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2-Aryl-3,4-dihydropyrans as building blocks for organic synthesis: ring-opening reactions with nucleophiles

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ABSTRACT

An electrophilic ring-opening reaction of 2-aryl-3,4-dihydropyran with many nucleophiles, such as thiophenols, thiols, benzenesulfinic acid, resorcin, 2-methylfuran, benzamide and allyltrimethylsilane, was developed. In the presence of an appropriate catalyst, a product that contains not only a moiety of the nucleophile but also a fragment of 1,3-dicarbonyl compound was obtained.

1. Introduction

Heterocyclic compounds display an intrinsic reactivity, which enables rich, versatile and productive transformations. Taking into account their ubiquitous presence in natural products and drugs, the development of new and efficient preparative protocols for these structures remains an urgent task in organic synthesis.[1] Dihydropyran derivatives, which are among the most investigated heterocycles in the past decade, are widely present in nature-occurring products.[2] Some of dihydropyrans showed important biological and pharmaceutical activities, and therefore, their synthesis have attracted much attention.[3]

Recently, we have described a three-component reaction of olefins, formaldehyde and β-dicarbonyl compounds, which generated a variety of 2,5,6-trisubstituted 3,4-dihydropyrans in high yields.[4] This reaction opens a facile method to prepare the dihydropyrans. Therefore, using of these dihydropyrans in organic synthesis becomes thus a downstream topic for us. Because skeletons of the dihydropyrans involve a benzyl ether fragment, that is, generally unstable in the presence of nucleophile under acidic condition,[5] the dihydropyran could be a valuable substrate in acid-catalyzed transformations. Out of this consideration, quite recently, we have developed a novel ring-opening reaction of 2-substituted 3,4-dihydropyrans with nucleophiles.[6] However, for the reactions of 2-aryl-3,4-dihydropyrans, only a few nucleophiles have been utilized. In this paper, we will mainly focus on the ring-opening reaction of 2-aryl-3,4-dihydropyrans, in which many nucleophiles, such as thiophenols, thiols, benzenesulfinic acid, resorcin, 2-methylfuran, benzamide and allyltrimethylsilane, were screened. These reactions along with our previous results offered comprehensive information about the ring-opening reaction of 2-aryl-3,4-dihydropyrans.

Initially, reaction of a 2-aryl-3,4-dihydropyran, **1a**, with thiophenol, **2a**, was investigated, and the results are listed in Table 1. In the absence of catalyst, no reaction occurred (entry 1). When some weak acids, such as $MnCl_2$ and boric acid, were used, a product, **3a**, was formed, but owing to the fact that most of the starting materials keep unaltered, as a result, the yields obtained are rather poor (entries 2 and 3). These results imply that the ring-opening reaction is, indeed, possible, and therefore, we screened the other Lewis acid catalysts in later study. $FeCl_3$ was found to be ineffective for this reaction because of the formation of a very messy mixture (entry 4). With other strong Lewis acids, such as $Sc(OTf)_3$, $InCl_3$, $ZrCl_4$ and $Bi(OTf)_3$, only moderate yields were obtained with a complete consumption of **1a** (entries 5–8). In these cases, many spots were observed by TLC detection. However, attempt to isolate the by-product was failed. Interestingly, an exclusive selectivity to **3a** was observed when using $MnBr_2$ as a catalyst. And after 11 h of

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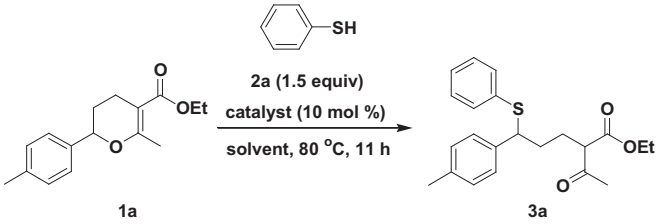
Table 1
Ring-opening reaction of **1a** with **2a** in different conditions[a]



Entry	Catalyst	Solvent	Yield%
1	—	CH_3NO_2	0
2	$MnCl_2$	CH_3NO_2	22
3	H_3BO_3	CH_3NO_2	31
4	$FeCl_3$	CH_3NO_2	10
5	$Sc(OTf)_3$	CH_3NO_2	45
6	$InCl_3$	CH_3NO_2	62
7	$ZrCl_4$	CH_3NO_2	55
8	$Bi(OTf)_3$	CH_3NO_2	46
9	$MnBr_2$	CH_3NO_2	87
10	$MnBr_2$	Toluene	Trace
11	$MnBr_2$	1,4-Dioxane	10
12	$MnBr_2$	DCE	29
13[b]	$MnBr_2$	CH_3NO_2	85

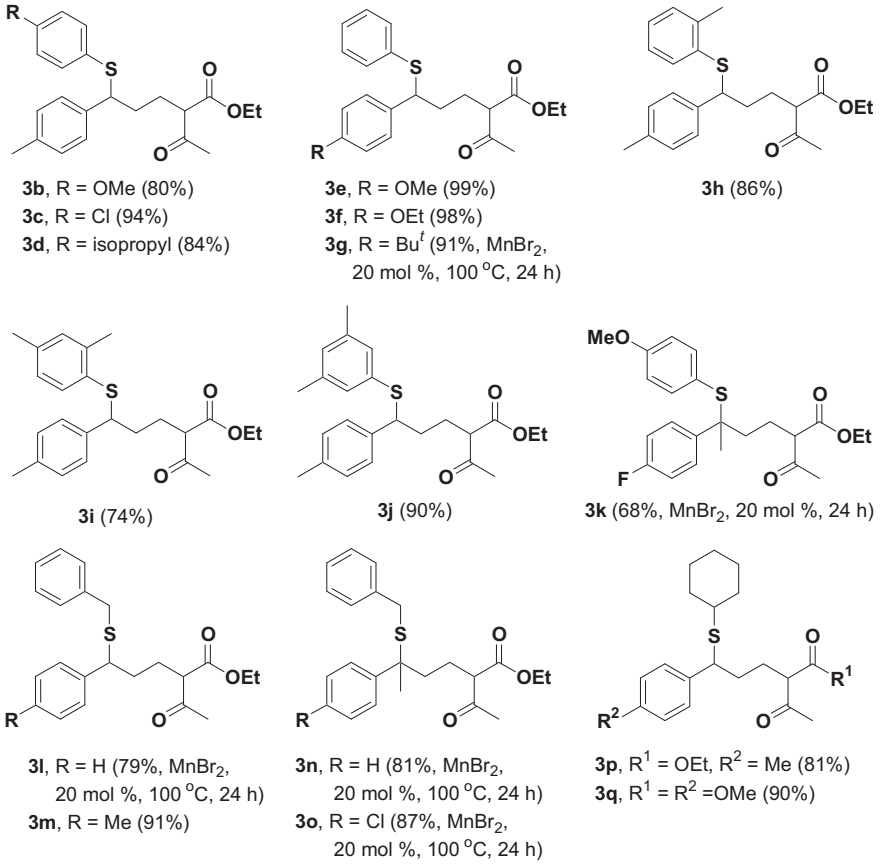
[a] The reaction was performed in 0.25 mmol scale in 1.0 ml of solvent.
[b] The reaction was performed in 20 mmol scale.

reaction at 80 °C, the yield reached to 87% (entry 9). Further investigation revealed that the solvent also played a key role in controlling the catalytic activity of $MnBr_2$, and nitromethane was proved to be an appropriate solvent for this system (entries 9–12).

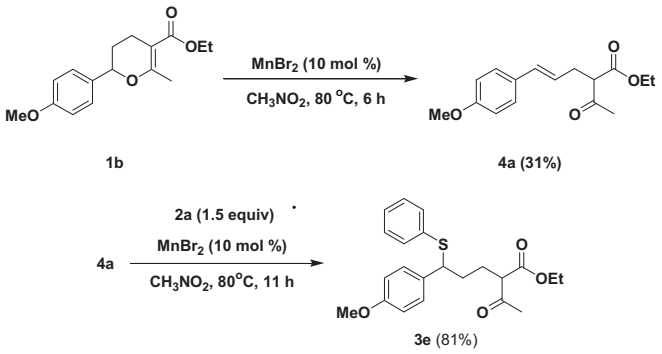
With the optimized conditions in hand, we probed the scope of the reaction with respect to both the dihydropyrans and thiophenols. As shown in Scheme 1, a variety of dihydropyrans and thiophenols could be applied in the ring-opening reaction, and the corresponding products were obtained in good to excellent yields. Thiols can also be used instead of thiophenol to react with **1a**-type dihydropyran under catalysis of $MnBr_2$ to generate the corresponding ring-opening products in high yields. A reaction in preparative-scale (20 mmol) was also investigated by using thiophenol **2a** as substrate, and it was found that the reaction proceeded uneventfully (Table 1, entry 13), indicating the usefulness of this method for practical synthesis. It should be noted that because the formed product contains not only a fragment of 1,3-dicarbonyl compound, but also a moiety of sulfide, it is thus conceivable that these products could be useful for organic synthesis.

The mechanism of the ring-opening reaction most likely involves a Lewis acid-assisted formation of a benzylcarbenium and the following electrophilic reaction with the nucleophile. In order to get an evidence, we then treated a 2-aryl-3,4-dihydropyran, **1b**, under the reaction condition in the absence of nucleophile. After 6 h of reaction, a styrene derivative, **4a**, was obtained in 31% of yield (Scheme 2). Interestingly, in the presence of $MnBr_2$, the isolated **4a** can react smoothly with thiophenol, **2a**, to form the ring-opening product, **3e**, in 81% of yield. This result implies (i) a benzylcarbenium might be, indeed, formed, which can then generate **4a** through a hydrogen transfer pathway; and (ii) **4a** might be the reaction intermediate for the model reaction.

On the basis of these results, we thus proposed a plausible mechanism in Fig. 1. In the beginning of the reaction, the dihydropyran was activated by $MnBr_2$ to form a benzylcarbenium (**I**) via cleavage of C(2)–O bond,[7] which then underwent a hydrogen



Scheme 1. Ring-opening reactions of 2-aryl-3,4-dihydropyrans with thiophenols or thiols catalyzed by $MnBr_2$. Unless otherwise specified, all the reactions were conducted under the optimized condition in Table 1.



Scheme 2. Subdivision of the ring-opening reaction and the intermediate isolated from the catalytic system.

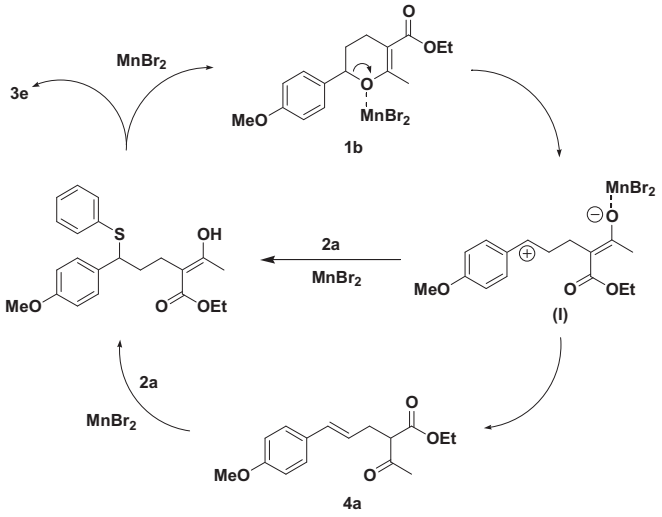
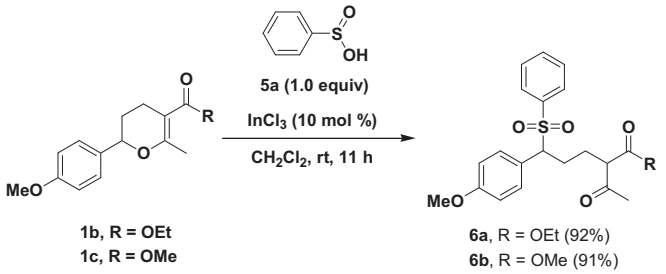


Fig. 1. Plausible mechanism of the ring-opening reaction of dihydropyran **1b** with **2a**.

transfer to form **4a**. It should be noted that, in the beginning of the catalytic cycle, $MnBr_2$ might also coordinate with the carbonyl group of the ester functionality of **1b**, activating indirectly the C–O bond of ether group, and leading to thus a formation of a benzylcarbenium (**I**). After an atom-economic addition of **2a** to **4a**, the final ring-opening product **3e** could be formed.[8] It should be noted that, in the presence of a Lewis acid catalyst, (**I**) could also be directly trapped with **2a** to form the desired product **3e**.[8b,9] Although these reaction pathways are both operative for the formation of **4a**, in view of the presence of a ketocarbonyl in the structures of the intermediate **4a** and the formed product **3e**, which are also reactive toward nucleophiles under acidic condition, controlling of the reaction selectivity is thus a challenge. The use of a weak Lewis acid as catalyst ensures the selectivity but may also be a reason of insufficient reaction. On the contrary, the reaction over a strong Lewis acid proceeds rapidly, but suffers from a bad control of the reaction selectivity. Thanks to the mild acid strength of $MnBr_2$ catalyst, we are able to make a good balance between the conversion and the selectivity to the ring-opening product. In addition, the unique performance of $MnBr_2$ as a Lewis acid catalyst may also be valuable for other organic transformations, and this point deserves further investigation.

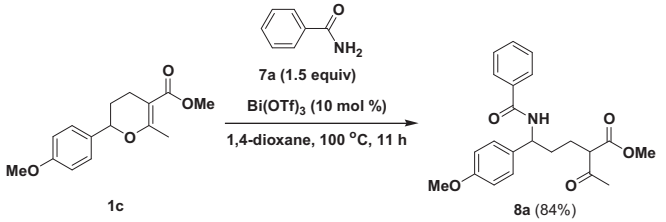
According to this mechanism, other nucleophiles might also be applicable. We thus explore the generality of this ring-opening reaction with respect to nucleophiles. In view of the huge difference on the reactivity of nucleophiles, the reaction condition has to be optimized for each substrate.[10] Catalyst and solvent proved to be both important for the screening of nucleophiles.

As shown in Scheme 3, benzenesulfinic acid, **5a**, can readily react, in the presence of catalytic amount of $InCl_3$, with dihydropyrans, **1b** and **1c**, to form the corresponding ring-opening products, **6a** and **6b**, in excellent yields. Instead of sulfide, the formed products, here, contain a fragment of sulfone in the structure. Although the sulfone product could be theoretically synthesized by means of an oxidation of sulfide that was prepared through the first ring-opening reaction, the reaction of benzenesulfinic acid offers a straightforward way for the synthesis of this kind of sulfone.



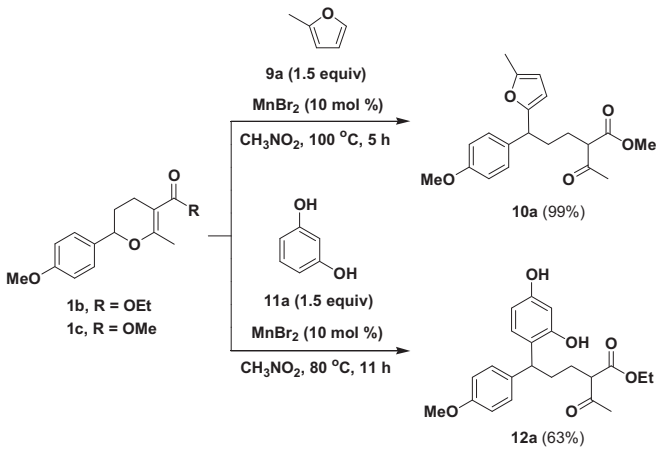
Scheme 3. Ring-opening reaction of the dihydropyrans, **1b** and **1c**, with benzenesulfinic acid **5a**.

Scheme 4 shows a ring-opening reaction of dihydropyran **1c** with a nitrogen-based nucleophile, benzamide **7a**. Because of the poor reactivity of benzamide, a strong Lewis acid, $Bi(OTf)_3$, has to be used in this case. It should be noted that, in view of the fact that $Bi(OTf)_3$ is unstable at high temperature,[11] the real catalyst here might be trifluoromethanesulfonic acid (TfOH) that was in situ generated during the decomposition of $Bi(OTf)_3$. This conjecture can be verified by a fact that 80% yield could be obtained by using TfOH as catalyst. Furthermore, the high reaction yield obtained here implies also that structure of the formed product is quite stable in the presence of strong acid. And therefore, the observed susceptibility of the model ring-opening reaction in Table 1 toward Lewis acid catalyst also has to be related to the reactivity of nucleophile. On the basis of our experience, an empiristic tendency could be summarized at this stage. That is more reactive the nucleophile is, more difficult to control the selectivity.



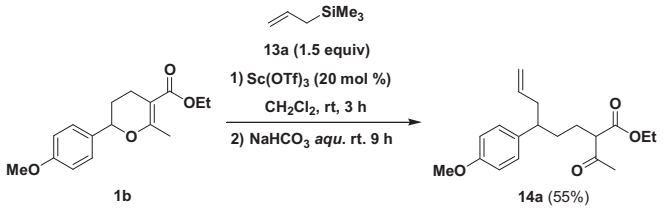
Scheme 4. Ring-opening reaction of dihydropyran **1c** with benzamide **7a**.

Carbon-based nucleophiles, such as 2-methylfuran and resorcin, can also be used in this type of ring-opening reaction. As shown in Scheme 5, in the presence of $MnBr_2$, the ring-opening reaction of **1c** with 2-methylfuran **9a** proceeded exclusively, and the corresponding ring-opening product **10a** was obtained in nearly quantitative yield. However, in the case of resorcin **11a**, only a moderate yield was obtained. Many other carbon-based nucleophiles might also be applicable in this reaction, and the study in this line is underway in our group.



Scheme 5. Ring-opening reaction of dihydropyrans, **1b** and **1c**, with 2-methylfuran **9a** and resorcin **11a**.

Finally, the reactivity of a silicon-containing nucleophile, allyltrimethylsilane, was examined in the ring-opening reaction (Scheme 6). In this case, the reaction has to be conducted in dichloromethane at room temperature by using $Sc(OTf)_3$ as catalyst. The obtained product contains not only a double bond but also a fragment of 1,3-dicarbonyl compound. Therefore, it might be valuable for organic synthesis.



Scheme 6. Ring-opening reaction of dihydropyran **1b** with allyltrimethylsilane **13a**.

In conclusion, an electrophilic ring-opening reaction of 2-aryl-3,4-dihydropyran with nucleophile was described. Many nucleophiles, such as thiophenols, thiols, benzenesulfinic acid, benzamide, 2-methylfuran, resorcin, and allyltrimethylsilane, were all successfully used in this type of ring-opening reaction. The generated products contain not only a core structure of the nucleophile, but also a fragment of 1,3-dicarbonyl compound. The ring-opening reaction might proceed through (i) a Lewis acid-assisted cleavage of C(2)–O bond that generates a benzylcarbenium intermediate, and (ii) the following electrophilic reaction of the reaction intermediate with a nucleophile. These results offered a complementary information about the ring-opening reaction of 2-aryl-3,4-dihydropyran, and demonstrated that many nucleophiles could be successfully used. The other nucleophiles might also be applicable in this type of ring-opening reaction, and the study in this line is underway in our group.

2. Experimental section

2.1. General

4-Methylstyrene, 4-fluoro-α-methylstyrene, *tert*-butylstyrene, 4-methoxystyrene, 4-ethoxystyrene, thiophenol, 3,5-dimethylthiophenol, 2,4-dimethylthiophenol, 4-chlorothiophenol, 4-isopropylthiophenol, 4-methoxythiophenol, 2-methylthiophenolethiol, benzenemethanethiol, 2-methylfuran, allyltrimethylsilane, benzenesulfinic acid, $Sc(OTf)_3$, $Bi(OTf)_3$, $InCl_3$, 4-hydroxy-6-methyl-2-pyrone and chloroform-*d* were purchased from Alfa Aesar Chemical Company. α-Methylstyrene, resorcin, $MnBr_2$, methyl acetoacetate, ethyl acetoacetate, acetylacetone, $FeCl_3$ (anhydrous), $MnCl_2$ (anhydrous), H_3BO_3, DMSO, 1,4-dioxane, 1,2-dichloroethane, acetonitrile, nitromethane, DMF, toluene, ethyl acetate, and formaldehyde aqueous solution (37 wt %) were purchased from Sinopharm Chemical Reagents Limited Company (SCRC). 2,5,6-Trisubstituted 3,4-dihydropyrans were prepared in water according to our reported method starting from olefins, 1,3-dicarbonyl compounds and formaldehyde aqueous solution.[4a] ^1H and ^{13}C NMR spectra were recorded on a Bruker AV-400. Chemical shifts are expressed in parts per million relative to Me_4Si in $CDCl_3$. IR spectra were recorded on an FT-IR Bruker (VERTEX 70) using KBr technology.

2.2. A typical procedure for ring-opening reaction of dihydropyran 1a with 2a

All reactions were conducted in a 10 ml of V-type flask equipped with triangle magnetic stirring. In a typical reaction, nitromethane (1.0 ml) was mixed with **1a** (65.1 mg, 0.25 mmol), **2a** (41.3 mg, 0.38 mmol) and $MnBr_2$ (5.4 mg, 10 mol %) under air. The mixture was stirred for 11 h at 80 °C. After reaction, the mixture was cooled to room temperature and the desired product, **3a**, was obtained by preparative TLC using a mixed solution of ethyl acetate and pet. ether as eluting solvent (the ratio of ethyl acetate/pet. ether is 1/6). 80.6 mg, Yield=87%. Tests for substrate scope and the reaction of using other nucleophile were all performed according to an analogous procedure with above mentioned. The reaction in 20 mmol was performed also in the same procedure, but the product was isolated by a silica column chromatography method.

2.3. A procedure for treating a dihydropyran 1b in the absence of nucleophile and the following reaction of 4a with 2a

All reactions were conducted in a 10 ml of V-type flask equipped with triangle magnetic stirring. In a typical reaction, nitromethane (2.0 ml) was mixed with **1b** (138.2 mg, 0.50 mmol) and $MnBr_2$ (10.7 mg, 10 mol %) under air. The mixture was stirred for 6 h at 80 °C. After reaction, the mixture was cooled to room temperature and a product, **4a**, was obtained by preparative TLC using a mixed solution of ethyl acetate and pet. ether as eluting solvent (the ratio of ethyl acetate/pet. ether is 1/8). Yield=31%, 42.8 mg. The obtained **4a** was then mixed with **2a** (25.6 mg, 0.23 mmol) and $MnBr_2$ (3.3 mg, 10 mol %) in 1 ml nitromethane, and then mixture was then heated at 80 °C for 11 h. At the end of the reaction, **3e** was obtained by preparative TLC isolation procedure (eluting solvent is a mixture of ethyl acetate and pet. ether, the ratio is v/v=1/6) in 81% yield (48.5 mg).

2.4. Procedure for ring-opening allylation reaction of dihydropyran 1b with allyltrimethylsilane 13a

The reaction was conducted in a 10 ml of V-type flask equipped with triangle magnetic stirring. Dichloromethane (1.0 ml) was mixed with dihydropyran **1b** (69.1 mg, 0.25 mmol), allyltrimethylsilane **13a** (42.9 mg, 0.38 mmol), and $Sc(OTf)_3$ (24.6 mg, 20 mol %) under air. The mixture was stirred for 3 h at room temperature. After reaction, the reaction mixture was then mixed with $NaHCO_3$ aqueous solution (2N, 2.0 ml) and stirred for 9 h at room temperature. Finally, 5.0 ml of brine was added and then the aqueous phase was extracted with dichloromethane (5.0 ml×3). The obtained organic phases were then combined together and dried with anhydrous Na_2SO_4. After evaporation under reduced pressure, the desired product, **14a**, was obtained by preparative TLC using a mixed

solution of ethyl acetate and pet. ether as eluting solvent (the ratio of ethyl acetate/pet. ether is 1/8). Yield=55%, 43.6 mg.

2.5. Spectroscopic data of newly synthesized products

*2.5.1. Ethyl 2-acetyl-5-(phenylthio)-5-(p-tolyl)pentanoate (**3a**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.22 (dt, J_a=2.0 Hz, J_b=7.2 Hz, 3H), 1.73–1.97 (m, 4H), 2.13 (d, J=4.8 Hz, 3H), 2.29 (s, 3H), 3.34 (q, J=6.4 Hz, 1H), 4.06–4.18 (m, 3H), 7.06 (d, J=8.0 Hz, 2H), 7.11 (d, J=8.0 Hz, 2H), 7.15–7.22 (m, 3H), 7.23–7.28 (m, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 21.1, 26.1, 26.2, 28.7, 28.8, 33.7, 33.8, 52.9, 53.0, 59.4, 59.4, 61.5, 61.5, 127.1, 127.1, 127.6, 128.7, 129.2, 132.3, 132.4, 134.9, 134.9, 137.0, 138.1, 138.2, 169.4, 169.5, 202.7; IR (cm^{-1}): 3053, 3020, 2980, 2925, 2866, 1738, 1716, 1642, 1583, 1512, 1443, 1359, 1243, 1145, 1023, 821, 742, 692; HRMS m/z (ESI) calcd for $C_{22}H_{26}NaO_3S$ $[M+Na]^+$ 393.1500 found 393.1495.

*2.5.2. Ethyl 2-acetyl-5-[(4-methoxyphenyl)thio]-5-(p-tolyl)pentanoate (**3b**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.21 (dt, J_a=1.2 Hz, J_b=7.2 Hz, 3H), 1.70–1.98 (m, 4H), 2.13 (d, J=2.4 Hz, 3H), 2.29 (s, 3H), 3.35 (q, J=5.6 Hz, 1H), 3.73 (s, 3H), 3.91 (t, J=8.0 Hz, 1H), 4.13 (q, J=6.8 Hz, 2H), 6.72 (d, J=8.4 Hz, 2H), 7.04 (t, J=8.8 Hz, 4H), 7.17 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 21.1, 26.2, 26.3, 28.7, 28.8, 33.2, 33.3, 54.1, 54.1, 55.3, 59.4, 59.5, 61.4, 114.2, 124.7, 127.7, 129.1, 135.9, 135.9, 136.8, 138.3, 138.4, 159.6, 169.5, 169.5, 202.8; IR (cm^{-1}): 2938, 2869, 2837, 1738, 1716, 1591, 1494, 1454, 1360, 1285, 1245, 1173, 1147, 1030, 826; HRMS m/z (ESI) calcd for $C_{23}H_{28}NaO_4S$ $[M+Na]^+$ 423.1606 found 423.1601.

*2.5.3. Ethyl 2-acetyl-5-[(4-chlorophenyl)thio]-5-(p-tolyl)pentanoate (**3c**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.23 (t, J=6.8 Hz, 3H), 1.69–1.97 (m, 4H), 2.14 (d, J=5.2 Hz, 3H), 2.29 (s, 3H), 3.35 (q, J=6.8 Hz, 1H), 4.04 (dd, J_a=2.4 Hz, J_b=7.6 Hz, 1H), 4.10–4.19 (m, 2H), 7.04–7.11 (m, 4H), 7.12–7.18 (m, 4H); ^{13}C NMR ($CDCl_3$): 14.1, 21.1, 26.1, 26.2, 28.8, 28.8, 33.6, 33.7, 53.2, 53.2, 59.3, 59.4, 61.5, 61.5, 127.6, 128.8, 129.3, 133.2, 133.3, 133.3, 133.8, 133.9, 137.2, 137.8, 137.9, 169.4, 169.5, 202.6; IR (cm^{-1}): 2981, 2930, 2866, 1737, 1715, 1644, 1512, 1474, 1450, 1359, 1243, 1145, 1095, 1013, 819; HRMS m/z (ESI) calcd for $C_{22}H_{25}ClNaO_3S$ $[M+Na]^+$ 427.1111 found 427.1105.

*2.5.4. Ethyl 2-acetyl-5-[(4-isopropylphenyl)thio]-5-(p-tolyl)pentanoate (**3d**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.18–2.04 (m, 9H), 1.72–1.97 (m, 4H), 2.12 (d, J=4.4 Hz, 3H), 2.30 (s, 3H), 2.84 (sept, J=7.2 Hz, 1H), 3.33 (q, J=6.4 Hz, 1H), 4.03 (dd, J_a=4.8 Hz, J_b=8.0 Hz, 1H), 4.08–4.17 (m, 2H), 7.02–7.13 (m, 6H), 7.18 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 21.2, 23.9, 26.2, 26.2, 28.7, 33.7, 33.8, 33.8, 53.1, 53.2, 59.4, 59.5, 61.4, 126.9, 127.6, 127.7, 129.2, 131.5, 131.6, 132.8, 132.9, 136.9, 138.3, 138.4, 148.2, 148.2, 169.5, 169.5, 202.8; IR (cm^{-1}): 2963, 2872, 1741, 1719, 1646, 1456, 1362, 1147, 1018, 828; HRMS m/z (ESI) calcd for $C_{25}H_{32}NaO_3S$ $[M+Na]^+$ 435.1970 found 435.1964.

*2.5.5. Ethyl 2-acetyl-5-(4-methoxyphenyl)-5-(phenylthio)pentanoate (**3e**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.21 (dt, J_a=2.8 Hz, J_b=7.2 Hz, 3H), 1.72–1.97 (m, 4H), 2.13 (d, J=4.4 Hz, 3H), 3.34 (q, J=6.0 Hz, 1H), 3.75 (s, 3H), 4.06–4.18 (m, 3H), 6.78 (td, J_a=2.4 Hz, J_b=8.8 Hz, 2H), 7.13 (dd, J_a=1.6 Hz, J_b=8.8 Hz, 2H), 7.16–7.22 (m, 3H), 7.22–7.28 (m, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 26.1, 26.2, 28.8, 28.8, 33.7, 33.8, 52.6, 52.6, 55.2, 59.3, 59.4, 61.5, 113.9, 127.2, 127.2, 128.7, 128.8, 132.5, 132.5, 133.1, 133.2, 134.7, 134.8, 158.8, 169.4, 169.5, 202.7; IR (cm^{-1}): 3060, 2960, 2937, 2837, 1738, 1716, 1608, 1510, 1454, 1360, 1303, 1249, 1176, 1035, 835, 744, 692; HRMS m/z (ESI) calcd for $C_{22}H_{26}NaO_4S$ $[M+Na]^+$ 409.1449 found 409.1444.

*2.5.6. Ethyl 2-acetyl-5-(4-ethoxyphenyl)-5-(phenylthio)pentanoate (**3f**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.20 (dt, J_a=2.4 Hz, J_b=7.2 Hz, 3H), 1.37 (t, J=6.8 Hz, 3H), 1.72–1.98 (m, 4H), 2.12 (d, J=4.4 Hz, 3H), 3.34 (q, J=6.0 Hz, 1H), 3.97 (q, J=6.8 Hz, 2H), 4.05–4.18 (m, 3H), 6.77 (td, J_a=2.0 Hz, J_b=6.4 Hz, 2H), 7.12 (dd, J_a=1.6 Hz, J_b=8.8 Hz, 2H), 7.15–7.21 (m, 3H), 7.21–7.27 (m, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 14.9, 26.1, 26.2, 28.7, 28.8, 33.7, 33.8, 52.6, 52.6, 59.3, 59.4, 61.4, 61.4, 63.4, 114.4, 127.2, 127.2, 128.8, 128.8, 132.5, 132.5, 132.9, 133.0, 134.8, 134.8, 158.2, 169.4, 169.5, 202.7; IR (cm^{-1}): 3061, 2982, 2938, 1967, 1887, 1742, 1720, 1609, 1510, 1477, 1363, 1248, 1177, 1049, 924, 840, 746, 695; HRMS m/z (ESI) calcd for $C_{23}H_{28}NaO_4S$ $[M+Na]^+$ 423.1606 found 423.1601.

*2.5.7. Ethyl 2-acetyl-5-(4-(tert-butyl)phenyl)-5-(phenylthio)pentanoate (**3g**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.20 (t, J=7.2 Hz, 3H), 1.29 (s, 9H), 1.64–2.00 (m, 4H), 2.11 (d, J=3.6 Hz, 3H), 3.34 (q, J=7.6 Hz, 1H), 4.12 (quint, J=6.8 Hz, 3H), 7.13–7.22 (m, 5H), 7.23–7.30 (m, 4H); ^{13}C NMR ($CDCl_3$): 14.1, 26.1, 26.2, 28.7, 28.8, 31.4, 33.7, 33.8, 34.5, 52.8, 52.8, 59.4, 59.5, 61.4, 61.5, 125.5, 127.1, 127.1, 127.4, 128.7, 128.7, 132.0, 132.3, 132.3, 135.0, 135.0, 138.0, 138.0, 150.2, 169.5, 169.5, 202.8; IR (cm^{-1}): 3056, 2965, 2905, 2869, 1739, 1717, 1643, 1584, 1470, 1362, 1146, 1024, 842, 744, 692, 570; HRMS m/z (ESI) calcd for $C_{25}H_{23}NaO_3S$ $[M+Na]^+$ 435.1970 found 435.1964.

*2.5.8. Ethyl 2-acetyl-5-(p-tolyl)-5-(o-tolylthio)pentanoate (**3h**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.21 (dt, J_a=2.4 Hz, J_b=7.2 Hz, 3H), 1.69–1.99 (m, 4H), 2.12 (d, J=4.8 Hz, 3H), 2.29 (s, 3H), 3.34 (q, J=6.8 Hz, 1H), 4.04 (dd, J_a=6.0 Hz, J_b=8.8 Hz, 1H), 4.13 (tq, J_a=2.0 Hz, J_b=7.2 Hz, 2H), 7.01–7.09 (m, 3H), 7.09–7.14 (m, 3H), 7.21–7.26 (m, 1H); ^{13}C NMR ($CDCl_3$): 14.1, 20.7, 21.1, 26.2, 26.2, 28.7, 28.8, 33.8, 33.9, 52.2, 52.2, 59.4, 59.5, 61.4, 126.3, 127.0, 127.1, 127.6, 127.6, 129.2, 130.2, 132.3, 132.4, 134.2, 134.3, 137.0, 138.1, 138.2, 139.8, 139.9, 169.5, 169.5, 202.7; IR (cm^{-1}): 3057, 2982, 2927, 2869, 1739, 1717, 1644, 1514, 1456, 1361, 1245, 1209, 1146, 1049, 1023, 821, 750; HRMS m/z (ESI) calcd for $C_{23}H_{28}NaO_3S$ $[M+Na]^+$ 407.1657 found 407.1651.

*2.5.9. Ethyl 2-acetyl-5-[(2,4-dimethylphenyl)thio]-5-(p-tolyl)pentanoate (**3i**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.21 (dq, J_a=3.6 Hz, J_b=6.8 Hz, 3H), 1.72–1.99 (m, 4H), 2.12 (d, J=4.0 Hz, 3H), 2.25 (s, 6H), 2.29 (s, 3H), 3.33 (q, J=6.8 Hz, 1H), 3.96 (dd, J_a=6.0 Hz, J_b=8.4 Hz, 1H), 4.09–4.18 (m, 2H), 6.86 (d, J=8.0 Hz, 1H), 6.95 (s, 1H), 7.05 (d, J=8.0 Hz, 2H), 7.09 (dd, J_a=2.0 Hz, J_b=8.4 Hz, 2H), 7.14 (d, J=7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): 14.1, 20.7, 21.0, 21.1, 26.2, 26.3, 28.7, 28.8, 33.6, 33.8, 52.6, 52.7, 59.4, 59.5, 61.4, 61.4, 127.0, 127.6, 129.2, 130.4, 130.4, 131.1, 133.5, 133.6, 136.9, 137.3, 137.4, 138.3, 138.3, 140.4, 140.4, 169.5, 169.5, 202.8; IR (cm^{-1}): 2923, 2867, 1738, 1716, 1642, 1451, 1359, 1241, 1146, 1056, 1020, 813; HRMS m/z (ESI) calcd for $C_{24}H_{30}NaO_3S$ $[M+Na]^+$ 421.1813 found 421.1827.

*2.5.10. Ethyl 2-acetyl-5-[(3,5-dimethylphenyl)thio]-5-(p-tolyl)pentanoate (**3j**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.21 (dt, J_a=3.2 Hz, J_b=7.2 Hz, 3H), 1.72–1.97 (m, 4H), 2.12 (d, J=4.8 Hz, 3H), 2.22 (s, 3H), 2.30 (s, 3H), 3.33 (q, J=8.0 Hz, 1H), 4.07 (dt, J_a=2.4 Hz, J_b=8.4 Hz, 1H), 4.10–4.18 (m, 2H), 6.80 (s, 1H), 6.87 (s, 2H), 7.07 (d, J=8.0 Hz, 2H), 7.12 (dd, J_a=1.2 Hz, J_b=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 21.1, 21.2, 26.2, 26.2, 28.7, 28.8, 33.7, 33.8, 52.6, 59.4, 61.4, 127.7, 128.9, 128.9, 129.2, 129.8, 129.9, 134.3, 134.3, 136.9, 138.2, 138.3, 169.5, 169.5, 202.8; IR (cm^{-1}): 2923, 2861, 1739, 1587, 1452, 1364, 1216, 1146, 1021, 849, 687; HRMS m/z (ESI) calcd for $C_{24}H_{30}NaO_3S$ $[M+Na]^+$ 421.1813 found 421.1808.

*2.5.11. Ethyl 2-acetyl-5-(4-fluorophenyl)-5-((4-methoxyphenyl)thio) hexanoate (**3k**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.25 (dt, J_a=2.8 Hz, J_b=7.2 Hz, 3H), 1.52–1.67 (m, 4H), 1.71–1.92 (m, 2H), 2.02–2.14 (m, 1H), 2.17 (d, J=14.4 Hz, 3H), 3.33 (q, J=6.0 Hz, 1H), 3.75 (s, 3H), 4.14–4.22 (m, 2H), 6.70 (td, J_a=2.4 Hz, J_b=8.8 Hz, 2H),

6.94 (dt, J_a=1.2 Hz, J_b=8.8 Hz, 2H), 6.98–7.03 (m, 2H), 7.23–7.29 (m, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 23.4, 23.5, 25.1, 25.2, 28.8, 28.9, 39.3, 39.4, 53.4, 55.2, 59.8, 61.5, 113.8, 113.9, 114.6, 114.6, 114.8, 114.8, 122.4, 128.7, 128.8, 138.4, 138.5, 139.8, 139.9, 160.1, 160.4, 162.6, 169.5, 169.5, 202.7; IR (cm^{-1}): 3066, 2974, 2940, 2838, 2532, 2045, 1892, 1739, 1717, 1594, 1498, 1461, 1405, 1369, 1285, 1246, 1166, 1102, 1028, 830, 737, 644, 527; HRMS *m*/*z* (ESI) calcd for $C_{23}H_{27}FNaO_4S$ $[M+Na]^+$ 441.1512 found 441.1506.

*2.5.12. Methyl 2-acetyl-5-(benzylthio)-5-phenylpentanoate (**3l**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.62–1.94 (m, 4H), 2.12 (d, *J*=9.6 Hz, 3H), 3.30 (quint, *J*=7.6 Hz, 1H), 3.38 (dd, J_a=4.0 Hz, J_b=13.6 Hz, 1H), 3.50 (d, *J*=13.6 Hz, 1H), 3.58 (dt, J_a=1.6 Hz, J_b=6.8 Hz, 1H), 3.67 (d, *J*=6.0 Hz, 3H), 7.17–7.22 (m, 2H), 7.22–7.29 (m, 5H), 7.29–7.36 (m, 3H); ^{13}C NMR ($CDCl_3$): 26.1, 26.2, 28.8. 28.9, 33.9, 34.0, 35.4, 35.4, 48.7, 48.7, 52.5, 59.1, 127.0, 127.4, 128.0, 128.1, 128.4, 128.5, 128.5, 128.6, 128.6, 129.0, 138.2, 138.2, 141.8, 141.9, 169.9, 169.9, 202.7; IR (cm^{-1}): 3074, 2965, 2905, 2869. 1739, 1717, 1643, 1470, 1362, 1270, 1178, 1147, 1024, 842, 744, 692, 570; HRMS *m*/*z* (ESI) calcd for $C_{21}H_{24}NaO_3S$ $[M+Na]^+$ 379.1344 found 379.1338.

*2.5.13. Ethyl 2-acetyl-5-(benzylthio)-5-(p-tolyl)pentanoate (**3m**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.22 (dq, J_a=2.0 Hz, J_b=7.2 Hz, 3H), 1.63–1.90 (m, 4H), 2.12 (d, *J*=8.8 Hz, 3H), 2.34 (s, 3H), 3.27 (quint, *J*=8.4 Hz, 1H), 3.38 (dd, J_a=3.6 Hz, J_b=13.2 Hz, 1H), 3.50 (d, *J*=13.6 Hz, 1H), 3.56 (dt, J_a=2.0 Hz, J_b=7.2 Hz, 1H), 4.13 (dq, J_a=3.2 Hz, J_b=6.8 Hz, 2H), 7.11–7.18 (m, 4H), 7.21 (dt, J_a=1.2 Hz, J_b=6.8 Hz, 3H), 7.24–7.31 (m, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 14.1, 21.2, 26.1, 26.2, 28.7, 28.8, 33.9, 34.0, 35.3, 35.4, 48.4, 48.4, 59.3, 59.3, 61.4, 126.9, 127.9, 128.4, 129.0, 129.3, 136.9, 138.3, 138.4, 138.7, 138.8, 169.4, 169.5, 202.8, 202.8; IR (cm^{-1}): 3029, 2982, 2925, 1740, 1718, 1454, 1361, 1244, 1151, 1030, 819, 769, 702; HRMS *m*/*z* (ESI) calcd for $C_{23}H_{28}NaO_3S$ $[M+Na]^+$ 407.1657 found 407.1651.

*2.5.14. Ethyl 2-acetyl-5-(benzylthio)-5-phenylhexanoate (**3n**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.23 (q, *J*=7.2 Hz, 3H), 1.55–1.71 (m, 1H), 1.74 (d, *J*=1.6 Hz, 3H), 1.86–1.88 (m, 1H), 1.88–2.06 (m, 2H), 2.13 (d, *J*=16.8 Hz, 3H), 3.23–3.31 (m, 2H), 3.43 (d, *J*=12.0 Hz, 1H), 4.10–4.21 (m, 2H), 7.09–7.14 (m, 2H), 7.16 (td, J_a=1.2 Hz, J_b=6.8 Hz, 1H), 7.18–7.27 (m, 3H), 7.30–7.38 (m, 2H), 7.50–7.59 (m, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 14.2, 23.4, 26.1, 26.2, 28.8, 28.9, 33.9, 34.0, 39.9, 40.0, 52.0, 52.0, 59.8, 61.4, 61.5, 125.8, 126.8, 126.8, 127.1, 127.2, 128.2, 128.2, 128.3, 128.3, 128.4, 129.0, 138.0, 138.0, 144.2, 144.3, 169.4, 169.5, 202.8; IR (cm^{-1}): 3086, 3061, 3029, 2977, 2936, 2873, 1952, 1885, 1739, 1717, 1603, 1450, 1360, 1243, 1206, 1154, 1097, 1070, 1028, 860, 763, 700; HRMS *m*/*z* (ESI) calcd for $C_{23}H_{28}NaO_3S$ $[M+Na]^+$ 407.1657 found 407.1651.

*2.5.15. Ethyl 2-acetyl-5-(benzylthio)-5-(4-chlorophenyl)hexanoate (**3o**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.25 (q, *J*=7.2 Hz, 3H), 1.54–1.68 (m, 1H), 1.71 (d, *J*=1.6 Hz, 3H), 1.74–1.84 (m, 1H), 1.85–1.97 (m, 2H), 2.16 (d, *J*=12.8 Hz, 3H), 3.23–3.32 (m, 2H), 3.45 (d, *J*=12.0 Hz, 1H), 4.17 (double quint, J_a=0.8 Hz, J_b=7.2 Hz, 2H), 7.09–7.14 (m, 2H), 7.15–7.26 (m, 3H), 7.30 (td, J_a=2.4 Hz, J_b=9.6 Hz, 2H), 7.45 (td, J_a=2.4 Hz, J_b=9.6 Hz, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 14.1, 23.3, 26.0, 26.1, 28.9, 29.0, 33.9, 34.0, 39.9, 40.0, 51.5, 51.5, 59.6, 59.7, 61.5, 61.5, 126.9, 128.4, 128.4, 128.4, 128.6, 128.7, 128.9, 132.5, 137.7, 137.7, 143.0, 143.1, 169.4, 169.4, 202.6; IR (cm^{-1}): 3085, 3062, 3029, 2976, 2934, 2873, 1739, 1717, 1645, 1601, 1488, 1454, 1397, 1369, 1258, 1151, 1096, 1012, 831, 710, 697; HRMS *m*/*z* (ESI) calcd for $C_{23}H_{27}ClNaO_3S$ $[M+Na]^+$ 441.1267 found 441.1262.

*2.5.16. Ethyl 2-acetyl-5-(cyclohexylthio)-5-(p-tolyl)pentanoate (**3p**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.10–1.36 (m, 8H), 1.44–1.57 (m, 1H), 1.58–1.86 (m, 6H), 1.86–1.99 (m, 2H), 2.16 (d, *J*=8.0 Hz, 3H), 2.30–2.39 (m, 4H), 3.35 (dq, J_a=1.6 Hz, J_b=6.8 Hz, 1H), 3.79 (dt, J_a=2.0 Hz, J_b=7.2 Hz, 1H), 4.16 (double quint, J_a=2.0 Hz, J_b=6.8 Hz, 2H), 7.10 (d, *J*=8.0 Hz, 2H), 7.17 (d, *J*=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): 14.1, 14.1, 21.1, 25.8, 25.9, 26.0, 26.3, 28.7, 28.8, 33.2, 33.8, 34.6, 34.6, 42.5, 42.5, 47.3, 47.4, 59.5, 59.5, 61.4, 61.4, 127.5, 127.5, 129.2, 136.6, 139.6, 139.7, 169.5, 169.6, 202.9; IR (cm^{-1}): 2928, 2852, 1738, 1716, 1643, 1510, 1449, 1359, 1242, 1145, 1021, 953, 887, 817, 779, 525; HRMS *m*/*z* (ESI) calcd for $C_{22}H_{32}NaO_3S$ $[M+Na]^+$ 399.1970 found 399.1964.

*2.5.17. Methyl 2-acetyl-5-(cyclohexylthio)-5-(4-methoxyphenyl) pentanoate (**3q**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.16–1.23 (m, 4H), 1.51–194 (m, 10H), 2.16 (d, *J*=9.2 Hz, 3H), 2.28–2.38 (m, 1H), 3.35–3.40 (m, 1H), 3.70 (d, 6.8 Hz, 3H), 3.79–3.91 (m, 4H), 6.84 (d, *J*=8.4 Hz, 2H), 7.20 (d, *J*=8.4 Hz, 2H); ^{13}C NMR: 25.7, 25.8, 25.9, 26.2, 28.7, 28.8, 33.2, 33.8, 34.5, 34.6, 42.4, 46.9, 47.0, 52.4, 52.5, 55.2, 59.1, 59.2, 113.8, 128.5, 134.5, 134.6, 158.5, 169.9, 170.0, 202.7, 202.8; IR (cm^{-1}): 3433, 2999, 2929, 2851, 1744, 1716, 1609, 1510, 1446, 1358, 1301, 1248, 1176, 1147, 1035, 834, 544; HRMS *m*/*z* (ESI) calcd for $C_{21}H_{30}NaO_4S$ $[M+Na]^+$ 401.1762 found 401.1753.

*2.5.18. (E)-Ethyl 2-acetyl-5-(4-methoxyphenyl)pent-4-enoate (**4a**).* White solid, mp=41–42 °C; ^{1}H NMR ($CDCl_3$): 1.25 (t, *J*=6.8 Hz, 3H), 2.25 (s, 3H), 2.72 (t, *J*=7.2 Hz, 2H), 3.57 (t, *J*=7.6 Hz, 1H), 3.79 (s, 3H), 4.19 (q, *J*=7.2 Hz, 2H), 5.96 (dt, J_a=15.6 Hz, J_b=7.6 Hz, 1H), 6.39 (d, *J*=15.6 Hz, 1H), 6.82 (d, *J*=8.4 Hz, 2H), 7.24 (d, *J*=8.4 Hz, 2H); ^{13}C NMR: 14.1, 29.2, 31.5, 55.2, 59.7, 61.4, 113.9, 123.4, 127.3, 129.8, 132.1, 159.0, 169.2, 202.5; IR (cm^{-1}): 3414, 3031, 2986, 2965, 2916, 2842, 1736, 1710, 1607, 1511, 1457, 1422, 1367, 1303, 1251, 1217, 1175, 1143, 1030, 974, 838, 795; HRMS *m*/*z* (ESI) calcd for $C_{16}H_{20}NaO_4$ $[M+Na]^+$ 299.1259 found 299.1256.

*2.5.19. Ethyl 2-acetyl-5-(4-methoxyphenyl)-5-(phenylsulfonyl)pentanoate (**6a**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.24 (dt, J_a=7.2 Hz, J_b=4.8 Hz, 3H); 1.67–1.74 (m, 2H), 1.99–2.20 (m, 4H), 2.32–2.36 (m, 1H), 3.41 (t, *J*=6.4 Hz, 1H), 3.76 (s, 3H), 3.98–4.03 (m, 1H), 4.16 (m, 2H), 6.75 (d, *J*=8.8 Hz, 2H), 6.98 (d, *J*=8.8 Hz, 2H), 7.37 (t, *J*=8.0 Hz, 2H), 7.51 (m, 3H); ^{13}C NMR: 14.0, 19.1, 25.0, 25.1, 25.2, 25.3, 28.9, 29.0, 30.5, 55.2, 59.0, 61.5, 65.5, 114.0, 123.1, 123.1, 123.2, 128.6, 128.8, 130.9, 133.4, 137.1, 160.0, 169.0, 169.1, 202.1; IR (cm^{-1}): 3064, 3036, 2962, 2936, 2839, 1737, 1713, 1609, 1513, 1446, 1362, 1298, 1253, 1180, 1145, 1084, 1031, 843, 724, 689, 607; HRMS *m*/*z* (ESI) calcd for $C_{22}H_{26}NaO_6S$ $[M+Na]^+$ 441.1348 found 441.1331.

*2.5.20. Methyl 2-acetyl-5-(4-methoxyphenyl)-5-(phenylsulfonyl) pentanoate (**6b**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.71–1.77 (m, 2H), 2.05–2.14 (m, 1H), 2.15 (d, *J*=4.0 Hz, 3H), 2.31–2.37 (m, 1H), 3.44 (dt, J_a=1.6 Hz, J_b=7.2 Hz, 1H); 3.70 (d, *J*=3.2 Hz, 3H), 3.76 (s, 3H), 3.98–4.03 (m, 1H), 6.75 (d, *J*=8.4 Hz, 2H), 6.98 (d, *J*=8.4 Hz, 2H), 7.36–7.40 (m, 2H), 7.48–7.50 (m, 3H); IR (cm^{-1}): 3063, 3003, 2955, 2841, 1741, 1715, 1610, 1513, 1445, 1360, 1297, 1253, 1145, 1083, 1032, 844, 725, 690, 607, 563, 527; HRMS *m*/*z* (ESI) calcd for $C_{21}H_{24}NaO_6S$ $[M+Na]^+$ 427.1191 found 427.1186.

*2.5.21. Ethyl 2-acetyl-5-benzamido-5-(4-methoxyphenyl)pentanoate (**8a**).* Colorless liquid; ^{1}H NMR ($CDCl_3$): 1.26 (dt, J_a=2.0 Hz, J_b=7.2 Hz, 3H), 1.72 (m, 1H), 1.90 (m, 3H), 2.20 (s, 3H), 3.51 (dt, J_a=20.4 Hz, J_b=6.4 Hz, 1H), 3.78 (s, 3H), 4.19 (q, *J*=7.2 Hz, 2H), 5.10 (m, 1H), 6.55 (t, *J*=6.8 Hz, 1H), 6.87 (d, *J*=8.4 Hz, 2H), 7.27 (d, *J*=7.6 Hz, 2H), 7.46 (m, 3H), 7.77 (d, *J*=7.2 Hz, 2H); ^{13}C NMR: 13.7, 14.0, 19.1, 24.6, 24.7, 29.0, 30.5, 33.4, 52.9, 53.2, 55.3, 58.9, 59.0, 61.5, 65.5, 114.2, 126.8, 126.9, 127.7, 127.8, 128.5, 128.8, 130.9, 131.5, 132.3, 133.6, 133.7, 134.4, 159.0, 166.7, 166.8, 169.5, 169.6, 203.0, 203.1; IR(cm^{-1}): 3308, 3062, 2959, 2934, 2871, 2837, 1732, 1714, 1637, 1611, 1532, 1514, 1488, 1461, 1359, 1280, 1248, 1179, 1149, 1032, 833, 696,

556; HRMS *m*/*z* (ESI) calcd for $C_{23}H_{27}NNaO_5S$ $[M+Na]^+$ 420.1787 found 420.1783.

*2.5.22. Methyl 2-acetyl-5-(4-methoxyphenyl)-5-(5-methylfuran-2-yl)pentanoate (**10a**).* Colorless liquid; ^1H NMR ($CDCl_3$): 1.76–1.85 (m, 3H), 1.97–2.05 (m, 1H), 2.15 (d, J=7.2 Hz, 3H), 2.20 (s, 3H), 3.40 (t, J=7.2 Hz, 1H), 3.70 (d, J=2.4 Hz, 3H), 3.76 (s, 3H), 3.80 (t, J=7.2 Hz, 1H), 5.83 (s, 1H), 5.87 (q, J=2.8 Hz, 1H), 6.82 (d, J=8.8 Hz, 2H), 7.13 (dd, J_a=2.0 Hz, J_b=8.4 Hz, 2H); ^{13}C NMR: 13.5, 26.4, 28.7, 32.5, 32.6, 44.3, 52.3, 55.2, 59.4, 105.8, 106.0, 113.9, 128.7, 134.3, 134.4, 150.8, 155.6, 155.7, 158.3, 170.0, 170.1, 202.8, 202.9; IR (cm^{-1}): 3102, 3000, 2953, 2927, 2868, 2838, 1743, 1715, 1611, 1562, 1512, 1439, 1358, 1299, 1248, 1216, 1178, 1148, 1032, 837, 786, 540; HRMS *m*/*z* (ESI) calcd for $C_{20}H_{24}NaO_5$ $[M+Na]^+$ 367.1521 found 367.1512.

*2.5.23. Ethyl 2-acetyl-5-(2,4-dihydroxyphenyl)-5-(4-methoxyphenyl)pentanoate (**12a**).* Colorless liquid; ^1H NMR ($CDCl_3$): 1.20 (t, J=7.2 Hz, 3H), 1.85 (m, 4H), 2.13 (d, 3.6 Hz, 3H), 3.46 (dd, J_a=16.4 Hz, J_b=6.8 Hz, 1H), 4.12 (m, 3H), 4.12 (t, J=7.2 Hz, 3H), 6.26 (s, 1H), 6.34 (dd, J_a=14.8 Hz, J_b=8.4 Hz, 2H), 6.58 (s, 1H), 6.76 (d, J=8.4 Hz, 2H), 7.12 (d, J=8.4 Hz, 2H); ^{13}C NMR: 13.7, 14.0, 14.1, 19.1, 26.6, 26.7, 28.8, 28.9, 30.5, 32.5, 42.1, 42.3, 55.2, 59.6, 59.7, 60.7, 61.8, 65.9, 103.3, 107.6, 107.7, 107.8, 113.8, 123.1, 123.3, 128.6, 128.8, 128.9, 130.3, 131.1, 136.2, 136.4, 154.3, 154.4, 154.9, 157.0, 157.7, 170.2, 170.3, 204.9; IR (cm^{-1}): 3401, 3033, 2959, 2935, 2870, 2837, 1727, 1699, 1607, 1511, 1456, 1369, 1302, 1246, 1212, 1178, 1149, 1112, 1033, 974, 910, 839, 732, 632, 552; HRMS *m*/*z* (ESI) calcd for $C_{22}H_{26}NaO_6$ $[M+Na]^+$ 409.1627 found 409.1619.

*2.5.24. Ethyl 2-acetyl-5-(4-methoxyphenyl)oct-7-enoate (**14a**).* Colorless liquid; ^1H NMR ($CDCl_3$): 1.24 (dt, J_a=3.2 Hz, J_b=7.2 Hz, 3H), 1.37–1.58 (m, 1H), 1.58–1.80 (m, 3H), 2.13 (d, J=8.4 Hz, 3H), 2.31 (t, J=6.8 Hz, 2H), 2.50–2.61 (m, 1H), 3.32 (quint, J=7.6 Hz, 1H), 3.78 (s, 3H), 4.11–4.20 (m, 2H), 4.90 (s, 0.5H), 4.92 (d, J=0.4 Hz, 1H), 4.97 (s, 0.5H), 5.57–5.69 (m, 1H), 6.83 (td, J_a=3.2 Hz, J_b=7.6 Hz, 2H), 7.06 (d, J=8.4 Hz, 2H); ^{13}C NMR: 14.1, 26.1, 26.3, 28.5, 28.8, 33.3, 33.6, 41.4, 41.5, 44.7, 44.9, 55.2, 59.8, 60.0, 61.3, 61.3, 113.8, 116.1, 128.5, 136.3, 136.3, 136.8, 158.0, 169.7, 169.8, 203.2; IR (cm^{-1}): 3072, 2976, 2956, 2921, 2838, 1738, 1714, 1640, 1610, 1511, 1451, 1361, 1298, 1246, 1206, 1178, 1148, 1119, 1035, 914, 831, 550, 419; HRMS *m*/*z* (ESI) calcd for $C_{19}H_{26}O_4$ $[M]^+$ 318.1831 found 318.1844.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.08.075.

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