1H), 6.00 (d, *J* = 5.6 Hz, 1H), 3.90 (dd, *J* = 8.5, 4.7 Hz, 1H), 3.44 (ddd, *J* = 22.3, 17.6, 6.6 Hz, 2H), 1.44 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.0, 172.1, 160.6, 152.39, 141.9, 136.4, 133.4, 128.7, 128.0, 120.4, 110.5, 108.4, 89.4, 41.3, 37.4, 21.4; FTIR (film): 2924, 1762, 1684, 1597, 1449, 1107, 956, 822, 761, 690, 562 cm⁻¹; HRMS (MALDI -TOF): m/z calcd for C₁₈H₁₆O₄ [M]⁺ 296.1049, found: 296.1046.

anti: 5-methyl-5-(3-oxo-3-phenyl-1-(thiophen-2-yl)propyl)furan-2(5H)-one (3s)

Purified with ethyl acetate/petroleum ether (1/5) to give **3s** as colorless oil liquid (88 mg, 94% yield); ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.87 (d, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46-7.42 (m, 3H), 7.21 (d, *J* = 5.1 Hz, 1H), 7.05 (d, *J* = 3.4 Hz, 1H), 6.97-6.95 (m, 1H), 6.00 (d, *J* = 5.6 Hz, 1H), 4.18 (t, *J* = 6.3 Hz, 1H), 3.35 (qd, *J* = 17.8, 6.3 Hz, 2H), 1.46 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.2, 172.2, 1108, 962, 906, 818, 764, 720, 689, 577, 543, 512 cm⁻¹; HRMS (MALDI -TOF): m/z calcd for C₁₈H₁₆O₃S [M+Na]⁺ 335.0712, found: 335.0713.

anti: 5-methyl-5-(3-oxo-1-phenylbutyl)furan-2(5H)-one (3t)⁶ⁱ

Purified with ethyl acetate/petroleum ether (1/2) to give **3t** as colorless liquid (56.4 mg, 77% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.37 (d, J = 5.6 Hz, 1H), 7.23 (m, 5H), 5.95 (d, 5.7 Hz, 1H), 3.76-3.51 (m, 1H), 3.00-2.69 (m, 2H), 2.03 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 206.2, 172.5, 161.2, 139.0, 129.3, 128.6, 127.5, 120.3, 90.1, 46.6, 44.3, 30.6, 22.6.

anti: 5-methyl-5-(3-oxocyclopentyl)furan-2(5H)-one (3u)⁶ⁱ

Purified with ethyl acetate/petroleum ether (1/2) to give **3u** as colorless liquid (27.6 mg, 51% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.40 (d, J = 5.7 Hz, 1H), 6.12 (d, J = 5.7 Hz, 1H), 2.64-2.55 (m, 1H), 2.46-2.33 (m, 2H), 2.26-2.15 (m, 2H), 1.97-1.89 (m, 1H), 1.63-1.55 (m, 1H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 216.1, 171.9, 158.7, 121.6, 88.9, 43.6, 39.6, 38.4, 23.7, 23.1.

5-methyl-5-(3-oxopentyl)furan-2(5H)-one (3v)

Purified with ethyl acetate/petroleum ether (1/3) to give **3v** as colorless liquid (20.8 mg, 38% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.30 (d, J = 5.6 Hz, 1H), 5.96 (d, J = 5.6 Hz, 1H), 2.41-2.29 (m, 4H), 2.09-2.04 (m, 2H), 1.45 (s, 3H), 0.99 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 209.9, 172.3, 160.3, 120.4, 88.1, 36.0, 35.0, 35.8, 31.0, 24.3; FTIR (film): 3568, 2928, 2384, 2348, 1753, 1712, 1383, 1113, 949, 566 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{O}_3$ $[\text{M}]^+$ 182.0943, Found: 182.0943.

methyl 3-(2-methyl-5-oxo-2,5-dihydrofuran-2-yl)propanoate (3w)

Purified with ethyl acetate/petroleum ether (1/3) to give **3w** as colorless liquid (39.2 mg, 71% yield); ^1H NMR (400 MHz, CDCl_3) δ = 7.33 (d, J = 5.6 Hz, 1H), 6.00 (d, J

= 5.6 Hz, 1H), 3.63 (s, 3H), 2.36-2.28 (m, 1H), 2.25-2.14 (m, 2H), 2.11-2.03 (m, 1H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 173.0, 172.1, 159.7, 120.9, 87.8, 32.7, 28.1, 24.2; FTIR (film): 1752, 1438, 1172, 1108, 950, 822 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_9\text{H}_{12}\text{O}_4$ $[\text{M}+\text{Na}]^+$ 207.0628, found: 207.0632.

tert-butyl 3-(2-methyl-5-oxo-2,5-dihydrofuran-2-yl)propanoate (3x)

Purified with ethyl acetate/petroleum ether (1/10) to give **3x** as colorless liquid (49.5 mg, 73% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.33 (d, J = 5.6 Hz, 1H), 5.96 (d, J = 5.6 Hz, 1H), 2.24-2.00 (m, 4H), 1.45 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 172.2, 171.8, 159.9, 120.7, 88.0, 80.7, 32.7, 29.5, 28.0, 24.2; FTIR (film): 2980, 2935, 1759, 1728, 1457, 1368, 1155, 1107, 950, 823 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_{12}\text{H}_{18}\text{O}_4$ $[\text{M}+\text{Na}]^+$ 249.1097, found: 249.1093.

3-(2-methyl-5-oxo-2,5-dihydrofuran-2-yl)propanenitrile (3y)

Purified with ethyl acetate/petroleum ether (1/3) to give **3y** as colorless liquid (20.9 mg, 46% yield); ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.44 (d, J = 5.6 Hz, 1H), 6.12 (d, J = 5.6 Hz, 1H), 2.46-2.36 (m, 1H), 2.31-2.23 (m, 2H), 2.15-2.05 (m, 1H), 1.53 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 171.5, 158.7, 121.8, 118.9, 86.8, 33.6, 24.0, 12.0; FTIR (film): 2938, 2249, 1754, 1604, 1185, 1110, 951, 900, 823, 521 cm^{-1} ; HRMS (MALDI -TOF): m/z calcd for $\text{C}_8\text{H}_9\text{NO}_2$ $[\text{M}+\text{Na}]^+$ 174.0526, found: 174.0526.

anti: 5-butyl-5-(1,3-diphenylpropyl)furan-2(5H)-one(3z)

Purified with acetone/petroleum ether (1/6) to give **3z** as white solid (91.3 mg, 82% yield); mp 72.4-75.8 $^\circ\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.85-7.82 (m, 2H), 7.55-7.51 (m, 1H), 7.49-7.36 (m, 5H), 7.34-7.30 (m, 2H), 7.27-7.23 (m, 1H), 6.02 (d, J = 5.6 Hz, 1H), 3.89 (t, J = 6.2 Hz, 1H), 3.23 (qd, J = 18.0, 6.4 Hz, 2H), 1.73-1.54 (m,

2H), 1.20-1.04 (m, 4H), 0.78 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.8, 172.9, 160.1, 139.5, 136.6, 133.4, 129.5, 128.6, 128.5, 127.9, 127.4, 121.4, 93.1, 45.9, 39.6, 35.2, 25.6, 22.6, 13.8; FTIR (film): 2953, 2859, 1746, 1684, 1446, 1234, 1000, 932, 822, 748, 704, 686, 548 cm^{-1} ; HRMS (MALDI-TOF): m/z calcd for $\text{C}_{23}\text{H}_{24}\text{O}_3$ $[\text{M}+\text{Na}]^+$ 371.1618, found: 371.1614.

anti: 5-(1,3-diphenylpropyl)-5-isobutylfuran-2(5H)-one(3aa)

Purified with acetone/petroleum ether (1/6) to give **3aa** as white solid (95.7 mg, 86% yield); mp 125.6-129.4 $^{\circ}\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.63 (d, $J = 7.1$ Hz, 2H), 7.53 (t, $J = 8.0$ Hz, 1H), 7.42-7.39 (m, 5H), 7.31 (t, $J = 7.0$ Hz, 2H), 7.26-7.23 (m, 1H), 6.02 (d, $J = 5.6$ Hz, 1H), 3.85 (t, $J = 6.2$ Hz, 1H), 3.24 (d, $J = 6.2$ Hz, 2H), 1.66-1.61 (m, 2H), 1.47-1.38 (m, 1H), 0.78 (d, $J = 6.6$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.8, 172.9, 160.2, 139.6, 136.5, 133.4, 129.6, 128.6, 128.5, 127.9, 127.4, 121.2, 93.3, 46.8, 44.1, 39.6, 24.6, 23.7, 23.6; FTIR (film): 2950, 2866, 1744, 1690, 1607, 1595, 1446, 1364, 1252, 932, 815, 746, 684, 552 cm^{-1} ; HRMS (MALDI-TOF): m/z calcd for $\text{C}_{23}\text{H}_{24}\text{O}_3$ $[\text{M}+\text{Na}]^+$ 371.1618, found: 371.1611.

anti: 5-(1,3-diphenylpropyl)-5-isopropylfuran-2(5H)-one(3ab)

Purified with acetone/petroleum ether (1/6) to give **3ab** as white solid (72.8 mg, 68% yield); mp 143.4-149.5 $^{\circ}\text{C}$ ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.81-7.78 (m, 2H), 7.54-7.50 (m, 3H), 7.41-7.38 (m, 3H), 7.34-7.30 (m, 2H), 7.26-7.22 (m, 1H), 6.10 (d, $J = 5.7$ Hz, 1H), 4.15 (t, $J = 6.1$ Hz, 1H), 3.15 (qd, $J = 18.1, 6.0$ Hz, 2H), 1.98 (heptet, $J = 6.8$ Hz 1H), 1.08 (d, $J = 6.9$ Hz, 3H), 0.66 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 198.1, 172.8, 157.5, 139.8, 136.5, 133.4, 129.6, 128.63, 128.57, 127.9, 127.3, 123.0, 96.2, 43.1, 40.3, 32.5, 18.1, 16.2; FTIR (film): 3113, 3060, 2959, 1744, 1684, 1448, 1366, 1230, 1129, 1011, 942, 822, 748, 707, 682 cm^{-1} ; HRMS (MALDI-TOF): m/z calcd for $\text{C}_{22}\text{H}_{22}\text{O}_3$ $[\text{M}+\text{Na}]^+$ 357.1461, found: 357.1465.

anti: 5-(3-oxo-1,3-diphenylpropyl)-5-phenylfuran-2(5H)-one (3ac)^{6d}

Purified with ethyl acetate/petroleum ether (1/5) to give **3ac** as white solid (99.4 mg, 90% yield); mp 124.8-126.6 $^{\circ}\text{C}$; ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.90 (dd, $J =$

8.4, 1.3 Hz, 2H), 7.80 (d, $J = 5.6$ Hz, 1H), 7.59-7.55 (m, 1H), 7.46 (t, $J = 7.7$ Hz, 2H), 7.28 - 7.20 (m, 5H), 7.15 - 7.09 (m, 5H), 5.99 (d, $J = 5.6$ Hz, 1H), 4.29 (t, $J = 6.3$ Hz, 1H), 3.43 (qd, $J = 18.1, 6.3$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.8, 172.2, 159.8, 138.4, 137.8, 136.6, 133.5, 129.7, 128.7, 128.4, 127.99, 127.97, 127.1, 125.5, 119.7, 93.3, 48.4, 39.1.

anti: 5-(3-oxo-1,3-diphenylpropyl)-5-(p-tolyl)furan-2(5H)-one (3ad)^{6d}

Purified with ethyl acetate/petroleum ether (1/5) to give **3ad** as white solid (94 mg, 82% yield); mp 204.3-206.7°C; ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.90-7.88 (m, 2H), 7.77 (d, $J = 5.6$ Hz, 1H), 7.59-7.55 (m, 1H), 7.45 (t, $J = 7.6$ Hz, 2H), 7.14-7.05 (m, 9H), 5.97 (d, $J = 5.6$ Hz, 1H), 4.26 (t, $J = 6.3$ Hz, 1H), 3.42 (qd, $J = 18.1, 6.3$ Hz, 2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.6, 172.3, 159.9, 138.5, 137.6, 136.6, 134.7, 133.4, 129.7, 129.0, 128.7, 127.97, 127.95, 127.1, 125.4, 119.5, 93.3, 48.4, 39.2, 21.0.

anti: 5-(4-chlorophenyl)-5-(3-oxo-1,3-diphenylpropyl)furan-2(5H)-one (3ae)^{6d}

Purified with ethyl acetate/petroleum ether (1/5) to give **3ae** as yellow solid (94.1 mg, 78% yield); mp 198.5-201.3°C; ^1H NMR (400 MHz, CDCl_3) δ (ppm) = 7.91-7.89 (m, 2H), 7.75 (d, $J = 5.6$ Hz, 1H), 7.58 (t, $J = 7.4$ Hz, 1H), 7.46 (t, $J = 7.7$ Hz, 2H), 7.24-7.10 (m, 9H), 6.00 (d, $J = 5.6$ Hz, 1H), 4.25 (t, $J = 6.2$ Hz, 1H), 3.41 (qd, $J = 18.2, 6.4$ Hz, 2H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) = 197.7, 171.9, 159.4, 138.2, 136.5, 136.4, 133.9, 133.6, 129.6, 128.7, 128.6, 128.1, 128.0, 127.3, 126.8, 120.0, 92.7, 48.2, 39.1.

**anti: 5-(3-(4-bromophenyl)-3-oxo-1-phenylpropyl)-5-phenylfuran-2(5H)-one
(3af)**

Purified with ethyl acetate/petroleum ether (1/5) to give **3af** as white solid (65.6 mg, 49% yield); mp 185.7-188.2°C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.79-7.74 (m, 3H), 7.61-7.58 (m, 2H), 7.28-7.21 (m, 5H), 7.14-7.08 (m, 5H), 6.01 (d, *J* = 5.6 Hz, 1H), 4.24 (t, *J* = 6.3 Hz, 1H), 3.38 (d, *J* = 18.0, 6.3 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 196.8, 172.0, 159.7, 138.2, 137.6, 135.2, 132.0, 129.6, 129.5, 128.7, 128.4, 128.0, 127.2, 125.5, 119.7, 93.1, 48.5, 39.1; FTIR (film): 3091, 2979, 2932, 1757, 1666, 1595, 1448, 1290, 1226, 1108, 962, 906, 818, 764, 720, 689, 577, 543, 512 cm⁻¹; HRMS (MALDI -TOF): *m/z* calcd for C₂₅H₁₉BrO₃ [M+Na]⁺ 469.0410, found: 469.0411.

**anti: 5-(1-(4-chlorophenyl)-3-oxo-3-phenylpropyl)-5-phenylfuran-2(5H)-one
(3ag)^{6d}**

Purified with ethyl acetate/petroleum ether (1/5) to give **3ag** as white solid (55.5 mg, 46% yield); mp 161.4-164.3°C; ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.89 (d, *J* = 7.2 Hz, 2H), 7.77 (d, *J* = 5.6 Hz, 1H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.29-7.23 (m, 5H), 7.08 (q, *J* = 8.4 Hz, 4H), 6.00 (d, *J* = 5.6 Hz, 1H), 4.28 (t, *J* = 6.3 Hz, 1H), 3.38 (qd, *J* = 17.9, 6.3 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 197.5, 172.0, 159.5, 137.6, 137.1, 136.4, 133.6, 133.0, 130.9, 128.8, 128.6, 128.1, 128.1, 128.0, 125.2, 119.8, 83.0, 47.7, 39.0.

Procedure for Control Experiment: α-angelica lactone **2a** (0.16 mmol, 15 μL) was dissolved in anhydrous THF (1.0 mL) and the solution was cooled to -78 °C, then

LDA (0.15 mmol, 75 μ L, 2M in THF) was added under N₂. Subsequently the reaction solution was stirred at -78 °C for 20 min, then compound **10** was added and the reaction mixture was allowed to warm to room temperature and stirred overnight. TLC indicated that the desired product **3a** was not generated. Then, the crude mixture was concentrated under vacuum and purified by flash silica gel column chromatography to recover compound **10** in 83% yield (57 mg).

ASSOCIATED CONTENT

Supporting Information

The copies of ¹H and ¹³C NMR spectra for all products and the X-ray data for compound **3j** are available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Author

*E-mail: duguangfen@shzu.edu.cn; helin@shzu.edu.cn; db_tea@shzu.edu.cn

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (Nos. 21262027, 21428302) and Shihezi University (No. 2012ZRKXJQ06).

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