Synthesis of Methyl (*E*)-2-Nitromethylcinnamates Derived from Baylis–Hillman Acetates and Conversion into Several Coumarin Derivatives

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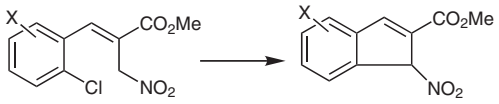
Received 4 August 2004; revised 17 September 2004

Abstract: Fast and easy access to methyl (*E*)-2-nitromethylcinnamates, from the corresponding Baylis–Hillman acetates with $NaNO_2$ in DMF is described. Several *ortho*-chloro-2-nitromethylcinnamates undergo intramolecular aromatic substitution reaction followed by rearrangement to yield coumarin derivatives.

Key words: Baylis–Hillman reaction, sodium nitrite, methyl (*E*)-2-nitromethylcinnamates, nitronate anion, coumarin

Aliphatic nitro compounds are potentially useful substrates in organic synthesis due to the high electron-withdrawing nature associated with the nitro group and the conversion of the nitro group into other functionalities.[1] Nitronate salts can act as carbon nucleophiles with a range of electrophiles including haloalkanes,[2] aldehydes[3,4] and Michael acceptors[5] leading to the carbon-carbon bond formation.

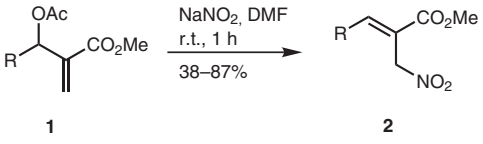
Much attention has recently been focused on the S_N2' nucleophilic substitution of the acetates, imines or bromo-derivatives of the Baylis–Hillman (BH) adducts. These include nucleophilic substitution of tosyl amide,[6] acrylonitrile,[7] cyanide,[8,9] hydride,[10] imidazole,[11] acetate ion,[12] phosphite,[13] azide,[14,15] nitronate anion,[16] active methylene anion[17] and nitric acid.[18] To the best of our knowledge, there is no report in the literature[19] for the conversion of the BH adducts into the corresponding 2-nitromethyl-2-propenoates stereoselectively. As part of our continuing studies towards development of the BH chemistry,[20,21] we desired to have the nitro group at the allylic position of the 3-aryl-2-propenoates. In principle, such nitro compounds might be extended further toward the building of indene derivatives (Equation 1).



Equation 1

Similar methods using Baylis–Hillman chemistry in the construction of benzannulated compounds such as 3-quinolincarboxylic acid esters,[6b] 1,4-dihydroquinolines,[22] and naphthalenes[16a] via intramolecular nucleophilic aromatic substitution reaction (S_NAr) were reported. We now describe a synthesis of methyl (*E*)-2-nitromethylcinnamates derived from BH acetates and conversion into coumarins by the intramolecular S_NAr reaction of several *ortho*-chloro-2-nitromethylcinnamates.

The coumarin nucleus is present in many naturally-occurring pharmacologically active compounds.[23] Various methods for preparing coumarin derivatives have been developed including the classic von Pechmann,[24] Claisen,[25] Perkin,[26] Reformatsky,[27] Knoevenagel,[28] and Wittig reactions.[29] Also, new methods of accessing these important compounds continue to be reported. These include: the reaction of *tert*-butyl isocyanide and dialkyl acetylenedicarboxylates in the presence of salicylaldehydes;[30] the reaction of the *N*-hydroxybenzotriazole ester of acetyl salicylic acids and active methylene compounds followed by cyclization;[31] palladium-catalyzed reaction of phenols with propiolic acids;[32] and cyclization of protected or unprotected BH adducts of salicylaldehyde.[33]



Scheme 1

In view of the report[14] that 1,4-diazabicyclo[2,2,2]octane (DABCO) assisted fast and easy access to azides of BH adducts from the corresponding acetates in aqueous media, we carried out the reaction of BH acetate **1a** with DABCO in aqueous THF for 10 minutes and then sodium nitrite ($NaNO_2$) was added and stirred at room temperature for one hour. Unfortunately, the desired 2-nitromethylcinnamic acid methyl ester **2a** was produced in poor yield (25%). But, the direct substitution reaction of **1a** with $NaNO_2$ in DMF at room temperature for one hour afforded **2a** in 87% yield. This success led us to transform the representative methyl 3-acetoxy-3-aryl-2-methylenepropanoates **1b–l** into methyl (*E*)-3-aryl-2-nitromethyl-2-propenoates **2b–l** stereoselectively under the similar reaction conditions (Scheme 1, Table 1 and Table 2). The *E* geometry of the olefinic bond was established on the basis of NOE experiment of **2d** in which irradiation of either of the allylic protons or the olefinic proton did not lead to the enhancement of the other peak. Also, in the ^1H NMR

SYNTHESIS 2005, No. 1, pp 0033–0038
Advanced online publication: 17.11.2004
DOI: 10.1055/s-2004-834916; Art ID: F11204SS

Table 1 Methyl (*E*)-3-Aryl-2-nitromethyl-2-propenoates **2**

Reactant	R	Product	Yield (%)	Time (h)	Mp (°C)
1a	C_6H_5	**2a**	87	1	oil
1b	4-ClC_6H_4	**2b**	76	1	64–66
1c	2-BrC_6H_4	**2c**	86	1	96–97
1d	4-BrC_6H_4	**2d**	83	1	73–74
1e	2-IC_6H_4	**2e**	64	1	90–91
1f	2-$O_2NC_6H_4$	**2f**	38	1	63–64
1g	4-$O_2NC_6H_4$	**2g**	70	1	128–130
1h	4-$MeOC_6H_4$	**2h**	79	1	oil
1i	4-$AcNHC_6H_4$	**2i**	82	1	150–152
1j	2-ClC_6H_4	**2j**	78	1	88–90
1k	2,6-$Cl_2C_6H_3$	**2k**	80	1	87–89
1l	2,3-$Cl_2C_6H_3$	**2l**	71	1	122–124

spectra, the vinyl peaks appeared at 7.87–8.44 ppm, which were well coincident with the reported data of similar compounds.[16b,18]

The simplicity of this reaction yielding 2-nitromethyl-*o*-chlorocinnamates **2j–l** has obvious some synthetic potential due to their conversion into the cyclic derivatives via intramolecular S_NAr reaction. Thus, in our initial experiment, the reaction of **2j** with K_2CO_3 in DMF led to an extremely complex reaction mixture as indicated by thin layer chromatography, from which we could isolate 3-methoxycarbonylcoumarin 2-oxime **7j** in 14% yield. But, dichlorocinnamates **2k** and **2l**, having another electron-attracting chlorine atom on benzene ring, gave coumarin 2-oximes **7k** and **7l** in 66% and 50% yields, respectively. Interestingly, the reaction of BH acetates **1m** and **1n**, having strong electron-withdrawing nitro group on benzene ring, with $NaNO_2$ in DMF directly gave the corresponding coumarin 2-oximes **7m** (70%) and **7n** (48%)[34] within 30 minutes (Scheme 2).[35] In all the cases indene derivatives **3** were not obtained. Although the isolation of the intermediate 2-nitromethylcinnamates **2m** and **2n** were unsuccessful in these reactions we presumed that the eliminated acetate anions could be considered as a base in this transformation, possibly because of some enhancement of the hydrogen acidity at the α-position of nitro group.

We believe that the oximes **7** might be produced by the rearrangement of the intermediate 4-methoxycarbonyl-1,2-benzoxazepine 2-oxides **4**. Conversion of **4** into **7** under the reaction condition was considered to proceed by way of the zwitterionic tricyclic oxaziridine *N*-oxide intermediate **5**, which was formed by the attack of the ring oxygen to the imminium carbon. The resulting oxaziridine intermediate **5** could be cleaved to produce nitroso compound **6**, then tautomerized to afford oxime **7**. This kind of the formation of 7-membered ring products, 3,2-benzoxazepin-5(4*H*)-one 2-oxides via intramolecular *O*-alkylation of the nitronate anion and rearrangement to isocoumarin-4-one 1-oximes was reported in the literature.[36] Oximes **7j–n** were easily hydrolyzed using concentrated HCl in THF to give the corresponding coumarins **8j–n** by the known method.[36]

The structures of oximes **7j–n** were assigned on the basis of their spectral data. IR spectra showed absorptions at 3395–3449 cm^{-1} for the hydroxyl groups, absorptions at 1703–1731 cm^{-1} for the ester carbonyl groups, and absorptions at 1641–1655 and 1603–1613 cm^{-1} for the carbon-nitrogen and carbon-carbon double bonds. The ^1H NMR spectra showed signals at δ = 7.62–7.78 ppm as a singlet for the methine hydrogen, signals at δ = 10.77–11.28 ppm as a singlet for oxime hydrogen and exchangeable in deuterium oxide, and signals corresponding to the methoxy peak appeared as a singlet at δ = 3.78–3.83 ppm. The ^{13}C NMR spectra showed eleven absorption peaks including ester carbonyl absorption (162.83–163.85 ppm).

The structures of coumains **8j–n** were established on the basis of their spectral data compared with literature values.[30,37] IR spectra revealed sharp bands at 1738–1779 and 1696–1720 cm^{-1} assigned to the carbonyl groups. The ^1H NMR spectra showed two single sharp lines readily recognized as arising from methoxy (δ = 3.97–4.00 ppm) and methine (δ = 8.55–8.90 ppm) protons along with multiplets for the aromatic protons. The ^{13}C NMR spectra exhibited signals at δ = 162.54–163.69 ppm for the ester carbonyl groups and signals at δ = 153.96–155.89 ppm for the lactone carbonyl groups.

In conclusion, a simple synthesis of methyl 2-nitromethylcinnamates from readily available Baylis–Hillman acetates and conversion to the several coumarin derivatives is disclosed.

Silica gel 60 (70–230 mesh ASTM) used for column chromatography was supplied by E. Merck. Analytical TLC was carried out on Merck silica gel 60 F_{254} TLC plates. Melting points were taken using an Electrothermal melting point apparatus and are uncorrected. Microanalyses were obtained using a Carlo Erba EA 1180 element analyzer. Electron impact (EI) and high resolution mass spectra (HRMS) were obtained using a Jeol SX102 mass spectrometer. IR spectra were recorded on a Nicolet Magna 550 FTIR spectrometer. The ^1H and ^{13}C NMR spectra were measured on a Gemini 300 spectrometer using $CDCl_3$ or DMSO-d_6. All chemical shifts are reported in ppm relative to TMS and coupling constants (*J*) are expressed in Hz.

Aromatic aldehydes, DABCO, THF, DMF, K_2CO_3, $NaNO_2$ and methyl acrylate were obtained from Aldrich and used without further purification. All the required Baylis–Hillman acetates **1a–n** were prepared by the reaction of the corresponding aldehydes with methyl acrylate in the presence of DABCO followed by acetylation with acetic anhydride according to the literature procedures.[16,38]

Preparation of Methyl (*E*)-3-Aryl-2-nitromethyl-2-propenoates 2a–l; General Procedure

$NaNO_2$ (207 mg, 3 mmol) was added to the solution of the Baylis–Hillman acetates **1a–l** (2 mmol) in DMF (8 mL) and stirred at r.t. for

Table 2 Spectral and Elemental Analysis Data of Methyl (*E*)-3-Aryl-2-nitromethyl-2-propenoates **2**

Product	IR (KBr) (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, *J* (Hz)	^{13}C NMR ($CDCl_3$/TMS) δ	Analysis (%) Calcd/Found C H N
2a	1714, 1639, 1555, 1387, 1357	3.88 (s, 3 H, OCH_3), 5.36 (s, 2 H, CH_2), 7.31–7.34 (m, 2 H, aromatic), 7.44–7.46 (m, 3 H, aromatic), 8.19 (s, 1 H, CH)	52.53, 71.66, 121.73, 128.69, 128.90, 130.04, 133.26, 147.44, 166.03	59.73 5.01 6.33 59.51 5.14 6.06
2b	1726, 1641, 1555, 1382, 1360	3.80 (s, 3 H, OCH_3), 5.25 (s, 2 H, CH_2), 7.20 (d, *J* = 7.6 Hz, 2 H, aromatic), 7.34 (d, *J* = 7.6 Hz, 2 H, aromatic), 8.05 (s, 1 H, CH)	52.76, 71.61, 122.37, 129.38, 130.16, 131.74, 136.40, 146.23, 165.86	51.68 3.94 5.48 51.46 3.97 5.29
2c	1709, 1639, 1561, 1387, 1356	3.90 (s, 3 H, OCH_3), 5.22 (s, 2 H, CH_2), 7.26–7.39 (m, 3 H, aromatic), 7.67 (d, *J* = 7.9 Hz, 1 H, aromatic), 8.17 (s, 1 H, CH)	52.70, 71.57, 123.37, 123.74, 127.77, 129.31, 131.18, 133.07, 133.89, 146.43, 165.43	44.02 3.36 4.67 44.25 3.34 4.69
2d	1718, 1641, 1554, 1389, 1359	3.88 (s, 3 H, OCH_3), 5.32 (s, 2 H, CH_2), 7.20 (d, *J* = 8.4 Hz, 2 H, aromatic), 7.59 (d, *J* = 8.4 Hz, 2 H, aromatic), 8.11 (s, 1 H, CH)	53.25, 71.95, 122.79, 125.09, 130.68, 132.54, 132.84, 146.68, 166.21	44.02 3.36 4.67 44.04 3.27 4.59
2e	1709, 1637, 1562, 1388, 1354	3.98 (s, 3 H, OCH_3), 5.27 (s, 2 H, CH_2), 7.20 (dd, *J* = 7.6, 7.6 Hz, 1 H, aromatic), 7.30 (d, *J* = 7.6 Hz, 1 H, aromatic), 7.50 (dd, *J* = 7.6, 7.6 Hz, 1 H, aromatic), 8.01 (d, *J* = 7.6 Hz, 1 H, aromatic), 8.13 (s, 1 H, CH)	52.89, 71.57, 98.64, 123.02, 128.64, 128.82, 131.10, 137.64, 139.47, 150.29, 165.50	38.06 2.90 4.04 38.31 2.91 3.93
2f	1724, 1649, 1555, 1518, 1379, 1342	3.91 (s, 3 H, OCH_3), 5.13 (s, 2 H, CH_2), 7.42 (d, *J* = 7.6 Hz, 1 H, aromatic), 7.63–7.78 (m, 2 H, aromatic), 8.29 (dd, *J* = 8.2, 1.2 Hz, 1 H, aromatic), 8.44 (s, 1 H, CH)	52.44, 71.58, 122.95, 125.52, 129.68, 130.51, 130.94, 134.75, 144.93, 147.04, 165.25	49.63 3.79 10.52 49.74 3.68 10.53
2g	1720, 1648, 1566, 1519, 1384, 1347	3.91 (s, 3 H, OCH_3), 5.30 (s, 2 H, CH_2), 7.52 (d, *J* = 8.6 Hz, 2 H, aromatic), 8.21 (s, 1 H, CH), 8.32 (d, *J* = 8.6 Hz, 2 H, aromatic)	53.10, 71.33, 124.29, 124.88, 129.59, 139.63, 144.85, 148.42, 165.27	49.63 3.79 10.52 49.35 3.75 10.53
2h	1710, 1633, 1555, 1391, 1358	3.85 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 5.40 (s, 2 H, CH_2), 6.96 (d, *J* = 8.7 Hz, 2 H, aromatic), 7.31 (d, *J* = 8.7 Hz, 2 H, aromatic), 8.12 (s, 1 H, CH)	52.31, 55.15, 71.92, 114.37, 119.12, 125.53, 130.99, 147.07, 161.14, 166.36	57.37 5.22 5.58 57.07 5.29 5.68
2i	1707, 1667, 1595, 1551, 1397, 1370	2.21 (s, 3 H, CH_3), 3.87 (s, 3 H, OCH_3), 5.38 (s, 2 H, CH_2), 7.30 (d, *J* = 8.6 Hz, 2 H, aromatic), 7.61 (d, *J* = 8.6 Hz, 2 H, aromatic), 7.69 (br s, 1 H, NH), 8.11 (s, 1 H, CH)	24.61, 52.69, 71.96, 119.83, 120.58, 128.88, 130.20, 139.93, 147.06, 166.39, 168.80	56.11 5.07 10.07 56.14 4.96 9.90
2j	1726, 1641, 1555, 1382, 1360	3.90 (s, 3 H, OCH_3), 5.24 (s, 2 H, CH_2), 7.25–7.50 (m, 4 H, aromatic), 8.24 (s, 1 H, CH)	52.80, 71.71, 123.72, 127.27, 129.34, 129.53, 130.51, 132.10, 134.13, 144.63, 165.56	51.68 3.94 5.48 51.50 3.99 5.83
2k	1717, 1654, 1561, 1386, 1358	3.91 (s, 3 H, OCH_3), 5.08 (s, 2 H, CH_2), 7.26–7.41 (m, 3 H, aromatic), 7.87 (s, 1 H, CH)	52.81, 71.21, 126.80, 128.25, 130.76, 131.02, 133.90, 141.04, 164.89	45.54 3.13 4.83 45.61 3.15 5.00
2l	1708, 1637, 1556, 1387, 1357	3.90 (s, 3 H, OCH_3), 5.21 (s, 2 H, CH_2), 7.19 (d, *J* = 7.6 Hz, 1 H, aromatic), 7.30 (dd, *J* = 7.9, 7.6 Hz, 1 H, aromatic), 7.55 (d, *J* = 7.9 Hz, 1 H, aromatic), 8.19 (s, 1 H, CH)	52.79, 71.47, 124.30, 127.39, 127.80, 131.59, 132.12, 133.96, 134.19, 144.01, 165.22	45.54 3.13 4.83 45.85 3.13 4.67

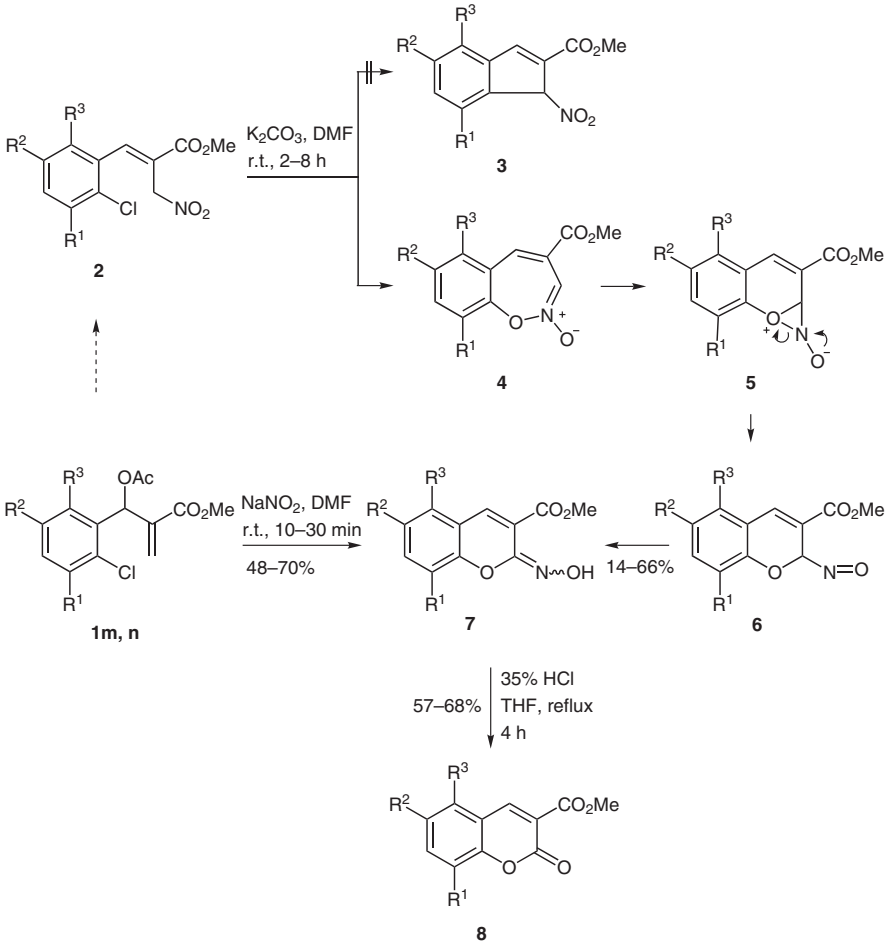
1 h. The reaction mixture was diluted with water (15 mL) and extracted with Et_2O (3 × 30 mL). The combined organic layers were dried over anhyd $MgSO_4$ and the solvent was evaporated in vacuo. The resulting mixture was chromatographed on silica gel eluting with hexane–EtOAc (4:1) to afford pure **2a–l**.

The physical and spectral data of **2a–l** prepared by this general method are listed in Table 1 and Table 2.

Methyl 2-Hydroxyimino-2*H*-chromene-3-carboxylate (7j)

K_2CO_3 (207 mg, 1.5 mmol) was added to the solution of **2j** (256 mg, 1.0 mmol) in DMF (5 mL) and stirred at r.t. for 8 h. The reaction mixture was neutralized with dilute aq HCl solution and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhyd $MgSO_4$ and the solvent was evaporated in vacuo. The resulting mixture was chromatographed on silica gel eluting with hexane–EtOAc (2:1) to afford **7j** (31 mg, 14%) as a yellow solid; mp 217–219 °C.

IR (KBr): 3423, 1725, 1643, 1603, 1450, 1438, 1351 cm^{-1}.



1, 2, 7, 8	R^1	R^2	R^3
j	H	H	H
k	H	H	Cl
l	Cl	H	H
m	H	NO_2	H
n	NO_2	H	Cl

Scheme 2

^{1}H NMR (DMSO-d_6): δ = 3.78 (s, 3 H, OCH_3), 7.16–7.21 (m, 2 H, aromatic), 7.43–7.55 (m, 2 H, aromatic), 7.63 (s, 1 H, CH), 10.77 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 52.47, 115.20, 118.52, 120.79, 124.09, 129.15, 132.29, 133.42, 145.33, 152.52, 163.85.

HRMS (EI): *m*/*z* calcd for $C_{11}H_9NO_4$: 219.0532; found: 219.0530.

Methyl 5-Chloro-2-hydroxyimino-2*H*-chromene-3-carboxylate (7k)

K_2CO_3 (207 mg, 1.5 mmol) was added to the solution of **2k** (290 mg, 1.0 mmol) in DMF (5 mL) and stirred at r.t. for 2 h. The reaction mixture was neutralized with dilute aq HCl solution and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhyd $MgSO_4$ and the solvent was evaporated in vacuo. The residue was crystallized with EtOAc to give **7k** (167 mg, 66%) as a yellow solid; mp 243–245 °C.

IR (KBr): 3435, 1727, 1646, 1604, 1594, 1450, 1353 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 3.80 (s, 3 H, OCH_3), 7.19 (d, *J* = 8.2 Hz, 1 H, aromatic), 7.32 (d, *J* = 8.2 Hz, 1 H, aromatic), 7.46 (dd, *J* = 8.2, 8.2 Hz, 1 H, aromatic), 7.62 (s, 1 H, CH), 11.01 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 52.76, 114.69, 116.89, 122.53, 124.76, 128.35, 131.76, 132.87, 144.76, 153.52, 163.48.

MS: *m*/*z* (%) = 255 (33), 253 (95) [M$^+$], 221 (100), 191 (72), 177 (24), 163 (22), 135 (29), 114 (65).

HRMS (EI): *m*/*z* calcd for $C_{11}H_8{}^{35}ClNO_4$: 253.0142; found: 253.0172.

Methyl 8-Chloro-2-hydroxyimino-2*H*-chromene-3-carboxylate (7l)

K_2CO_3 (207 mg, 1.5 mmol) was added to the solution of **2l** (290 mg, 1.0 mmol) in DMF (5 mL) and stirred at r.t. for 6 h. The work-up procedure was the same as described above to give **7l** (127 mg, 50%) as a yellow solid; mp 217–219 °C.

IR (KBr): 3395, 1705, 1650, 1612, 1455, 1434, 1373 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 3.79 (s, 3 H, OCH_3), 7.18 (dd, *J* = 7.9, 7.9 Hz, 1 H, aromatic), 7.50 (d, *J* = 7.9 Hz, 1 H, aromatic), 7.58 (d, *J* = 7.9 Hz, 1 H, aromatic), 7.64 (s, 1 H, CH), 10.95 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 52.53, 119.20, 120.36, 121.48, 124.62, 127.91, 132.25, 132.84, 144.47, 147.99, 163.50.

MS: *m*/*z* (%) = 255 (32), 253 (100) [M$^+$], 221 (89), 191 (48), 177 (22), 163 (12), 135 (8), 114 (20).

HRMS (EI): *m*/*z* calcd for $C_{11}H_8{}^{35}ClNO_4$: 253.0142; found: 253.0151.

Methyl 6-Nitro-2-hydroxyimino-2*H*-chromene-3-carboxylate (7m)

$NaNO_2$ (104 mg, 1.5 mmol) was added to the solution of the Baylis–Hillman acetate **1m** (314 mg, 1.0 mmol) in DMF (5 mL) and stirred at r.t. for 30 min. The reaction mixture was quenched by water (15 mL). The precipitated solid was collected by filtration and dried in vacuo to give **7m** (185 mg, 70%) as a yellow solid; mp 259–260 °C.

IR (KBr): 3423, 1703, 1655, 1613, 1570, 1531, 1514, 1377, 1340, 1292 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 3.83 (s, 3 H, OCH_3), 7.41 (d, *J* = 9.2 Hz, 1 H, aromatic), 7.78 (s, 1 H, CH), 8.29 (dd, *J* = 9.2, 2.8 Hz, 1 H, aromatic), 8.52 (d, *J* = 2.8 Hz, 1 H, aromatic), 11.18 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 52.76, 116.55, 119.56, 122.71, 124.80, 127.19, 131.68, 143.36, 144.46, 156.63, 163.45.

MS: *m*/*z* (%) = 264 (100) [M$^+$], 232 (92), 202 (63), 186 (35), 158 (36), 114 (41).

HRMS (EI): *m*/*z* calcd for $C_{11}H_8N_2O_6$: 264.0382; found: 264.0380.

Methyl 5-Chloro-8-nitro-2-hydroxyimino-2*H*-chromene-3-carboxylate (7n)

$NaNO_2$ (104 mg, 1.5 mmol) was added to the solution of the Baylis–Hillman acetate **1n** (348 mg, 1.0 mmol) in DMF (5 mL) and stirred at r.t. for 10 min. The reaction mixture was quenched by water (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over anhyd $MgSO_4$ and the solvent was evaporated in vacuo. The residue was crystallized with EtOAc to give **7n** (143 mg, 48%) as a yellow solid; mp 235–236 °C.

IR (KBr): 3449, 1731, 1641, 1613, 1590, 1571, 1449, 1345, 1255 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 3.82 (s, 3 H, OCH_3), 7.49 (d, *J* = 9.2 Hz, 1 H, aromatic), 7.64 (s, 1 H, CH), 8.07 (d, *J* = 9.2 Hz, 1 H, aromatic), 11.28 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 52.91, 119.28, 123.47, 124.35, 127.50, 127.64, 135.59, 136.38, 142.82, 146.24, 162.83.

MS: *m*/*z* (%) = 300 (33), 298 (100) [M$^+$], 266 (86), 236 (45), 222 (23), 192 (15), 148 (30).

HRMS (EI): *m*/*z* calcd for $C_{11}H_7{}^{35}ClN_2O_6$: 297.9993; found: 297.9985.

Methyl 2-Oxo-2*H*-chromene-3-carboxylate (8j)

To a solution of oxime **7j** (219 mg, 1.0 mmol) in THF (3 mL) was added 35% HCl (0.16 mL, 1.5 mmol) and stirred at reflux temperature for 4 h. The reaction mixture was concentrated under reduced pressure and the residue was partitioned between CH_2Cl_2 (20 mL) and water (5 mL). The organic layer was separated, dried and evaporated in vacuo. The resulting residue was chromatographed on silica gel eluting with hexane–EtOAc (2:1) to afford **8j** (138 mg, 68%) as a white solid after it was crystallized with Et_2O; mp 107–109 °C (lit.[30] 107–109).

IR (KBr): 1738, 1703, 1613, 1566, 1459, 1261 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.97 (s, 3 H, OCH_3), 7.35–7.39 (m, 2 H, aromatic), 7.62–7.67 (m, 2 H, aromatic), 8.58 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 52.89, 116.43, 117.84, 117.94, 124.88, 129.55, 134.45, 149.25, 155.21, 156.67, 163.69.

MS: *m*/z (%) = 204 (79) [M$^+$], 173 (100), 146 (70), 89 (75), 63 (50).

Methyl 5-Chloro-2-oxo-2*H*-chromene-3-carboxylate (8k)

To a solution of oxime **7k** (254 mg, 1.0 mmol) in THF (3 mL) was added 35% HCl (0.16 mL, 1.5 mmol) and stirred at reflux temperature for 4 h. The work-up procedure was the same as described above to afford **8k** (150 mg, 63%) as a white solid after it was crystallized with Et_2O; mp 135–137 °C.

IR (KBr): 1746, 1720, 1608, 1563, 1450, 1294 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.98 (s, 3 H, OCH_3), 7.28 (d, *J* = 8.2 Hz, 1 H, aromatic), 7.39 (dd, *J* = 7.9, 0.9 Hz, 1 H, aromatic), 7.58 (dd, *J* = 8.2, 8.2 Hz, 1 H, aromatic), 8.90 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 53.04, 115.59, 116.53, 118.59, 125.45, 134.04, 134.35, 145.14, 155.82, 155.89, 163.24.

MS: *m*/*z* (%) = 240 (25), 238 (51) [M$^+$], 207 (100), 180 (54), 123 (34).

HRMS (EI): *m*/*z* calcd for $C_{11}H_7{}^{35}ClO_4$: 238.0033; found: 238.0047.

Methyl 8-Chloro-2-oxo-2*H*-chromene-3-carboxylate (8l)

To a solution of oxime **7l** (254 mg, 1.0 mmol) in THF (3 mL) was added 35% HCl (0.16 mL, 1.5 mmol) and stirred at reflux temperature for 4 h. The work-up procedure was the same as described in the preparation of **8j** to afford **8l** (150 mg, 63%) as a white solid after it was crystallized with Et_2O; mp 133–135 °C.

IR (KBr): 1758, 1698, 1614, 1561, 1452, 1316 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.97 (s, 3 H, OCH_3), 7.29 (dd, *J* = 7.9, 7.6 Hz, 1 H, aromatic), 7.54 (dd, *J* = 7.6, 1.2 Hz, 1 H, aromatic), 7.73 (dd, *J* = 7.9, 1.2 Hz, 1 H, aromatic), 8.55 (s, 1 H, CH).

^{13}C NMR ($CDCl_3$): δ = 53.13, 118.75, 119.06, 121.81, 125.03, 128.01, 134.64, 148.61, 150.88, 155.42, 163.36.

MS: *m*/*z* (%) = 240 (7), 238 (22) [M$^+$], 207 (100), 180 (60), 123 (36).

HRMS (EI): *m*/*z* calcd for $C_{11}H_7{}^{35}ClO_4$: 238.0033; found: 238.0028.

Methyl 6-Nitro-2-oxo-2*H*-chromene-3-carboxylate (8m)

To a solution of oxime **7m** (264 mg, 1.0 mmol) in THF (3 mL) was added 35% HCl (0.16 mL, 1.5 mmol) and stirred at reflux temperature for 4 h. The work-up procedure was the same as described in the preparation of **8j** to afford **8m** (160 mg, 64%) as a white solid after it was crystallized with MeOH; mp 219–220 °C. (lit.[37] 220–221).

IR (KBr): 1779, 1696, 1619, 1570, 1523, 1478, 1349, 1307 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.00 (s, 3 H, OCH_3), 7.51 (d, *J* = 9.1 Hz, 1 H, aromatic), 8.50 (dd, *J* = 9.1, 2.5 Hz, 1 H, aromatic), 8.57 (d, *J* = 2.5 Hz, 1 H, aromatic), 8.62 (s, 1 H, CH).

^{13}C NMR (DMSO-d_6): δ = 52.71, 117.77, 118.17, 119.18, 126.09, 128.65, 143.65, 147.94, 154.99, 158.09, 162.62.

MS: *m*/*z* (%) = 249 (50) [M$^+$], 218 (100), 191 (51), 172 (48), 88 (31), 62 (25).

Methyl 5-Chloro-8-nitro-2-oxo-2*H*-chromene-3-carboxylate (8n)

To a solution of oxime **7n** (299 mg, 1.0 mmol) in THF (3 mL) was added 35% HCl (0.16 mL, 1.5 mmol) and stirred at reflux temperature for 4 h. The work-up procedure was the same as described in the preparation of **8j** to afford **8n** (162 mg, 57%) as a white solid after it was crystallized with MeOH; mp 210–212 °C.

IR (KBr): 1775, 1711, 1608, 1563, 1536, 1453, 1356, 1266 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.00 (s, 3 H, OCH_3), 7.51 (d, *J* = 8.6 Hz, 1 H, aromatic), 8.19 (d, *J* = 8.6 Hz, 1 H, aromatic), 8.89 (s, 1 H, CH).

^{13}C NMR (DMSO-d_6): δ = 53.33, 118.30, 119.73, 125.39, 130.41, 135.76, 138.74, 143.85, 148.15, 153.96, 162.54.

MS: *m*/*z* (%) = 285 (38), 283 (100) [M^+], 252 (87), 225 (34), 206 (17), 178 (21), 150 (16), 122 (14), 87 (34).

HRMS (EI): *m*/*z* calcd for $C_{11}H_6{}^{35}ClNO_6$: 282.9884; found: 282.9871.

Acknowledgment

This study was supported by a grant of the Korea Health 21 R & D Project, Ministry of Health & Welfare, Republic of Korea (01-PJ1-01CH03-0003).

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