

Synthesis of Allyl Aryl Sulfone Derivatives from *Baylis–Hillman* Acetates in Water

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Various phenyl and *p*-tolyl allyl sulfone derivatives were prepared stereoselectively by reacting *Baylis–Hillman* acetates with sodium 4-*R*-benzenesulfinate (*R* = H, Me) in H₂O. The reaction was very efficient in providing the corresponding sulfone derivatives in good to excellent yields (*Table*).

Introduction. – As a part of our ongoing programme initiated towards the development of ecological chemical methodologies [1], we became interested in *Baylis–Hillman* acetates as reactive intermediates. Herein, we report the synthesis of disubstituted phenyl or *p*-tolyl allyl sulfone derivatives in H₂O under catalyst-free conditions.

Results. – In the course of the present work, *Baylis–Hillman* acetates were treated with sodium benzenesulfonates in H₂O at room temperature. The reaction resulted in the corresponding allyl sulfone derivatives in 71% yield. However, the same reaction in H₂O under heating proceeded in a much better way. After having optimized the reaction conditions, *Baylis–Hillman* acetates and sodium 4-*R*-benzenesulfonates (*R* = H, Me) in H₂O were heated at 70–80° to give the products in excellent yields of up to 94% within 6 h (*Scheme*; *Table*, *Entry 1*). Encouraged by the result, we first prepared various *Baylis–Hillman* acetates by reported literature procedures from commercially available aldehydes R¹–CHO and *Michael* acceptors such as methyl or ethyl acrylate (CH₂=CHCOOR) or acrylonitrile (CH₂=CHCN) in the presence of DABCO (=1,4-

Scheme. Synthesis of Allyl Aryl Sulfone Derivatives from Baylis–Hillman Acetates and Sodium Benzenesulfonates

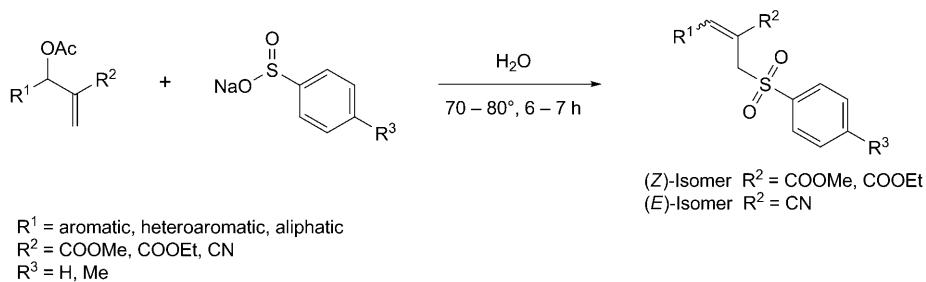
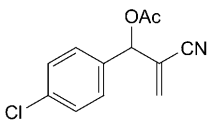
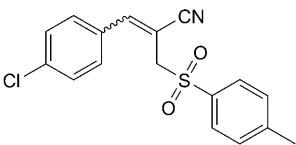
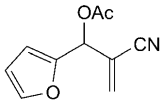
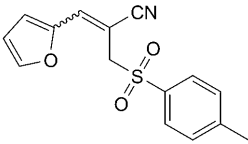
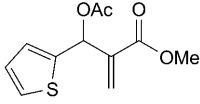
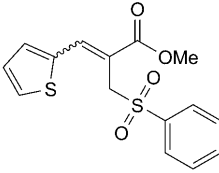
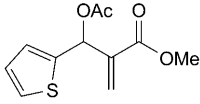
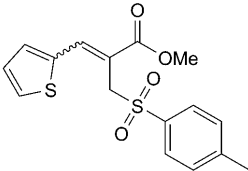
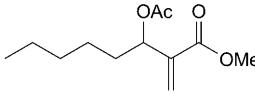
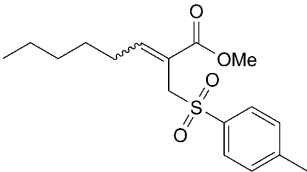
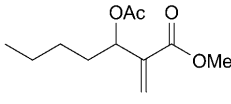
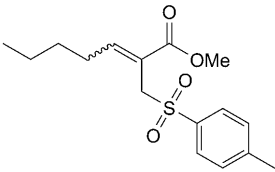
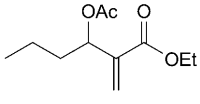
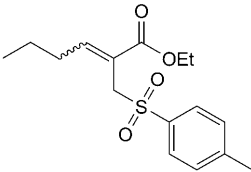


Table. *Synthesis of Allyl Phenyl or Allyl p-Tolyl Sulfone Derivatives from Baylis–Hillman Acetates and Sodium Benzenesulfinate or Sodium 4-Methylbenzenesulfonates^a*

Entry	Substrate	Product	Time [h]	Yield [%] ^b	(<i>E</i>)/(<i>Z</i>) ^c
1			6	94	2 : 98
2			7	92	3 : 97
3			6	91	3 : 97
4			6	91	3 : 97
5			6	87	95 : 5
6			6	95	4 : 96
7			6	91	95 : 5

Table (cont.)

Entry	Substrate	Product	Time [h]	Yield [%] ^b	(<i>E</i>)/(<i>Z</i>) ^c
8			6	89	95 : 5
9			7	84	95 : 5
10			6	89	3 : 97
11			6	87	3 : 97
12			7	74	5 : 95
13			7	73	5 : 95
14			7	73	4 : 96

^a) Reaction conditions: *Baylis–Hillman* acetate (1.0 mmol), sodium sulfinate (1.2 mmol), H₂O (15 ml), 70–80°, 6–7 h. ^b) Yield of isolated sulfone derivatives. ^c) Selectivity was determined by ¹H-NMR analysis.

diazabicyclo[2.2.2]octane) as catalyst and Ac_2O as acetylating agent. The resulting adducts were then treated with sodium benzenesulfinate or sodium 4-methylbenzenesulfinate (Table). In the present study, aldehydes $\text{R}^1\text{-CHO}$ with electron-donating groups gave the corresponding allyl sulfone derivatives in lower yields in comparison to aldehydes with electron-withdrawing groups. In the case of acetates of aliphatic *Baylis–Hillman* adducts, the corresponding allyl sulfone derivatives were also obtained in lower yields (Table, Entries 12–14). The (2*Z*)-configuration of the 2-(sulfonylmethyl)acrylates were assigned on the basis of ^1H - and ^{13}C -NMR shifts in comparison with literature values [2]. In the case of *Baylis–Hillman* adducts prepared from acrylonitrile, the reaction with sodium 4-methylbenzenesulfinate gave the corresponding 2-(sulfonylmethyl)acrylonitriles with reversal of selectivity, i.e., the (2*E*)-isomers were the major product. This fact was also confirmed by ^1H - and ^{13}C -NMR measurements and by comparison with reported values.

In conclusion, we developed an elegant protocol for the synthesis of allyl sulfone derivatives in high yields by reaction of *Baylis–Hillman* acetates with sodium 4-*R*-benzenesulfinate ($\text{R} = \text{H}, \text{Me}$) in H_2O . This practical method may have widespread applications in the context of ecologically oriented organic synthesis.

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Experimental Part

General. TLC: Precoated silica-gel plates (60 F_{254} , 0.2-mm layer, E. Merck). Column chromatography (CC): Silica gel, 60–120 mesh. M.p.: Fischer–Johns apparatus; uncorrected. IR Spectra: Thermo Nicolet Nexus 670 FT-IR spectrophotometer; in KBr; $\bar{\nu}$ in cm^{-1} . ^1H - and ^{13}C -NMR Spectra: Bruker Avance 300, Innova 400 MHz and Bruker Gemini 200 MHz instrument; in CDCl_3 ; δ in ppm rel. to Me_4Si as internal standard, J in Hz. ESI-MS: Finnigan MAT 1020 mass spectrometer; in m/z .

Allyl Aryl Sulfone Derivatives: General Procedure. To a flask containing the *Baylis–Hillman* acetate (1 mmol) in H_2O (15 ml), the sodium benzenesulfinate (1.2 mmol) was added. The suspension was magnetically stirred at 70–80° until the reaction was complete (TLC monitoring). The mixture was then extracted with AcOEt (4×10 ml), the extract washed with H_2O and brine dried (anh. Na_2SO_4), and concentrated, and the resulting crude product purified by CC (AcOEt /hexane 1:9): substituted allyl sulfone derivative in yields up to 94% (Table).

Methyl (2*Z*)-2-[(4-Methylphenyl)sulfonyl]methyl]-3-phenylprop-2-enoate (Table, Entry 1): Light brown solid. M.p. 120°. IR: 2982, 1713, 1317, 1266, 1141. ^1H -NMR: 7.91 (s, 1 arom. H); 7.74 (d, $J = 8.3$, 2 arom. H); 7.52 (d, $J = 7.5$, 2 arom. H); 7.38 (m, 3 arom. H); 7.29 (d, $J = 7.5$, 2 arom. H); 4.41 (s, CH_2SO_2); 3.61 (s, MeO); 2.46 (s, Me). ^{13}C -NMR: 166.8; 146.0; 144.6; 136.1; 133.5; 129.5; 129.0; 128.6; 128.4; 120.9; 55.0; 52.2; 21.5. ESI-MS: 353 ($[M + \text{Na}]^+$).

Ethyl (2*Z*)-3-(4-Methoxyphenyl)-2-[(4-methylphenyl)sulfonyl]methyl]prop-2-enoate (Table, Entry 2): Yellow oil. IR: 2987, 1713, 1610, 1510, 1319, 1144. ^1H -NMR: 7.89 (s, 1 H); 7.76 (d, $J = 8.1$, 2 arom. H); 7.58 (d, $J = 8.6$, 2 arom. H); 7.28 (d, $J = 8.8$, 2 arom. H); 6.92 (d, $J = 8.8$, 2 arom. H); 4.50 (s, CH_2SO_2); 4.00 (q, $J = 7.1$, MeCH_2O); 3.84 (s, MeO); 2.42 (s, Me); 1.20 (t, $J = 7.1$, MeCH_2O). ^{13}C -NMR: 166.7; 160.9; 145.2; 131.5; 129.5; 128.6; 126.2; 114.1; 61.3; 55.4; 55.3; 21.5; 14.0. ESI-MS: 397 ($[M + \text{Na}]^+$).

Ethyl (2*Z*)-3-(4-Fluorophenyl)-2-[(4-methylphenyl)sulfonyl]methyl]prop-2-enoate (Table, Entry 3): White solid. M.p. 65°. IR: 2984, 1710, 1600, 1508, 1317, 1142. ^1H -NMR: 7.86 (s, 1 H); 7.71 (d, $J = 7.1$, 2 H); 7.54 (t, $J = 6.7$, 2 H); 7.27 (d, $J = 7.7$, 2 H); 7.05 (t, $J = 8.4$, 2 H); 4.41 (s, 2 H); 4.02 (q, $J = 6.9$, 2 H); 2.41 (s, 3 H); 1.22 (t, $J = 6.9$, 3 H). ^{13}C -NMR: 164.8; 161.5; 144.5; 132.5; 131.3; 131.2; 129.7; 129.4; 128.3; 121.0; 115.7; 115.4; 61.2; 54.8; 21.4; 14.0. ESI-MS: 385 ($[M + \text{Na}]^+$).

Ethyl (2Z)-3-(4-Chlorophenyl)-2-[(4-methylphenyl)sulfonyl]methyl]prop-2-enoate (Table, Entry 4): Colorless oil. IR: 2985, 1715, 1315, 1268, 1131. ¹H-NMR: 7.85 (s, 1 H); 7.70 (d, *J* = 8.3, 2 H); 7.44 (d, *J* = 9.0, 2 H); 7.24–7.33 (m, 4 H); 4.44 (s, 2 H), 4.06 (q, *J* = 6.7, 2 H); 2.40 (s, 3 H); 1.22 (t, *J* = 6.7, 3 H). ¹³C-NMR: 166.1; 144.9; 136.2; 132.1; 130.5; 129.6; 128.9; 128.4; 121.7; 61.6; 54.9; 21.5; 14.0. ESI-MS: 379 ([*M* + H]⁺).

(2E)-2-[(4-Methylphenyl)sulfonyl]methyl]-3-phenyl-prop-2-enenitrile (Table, Entry 5): Light brown solid. M.p. 90°. IR: 2212, 1623, 1311, 1146. ¹H-NMR: 7.81 (d, *J* = 8.3, 2 H); 7.55 (s, 1 H); 7.34–7.40 (m, 7 H); 4.17 (s, 2 H); 2.46 (s, 3 H). ¹³C-NMR: 152.0; 132.2; 130.5; 130.1; 129.0; 128.9; 128.7; 118.1; 103.2; 56.4; 21.7. ESI-MS: 320 ([*M* + Na]⁺).

Methyl (2Z)-2-[(4-Methylphenyl)sulfonyl]methyl]-3-(3-nitrophenyl)prop-2-enoate (Table, Entry 6): Light yellow solid. M.p. 110°. IR: 2982, 1713, 1317, 1266, 1141. ¹H-NMR: 8.20 (d, *J* = 8.3, 2 H); 7.94 (d, *J* = 7.8, 1 H); 7.91 (s, 1 H); 7.71 (d, *J* = 7.8, 2 H); 7.60 (t, *J* = 7.8, 1 H); 7.28 (d, *J* = 7.8, 2 H); 4.33 (s, 2 H); 3.69 (s, 3 H); 2.43 (s, 3 H). ¹³C-NMR: 166.5; 145.3; 140.3; 138.4; 135.6; 133.7; 129.5; 128.3; 127.4; 123.2; 56.5; 52.2; 21.2. ESI-MS: 376 ([*M* + H]⁺).

(2E)-3-(4-Ethoxyphenyl)-2-[(4-methylphenyl)sulfonyl]methyl]prop-2-enenitrile (Table, Entry 7): Yellow oil. IR: 2927, 2210, 1627, 1321, 1148. ¹H-NMR: 7.54 (d, *J* = 8.6, 2 H); 7.40 (d, *J* = 6.7, 2 H); 7.26 (t, *J* = 6.7, 2 H); 6.81 (d, *J* = 8.6, 2 H); 6.54 (s, 1 H), 4.01 (q, *J* = 6.7, 2 H); 3.69 (s, 2 H); 2.43 (s, 3 H); 1.41 (t, *J* = 6.7, 3 H). ¹³C-NMR: 160.4; 144.0; 138.4; 133.2; 130.5; 129.3; 128.5; 127.4; 114.2; 104.2; 63.7; 57.2; 21.3; 14.6. ESI-MS: 364 ([*M* + Na]⁺).

(2E)-3-(4-Chlorophenyl)-2-[(4-methylphenyl)sulfonyl]methyl]prop-2-enenitrile (Table, Entry 8): White solid. M.p. 110°. IR: 2928, 2212, 1627, 1313, 1144. ¹H-NMR: 7.80 (d, *J* = 8.1, 1 H); 7.38 (m, 6 H); 7.30 (d, *J* = 8.3, 2 H); 4.42 (s, 2 H); 2.47 (s, 3 H). ¹³C-NMR: 150.8; 145.2; 136.2; 134.9; 131.4; 130.7; 130.1; 129.3; 129.1; 128.6; 118.0; 103.4; 56.3; 21.7. ESI-MS: 354 ([*M* + Na]⁺).

(2E)-3-(Furan-2-yl)-2-[(4-methylphenyl)sulfonyl]methyl]prop-2-enenitrile (Table, Entry 9): Brown solid. M.p. 125°. IR: 2925, 2212, 1623, 1311, 1146. ¹H-NMR: 7.78 (d, *J* = 8.1, 2 H); 7.57 (s, 1 H); 7.38 (d, *J* = 8.1, 2 H); 7.04 (d, *J* = 3.5, 1 H); 6.96 (s, 1 H); 6.54 (s, 1 H); 3.98 (s, 2 H), 2.45 (s, 3 H). ¹³C-NMR: 148.7; 145.8; 137.1; 134.5; 130.0; 128.5; 119.6; 117.1; 112.7; 112.2; 60.5; 21.6. ESI-MS: 305 ([*M* + NH₄]⁺).

Methyl (2Z)-2-[(Phenylsulfonyl)methyl]-3-(thiophen-2-yl)prop-2-enoate (Table, Entry 10): Light brown oil. IR: 2984, 1710, 1600, 1508, 1317, 1142. ¹H-NMR: 8.00 (s, 1 H); 7.78 (d, *J* = 8.3, 2 H); 7.57 (d, *J* = 3.7, 1 H); 7.52 (d, *J* = 5.2, 1 H); 7.30 (d, *J* = 8.3, 3 H); 7.12 (t, *J* = 3.7, 1 H); 4.55 (s, 2 H); 3.54 (s, 3 H). ¹³C-NMR: 166.4; 139.0; 137.5; 134.2; 133.5; 131.5; 129.3; 128.5; 128.2; 62.4; 52.7. ESI-MS: 345 ([*M* + Na]⁺).

Methyl (2Z)-2-[(4-Methylphenyl)sulfonyl]methyl]-3-(thiophen-2-yl)prop-2-enoate (Table, Entry 11): Light brown oil. IR: 2984, 1710, 1600, 1508, 1317, 1142. ¹H-NMR: 8.00 (s, 1 H); 7.78 (d, *J* = 8.3, 2 H); 7.57 (d, *J* = 3.7, 1 H); 7.52 (d, *J* = 5.2, 1 H); 7.30 (d, *J* = 8.3, 2 H); 7.12 (t, *J* = 3.7, 1 H); 4.55 (s, 2 H); 3.54 (s, 3 H); 2.45 (s, 3 H). ¹³C-NMR: 166.4; 139.0; 137.5; 134.2; 133.5; 131.5; 129.3; 128.5; 128.2; 62.4; 52.7; 21.4. ESI-MS: 359 ([*M* + Na]⁺).

Methyl (2Z)-2-[(4-Methylphenyl)sulfonyl]methyl]oct-2-enoate (Table, Entry 12): Colorless oil. IR: 2953, 1720, 1321, 1143, 1085. ¹H-NMR: 7.72 (d, *J* = 8.3, 2 H); 7.32 (d, *J* = 8.3, 2 H); 7.09 (t, *J* = 7.5, 1 H); 4.22 (s, 2 H); 3.05 (s, 3 H); 2.42 (s, 3 H); 2.14 (q, *J* = 6.7, 2 H); 2.0 (m, 2 H); 1.32 (m, 4 H); 0.87 (t, *J* = 7.5, 3 H). ¹³C-NMR: 165.7; 151.3; 144.3; 131.5; 129.2; 128.2; 120.2; 60.2; 53.6; 29.9; 28.7; 22.7; 21.9; 21.1; 13.7. ESI-MS: 347 ([*M* + Na]⁺).

Methyl (2Z)-2-[(4-Methylphenyl)sulfonyl]methyl]hept-2-enoate (Table, Entry 13): Colorless oil. IR: 2956, 1720, 1318, 1144, 1084. ¹H-NMR: 7.72 (d, *J* = 8.3, 2 H); 7.32 (d, *J* = 8.3, 2 H); 7.09 (t, *J* = 7.5, 1 H); 4.22 (s, 2 H); 3.05 (s, 3 H); 2.42 (s, 3 H); 2.14 (q, *J* = 6.7, 2 H); 1.32 (m, 4 H); 0.87 (t, *J* = 7.5, 3 H). ¹³C-NMR: 165.7; 151.3; 144.5; 131.5; 129.2; 128.2; 120.2; 60.2; 53.6; 29.9; 28.7; 21.9; 21.1; 13.7. ESI-MS: 333 ([*M* + Na]⁺).

Ethyl (2Z)-2-[(4-Methylphenyl)sulfonyl]methyl]hex-2-enoate (Table, Entry 14): Colorless oil. IR: 2948, 1720, 1319, 1146, 1087. ¹H-NMR: 7.68 (d, *J* = 6.9, 2 H); 7.28 (d, *J* = 6.9, 2 H); 7.03 (t, *J* = 7.5, 1 H); 4.15 (s, 2 H); 3.91 (q, *J* = 7.1, 2 H); 2.42 (s, 3 H); 2.20 (q, *J* = 7.5, 2 H); 1.46 (m, 2 H); 1.13 (t, *J* = 7.1, 3 H); 0.94 (t, *J* = 7.1, 3 H). ¹³C-NMR: 165.0; 150.4; 136.4; 129.3; 128.8; 128.7; 60.6; 53.9; 31.8; 31.3; 21.5; 14.0; 13.8. ESI-MS: 333 ([*M* + Na]⁺).

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