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Reactions of salicyl *N*-tosylimines or salicylaldehydes with diethyl acetylenedicarboxylate for the synthesis of highly functionalized chromenes

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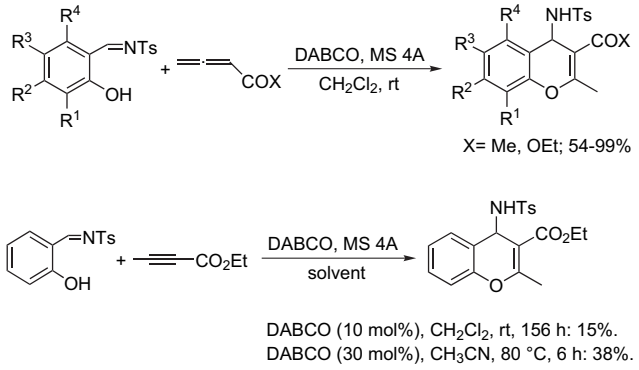
Abstract—Reactions of diethyl acetylenedicarboxylate with salicyl *N*-tosylimines or salicylaldehydes proceeded smoothly in the presence of DABCO or dimethylphenylphosphine under mild conditions to give the corresponding chromenes in excellent yields.

1. Introduction

Due to the unique biological and pharmacological activity, chromene derivatives have attracted considerable attention.[1] Different processes for the synthesis of chromenes have been reported during the past few years.[2] We have recently reported an efficient approach to substituted chromenes by amine-catalyzed reaction of allenic esters, allenic ketones or ethyl 2-butynoate with salicyl *N*-tosylimines (Scheme 1).[3] However, the reaction between ethyl 2-butynoate and salicyl *N*-tosylimine did not give the corresponding chromene in satisfactory yield under various reaction conditions (Scheme 1). During our continuing research in this area, we found that diethyl acetylenedicarboxylate showed higher reactivity than ethyl 2-butynoate for this reaction. In this paper, we report the reactions of salicyl *N*-tosylimines or salicylaldehydes with diethyl acetylenedicarboxylate to give the corresponding chromenes in excellent yields in the presence of DABCO or dimethylphenylphosphine under mild conditions.



Scheme 1. Reaction of allenes or ethyl 2-butynoate with salicyl *N*-tosylimines.

2. Results and discussion

Different solvents and catalysts were first examined using the reaction of salicyl *N*-tosylimine **1a** (1.0 equiv) with diethyl acetylenedicarboxylate **2a** (1.2 equiv) as a model. The results are summarized in Table 1. Using 1,4-diazabicyclo[2,2,2]octane (DABCO) (10 mol %) as the catalyst and performing the reaction in dichloromethane did not give the corresponding chromene and alternatively, acyclic product **3a** was obtained in 50% yield (Table 1, entry 1). Compound **3a** is confirmed to be a mixture of *E:Z* isomers (12:1) by comparison of the ^{1}H NMR chemical shifts of the olefinic protons with those of similar known compounds.[4] Then, several other solvents were examined under the similar conditions (Table 1, entries 2–6). As a consequence, DMSO was found to be the best solvent. Under the catalysis of DABCO, the reaction could be completed in DMSO within 2 h giving the corresponding chromene **4a** in 98% yield (Table 1, entry 6). Other amine or phosphine

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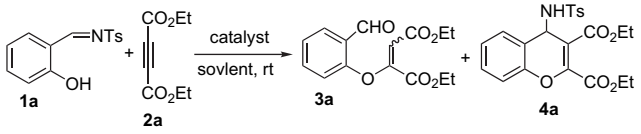
Table 1. Reactions of salicyl *N*-tosylimine **1a** (1.0 equiv) with diethyl acetylenedicarboxylate **2a** (1.2 equiv) in the presence of 10 mol % of catalyst in various solvents



Entry	Solvent	Time (h)	Catalyst	Yield (%)[a]	
				3a	**4a**
1	CH_2Cl_2	25	DABCO	50	—
2	THF	25	DABCO	43	—
3	PhMe	25	DABCO	—	33
4	CH_3CN	25	DABCO	—	60
5	DMF	25	DABCO	—	95
6	DMSO	2	DABCO	—	98
7	DMSO	0.5	DBU	—	94
8	DMSO	0.5	DMAP	—	90
9	DMSO	1	Et_3N	—	91
10	DMSO	0.5	PMe_3	—	92
11	DMSO	2.5	PPh_2Me	—	89
12	DMSO	2	$PPhMe_2$	—	88
13	DMSO	1	PBu_3	—	85
14	DMSO	1	PPh_3	—	90
15	DMSO	3	$^iPr_2NEt$	—	72
16	DMSO	2	K_2CO_3	—	72

[a] Isolated yields.

catalysts also showed catalytic activity for the reaction in DMSO while the yields of **4a** were slightly lower (Table 1, entries 7–14). It should be noted that the weak nucleophile ethyldiisopropylamine ($^iPr_2NEt$) and inorganic catalyst K_2CO_3 could also promote this reaction to give the corresponding chromene **4a** in moderate yields (72%) (Table 1, entries 15 and 16). Thus, we established the optimal reaction conditions for this reaction using DABCO as catalyst and performing the reaction in DMSO.

Under these optimized reaction conditions, the reaction of several other salicyl *N*-tosylimines **1** with **2a** was also examined. Both electron-withdrawing and electron-donating substituents were tolerated at various positions on the benzene rings in the imines. The corresponding chromenes **3** were obtained in good yields (Table 2, entries 1–5).

In the previous study, we found that weak nucleophilic catalysts showed no catalytic activity for the reaction between

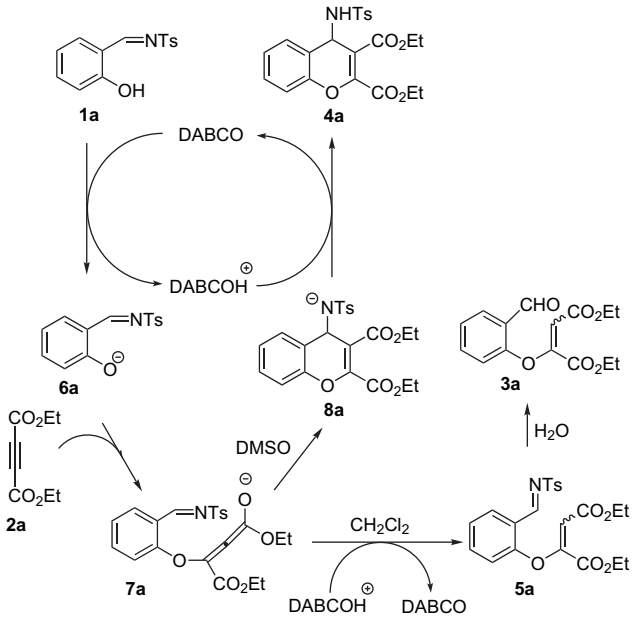
Table 2. Reactions of other salicyl *N*-tosylimines **1** (1.0 equiv) with diethyl acetylenedicarboxylate **2a** (1.2 equiv) in the presence of 10 mol % of DABCO

Entry	R^1	R^2	R^3	Time (h)	Yield of **4** (%)[a]
1	OMe	H	H	1	**4b**: 97
2	H	OMe	H	1	**4c**: 98
3	H	H	OMe	1	**4d**: 90
4	H	H	Cl	2	**4e**: 94
5	Cl	H	Cl	24	**4f**: 83

[a] Isolated yields.

allenic esters and salicyl *N*-tosylimines.[3] While now weak nucleophilic catalyst ethyldiisopropylamine ($^iPr_2NEt$) or K_2CO_3 can also promote the reaction of salicyl *N*-tosylimine **1a** with diethyl acetylenedicarboxylate **2a** effectively. Thus, the reaction was most likely to proceed through a different pathway.

On the basis of the above results, one reasonable mechanism is shown in Scheme 2.[5,6] DABCO first abstracts a proton from imine **1a** to generate anion **6a** and release $DABCOH^+$. Then, Michael addition occurs between intermediate **6a** and **2a** to give intermediate **7a**. Then, the reaction follows different pathways depending on the solvent. In DMSO, intramolecular Mannich reaction occurs in intermediate **7a** to afford intermediate **8a** and subsequent protonation gives product **4a** and regenerates DABCO. In CH_2Cl_2, intermediate **7a** abstracts a proton from $DABCOH^+$ to give compound **5a**, which is hydrolyzed to **3a** upon work up. The reason why the reaction proceeds through different pathways in different solvents has not been fully understood. Based on the previous reports,[7] one reasonable explanation is the medium effect in which the ionic intermediate 8a can be stabilized in the solvent such as DMSO better than in CH_2Cl_2 so that intramolecular Mannich reaction readily occurs in DMSO rather than in CH_2Cl_2. Another explanation is that the proton transfer step for the conversion of intermediate 8a to 4a is rate determining[7,8] and the intramolecular Mannich reaction is a reversible one. Proton transfer in DMSO is much faster, which allows the Mannich reaction to be predominant, while in CH_2Cl_2 the proton transfer is slower and retro-Mannich reaction effectively competes to give the starting anionic intermediate **7a** and subsequent protonation gives **5a**.



Scheme 2. Possible mechanism for the formation of **3a** and **4a**.

To confirm, compound **5a** was indeed obtained during the reaction, we monitored the reaction process of **1a** and **2a** in $CDCl_3$ by ^1H NMR spectra. Molecular sieves 4 Å were added to prevent the decomposition of **1a** during the spectroscopic trace process. Some selected spectra are shown in Figures 1–3. As can be seen from Figure 3, intermediate

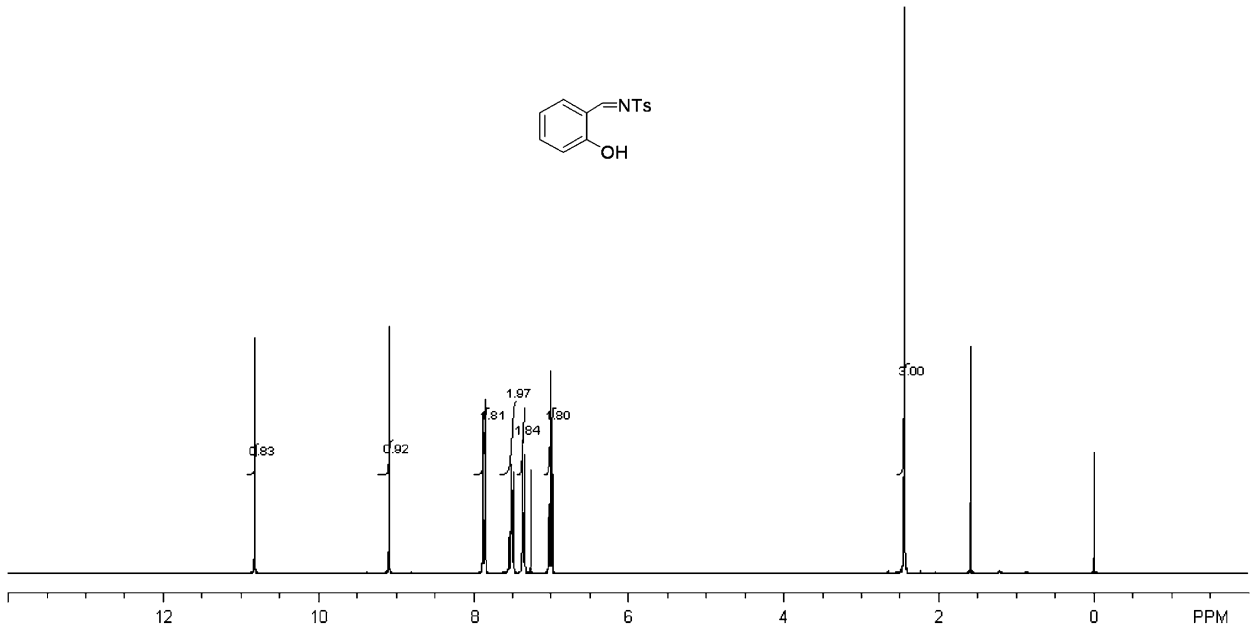


Figure 1. ^{1}H NMR spectroscopy of **1a** in $CDCl_3$.

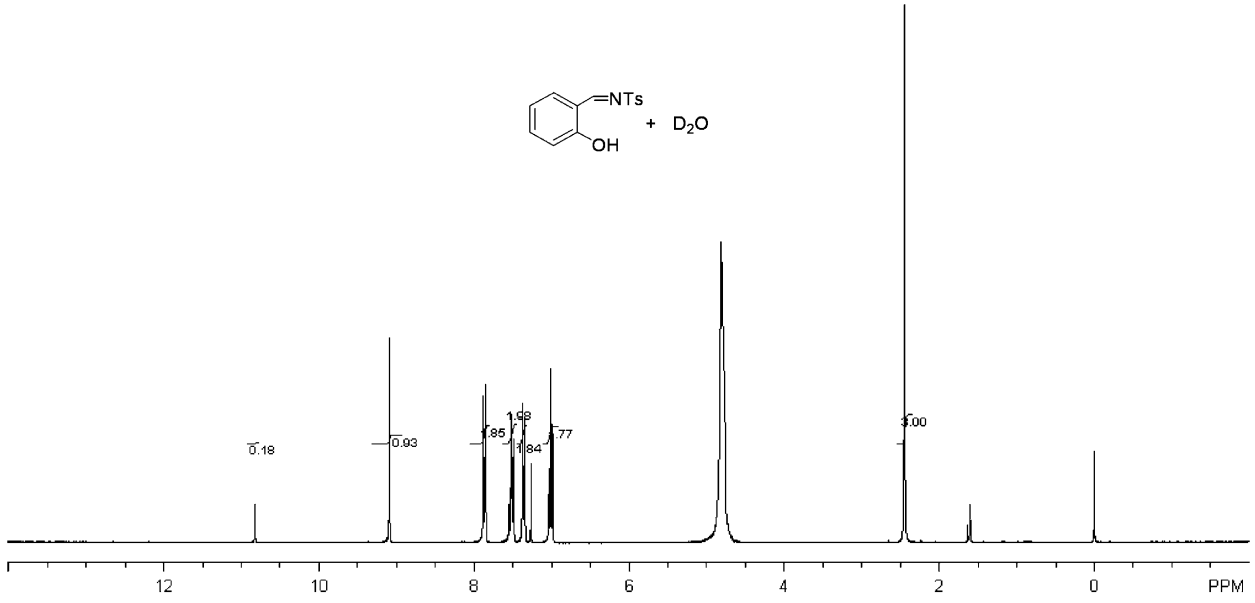


Figure 2. D_2O was added to the solution of **1a** in $CDCl_3$.

5a was indeed observed and the specific peaks for iminium proton and olefinic proton were assigned. Therefore, the reaction is most likely to proceed via the pathway shown in Scheme 2.

When the strongly nucleophilic and weakly basic phosphine is used as the catalyst, the reaction might proceed through an alternative pathway as shown in Scheme 3. The phosphine first attacks **2a** to generate a zwitterionic intermediate **7b**. Then, Mannich reaction between **7b** and **1a** followed by proton transfer provides intermediate **8b**. Subsequent cyclization of **8b** yields product **4a** and regenerates the catalyst.

Since the reaction between salicyl *N*-tosylimine **1a** and diethyl acetylenedicarboxylate **2a** proceeded effectively, we further attempted to know whether the less reactive salicylaldehyde could also react with **2a** to give the corresponding chromene under the similar conditions. Although the reaction of dimethyl acetylenedicarboxylate with salicylaldehyde was reported in the literature, yet the yield of the corresponding chromene was rather low (22%).[4] Thus, it is necessary to study the reaction of salicylaldehyde and **2a** systematically.

The optimization for the reaction conditions of salicylaldehyde **9a** and **2a** is shown in Table 3. Under the same optimal reaction conditions for **1a** and **2a**, the corresponding chromene **10a** could be obtained in 93% yield in 24 h (Table 3, entry 1). Several other catalysts were also screened (Table 3, entries 2–11) and $PPhMe_2$ was found to be the most

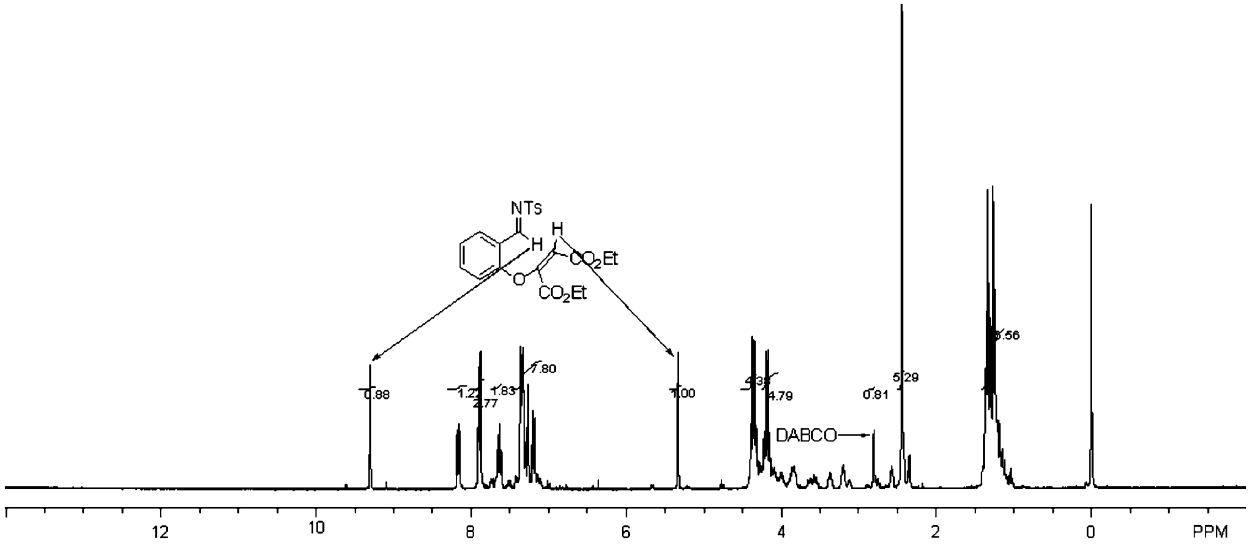
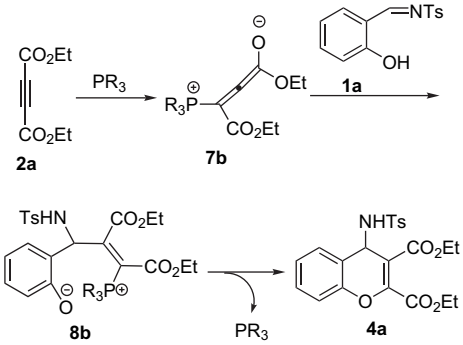
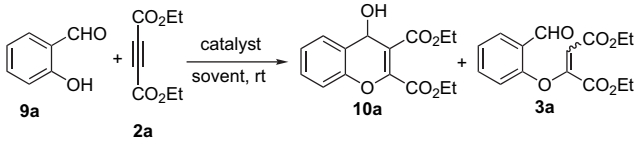


Figure 3. Twelve hours after DABCO was added to the solution of **1a** and **2a** in $CDCl_3$.



Scheme 3. An alternative pathway for the formation of **4a** under the catalysis of phosphine.

Table 3. Reactions of salicylaldehyde **9a** (1.0 equiv) with diethyl acetylenedicarboxylate **2a** (1.2 equiv) in the presence of 10 mol % of catalyst



Entry	Solvent	Time (h)	Catalyst	Yield (%)[a]	
				10a	**3a**
1	DMSO	24	DABCO	93	—
2	DMSO	11	DBU	87	—
3	DMSO	4	Et_3N	82	—
4	DMSO	1	DMAP	74	—
5	DMSO	30	PPh_3	93	—
6	DMSO	7	PBu_3	85	—
7	DMSO	2	PMe_3	95	—
8	DMSO	4	PPh_2Me	88	—
9	DMSO	2	$PPhMe_2$	97	—
10	DMSO	1	$^iPr_2NEt$	73	—
11	DMSO	13	K_2CO_3	77	—
12	CH_3CN	25	$PPhMe_2$	40	—
13	DMF	25	$PPhMe_2$	20	—
14	CH_2Cl_2	25	$PPhMe_2$	—	24
15	THF	25	$PPhMe_2$	—	22
16	PhMe	100	$PPhMe_2$	—[b]	

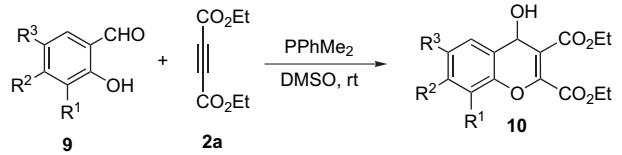
[a] Isolated yields.
[b] Disordered reaction.

effective catalyst (Table 3, entry 9). Using $PPhMe_2$ as the catalyst, solvent effect was also examined (Table 3, entries 12–16). Performing the reaction in acetonitrile and *N*,*N*-dimethylformamide (DMF), both provided **10a** in low yields (Table 3, entries 12 and 13). When carrying out the reaction in CH_2Cl_2 or THF, acyclic product **3a** was obtained as well (Table 3, entries 14 and 15). Changing the solvent to toluene, the reaction became disordered and from which no products could be identified (Table 3, entry 16). Thus, these optimized reaction conditions for this reaction were using $PPhMe_2$ as the catalyst and DMSO as the solvent.

Under the above optimal reaction conditions, several other salicylaldehydes (**9**) can also react with **2a** to give the corresponding chromenes **10** in excellent yields (Table 4, entries 1–5). Therefore, the reaction of salicylaldehyde **9** with **2a** has been significantly improved in comparison with the previous synthetic procedures.[4]

With the acyclic compound **3a** in hand, we further attempted to know if **3a** could be cyclized to chromene **10a** by intramolecular Baylis–Hillman reaction.[9] To test this hypothesis, **3a** was treated with DABCO in DMSO. However, no reaction occurred within 48 h (Scheme 4). This result suggests

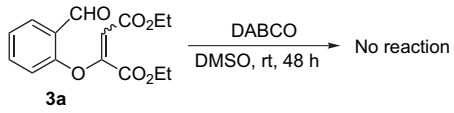
Table 4. Reactions of other salicylaldehydes **9** (1.0 equiv) with diethyl acetylenedicarboxylate **2a** (1.2 equiv) in the presence of 10 mol % of $PPhMe_2$



Entry	R^1	R^2	R^3	Time (h)	Yield of **10** (%)[a]
1	OMe	H	H	3	**10b**: >99
2	H	OMe	H	3	**10c**: 94
3	H	H	OMe	3	**10d**: 92
4	H	H	Cl	24	**10e**: 89
5	Cl	H	Cl	24	**10f**: 83

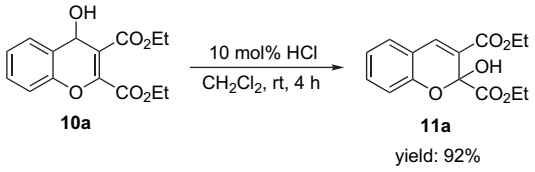
[a] Isolated yields.

again that chromenes **4** and **10** would be formed via the pathway shown in Scheme 2.



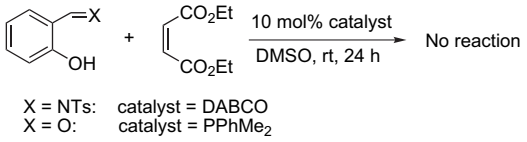
Scheme 4. The attempted intramolecular Baylis–Hillman reaction.

On the other hand, similar to the reported procedure,[4] compound **10a** could be converted to another type of chromene derivative **11a** in 92% yield via hydroxy migration simply by treating with catalytic amount of hydrochloric acid (Scheme 5).



Scheme 5. Transformation of product **10a**.

Since diethyl acetylenedicarboxylate shows excellent reactivity, we further envisioned whether diethyl maleate was also suitable substrate for this kind of reaction. To test this hypothesis, diethyl maleate was subjected to the reaction with salicyl *N*-tosylimine or salicylaldehyde under these above optimized conditions (Scheme 6). However, no reaction occurred presumably due to the reason that diethyl maleate is less electrophilic than diethyl acetylenedicarboxylate as a Michael acceptor.



Scheme 6. The attempted reaction of diethyl maleate with salicyl *N*-tosylimine or salicylaldehyde.

3. Conclusions

We have shown an efficient process for the synthesis of highly functionalized chromene derivatives by reaction of diethyl acetylenedicarboxylate with salicyl *N*-tosylimines or salicylaldehydes. The reaction proceeded smoothly under mild conditions in the presence of DABCO and $PPhMe_2$, respectively, and the corresponding chromenes were obtained in excellent yields. Further application of these products is under progress in our laboratory.

4. Experimental

4.1. General remarks

Mps were obtained with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; *J*-values are in Hertz. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by an Ion Spec 4.7 Tesla FTMS mass spectrometer. Some of the solid compounds reported in this paper gave satisfactory CHN microanalyses with a Carlo-Erba 1106 analyzer and other compounds reported in this paper gave satisfactory HRMS analytic data. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 200–300 mesh silica gel at increased pressure. The starting materials such as salicylic aldehydes and diethyl acetylenedicarboxylate were bought from Aldrich Company. Salicyl *N*-tosylimines[10] were prepared according to the literature.

4.2. Typical procedure for the reaction of salicyl *N*-tosylimine with diethyl acetylenedicarboxylate catalyzed by DABCO in CH_2Cl_2

To a Schlenk tube with CH_2Cl_2 (1.0 mL) were added salicyl *N*-tosylimine (68.9 mg, 0.25 mmol), diethyl acetylenedicarboxylate (51 mg, 0.3 mmol) and DABCO (2.8 mg, 0.025 mmol). The solution was stirred for 25 h at room temperature. Then, the solvent was removed under reduced pressure and the residue was purified by a silica gel column chromatography to give **3a** (eluent: EtOAc/petroleum=1:6, 36.5 mg, yield 50%) as a colorless liquid. We obtained product **3a** as a mixture of *E*,*Z*-isomers (*E*/*Z*=12:1). The *E*,*Z*-isomers of **3a** could not be isolated by SiO_2 flash chromatography. The ratio of the two isomers was obtained based on ^{1}H NMR spectroscopic data and the corresponding ^{1}H NMR spectroscopic data for *E*-isomers of **3a** could be assigned.

4.2.1. 2-(2-Formyl-phenoxy)-but-2-enedioic acid diethyl ester (3a). A colorless liquid, IR (KBr) ν 1744, 1719, 1697, 1211, 1189 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.27 (t, *J*=7.2 Hz, 3H, CH_3), 1.35 (t, *J*=7.2 Hz, 3H, CH_3), 4.13 (q, *J*=7.2 Hz, 2H, CH_2), 4.37 (q, *J*=7.2 Hz, 2H, CH_2), 5.24 (s, 1H, CH), 7.21 (d, *J*=5.4 Hz, 1H, Ar), 7.40 (t, *J*=7.2 Hz, 1H, Ar), 7.66 (td, *J*=5.4, 1.8 Hz, 1H, Ar), 7.97 (dd, *J*=7.8, 1.8 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 13.9, 60.8, 62.5, 102.1, 121.5, 126.7, 127.7, 128.9, 135.9, 155.3, 159.6, 161.9, 164.6, 187.6; MS (EI) *m*/*z* 293 (M^+, 0.63), 342 (M^+−170, 53.58), 242 (M^+−270, 35.82), 270 (M^+−242, 12.05), 170 (M^+−342, 4.57), 155 (M^+−357, 11.84); HRMS calcd for $C_{15}H_{16}O_6$ requires 292.0947. Found: 292.0958.

4.3. Typical procedure for the reaction of salicyl *N*-tosylimine with diethyl acetylenedicarboxylate catalyzed by DABCO in DMSO

To a Schlenk tube with DMSO (1.0 mL) were added salicyl *N*-tosylimine (68.9 mg, 0.25 mmol), diethyl acetylenedicarboxylate (51 mg, 0.3 mmol) and DABCO (2.8 mg, 0.025 mmol). The solution was stirred for 2 h at room temperature. CH_2Cl_2 (40 mL) was added and the solution was washed with water (20 mL×3) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a silica gel column

chromatography to give **4a** (eluent: EtOAc/petroleum=1:4, 109.3 mg, yield 98%) as a white solid.

4.3.1. Diethyl 4-(4-methylphenylsulfonamido)-4*H*-chromene-2,3-dicarboxylate (4a). A white solid, mp: 148–150 °C; IR (KBr) ν 3270, 2988, 1712, 1275, 1224, 1158, 1102, 764, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.17 (t, J=7.2 Hz, 3H, CH_3), 1.37 (t, J=7.2 Hz, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.88–4.00 (m, 1H, CH_2), 4.32–4.39 (m, 1H, CH_2), 4.35 (q, J=7.2 Hz, CH_2), 5.08 (d, J=7.2 Hz, 1H, NH), 5.65 (d, J=7.2 Hz, 1H, CH), 7.08–7.12 (m, 2H, Ar), 7.22–7.29 (m, 3H, Ar), 7.40 (d, J=7.2 Hz, 1H, CH), 7.66 (d, J=8.1 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 13.8, 21.4, 46.80, 61.3, 62.5, 106.8, 116.6, 119.4, 125.5, 126.8, 129.2, 129.4, 129.7, 138.8, 142.9, 149.7, 149.8, 161.7, 164.6; MS (EI) m/z 371 (M^+−74, 3.68), 312 (M^+−133, 2.18), 244 (M^+−203, 4.07), 203 (M^+−244, 3.75), 133 (M^+−312, 87.98), 74 (M^+−371, 100.00); Anal. Calcd for $C_{22}H_{23}NO_7S$: C, 59.32; H, 5.20; N, 3.14%. Found: C, 59.43; H, 5.18; N, 2.96%.

4.3.2. Diethyl 8-methoxy-4-(4-methylphenylsulfonamido)-4*H*-chromene-2,3-dicarboxylate (4b). A white solid, mp: 118–122 °C; IR (KBr) ν 3728, 2983, 1718, 1649, 1303, 1214, 1100, 1025, 944, 860, 816, 563 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.17 (t, J=7.2 Hz, 3H, CH_3), 1.37 (t, J=7.2 Hz, 3H, CH_3), 2.42 (s, 3H, CH_3), 3.86 (s, 3H, CH_3), 3.87–3.90 (m, 1H, CH_2), 3.98–4.00 (m, 1H, CH_2), 4.36 (q, J=7.2 Hz, 2H, CH_2), 4.86 (d, J=8.6 Hz, 1H, NH), 5.67 (d, J=8.6 Hz, 1H, CH), 6.85 (d, J=8.1 Hz, 1H, Ar), 7.01–7.06 (m, 2H, Ar), 7.24 (d, J=8.0 Hz, 2H, Ar), 7.69 (d, J=8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 13.8, 21.4, 46.8, 56.1, 61.4, 62.5, 106.8, 111.4, 120.5, 120.6, 125,4 126.9, 129.3, 138.8, 139.6, 142.9, 147.6, 149.7, 161.6, 164.6; MS (ESI) m/z 498 (M^++23); Anal. Calcd for $C_{23}H_{25}NO_8S$: C, 58.10; H, 5.30; N, 2.95%. Found: C, 58.05; H, 5.23; N, 2.61%.

4.3.3. Diethyl 7-methoxy-4-(4-methylphenylsulfonamido)-4*H*-chromene-2,3-dicarboxylate (4c). A white solid, mp: 136–140 °C; IR (KBr) ν 3261, 2908, 1725, 1574, 1224, 1492, 1276, 1209, 1156, 1024, 764 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.17 (t, J=7.2 Hz, 3H, CH_3), 1.38 (t, J=7.2 Hz, 3H, CH_3), 2.41 (s, 3H, CH_3), 3.79 (s, 3H, CH_3), 3.91–4.05 (m, 1H, CH_2), 4.33–4.37 (m, 1H, CH_2), 4.36 (q, J=7.2 Hz, 2H, CH_2), 4.85 (d, J=6.0 Hz, 1H, NH), 5.59 (d, J=6.0 Hz, 1H, CH), 6.60–6.68 (m, 2H, Ar), 7.20–7.40 (m, 3H, Ar), 7.67 (d, J=8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 13.8, 21.4, 46.8, 55.5, 61.4, 62.5, 100.8, 107.6, 111.5, 113.0, 126.9, 129.3, 130.4, 138.8, 142.9, 149.2, 150.5, 160.3, 161.7, 164.8; MS (EI) m/z 431 (M^+−44, 0.62), 319 (M^+−155,11.71), 245 (M^+−230, 4.57), 230 (M^+−245, 30.14); 155 (M^+−319, 22.77); Anal. Calcd for $C_{23}H_{25}NO_8S$: C, 58.10; H, 5.30; N, 2.95%. Found: C, 57.83; H, 5.33; N, 2.67%.

4.3.4. Diethyl 6-methoxy-4-(4-methylphenylsulfonamido)-4*H*-chromene-2,3-dicarboxylate (4d). A white solid, mp: 174–176 °C; IR (KBr) ν 3279, 2984, 1742, 1651, 1489, 1342, 1276, 1215, 1157 1101, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.19 (t, J=7.2 Hz, 3H, CH_3), 1.38 (t, J=7.2 Hz, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.67 (s, 3H, CH_3), 3.91–4.04 (m, 1H, CH_2), 4.32–4.37 (m, 1H, CH_2), 4.36 (q, J=7.2 Hz, 2H, CH_2), 4.97 (d, J=7.5 Hz, 1H, NH), 5.63 (d, J=7.5 Hz, 1H, CH), 6.82–6.86 (m, 2H, Ar), 7.04 (d, J=8.4 Hz, 1H, Ar), 7.23–7.27 (m, 2H, Ar), 7.66 (d, J=6.3 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 21.4, 47.5, 55.4, 61.4, 62.5, 105.8, 111.9, 117.1, 117.9, 119.7, 126.9, 129.3, 138.9, 143.0, 143.9, 150.1, 156.9, 161.9, 164.8; MS (EI) m/z 431 (M^+−44, 1.82), 319 (M^+−155, 100), 245 (M^+−230, 37.21) 230 (M^+−245, 8.12); 155 (M^+−319, 1.48); Anal. Calcd for $C_{23}H_{25}NO_8S$: C, 58.10; H, 5.30; N, 2.95%. Found: C, 58.02; H, 5.26; N, 2.70%.

4.3.5. Diethyl 6-bromo-4-(4-methylphenylsulfonamido)-4*H*-chromene-2,3-dicarboxylate (4e). A white solid, mp: 160–162 °C; IR (KBr) ν 3250, 2985, 1722, 1479, 1346, 1276, 1158, 1030, 813 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.23 (t, J=7.2 Hz, 3H, CH_3), 1.39 (t, J=7.2 Hz, 3H, CH_3), 2.42 (s, 3H, CH_3), 4.01–4.04 (m, 1H, CH_2), 4.07–4.09 (m, 1H, CH_2), 4.54 (q, J=7.2 Hz, 2H, CH_2), 5.13 (d, J=6.9 Hz, 1H, NH), 5.53 (d, J=6.9 Hz, 1H, CH), 6.98 (d, J=8.7 Hz, 1H, Ar), 7.22–7.26 (m, 3H, Ar), 7.36 (dd, J=8.7, 2.4 Hz, 1H, Ar), 7.61 (d, J=8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 21.5, 46.7, 61.7, 62.7, 106.9, 117.8, 118.6, 120.7, 126.8, 129.5, 132.3, 132.6, 138.5, 143.5, 148.9, 149.5, 161.5, 164.4; MS (EI) m/z 367 (M^+−155, 51.60), 352 (M^+−171,37.39), 171 (M^+−352, 4.76), 155 (M^+−367, 14.84); Anal. Calcd for $C_{22}H_{22}BrNO_7S$: C, 50.39; H, 4.23; N, 2.67%. Found: C, 50.41; H, 4.17; N, 2.49%.

4.3.6. 6,8-Dichloro-4-(toluene-4-sulfonylamino)-4*H*-chromene-2,3-dicarboxylic acid diethyl ester (4f). A white solid, mp: 136–140 °C; IR (KBr) ν 3281, 2984, 1745, 1654, 1587, 1489, 1302, 815, 765 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.21 (t, J=7.2 Hz, 3H, CH_3), 1.39 (t, J=7.2 Hz, 3H, CH_3), 2.42 (s, 3H, CH_3) 3.99–4.06 (m, 2H, CH_2), 4.37 (q, J=7.2 Hz, 2H, CH_2), 5.07 (d, J=7.6 Hz, 1H, NH), 5.65 (d, J=7.6 Hz, 1H, CH), 7.10 (s, 1H, Ar), 7.26–7.33 (m, 2H, Ar), 7.33 (s, 1H, Ar), 7.64 (d, J=7.5 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.80, 13.85, 21.5, 46.9, 61.8, 62.8, 107.4, 121.8, 123.0, 126.9, 127.8, 129.5, 130.0, 130.2, 138.3, 143.6, 144.7, 149.2, 160.9, 164.0; MS (EI) m/z 357 (M^+−155, 76.77), 342 (M^+−170, 53.58), 242 (M^+−270, 35.82), 270 (M^+−242, 12.05), 170 (M^+−342, 4.57), 155 (M^+−357, 11.84); Anal. Calcd for $C_{22}H_{21}Cl_2NO_7S$: C, 51.37; H, 4.12; N, 2.72%. Found: C, 51.07; H, 4.34; N, 2.45%.

4.4. Typical procedure for the reaction of salicylaldehyde with diethyl acetylenedicarboxylate catalyzed by $PPhMe_2$ in DMSO

To a Schlenk tube with DMSO (1.0 mL) were added salicylaldehyde (30.5 mg, 0.25 mmol), diethyl acetylenedicarboxylate (51 mg, 0.3 mmol) and $PPhMe_2$ (3.5 mg, 0.025 mmol). The solution was stirred for 2 h at room temperature. CH_2Cl_2 (40 mL) was added and the solution was washed with water (20 mL×3) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by a silica gel column chromatography to give **10a** (eluent: EtOAc/petroleum=1:4, 70.8 mg, yield 97%) as a white solid.

4.4.1. 4-Hydroxy-4*H*-chromene-2,3-dicarboxylic acid diethyl ester (10a). A white solid, mp: 63–64 °C; IR (KBr) ν 2985, 1746, 1654, 1275, 1587, 1488, 1301, 1222, 1045, 1015, 892, 759 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.32 (t, J=7.2 Hz, 3H, CH_3), 1.38 (t, J=7.2 Hz, 3H, CH_3), 3.11 (d, J=4.8 Hz, 1H, CH), 4.33 (q, J=7.2 Hz, 2H, CH_2), 4.39 (q, J=7.2 Hz, 2H, CH_2), 5.76 (d, J=4.8 Hz, 1H, OH), 7.15 (d, J=6.9 Hz, 1H, Ar), 7.25–7.54 (m, 2H, Ar), 7.56 (dd, J=7.5, 1.5 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 14.0, 60.3, 61.5, 62.5, 107.4, 116.6, 120.8, 125.5, 129.6, 129.9, 149.0, 150.2, 162.3, 165.7; MS (EI) *m/z* 291 (M^+, 8.39), 191 (M^+-101, 8.49) 173 (M^+-118, 100), 118 (M^+-173, 6.78), 101 (M^+-191, 17.59); Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52%. Found: C, 61.52; H, 5.56%.

4.4.2. Diethyl 4-hydroxy-8-methoxy-4*H*-chromene-2,3-dicarboxylate (10b). A white solid, mp: 100–102 °C; IR (KBr) ν 3270, 2988, 1712, 1275, 1224, 1158, 1102, 764, 758 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.34 (t, J=7.2 Hz, 3H, CH_3), 1.39 (t, J=7.2 Hz, 3H, CH_3), 3.10 (d, J=5.1 Hz, 1H, CH), 3.89 (s, 3H, CH_3), 4.26 (q, J=7.2 Hz, 2H, CH_2), 4.35 (q, J=7.2 Hz, 2H, CH_2), 5.74 (d, J=5.1 Hz, 1H, OH), 6.90 (d, J=6.6 Hz, 1H, Ar), 7.10–7.27 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 14.0, 56.1, 60.5, 61.5, 62.5, 107.3, 111.6, 120.8, 121.7, 125.4, 139.0, 147.6, 150.1, 162.3, 165.7; MS (EI) *m/z* 280 (M^+-43, 21.64), 235 (M^+-89, 10.16) 89 (M^+-235, 11.30), 43 (M^+-280, 8.81), 101 (M^+-191, 17.59); Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63%. Found: C, 59.52; H, 5.61%.

4.4.3. Diethyl 4-hydroxy-7-methoxy-4*H*-chromene-2,3-dicarboxylate (10c). A white solid, mp: 98–100 °C; IR (KBr) ν 3627, 2983, 1748, 1294, 1236, 1100, 1033, 858, 818, 775 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.31 (t, J=7.2 Hz, 3H, CH_3), 1.37 (t, J=7.2 Hz, 3H, CH_3), 3.59 (d, J=5.4 Hz, 1H, CH), 3.85 (s, 3H, CH_3), 4.27 (q, J=7.2, Hz, 2H, CH_2), 4.40 (q, J=7.2 Hz, 2H, CH_2), 5.69 (d, J=5.4 Hz, 1H, OH), 6.86 (dd, J=9.0, 2.0 Hz, 1H, Ar), 7.07–7.13 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.6, 13.8, 55.9, 60.1, 61.3, 62.3, 107.4, 111.3, 120.7, 121.8, 125.1, 138.8, 147.4, 149.8, 162.0, 165.6; MS (EI) *m/z* 203 (M^+-119, 100), 188 (M^+-133, 0.68) 119 (M^+-203, 16.24), 133 (M^+-188, 3.32); Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63%. Found: C, 59.45; H, 5.55%.

4.4.4. Diethyl 4-hydroxy-6-methoxy-4*H*-chromene-2,3-dicarboxylate (10d). A white solid, mp: 124–126 °C; IR (KBr) ν 3454, 2982, 1750, 1288, 1224, 1113, 1098, 974, 837, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.32 (t, J=7.2 Hz, 3H, CH_3), 1.37 (t, J=7.2 Hz, 3H, CH_3), 3.40 (d, J=5.1 Hz, 1H, CH), 3.80 (s, 3H, CH_3), 4.26 (q, J=7.2 Hz, 2H, CH_2), 4.37 (q, J=7.2 Hz, 2H, CH_2), 5.71 (d, J=5.1 Hz, 1H, OH), 6.77 (dd, J=9.0, 2.4 Hz, 1H, Ar), 6.99 (d, J=2.4 Hz, 1H, Ar) 7.06 (d, J=8.7 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 13.9, 55.5, 60.6, 61.3, 62.3, 106.3, 112.3, 116.8, 117.6, 121.4, 143.0, 150.3, 156.7, 162.3, 165.7; MS (EI) *m/z* 203 (M^+-119, 100.00), 119 (M^+-203, 21.76); Anal. Calcd for $C_{16}H_{18}O_7$: C, 59.62; H, 5.63%. Found: C, 59.34; H, 5.53%.

4.4.5. Diethyl 6-chloro-4-hydroxy-4*H*-chromene-2,3-dicarboxylate (10e). A white solid, mp: 78–80 °C; IR (KBr) ν 3464, 2983, 1719, 1653, 1480, 1375, 1283, 860, 818, 760 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.34 (t, J=7.2 Hz, 3H, CH_3), 1.42 (t, 3H, J=7.2 Hz, CH_3), 3.21 (d, J=6.0 Hz, 1H, CH), 4.31 (q, J=7.2 Hz, 2H, CH_2), 4.37 (q, J=7.2 Hz, 2H, CH_2), 5.76 (d, J=7.2 Hz, 1H, OH), 7.09 (d, J=9.0 Hz, 1H, Ar), 7.29 (dd, J=5.7, 2.4 Hz, 1H, Ar), 7.40 (d, J=2.4 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 13.8, 59.9, 61.5, 62.5, 107.4, 118.0, 122.4, 129.4, 129.7, 130.2, 147.4, 149.6, 161.9, 165.4; MS (EI) *m/z* 326 (M^+, 6.17), 207 (M^+-119, 100) 191 (M^+-135, 4.92); Anal. Calcd for $C_{15}H_{15}ClO_6$: C, 55.14; H, 4.63%. Found: C, 55.10; H, 4.56%.

4.4.6. Diethyl 6,8-dichloro-4-hydroxy-4*H*-chromene-2,3-dicarboxylate (10f). A white solid, mp: 96–100 °C; IR (KBr) ν 3458, 2984, 1721, 1656, 1578, 1461, 1305, 1206, 1051, 1014, 987 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.34 (t, J=7.2 Hz, 3H, CH_3), 1.41 (t, J=7.2 Hz, 3H, CH_3), 3.20 (d, J=6.0 Hz, 1H, CH), 4.32 (q, J=7.2 Hz, 2H, CH_2), 4.42 (q, J=7.2 Hz, 2H, CH_2), 5.71 (d, J=6.0 Hz, 1H, OH), 7.42 (d, J=1.2 Hz, 1H, Ar), 7.45 (d, J=1.2 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 13.8, 60.0, 61.7, 62.6, 108.2, 122.7, 123.7, 127.9, 129.9, 143.7, 148.9, 161.3, 165.1; MS (EI) *m/z* 286 (M^+-75, 100), 189 (M^+-173, 7.60), 173 (M^+-189, 16.32), 75 (M^+-286, 13.87); Anal. Calcd for $C_{15}H_{14}Cl_2O_6$: C, 49.88; H, 3.91%. Found: C, 49.80; H, 3.80%.

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References and notes

1. (a) Bower, R. S.; Ohta, T.; Cleere, J. S.; Marsella, P. A. *Science* **1976**, *193*, 542–547; (b) Ellis, G. P. Chromenes, Chromanones, and Chromones. In *The Chemistry of Heterocyclic Compounds*; Wiley: New York, NY, 1977; Vol. 31, pp 11–141; (c) Kemnitzer, W.; Drewe, J.; Jiang, S.; Zhang, H.; Wang, Y.; Zhao, J. *J. Med. Chem.* **2004**, *47*, 6299–6310; (d) Brown, C. W.; Liu, S.; Klucik, J.; Berlin, K. D.; Brenman, P. J.; Kaur, D.; Benbrook, D. M. *J. Med. Chem.* **2004**, *47*, 1008–1017; (e) Sanvicens, N.; Gomez-Vicente, V.; Masip, I.; Messeguer, A.; Cotter, T. G. *J. Biol. Chem.* **2004**, *279*, 39268–39278.
2. (a) Trost, B. M.; Toste, F. D. *J. Am. Chem. Soc.* **1998**, *120*, 9074–9075; (b) Trost, B. M.; Shen, H. C.; Dong, L.; Surivet, J.-P.; Sylvain, C. *J. Am. Chem. Soc.* **2004**, *126*, 11966–11983; (c) Mondal, M.; Argade, N. P. *Synlett* **2004**, 1243–1246; (d) Sosnovskikh, V. Y.; Usachev, B. I.; Sizov, A. Y.; Kodess, M. I. *Tetrahedron Lett.* **2004**, *45*, 7351–7354; (e) Pettigrew, J. D.; Cadieux, J. A.; So, S. S. S.; Wilson, P. D. *Org. Lett.* **2005**, *7*, 467–470.
3. Shi, Y.-L.; Shi, M. *Org. Lett.* **2005**, *7*, 3057–3060.
4. Gupta, R. K.; George, M. V. *Tetrahedron* **1975**, *31*, 1263–1275.

5. For the reactions of 2-hydroxybenzaldehydes with activated olefins; (a) Kawase, Y.; Yamaguchi, S.; Horita, H.; Takeno, J.; Kameyama, H. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 1153–1155; (b) Yamaguchi, S.; Saitoh, T.; Kamiumezawa, M.; Enomoto, H.; Kawase, Y. *J. Heterocycl. Chem.* **1992**, *29*, 755–758; (c) Kaye, P. T.; Musa, M. A.; Nocanda, X. W.; Robinson, R. S. *Org. Biomol. Chem.* **2003**, *1*, 1133–1138; (d) Kaye, P. T.; Musa, M. A. *Synthesis* **2003**, 531–534; (e) Lesch, B.; Bräse, S. *Angew. Chem., Int. Ed.* **2004**, *43*, 115–118; (f) Lesch, B.; Toräng, J.; Vanderheiden, S.; Bräse, S. *Adv. Synth. Catal.* **2005**, *347*, 555–562; (g) Zhao, G.-L.; Shi, Y.-L.; Shi, M. *Org. Lett.* **2005**, *7*, 4527–4530.

6. For the reactions of salicyl *N*-tosylimines with 2-cyclohexenone: Shi, Y.-L.; Shi, M. *Synlett* **2005**, 2623–2626.

7. (a) Price, K. E.; Broadwater, S. J.; Jung, H. M.; McQuade, D. T. *Org. Lett.* **2005**, *7*, 147–150; (b) Price, K. E.; Broadwater, S. J.; Walker, B. J.; McQuade, D. T. *J. Org. Chem.* **2005**, *70*, 3980–3987.

8. (a) Raheem, I. T.; Jacobsen, E. N. *Adv. Synth. Catal.* **2005**, *347*, 1701–1708; (b) Buskens, P.; Klankermayer, J.; Leitner, W. *J. Am. Chem. Soc.* **2005**, *127*, 16762–16763; (c) Aggarwal, V. K.; Fulford, S. Y.; Lloyd-Jones, G. C. *Angew. Chem., Int. Ed* **2005**, *44*, 1706–1708.

9. For intramolecular Baylis–Hillman reactions: (a) Roth, F.; Gygax, P.; Fráter, G. *Tetrahedron Lett.* **1992**, *33*, 1045–1048; (b) Keck, G. E.; Welch, D. S. *Org. Lett.* **2002**, *4*, 3687–3690; (c) Yeo, J. E.; Yang, X.; Kim, H. J.; Koo, S. *Chem. Commun.* **2004**, 236–237; (d) Krishna, P. R.; Kannan, V.; Sharma, G. V. M. *J. Org. Chem.* **2004**, *69*, 6467–6469; (e) Krafft, M. E.; Haxell, T. F. N. *J. Am. Chem. Soc.* **2005**, *127*, 10168–10169; (f) Thalji, R. K.; Roush, W. R. *J. Am. Chem. Soc.* **2005**, *127*, 16778–16779; (g) Teng, W.-D.; Huang, R.; Kwong, C. K.-W.; Shi, M.; Toy, P. H. *J. Org. Chem.* **2006**, *71*, 368–371.

10. Wynne, J. H.; Price, S. E.; Rorer, J. R.; Stalick, W. M. *Synth. Commun* **2003**, *33*, 341–352.