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Aza-Baylis–Hillman reaction of salicyl *N*-tosylimines with methyl vinyl ketone, ethyl vinyl ketone or phenyl vinyl ketone

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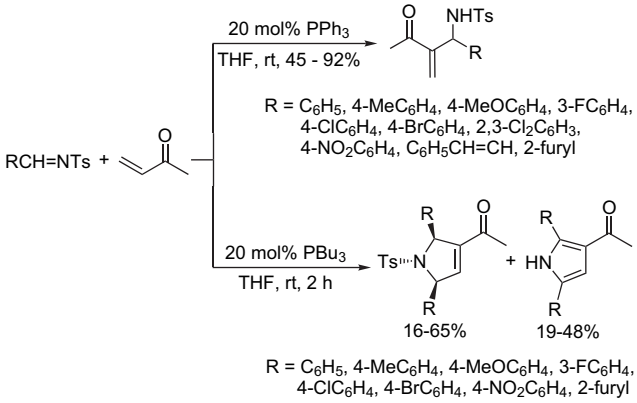
Abstract—Reactions of salicyl *N*-tosylimines with methyl vinyl ketone, ethyl vinyl ketone or phenyl vinyl ketone proceeded smoothly under mild conditions to give the corresponding chromanes or aza-Baylis–Hillman adducts in moderate to excellent yields in the presence of phosphine or nitrogen Lewis base.

1. Introduction

The Baylis–Hillman reaction, one of the most atom economical and important carbon–carbon bond-forming reactions,[1,2] has made great progress recently in the areas of shortening reaction time, extending the scope of the substrates, asymmetric catalysis and mechanistic studies.[3–5] For its great potential of the products for further transformation and the superior mild reaction conditions, the aza version of this reaction is extremely fascinating.[6–8] During the course of our investigations on the aza-Baylis–Hillman reaction of *N*-tosylimines with various activated alkenes, we have found that many unexpected products were obtained besides the normal aza-Baylis–Hillman adducts.[6b–f] For example, the reaction between *N*-tosylimines and methyl vinyl ketone proceeded smoothly to give the aza-Baylis–Hillman adducts in moderate to excellent yields under the catalysis of PPh_3, while a more nucleophilic catalyst PBu_3 resulted in two types of cyclized products (Scheme 1).[6b]

Recently, the reaction of salicyl aldehydes or salicyl *N*-tosylimines with various α,β-unsaturated compounds has been well studied.[9,10] However, the aza-Baylis–Hillman reaction of salicyl *N*-tosylimines with methyl vinyl ketone, which is one of the simplest activated alkenes, has never been reported yet. Herein, we wish to report the aza-Baylis–Hillman reactions of *N*-tosylimines with methyl vinyl ketone, ethyl vinyl ketone or phenyl vinyl ketone under mild conditions.



Scheme 1. Aza-Baylis–Hillman reaction of methyl vinyl ketone with *N*-tosylimines.

2. Results and discussion

The reaction conditions were optimized by the reaction of salicyl *N*-tosylimine **1a** (1.0 equiv) with methyl vinyl ketone **2a** (2.0 equiv) as a model and the results are summarized in Table 1. Different catalysts were screened using THF as the solvent (Table 1, entries 1–8). Under the catalysis of DABCO, the reaction yielded the aza-Baylis–Hillman adduct **3a** in 68% yield along with the cyclized chromane product **4a** in 20% yield as a mixture of *syn*- and *anti*-isomers (Table 1, entry 1). Using PPh_3 as the catalyst resulted in the chromane product **4a** exclusively in 83% yield as a mixture of *syn*- and *anti*-isomers (Table 1, entry 2).[11] The configuration of the major isomer of **4a** was confirmed by an X-ray diffraction (Fig. 1).[12] Other catalysts, such as DBU,

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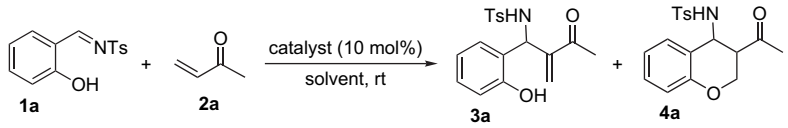
Table 1. Aza-Baylis–Hillman reaction of salicyl *N*-tosylimine **1a** (1.0 equiv) with methyl vinyl ketone **2a** (2.0 equiv) in the presence of various catalysts and solvents



Entry	Catalyst	Solvent	Time (h)	Yield[a] (%)	
				3a	**4a** (*anti*/*syn*)[b]
1	DABCO	THF	4	68	20 (3/1)
2	PPh_3	THF	6	0	83 (3/1)
3	DBU	THF	45	Trace	Trace
4	PMe_3	THF	120	Trace	13 (2/1)
5	$PPhMe_2$	THF	120	Trace	13 (2/1)
6	PPh_2Me	THF	106	Trace	33 (2/1)
7	PBu_3	THF	96	Trace	13 (2/1)
8	DMAP	THF	20	Trace	49 (4/1)
9	DABCO	CH_2Cl_2	7	10	32 (1.3/1)
10	DABCO	PhMe	6	Trace	83 (*anti*)
11	DABCO	DMF	20	Trace	64 (1/1)
12	DABCO	DMSO	23	24	44 (1/1)
13	DABCO	CH_3CN	29	Trace	13 (3/1)
14[c]	DABCO	THF	4	89	0
15	PPh_3	CH_2Cl_2	16	0	51 (3/1)
16	PPh_3	PhMe	20	0	80 (7/1)
17	PPh_3	DMF	20	0	72 (2/1)
18	PPh_3	DMSO	23	0	30 (9/1)
19	PPh_3	CH_3CN	48	0	26 (3/1)

[a] Isolated yields.
[b] The ratio of *anti*/*syn* was determined by ^1H NMR.
[c] Amount used: 1.5 equiv of methyl vinyl ketone.

DMAP, PBu_3, PMe_3, PPh_2Me, or $PPhMe_2$ were all less effective than DABCO or PPh_3 (Table 1, entries 3–8). Then, various solvents were also examined using DABCO or PPh_3 as the catalyst, respectively. It was found that the solvent affected the product distribution significantly under the catalysis of DABCO. PhMe favored the formation of chromane product **4a** and THF favored the formation of aza-Baylis–Hillman adduct **3a** (Table 1, entries 1 and 10). It should be noted that using DABCO as the catalyst in PhMe, chromane product **4a** was obtained as the *anti*-isomer stereoselectively (Table 1, entry 10). If the amount of methyl vinyl ketone was reduced to 1.5 equiv, aza-Baylis–Hillman product **3a** was obtained exclusively (Table 1, entry 14).

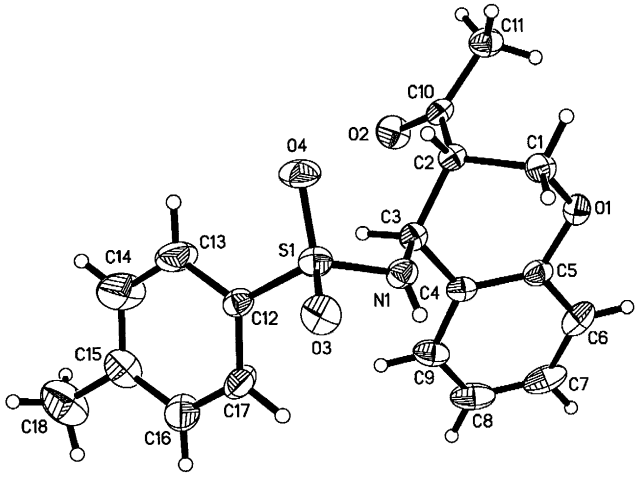


Figure 1. ORTEP diagram of **4a**.

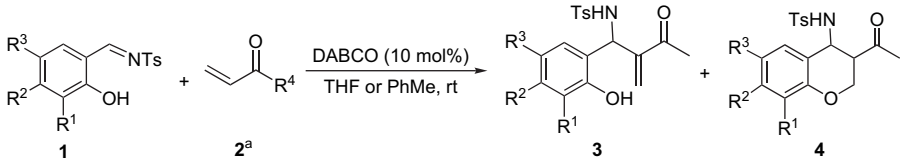
While under the catalysis of PPh_3, the solvent effect was not so obvious and chromane product **4a** was always obtained exclusively as a mixture of *syn*- and *anti*-isomers (Table 1, entries 15–19). Of the solvents examined for PPh_3, THF was the best one considering the yield of **4a** (Table 1, entry 2).

According to the above results, we decided to examine the substrate scope under three different reaction conditions: (a) using DABCO as the catalyst and THF as the solvent, 1.5 equiv of methyl vinyl ketone as the substrate; (b) using DABCO as the catalyst and PhMe as the solvent, 2.0 equiv of methyl vinyl ketone as the substrate; (c) using PPh_3 as the catalyst and PhMe as the solvent, 2.0 equiv of methyl vinyl ketone as the substrate.

Under the catalysis of DABCO, several other salicyl *N*-tosylimines could also react with methyl vinyl ketone at room temperature in THF or PhMe and the results are summarized in Table 2.

For the imines with electron-donating groups on the aromatic rings, prolonged reaction time was required (Table 2, entries 1–8). For 3-methoxy salicyl *N*-tosylimine **1b**, aza-Baylis–Hillman adduct **3b** was obtained as the major product either in THF or in PhMe, possibly due to the hydrogen bonding between the methoxy group and phenol group, which made the proton in the phenol group leave more difficultly (Table 2, entries 1 and 2). For the imines with electron-withdrawing groups on the aromatic rings, the reaction could be completed within 12 h to give the chromane product either in THF or in PhMe as a mixture of *syn*- and *anti*-isomers (Table 2, entries 9–14). For the aza-Baylis–

Table 2. Aza-Baylis–Hillman reaction of salicyl *N*-tosylimines with vinyl ketones in the presence of DABCO at room temperature



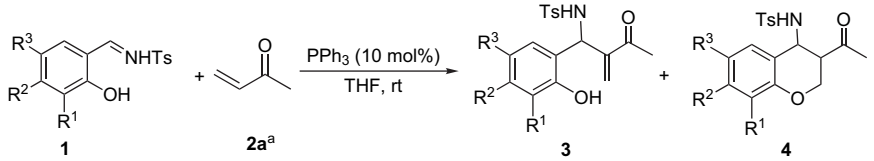
Entry	R^1	R^2	R^3		R^4	Solvent	Time (h)	Yield[b] (%)			
								3		**4** (*anti*/*syn*)[c]	
1	OMe	H	H	**1b**	Me	THF	18	**3b**:	56	**4b**:	0
2	—	—	—		—	PhMe	18		56		11 (4/1)
3	H	OMe	H	**1c**	Me	THF	20	**3c**:	Trace	**4c**:	42 (4/1)
4	—	—	—		—	PhMe	12		0		54 (4/1)
5	H	H	OMe	**1d**	Me	THF	12	**3d**:	50	**4d**:	48 (2/1)
6	—	—	—		—	PhMe	12		0		94 (4/1)
7	H	H	Me	**1e**	Me	THF	12	**3e**:	84	**4e**:	4 (2/1)
8	—	—	—		—	PhMe	12		Trace		69 (3/1)
9	H	H	Br	**1f**	Me	THF	12	**3f**:	Trace	**4f**:	49 (3/1)
10	—	—	—		—	PhMe	12		0		78 (3/1)
11	Cl	H	Cl	**1g**	Me	THF	12	**3g**:	0	**4g**:	26 (1/1)
12	—	—	—		—	PhMe	12		0		99 (2/1)
13	H	H	Cl	**1h**	Me	THF	12	**3h**:	Trace	**4h**:	99 (3/1)
14	—	—	—		—	PhMe	12		0		92 (3/1)
15	H	H	H	**1a**	Et	THF	12	**3i**:	63	**4i**:	0
16	—	—	—		—	PhMe	24		0		67 (8/3)
17	OMe	H	H	**1c**	Et	THF	36	**3j**:	48	**4j**:	0
18	—	—	—		—	PhMe	36		32		32 (2/1)
19	H	H	OMe	**1d**	Et	THF	20	**3k**:	56	**4k**:	Trace
20	—	—	—		—	PhMe	20		Trace		62 (2/1)
21	H	H	Br	**1f**	Et	THF	12	**3l**:	19	**4l**:	80 (3/1)
22	—	—	—		—	PhMe	12		Trace		79 (5/2)
23	H	H	H	**1a**	Ph	THF	48	**3m**:	63	**4m**:	0
24	—	—	—		—	PhMe	48		0		67 (8/3)

[a] Amount used: 1.5 equiv of **2** in THF or 2 equiv of **2** in PhMe.
[b] Isolated yields.
[c] The ratio of *anti*/*syn* was determined by ^{1}H NMR.

Hillman reaction of ethyl vinyl ketone or phenyl vinyl ketone with salicyl *N*-tosylimines, similar results were obtained (Table 2, entries 15–22).

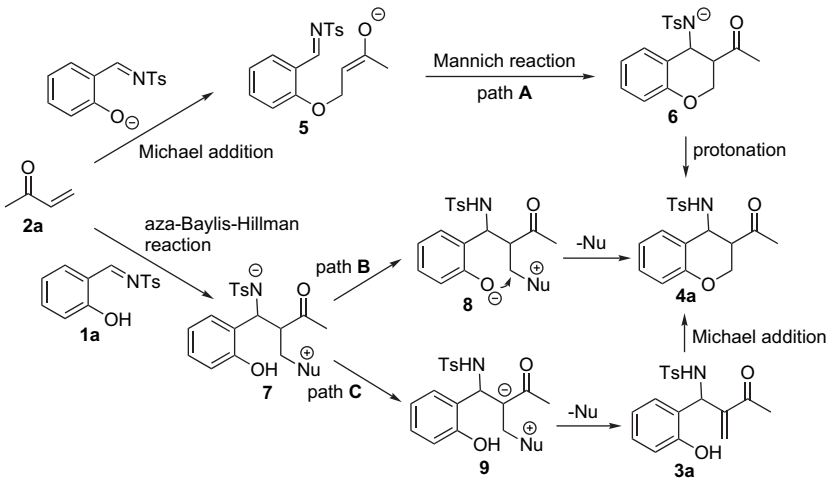
Using PPh_3 as the catalyst, it was found that other salicyl *N*-tosylimines also reacted with methyl vinyl ketone in THF to give the corresponding chromanes **4** as the major products and the results are summarized in Table 3. The reaction required relatively longer time than those catalyzed by DABCO, compared with the results in Table 2. Unlike unsubstituted salicyl *N*-tosylimine **1a** (Table 1, entry 2), several substituted salicyl *N*-tosylimines yielded mixtures of aza-Baylis–Hillman adducts **3** and chromane products **4** (Table 3, entries 1, 2, and 5) and only 5-methyl or 5-bromo salicyl *N*-tosylimines gave chromane products **4** exclusively (Table 3, entries 3 and 4). In toluene, similar results were obtained.

Table 3. Aza-Baylis–Hillman reaction of salicyl *N*-tosylimines with methyl vinyl ketone in the presence of PPh_3 at room temperature



Entry	R^1	R^2	R^3		Time (h)	Yield[b] (%)	
						3	**4** (*anti*/*syn*)[c]
1	OMe	H	H	**1b**	240	**3b**: 18	**4b**: 52 (6/1)
2	H	H	OMe	**1d**	24	**3d**: 48	**4d**: 41 (3/2)
3	H	H	Me	**1e**	18	**3e**: 0	**4e**: 82 (2/1)
4	H	H	Br	**1f**	18	**3f**: 0	**4f**: 67 (2/1)
5	H	H	Cl	**1h**	18	**3h**: 35	**4h**: 64 (2/1)

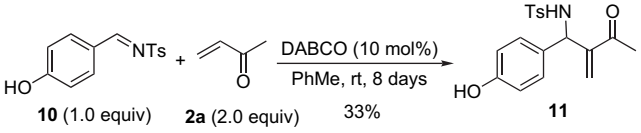
[a] Amount used: 2.0 equiv of **2a**.
[b] Isolated yields.
[c] The ratio of *anti*/*syn* was determined by ^{1}H NMR.



Scheme 2. Plausible reaction pathways for the formation of chromane product **4a**.

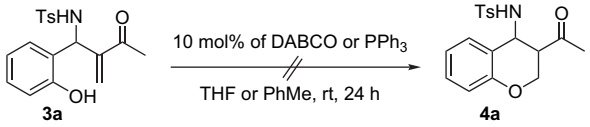
Considering the mechanism for the formation of chromane product **4a**, there might be three different pathways as shown in Scheme 2 based on the earlier reports.[9,10] Path **A** started with Michael addition of the phenolic anion group in the imine to **2a**, then intramolecular Mannich reaction and protonation gave product **4a**. Path **B** started with the aza-Baylis–Hillman reaction to form intermediate **7**, then the nitrogen anion abstracted a proton from the phenolic group in intermediate **7** to give intermediate **8** and subsequent cyclization yielded product **4a**. Path **C** also started with the aza-Baylis–Hillman reaction, but unlike path **B**, the nitrogen anion abstracted a proton from the α-position of the carbonyl group rather than from the phenolic group in intermediate **7** to give intermediate **9**. Subsequent elimination of the catalyst gave the aza-Baylis–Hillman product **3a** and then intramolecular Michael addition occurred to give product **4a**.

In order to clarify which pathway the reaction followed, some control experiments were performed. First we used *N*-tosylimine of 4-hydroxybenzaldehyde instead of salicyl *N*-tosylimine to react with methyl vinyl ketone to examine whether Michael addition was competitive with the aza-Baylis–Hillman reaction (Scheme 3). After 8 days, aza-Baylis–Hillman product **10** was obtained in 33% yield and no Michael addition product was formed. Thus, path **A** was less probable.



Scheme 3. The reaction of *N*-tosylimine of 4-hydroxybenzaldehyde with methyl vinyl ketone under the catalysis of DABCO.

Next we also tested whether the aza-Baylis–Hillman product **3a** could be cyclized under the reaction conditions. To the THF or PhMe solution of **3a** was added 10 mol % of PPh_3 or DABCO and after 24 h, no cyclized product **4a** was detected by TLC (Scheme 4). Thus, path **C** was also less probable and the chromane product **4a** was most likely to be obtained from path **B**.



Scheme 4. The attempted cyclization of aza-Baylis–Hillman product **3a**.

Why THF favored the formation of aza-Baylis–Hillman product **3a** and PhMe favored the formation of chromane product **4a** is explained as follows: there might be a hydrogen bonding between THF and the phenolic group in intermediate **7** (Scheme 2), which made the phenolic group relatively more difficult to be deprotonated. Therefore, the nitrogen anion abstracted a proton from the α-position of the carbonyl group and aza-Baylis–Hillman product **3a** was obtained. In PhMe, there was no similar hydrogen bonding and the phenolic group in intermediate **7** was more easily to be deprotonated to give chromane **4a** as the major product. For the imines with the substituents (Cl, Br or 4-OMe) that could stabilize the phenolic anion in intermediate **8**, the reaction was prone to follow path **B** to give chromane **4** as the major products (Table 2, entries 3, 4, and 9–14). At the present stage, the reason for different catalytic activities using PPh_3 and DABCO has not been understood clearly yet.

3. Conclusions

We have studied the aza-Baylis–Hillman reaction of salicyl *N*-tosylimines with methyl vinyl ketone, ethyl vinyl ketone or phenyl vinyl ketone. These reaction conditions have been optimized by verifying the catalysts and solvents. Using DABCO as the catalyst, the reaction mostly gave chromanes as the major products in PhMe and aza-Baylis–Hillman products as the major products in THF. A plausible mechanism for the formation of the chromane products was proposed based on some controlled experiments. Further transformation 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 300–400 mesh silica gel at increased pressure. Salicyl *N*-tosylimines were prepared according to the literature.[13]

4.2. Typical procedure for the synthesis of aza-Baylis–Hillman product 3a

To a Schlenk tube with salicyl *N*-tosylimine (69 mg, 0.25 mmol) and DABCO (2.8 mg, 0.025 mmol) were added THF (1.0 mL) and methyl vinyl ketone (31 μL, 0.38 mmol). The solution was stirred at room temperature for 4 h. Then the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to give **3a** (eluant: EtOAc/petroleum=1/1, 78 mg, yield 89%) as a white solid.

4.2.1. *N*-(3-Acetyl-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 3a. A white solid: mp 158–160 °C; IR (KBr) *ν* 3411, 3161, 1688, 1599, 1454, 1322, 1152 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.25 (3H, s, Me), 2.38 (3H, s, Me), 5.49 (1H, d, *J*=7.3 Hz, CH), 5.70 (1H, d, *J*=7.3 Hz, NH), 6.17 (1H, s, =CH), 6.22 (1H, s, =CH), 6.66 (1H, s, OH), 6.72–6.79 (2H, m, Ar), 6.94 (1H, d, *J*=7.2 Hz, Ar), 7.08 (1H, t, *J*=7.2 Hz, Ar), 7.18 (2H, d, *J*=8.3 Hz, Ar), 7.61 (2H, d, *J*=8.3 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) *δ* 21.5, 26.2, 53.4, 117.0, 120.7, 124.8, 127.1, 128.0, 128.1, 129.1, 129.4, 136.4, 143.5, 146.4, 153.1, 200.0. MS (EI) *m/e* 190 (M^+−155, 64.2), 148 (M^+−167, 62.7), 131 (M^+−214, 76.7), 91 (M^+−254, 100.0), 65 (M^+−280, 45.4), 43 (M^+−302, 93.2). HRMS (MALDI) calcd for $C_{18}H_{19}NO_4SNa^+$: 368.0927, found: 368.0934.

4.2.2. *N*-(1-(2-Hydroxy-3-methoxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 3b. A yellow solid: mp 107–110 °C; IR (KBr) *ν* 3306, 2925, 1673, 1596, 1481, 1442, 1333, 1273, 1223, 1159, 1055 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.20 (3H, s, Me), 2.35 (3H, s, Me), 3.81(3H, s, OMe), 5.58 (1H, d, *J*=9.6 Hz, CH), 5.79 (1H, s, OH), 5.99 (1H, d, *J*=9.6 Hz, NH), 6.09 (1H, s, =CH), 6.18 (1H, s, =CH), 6.64–6.66 (2H, m, Ar), 6.70–6.72 (1H, m, Ar), 7.12 (2H, d, *J*=8.0 Hz, Ar), 7.60 (2H, d, *J*=8.0 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) *δ* 21.4, 26.3, 54.0, 56.0, 109.7, 119.6, 121.1, 124.0, 127.1, 127.2, 127.2, 129.1, 137.3, 142.5, 142.9, 146.2, 198.6. MS (EI) *m/e* 375 (M^+, 0.6), 204 (M^+−171, 66.5), 161 (M^+−214, 100.0). HRMS (MALDI) calcd for $C_{19}H_{21}NO_5SNa^+$: 398.1032, found: 398.1024.

4.2.3. *N*-(1-(2-Hydroxy-4-methoxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 3c. A yellow solid; mp: 110–112 °C; IR (KBr) *ν* 2923, 2839, 1920, 1703, 1674, 1618, 1519, 1444, 1320, 1160, cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.22 (3H, s, Me), 2.37 (3H, s, Me), 3.67 (3H, s, Me), 5.45 (1H, d, *J*=7.8 Hz, CH), 5.99 (1H, d, *J*=7.8 Hz, NH), 6.12 (1H, s, =CH), 6.17 (1H, s, =CH), 6.22–6.25 (2H, m, Ar), 6.82 (1H, d, *J*=9.3 Hz, Ar), 7.16 (2H, d, *J*=8.1 Hz, Ar), 7.27 (1H, s, OH), 7.59 (2H, d, *J*=8.1 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) *δ* 21.4, 26.2, 53.1, 55.2, 102.5, 106.5, 117.2, 127.1, 127.7, 128.8, 129.4, 136. 4, 143.4, 146.6, 154.3, 160.2, 200.0. MS (MALDI) *m/e* 398 (M^++23, 100.0). HRMS (MALDI) calcd for $C_{19}H_{21}NO_5SNa^+$: 398.1032, found: 398.1030.

4.2.4. *N*-(1-(2-Hydroxy-5-methoxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 3d. A white solid: mp 107–110 °C; IR (KBr) *ν* 3306, 1676, 1596, 1481, 1442, 1335, 1274, 1222, 1160, 1055 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.20 (3H, s, Me), 2.34 (3H, s, Me), 3.81 (3H, s, Me), 5.57 (1H, d, *J*=9.7 Hz, CH), 5.82 (1H, s, OH), 6.01 (1H, d, *J*=9.7 Hz, NH), 6.09 (1H, s, =CH), 6.17 (1H, s, =CH), 6.64–6.73 (3H, m, Ar), 7.12 (2H, d, *J*=8.1 Hz, Ar), 7.60 (2H, d, *J*=8.1 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) *δ* 21.4, 26.3, 54.0, 55.9, 109.7, 119.5, 121.1, 124.0, 127.1, 127.2, 129.1, 137.3, 142.5, 142.8, 146.2, 146.2, 198.6. MS (EI) *m/e* 204 (M^+−171, 54.4), 161 (M^+−214, 100.0), 91 (M^+−284, 26.9), 43 (M^+−332, 44.5). HRMS (EI) calcd for $C_{19}H_{21}NO_5S$: 375.1140, found: 375.1131.

4.2.5. *N*-[2-Acetyl-1-(2-hydroxy-5-methylphenyl)-allyl]-4-methylbenzenesulfonamide 3e. A white solid: mp 148–150 °C; IR (KBr) *ν* 3400, 3300, 2924, 2860, 1919, 1678, 1598, 1511, 1431, 1334, 1165, 1057 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.07 (3H, s, Me), 2.20 (3H, s, Me), 2.33 (3H, s, Me), 5.50 (1H, d, *J*=9.0 Hz, CH), 6.11 (1H, s, =CH), 6.19 (1H, s, =CH), 6.28 (1H, d, *J*=9.0 Hz, NH), 6.57 (1H, d, *J*=8.1 Hz, Ar), 6.69 (1H, d, *J*=2.0 Hz, Ar), 6.76 (1H, dd, *J*=2.0, 8.1 Hz, Ar), 7.06 (1H, s, OH), 7.10 (2H, d, *J*=8.7 Hz, Ar), 7.62 (2H, d, *J*=8.7 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) *δ* 20.2, 21.3, 26.1, 53.4, 116.4, 124.1, 126.1, 127.0, 127.7, 128.9, 129.2, 129.5, 136.5, 143.2, 146.5, 150.9, 199.8. MS (MALDI) *m/e* 382 (M^++23, 100.0). HRMS (MALDI) calcd for $C_{19}H_{21}NO_4SNa^+$: 382.1083, found: 382.1098.

4.2.6. *N*-(1-(5-Bromo-2-hydroxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 3f. A white solid: mp 124–126 °C; IR (KBr) *ν* 3309, 2922, 1916, 1673, 1598, 1494, 1328, 1159 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) *δ* 2.17 (3H, s, Me), 2.30 (3H, s, Me), 5.40 (1H, d, *J*=9.0 Hz, CH), 6.01 (1H, d, *J*=9.0 Hz, NH), 6.10 (1H, s, =CH), 6.13 (1H, s, =CH), 6.52 (1H, d, *J*=8.4 Hz, Ar), 6.89 (1H, d, *J*=1.8 Hz, Ar), 7.02 (1H, dd, *J*=1.8, 8.4 Hz, Ar), 7.07 (1H, s, OH), 7.13 (2H, d, *J*=7.2 Hz, Ar), 7.71 (2H, d, *J*=7.2 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) *δ* 21.5, 26.2, 53.2, 112.6, 118.6, 126.6, 127.0, 128.5, 129.5, 131.0, 131.6, 136.1, 143.8, 145.8, 152.4, 199.8. MS (MALDI)

m/e 446 (M^++23), 448 (M^++25, 100.0). HRMS (MALDI) calcd for $C_{18}H_{18}NO_4SBrNa^+$: 446.0031, found: 446.0032.

4.2.7. *N*-(1-(3,5-Dichloro-2-hydroxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 3g. A white solid: mp 109–110 °C; IR (KBr) ν 3273, 2924, 2853, 2101, 1712, 1674, 1598, 1557, 1495, 1332, 1161, 1093, 1068 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.23 (3H, s, Me), 2.36 (3H, s, Me), 5.52 (1H, d, *J*=9.6 Hz, CH), 6.11 (1H, d, *J*=9.6 Hz, NH), 6.15 (1H, s, =CH), 6.16 (1H, s, =CH), 6.20 (1H, s, OH), 6.94 (1H, d, *J*=2.4 Hz, Ar), 7.09 (1H, d, *J*=2.4 Hz, Ar), 7.15 (2H, d, *J*=8.4 Hz, Ar), 7.58 (2H, d, *J*=8.4 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.3, 26.0, 63.8, 120.8, 125.2, 126.8, 127.1, 127.5, 127.7, 128.4, 129.1, 136.6, 143.4, 145.0, 146.9, 197.0. MS (EI) *m/e* 201 (M^+−212, 21.2), 199 (M^+−214, 35.5), 171 (M^+−242, 25.0), 155 (M^+−258, 28.9), 91 (M^+−322, 100.0), 43 (M^+−370, 86.7). HRMS (EI) calcd for $C_{18}H_{17}Cl_2NO_4S$: 413.0255, found: 413.0258.

4.2.8. *N*-(1-(5-Chloro-2-hydroxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 3h. A white solid: mp 124–126 °C; IR (KBr) ν 3281, 2923, 1709, 1486, 1332, 1161, 1093 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.26 (3H, s, Me), 2.38 (3H, s, Me), 5.44 (1H, d, *J*=8.4 Hz, CH), 5.85 (1H, d, *J*=8.4 Hz, NH), 6.19 (1H, s, =CH), 6.20 (1H, s, =CH), 6.66 (1H, d, *J*=8.1 Hz, Ar), 6.83 (1H, d, *J*=2.4 Hz, Ar), 6.97 (1H, dd, *J*=2.4, 8.1 Hz, Ar), 6.99 (1H, s, OH), 7.18 (2H, d, *J*=8.1 Hz, Ar), 7.59 (2H, d, *J*=8.1 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.5, 26.2, 53.2, 118.5, 125.5, 126.4, 127.1, 127.8, 128.6, 128.9, 129.5, 136.2, 143.8, 145.9, 151.9, 199.9. MS (MALDI) *m/e* 402 (M^++23, 100.0). HRMS (MALDI) calcd for $C_{18}H_{18}NO_4SClNa^+$: 402.0533, found: 402.0537.

4.2.9. *N*-(1-(2-Hydroxyphenyl)-2-methylene-3-oxopentyl)-4-methylbenzenesulfonamide 3i. A white solid: mp 185–186 °C; IR (KBr) ν 3301, 2979, 2939, 2879, 1919, 1676, 1598, 1458, 1414, 1332, 1158, 1093, 950 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.98 (3H, t, *J*=7.2 Hz, Me), 2.36 (3H, s, Me), 2.49–2.72 (2H, m, CH_2), 5.51 (1H, d, *J*=8.3 Hz, CH), 5.90 (1H, d, *J*=8.3 Hz, NH), 6.15 (1H, s, =CH_2), 6.17 (1H, s, =CH_2), 6.71–6.76 (2H, m, Ar), 6.87 (1H, s, OH), 6.94 (1H, dd, *J*=8.1, 1.5 Hz, Ar), 7.02–7.09 (1H, m, Ar), 7.16 (2H, d, *J*=8.7 Hz, Ar), 7.60 (2H, d, *J*=8.7 Hz, Ar); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 7.9, 21.4, 31.1, 55.5, 112.9, 114.4, 117.9, 125.8, 126.3, 127.0, 129.3, 129.6, 136.5, 143.4, 146.9, 153.4, 202.5; MS (EI) *m/e* 204 (M^+−155, 42.8), 148 (M^+−211, 66.0), 146 (M^+−213, 20.0), 131 (M^+−228, 43.4), 91 (M^+−268, 100.0), 65 (M^+−294, 30.2), 57 (M^+−302, 81.2), 55 (M^+−304, 16.3). Anal. Calcd for $C_{19}H_{21}NO_4S$ requires: C, 63.49; H, 5.89; N, 3.90%. Found: C, 63.53; H, 5.89; N, 3.74%.

4.2.10. *N*-(1-(2-Hydroxy-3-methoxyphenyl)-2-methylene-3-oxopentyl)-4-methylbenzenesulfonamide 3j. A colorless solid: mp 144–146 °C; IR (KBr) ν 3355, 3268, 2977, 2939, 2843, 1918, 1679, 1597, 1482, 1443, 1158, 1093, 955, 904, 815, 670 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.87 (3H, t, *J*=7.4 Hz, Me), 2.51 (3H, s, Me), 2.33–2.56 (2H, m, CH_2), 3.70 (3H, s, OCH_3), 5.53 (1H, d, *J*=9.6 Hz, CH), 5.85 (1H, s, OH), 5.98 (1H, s, =CH_2), 6.02 (1H, s, =CH_2), 6.06 (1H, d, *J*=9.6 Hz, NH), 6.54–6.64 (3H, m, Ar), 7.02 (2H, d, *J*=8.3 Hz, Ar), 7.51 (2H, d, *J*=8.3 Hz, Ar); ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 7.8, 21.3, 31.2, 54.1, 55.9, 109.6, 119.4, 120.9, 124.0, 125.6, 127.0, 129.0, 137.2, 142.4, 142.8, 145.7, 146.2, 201.3; MS (EI) *m/e* 171 (M^+−218, 17.3), 155 (M^+−234, 20.9), 108 (M^+−281, 13.1), 107 (M^+−282, 25.7), 91 (M^+−298, 100.0), 89 (M^+−300, 11.2), 65 (M^+−324, 34.4), 63 (M^+−326, 12.4). Anal. Calcd for $C_{20}H_{23}NO_5S$ requires: C, 61.68; H, 5.95; N, 3.60%. Found: C, 61.46; H, 5.65; N, 3.22%.

4.2.11. *N*-(1-(2-Hydroxy-5-methoxyphenyl)-2-methylene-3-oxopentyl)-4-methylbenzenesulfonamide 3k. A colorless solid: mp 166–168 °C; IR (KBr) ν 3357, 3272, 2977, 2986, 2785, 1901, 1711, 1597, 1482, 1443, 1158, 1093 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 1.00 (3H, t, *J*=7.5 Hz, Me), 2.37 (3H, s, Me), 2.50–2.74 (2H, m, CH_2), 3.65 (1H, s, OCH_3), 5.47 (1H, d, *J*=8.4 Hz, CH), 5.79 (1H, d, *J*=8.4 Hz, NH), 6.17 (1H, s, =CH_2), 6.20 (1H, s, =CH_2), 6.45 (1H, d, *J*=2.7 Hz, Ar), 6.49 (1H, s, OH), 6.01 (1H, dd, *J*=8.7, 2.6 Hz, Ar), 6.68 (1H, d, *J*=8.7 Hz, Ar), 7.16 (2H, d, *J*=8.2 Hz, Ar), 7.60 (2H, d, *J*=8.2 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 7.9, 21.4, 31.1, 53.2, 55.5, 112.9, 114.0, 117.9, 125.8, 126.3, 127.0, 129.3, 129.6, 136.5, 143.4, 146.9, 153.3, 202.5; MS (EI) *m/e* 218 (M^+−171, 57.74), 203 (M^+−186, 25.7), 189 (M^+−200, 31.1), 178 (M^+−211, 19.1), 161 (M^+−228, 69.8), 91 (M^+−298, 100.0), 65 (M^+−324, 44.3), 57 (M^+−332, 60.8). Anal. Calcd for $C_{20}H_{23}NO_5S$ requires: C, 61.68; H, 5.95; N, 3.60%. Found: C, 61.60; H, 5.79; N, 3.18%.

4.2.12. *N*-(1-(5-Bromo-2-hydroxyphenyl)-2-methylene-3-oxopentyl)-4-methylbenzenesulfonamide 3l. A colorless solid: mp 290–292 °C; IR (KBr) ν 3277, 2983, 1938, 1676, 1598, 1493, 1416, 1331, 1159, 1093, 813, 670 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 0.91 (3H, t, *J*=7.2 Hz, Me), 2.92 (3H, s, Me), 2.44–2.61 (2H, m, CH_2), 5.40 (1H, d, *J*=9.3 Hz, CH), 6.03 (1H, d, *J*=9.3 Hz, NH), 6.06 (1H, s, =CH_2), 6.08 (1H, s, =CH_2), 6.52 (1H, d, *J*=8.4 Hz, Ar), 6.88 (1H, s, OH), 6.99 (1H, dd, *J*=8.4, 1.8 Hz, Ar), 7.08 (2H, d, *J*=7.8 Hz, Ar), 7.15–7.24 (1H, m, Ar), 7.49 (2H, d, *J*=7.8 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 7.8, 21.44, 31.1, 53.2, 112.5, 118.6, 126.3, 126.7, 127.0, 129.4, 129.6, 131.5, 136.1, 143.7, 145.4, 152.3, 202.4; MS (EI) *m/e* 209 (M^+−228, 15.9), 171 (M^+−266, 16.6), 155 (M^+−282, 18.3), 91 (M^+−346, 100.0), 65 (M^+−372, 28.0), 63 (M^+−374, 15.3), 57 (M^+−380, 52.3), 51 (M^+−386, 15.5). Anal. Calcd for $C_{19}H_{20}BrNO_4S$ requires: C, 52.06; H, 4.60; N, 3.20%. Found: C, 51.73; H, 4.61; N, 3.07%.

4.2.13. *N*-(2-Benzoyl-1-(2-hydroxyphenyl)allyl)-4-methylbenzenesulfonamide 3m. White solid; mp 174–176 °C; IR (KBr) ν 3273, 3064, 2922, 2850, 1658, 1597, 1449, 1332, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.27 (3H, s, Me), 5.64 (1H, s, =CH), 5.70 (1H, d, *J*=8.7 Hz, CH), 6.08 (1H, s, =CH), 6.57 (1H, d, *J*=8.7 Hz, NH), 6.60 (1H, t, *J*=7.5 Hz, Ar), 6.69 (1H, d, *J*=7.5 Hz, Ar), 6.92–6.99 (2H, m, Ar), 7.05 (2H, d, *J*=8.4 Hz, Ar), 7.21–7.26 (1H, m, Ar), 7.44–7.49 (2H, m, Ar), 7.57–7.62 (4H, m, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.3, 55.4, 116.3, 120.3, 124.0, 126.2, 126.9, 128.1, 129.3, 129.5, 129.6, 132.8, 136.8, 139.0, 143.2,

143.3, 145.7, 153.3, 197.5. MS (EI) *m/e* 77 (M^+-330, 26.2), 91 (M^+-316, 39.1), 105 (M^+-302, 46.4), 131 (M^+-276, 58.6), 155 (M^+-252, 26.1), 171 (M^+-236, 29.1), 236 (M^+-171, 100.0), 252 (M^+-155, 23.8). HRMS (EI) calcd for $C_{23}H_{21}NO_4S$: 407.1191, found: 407.1191.

4.3. Typical procedure for the synthesis of chromane product 4a

To a Schlenk tube with salicyl *N*-tosylimine (69 mg, 0.25 mmol) and DABCO (2.8 mg, 0.025 mmol) were added THF (1.0 mL) and methyl vinyl ketone (41 μL, 0.5 mmol). The solution was stirred at room temperature for 6 h. Then the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to give **4a** (eluant: EtOAc/petroleum=1/4, 72 mg, yield 83%) as a white solid.

4.3.1. *N*-(1-(2-Hydroxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 4a. A white solid: mp 182–184 °C; IR (KBr) ν 3290, 2932, 1711, 1582, 1488, 1456, 1222, 1157 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) Major isomer: δ 2.25 (3H, s, Me), 2.49 (3H, s, Me), 3.26 (1H, q, *J*=2.6 Hz, CH), 4.33 (1H, dd, *J*=2.6, 12.0 Hz, CH), 4.63 (1H, dd, *J*=2.6, 12.0 Hz, CH), 4.65 (1H, d, *J*=5.1 Hz, CH), 4.74 (1H, d, *J*=5.1 Hz, NH), 6.49 (1H, d, *J*=7.5 Hz, Ar), 6.72–6.78 (2H, m, Ar), 7.10 (1H, t, *J*=7.8 Hz, Ar), 7.40 (2H, d, *J*=8.3 Hz, Ar), 7.82 (2H, d, *J*=8.3 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.6, 28.2, 47.7, 52.9, 62.8, 117.2, 119.6, 121.6, 127.3, 129.4, 129.6, 130.0, 136.4, 144.1, 154.1, 205.6 (major isomer). MS (EI) *m/e* 190 (M^+-155, 76.3), 148 (M^+-167, 100.0), 131 (M^+-214, 38.5), 91 (M^+-254, 75.9), 65 (M^+-280, 37.8), 43 (M^+-302, 88.0). Anal. Calcd for $C_{18}H_{19}NO_4S$ requires: C, 62.59; H, 5.54; N, 4.06%. Found: C, 62.45; H, 5.47; N, 3.89%.

4.3.2. *N*-(3-Acetyl-8-methoxy-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4b. A white solid: mp 159–160 °C; IR (KBr) ν 3168, 2926, 1712, 1589, 1488, 1330, 1159, 816 cm^{-1}; *anti*-isomer: ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.28 (3H, s, Me), 2.50 (3H, s, Me), 3.30 (1H, s, CH), 3.81 (3H, s, Me), 4.39 (1H, dd, *J*=12.0, 2.6 Hz, CH), 4.64 (2H, s, CH_2), 4.87 (1H, dd, *J*=12.0, 2.6 Hz, NH), 6.07 (1H, dd, *J*=6.8, 2.6 Hz, Ar), 6.69–6.76 (2H, m, Ar), 7.41 (2H, d, *J*=8.4 Hz, Ar), 7.84 (2H, d, *J*=8.4 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.4, 29.9, 42.7, 47.2, 55.7, 63.2, 110.6, 120.2, 120.8, 121.1, 126.8, 129.6, 136.6, 143.3, 143.9, 147.9, 207.8. MS (EI) *m/e* 204 (M^+-171, 62.9), 171 (M^+-204, 42.3), 161 (M^+-214, 100.0), 91 (M^+-284, 79.5. HRMS (MALDI) calcd for $C_{19}H_{21}NO_5S$: 375.1140, found: 375.1140.

4.3.3. *N*-(3-Acetyl-7-methoxy-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4c. A white solid: mp 163–165 °C; IR (KBr) ν 3280, 2953, 2838, 1712, 1620, 1586, 1505, 1443, 1332, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 2.22 (3H, s, Me), 2.48 (3H, s, Me), 3.17–3.20 (1H, m, CH), 3.69 (3H, s, Me), 4.33 (1H, d, *J*=9.6 Hz, CH), 4.78 (2H, d, *J*=10.5 Hz, CH_2), 5.00 (1H, d, *J*=1.8 Hz, NH), 6.24 (1H, s, Ar), 6.31–6.42 (2H, m, Ar), 7.37 (2H, d, *J*=8.1 Hz, Ar), 7.79 (2H, d, *J*=8.1 Hz, Ar); minor isomer: δ 2.14 (3H, s, Me), 2.43 (3H, s, Me), 2.88–3.01 (1H, m, CH), 3.69 (3H, s, Me), 4.34–4.40 (1H, m, CH), 4.81 (1H, dd, *J*=4.5, 9.6 Hz, CH), 4.90–5.0 (1H, m, CH), 5.65 (1H, d, *J*=9.6 Hz, NH), 6.24–6.42 (2H, m, Ar), 6.82 (1H, d, *J*=8.4 Hz, Ar), 7.31 (2H, d, *J*=8.1 Hz, Ar), 7.74 (2H, d, *J*=8.1 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.5, 28.1, 47.4, 52.8, 55.2, 62.8, 101.2, 109.1, 111.7, 127.2, 129.7, 129.9, 136.5, 144.0, 155.1, 160.5, 205.6 (major isomer). MS (MALDI) *m/e* 398 (M^++23, 100.0). HRMS (MALDI) calcd for $C_{19}H_{21}NO_5SNa^+$: 398.1032, found: 398.1047.

4.3.4. *N*-(3-Acetyl-6-methoxy-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4d. A white solid: mp 174–180 °C; IR (KBr) ν 3326, 2931, 1703, 1596, 1502, 1424, 1329, 1206, 1159, 1047 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 2.27 (3H, s, Me), 2.47 (3H, s, Me), 3.21 (1H, q, *J*=3.0 Hz, CH), 3.50 (3H, s, Me), 4.25 (1H, dd, *J*=3.0, 17.0 Hz, CH), 4.55–4.60 (2H, m, CH_2), 4.65–4.73 (1H, m, CH), 4.80 (1H, d, *J*=9.0 Hz, NH), 5.89 (1H, d, *J*=1.2 Hz, Ar), 6.63–6.67 (2H, m, Ar), 7.41 (2H, d, *J*=8.6 Hz, Ar), 7.85 (2H, d, *J*=8.6 Hz, Ar); minor isomer: δ 2.17 (3H, s, Me), 2.44 (3H, s, Me), 3.04–3.06 (1H, m, CH), 4.24 (1H, dd, *J*=2.7, 12.3 Hz, CH), 4.47 (1H, dd, *J*=4.8, 12.3 Hz, CH), 4.82 (1H, dd, *J*=5.3, 9.9 Hz, CH), 5.72 (1H, d, *J*=9.9 Hz, NH), 6.58 (1H, d, *J*=1.2 Hz, Ar), 6.62–6.63 (2H, m, Ar), 7.25 (2H, d, *J*=8.1 Hz, Ar), 7.80 (2H, d, *J*=8.1 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.5, 28.2, 47.9, 53.3, 55.3, 63.0, 112.1, 117.0, 118.1, 119.8, 127.3, 130.0, 136.6, 144.0, 148.1, 153.9, 206.0 (major isomer). MS (EI) *m/e* 375 (M^+, 14.9), 220 (M^+-155, 66.4), 178 (M^+-197, 100.0), 91 (M^+-284, 38.5). HRMS (EI) calcd for $C_{19}H_{21}NO_5S^{+1}$: 375.1136, found: 375.1140.

4.3.5. *N*-(3-Acetyl-6-methylchroman-4-yl)-4-methyl-benzenesulfonamide 4e. A white solid: mp 171–173 °C; IR (KBr) ν 3263, 2922, 2886, 1619, 1597, 1501, 1421, 1334, 1303, 1227, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 2.04 (3H, s, Me), 2.22 (3H, s, Me), 2.48 (3H, s, Me), 3.15 (1H, q, *J*=2.7 Hz, CH), 4.24 (1H, dd, *J*=2.7, 12 Hz, CH), 4.54 (1H, dd, *J*=2.7, 12 Hz, CH), 4.61 (1H, d, *J*=5.1 Hz, CH), 5.03 (1H, d, *J*=5.1 Hz, NH), 6.14 (1H, d, *J*=2.1 Hz, Ar), 6.68 (1H, d, *J*=8.4 Hz, Ar), 6.84 (1H, dd, *J*=2.1, 8.4 Hz, Ar), 7.38 (2H, d, *J*=8.4 Hz, Ar), 7.80 (2H, d, *J*=8.4 Hz, Ar); minor isomer: δ 2.02 (3H, s, Me), 2.16 (3H, s, Me), 2.44 (3H, s, Me), 2.97–3.02 (1H, m, CH), 4.23–4.27 (1H, m, CH), 4.38 (1H, dd, *J*=4.4, 12.6 Hz, CH), 4.80 (1H, dd, *J*=4.4, 9.6 Hz, CH), 5.72 (1H, d, *J*=9.6 Hz, NH), 6.56 (1H, d, *J*=8.4 Hz, Ar), 6.57 (1H, d, *J*=2.1 Hz, Ar), 6.84 (1H, dd, *J*=2.1, 8.4 Hz, Ar), 7.32 (2H, d, *J*=8.0 Hz, Ar), 7.76 (2H, d, *J*=8.0 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 20.3, 20.4, 21.5, 21.6, 28.2, 28.5, 29.5, 47.6, 49.8, 53.1, 62.8, 65.1, 116.3, 116.9, 119.2, 121.0, 127.1, 127.4, 128.1, 129.5, 129.7, 129.8, 130.0, 130.4, 130.5, 130.8, 136.6, 138.2, 139.0, 144.1, 151.6, 151.9, 205.7, 206.8 (major isomer and minor isomer). MS (MALDI) *m/e* 482 (M^++23, 100.0). HRMS (MALDI) calcd for $C_{19}H_{21}NO_4SNa^+$: 382.1083, found: 382.1098.

4.3.6. *N*-(3-Acetyl-6-bromo-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4f. A colorless solid: mp 168–170 °C; IR (KBr) ν 3254, 2888, 1708, 1598, 1482, 1322, 1221, 1157, 1091 cm^{-1}; ^1H NMR ($CDCl_3$,

TMS, 300 MHz) major isomer: δ 2.27 (3H, s, Me), 2.51 (3H, s, Me), 3.23 (1H, q, J=3.1 Hz, CH), 4.28 (1H, dd, J=3.0, 12.0 Hz, CH), 4.59–4.62 (2H, m, CH), 4.73–4.75 (1H, d, J=3.0 Hz, NH), 6.33 (1H, d, J=2.7 Hz, Ar), 6.62 (1H, d, J=9.0 Hz, Ar), 7.17 (1H, dd, J=2.7, 9.0 Hz, Ar), 7.43 (2H, d, J=8.1 Hz, Ar), 7.80 (2H, d, J=8.1 Hz, Ar); minor isomer: δ 2.20 (3H, s, Me), 2.47 (3H, s, Me), 3.03–3.06 (1H, m, CH), 4.28 (1H, dd, J=3.0, 12.0 Hz, CH), 4.49 (1H, dd, J=12.4, 5.0 Hz, CH), 4.63 (1H, dd, J=12.4, 5.0 Hz, CH), 5.63 (1H, d, J=9.9 Hz, NH), 6.57 (1H, d, J=8.7 Hz, Ar), 6.89 (1H, d, J=2.4 Hz, Ar), 7.15 (1H, dd, J=2.4, 9.0 Hz, Ar), 7.29 (2H, d, J=8.1 Hz, Ar), 7.78 (2H, d, J=8.1 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.6, 21.6, 28.1, 28.5, 47.3, 49.4, 49.4, 52.7, 63.0, 65.1, 113.3, 113.3, 118.4, 119.0, 121.7, 123.4, 126.9, 127.2, 130.0, 130.1, 130.5, 131.9, 132.0, 132.4, 136.4, 144.1, 144.4, 152.9, 153.1, 205.4, 206.4 (major isomer and minor isomer). MS (MALDI) *m/e* 446 (M^++23), 448 (M^++25, 100.0). HRMS (MALDI) calcd for $C_{18}H_{18}NO_4SBrNa^+$: 446.0045, found: 446.0032.

4.3.7. *N*-(3-Acetyl-6,8-dichloro-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4g. A white solid: mp 150–152 °C; IR (KBr) ν 3257, 2878, 1709, 1594, 1568, 1472, 1325, 1156, 1092 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 2.28 (3H, s, Me), 2.51 (3H, s, Me), 3.27 (1H, q, J=9.0 Hz, CH), 4.36 (1H, dd, J=2.7, 15.0 Hz, CH), 4.63 (1H, d, J=4.2 Hz, NH), 4.72–4.77 (2H, m, CH_2), 6.21 (1H, d, J=2.4 Hz, Ar), 7.19 (1H, d, J=2.4 Hz, Ar), 7.43 (2H, d, J=8.1 Hz, Ar), 7.81 (2H, d, J=8.1 Hz, Ar); minor isomer: δ 2.20 (3H, s, Me), 2.46 (3H, s, Me), 3.06 (1H, q, J=9.0 Hz, CH), 4.36 (1H, dd, J=2.7, 15.0 Hz, CH), 4.60–4.62 (1H, m, CH), 4.79–4.81 (1H, m, CH), 5.71 (1H, d, J=10.2 Hz, NH), 6.82 (1H, d, J=2.1 Hz, Ar), 7.17 (1H, d, J=2.1 Hz, Ar), 7.36 (2H, d, J=8.1 Hz, Ar), 7.79 (2H, d, J=8.1 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.6, 21.6, 28.1, 28.5, 47.3, 49.4, 49.4, 52.7, 63.0, 65.1, 113.3, 113.3, 118.4, 119.0, 121.7, 123.4, 126.9, 127.2, 130.0, 130.1, 130.5, 131.9, 132.0, 132.4, 136.4, 144.1, 144.4, 152.9, 153.1, 205.4, 206.4 (major isomer and minor isomer). MS (MALDI) *m/e* 436 (M^++23, 100.0). HRMS (MALDI) calcd for $C_{18}H_{17}NO_4SCl_2Na^+$: 436.0147, found: 436.0145.

4.3.8. *N*-(3-Acetyl-6-chloro-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4h. A colorless solid: mp 164–166 °C; IR (KBr) ν 3280, 1712, 1597, 1485, 1334, 1239, 1160, 1093 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 2.22 (3H, s, Me), 2.49 (3H, s, Me), 3.17 (1H, q, J=3.1 Hz, CH), 4.25 (1H, dd, J=3.1, 12.0 Hz, CH), 4.56 (1H, dd, J=3.1, 12.0 Hz, CH), 4.57–4.61 (1H, m, CH), 5.25 (1H, d, J=6.8 Hz, NH), 6.30 (1H, d, J=2.4 Hz, Ar), 6.62 (1H, d, J=8.7 Hz, Ar), 7.00 (1H, dd, J=2.4, 8.7 Hz, Ar), 7.40 (2H, d, J=8.1 Hz, Ar), 7.78 (2H, d, J=8.1 Hz, Ar); minor isomer: δ 2.17 (3H, s, Me), 2.45 (3H, s, Me), 3.01–3.05 (1H, m, CH), 4.24–4.29 (1H, m, CH), 4.44 (1H, dd, J=5.7, 11.7 Hz, CH), 4.77 (1H, dd, J=4.8, 9.9 Hz, CH), 5.84 (1H, d, J=9.9 Hz, NH), 6.60 (1H, d, J=8.7 Hz, Ar), 6.70 (1H, d, J=2.4 Hz, Ar), 7.00 (1H, dd, J=2.4, 8.7 Hz, Ar), 7.34 (2H, d, J=8.4 Hz, Ar), 7.74 (2H, d, J=8.4 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.5, 21.56, 3.11, 28.4, 47.4, 49.3, 49.5, 52.7, 63.0, 65.2, 118.0, 118.6, 121.2, 122.9, 125.95, 126.0, 126.9, 127.2, 127.6, 129.0, 129.1, 129.5, 130.0, 130.1, 136.4, 137.8, 144.1, 144.4, 152.4, 152.6, 205.5, 206.6 (major isomer and minor isomer). MS (EI) *m/e* 224 (M^+−156, 66.7), 182 (M^+−198, 60.9), 180 (M^+−200, 24.4), 91 (M^+−289, 85.5), 43 (M^+−337, 85.5). Anal. Calcd for $C_{18}H_{18}ClNO_4S$ requires: C, 56.91; H, 4.78; N, 3.69%. Found: C, 56.94; H, 4.82; N, 3.56%.

4.3.9. 4-Methyl-*N*-(3-propionyl-3,4-dihydro-2*H*-chromen-4-yl)benzenesulfonamide 4i. A colorless solid: mp 180–181 °C; IR (KBr) ν 3283, 2979, 2937, 1712, 1585, 1490, 1455, 1336, 1225, 1160, 1093, 758 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 0.98 (3H, t, J=7.2 Hz, Me), 2.48 (3H, s, Me), 2.43–2.66 (2H, m, CH_2), 3.21 (1H, q, J=3.3 Hz, CH), 4.28 (1H, dd, J=12.0, 2.7 Hz, CH_2), 4.50 (1H, dd, J=1.2, 7.8 Hz, CH_2), 4.68 (1H, t, J=4.4 Hz, CH), 4.92 (1H, d, J=6.0 Hz, NH), 6.56 (1H, d, J=6.9 Hz, Ar), 6.73 (1H, t, J=8.1 Hz, Ar), 6.75 (1H, t, J=8.1 Hz, Ar), 7.07 (1H, td, J=1.2, 6.9 Hz, Ar), 7.37 (2H, d, J=8.4 Hz, Ar), 7.80 (2H, d, J=8.4 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 7.2, 21.6, 34.2, 48.1, 52.0, 63.2, 117.1, 120.0, 121.5, 127.3, 129.3, 129.5, 130.0, 136.5, 144.0, 154.2, 208.3 (major isomer); MS (EI) *m/e* 204 (M^+−155, 55.9), 148 (M^+−211, 94.7), 146 (M^+−213, 30.9), 131 (M^+−228, 29.7), 91 (M^+−268, 72.8), 65 (M^+−294, 30.1), 57 (M^+−302, 100.0), 55 (M^+−304, 18.4). Anal. Calcd for $C_{19}H_{21}NO_4S$ requires: C, 63.49; H, 5.89; N, 3.90%. Found: C, 63.27; H, 5.74; N, 3.61%.

4.3.10. *N*-(8-Methoxy-3-propionyl-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4j. A colorless solid: mp 181–182 °C; IR (KBr) ν 3277, 2978, 2940, 1918, 1711, 1589, 1487, 1439, 1330, 1265, 1161, 1092, 1009, 815, 735, 668 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 0.98 (3H, t, J=7.2 Hz, Me), 2.45 (3H, s, Me), 2.31–2.43 (1H, m, CH_2), 2.45–2.65 (1H, m, CH_2), 3.04–3.08 (1H, m, CH), 3.80 (3H, s, OCH_3), 4.33 (1H, dd, J=12.3, 2.5 Hz, CH), 4.59 (1H, dd, J=9.3, 5.1 Hz, CH), 4.86 (1H, dd, J=5.4, 9.9 Hz, CH), 5.64 (1H, d, J=10.2 Hz, NH), 6.70–6.82 (3H, m, Ar), 7.33 (2H, d, J=8.3 Hz, Ar), 7.78 (2H, d, J=8.3 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz): δ 7.1, 21.5, 34.1, 48.5, 49.8, 55.8, 66.0, 110.5, 119.3, 120.9, 122.4, 127.0, 129.8, 138.1, 143.4, 143.7, 147.7, 209.2 (major isomer); MS (EI) *m/e* 178 (M^+−211, 57.2), 177 (M^+−212, 30.7), 161 (M^+−228, 36.7), 150 (M^+−239, 68.0), 135 (M^+−254, 28.5), 91 (M^+−298, 100.0), 65 (M^+−324, 33.8), 57 (M^+−332, 94.8). Anal. Calcd for $C_{20}H_{23}NO_5S$ requires: C, 61.68; H, 5.95; N, 3.60%. Found: C, 61.36; H, 5.81; N, 3.26%.

4.3.11. *N*-(6-Methoxy-3-propionyl-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4k. A colorless solid: mp 166–168 °C; IR (KBr) ν 3283, 2984, 2939, 1712, 1598, 1499, 1334, 1207, 1160, 1094, 1057, 910, 817, 667 cm^{-1}; ^{1}H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 1.02 (3H, t, J=7.2 Hz, Me), 2.46 (3H, s, Me), 2.50–2.69 (2H, m, CH_2), 3.19 (1H, q, J=3.0 Hz, CH), 3.49 (3H, s, CH_3), 4.24 (1H, dd, J=11.7, 3.0 Hz, CH), 4.50 (1H, dd, J=11.7, 4.2 Hz, CH), 4.65–4.72 (2H, m, CH+NH), 5.92 (1H, s, Ar), 6.66–6.67 (2H, m, Ar), 7.40 (2H, d, J=8.3 Hz, Ar), 7.84 (2H, d, J=8.3 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 7.2, 21.5, 34.2, 48.3, 52.5, 55.3, 63.3, 112.0, 116.9, 118.1, 120.1, 127.3, 130.0, 136.7, 144.0, 148.2,

153.9, 208.4 (major isomer); MS (EI) *m/e* 85 (M^+-304, 42.8), 83 (M^+-306, 20.6), 71 (M^+-318, 78.6), 57 (M^+-332, 100.0), 56 (M^+-333, 25.1), 55 (M^+-334, 31.5), 43 (M^+-346, 67.0), 41 (M^+-348, 24.9). Anal. Calcd for $C_{20}H_{23}NO_5S$ requires: C, 61.68; H, 5.95; N, 3.60%. Found: C, 61.85; H, 6.06; N, 3.47%.

4.3.12. *N*-(6-Bromo-3-propionyl-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4l. A colorless solid: mp 164–166 °C; IR (KBr) ν 3270, 1752, 1712, 1483, 1160, 1091, 816, 666 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) major isomer: δ 1.01 (3H, t, J=7.4 Hz, Me), 2.47 (3H, s, Me), 2.34–2.69 (2H, m, CH_2), 3.20–3.24 (1H, m, CH), 4.27 (1H, dd, J=11.7, 2.6 Hz, CH), 4.54 (1H, dd, J=11.7, 5.1 Hz, CH), 4.60–4.72 (2H, m, NH+CH), 6.35 (1H, d, J=2.4 Hz, Ar), 6.63 (1H, d, J=9.0 Hz, Ar), 7.16 (1H, dd, J=8.1, 2.1 Hz, Ar), 7.42 (2H, d, J=8.3 Hz, Ar), 7.83 (2H, d, J=8.3 Hz, Ar); minor isomer: δ 1.01 (3H, t, J=7.4 Hz, Me), 2.44 (3H, s, Me), 2.34–2.69 (2H, m, CH_2), 3.0–3.10 (1H, m, CH), 4.27 (1H, dd, J=11.7, 2.6 Hz, CH), 4.48 (1H, dd, J=11.7, 5.1 Hz, CH), 4.77 (1H, dd, J=9.6, 4.8 Hz, CH), 5.58 (1H, d, J=9.9 Hz, NH), 6.57 (1H, d, J=9.0 Hz, Ar), 6.89 (1H, d, J=2.4 Hz, Ar), 7.16 (1H, dd, J=8.1, 2.1 Hz, Ar), 7.36 (2H, d, J=8.3 Hz, Ar), 7.78 (2H, d, J=8.3 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 7.2, 21.6, 34.2, 47.3, 51.8, 63.4, 66.4, 113.3, 119.0, 122.0, 127.2, 130.1, 131.9, 132.4, 136.5, 144.4, 208.0 (major isomer); MS (MALDI) *m/e* 476 (M^++K^+). Anal. Calcd for $C_{19}H_{20}BrNO_4S$ requires: C, 52.06; H, 4.60; N, 3.20%. Found: C, 51.81; H, 4.45; N, 3.02%.

4.3.13. *N*-(3-Benzoyl-3,4-dihydro-2*H*-chromen-4-yl)-4-methylbenzenesulfonamide 4m. A white solid: mp 180–182 °C; IR (KBr) ν 3296, 2920, 2355, 1675, 1489, 1161 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) *anti*-isomer: δ 2.45 (3H, s, Me), 4.19–4.22 (1H, m, CH), 4.40–4.40 (2H, m, CH_2), 4.75 (2H, s, NH+CH), 6.77–6.80 (1H, m, Ar), 6.81–6.87 (2H, m, Ar), 7.14–7.20 (1H, m, Ar), 7.31 (2H, d, J=8.1 Hz, Ar), 7.48 (2H, t, J=7.5 Hz, Ar), 7.60 (1H, t, J=7.5 Hz, Ar), 7.77 (2H, d, J=7.0 Hz, Ar), 7.86 (2H, d, J=7.0 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.4, 47.5, 49.0, 64.4, 116.9, 120.7, 121.5, 127.1, 128.3, 128.6, 129.3, 129.7, 133.5, 135.2, 136.7, 137.9, 143.6, 154.2, 198.2 (*anti*-isomer); MS (ESI) *m/e* 425 (M^++18, 100). Anal. Calcd for $C_{23}H_{21}NO_4S$ requires: C, 67.79; H, 5.19; N, 3.44%. Found: C, 67.94; H, 5.19; N, 3.34%.

4.4. Reaction procedure for the synthesis of aza-Baylis–Hillman product 11

To a Schlenk tube with *N*-tosylimine of 4-hydroxybenzaldehyde (69 mg, 0.25 mmol) and DABCO (2.8 mg, 0.025 mmol) were added PhMe (1.0 mL) and methyl vinyl ketone (42 μL, 0.50 mmol). The solution was stirred at room temperature for 8 days. Then the solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography to give **4a** (eluant: EtOAc/petroleum=1/1, 28 mg, yield 33%) as a white solid.

4.4.1. *N*-(1-(4-Hydroxyphenyl)-2-methylene-3-oxobutyl)-4-methylbenzenesulfonamide 11. A white solid: mp 178–180 °C; IR (KBr) ν 3370, 3065, 2923, 2853, 1591, 1568, 1441, 1289, 1152, 1068 cm^{-1}; ^1H NMR ($CDCl_3$, TMS, 300 MHz) δ 2.17 (3H, s, Me), 2.42 (3H, s, Me), 3.76 (1H, s, OH), 5.20 (1H, d, J=7.5 Hz, CH), 5.49 (1H, d, J=7.5 Hz, NH), 6.09 (1H, s, =CH), 6.10 (1H, s, =CH), 6.66 (2H, d, J=8.4 Hz, Ar), 6.95 (2H, d, J=8.4 Hz, Ar), 7.25 (2H, d, J=8.4 Hz, Ar), 7.66 (2H, d, J=8.4 Hz, Ar). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 21.5, 26.2, 48.0, 116.5, 124.3, 126.2, 127.6, 129.8, 134.1, 135.0, 144.5, 163.1, 169.7, 196.7. MS (EI) *m/e* 190 (M^+-155, 93.7), 155 (M^+-190, 21.7), 131 (M^+-214, 20.1), 96 (M^+-249, 16.5), 91 (M^+-254, 100.0), 43 (M^+-302, 67.1). Anal. Calcd for $C_{18}H_{19}NO_4S$ requires: C, 62.59; H, 5.54; N, 4.06%. Found: C, 62.67; H, 5.63; N, 3.86%.

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