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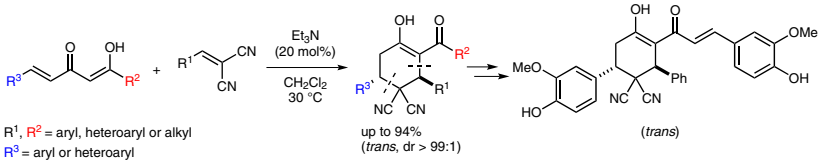
Base-Catalyzed Domino Double Michael Reactions of 1-Hydroxy-1,4-dien-3-ones and 2-Alkylidenemalononitriles: A Diastereoselective Route to Polysubstituted 3-Alkanoyl-4-hydroxycyclohex-3-enes

Yeong-Jiunn Jang[a,b,c]
Yu-Shan Chen[a]
Chia-Jui Lee[a]
Chi-Han Chen[a]
Wenwei Lin*[a]

[a] Department of Chemistry, National Taiwan Normal University, No. 88, Sec. 4, Tingchow Road, Taipei, Taiwan 11677, R.O.C. wenweilin@ntnu.edu.tw
[b] School of Pharmacy, College of Pharmacy, China Medical University, No. 91 Hsueh-Shih Road, Taichung, Taiwan 40402, R.O.C.
[c] Chinese Medicine Research and Development Center, China Medical University Hospital, No. 2 Yuh-Der Road, Taichung, Taiwan 40447, R.O.C.



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Abstract The diastereoselective synthesis of 2,6-disubstituted 3-alkanoyl-4-hydroxycyclohex-3-ene-1,1-dicarbonitriles has been developed through domino double Michael addition of 1,5-disubstituted 1-hydroxy-1,4-dien-3-ones to 2-alkylidenemalononitriles catalyzed by triethylamine. This simple domino process affords a variety of highly functionalized 3-alkanoyl-4-hydroxycyclohex-3-enes, some of which are not easily accessible using other methodologies, in moderate to good yields and excellent diastereoselectivity (dr > 95:5). Thus, the generality of this process and feasibility of introducing bioactive moieties make this reaction highly valuable in synthetic and medicinal chemistry.

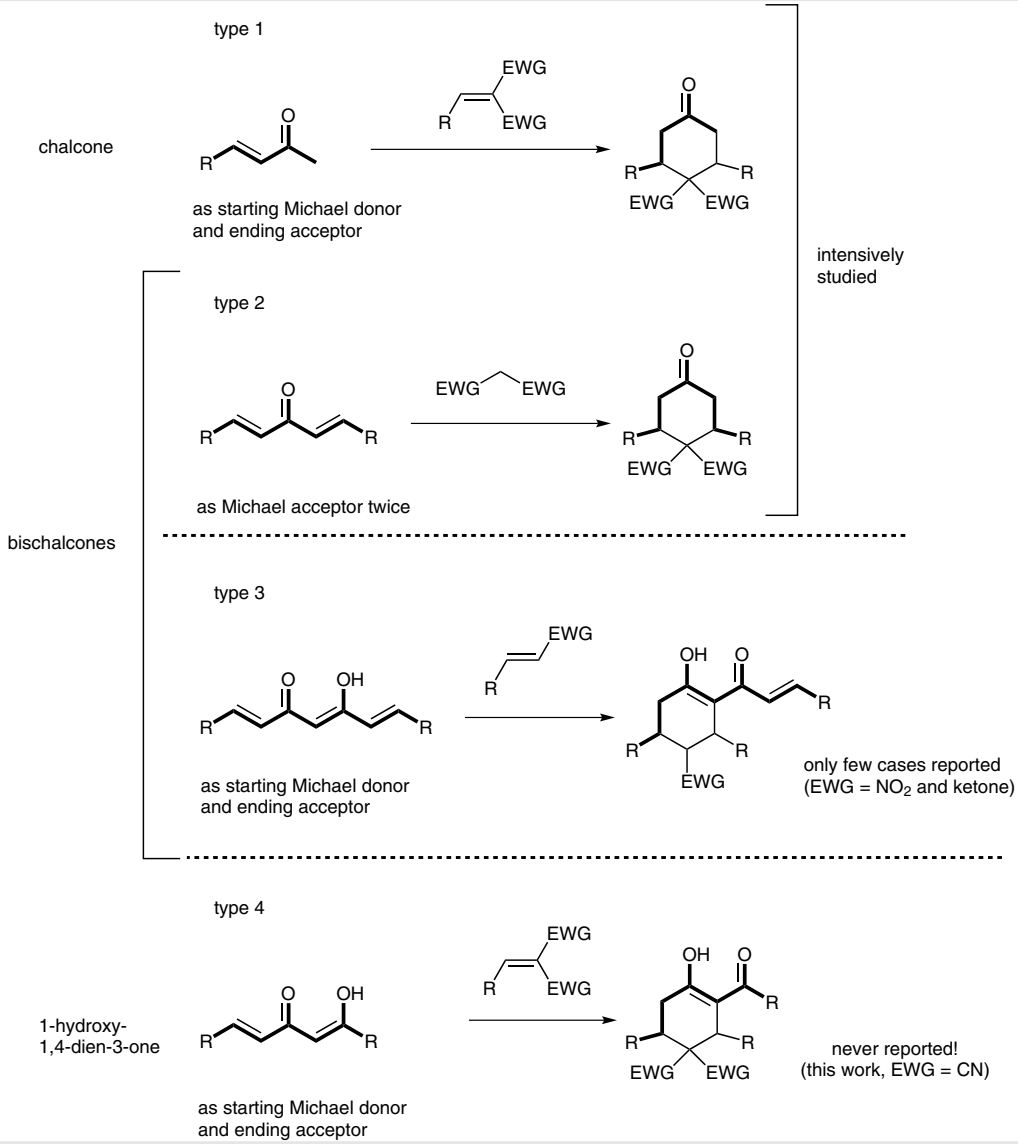
Key words domino reaction, Michael addition, diastereoselectivity, cyclohexanone, curcumin

The construction of suitably functionalized cyclohexanones and related cyclohexanol skeletons plays a central role in many natural product syntheses due to their significant biological and pharmaceutical importance.[1] In literature reports, many methods for the synthesis of substituted cyclohexanones have arisen from different approaches, such as [4+2] cycloaddition,[2] rhodium(I)-catalyzed Pauson–Khand reaction,[3] palladium-catalyzed intramolecular hydroalkylation,[4] organocatalyzed domino annulation,[5] and reductive tandem double Michael cascade,[6a] highlighting the continued interest in these frameworks from the synthetic community. In particular, domino processes are a powerful strategy for the construction of complex molecular skeletons by simultaneous formation of two or more bonds from simple materials in a one-pot manner.[7] These benefits are of particular interest in pharmaceutical research for the construction of libraries of biologically active compounds. Therefore, developing novel domino reactions for the preparation of structurally diverse chemical libraries of polyfunctional compounds remains an interest for synthetic chemists. In this field, the usefulness of sequential Michael additions has been demonstrated,[8] and domino Michael reactions have especially emerged as one of the most potent tools for the synthesis of various important cyclic building blocks during recent decades.

It is well documented that the Michael reaction of chalcones containing an activated alkene, such as nitroolefins and 1,5-disubstituted penta-1,4-dien-3-ones, with active methylene substrates, such as malononitrile and 1,3-dicarbonyl compounds, can be employed to prepare highly substituted cyclohexanones, while chalcones can serve both as the starting Michael donor and ending acceptor in domino double Michael reactions (Scheme 1, type 1) and bischalcones as the Michael acceptors twice in the reaction course (type 2). Recently, curcumin and its derivatives, also bischalcones, are reported to have chalcone-like behavior and they have been used to build substituted cyclohexanones with nitroolefins and chalcones (type 3).[6b,c] Although, there are several reports of the use of δ-aryl-β-oxo-γ,δ-unsaturated esters,[9] to the best of our knowledge there are no reports in the literature of the highly functionalized syntheses of 3-alkanoyl-4-hydroxycyclohex-3-enes using 1-hydroxy-1,4-dien-3-ones as both the starting Michael donor and ending acceptor in domino double Michael reactions (type 4).

Herein, we disclose that only *trans*-isomers of 2,6-disubstituted 3-alkanoyl-4-hydroxycyclohex-3-ene-1,1-dicarbonitriles **3** are obtained in an efficient synthesis in good yields with excellent diastereoselectivity through the domino Michael addition of 1-hydroxy-1,4-dien-3-ones **1** with 2-alkylidenemalononitriles **2** catalyzed by triethylamine.

The starting materials, 1-hydroxy-1,4-dien-3-ones **1**, were readily prepared by benzoylation of methyl vinyl ketones and acid chlorides with lithium diisopropylamide.[10a] Initially, to identify the optimal reaction conditions, a representative reaction affording **3aaa** was investigated in the

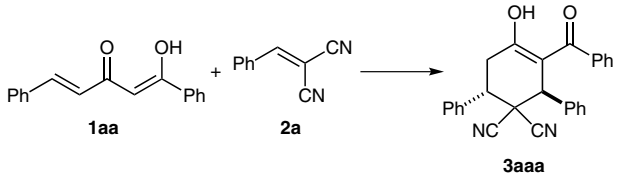


Scheme 1 Domino double Michael reactions for the construction of cyclohexanones

presence of different bases in dichloromethane at 30 °C. First of all, the reaction of **1aa** with 1.2 equivalents of 2-benzylidenemalononitrile (**2a**), in the presence of piperidine as base catalyst (20 mol%) for two days, afforded an 85% NMR yield of **3aaa** (Table 1, entry 1). The reaction was then performed in the presence of pyrrolidine and 4-(dimethylamino)pyridine, which led to a noticeable decrease in the yield of **3aaa** to 72% and 70%, respectively, with 11% remaining of **1aa** (entries 2 and 3). The reaction completely failed to occur when pyridine was used as the base (entry 4). The representative reaction was then carried out in the presence of triethylamine which led to slight enhancement in the yield to 91% with no remaining **1aa** after 22 hours (entry 5). DABCO gave a moderate yield (69%), whereas a very poor yield was observed with 4-methylmorpholine (NMM) (entries 6 and 7). From these results, triethylamine emerged as the best choice of base for the domino reaction.[11] Having determined the optimal base for the reaction, investigating the choice of a suitable solvent was performed. From the results in Table 1, dichloromethane was the best solvent giving the maximum yield of the product (entries 8–15 vs. 5). Incidentally, using a higher temperature (60 °C) in 1,2-dichloroethane or toluene resulted in a somewhat faster reaction rate or higher yield and this shows the low level of temperature dependence of the reactions (entries 10 vs. 9 or 14 vs. 13). The ideal conditions thus established were then applied to the synthesis of a library of novel 2,6-disubstituted 3-alkanoyl-4-hydroxycy-

clohex-3-ene-1,1-dicarbonitriles **3** via the domino double Michael reactions of 1-hydroxy-1,4-dien-3-ones **1** and 2-alkylidenemalononitriles **2**.

Table 1 Condition Screening for the Formation of Cyclohexanone **3** via Domino Double Michael Reactions of **1aa** and **2a**[a]

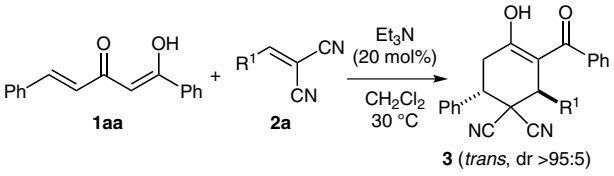


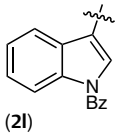
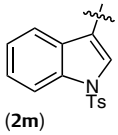
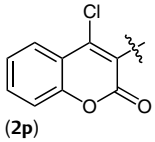
Entry	Catalyst	Solvent	Temp (°C)	Time	Yield[b] (%)	
					3aaa	**1aa**
1	piperidine	CH_2Cl_2	30	2 d	85	0
2	pyrrolidine	CH_2Cl_2	30	2 d	72	11
3	DMAP	CH_2Cl_2	30	2 d	70	11
4	pyridine	CH_2Cl_2	30	1 d	–[c]	–[c]
5	Et_3N	CH_2Cl_2	30	22 h	91	0
6	NMM	CH_2Cl_2	30	2 d	8	82
7	DABCO	CH_2Cl_2	30	2 d	69	13
8	Et_3N	$CHCl_3$	30	1 d	74	11
9	Et_3N	DCE	30	1 d	79	2
10	Et_3N	DCE	60	18 h	79	2
11	Et_3N	THF	30	1 d	58	11
12	Et_3N	MeCN	30	1 d	80	0
13	Et_3N	toluene	30	1 d	20	68
14	Et_3N	toluene	60	1 d	26	51
15	Et_3N	xylenes	30	1 d	21	66

[a] Reaction conditions: **1aa** (0.25 mmol), **2a** (0.3 mmol, 1.2 equiv), catalyst (20 mol%), ACS-grade solvent (2 mL), 30 °C.
[b] NMR analysis: a known amount of Ph_3CH was added to the crude products and used as internal reference for determination of yields of products and remaining starting materials.
[c] No reaction.

With the optimum conditions in hand, we explored the scope and limitation of this route to highly functionalized 3-alkanoyl-4-hydroxycyclohex-3-enes **3** by changing the substitution pattern of the R^1 group in the methylenemalononitrile **2** to modify the nature of the double bond. The reactions proceeded with excellent diastereoselectivity, leading to the formation of the corresponding compound **3** as a single diastereomer. The *trans* configuration of the 2,6-disubstitution of **3aaa** was confirmed by X-ray crystallography.[12] These results are depicted in Table 2. Various electron-poor and electron-rich R^1 substituents on 2-methylenemalonitriles **2** were well-tolerated in the reaction with **1aa**. In general, reactions when R^1 is an *ortho*- or *para*-electron-withdrawing group substituted phenyl (entries 4–7) or when R^1 is a steric hindered naphthyl substituent (entries 2 and 3) all give similar results to that of the unsubstituted 2-benzylidenemalononitrile (**2a**; entry 1). However, when R^1 was a *para*-electron-donating group substituted phenyl stoichiometric **2h** was consumed by excess **1aa** (entry 8). Heteroaryl motifs in **2i**–**k** were successfully incorporated, and the products were obtained in 60–79% yields within nine hours to four days (entries 9–11). Additionally, it should be noted that indoles and coumarins are valuable building blocks found in numerous biologically active natu-

Table 2 Domino Double Michael Reactions of **1aa** and R^1-Substituted **2**[a]



Entry	R^1 (**2**)	Time (h)	Yield[b,c] (%)
1	Ph (**2a**)	22	**3aaa**, 87
2	1-naphthyl (**2b**)	24	**3aab**, 85
3	2-naphthyl (**2c**)	16	**3aac**, 77
4	4-ClC_6H_4 (**2d**)	16	**3aad**, 80
5	4-BrC_6H_4 (**2e**)	16	**3aae**, 77
6	2-ClC_6H_4 (**2f**)	24	**3aaf**, 76
7	2-BrC_6H_4 (**2g**)	9	**3aag**, 75
8[d]	4-$MeOC_6H_4$ (**2h**)	96	**3aah**, 74
9	2-thienyl (**2i**)	96	**3aai**, 79
10	2-furyl (**2j**)	72	**3aaj**, 60
11	3-pyridyl (**2k**)	9	**3aak**, 72
12	 (**2l**)	48	**3aal**, 62
13	 (**2m**)	48	**3aam**, 60
14	*i*-Pr (**2n**)	72	**3aan**, 20
15	*t*-Bu (**2o**)	144	**3aao**-keto, 37
16	 (**2p**)	24	**3aap**, 66

[a] Reaction conditions: **1aa** (0.25 mmol), **2** (0.3 mmol, 1.2 equiv), Et_3N (20 mol%), CH_2Cl_2 (2 mL), 30 °C.
[b] Diastereomeric ratio (dr) measured by ^1H NMR analysis of the crude reaction mixture.
[c] Isolated yield.
[d] Reaction conditions: **1aa** (0.3 mmol, 1.2 equiv), **2h** (0.25 mmol), Et_3N (20 mol%), CH_2Cl_2 (2 mL), 30 °C.

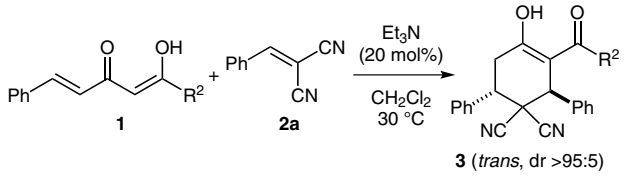
ral products and pharmacologically relevant therapeutic agents.[13–15] Molecules containing these scaffolds exhibit a broad range of bioactivity, therefore, they were also used in our method to expand the library of **3**. Remarkably, indole- and coumarin-substituted methylenemalononitriles were used successfully in the reaction to give **3aal**, **3aam**, and **3aap** in 60–66 % yields (entries 12, 13, and 16); these compounds have a high possibility of having interesting bioactivity. However, other attempts to react alkylidenemalononitriles under the standard conditions gave unsatisfied results, even after prolonged reaction times (entries 14 and 15). Furthermore, only the keto form product (entry 15)[16] was surprisingly generated without any enol product when R^1 = *tert*-butyl (i.e., **2o**) because the intramolecular hydrogen bonding of keto and enol residues was twisted and corrupted due to the steric hindrance between R^1 (*tert*-butyl) and R^2 (phenyl) groups in the product. Obviously, the substituent R^1 and interactions between R^1 and R^2 have a large influence on not only the yield and rate, but also on the product distribution.

Under the optimized conditions, the scope of this new domino double Michael reaction was next examined using various 1-R^2-5-phenyl-substituted **1**, prepared from benzylideneacetone and various readily available acid chlorides (Table 3),[10] and 2-benzylidenemalononitrile (**2a**). It was pleasing to find that most reactions afforded the corresponding products in good yields and with excellent diastereoselectivities. When the R^2 functionality was an electron-withdrawing group containing phenyl group in **1ab** and **1ac**, the desired products were achieved with good efficiency, relatively higher yields, while in the case of an electron-donating group containing phenyl group in **1ad** only a moderate yield was observed as it inactivated the nucleophilic enolate (Scheme 2, intermediate I) and therefore retarded the first addition step (entries 1 and 2 vs. 3). These results indicated that the electronic properties of R^2 play an important role in this process and they are especially beneficial to the first Michael reaction. Furthermore, heteroaryl motifs such as **1ae**–**af** were successfully incorporated, and in similar results **3aea** and **3afa** were obtained in 81–85% yields (entries 4 and 5). The reactions of aliphatic R^2 were also examined (entries 6 and 7), and the corresponding products were produced smoothly with a significant increase both in yields and reaction rates while steric effects were not involved. On the other hand, when a sterically hindered R^2 was investigated (entry 8), a noticeable decrease in reaction rate and yield was found in comparison with electron-withdrawing group substituted phenyls (entries 8 vs. 1 and 2), but remarkably it was still better than that of electron-donating group substituted phenyls (entries 8 vs. 3). It is interesting that electronic effects at R^2 have a larger influence on the yield and rate than steric effects. Similarly, it was found that the keto-form product was predominates when R^2 = *tert*-butyl (entry 8),[17] and it resulted from the steric hindrance between R^2 = *tert*-butyl and R^1 = phenyl groups in the product, which are reversed substituents compared with **3aao** (Table 2, entry 15).

To thoroughly extend the generality of this method, 1-phenyl-5-R^3-substituted **1**, synthesized from benzoyl chloride and methyl vinyl ketones readily prepared through the Aldol condensation or the Wittig reaction, were reacted with 2-benzylidenemalononitrile (**2a**) and the results are summarized in Table 4. To our delight, a wide variety of functionalized **3** were obtained in medium to good yields and with excellent diastereoselectivity. Similar yields and rates were afforded no matter if electron-rich- or electron-poor-substituted phenyl, or heteroaryl motifs were involved. This suggests that 5-R^3 substituents on **1** have less influence on the overall reactivity as compared with R^1 and R^2 substituents and the second addition step on the conjugated ketone was too fast to be retarded by R^3 substituents due to intramolecular addition. Inspired by ideas in Table 2, indolyl motifs were also successfully introduced and provided similar results to other heteroaryl motifs in this position (entries 7 and 8 vs. 4–6).

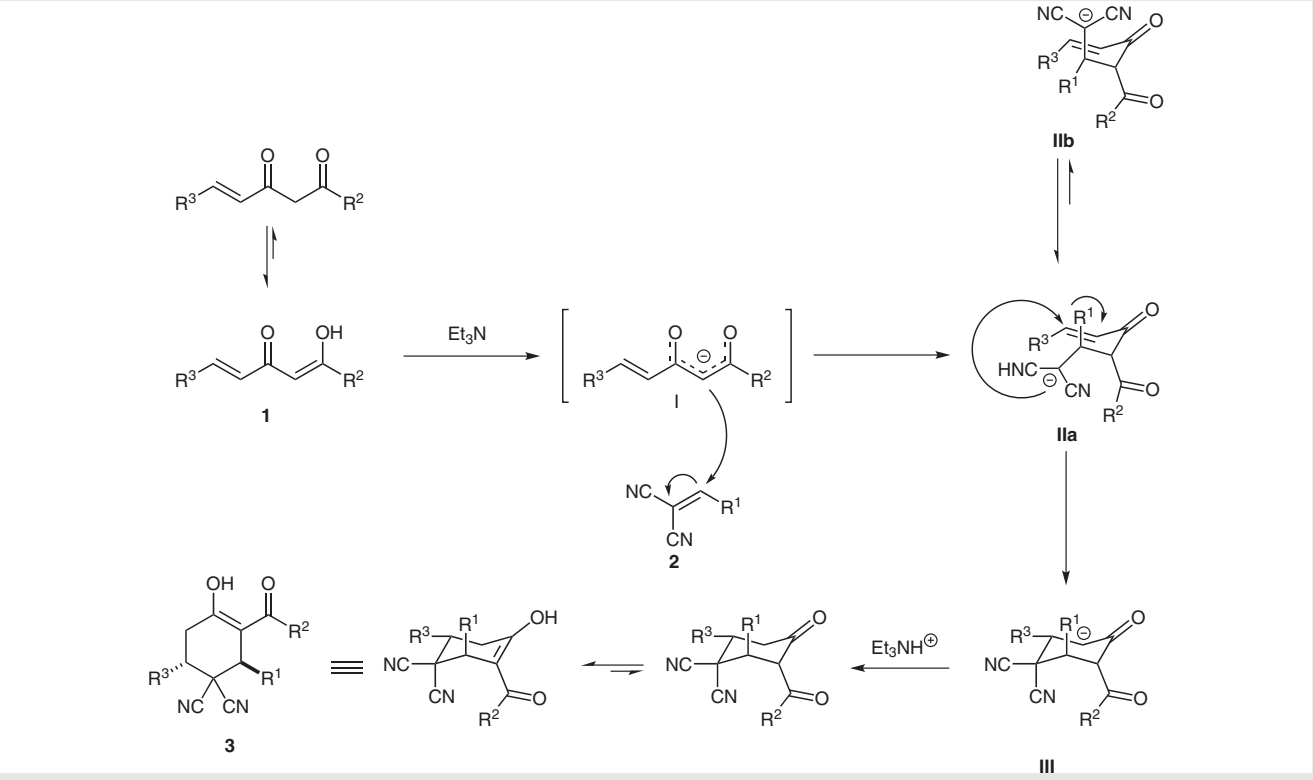
In addition, the scope of the work was further extended to the one-pot reaction due to the easy and mild preparation of **2**. To study this proposal, **1aa** was treated with benzaldehyde and malononitrile in the presence of triethylamine under similar conditions, and it is pleasing to find that the corresponding product **3aaa** was obtained as the sole diastereomer in similar yield to that obtained in a stepwise reaction, although a prolonged reaction time was nec-

Table 3 Domino Double Michael Reactions of **2a** and R^2-Substituted **1**[a]



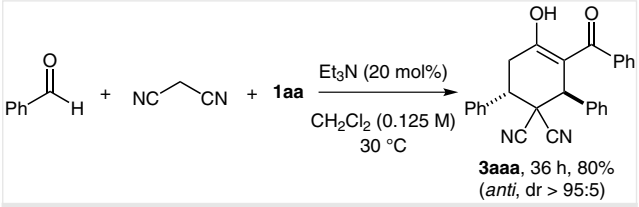
Entry	R^2 (**1**)	Time (h)	Yield[b,c] (%)
1	4-ClC_6H_4 (**1ab**)	24	**3aba**, 77
2	4-BrC_6H_4 (**1ac**)	24	**3aca**, 78
3	4-$MeOC_6H_4$ (**1ad**)	24	**3ada**, 39
4	2-thienyl (**1ae**)	12	**3aea**, 81
5	2-furyl (**1af**)	8	**3afa**, 85
6	Et (**1ag**)	8	**3aga**, 88
7	*i*-Pr (**1ah**)	13	**3aha**, 94
8	*t*-Bu (**1ai**)	48	**3aia**-enol, 18 **3aia**-keto, 55

[a] Reaction conditions: **1** (0.25 mmol), **2a** (0.3 mmol, 1.2 equiv), Et_3N (20 mol%), CH_2Cl_2 (2 mL), 30 °C.
[b] Diastereomeric ratio (dr) measured by ^1H NMR analysis of crude reaction mixture.
[c] Isolated yield.



Scheme 2 Proposed mechanism for the formation of **3** from **1**

essary (Scheme 3 vs. Table 2, entry 1). On the other hand, it is worthy of note that such highly functional products **3** were conveniently generated for the first time from commercially available materials in a one-pot reaction comparing to literature reports.[2–6]

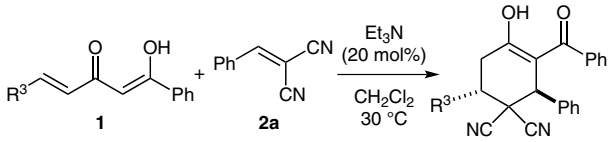


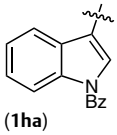
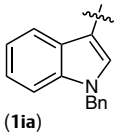
Scheme 3 Preparation of **3aaa** from benzaldehyde and malononitrile in a one-pot manner. *Reagents and conditions*: **1aa** (0.25 mmol), benzaldehyde (1.2 equiv), malononitrile (1.2 equiv), Et_3N (20 mol%), CH_2Cl_2 (2 mL), 30 °C. Isolated yield, dr measured by ^1H NMR analysis of crude reaction mixture.

Pleased by our results so far, we turned our attention to synthetic applications related to the introduction of more functionalities on the carbocycles, and it would be definitely attractive to apply our method to compounds existing in nature or that have interesting bioactivity. For this purpose, curcumin-related derivatives **4a** and **4b** were prepared for the reaction with **2a** under typical conditions.[10b] To our delight, our method can be used directly as expected and gave very highly functionalized 6-aryl-3-(3-arylpropenoyl)-4-hydroxy-2-phenylcyclohex-3-ene-1,1-dicarbonitriles **5aa** (65%) and **5ba** (75%) with excellent diastereoselectivity in 12 hours (Scheme 4). Moreover, as chalcones are an important and enormous class of natural compounds that display interesting biological activity, and recent research suggests that the development of hybrid compounds through the combination of different pharmacophores may lead to molecules with interesting profiles. Based on these criteria, our methodology allowed practical and versatile functionalization, which makes it attractive from a medicinal chemistry point of view.

In summary, we have developed a novel domino method to construct highly functionalized cyclohexanone derivatives via a double Michael reaction of 1-hydroxy-1,4-dien-3-ones and 2-alkylidenemalononitriles. The attractive features of this process are the practicability and the mild reaction conditions, which provide a series of cyclohexanone derivatives in moderate to good yields with extremely high diastereoselectivity. In addition, considering the high functional group tolerance of our method, this protocol should also offer an efficient and stereoselective entry to structurally more diverse, bioactive, and potentially pharmacological compounds. Current efforts are focused in two categories in order to: (1) broaden the substrate scope and study substrates other than methylenemalononitriles such as α-cyanocinnamates, and (2) develop new applications for this versatile methodology especially for the asymmetric synthesis of valuable compounds. Further investigations in these areas will be reported in due course.[18]

Table 4 Domino Double Michael Reactions of **2a** and R^3-Substituted **1**[a]



Entry	R^3 (**1**)	Time (h)	Yield[b,c] (%)
1	4-ClC_6H_4 (**1ba**)	12	**3baa**, 68
2	4-BrC_6H_4 (**1ca**)	12	**3caa**, 75
3	4-$MeOC_6H_4$ (**1da**)	12	**3daa**, 72
4	2-thienyl (**1ea**)	14	**3eaa**, 66
5	2-furyl (**1fa**)	24	**3faa**, 65
6	3-pyridyl (**1ga**)	12	**3gaa**, 59
7	 (**1ha**)	24	**3haa**, 70
8	 (**1ia**)	24	**3iaa**, 66

[a] Reaction conditions: **1** (0.25 mmol), **2a** (0.3 mmol, 1.2 equiv), Et_3N (20 mol%), CH_2Cl_2 (2 mL), 30 °C.
[b] Diastereomeric ratio (dr) measured by ^1H NMR analysis of crude reaction mixture.
[c] Isolated yield.

All reactions were carried out under an ordinary atmosphere in glass vials, unless otherwise noted. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. Yields refer to isolated yields of compounds estimated to be > 95% pure as determined by ^1H NMR. ^1H and ^{13}C NMR spectra were generally recorded on Bruker AV-400 or AV-500 spectrometers using $CDCl_3$ as solvent at 400 or 500 and 100 or 125 MHz, respectively. Chemical shifts are reported in ppm relative to $CDCl_3$ (δ = 7.26 ppm) in indicated cases. Analytical thin-layer chromatography (TLC) was performed using Merck 60 F254 precoated silica gel plates (0.2 mm thickness). Flash chromatography was performed using Merck silica gel 60. Key experimental procedures as well as spectroscopic data of products are summarized in the following experimental section.

2,6-Disubstituted 3-Alkanoyl-4-hydroxycyclohex-3-ene-1,1-dicarbonitriles 3 or 5; General Procedure

In an ordinary vial equipped with a magnetic stirring bar, compound **1** or **4** (0.25 mmol), **2** (0.3 mmol, 1.2 equiv), and Et_3N (0.05 mmol, 20 mol%) were dissolved in CH_2Cl_2 (2.0 mL) and stirred at 30 °C. After the completion of the reaction, the mixture was subjected directly to flash column chromatography (silica gel) to give the corresponding products **3** or **5**.

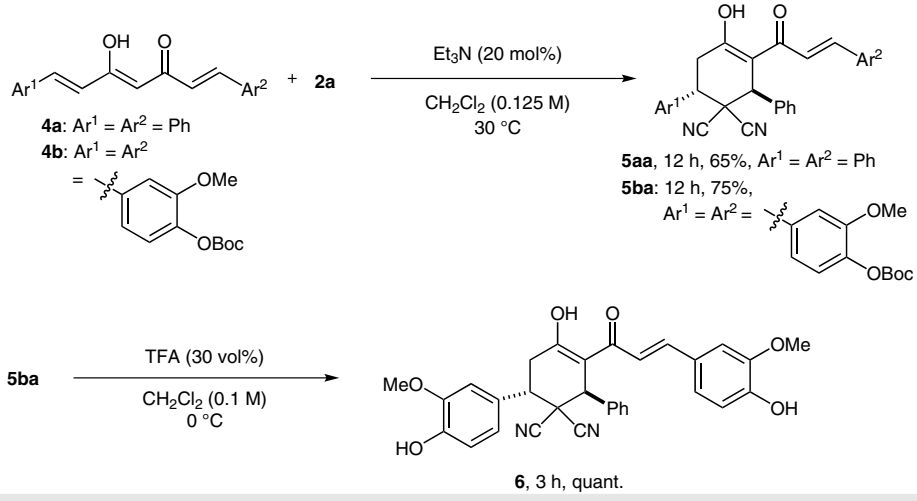
One-Pot Procedure for 3aa

In an ordinary vial equipped with a magnetic stirring bar, compound **1aa** (0.25 mmol), benzaldehyde (0.3 mmol, 1.2 equiv), malononitrile (0.3 mmol, 1.2 equiv), and Et_3N (20 mol%) were dissolved in CH_2Cl_2 (2.0 mL) and stirred at 30 °C. After completion of the reaction (36 h), the mixture was subjected directly to flash column chromatography (silica gel) to give the corresponding product **3aaa**.

3aaa

White solid; yield: 87.9 mg (87%); R_f = 0.21 (CH_2Cl_2–hexanes, 2:3); 100% enol form; mp 248.3–249.2 °C.

IR (KBr): 3448 (s), 3059 (w), 2374 (w), 1608 (s), 1458 (w), 1240 (m), 702 cm^{-1} (s).



Scheme 4 Domino double Michael reactions on curcumin-related derivatives **4a** and **4b**

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.41 (s, 1 H), 7.44–7.34 (m, 7 H), 7.34–7.29 (m, 2 H), 7.30 (t, *J* = 7.6 Hz, 2 H), 7.16–7.09 (m, 2 H), 7.01 (d, *J* = 7.9 Hz, 2 H), 4.52 (s, 1 H), 3.47 (dd, *J* = 11.7, 6.2 Hz, 1 H), 3.32 (dd, *J* = 19.7, 11.7 Hz, 1 H), 3.10 (dd, *J* = 19.6, 6.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 182.3, 136.5, 135.9, 135.0, 130.7, 130.2, 129.5, 129.3, 129.2, 128.9, 128.32, 128.3, 126.1, 114.4, 113.1, 105.4, 49.1, 44.4, 40.2, 34.7.

MS (70 eV, EI): *m*/*z* (%) = 404 $[M]^+$ (10), 250 (30), 232 (15), 155 (18), 105 (100), 77 (70).

HRMS (APCI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{20}N_2O_2Na$: 427.1422; found: 427.1415.

3aab

White solid; yield: 96.5 mg (85%); R_f = 0.18 (CH_2Cl_2–hexanes, 2:3); 100% enol form; mp 152.9–153.8 °C.

IR (KBr): 3448 (s), 3055 (w), 2369 (w), 1598 (s), 1406 (m), 1295 (m), 701 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.21 (s, 1 H), 7.88 (d, *J* = 8.2 Hz, 1 H), 7.80 (d, *J* = 8.1 Hz, 1 H), 7.60 (d, *J* = 8.6 Hz, 1 H), 7.53 (t, *J* = 7.68 Hz, 1 H), 7.46–7.37 (m, 2 H), 7.37–7.29 (m, 6 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 6.94 (t, *J* = 7.7 Hz, 2 H), 6.83 (d, *J* = 7.4 Hz, 2 H), 5.55 (s, 1 H), 3.73 (dd, *J* = 11.8, 6.1 Hz, 1 H), 3.39 (dd, *J* = 19.8, 11.9 Hz, 1 H), 3.16 (dd, *J* = 19.8, 6.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 180.6, 136.6, 135.0, 133.7, 132.7, 131.7, 130.3, 130.0, 129.5, 129.1, 128.8, 128.7, 128.4, 128.2, 126.4, 126.3, 125.5, 124.5, 122.8, 114.8, 112.9, 106.8, 43.2, 43.1, 40.5, 34.2.

MS (70 eV, EI): *m*/*z* (%) = 454 $[M]^+$ (45), 205 (40), 105 (100), 77 (50).

HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{31}H_{22}N_2O_2Na$: 477.1579; found: 477.1581.

3aac

Yellow solid; yield: 87.5 mg (77%); R_f = 0.41 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 193.6–194.4 °C.

IR (KBr): 3448 (s), 3055 (w), 2369 (w), 1612 (s), 1413 (w), 1241 (s), 700 cm^{-1} (s).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 16.54 (s, 1 H), 7.88 (d, *J* = 7.2 Hz, 1 H), 7.85 (d, *J* = 8.5 Hz, 2 H), 7.61 (s, 1 H), 7.60–7.54 (m, 2 H), 7.40–7.32 (m, 4 H), 7.32–7.27 (m, 2 H), 7.25–7.20 (m, 3 H), 7.00 (t, *J* = 7.6 Hz, 2 H), 4.87 (s, 1 H), 3.54 (dd, *J* = 11.7, 6.4 Hz, 1 H), 3.37 (dd, *J* = 19.9, 11.7 Hz, 1 H), 3.18 (dd, *J* = 19.9, 6.4 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 196.6, 182.6, 136.4, 134.9, 133.6, 133.4, 132.9, 130.8, 129.9, 129.5, 129.2, 128.8, 128.4, 128.33, 128.28, 127.8, 127.3, 127.2, 126.9, 126.2, 114.4, 113.2, 105.5, 49.2, 44.4, 40.4, 34.8.

MS (70 eV, EI): *m*/*z* (%) = 454 $[M]^+$ (40), 205 (15), 105 (100), 77 (95).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{31}H_{21}N_2O_2$: 453.1603; found: 453.1594.

3aad

White solid; yield: 87.8 mg (80%); R_f = 0.43 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 153.4–154.2 °C.

IR (KBr): 3702 (w), 2923 (m), 2358 (m), 2328 (m), 1596 (s), 1489 (m), 1234 (m), 697 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.35 (s, 1 H), 7.45–7.37 (m, 4 H), 7.37–7.28 (m, 6 H), 7.04 (dd, *J* = 11.6, 8.6 Hz, 4 H), 4.51 (s, 1 H), 3.42–3.27 (m, 2 H), 3.10 (dd, *J* = 18.4, 4.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.9, 182.0, 136.4, 135.5, 134.7, 134.5, 131.4, 130.8, 129.6, 129.3, 129.1, 128.5, 128.3, 126.0, 114.2, 113.0, 105.2, 48.2, 44.3, 40.2, 34.5.

MS (70 eV, EI): *m*/*z* (%) = 438 $[M]^+$ (50), 440 $[M + 2]^+$ (17), 249 (85), 189 (20), 105 (100), 77 (70).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{27}H_{18}N_2O_2Cl$: 437.1057; found: 437.1063.

3aae

White solid; yield: 93.0 mg (77%); R_f = 0.56 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 259.9–260.7 °C.

IR (KBr): 3448 (s), 3063 (w), 2369 (w), 1618 (s), 1413 (s), 1239 (s), 702 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.35 (s, 1 H), 7.50 (d, *J* = 8.4 Hz, 2 H), 7.46–7.37 (m, 4 H), 7.36–7.28 (m, 4 H), 7.02 (d, *J* = 7.5 Hz, 2 H), 6.99 (d, *J* = 8.4 Hz, 2 H), 4.49 (s, 1 H), 3.42–3.26 (m, 2 H), 3.10 (dd, *J* = 18.2, 4.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.8, 182.0, 136.4, 135.0, 134.7, 132.1, 131.6, 130.8, 129.6, 129.3, 128.5, 128.3, 126.0, 123.8, 114.1, 113.0, 105.1, 48.6, 44.2, 40.2, 34.5.

MS (70 eV, EI): *m*/*z* (%) = 484 $[M]^+$ (10), 484 $[M + 2]^+$ (10), 249 (60), 105 (100), 77 (50).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{27}H_{18}N_2O_2Br$: 481.0552; found: 481.0545.

3aaf

White solid; yield: 83.4 mg (76%); R_f = 0.57 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 213.9–214.7 °C.

IR (KBr): 3442 (w), 3059 (w), 2243 (w), 1618 (s), 1406 (w), 1268 (m), 702 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.15 (s, 1 H), 7.46–7.32 (m, 7 H), 7.32–7.21 (m, 5 H), 6.96 (d, *J* = 7.4 Hz, 2 H), 5.28 (s, 1 H), 3.54 (dd, *J* = 12.0, 5.8 Hz, 1 H), 3.36 (dd, *J* = 19.5, 12.0 Hz, 1 H), 3.09 (dd, *J* = 19.6, 5.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.5, 180.5, 136.7, 136.3, 134.7, 134.1, 131.1, 130.44, 130.42, 129.6, 129.3, 128.6, 128.5, 127.0, 125.4, 114.3, 112.3, 105.8, 44.6, 42.8, 40.5, 34.1.

MS (70 eV, EI): *m*/*z* (%) = 438 $[M]^+$ (18), 440 $[M + 2]^+$ (6), 403 (20), 249 (60), 105 (100), 77 (70).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{27}H_{18}N_2O_2Cl$: 437.1057; found: 437.1055.

3aag

White solid; yield: 90.6 mg (75%); R_f = 0.57 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 208.1–209.0 °C.

IR (KBr): 3435 (m), 3025 (w), 2369 (w), 1618 (s), 1405 (s), 1269 (s), 764 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.12 (s, 1 H), 7.45 (d, *J* = 8.0 Hz, 1 H), 7.42–7.32 (m, 7 H), 7.30 (t, *J* = 7.6 Hz, 2 H), 7.25–7.16 (m, 2 H), 6.96 (d, *J* = 7.4 Hz, 2 H), 5.26 (s, 1 H), 3.54 (dd, *J* = 12.0, 5.8 Hz, 1 H), 3.36 (dd, *J* = 19.6, 12.0 Hz, 1 H), 3.09 (dd, *J* = 19.6, 5.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.7, 180.3, 136.8, 135.6, 134.7, 133.9, 131.2, 130.5, 130.4, 129.6, 129.2, 128.7, 128.5, 127.6, 127.5, 125.5, 114.2, 112.3, 105.9, 47.0, 42.7, 40.4, 34.0.

MS (70 eV, EI): *m*/*z* (%) = 483 $[M]^+$ (5), 485 $[M + 2]^+$ (5), 403 (50), 249 (70), 105 (100), 77 (70).

HRMS (ESI-TOF): *m*/*z* [M – H]⁻ calcd for $C_{27}H_{18}N_2O_2Br$: 481.0552; found: 481.0555.

3aah

White solid; yield: 80.4 mg (74%); R_f = 0.28 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 209.0–209.3 °C.

IR (KBr): 3448 (s), 3059 (w), 2374 (w), 1608 (s), 1458 (w), 1240 (m), 702 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.42 (s, 1 H), 7.44–7.36 (m, 4 H), 7.35–7.27 (m, 4 H), 7.04 (t, *J* = 7.7 Hz, 4 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 4.47 (s, 1 H), 3.84 (s, 3 H), 3.44 (dd, *J* = 11.8, 6.2 Hz, 1 H), 3.30 (dd, *J* = 19.7, 11.9 Hz, 1 H), 3.08 (dd, *J* = 19.8, 6.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.8, 182.0, 160.2, 136.6, 135.1, 131.4, 130.7, 129.5, 129.2, 128.32, 128.30, 127.8, 126.1, 114.5, 114.2, 113.3, 105.7, 55.3, 48.5, 44.6, 40.1, 34.7.

MS (70 eV, EI): *m*/*z* (%) = 434 $[M]^+$ (30), 262 (70), 249 (60), 105 (100), 77 (100).

HRMS (ESI-TOF): *m*/*z* [M – H]⁻ calcd for $C_{28}H_{21}N_2O_3$: 433.1552; found: 433.1551.

3aai

Yellow solid; yield: 81.1 mg (79%); R_f = 0.59 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 231.7–232.6 °C.

IR (KBr): 3424 (w), 2921 (m), 2369 (w), 1608 (s), 1411 (s), 1238 (s), 700 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.41 (s, 1 H), 7.48–7.32 (m, 9 H), 7.15 (d, *J* = 7.4 Hz, 2 H), 7.05 (t, *J* = 4.3 Hz, 1 H), 6.95 (d, *J* = 3.3 Hz, 1 H), 4.83 (s, 1 H), 3.59 (dd, *J* = 11.8, 6.4 Hz, 1 H), 3.29 (dd, *J* = 19.7, 11.8 Hz, 1 H), 3.07 (dd, *J* = 19.8, 6.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.4, 182.2, 140.5, 136.3, 135.0, 130.9, 129.6, 129.31, 129.29, 128.6, 128.3, 128.2, 127.7, 126.2, 114.0, 113.5, 107.0, 44.9, 44.5, 40.8, 34.6.

MS (70 eV, EI): *m*/*z* (%) = 410 $[M]^+$ (10), 326 (25), 256 (30), 161 (18), 105 (100), 77 (90).

HRMS (ESI-TOF): *m*/*z* [M – H]⁻ calcd for $C_{25}H_{17}N_2O_2S$: 409.1011; found: 409.1007.

3aaj

Yellow solid; yield: 59.2 mg (60%); R_f = 0.45 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 230.5.4–231.4 °C.

IR (KBr): 3448 (s), 3122 (w), 2374 (w), 1609 (s), 1414 (s), 1272 (s), 701 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.44 (s, 1 H), 7.48 (t, *J* = 6.9 Hz, 2 H), 7.43–7.35 (m, 7 H), 7.16 (t, *J* = 7.3 Hz, 2 H), 6.41 (dd, *J* = 3.1, 1.8 Hz, 1 H), 6.21 (d, 1 H), 4.66 (s, 1 H), 3.53 (dd, *J* = 11.7, 6.4 Hz, 1 H), 3.27 (dd, *J* = 19.7, 11.8 Hz, 1 H), 3.06 (dd, *J* = 19.7, 6.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.3, 183.6, 149.3, 144.2, 136.1, 135.1, 131.0, 129.6, 129.3, 128.6, 128.3, 126.2, 113.7, 113.1, 112.4, 111.2, 103.7, 43.7, 43.5, 41.6, 34.9.

MS (70 eV, EI): *m*/*z* (%) = 394 $[M]^+$ (10), 240 (40), 105 (100), 77 (90).

HRMS (ESI-TOF): *m*/*z* [M – H]⁻ calcd for $C_{25}H_{17}N_2O_3$: 393.1239; found: 393.1239.

3aak

White solid; yield: 73.0 mg (72%); R_f = 0.62 (EtOAc–hexanes, 1:1); 100% enol form; mp 251.0–251.9 °C.

IR (KBr): 3448 (m), 2922 (m), 2254 (w), 1576 (s), 1414 (s), 1272 (s), 698 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.29 (s, 1 H), 8.63 (s, 1 H), 8.38 (s, 1 H), 7.46–7.37 (m, 5 H), 7.37–7.27 (m, 5 H), 7.02 (d, *J* = 7.4 Hz, 2 H), 4.57 (s, 1 H), 3.44–3.30 (m, 2 H), 3.21–3.08 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.0, 181.8, 150.9, 150.4, 137.7, 136.4, 134.4, 132.0, 130.9, 129.8, 129.4, 128.6, 128.3, 125.8, 123.5, 114.0, 112.9, 104.4, 47.1, 44.1, 40.4, 34.4.

MS (70 eV, EI): *m*/*z* (%) = 405 $[M]^+$ (30), 251 (95), 105 (100), 77 (90).

HRMS (ESI-TOF): *m*/*z* [M – H]⁻ calcd for $C_{26}H_{18}N_3O_2$: 404.1399; found: 404.1400.

3aal

Yellow solid; yield: 84.9 mg (62%); R_f = 0.20 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 227.1–228.0 °C.

IR (KBr): 3725 (w), 3053 (w), 2947 (w), 2359 (w), 1695 (m), 1600 (m), 1448 (m), 1349 (s), 697 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.25 (s, 1 H), 8.28 (d, *J* = 8.2 Hz, 1 H), 7.71–7.67 (m, 3 H), 7.49 (t, *J* = 7.4 Hz, 2 H), 7.38–7.25 (m, 9 H), 7.18 (t, *J* = 7.5 Hz, 2 H), 7.09 (s, 1 H), 7.03 (d, *J* = 7.4 Hz, 2 H), 4.78 (s, 1 H), 3.69 (dd, *J* = 11.2, 6.0 Hz, 1 H), 3.35 (dd, *J* = 11.5, 19.7 Hz, 1 H), 3.10 (dd, *J* = 19.8, 5.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.9, 180.9, 168.1, 136.5, 136.3, 134.9, 133.5, 132.6, 130.5, 129.5, 129.2, 129.1, 128.9, 128.3, 128.1, 125.7, 124.3, 119.1, 117.3, 116.3, 114.1, 113.6, 105.4, 44.5, 41.9, 41.4, 34.4.

MS (70 eV, EI): *m*/*z* (%) = 547 $[M]^+$ (6), 105 (100), 77 (70).

HRMS (MALDI-TOF): *m*/*z* [M + Na]⁺ calcd for $C_{36}H_{25}N_3O_3Na$: 570.1794; found: 570.1812.

3aam

Yellow solid; yield: 89.7 mg (60%); R_f = 0.45 (CH_2Cl_2–hexanes, 2:1); 100% enol form; mp 260.1–261.0 °C.

IR (KBr): 3688 (w), 3057 (w), 2920 (w), 2357 (w), 1595 (s), 1444 (s), 1172 (s), 672 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.15 (s, 1 H), 7.99 (d, *J* = 8.4 Hz, 1 H), 7.77 (d, *J* = 8.4 Hz, 2 H), 7.45 (s, 1 H), 7.39–7.28 (m, 4 H), 7.25 (d, *J* = 8.5 Hz, 4 H), 7.22–7.09 (m, 3 H), 6.94 (t, *J* = 7.9 Hz, 2 H), 6.76 (d, *J* = 7.2 Hz, 2 H), 4.82 (s, 1 H), 3.56 (dd, *J* = 11.8, 6.0 Hz, 1 H), 3.34 (dd, *J* = 19.7, 11.9 Hz, 1 H), 3.11 (dd, *J* = 19.7, 6.0 Hz, 1 H), 2.34 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 180.2, 145.6, 136.3, 135.0, 134.9, 134.7, 130.4, 129.5, 129.2, 129.0, 128.21, 128.17, 127.9, 126.8, 125.7, 125.6, 123.6, 120.1, 119.6, 114.1, 113.7, 113.2, 106.0, 43.3, 41.1, 40.8, 34.0, 21.5.

HRMS (MALDI-TOF): *m*/*z* [M + Na]⁺ calcd for $C_{36}H_{27}N_3O_4SNa$: 620.1620; found: 620.1641.

3aan

White solid; yield: 18.5 mg (20%); R_f = 0.61 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 211.8–212.5 °C.

IR (CH_2Cl_2): 3328 (m), 2962 (m), 2244 (w), 1589 (s), 1265 (s), 708 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.12 (s, 1 H), 7.59–7.51 (m, 5 H), 7.51–7.42 (m, 5 H), 3.64 (d, *J* = 3.4 Hz, 1 H), 3.52 (dd, *J* = 11.7, 6.7 Hz, 1 H), 3.21 (dd, *J* = 19.7, 11.8 Hz, 1 H), 2.94 (dd, *J* = 19.8, 6.7 Hz, 1 H), 2.08 (m, 1 H), 0.85 (d, *J* = 7.0 Hz, 3 H), 0.62 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.7, 184.3, 136.6, 135.4, 131.2, 129.6, 129.4, 128.9, 128.2, 127.6, 114.6, 114.2, 105.0, 47.7, 43.9, 40.8, 35.3, 32.4, 24.0, 21.8.

MS (70 eV, EI): *m*/*z* (%) = 370 $[M]^+$ (6), 327 (40), 223 (85), 105 (100), 77 (65).

HRMS (MALDI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{22}N_2O_2Na$: 393.1579; found: 393.1596.

3aao-keto

Yellow solid; yield: 35.6 mg (37%); R_f = 0.63 (CH_2Cl_2–hexanes, 1:1); 100% keto form; mp 214.2–215.1 °C.

IR (KBr): 2962 (m), 2359 (w), 1707 (s), 1672 (s), 1592 (w), 1486 (w), 1261 (m), 697 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29–8.12 (m, 2 H), 7.66 (t, *J* = 7.4 Hz, 1 H), 7.48–7.60 (m, 4 H), 7.48–7.36 (m, 3 H), 4.98 (d, *J* = 3.5 Hz, 1 H), 4.18 (dd, *J* = 12.3, 6.9 Hz, 1 H), 3.51 (d, *J* = 4.2 Hz, 1 H), 3.01 (ddd, *J* = 19.2, 12.4, 1.5 Hz, 1 H), 2.79 (dd, *J* = 19.2, 6.9 Hz, 1 H), 1.21 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.4, 192.9, 135.3, 134.7, 134.3, 129.9, 129.5, 129.09, 129.07, 128.8, 115.8, 113.8, 61.6, 53.8, 46.5, 41.2, 40.1, 36.2, 28.3.

MS (70 eV, EI): *m*/*z* (%) = 384 $[M]^+$ (10), 250 (10), 105 (100), 77 (65).

HRMS (EI-magnetic sector): *m*/*z* $[M]^+$ calcd for $C_{25}H_{24}N_2O_2$: 384.1838; found: 384.1841.

3aap

Yellow solid; yield: 83.6 mg (66%); R_f = 0.24 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 201.6–202.3 °C.

IR (KBr): 3710 (w), 3038 (m), 2916 (m), 2351 (m), 1714 (m), 1604 (m), 1482 (w), 1288 (m), 705 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.51 (s, 1 H), 7.73 (d, *J* = 8.0 Hz, 1 H), 7.65 (t, *J* = 7.6 Hz, 1 H), 7.48–7.32 (m, 8 H), 7.28 (t, *J* = 7.4 Hz, 2 H), 7.20 (d, *J* = 7.3 Hz, 2 H), 5.26 (s, 1 H), 4.00 (dd, *J* = 10.2, 7.3 Hz, 1 H), 3.32–3.14 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.7, 188.5, 158.9, 152.7, 152.1, 135.4, 135.2, 134.0, 130.2, 129.4, 129.1, 128.9, 128.5, 126.8, 126.0, 125.3, 120.3, 117.2, 116.6, 113.9, 112.9, 102.0, 44.9, 43.4, 43.1, 36.8.

MS (70 eV, EI): *m*/*z* (%) = 506 $[M]^+$ (30), 311 (30), 105 (100), 77 (70).

HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{30}H_{19}N_2O_4ClNa$: 529.0931; found: 529.0923.

3aba

White solid; yield: 84.5 mg (77%); R_f = 0.59 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 234.2–235.1 °C.

IR (KBr): 3448 (m), 3060 (w), 2369 (w), 1608 (s), 1413 (s), 1274 (s), 703 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.39 (s, 1 H), 7.46–7.36 (m, 6 H), 7.34–7.29 (m, 4 H), 7.28–7.24 (m, 2 H), 7.16 (t, *J* = 3.7 Hz, 2 H), 4.46 (s, 1 H), 3.46 (dd, *J* = 11.6, 6.2 Hz, 1 H), 3.32 (dd, *J* = 20.0, 11.4 Hz, 1 H), 3.12 (dd, *J* = 19.6, 6.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 182.7, 137.1, 135.8, 134.9, 134.8, 130.2, 129.54, 129.48, 129.3, 129.0, 128.7, 128.3, 127.7, 114.3, 113.0, 105.4, 49.1, 44.4, 40.2, 34.7.

MS (70 eV, EI): *m*/*z* (%) = 438 $[M]^+$ (15), 440 $[M + 2]^+$ (5), 284 (40), 139 (100), 77 (20).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{27}H_{18}N_2O_2Cl$: 437.1057; found: 437.1057.

3aca

White solid; yield: 94.3 mg (78%); R_f = 0.57 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 242.4–243.2 °C.

IR (KBr): 3448 (m), 3054 (w), 2374 (w), 1592 (s), 1414 (s), 1275 (s), 703 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.34 (s, 1 H), 7.45–7.35 (m, 8 H), 7.34–7.28 (m, 2 H), 7.20–7.12 (m, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 4.46 (s, 1 H), 3.45 (dd, *J* = 11.6, 6.2 Hz, 1 H), 3.31 (dd, *J* = 19.7, 11.7 Hz, 1 H), 3.11 (dd, *J* = 19.7, 6.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 182.7, 135.8, 135.2, 134.8, 131.6, 130.2, 129.52, 129.47, 129.2, 129.0, 128.3, 127.8, 125.4, 114.3, 113.0, 105.4, 49.0, 44.3, 40.2, 34.7.

MS (70 eV, EI): *m*/*z* (%) = 482 $[M]^+$ (10), 484 $[M + 2]^+$ (10), 330 (55), 312 (30), 182 (100), 155 (100), 104 (70), 77 (50).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{27}H_{18}N_2O_2Br$: 481.0552; found: 481.0558.

3ada

White solid; yield: 42.4 mg (39%); R_f = 0.36 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 205.4–206.4 °C.

IR (CH_2Cl_2): 3313 (w), 3038 (w), 2969 (w), 2351 (s), 1596 (s), 1413 (m), 1303 (s), 1259 (s), 701 cm^{-1} (m).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.76 (s, 1 H), 7.45–7.39 (m, 3 H), 7.39–7.35 (m, 3 H), 7.34–7.27 (m, 2 H), 7.25–7.20 (m, 2 H), 7.09 (d, *J* = 8.8 Hz, 2 H), 6.79 (d, *J* = 8.8 Hz, 2 H), 4.64 (s, 1 H), 3.81 (s, 3 H), 3.45 (dd, *J* = 11.6, 6.4 Hz, 1 H), 3.30 (dd, *J* = 20.0, 11.2 Hz, 1 H), 3.10 (dd, *J* = 19.8, 6.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.0, 182.9, 161.8, 136.1, 135.1, 130.2, 129.4, 129.3, 129.2, 129.0, 128.8, 128.7, 128.3, 114.4, 113.7, 113.3, 105.2, 55.4, 49.1, 44.5, 40.4, 35.0.

MS (70 eV, EI): *m*/*z* (%) = 434 $[M]^+$ (20), 280 (55), 172 (75), 134 (100), 104 (50), 77 (60).

HRMS (MALDI-TOF): *m*/*z* $[M + H]^+$ calcd for $C_{28}H_{23}N_2O_3$: 435.1708; found: 435.1717.

3aea

White solid; yield: 83.1 mg (81%); R_f = 0.31 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 243.5–244.2 °C.

IR (KBr): 3448 (m), 2920 (w), 2375 (w), 1592 (s), 1413 (s), 1239 (s), 702 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 17.51 (s, 1 H), 7.59 (d, *J* = 4.8 Hz, 1 H), 7.54–7.42 (m, 5 H), 7.42–7.34 (m, 3 H), 7.33–7.24 (m, 3 H), 7.00 (t, *J* = 4.4 Hz, 1 H), 5.01 (s, 1 H), 3.48–3.24 (m, 2 H), 3.11 (dd, *J* = 19.2, 6.0 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.8, 184.5, 139.6, 135.4, 135.1, 133.5, 132.2, 130.4, 129.7, 129.5, 129.2, 128.3, 128.1, 114.3, 113.4, 103.7, 48.5, 44.8, 40.1, 35.5.

MS (70 eV, EI): *m*/*z* (%) = 410 $[M]^+$ (10), 256 (15), 172 (45), 111 (100), 105, 77 (20).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{25}H_{17}N_2O_2S$: 409.1011; found: 409.1012.

3afa

Yellow solid; yield: 83.8 mg (85%); R_f = 0.34 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 241.8–242.6 °C.

IR (KBr): 3436 (m), 2922 (m), 2244 (w), 1591 (s), 1411 (s), 1246 (m), 704 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 17.36 (s, 1 H), 7.52 (s, 1 H), 7.47–7.35 (m, 8 H), 7.34–7.29 (m, 2 H), 7.25 (d, *J* = 3.4 Hz, 1 H), 6.48 (q, *J* = 1.6 Hz, 1 H), 5.48 (s, 1 H), 3.47 (dd, *J* = 12.0, 6.0 Hz, 1 H), 3.33 (dd, *J* = 19.5, 12.0 Hz, 1 H), 3.07 (dd, *J* = 19.6, 6.1 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.2, 178.7, 150.4, 146.8, 136.4, 135.2, 130.3, 129.4, 129.2, 129.1, 128.6, 128.3, 120.5, 114.6, 113.5, 112.7, 103.4, 47.5, 44.6, 39.5, 35.3.

MS (70 eV, EI): *m*/*z* (%) = 394 $[M]^+$ (35), 239 (25), 159 (30), 95 (100), 77 (40).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{25}H_{17}N_2O_3$: 393.1239; found: 393.1238.

3aga

White solid; yield: 78.4 mg (88%); R_f = 0.45 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 171.5–172.0 °C.

IR (KBr): 3448 (m), 2938 (m), 2374 (w), 1618 (s), 1414 (s), 1212 (s), 704 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.13 (s, 1 H), 7.52–7.45 (m, 3 H), 7.43–7.35 (m, 5 H), 7.33–7.27 (m, 2 H), 4.58 (s, 1 H), 3.41 (dd, *J* = 12.3, 6.8 Hz, 1 H), 3.25 (dd, *J* = 19.4, 12.3 Hz, 1 H), 2.96 (dd, *J* = 19.4, 5.9 Hz, 1 H), 2.47 (dq, *J* = 17.1, 5.9 Hz, 1 H), 1.95 (dq, *J* = 17.1, 5.9 Hz, 1 H), 0.95 (t, *J* =7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 203.8, 176.6, 135.3, 135.0, 130.2, 129.7, 129.5, 129.2, 129.1, 128.3, 114.5, 113.2, 104.9, 48.6, 44.4, 39.7, 33.5, 30.9, 7.6.

MS (70 eV, EI): *m*/*z* (%) = 356 $[M]^+$ (70), 223 (30), 202 (60), 155 (100), 77 (70), 57 (80).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{23}H_{19}N_2O_2$: 355.1447; found: 355.1448.

3aha

White solid; yield: 87.1 mg (94%); R_f = 0.51 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 224.5–225.1 °C.

IR (KBr): 3449 (m), 2962 (m), 2244 (w), 1618 (s), 1412 (s), 1213 (m), 704 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.64 (s, 1 H), 7.52–7.42 (m, 3 H), 7.42–7.34 (m, 5 H), 7.33–7.27 (m, 2 H), 4.63 (s, 1 H), 3.42 (dd, *J* = 12.3, 5.9 Hz, 1 H), 3.25 (dd, *J* = 19.5, 12.3 Hz, 1 H), 2.97 (dd, *J* = 19.5, 5.9 Hz, 1 H), 2.57 (sept, *J* = 6.7 Hz, 1 H), 1.60 (d, *J* = 6.8 Hz, 3 H), 0.64 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.9, 179.4, 135.7, 135.0, 130.2, 129.6, 129.4, 129.2, 129.0, 128.2, 114.4, 113.2, 104.1, 48.5, 44.5, 39.7, 34.0, 33.9, 19.7, 17.9.

MS (70 eV, EI): *m*/*z* (%) = 370 $[M]^+$ (60), 327 (15), 223 (60), 216 (65), 155 (100), 105 (60), 77 (40).

HRMS (ESI-TOF): *m*/*z* $[M - H]^-$ calcd for $C_{24}H_{21}N_2O_2$: 369.1603; found: 369.1599.

3aia-enol

White solid; yield: 17.3 mg (18%); R_f = 0.49 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 182.6–183.6 °C.

IR (KBr): 3443 (w), 2962 (m), 2252 (w), 1726 (s), 1699 (s), 1596 (w), 1478 (s), 1283 (m), 693 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 17.19 (s, 1 H), 7.51–7.42 (m, 3 H), 7.41–7.31 (m, 5 H), 7.31–7.26 (m, 2 H), 5.05 (s, 1 H), 3.31–3.16 (m, 2 H), 3.08–2.94 (m, 1 H), 1.15 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.2, 181.0, 135.8, 135.2, 130.3, 129.4, 129.3, 129.2, 129.0, 128.3, 114.3, 113.8, 104.5, 47.7, 44.4, 43.1, 40.0, 34.7, 27.8.

MS (70 eV, EI): *m*/*z* (%) = 384 $[M]^+$ (10), 327 (30), 223 (40), 83 (100), 57 (15).

HRMS (FAB-magnetic sector): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{25}N_2O_2$: 385.1916; found: 385.1917.

3aia-keto

White solid; yield: 52.9 mg (55%); R_f = 0.33 (CH_2Cl_2–hexanes, 1:1); 100% keto form; mp 201.1–202.0 °C.

IR (KBr): 3695 (m), 2962 (s), 2358 (s), 1585 (s), 1455 (s), 1166 (s), 705 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.43 (m, 3 H), 7.42–7.26 (m, 7 H), 4.74 (d, *J* = 12.5 Hz, 1 H), 4.18–4.02 (m, 2 H), 3.41 (dd, *J* = 16.7, 7.1 Hz, 1 H), 3.02 (d, *J* = 16.7 Hz, 1 H), 0.89 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 210.6, 203.5, 134.7, 134.0, 129.7, 129.6, 129.2, 129.1, 128.9, 115.3, 112.8, 59.1, 48.1, 45.8, 44.9, 44.0, 42.3, 25.7.

MS (70 eV, EI): *m*/*z* (%) = 384 $[M]^+$ (10), 146 (100), 131 (30), 57 (15).

HRMS (FAB-magnetic sector): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{25}N_2O_2$: 385.1916; found: 385.1915.

3baa

White solid; yield: 74.6 mg (68%); R_f = 0.27 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 204.5–205.3 °C.

IR (KBr): 3432 (m), 3063 (w), 2369 (w), 1610 (s), 1413 (w), 1237 (m), 702 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.44 (s, 1 H), 7.47–7.31 (m, 6 H), 7.30–7.22 (m, 4 H), 7.11 (d, *J* = 6.2 Hz, 2 H), 7.00 (d, *J* = 7.6 Hz, 2 H), 4.52 (s, 1 H), 3.45 (dd, *J* = 11.7, 6.4 Hz, 1 H), 3.26 (dd, *J* = 19.7, 11.7 Hz, 1 H), 3.08 (dd, *J* = 19.7, 6.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 181.9, 136.3, 135.8, 135.6, 133.4, 130.7, 130.1, 129.6, 129.43, 129.35, 128.9, 128.3, 126.1, 114.1, 113.0, 105.3, 48.9, 44.2, 39.7, 34.5.

MS (70 eV, EI): *m*/*z* (%) = 438 $[M]^+$ (40), 440 $[M + 2]^+$ (15), 250 (80), 232 (75), 155 (70), 145 (60), 105 (100), 77 (85).

HRMS (EI-magnetic sector): *m*/*z* $[M]^+$ calcd for $C_{27}H_{19}N_2O_2Cl$: 438.1135; found: 438.1137.

3caa

White solid; yield: 90.6 mg (75%); R_f = 0.25 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 227.3–228.2 °C.

IR (KBr): 3435 (m), 3062 (w), 2369 (w), 1611 (s), 1414 (s), 1236 (s), 702 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 16.43 (s, 1 H), 7.50 (d, *J* = 8.4 Hz, 2 H), 7.44–7.34 (m, 4 H), 7.27 (t, *J* = 7.5 Hz, 2 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 7.14–7.08 (m, 2 H), 7.00 (d, *J* = 7.8 Hz, 2 H), 4.52 (s, 1 H), 3.43 (dd, *J* = 11.7, 6.4 Hz, 1 H), 3.25 (dd, *J* = 19.7, 11.7 Hz, 1 H), 3.08 (dd, *J* = 19.7, 6.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 181.9, 136.3, 135.8, 134.0, 132.4, 130.7, 130.1, 129.9, 129.4, 128.9, 128.4, 126.1, 123.8, 114.1, 113.0, 105.3, 49.0, 44.2, 39.8, 34.5.

MS (70 eV, EI): *m*/*z* (%) = 482 [M]$^+$ (10), 484 [M + 2]$^+$ (10), 250 (55), 155 (25), 145 (20), 105 (100), 77 (75).

HRMS (ESI-TOF): *m*/*z* [M – H]$^-$ calcd for $C_{27}H_{18}N_2O_2Br$: 481.0552; found: 481.0546.

3daa

White solid; yield: 78.2 mg (72%); R_f = 0.47 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 207.8–208.4 °C.

IR (KBr): 3439 (m), 2836 (w), 2244 (w), 1616 (s), 1406 (s), 1258 (s), 700 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.42 (s, 1 H), 7.46–7.32 (m, 4 H), 7.25 (dd, *J* = 17.5, 8.3 Hz, 4 H), 7.14–7.08 (m, 2 H), 7.00 (d, *J* = 7.5 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 4.50 (s, 1 H), 3.78 (s, 3 H), 3.43 (dd, *J* = 11.6, 6.3 Hz, 1 H), 3.28 (dd, *J* = 19.7, 11.7 Hz, 1 H), 3.07 (dd, *J* = 19.6, 6.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 182.4, 160.3, 136.5, 136.0, 130.6, 130.2, 129.5, 129.2, 128.8, 128.3, 126.8, 126.1, 114.53, 114.46, 113.3, 105.4, 55.3, 49.0, 44.8, 39.5, 34.8.

MS (70 eV, EI): *m*/*z* (%) = 434 [M]$^+$ (50), 250 (60), 155 (35), 104 (100), 77 (80).

HRMS (ESI-TOF): *m*/*z* [M – H]$^-$ calcd for $C_{28}H_{21}N_2O_3$: 433.1552; found: 433.1556.

3eaa

White solid; yield: 67.7 mg (66%); R_f = 0.32 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 220.1–221.0 °C.

IR (KBr): 3448 (m), 3055 (w), 2375 (w), 1602 (s), 1416 (s), 1256 (s), 747 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.34 (s, 1 H), 7.44–7.30 (m, 5 H), 7.29–7.22 (m, 2 H), 7.14–7.06 (m, 3 H), 7.04–6.96 (m, 3 H), 4.52 (s, 1 H), 3.82 (t, *J* = 8.8 Hz, 1 H), 3.26 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 181.2, 137.5, 136.5, 135.8, 130.7, 130.1, 129.3, 128.9, 128.3, 127.8, 127.4, 126.3, 126.0, 114.1, 113.1, 105.4, 48.7, 45.3, 36.5, 36.4.

MS (70 eV, EI): *m*/*z* (%) = 410 [M]$^+$ (15), 250 (35), 105 (100), 77 (90).

HRMS (ESI-TOF): *m*/*z* [M – H]$^-$ calcd for $C_{25}H_{17}N_2O_2S$: 409.1011; found: 409.1017.

3faa

Yellow solid; yield: 64.1 mg (65%); R_f = 0.36 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 215.7–216.6 °C.

IR (KBr): 3449 (m), 3056 (m), 2236 (w), 1603 (s), 1412 (s), 1251 (s), 702 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.41 (s, 1 H), 7.50–7.32 (m, 5 H), 7.27 (t, *J* = 7.2 Hz, 2 H), 7.16–7.06 (m, 2 H), 7.00 (d, *J* = 7.5 Hz, 2 H), 6.34 (d, *J* = 14.2 Hz, 2 H), 4.49 (s, 1 H), 3.67 (dd, *J* = 11.3, 6.5 Hz, 1 H), 3.31 (dd, *J* = 19.8, 11.4 Hz, 1 H), 3.12 (dd, *J* = 19.8, 6.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 181.7, 148.5, 143.7, 136.4, 135.8, 130.8, 130.1, 129.4, 129.0, 128.4, 126.2, 113.9, 113.2, 110.9, 109.7, 105.4, 48.6, 43.1, 34.9, 33.2.

MS (70 eV, EI): *m*/*z* (%) = 394 [M]$^+$ (15), 250 (70), 155 (20), 145 (15), 105 (100), 77 (60).

HRMS (ESI-TOF): *m*/*z* [M – H]$^-$ calcd for $C_{25}H_{17}N_2O_3$: 393.1239; found: 393.1244.

3gaa

Yellow solid; yield: 59.8 mg (59%); R_f = 0.24 (CH_2Cl_2–EtOAc–hexanes, 1:2:3); 100% enol form; mp 231.7–232.5 °C.

IR (KBr): 3448 (m), 3060 (w), 2246 (w), 1604 (s), 1412 (s), 1254 (s), 704 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.44 (s, 1 H), 8.64 (s, 1 H), 8.47 (s, 1 H), 7.79 (d, *J* = 8.0 Hz, 1 H), 7.45–7.35 (m, 5 H), 7.28 (t, *J* = 7.6 Hz, 2 H), 7.17–7.08 (m, 2 H), 7.01 (d, *J* = 7.4 Hz, 2 H), 4.56 (s, 1 H), 3.51 (dd, *J* = 11.7, 6.5 Hz, 1 H), 3.29 (dd, *J* = 19.7, 11.7 Hz, 1 H), 3.11 (dd, *J* = 19.7, 6.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 181.6, 150.9, 150.0, 136.2, 135.6, 135.2, 130.9, 130.8, 130.1, 129.5, 129.0, 128.3, 126.1, 123.9, 114.0, 112.8, 105.3, 48.8, 44.0, 38.0, 34.3.

MS (70 eV, EI): *m*/*z* (%) = 405 [M]$^+$ (10), 300 (100), 156 (40), 105 (80), 77 (60).

HRMS (EI-magnetic sector): *m*/*z* [M]$^+$ calcd for $C_{26}H_{19}N_3O_2$: 405.1477; found: 405.1469.

3haa

Yellow solid; yield: 95.8 mg (70%); R_f = 0.27 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 258.9–259.8 °C.

IR (KBr): 3664 (s), 3092 (w), 2359 (w), 1684 (w), 1600 (w), 1455 (w), 1082 (s), 700 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.44 (s, 1 H), 8.35 (d, *J* = 8.3 Hz, 1 H), 7.77 (d, *J* = 7.4 Hz, 2 H), 7.63 (t, *J* = 7.4 Hz, 1 H), 7.57 (s, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H), 7.46–7.32 (m, 5 H), 7.28 (t, *J* = 7.7 Hz, 2 H), 7.22–7.16 (m, 3 H), 7.07 (d, *J* = 7.9 Hz, 1 H), 7.02 (d, *J* = 7.6 Hz, 2 H), 4.55 (s, 1 H), 3.96 (dd, *J* = 11.1, 7.1 Hz, 1 H), 3.24–3.06 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 182.0, 168.3, 136.3, 136.0, 133.7, 132.5, 130.8, 130.7, 129.5, 129.0, 128.8, 128.4, 126.1, 126.04, 125.95, 124.0, 118.3, 116.7, 116.5, 114.5, 113.5, 105.3, 48.7, 44.2, 35.1, 31.4.

MS (70 eV, EI): *m*/*z* (%) = 547 [M]$^+$ (10), 105 (100), 77 (30).

HRMS (MALDI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{36}H_{25}N_3O_3Na$: 570.1794; found: 570.1814.

3iaa

Yellow solid; yield: 88.0 mg (66%); R_f = 0.49 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 222.4–223.2 °C.

IR (KBr): 3748 (w), 3031 (w), 2916 (w), 2359 (w), 1726 (w), 1592 (s), 1474 (m), 1467 (m), 1230 (m), 697 cm^{-1} (s).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.46 (s, 1 H), 7.47–7.37 (m, 4 H), 7.34 (s, 1 H), 7.32–7.21 (m, 6 H), 7.21–7.16 (m, 3 H), 7.14 (t, *J* = 7.4 Hz, 1 H), 7.07 (d, *J* = 6.9 Hz, 2 H), 7.02 (t, *J* = 8.0 Hz, 3 H), 5.31 (d, *J* = 4.2 Hz, 2 H), 4.54 (s, 1 H), 4.02 (dd, *J* = 11.1, 6.9 Hz, 1 H), 3.29 (dd, *J* = 20.0, 11.2 Hz, 1 H), 3.21 (dd, *J* = 20.0, 6.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 182.6, 136.7, 136.6, 136.3, 136.2, 130.6, 130.2, 129.2, 128.9, 128.3, 127.8, 127.0, 126.73, 126.66, 126.1, 122.7, 120.0, 118.5, 115.0, 113.8, 110.2, 110.1, 105.6, 50.3, 48.8, 45.1, 35.9, 32.1.

MS (70 eV, EI): *m*/*z* (%) = 534 [M]$^+$ (15), 207 (10), 115 (5), 105 (40), 92 (100), 77 (25).

HRMS (EI-magnetic sector): *m*/*z* [M]$^+$ calcd for $C_{36}H_{27}N_3O_2$: 533.2103; found: 533.2099.

5aa

Yellow solid; yield: 70.0 mg (65%); R_f = 0.50 (CH_2Cl_2–hexanes, 1:1); 100% enol form; mp 235.5–236.3 °C.

IR (KBr): 3702 (w), 3030 (m), 2358 (w), 1733 (w), 1627 (s), 1451 (s), 1204 (m), 701 cm^{-1} (s).

^1H NMR (400 MHz, $CDCl_3$): δ = 17.19 (s, 1 H), 7.74 (d, *J* = 15.4 Hz, 1 H), 7.52–7.41 (m, 5 H), 7.40–7.29 (m, 10 H), 6.59 (d, *J* = 15.4 Hz, 1 H), 4.79 (s, 1 H), 3.50 (dd, *J* = 12.3, 5.8 Hz, 1 H), 3.30 (dd, *J* = 19.5, 12.3 Hz, 1 H), 3.03 (dd, *J* = 19.5, 5.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.8, 183.7, 145.0, 136.3, 135.1, 134.3, 130.9, 130.1, 129.7, 129.4, 129.25, 129.21, 129.0, 128.5, 128.2, 119.0, 114.4, 113.2, 104.8, 48.5, 44.6, 39.9, 35.2.

MS (70 eV, EI): *m*/*z* (%) = 430 $[M]^+$ (40), 276 (20), 172 (20), 154 (25), 131 (70), 105 (70), 103 (100), 77 (90).

HRMS (EI-magnetic sector): *m*/*z* $[M]^+$ calcd for $C_{29}H_{22}N_2O_2$: 430.1684; found: 430.1681.

5ba

Yellow solid; yield: 135.3 mg (75%); R_f = 0.39 (EtOAc–CH_2Cl_2–hexanes, 1:1:4); 100% enol form; mp 153.9–154.3 °C.

IR (KBr): 3336 (w), 2977 (w), 2351 (w), 1764 (s), 1600 (m), 1512 (m), 1253 (s), 1145 (s), 743 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 17.11 (s, 1 H), 7.66 (d, *J* = 15.3 Hz, 1 H), 7.55–7.40 (m, 5 H), 7.10 (t, *J* = 8.3 Hz, 2 H), 6.98–6.90 (m, 2 H), 6.88–6.80 (m, 2 H), 6.48 (d, *J* = 15.3 Hz, 1 H), 4.77 (s, 1 H), 3.83 (s, 6 H), 3.48 (dd, *J* = 12.0, 5.9 Hz, 1 H), 3.25 (dd, *J* = 19.5, 12.1 Hz, 1 H), 3.04 (dd, *J* = 19.5, 5.9 Hz, 1 H), 1.54 (d, *J* = 3.0 Hz, 18 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 186.7, 183.1, 151.7, 151.5, 151.1, 150.9, 144.1, 142.3, 141.0, 136.3, 133.7, 133.1, 130.1, 129.7, 129.3, 123.1, 123.0, 121.7, 120.7, 119.3, 114.4, 113.0, 112.0, 111.4, 104.8, 83.8, 83.6, 56.1, 55.8, 48.4, 44.4, 39.8, 35.3, 27.5.

MS (70 eV, EI): *m*/*z* (%) = 522 $[M - 200]^+$ (100), 177 (60), 150 (100), 135 (60), 77 (20).

HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{41}H_{42}N_2O_{10}Na$: 745.2737; found: 745.2728.

Deprotection of 5ba with TFA

A dry and nitrogen-flushed 10 mL Schlenk flask, equipped with a magnetic stirring bar and a septum, was sequentially charged with a solution of **5ba** (0.3 mmol) and trifluoroacetic acid (30 vol%) in anhyd CH_2Cl_2 (3 mL). The reaction mixture was stirred for 3 h at 0 °C. Thereafter, the solvent was removed by evaporation in vacuo. Purification by flash chromatography (CH_2Cl_2–hexanes, 2:1) furnished **6** as a yellow solid; 52.3 mg (quant.).

Yellow solid; yield: 52.3 mg (100%); R_f = 0.35 (CH_2Cl_2–hexanes, 2:1); 100% enol form; mp 147.9–148.8 °C.

IR (KBr): 3466 (s), 3382 (m), 3191 (w), 2962 (w), 2200 (w), 1581 (s), 1451 (m), 1272 (s), 777 cm^{-1} (w).

^1H NMR (400 MHz, $CDCl_3$): δ = 17.24 (s, 1 H), 7.67 (d, *J* = 15.2 Hz, 1 H), 7.52–7.41 (m, 5 H), 6.93 (dd, *J* = 8.2, 2.2 Hz, 1 H), 6.87 (dd, *J* = 8.2, 2.2 Hz, 3 H), 6.80–6.74 (m, 2 H), 6.39 (d, *J* = 15.2 Hz, 1 H), 5.94 (br s, 1 H), 5.71 (br s, 1 H), 4.76 (s, 1 H), 3.88 (d, *J* = 2.8 Hz, 6 H), 3.43 (dd, *J* = 12.1, 5.9 Hz, 1 H), 3.24 (dd, *J* = 19.4, 12.2 Hz, 1 H), 3.02 (dd, *J* = 19.4, 5.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.0, 182.9, 148.8, 146.9, 146.8, 146.6, 145.2, 136.6, 130.2, 129.6, 129.2, 127.0, 129.9, 123.9, 121.8, 116.7, 114.9, 114.8, 114.7, 113.4, 110.1, 109.6, 104.5, 56.1, 55.8, 48.5, 45.0, 39.8, 35.4.

MS (70 eV, EI): *m*/*z* (%) = 522 $[M]^+$ (40), 367 (25), 190 (30), 177 (100), 150 (60), 77 (30).

HRMS (MALDI): *m*/*z* $[M + H]^+$ calcd for $C_{31}H_{27}N_2O_6$: 523.1869; found: 523.1888.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1379143.

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(10) (a) MacDonald, F. K.; Burnell, D. J. *J. Org. Chem.* **2009**, *74*, 6973; all the starting materials, 1-hydroxy-1,4-dien-3-ones **1**, were readily prepared according to the protocol mentioned in this article, and **1ae-ag**, **1ca**, and **1ga-ia** were new compounds. (b) Qiu, X.; Liu, Z.; Shao, W.-Y.; Liu, X.; Jing, D.-P.; Yu, Y.-J.; An, L.-K.; Huang, S.-L.; Bu, X.-Z.; Huang, Z.-S.; Gu, L.-Q. *Bioorg. Med. Chem.* **2008**, *16*, 8035; starting materials, curcumin-related derivatives **4a** and **4b**, were prepared according to this article, and **4b** was a new compound.

(11) This reaction was carried out using **1aa** (0.25 mmol) and **2a** (0.3 mmol, 1.2 equiv) in the absence of an added base in MeOH (10.5 mL, much more solvent than before due to the low solubility of **1aa** in MeOH) at 30 °C for 1d. After purification as usual, only 14% of product was obtained. It indicated that an added base was necessary for acceptable results although the reaction could occur via enol very slowly.

(12) The structure of **3aaa** was determined by X-ray crystal structure analysis (CCDC number: 940043), and further information is provided in the Supporting Information.

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(16) The structure of **3aao**-keto was determined by NMR analysis, and more information is provided in the Supporting Information.

(17) The structures of **3aia** were determined by X-ray crystal structure analysis (CCDC number for **3aia**-enol: 940045; for **3aia**-keto: 940044), and more information is provided in the Supporting Information.

(18) Our reaction was not only suitable for 2-alkylidenemalononitriles, but can also be employed using substrates such as α-cyanocinnamates and β-nitrostyrenes. In fact, we already have some results from these substrates and believe further results under investigation in these areas will be reported in due course.

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