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# Reexamination of the traditional Baylis–Hillman reaction

Min Shi,* Chao-Qun Li and Jian-Kang Jiang

*Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, People's Republic of China*

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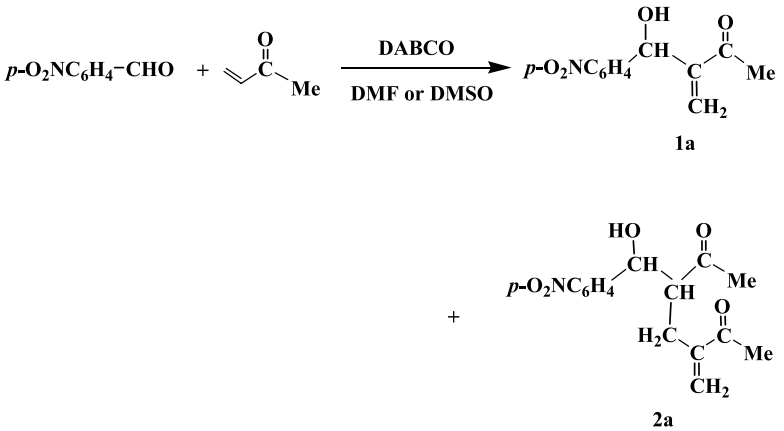
**Abstract**—In the Baylis–Hillman reaction of arylaldehydes with methyl vinyl ketone (MVK), we found that, besides the normal Baylis–Hillman adduct **1**, the diadduct **2** can also be formed at the same time and the yield of **2** can reach to 55% if increasing the amount of methyl vinyl ketone. But for ethyl vinyl ketone (EVK), methyl acrylate or acrylonitrile, only the normal Baylis–Hillman adduct **4**, **7** or **8** was obtained, respectively. The substituent's effects and Lewis base effects were also examined and a plausible reaction mechanism was proposed for the formation of **2**. 

## 1. Introduction

Recently, the Baylis–Hillman reaction has progressed,[1] and now includes a catalytic asymmetric version,[2] since Baylis and Hillman first reported the reaction of acetaldehyde with ethyl acrylate and acrylonitrile in the presence of catalytic amounts of 1,4-diazabicyclo[2,2,2]octane (DABCO) in 1972.[3] However, during our own investigation on this simple and useful reaction,[4] we found that, in the reaction of arylaldehydes with methyl vinyl ketone (MVK) or ethyl vinyl ketone (EVK) catalyzed by DABCO, the reaction products are not as simple as those reported before. For example, using *p*-nitrobenzaldehyde (1.0 equiv.) and MVK (2.0 equiv.) as substrates in the presence of catalytic amounts of DABCO (0.1 equiv.) in DMSO or DMF, we found that, besides the normal Baylis–Hillman reaction product **1a**, compound **2a** was also formed at the same time as a *syn* and *anti* mixture (2:3) (Scheme 1).[5]

The compound **2a** has never been realized as a Baylis–Hillman reaction product so far. In order to clarify this unexpected phenomenon, herein we wish to report our full results of the reexamination of the Baylis–Hillman reaction of arylaldehydes with MVK and EVK under the traditional Lewis base promoted reaction conditions. Moreover, a plausible reaction mechanism for the formation of **2** was proposed in this paper, along with the substituent's effects and the interesting Lewis base effects.




**Scheme 1.**

*Keywords*: Baylis–Hillman reaction; Lewis base; methyl vinyl ketone (MVK); ethyl vinyl ketone (EVK); DABCO; conjugated addition; DMAP.
* Corresponding author. Fax: +86-21-64166128; e-mail: mshi@pub.sioc.ac.cn

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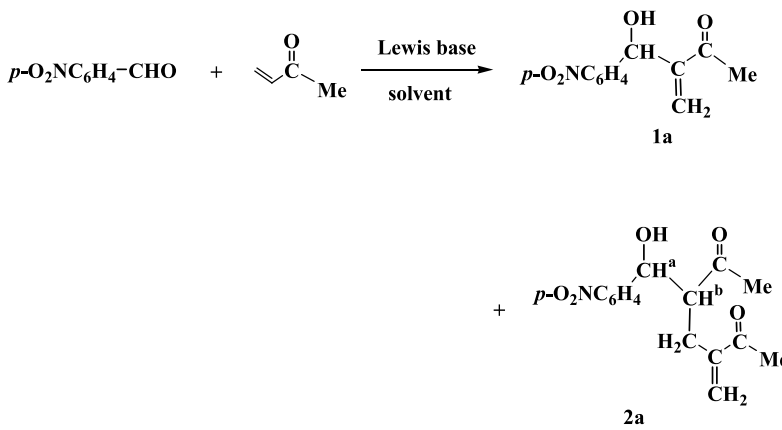
**Table 1**. Baylis–Hillman reactions of *p*-nitrobenzaldehyde (1.0 equiv.) with methyl vinyl ketone (2.0 equiv.) in the presence of Lewis base (0.1 equiv.)

| Entry | Lewis base | Solvent | Temperature (°C) | Time (h) | Yield (%)[a] | |
|---|---|---|---|---|---|---|
| | | | | | **1a** | **2a**[b] |
| 1 | DABCO | DMSO | 20 | 40 | 60 | 20 |
| 2 | DABCO | DMF | 20 | 40 | 63 | 23 |
| 3 | DABCO | $CH_2Cl_2$ | 20 | 40 | 61 | 34 |
| 4 | DMAP | DMSO | 20 | 40 | 85 | 0 |
| 5 | DMAP | DMF | 20 | 40 | 83 | 0 |
| 6 | DABCO | DMF[c] | 20 | 60 | 41 | 53 |
| 7 | DABCO | DMF[d] | 20 | 60 | 41 | 55 |
| 8 | DABCO | DMF[c] | −30 | 60 | 54 | 40 |
| 9[e] | DABCO | DMF[c] | 70 | 60 | 37 | 56 |

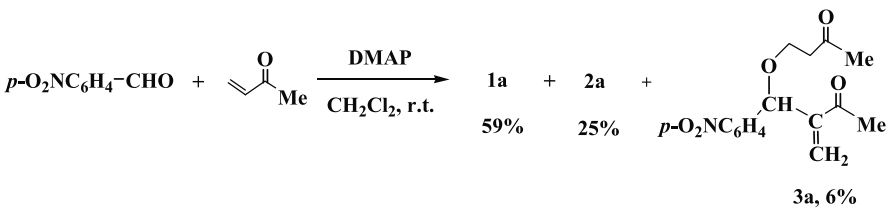
[a] Isolated yields.
[b] *syn*/*anti*=2:3.
[c] Mole ratio of aldehyde/MVK=1:4.
[d] Mole ratio of aldehyde/MVK=1:8.
[e] Dimer of MVK was formed.

as a Lewis base, **1a** and **2a** were formed at the same time along with the formation of **3a**, a Michael addition product of **1a** with MVK (Scheme 3). At present stage, we do not understand why **3a** could be formed in $CH_2Cl_2$ because no reactions occurred between benzyl alcohol or *sec*-phenethyl alcohol with MVK under the same reaction conditions (Scheme 4). Increasing the amount of MVK in reaction system raised the yields of **2a**. Using 4.0 or 8.0 equiv. of MVK, the yields of **2a** were 53 and 55%, respectively (Table 1, entries 6 and 7). The reaction temperatures slightly affected the yields of **2a** (Table 1, entries 8 and 9). However, at higher temperature, the dimer of MVK was formed as well. Thus, based on our own investigations, the compound **2a** can never be realized as a side reaction product of Baylis–Hillman reaction. As a matter of fact, another important reaction process operates in the traditional Baylis–Hillman reaction.

For *m*-nitrobenzaldehyde, *p*-bromo-, *p*-chlorobenzaldehyde, 2- or 3-pyridylaldehyde, or *trans*-cinnamaldehyde the



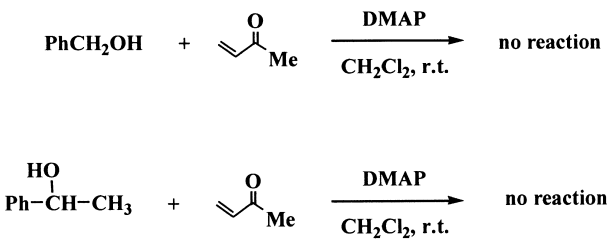

**Scheme 2.**



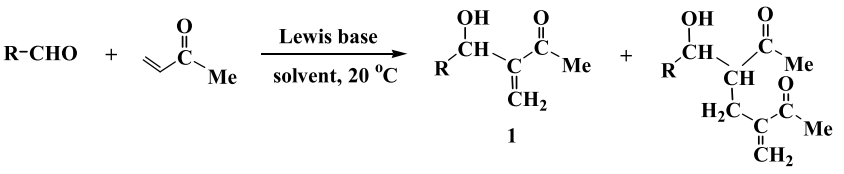

**Scheme 3.**

## 2. Results and discussion

As shown in Table 1, we found that the Lewis base played a very important role in this reaction (Scheme 2, Table 1). Using DABCO as a Lewis base, two products **1a** and **2a** were obtained at the same time (Table 1, entries 1–3). The *syn* and *anti* ratio of **2a** was determined by the $^1H$ NMR spectral data based on the *J* value of $H^a$ and $H^b$ (Scheme 2) because *anti*-isomer usually has bigger *J* value (for *anti*-**2a**: $JH^aH^b$=6.3 Hz, for *syn*-**2a**: $JH^aH^b$=2.8 Hz). DMF, DMSO or $CH_2Cl_2$ generally gave the similar results. When *p*-dimethylaminopyridine (DMAP) as a Lewis base in DMSO or DMF was used, **1a** was exclusively obtained in high yields under the same reaction conditions (Scheme 2, Table 1, entries 4 and 5). However, in $CH_2Cl_2$ using DMAP similar results were obtained (Scheme 5, Table 2, entries 1–3, 8 and 9, 11, 17, 19). Using DMAP as a Lewis base, **1** was exclusively formed as well (Scheme 5, Table 2, entries 4, 10, 12, 16, 18, 20). For benzaldehyde or aliphatic




**Scheme 4.**




**b: R= *m*-$NO_2C_6H_4$, c: R= *o*-$NO_2C_6H_4$, d: R= *p*-$BrC_6H_4$, e: R= *p*-$ClC_6H_4$, f: R= $C_6H_5$, g: R= *p*-$EtC_6H_4$, h: R= 2-pyridyl, i: R= 3-pyridyl, j: R= $C_6H_5CH$=CH, k: R= $CH_3(CH_2)_3$.**

**Scheme 5.**

**Table 2**. Baylis–Hillman reactions of aldehydes (1.0 equiv.) with methyl vinyl ketone (2.0 equiv.) in the presence of Lewis base (0.1 equiv.)

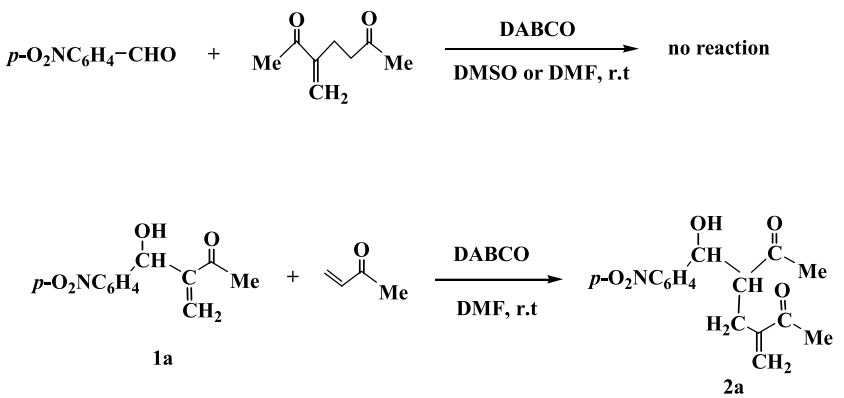
| Entry | R | Lewis base | Solvent | Time (h) | Yield (%)[a] | |
|---|---|---|---|---|---|---|
| | | | | | **1** | **2** (*syn*/*anti*) |
| 1 | *m*-$NO_2C_6H_4$ | DABCO | DMSO | 20 | 50 | 27 (1:1) |
| 2 | *m*-$NO_2C_6H_4$ | DABCO | DMF | 20 | 50 | 27 (1:1) |
| 3 | *m*-$NO_2C_6H_4$ | DABCO | DMF[b] | 20 | 50 | 41 (1:1) |
| 4 | *m*-$NO_2C_6H_4$ | DMAP | DMF | 20 | 87 | 0 |
| 5 | *o*-$NO_2C_6H_4$ | DABCO | DMF | 50 | 83 | 0 |
| 6 | *o*-$NO_2C_6H_4$ | DMAP | DMF | 20 | 83 | 0 |
| 7 | *o*-$NO_2C_6H_4$ | DMAP | $CH_2Cl_2$ | 40 | 81 | 0 |
| 8 | *p*-$BrC_6H_4$ | DABCO | DMF | 140 | 57 | 25 (1:3) |
| 9 | *p*-$BrC_6H_4$ | DABCO | DMF[b] | 80 | 51 | 36 (1:3) |
| 10 | *p*-$BrC_6H_4$ | DMAP | DMF | 120 | 88 | 0 |
| 11 | *p*-$BrC_6H_4$ | DABCO | DMF[b] | 160 | 62 | 33 (1:1) |
| 12 | *p*-$BrC_6H_4$ | DMAP | DMF | 60 | 67 | 0 |
| 13 | $C_6H_5$ | DMAP | DMF | 90 | 73 | 0 |
| 14 | $C_6H_5$ | DMAP | DMF | 130 | 54 | 0 |
| 15 | *p*-$EtC_6H_4$ | DMAP | DMF | 7d | 0 | 0 |
| 16 | 2-Pyridyl | DMAP | DMF[b] | 90 | 60 | 0 |
| 17 | 2-Pyridyl | DABCO | DMF[b] | 60 | 57 | 24 (3:2) |
| 18[c] | 3-Pyridyl | DMAP | DMF[b] | 90 | 70 | 0 |
| 19 | $C_6H_5CH$=CH | DABCO | DMF[b] | 60 | 57 | 24 (1:1) |
| 20 | $C_6H_5CH$=CH | DMAP | DMF[b] | 49 | 60 | 0 |
| 21[d] | $CH_3(CH_2)_3$ | DABCO | DMF[b] | 49 | 15 | 0 |

[a] Isolated yields.
[b] Mole ratio of aldehyde/MVK=1:4.
[c] Compound **3i** was formed in 10%.
[d] Dimer of MVK was formed.

aldehyde, only the corresponding normal Baylis–Hillman adducts **1** were formed under the same reaction conditions (Scheme 5, Table 2, entries 13, 21). For *p*-ethylbenzaldehyde, no reactions occurred (Scheme 5, Table 2, entry 15). But we surprisingly found that, for *o*-nitrobenzaldehyde, the Baylis–Hillman adduct **1** was produced as the single product under the same reaction conditions (Table 2, entries 5–7). This result suggested that *o*-nitro group on the phenyl ring could block out the further reaction of **1** with MVK.

In Baylis–Hillman reaction for simple methyl vinyl ketone (MVK), this phenomenon has never been reported before. Only in the reaction of dicarbonyl compounds with acrylonitrile in the presence of DABCO, the diadduct, which was thought to be derived either from reaction of acrylonitrile dimer with starting material or from the conjugated addition of the anion derived from a second molecule of acrylonitrile to the Baylis–Hillman adduct, was obtained as a minor product.[6] In order to clarify the true formation route of **2a**, we carried out the reactions of **1a** (1.0 equiv.) with MVK (2.0–8.0 equiv.) and *p*-nitrobenzaldehyde (1.0 equiv.) with MVK dimer (1.0 equiv.) in the presence of catalytic amounts of DABCO (0.1 equiv.), respectively (Scheme 6). We found that, **2a** was formed indeed from the reaction of **1a** with methyl vinyl ketone (MVK) in the presence of catalytic amounts of DABCO (0.1 equiv.) with *syn* and *anti* mixture (2:3), but no reactions occurred between *p*-nitrobenzaldehyde and MVK dimer under the same reaction conditions (Scheme 6). The yield of **2a** can reach to 41 or 48% using 4.0 or 8.0 equiv. of MVK, respectively (Table 3, entries 2 and 3).

Thus, we can conclude that two reaction processes occur for the traditional Baylis–Hillman reaction of arylaldehydes with MVK. One is the normal Baylis–Hillman reaction which is the 1,2-addition of the anion derived from MVK to *p*-nitrobenzaldehyde. Another is the conjugated addition (Michael addition) of the anion derived from a second molecule of MVK to **1**. In Scheme 7, we elucidated the plausible reaction mechanism for the formation of **2**.



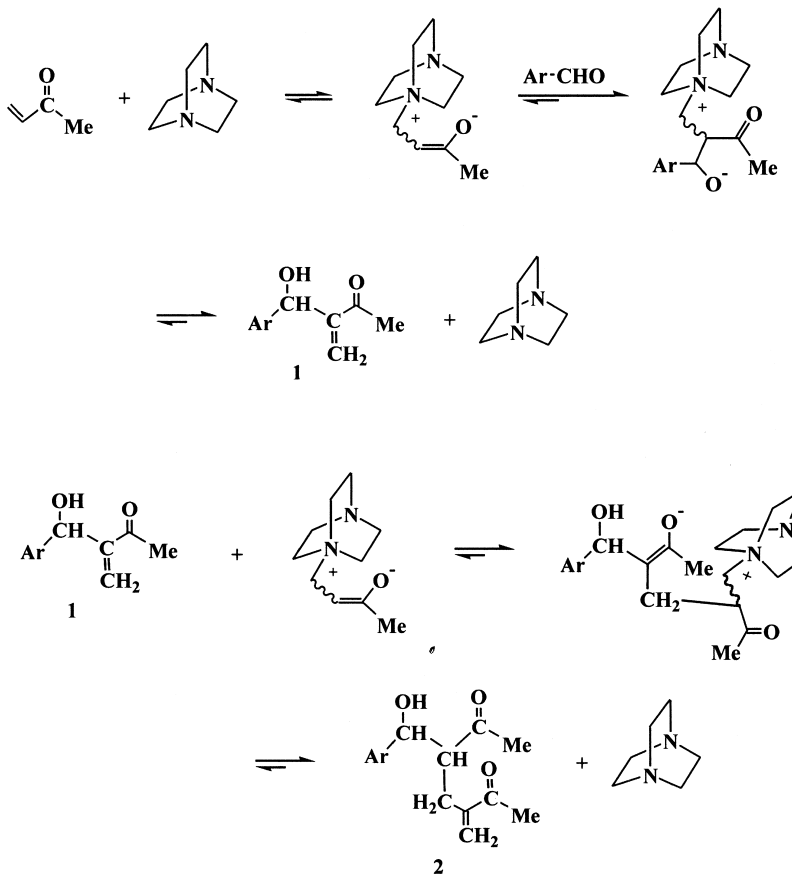

**Scheme 6.**

**Table 3**. Baylis–Hillman reactions of *p*-nitrobenzaldehyde with methyl vinyl ketone in the presence of Lewis base (0.1 equiv.)

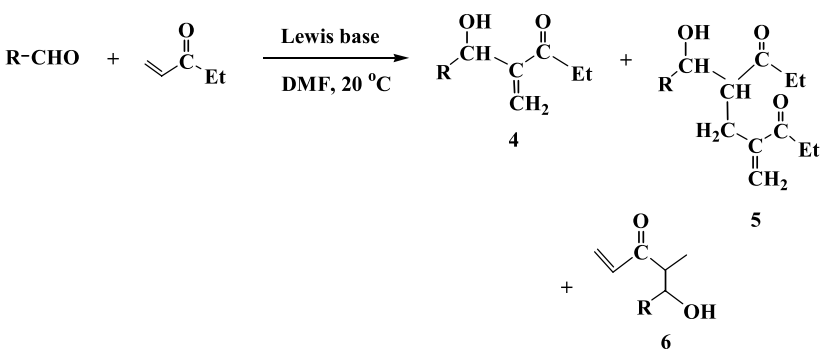
| Entry | Lewis base | **1a**/MVK | Time (h) | Yield (%)[a] of **2a**[b] |
|---|---|---|---|---|
| 1 | DABCO | 1:2 | 48 | 29 |
| 2 | DABCO | 1:4 | 48 | 41 |
| 3 | DABCO | 1:8 | 48 | 48 |

[a] Isolated yields.
[b] *syn*/*anti*=2:3.

On the other hand, we also examined the reaction of ethyl vinyl ketone (EVK) with aldehydes under the same reaction conditions (Scheme 8, Table 4). We found that the reaction rates were relatively slower than those using MVK as a substrate. In the reaction of *p*-nitrobenzaldehyde, *m*-nitrobenzaldehyde, pyridylaldehyde or *trans*-cinnamaldehyde with EVK, the diadduct **5** was only obtained in very low yields (trace amount) (Table 4, entries 1 and 2, entries 7–9). For *p*-bromo-, *p*-chloro-, or *p*-ethylbenzaldehyde, no




**Scheme 7.**



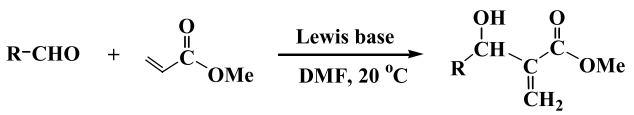

**a**: R= *p*-$NO_2C_6H_4$, **b**: R= *m*-$NO_2C_6H_4$, **c**: R= *o*-$NO_2C_6H_4$, **d**: R= *p*-$BrC_6H_4$, **e**: R= *p*-$ClC_6H_4$, **f**: R= $C_6H_5$, **g**: 2-pyridyl, **h**: R= 3-pyridyl, **i**: R= $C_6H_5CH$=CH.

**Scheme 8.**

**Table 4**. Baylis–Hillman reactions of aldehydes (1.0 equiv.) with methyl vinyl ketone (4.0 equiv.) in the presence of Lewis base (0.1 equiv.)

| Entry | R | Lewis base | Time (h) | Yield (%)[a] | | |
|---|---|---|---|---|---|---|
| | | | | **4** | **5** | **6** |
| 1 | *p*-$NO_2C_6H_4$ | DABCO | 60 | 80 | Trace | 0 |
| 2 | *m*-$NO_2C_6H_4$ | DABCO | 60 | 81 | Trace | 0 |
| 3 | *o*-$NO_2C_6H_4$ | DABCO | 60 | 41 | 0 | 40 |
| 4 | *p*-$BrC_6H_4$ | DABCO | 80 | 0 | 0 | 0 |
| 5 | *p*-$ClC_6H_4$ | DABCO | 80 | 0 | 0 | 0 |
| 6 | $C_6H_5$ | DABCO | 80 | 0 | 0 | 0 |
| 7 | 2-Pyridyl | DABCO | 60 | 83 | Trace | 0 |
| 8 | 3-Pyridyl | DABCO | 60 | 82 | Trace | 0 |
| 9 | $C_6H_5CH{=}CH$ | DABCO | 60 | 70 | Trace | 0 |

[a] Isolated yields.

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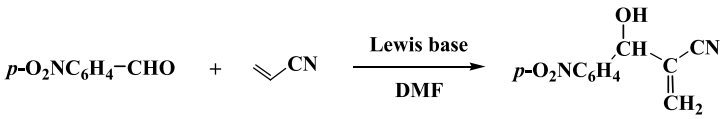
**a: R= *p*-$NO_2C_6H_4$, b: R= *m*-$NO_2C_6H_4$.**

**Scheme 9.**

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**Scheme 10.**

reactions occurred under the same reaction conditions (Scheme 8, Table 4, entries 4–6). In addition, we surprisingly found that, in the reaction of *o*-nitrobenzaldehyde with EVK, an aldol reaction product **6** was obtained along with the normal Baylis–Hillman adduct **4** (Table 4, entry 3). This phenomenon has never been disclosed before.

**Table 5**. Baylis–Hillman reactions of aldehydes (1.0 equiv.) with methyl vinyl ketone (4.0 equiv.) in the presence of Lewis base (0.1 equiv.)

| Entry | R | Lewis base | Time (h) | Yield (%)[a] of **7** |
|---|---|---|---|---|
| 1 | *p*-$NO_2C_6H_4$ | DABCO | 45 | 85 |
| 2 | *p*-$NO_2C_6H_4$ | DMAP | 45 | 80 |
| 3 | *m*-$NO_2C_6H_4$ | DABCO | 22 | 87 |
| 4 | *m*-$NO_2C_6H_4$ | DMAP | 22 | 60 |

[a] Isolated yields.

**Table 6**. Baylis–Hillman reactions of *p*-nitrobenzaldehyde (1.0 equiv.) with acrylonitrile (4.0 equiv.) in the presence of Lewis base (0.1 equiv.)

| Entry | R | Lewis base | Time (h) | Yield (%)[a] of **8** |
|---|---|---|---|---|
| 1 | *p*-$NO_2C_6H_4$ | DABCO | 120 | 70 |
| 2 | *p*-$NO_2C_6H_4$ | DMAP | 120 | 20 |

[a] Isolated yields.

This result suggested that, for some substrates, the Baylis–Hillman reaction can accompany a normal aldol condensation reaction. At present, we cannot give a reasonable explanation for the formation of **6** in the Baylis–Hillman reaction of *o*-nitrobenzaldehyde with EVK.

It should be emphasized here that, for methyl acrylate and acrylonitrile under the traditional Baylis–Hillman reaction conditions, only the corresponding normal Baylis–Hillman adduct **7** or **8** was obtained (Schemes 9 and 10). The results are summarized in Tables 5 and 6, respectively. Using DABCO as a Lewis base in DMF or DMSO, the reaction rates are fairly faster. The Baylis–Hillman adducts **7** or **8** could be obtained in good yields.

In conclusion, we found that, in the Baylis–Hillman reaction of arylaldehydes with methyl vinyl ketone, besides the normal Baylis–Hillman adduct **1**, diadduct **2** was formed at the same time which was confirmed to be derived from the further reaction of **1** with MVK via a conjugated addition. Efforts are underway to elucidate the mechanistic details of this reaction and to disclose the scope and limitations of this reaction. Work along this line is currently in progress.

## 3. Experimental

### 3.1. General

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 Hz. Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA+ mass spectrometer. Organic solvents were dried by standard methods when necessary. Some of the solid compounds reported in this paper gave satisfactory CHN microanalyses with a Carlo-Erba 1106 analyzer. 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.

### 3.2. Typical reaction procedure for the Baylis–Hillman reaction

To DABCO (11 mg, 0.10 mmol) and *p*-nitrobenzaldehyde (76 mg, 0.50 mmol) in DMF solution (0.50 mL) was added methyl vinyl ketone (MVK) (140 mg, 166 μL, 2.0 mmol) and the reaction mixture was stirred at room temperature for

40 h. The reaction product was extracted by dichloromethane (10.0 mL) and washed with water (10 mL×3). The organic layer was dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatography to give compound **1a** (70 mg, 63%) as a colorless solid and **2a** (34 mg, 23%) as a colorless oil (eluent: ethyl acetate/petroleum ether=1:4).

**3.2.1. Compound 1a.** Mp 76–77°C. IR (KBr) $\nu$ 3483 (O–H), 2935, 1658 (C=O), 1305, 856 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.37 (3H, s, Me), 3.34 (1H, d, $J$=5.3 Hz, OH), 5.69 (1H, d, $J$=5.3 Hz), 6.04 (1H, s), 6.28 (1H, s), 7.56 (2H, d, $J$=8.6 Hz, Ar), 8.25 (2H, d, $J$=8.6 Hz, Ar); MS (EI) $m/z$ 220 ($M^+-1$, 20.9), 204 ($M^+-17$, 100), 174 ($M^+-47$, 88.1). [Found: HRMS (EI) $m/z$ 222.0749 $(M+1)^+$; $C_{11}H_{12}O_4N$ requires M+1, 222.0766].

**3.2.2. Compound 2a.** *syn*-**2a**. IR (KBr) $\nu$ 3483 (O–H), 2935, 1658 (C=O), 1520, 856 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.04 (3H, s, Me), 2.25 (3H, s, Me), 2.52 (1H, dd, $J$=13.8, 5.2 Hz, CH), 2.60 (1H, dd, $J$=13.8, 7.9 Hz, CH), 3.15–3.25 (1H, m, CH), 3.67 (1H, d, $J$=2.8 Hz, OH), 5.0 (1H, dd, $J$=2.8, 2.4 Hz, CH), 5.73 (1H, s), 5.97 (1H, s), 7.53 (2H, d, $J$=9.4 Hz, Ar), 8.20 (2H, d, $J$=9.4 Hz, Ar); MS (EI) $m/z$ 274 ($M^+-18$, 13.2), 232 ($M^+-59$, 24.5), 97 ($M^+-194$, 44), 43 ($M^+-248$, 100). [Found: HRMS (EI) $m/z$ 292.1198 $(M+1)^+$; $C_{15}H_{18}O_5N$ requires M+1, 292.1185].

*anti*-**2a**. IR (KBr) $\nu$ 3483 (O–H), 2935, 1658 (C=O), 1305, 856 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.07 (3H, s, Me), 2.37 (3H, s, Me), 2.52 (1H, dd, $J$=13.8, 5.2 Hz, CH), 2.60 (1H, dd, $J$=13.8, 7.9 Hz, CH), 3.15–3.25 (1H, m, CH), 3.76 (1H, d, $J$=7.4 Hz, OH), 4.80 (1H, dd, $J$=7.9, 7.4 Hz, CH), 5.92 (1H, s), 6.12 (1H, s), 7.55 (2H, d, $J$=9.4 Hz, Ar), 8.22 (2H, d, $J$=9.4 Hz, Ar); MS (EI) $m/z$ 274 ($M^+-18$, 13.2), 232 ($M^+-59$, 24.5), 97 ($M^+-194$, 44), 43 ($M^+-248$, 100). [Found: HRMS (EI) $m/z$ 292.1198 $(M+1)^+$; $C_{15}H_{18}O_5N$ requires M+1, 292.1185].

**3.2.3. Compound 3a.** The compound **3a** was obtained in the reaction of *p*-nitrobenzaldehyde (76 mg, 0.50 mmol) with methyl vinyl ketone (140 mg, 166 μL, 2.0 mmol) in dichloromethane using DMAP as a Lewis base as a colorless oil (10 mg, 6%). IR (KBr) $\nu$ 2923, 1712 and 1675 (C=O), 1520, 856 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.15 (3H, s, Me), 2.20 (3H, s, Me), 2.69 (2H, t, $J$=7.2 Hz, $CH_2$), 3.50–3.62 (1H, m, CH), 3.62–3.74 (1H, m, CH), 5.4 (1H, s), 6.17 (1H, s), 6.23 (1H, s), 7.53 (2H, d, $J$=9.4 Hz, Ar), 8.20 (2H, d, $J$=9.4 Hz, Ar); MS (EI) $m/z$ 291 ($M^+$, 3.2), 274 ($M^+-18$, 10.5), 72 ($M^+-219$, 24.2), 43 ($M^+-248$, 100). [Found: HRMS (EI) $m/z$ 291.1100 ($M^+$); $C_{15}H_{17}O_5N$ requires M, 291.1107].

The spectral data of MVK dimer. A colorless oil. IR (KBr) $\nu$ 3423 (O–H), 2933, 1714 and 1676 (C=O), 1430 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz) $\delta$ 2.07 (3H, s, Me), 2.29 (3H, s, Me), 2.40–2.54 (4H, m, $CH_2$), 5.80 (1H, s, CH), 6.0 (1H, s, CH); MS (EI) $m/z$ 141 ($MH^+$, 0.84), 125 ($M^+-15$, 60), 97 ($M^+-43$, 100), 43 ($M^+-97$, 100). [Found: HRMS (EI) $m/z$ 140.0834 ($M^+$); $C_8H_{12}O_2$ requires M, 140.0837].

Compounds **1b** and **2b** (*syn* and *anti* mixture) were prepared in the same manner as that described above.

**3.2.4. Compound 1b.** 55 mg, 50%; a colorless solid; mp 79–80°C. IR (KBr) $\nu$ 3431 (O–H), 2930, 1654 (C=O), 1585, 834 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.37 (3H, s, Me), 3.35 (1H, d, $J$=5.4 Hz, OH), 5.68 (1H, d, $J$=5.4 Hz), 6.09 (1H, s), 6.30 (1H, s), 7.56 (1H, dd, $J$=8.0, 8.0 Hz, Ar), 7.78 (1H, d, $J$=8.0 Hz, Ar), 8.16 (1H, d, $J$=8.0 Hz, Ar), 8.26 (1H, s, Ar); MS (EI) $m/z$ 221 ($M^+$, 5.0), 220 ($M^+-1$, 43.0), 204 ($M^+-17$, 85.4), 77 ($M^+-144$, 36.8), 43 ($M^+-178$, 100). [Found: HRMS (EI) $m/z$ 222.0766 $(M+1)^+$, $C_{11}H_{12}O_4N$ requires M+1, 222.0774].

**3.2.5. Compound 2b.** *syn*-**2b**+*anti*-**2b**, 60 mg, 41%.

*syn*-**2b**. IR (KBr) $\nu$ 3448 (O–H), 2929, 1676 and 1709 (C=O), 1520, 810 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.06 (3H, s, Me), 2.22 (3H, s, Me), 2.52 (1H, dd, $J$=13.5, 5.1 Hz, CH), 2.61 (1H, dd, $J$=13.5, 7.8 Hz, CH), 3.21–3.29 (1H, m, CH), 3.78 (1H, d, $J$=5.2 Hz, OH), 5.04 (1H, dd, $J$=5.2, 2.5 Hz, CH), 5.73 (1H, s), 5.96 (1H, s), 7.54 (1H, t, $J$=8.1 Hz, Ar), 7.64 (1H, d, $J$=8.1 Hz, Ar), 8.10–8.15 (1H, m, Ar), 8.26 (1H, s, Ar); MS (EI) $m/z$ 274 ($M^+-18$, 12.4), 232 ($M^+-59$, 20.0), 97 ($M^+-194$, 40.8), 43 ($M^+-248$, 100). [Found: HRMS (EI) $m/z$ 292.1185 $(M+1)^+$, $C_{15}H_{18}O_5N$ requires M+1, 292.1195].

*anti*-**2b**. IR (KBr) $\nu$ 3448 (O–H), 2929, 1676 and 1709 (C=O), 1520, 810 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.05 (3H, s, Me), 2.34 (3H, s, Me), 2.42 (1H, dd, $J$=13.5, 5.1 Hz, CH), 2.48 (1H, dd, $J$=13.5, 7.8 Hz, CH), 3.21–3.29 (1H, m, CH), 3.78 (1H, d, $J$=6.9 Hz, OH), 4.83 (1H, dd, $J$=7.0, 6.9 Hz, CH), 5.92 (1H, s), 6.01 (1H, s), 7.52 (1H, t, $J$=8.1 Hz, Ar), 7.69 (1H, d, $J$=8.1 Hz, Ar), 8.10–8.15 (1H, m, Ar), 8.17 (1H, s, Ar); MS (EI) $m/z$ 274 ($M^+-18$, 12.4), 232 ($M^+-59$, 20.0), 97 ($M^+-194$, 40.8), 43 ($M^+-248$, 100). [Found: HRMS (EI) $m/z$ 292.1185 $(M+1)^+$, $C_{15}H_{18}O_5N$ requires M+1, 292.1195].

**3.2.6. Compound 1c.** The title compound was prepared in the same manner as that described above. 92 mg, 83%; mp 75–76°C. IR (KBr) $\nu$ 3362 (O–H), 2961, 1663 (C=O), 1571, 859 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.39 (3H, s, Me), 3.53 (1H, d, $J$=4.1 Hz, OH), 5.80 (1H, s), 6.19 (1H, s), 6.25 (1H, d, $J$=4.1 Hz, CH), 7.50 (1H, dd, $J$=7.1, 7.1 Hz, Ar), 7.70 (1H, dd, $J$=7.6, 7.6 Hz, Ar), 7.79 (1H, d, $J$=7.6 Hz, Ar), 8.0 (1H, d, $J$=8.2 Hz, Ar); MS (EI) $m/z$ 204 ($M^+-17$, 31.0), 162 ($M^+-59$, 100), 144 ($M^+-77$, 26.5), 43 ($M^+-178$, 86.6). [Found: HRMS (EI) $m/z$ 222.0766 $(M+1)^+$, $C_{11}H_{12}O_4N$ requires M+1, 222.0771].

Compounds **1d** and **2d** (*syn* and *anti* mixture) were prepared in the same manner as that described above

**3.2.7. Compound 1d.** 65 mg, 51%. IR (KBr) $\nu$ 3423 (O–H), 2963, 1676 (C=O), 1487, 822 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.33 (3H, s, Me), 3.20 (1H, d, $J$=4.8 Hz, OH), 5.58 (1H, d, $J$=4.8 Hz, CH), 5.99 (1H, s), 6.22 (1H, s), 7.25 (2H, d, $J$=8.4 Hz, Ar), 7.48 (2H, d, $J$=8.4 Hz); MS (EI) $m/z$ 255 ($M^+$, 38.5), 239 ($M^+-17$, 10.3), 175 ($M^+-80$, 100), 157 ($M^+-98$, 45.1), 77 ($M^+-178$, 42.6), 43

($M^+-212$, 54.7). [Found: HRMS (EI) *m/z* 253.9946 ($M^+$), $C_{11}H_{11}O_2Br$ requires M, 253.9942].

**3.2.8. Compound 2d.** *syn*-**2d**+*anti*-**2d**: 59 mg, 36%.

*syn*-**2d**. IR (KBr) $\nu$ 3438 (O–H), 2926, 1676 and 1709 (C=O), 1592, 838 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.88 (3H, s, Me), 2.24 (3H, s, Me), 2.30 (1H, dd, *J*=13.5, 6.2 Hz, CH), 2.60 (1H, dd, *J*=13.5, 8.3 Hz, CH), 3.14–3.21 (1H, m, CH), 3.40 (1H, d, *J*=2.1 Hz, OH), 4.78 (1H, dd, *J*=2.1, 1.9 Hz, CH), 5.68 (1H, s), 5.96 (1H, s), 7.20 (2H, d, *J*=8.4 Hz, Ar), 7.50 (2H, d, *J*=8.4 Hz, Ar); MS (EI) *m/z* 307 ($M^+-18$, 7.1), 265 ($M^+-70$, 18.2), 185 ($M^+-150$, 66.5), 125 ($M^+-210$, 66.7), 97 ($M^+-238$, 68.2), 43 ($M^+-292$, 100). [Found: HRMS (EI) *m/z* 325.0446 $(M+1)^+$, $C_{15}H_{18}O_3Br$ requires M+1, 325.0439].

*anti*-**2d**. IR (KBr) $\nu$ 3438 (O–H), 2926, 1676 and 1709 (C=O), 1592, 838 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.01 (3H, s, Me), 2.30 (3H, s, Me), 2.17 (1H, dd, *J*=13.5, 6.2 Hz, CH), 2.48 (1H, dd, *J*=13.5, 8.3 Hz, CH), 3.14–3.21 (1H, m, CH), 3.40 (1H, d, *J*=6.4 Hz, OH), 4.68 (1H, dd, *J*=6.4, 6.3 Hz, CH), 5.83 (1H, s), 6.17 (1H, s), 7.20 (2H, d, *J*=8.4 Hz, Ar), 7.49 (2H, d, *J*=8.4 Hz, Ar); MS (EI) *m/z* 307 ($M^+-18$, 7.1), 265 ($M^+-70$, 18.2), 185 ($M^+-150$, 66.5), 125 ($M^+-210$, 66.7), 97 ($M^+-238$, 68.2), 43 ($M^+-292$, 100). [Found: HRMS (EI) *m/z* 325.0446 $(M+1)^+$, $C_{15}H_{18}O_3Br$ requires M+1, 325.0439].

Compounds **1e** and **2e** (*syn* and *anti* mixture) were prepared in the same manner as that described above.

**3.2.9. Compound 1e.** 65 mg, 62%. IR (KBr) $\nu$ 3434 (O–H), 2936, 1676 (C=O), 1490, 827 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.37 (3H, s, Me), 3.23 (1H, d, *J*=4.9 Hz, OH), 5.59 (1H, d, *J*=4.9 Hz, CH), 5.99 (1H, s), 6.23 (1H, s), 7.33 (4H, s, Ar); MS (EI) *m/z* 210 ($M^+$, 9.6), 193 ($M^+-17$, 15.1), 175 ($M^+-35$, 100), 77 ($M^+-133$, 70.2), 43 ($M^+-167$, 76.4). [Found: HRMS (EI) *m/z* 222.0448 ($M^+$). $C_{11}H_{11}O_2Cl$ requires M, 222.0428].

**3.2.10. Compound 2e.** *syn*-**2e**+*anti*-**2e**: 46 mg, 33%.

*syn*-**2e**. IR (KBr) $\nu$ 3442 (O–H), 2936, 16768 and 1709 (C=O), 1596, 831 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.98 (3H, s, Me), 2.28 (3H, s, Me), 2.35 (1H, dd, *J*=13.6, 8.7 Hz, CH), 2.45 (1H, dd, *J*=14.5, 7.8 Hz, CH), 3.13–3.22 (1H, m, CH), 3.48 (1H, d, *J*=1.0 Hz, OH), 4.86 (1H, d, *J*=2.3, 1.0 Hz, CH), 5.73 (1H, s), 5.98 (1H, s), 7.23–7.32 (4H, m, Ar); MS (EI) *m/z* 263 ($M^+-17$, 11.9), 221 ($M^+-59$, 21.0), 125 ($M^+-155$, 56.3), 43 ($M^+-237$, 100). [Found: HRMS (EI) *m/z* 281.0939 $(M+1)^+$, $C_{15}H_{18}O_3Cl$ requires M+1, 281.0934].

*anti*-**2e**. IR (KBr) $\nu$ 3442 (O–H), 2936, 16768 and 1709 (C=O), 1596, 831 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.02 (3H, s, Me), 2.31 (3H, s, Me), 2.38 (1H, dd, *J*=13.6, 5.7 Hz, CH), 2.60 (1H, dd, *J*=13.6, 4.8 Hz, CH), 3.13–3.22 (1H, m, CH), 3.48 (1H, d, *J*=5.3 Hz, OH), 4.69 (1H, dd, *J*=5.5, 5.3 Hz, CH), 5.83 (1H, s), 6.07 (1H, s), 7.23–7.32 (4H, m, Ar); MS (EI) *m/z* 263 ($M^+-17$, 11.9), 221 ($M^+-59$, 21.0), 125 ($M^+-155$, 56.3), 43 ($M^+-237$, 100). [Found: HRMS (EI) *m/z* 281.0939 $(M+1)^+$, $C_{15}H_{18}O_3Cl$ requires M+1, 281.0934].

**3.2.11. Compound 1f.** The title was prepared in the same manner as that described above.

64 mg, 73%. IR (KBr) $\nu$ 3427 (O–H), 3031, 1673 (C=O), 1492, 840 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.38 (3H, s, Me), 3.20 (1H, d, *J*=4.3 Hz, OH), 5.62 (1H, d, *J*=4.3 Hz, CH), 6.0 (1H, s), 6.23 (1H, s), 7.30–7.40 (5H, m, Ar); MS (EI) *m/z* 176 ($M^+$, 22.0), 157 ($M^+-1$, 100.0), 77 ($M^+-99$, 33.0), 43 ($M^+-133$, 49.0). [Found: HRMS (EI) *m/z* 176.0837 ($M^+$), $C_{11}H_{12}O_2$ requires M, 176.0826].

Compounds **1h** and **2h** (*syn* and *anti* mixture) were prepared in the same manner as that described above.

**3.2.12. Compound 1h.** 51 mg, 57%. IR (KBr) $\nu$ 3398 (O–H), 2937, 1714 (C=O), 1570, 917 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.21 (3H, s, Me), 4.78 (1H, br., s, OH), 5.60 (1H, s, CH), 6.06 (1H, s), 6.11 (1H, s), 7.08 (1H, dd, *J*=6.8, 5.2 Hz, Ar), 7.30 (1H, d, *J*=7.8 Hz, Ar), 7.54 (1H, dd, *J*=7.8, 7.8 Hz, Ar), 8.39 (1H, d, *J*=4.8 Hz, Ar); MS (EI) *m/z* 178 [$(M+1)^+$, 100], 160 ($M^+-17$, 9.2), 80 ($M^+-97$, 25.4), 43 ($M^+-134$, 43.5). [Found: HRMS (EI) *m/z* 177.9783 ($M^+$), $C_{10}H_{11}O_2N$ requires M, 177.0790].

**3.2.13. Compound 2h.** *syn*-**2h**+*anti*-**2h**: 30 mg, 24%.

*syn*-**2h**. IR (KBr) $\nu$ 3405, 2928, 1627 and 1675 (C=O), 1592, 843 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.12 (3H, s, Me), 2.18 (3H, s, Me), 2.42 (1H, dd, *J*=16.2, 5.1 Hz, CH), 2.55–2.70 (1H, m, CH), 3.20–3.30 (1H, m, CH), 4.47 (1H, br., s, OH), 4.98 (1H, d, *J*=1.8 Hz, CH), 5.66 (1H, s, CH), 5.85 (1H, s, CH), 7.15 (1H, dd, *J*=12.3, 6.2 Hz, Ar), 7.30 (1H, d, *J*=7.9 Hz, Ar), 7.65 (1H, t, *J*=7.9 Hz, Ar), 8.47 (1H, t, *J*=5.0 Hz, Ar); MS (EI) *m/z* 230 ($M^+-17$, 1.6), 159 ($M^+-71$, 93.0), 134 ($M^+-113$, 49.0), 43 ($M^+-204$, 100). [Found: HRMS (EI) *m/z* 247.1196 $(M+1)^+$, $C_{14}H_{17}O_3N$ requires M+1, 247.1208].

*anti*-**2h**. IR (KBr) $\nu$ 3405, 2928, 1627 and 1675 (C=O), 1592, 843 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.0 (3H, s, Me), 2.28 (3H, s, Me), 2.49 (1H, dd, *J*=7.1, 7.1 Hz, CH), 2.55–2.70 (1H, m, CH), 3.30–3.40 (1H, m, CH), 4.35 (1H, d, *J*=7.2 Hz, OH), 4.74 (1H, dd, *J*=7.5, 7.2 Hz, CH), 5.87 (1H, s, CH), 6.04 (1H, s), 7.15 (1H, dd, *J*=12.3, 6.2 Hz, Ar), 7.34 (1H, d, *J*=7.9 Hz, Ar), 7.65 (1H, t, *J*=7.9 Hz, Ar), 8.47 (1H, t, *J*=5.0 Hz, Ar); MS (EI) *m/z* 230 ($M^+-17$, 1.6), 159 ($M^+-71$, 93.0), 134 ($M^+-113$, 49.0), 43 ($M^+-204$, 100). [Found: HRMS (EI) *m/z* 247.1196 $(M+1)^+$, $C_{14}H_{17}O_3N$ requires M, 247.1208].

**3.2.14. Compound 1i.** The title compound was prepared in the same manner as that described above.

62 mg, 70%; mp 85–86°C. IR (KBr) $\nu$ 3354 (O–H), 2930, 1714 (C=O), 896 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.33 (3H, s, Me), 3.88 (1H, br., s, OH), 5.65 (1H, s, CH), 6.09 (1H, s), 6.27 (1H, s), 7.20–7.30 (1H, m, Ar), 7.73 (1H, dd, *J*=8.0, 1.5 Hz, Ar), 8.46 (1H, dd, *J*=8.0, 6.2 Hz, Ar), 8.50 (1H, d, *J*=5.9 Hz, Ar); MS (EI) *m/z* 177 ($M^+$, 14.2), 160 ($M^+-17$, 100), 43 ($M^+-134$, 52.7). [Found:

HRMS (EI) *m/z* 177.0786 ($M^+$), $C_{10}H_{11}O_2N$ requires M, 177.0788].

**3.2.15. Compound 3i.** 25 mg, 10%; a colorless oil. IR (KBr) $\nu$ 2930, 1714 (C=O), 896 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.16 (3H, s, Me), 2.32 (3H, s, Me), 2.68–2.74 (2H, m, $CH_2$), 3.59–3.65 (1H, m), 3.67–3.77 (1H, m), 5.88 (1H, s, CH), 6.21 (1H, s, CH), 6.25 (1H, s, CH), 7.20–7.28 (1H, m, Ar), 7.68 (1H, dd, *J*=9.6, 3.6 Hz, Ar), 8.5 (1H, d, *J*=3.6 Hz, Ar), 8.56 (1H, s, Ar); MS (EI) *m/z* 230 ($M^+-17$, 1.6), 176 ($M^+-71$, 93.1), 134 ($M^+-113$, 49.7), 43 ($M^+-204$, 100). [Found: HRMS (EI) *m/z* 247.1216 ($M^+$), $C_{14}H_{17}O_3N$ requires M, 247.1208].

Compounds **1j** and **2j** (*syn* and *anti* mixture) were prepared in the same manner as that described above.

**3.2.16. Compound 1j.** 58 mg, 57%. IR (KBr) $\nu$ 3438 (O–H), 2924, 1672 (C=O), 1575, 852 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.40 (3H, s, Me), 3.10 (1H, d, *J*=5.9 Hz, OH), 5.69 (1H, t, *J*=5.9 Hz, CH), 6.13 (1H, s), 6.17 (1H, s), 6.31 (1H, dd, *J*=16.3, 6.2 Hz, CH), 6.68 (1H, d, *J*=16.3 Hz), 7.26–7.41 (5H, m, Ar); MS (EI) *m/z* 202 ($M^+$, 42.5), 184 ($M^+-18$, 50.3), 70 ($M^+-132$, 66.2), 43 ($M^+-159$, 100). [Found: HRMS (EI) *m/z* 202.1006 ($M^+$), $C_{13}H_{14}O_2$ requires M, 202.0994].

**3.2.17. Compound 2j.** 33 mg, 24%.

*syn*-**2j**. IR (KBr) $\nu$3442 (O–H), 2938, 1676 and 1709 (C=O), 831 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.18 (3H, s, Me), 2.30 (3H, s, Me), 2.60 (1H, dd, *J*=7.0, 7.0 Hz, CH), 2.64 (1H, dd, *J*=7.0, 7.0 Hz, CH), 2.99–3.11 (1H, m, CH), 4.28 (1H, d, *J*=2.2 Hz, OH), 4.50 (1H, dd, *J*=2.2, 2.0 Hz, CH), 5.87 (1H, s), 5.91 (1H, s), 6.29 (1H, dd, *J*=16.4, 6.2 Hz), 6.64 (1H, d, *J*=16.4 Hz), 7.28–7.41 (5H, m, Ar); MS (EI) *m/z* 272 ($M^+$, 0.6), 255 ($M^+-17$, 35.6), 211 ($M^+-61$, 27.0), 125 ($M^+-147$, 44.0), 43 ($M^+-229$, 100). [Found: HRMS (EI) *m/z* 273.1492 $(M+1)^+$, $C_{17}H_{21}O_3$ requires M+1, 273.1491].

*anti*-**2j**. IR (KBr) $\nu$ 3442 (O–H), 2938, 1676 and 1709 (C=O), 831 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 2.19 (3H, s, Me), 2.33 (3H, s, Me), 2.50 (1H, dd, *J*=7.0, 7.0 Hz, CH), 2.58 (1H, dd, *J*=7.0, 7.0 Hz, CH), 2.8 (1H, d, *J*=6.2 Hz, OH), 2.99–3.11 (1H, m, CH), 4.37 (1H, dd, *J*=7.4, 6.2 Hz, CH), 6.07 (1H, s), 6.10 (1H, s), 6.29 (1H, dd, *J*=16.4, 6.2 Hz), 6.64 (1H, d, *J*=16.4 Hz), 7.28–7.41 (5H, m, Ar); MS (EI) *m/z* 272 ($M^+$, 0.6), 255 ($M^+-17$, 35.6), 211 ($M^+-61$, 27.0), 125 ($M^+-147$, 44.0), 43 ($M^+-229$, 100). [Found: HRMS (EI) *m/z* 273.1492 $(M+1)^+$, $C_{17}H_{21}O_3$ requires M+1, 273.1491].

**3.2.18. Compound 1k.** The title compound was prepared in the same manner as that described above.

20 mg, 15%; a colorless oil. IR (KBr) $\nu$ 3420 (O–H), 1712 (C=O), 830 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 0.89 (3H, t, *J*=7.7 Hz, $CH_3$), 1.25–1.54 (4H, m, $CH_2$), 1.55–1.70 (2H, m, $CH_2$), 2.12 (3H, s, $CH_3$), 2.74 (1H, br., s, OH), 4.35–4.47 (1H, m, CH), 6.0 (1H, s, CH), 6.10 (1H, s, CH); MS (EI) *m/z* 156 ($M^+$, 1.1), 97 ($M^+-59$, 100), 57 ($M^+-99$, 100). [Found: HRMS (EI) *m/z* 157.1216 $(M+1)^+$, $C_9H_{17}O_2$ requires M+1, 157.1229].

**3.2.19. Compound 4a.** The title compound was prepared in the same manner as that described above.

94 mg, 80%; a colorless oil. IR (KBr) $\nu$ 3486 (O–H), 2939, 1672 (C=O), 1517, 855 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.01 (3H, t, *J*=7.1 Hz, $CH_3$), 2.70 (2H, q, *J*=7.1 Hz, $CH_2$), 3.44 (1H, d, *J*=5.9 Hz, OH), 5.68 (1H, d, *J*=5.9 Hz, CH), 6.03 (1H, s), 6.29 (1H, s), 7.52 (1H, dd, *J*=7.8, 7.8 Hz, Ar), 7.76 (1H, d, *J*=7.8 Hz, Ar), 8.16 (1H, d, *J*=7.8 Hz, Ar), 8.23 (1H, s, Ar); MS (EI) *m/z* 234 [$(M-H)^+$, 40.2], 218 ($M^+-17$, 100), 206 ($M^+-29$, 40.7), 188 ($M^+-47$, 57.9). [Found: HRMS (EI) *m/z* 218.0838 ($M^+-17$), $C_{12}H_{12}O_3N$ requires M−17, 218.0817].

**3.2.20. Compound 4b.** 95 mg, 81%; a colorless oil. IR (KBr) $\nu$ 3459 (O–H), 2938, 1672 (C=O), 1526, 808 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.08 (3H, t, *J*=7.1 Hz, $CH_3$), 2.70 (2H, q, *J*=7.1 Hz, $CH_2$), 3.44 (1H, s, OH), 5.60 (1H, s, CH), 6.06 (1H, s), 6.11 (1H, s), 7.08 (1H, dd, *J*=6.8, 5.2 Hz, Ar), 7.30 (1H, d, *J*=7.8 Hz, Ar), (1H, dd, *J*=7.8, 7.8 Hz, Ar), (1H, d, *J*=4.8 Hz, Ar); MS (EI) *m/z* 234 [$(M-H)^+$, 38.0], 218 ($M^+-17$, 100), 206 ($M^+-29$, 66.8), 188 ($M^+-47$, 31.5). [Found: HRMS (EI) *m/z* 218.0769 ($M^+-17$), $C_{12}H_{12}O_3N$ requires M−17, 218.0817].

**3.2.21. Compound 4c.** 48 mg, 41%; a colorless oil. IR (KBr) $\nu$ 3454 (O–H), 2938, 1675 (C=O), 1522, 835 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.07 (3H, t, *J*=7.3 Hz, $CH_3$), 2.56 (1H, s, OH), 2.70 (2H, q, *J*=7.1 Hz, $CH_2$), 5.71 (1H, s, CH), 6.12 (1H, s), 6.20 (1H, s), 7.42 (1H, td, *J*=7.8, 1.2 Hz, Ar), 7.62 (1H, td, *J*=7.8, 1.2 Hz, Ar), 7.90 (1H, dd, *J*=7.8, 1.2 Hz, Ar), 8.0 (1H, dd, *J*=7.8, 1.2 Hz, Ar); MS (EI) *m/z* 218 ($M^+-17$, 1.9), 161 ($M^+-74$, 23.8), 104 ($M^+-131$, 38.5), 57 ($M^+-178$, 100). [Found: HRMS (EI) *m/z* 218.0802 ($M^+-17$), $C_{12}H_{12}O_3N$ requires M-17, 218.0817].

**3.2.22. Compound 6.** 47 mg, 40%; a colorless oil. IR (KBr) $\nu$ 3452 (O–H), 2980, 1688 (C=O), 880 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.07 (3H, d, *J*=7.3 Hz, $CH_3$), 3.39 (1H, q, *J*=7.3 Hz, CH), 3.50 (1H, br., s, OH), 5.72 (1H, d, *J*=2.0 Hz, CH), 6.13 (1H, dd, *J*=9.8, 1.6 Hz, CH), 6.35 (1H, dd, *J*=17.5, 1.6 Hz, CH), 6.45 (1H, dd, *J*=17.5, 9.8 Hz, CH), 7.42 (1H, td, *J*=7.8, 1.2 Hz, Ar), 7.62 (1H, td, *J*=7.8, 1.2 Hz, Ar), 7.90 (1H, dd, *J*=7.8, 1.2 Hz, Ar), 8.0 (1H, dd, *J*=7.8, 1.2 Hz, Ar); MS (EI) *m/z* 186 ($M^+-46$, 1.1), 152 ($M^+-83$, 20.0), 104 ($M^+-131$, 100), 87 ($M^+-151$, 90.4). [Found: HRMS (EI) *m/z* 235.034 ($M^+$), $C_{12}H_{13}O_4N$ requires M, 235.0845].

**3.2.23. Compound 4g.** 79 mg, 83%; a colorless oil. IR (KBr) $\nu$ 3366 (O–H), 2938, 1675 (C=O), 1569, 857 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.03 (3H, t, *J*=7.3 Hz, $CH_3$), 2.68 (2H, q, *J*=7.3 Hz, $CH_2$), 4.85 (1H, d, *J*=4.1 Hz, OH), 5.69 (1H, d, *J*=4.1 Hz, CH), 6.08 (1H, s), 6.19 (1H, s), 7.18 (1H, dd, *J*=7.6, 4.9 Hz, Ar), 7.45 (1H, d, *J*=7.8 Hz, Ar), 7.68 (1H, dd, *J*=7.6, 6.0 Hz, Ar), 8.50 (1H, d, *J*=4.9 Hz, Ar); MS (EI) *m/z* 192 [$(MH)^+$, 61.1], 174 ($M^+-17$, 87.4), 162 ($M^+-29$, 93.8), 108 ($M^+-83$, 100). [Found: HRMS (EI) *m/z* 174.0934 ($M^+-17$), $C_{11}H_{12}ON$ requires M-17, 174.0919].

**3.2.24. Compound 4h.** 78 mg, 82%; a colorless oil. IR (KBr) $\nu$ 3181 (O–H), 2938, 1675 (C=O), 1592, 850 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.0 (3H, t, $J$=7.5 Hz, $CH_3$), 2.68 (2H, q, $J$=7.5 Hz, $CH_2$), 5.18 (1H, d, $J$=5.3 Hz, OH), 5.64 (1H, s, CH), 6.15 (1H, s), 6.20 (1H, s), 7.20 (1H, dd, $J$=8.3, 4.9 Hz, Ar), 7.71 (1H, d, $J$=7.8 Hz, Ar), 8.31 (1H, d, $J$=6.3 Hz, Ar), 8.44 (1H, s, Ar); MS (EI) $m/z$ 192 [$(M+H)^+$, 100), 162 ($M^+-29$, 63.9), 118 ($M^+-73$, 41.5), 80 ($M^+-111$, 30.3). [Found: HRMS (EI) $m/z$ 191.0897 ($M^+$), $C_{11}H_{13}O_2N$ requires M, 191.0946].

**3.2.25. Compound 4i.** 76 mg, 70%; a colorless oil. IR (KBr) $\nu$ 3432 (O–H), 2977, 1672 (C=O), 1491, 823 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 1.14 (3H, t, $J$=7.2 Hz, $CH_3$), 2.78 (2H, q, $J$=7.2 Hz, $CH_2$), 3.15 (1H, d, $J$=5.8 Hz, OH), 5.17 (1H, t, $J$=5.5 Hz, CH), 6.08 (1H, s), 6.18 (1H, s), 6.29 (1H, dd, $J$=16.1, 6.2 Hz, Ar), 6.58 (1H, dd, $J$=16.1, 0.8 Hz, Ar), 7.20–7.43 (5H, m, Ar); MS (EI) $m/z$ 216 ($M^+$, 20.2), 199 ($M^+-17$, 100), 115 ($M^+-101$, 14.5), 57 ($M^+-159$, 33.3). [Found: HRMS (EI) $m/z$ 216.1122 ($M^+$), $C_{14}H_{16}O_2$ requires M, 216.1150].

**3.2.26. Compound 7a.** 101 mg, 85%; a colorless oil. IR (KBr) $\nu$ 3492 (O–H), 2956, 1714 (C=O), 1629, 834 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 3.45 (1H, d, $J$=6.0 Hz, OH), 3.71 (3H, s, $OCH_3$), 5.61 (1H, d, $J$=6.0 Hz, CH), 5.90 (1H, s, CH), 6.40 (1H, s), 7.57 (2H, d, $J$=8.5 Hz, Ar), 8.18 (2H, d, $J$=8.5 Hz, Ar); MS (EI) $m/z$ 237 ($M^+$, 11.2), 220 ($M^+-17$, 60.9), 177 ($M^+-60$, 100), 150 ($M^+-87$, 78.0), 77 ($M^+-160$, 33.7). [Found: HRMS (EI) $m/z$ 237.0623 ($M^+$), $C_{11}H_{11}O_5N$ requires M, 237.0637].

**3.2.27. Compound 7b.** 103 mg, 87%; a colorless oil. IR (KBr) $\nu$ 3492 (O–H), 2956, 1710 (C=O), 1583, 857 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 3.54 (1H, d, $J$=6.0 Hz, OH), 3.79 (3H, s, $OCH_3$), 5.67 (1H, d, $J$=6.0 Hz, CH), 5.97 (1H, s, CH), 6.45 (1H, s), 7.58 (1H, dd, $J$=8.0, 8.0 Hz, Ar), 7.77 (1H, d, $J$=8.0 Hz, Ar), 8.17 (1H, d, $J$=8.0 Hz, Ar), 8.28 (1H, s, Ar); MS (EI) $m/z$ 237 ($M^+$, 1.0), 220 ($M^+-17$, 100), 188 ($M^+-49$, 90.4), 150 ($M^+-87$, 61.8), 77 ($M^+-160$, 43.3). [Found: HRMS (EI) $m/z$ 237.0636 ($M^+$), $C_{11}H_{11}O_5N$ requires M, 237.0637].

**3.2.28. Compound 8.** 72 mg, 70%; mp 78–79°C; a colorless oil. IR (KBr) $\nu$ 3461 (O–H), 2987, 1606 (C=O), 1522, 859 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 300 MHz, TMS) $\delta$ 3.20 (1H, br., s, OH), 5.44 (1H, s, CH), 6.10 (1H, s, CH), 6.20 (1H, s), 7.58 (2H, d, $J$=8.0 Hz, Ar), 8.27 (2H, d, $J$=8.0 Hz, Ar); MS (EI) $m/z$ 204 ($M^+$, 2.8), 187 ($M^+-17$, 4.0), 152 ($M^+-52$, 100), 77 ($M^+-127$, 30.7). [Found: HRMS (EI) $m/z$ 204.0533 ($M^+$), $C_{10}H_8O_3N_2$ requires M, 204.0535].

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