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Different Reaction Patterns in the *Baylis-Hillman* Reaction of Aryl Aldehydes with Phenyl Vinyl Ketone, Phenyl Acrylate and Phenyl Thioacrylate

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Abstract: In the Baylis-Hillman reaction of aryl aldehydes with phenyl vinyl ketone we have observed exclusive formation of diadducts **4**, and that the yields of diadduct can reach 80% with increasing amounts of phenyl vinyl ketone. On the other hand, for phenyl acrylate and phenyl thioacrylate, only the normal Baylis-Hillman adduct was obtained. The effects of substituents were also examined and a plausible reaction mechanism is proposed for the formation of compounds **4**.
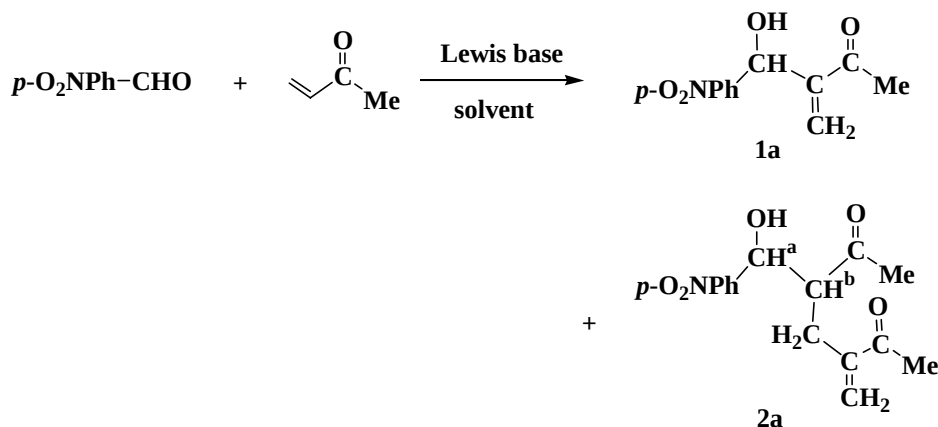
Keywords: Baylis-Hillman reaction; Lewis base; Phenyl vinyl ketone (PVK); Phenyl acrylate; DABCO; Conjugate addition; DMAP.

Introduction

Great progress has been made in the implementation of the Baylis-Hillman reaction [1], since Baylis and Hillman first reported in 1972 the reaction of acetaldehyde with ethyl acrylate and acrylonitrile in the presence of catalytic amounts of 1,4-diazabicyclo[2,2,2]octane (DABCO) [2], and even a catalytic asymmetric version has been published [3]. During our own investigations of this simple and useful reaction [4], we found that in the reaction of aryl aldehydes with methyl vinyl ketone (MVK) catalyzed by DABCO, the reaction products are not as simple as those reported before. For

example, using *p*-nitrobenzaldehyde (1.0 eq) and MVK (2.0 eq) as substrates in the presence of catalytic amounts of DABCO (0.1 eq) 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 2:3 mixture of *syn*- and *anti*-isomers [5] (Scheme 1) and the substituent effects of aryl aldehydes were also examined in detail [5].

Scheme 1

This interesting result stimulated us to further examine the influence of the R group of the Baylis-Hillman acceptor [C=C-C(O)R] on this reaction. Thus, we synthesized phenyl vinyl ketone (PVK) [6], phenyl acrylate [7], and phenyl thioacrylate [8] as the Baylis-Hillman acceptors and carefully examined the reaction products formed under the traditional Baylis-Hillman reaction conditions.

Results and Discussion

We found that, in the reaction of *p*-nitrobenzaldehyde (1.0 eq.) with PVK (1.0 eq.) in the presence of DABCO (10 mol-%) in DMF, the corresponding Baylis-Hillman adduct **3a** (*i.e.*, the normal Baylis-Hillman adduct) was not formed at all. The major reaction product was a mixture of *syn*- and *anti*-isomers of the 1:2 adduct **4a**, along with some PVK dimer (Scheme 2). Of course, as expected, **4a** was obtained in higher yields when 1.0 eq. *p*-nitrobenzaldehyde and 2.0 eq. of PVK were used in the presence of DABCO (10 mol-%). Results are summarized in Table 1. When the reaction was carried out in DMSO, THF or dichloromethane (CH_2Cl_2), similar results were obtained (Table 1, Entries 1-3). Using 4-(dimethylamino)pyridine (DMAP) as the Lewis base under the same reaction conditions, **4a** was obtained in lower yields (Table 1, entries 4-5). Increasing the amounts of PVK did not improve the yields of **4a** (Table 1, Entries 6-7). At lower temperatures (-30 ^{o}C), **4a** was obtained in 70% yield (Table 1, Entry 9) and with PBu_3 as the Lewis base, only traces of **4a** were obtained. The optimized reaction conditions were found to be reaction of 1.0 eq. aryl aldehyde with 2.0 eq. PVK in the presence of 10 mol-% DABCO in DMF.

Scheme 2
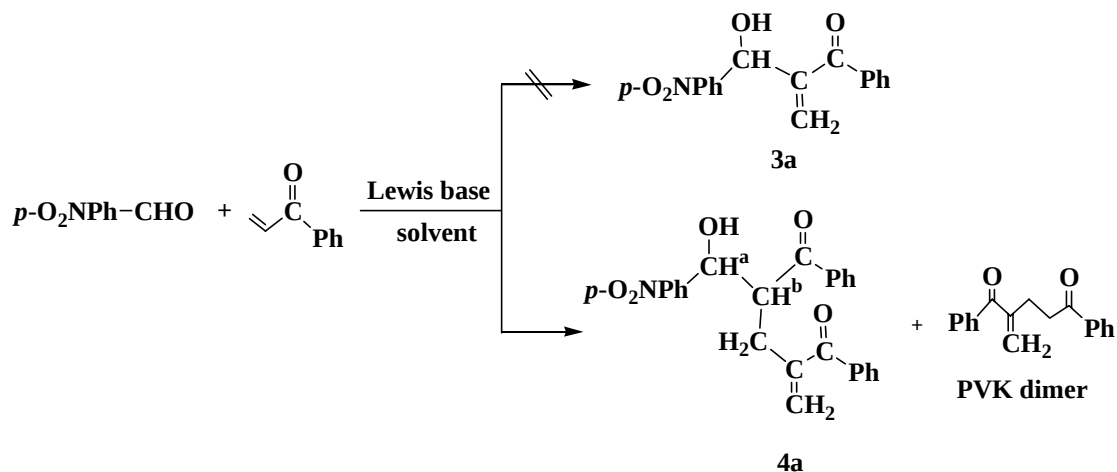
Table 1. Baylis-Hillman reactions of p-nitrobenzaldehyde (1.0 eq.) with phenyl vinyl ketone (2.0 eq.) in the presence of Lewis base (0.1 eq.).

entry	Lewis base	solvent	Temp. [^{o}C]	Time [h]	Yield [%][a]	
					4a[e]	PVK dimer
1	DABCO	DMSO	20	60	75	10
2	DABCO	DMF	20	60	88	14
3	DABCO	CH$_2$Cl$_2$	20	60	81	12
4	DABCO	THF	20	60	78	16
5	DMAP	DMSO	20	60	65	21
6	DMAP	DMF	20	60	63	20
7	DABCO	DMF[b]	20	60	80	11
8	DABCO	DMF[c]	20	60	60	13
9	PBu$_3$	DMF	20	60	trace	36
10	DABCO	DMF	-30	60	70	8

[a] Isolated yields. [b] Mole ratio of *p*-nitrobenzaldehyde:PVK= 1:3.0.
[c] Mole ratio of *p*-nitrobenzaldehyde:PVK= 1:4. [d] syn:anti= 2:3.

We next investigated the reactions of other aryl aldehydes with PVK under the optimized reaction conditions (Scheme 3). With electron deficient aryl aldehydes, such as nitrobenzaldehydes or pyridylaldehydes, the reaction proceeded smoothly to give **4** in good yields. However, with

p-chlorobenzaldehyde or benzaldehyde, only trace amounts of the 1:2 adduct **4** were obtained and the PVK dimer was formed almost exclusively (Scheme 3, Table 2) [7]. In all cases, the normal Baylis-Hillman adduct **3** was not formed.

Scheme 3

b: R= *m*-NO$_2$Ph, c: R= *o*-NO$_2$Ph, d: R=2-pyridyl,   **4**
e: R= 3-pyridyl, f: R= Ph, g: R=*p*-ClPh.
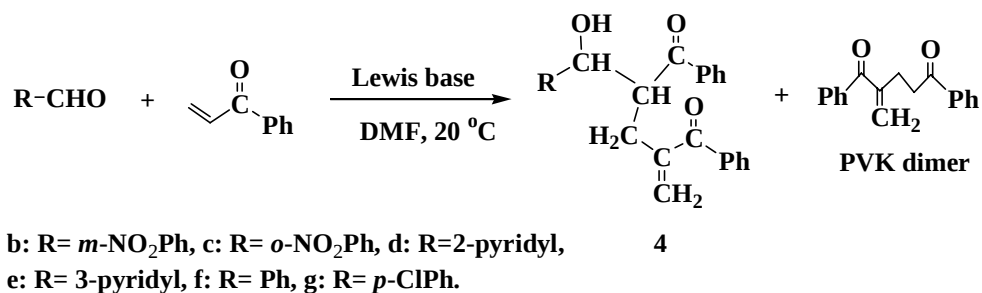
Table 2. Baylis-Hillman reactions of aryl aldehydes (1.0 eq) with phenyl vinyl ketone (2.0 eq.) in the presence of DABCO (0.1 eq).

entry	R	Lewis base	Time [h]	Yield [%][a]	
				4[b]	PVK dimer
1	*m*-NO$_2$Ph	DABCO	60	76 (2:3)	15
2	*o*-NO$_2$Ph	DABCO	60	79 (3:4)	16
3	2-pyridyl	DABCO	70	82 (3:5)	20
4	3-pyridyl	DABCO	70	81 (2:3)	16
5	Ph	DABCO	70	trace	33
6	*p*-ClPh	DABCO	70	trace	29

[a] Isolated yields. [b] syn- and anti mixture.

On the other hand, the Baylis-Hillman reactions with phenyl acrylate or phenyl thioacrylate as an acceptor were also examined (Schemes 4 and 5; results are summarized in Table 3). With phenyl acrylate as the acceptor, the normal Baylis-Hillman adducts **5** was exclusively obtained in most cases (Table 3, entries 1-2 and 4-8). Only in the reaction of *o*-nitrobenzaldehyde with phenyl acrylate, was diadduct **6c** formed in 29% (Table 3, Entry 3). However, with phenyl thioacrylate as a Baylis-Hillman acceptor, only in the reaction of *p*-chlorobenzaldehyde with phenyl thioacrylate, the corresponding Baylis-Hillman adduct **7** was obtained in good yield (Scheme 5). The reactions of other aryl aldehydes with phenyl thioacrylate were either very sluggish or gave many unidentified products.

Scheme 4

a: R= *p*-NO₂Ph, b: R= *m*-NO₂Ph, c: R= *o*-NO₂Ph,
d: R= *p*-BrPh, e: R= *p*-ClPh, f: R= Ph, g: R= PhCH=CH,
h: R= 3-pyridyl.
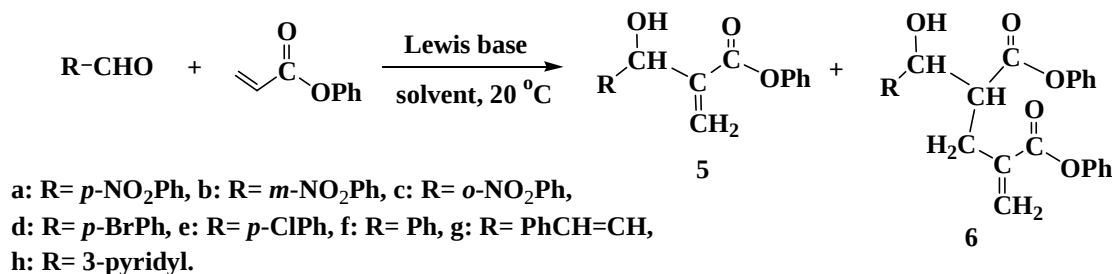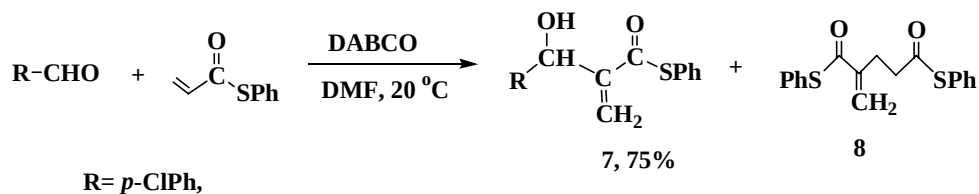
Table 3. Baylis-Hillman reactions of aldehydes (1.0 eq) with phenyl acrylate (2.0 eq) in the presence of Lewis base (0.1 eq).

entry	R	Lewis base	solvent	Time [h]	Yield [%][a]	
					5	6
1	*p*-NO₂Ph	DABCO	DMSO	40	75	0
2	*m*-NO₂Ph	DABCO	DMF	40	74	0
3	*o*-NO₂Ph	DABCO	DMF	40	53	29
4	*p*-BrPh	DABCO	DMF	50	78	0
5	*p*-ClPh	DABCO	DMF	50	71	0
6	Ph	DABCO	DMF	50	79	0
7	PhCH=CH	DABCO	DMF	40	57	0
8	3-pyridyl	DABCO	DMF	40	78	0

[a] Isolated yields.

Scheme 5

R= *p*-ClPh,
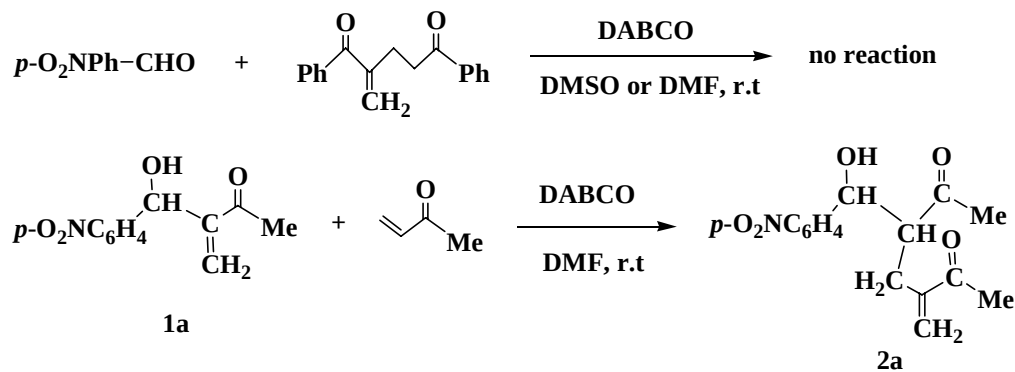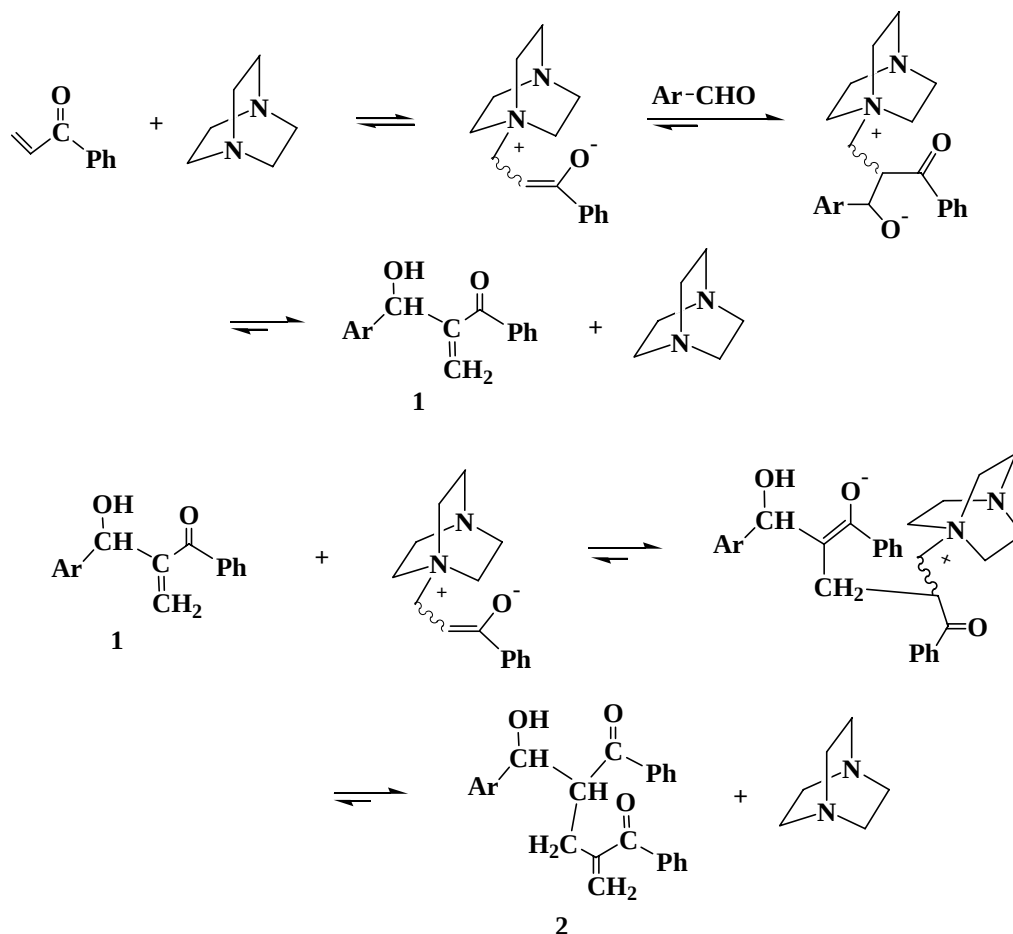
To the best of our knowledge, the exclusive formation of a diadduct in the traditional Baylis-Hillman reaction in which phenyl vinyl ketone (PVK) is used as the acceptor has never been disclosed before. To clarify the mechanism of formation of **4**, we carried out reactions of *p*-nitrobenzaldehyde

(1.0 equiv.) with PVK dimer (1.0 equiv.) in the presence of catalytic amounts of DABCO (0.1 equiv.). Since we found that no reaction occurred under these conditions (Scheme 6), we believe that the diadduct **4** was derived from a second reaction of normal Baylis-Hillman adduct **3** with PVK because we have already proven that the diadduct **2a** can be obtained from the reaction of **1a** with MVK in the presence of DABCO (10 mol-%) in DMF (Scheme 6).

Scheme 6

Scheme 7

In Scheme 7, we formulate a plausible reaction mechanism. Two reactions occur for the traditional Baylis-Hillman reaction of aryl aldehydes with PVK. One is the normal Baylis-Hillman reaction, which involves the 1,2-addition of the PVK-derived anion to *p*-nitrobenzaldehyde. Another is the conjugated addition (Michael addition) of the anion derived from a second molecule of PVK to **3** *via* intermediate **4'** (Scheme 7). Thus, the normal Baylis-Hillman adduct **3** formed can more easily undergo the next conjugate addition (Michael addition) of the anion derived from a second molecule of PVK to afford exclusively the diadduct **4**.

Conclusions

We have found that a diadduct **4** was formed exclusively in the Baylis-Hillman reaction of aryl aldehydes with phenyl vinyl ketone (PVK). It was confirmed the **4** was derived from a second reaction of the normal Baylis-Hillman adduct with PVK *via* a conjugate addition reaction. On the other hand, with phenyl acrylate or phenyl thioacrylate as acceptors, only the normal Baylis-Hillman reaction products were produced. Efforts are currently underway to further elucidate the mechanistic details of this reaction and to disclose its scope and limitations.

Acknowledgements
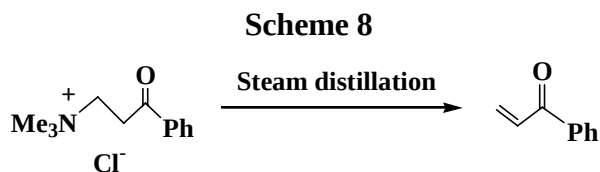
Experimental

General

IR spectra were recorded on a Nicolet AV-360 spectrometer. ^{1}H-NMR spectra (300 MHz) were recorded for $CDCl_3$ solutions on a Bruker AM-300 spectrometer with tetramethylsilane (TMS) as internal standard; J-values are in Hz. Mass spectra were recorded with a HP-5989 instrument and HRMS were measured on a Finnigan MA+ mass spectrometer. Organic solvents were dried by standard methods when necessary. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC using Huanghai GF_{254} silica gel coated plates. Flash Column Chromatography was carried out using 200-300 mesh silica gel under pressure. The *syn-* and *anti*-isomers of **4** were not separable, thus, the ratios of *syn* and *anti* isomers are determined from ^{1}H-NMR spectroscopic data and their HRMS data were obtained from *anti-* and *syn*-mixtures as well.

Preparation of phenyl vinyl ketone.
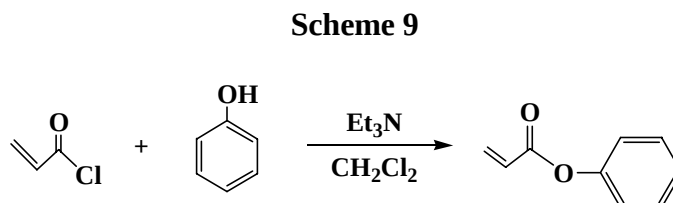
The phenyl vinyl ketone starting material was prepared according to Scheme 8 [6].

Scheme 8

A solution of the ammonium salt (5 g) in water (200 mL) was distilled at 90 °C. The distillate was extracted with ether (3 x 20 mL) and the organic layer was dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and residue was purified by flash silica gel chromatography (eluent: ethyl acetate/petroleum ether = 1/10) to give phenyl vinyl ketone (PVK) (1.6 g, 30%) as a colorless oil; ^{1}H-NMR: δ 5.94 (1H, *dd*, *J* = 10.5, 1.8 Hz, =CH), 6.45 (1H, *dd*, *J* = 16.8, 1.8 Hz, =CH), 7.17 (1H, *dd*, *J* = 16.8, 10.5 Hz, =CH), 7.46-7.51 (2H, *m*, Ar), 7.56-7.59 (1H, *m*, Ar), 7.94-7.97 (2H, *m*, Ar).

Preparation of phenyl acrylate.

The phenyl acrylate starting material was prepared according to Scheme 9 [7]. Acroylchloride (7.28 g, 80 mmol) in dichloromethane (10 mL) was added within 0.5 h. to a solution of phenol (7.5 g, 80 mmol) and triethylamine (10.1 g, 100 mmol) in dichloromethane (20 mL).

Scheme 9

The reaction mixture was stirred at room temperature for 24 h, then washed with water (2 x 30 mL) and extracted with dichloromethane (2 x 10 mL). The organic layer was dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and residue was purified by flash silica gel chromatography (eluent: petroleum ether) to give phenyl acrylate (9.0 g, 76%) as a colorless oil; ^{1}H-NMR: δ 6.00 (1H, *d*, *J* = 11.1 Hz, =CH), 6.32 (1H, *dd*, *J* = 17.1, 11.1 Hz, =CH), 6.60 (1H, *d*, *J* = 17.1 Hz, =CH), 7.11-7.14 (2H, *m*, Ar), 7.24-7.26 (1H, *m*, Ar), 7.37-7.42 (2H, *m*, Ar).

Typical reaction procedure for the Baylis-Hillman reaction.

Phenyl vinyl ketone (PVK) (138 mg, 1.0 mmol) was added to a solution of DABCO (6 mg, 0.05 mmol) and *p*-nitrobenzaldehyde (76 mg, 0.50 mmol) in DMF (0.50 mL) and the reaction mixture was stirred at room temperature for 60 h. The reaction product was extracted with dichloromethane (10.0

mL) and washed with water (10.0 mL x 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 column chromatography (eluent: 1:4 ethyl acetate-petroleum ether) to give the product **4a** (a 2:3 *syn* and *anti* mixture, 180 mg, 88%) and PVK dimer (25 mg, 14%) as colorless oils. The *syn* and *anti* ratio of **4a** was determined from the ^{1}H-NMR spectral data based on the J values of H$_a$ and H$_b$ (see Scheme 1) because the *anti*-isomer usually shows a bigger *J* value (for *anti*-**4a**: J$_{HaHb}$ = 6.3 Hz, for *syn*-**4a**: J$_{HaHb}$ = 2.8 Hz).

2-[Hydroxy-(4-nitrophenyl)methyl]-4-methylene-1,5-diphenylpentane-1,5-dione   (**4a**):   *syn*-**4a**:   IR (KBr): ν 1649 and 1668 cm^{-1} (C=O); ^{1}H-NMR: δ 2.86-2.93 (2H, *m*, CH$_2$), 4.09 (1H, *d*, *J* = 2.6 Hz, OH), 4.20-4.30 (1H, m, CH), 5.16 (1H, *dd*, *J* = 4.8, 2.6 Hz, CH), 5.55 (1H, *s*), 5.82 (1H, *s*), 7.20-7.60 (10H, *m*, Ar), 7.87 (2H, *d*, *J* = 8.6 Hz, Ar), 8.10 (2H, *d*, *J* = 8.6 Hz, Ar); EI-MS: *m/e* 397 (M$^+$-18, 0.2), 378 (M$^+$-37, 0.2), 159 (M$^+$-256, 50.1), 105 (M$^+$-310, 100); HRMS: C$_{18}$H$_{16}$O$_2$ requires 264.1150, found: (EI) *m/z* 264.1135 (M$^+$-151.0270); *anti*-**4a**: IR (KBr): ν 1649 and 1668 cm^{-1} (C=O); ^{1}H-NMR: δ 2.93-3.10 (2H, *m*, CH$_2$), 4.30-4.40 (1H, *m*, CH), 4.42 (1H, *d*, *J* = 8.2 Hz, OH), 5.06 (1H, *dd*, *J* = 8.2, 4.6 Hz, CH), 5.74 (1H, *s*), 6.07 (1H, *s*), 7.20-7.60 (10H, *m*, Ar), 7.87 (2H, *d*, *J* = 8.6 Hz, Ar), 8.10 (2H, *d*, *J* = 8.6 Hz, Ar); EI-MS: *m/e* 397 (M$^+$-18, 0.2), 378 (M$^+$-37, 0.2), 159 (M$^+$-256, 50.1), 105 (M$^+$-310, 100); HRMS: C$_{18}$H$_{16}$O$_2$ requires 264.1150, found: (EI) *m/z* 264.1135 (M$^+$-151.0270).

4-Methylene-1,5-diphenylpentane-1,5-dione (PVK dimer): a colorless oil; IR (KBr): ν 1650 and 1680 cm^{-1} (C=O); ^{1}H-NMR: δ 2.91 (2H, *t*, *J* = 7.3 Hz, CH$_2$), 3.23 (2H, *t*, *J* = 7.3 Hz, CH$_2$), 5.67 (1H, *s*), 5.96 (1H, *s*), 7.30-7.55 (6H, *m*, Ar), 7.70-7.75 (2H, *m*, Ar), 7.90-8.0 (2H, *m*, Ar); EI-MS: *m/e* 264 (M$^+$, 1.0), 159 (M$^+$-105, 63.8), 105 (M$^+$-159, 100), 77 (M$^+$-187, 54.2); HRMS: C$_{18}$H$_{16}$O$_2$ requires 264.1150, found: (EI) *m/z* 264.1185 (M$^+$).

2-[Hydroxy-(3-nitrophenyl)methyl]-4-methylene-1,5-diphenylpentane-1,5-dione (**4b**) (*syn*- and *anti*-mixture= 2:3): *syn*-**4b**: a colorless oil; IR (KBr): ν 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 2.90-3.0 (1H, *m*, CH$_2$), 3.10 (1H, *dd*, *J* = 13.7, 8.6 Hz, CH$_2$), 4.09 (1H, *d*, *J* = 2.6 Hz, OH), 4.20-4.30 (1H, *m*), 5.17 (1H, *dd*, *J* = 2.6, 2.6 Hz), 5.56 (1H, *s*, CH), 5.82 (1H, *s*, CH), 7.20-7.52 (9H, *m*, Ar), 7.55-7.82 (1H, *m*, Ar), 7.83-7.95 (2H, *m*, Ar), 8.0-8.08 (1H, *m*, Ar), 8.33 (1H, *s*, Ar); EI-MS: *m/e* 397 (M$^+$-18, 0.12), 378 (M$^+$-37, 1.0), 159 (M$^+$-256, 55.0), 105 (M$^+$-310, 100); HRMS: C$_{25}$H$_{21}$NO$_5$ requires 415.1420, found: (EI) *m/z* 415.1431 (M$^+$); *anti*-**4b**: a colorless oil; IR (KBr): ν 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 2.95 (2H, *dd*, *J* = 14.2 7.4 Hz, CH$_2$), 4.32 (1H, *d*, *J* = 5.2 Hz, OH), 4.38-4.45 (1H, *m*, CH), 5.12 (1H, *dd*, *J* = 5.2 2.0 Hz), 5.73 (1H, *s*, CH), 6.07 (1H, *s*, CH), 7.20-7.52 (9H, *m*, Ar), 7.55-7.82 (1H, *m*, Ar), 7.83-7.95 (2H, *m*, Ar), 8.0-8.08 (1H, *m*, Ar), 8.24 (1H, *s*, Ar); EI-MS: *m/e* 397 (M$^+$-18, 0.12), 378 (M$^+$-37, 1.0), 159 (M$^+$-256, 55.0), 105 (M$^+$-310, 100); HRMS: C$_{25}$H$_{21}$NO$_5$ requires 415.1420, found: (EI) *m/z* 415.1431 (M$^+$).

2-[Hydroxy-(2-nitrophenyl)methyl]-4-methylene-1,5-diphenylpentane-1,5-dione (**4c**) (*syn-* and *anti-*mixture = 3:4): *syn*-**4c**: a colorless oil; IR (KBr): v 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 2.85 (1H, *dd*, *J* = 13.4 4.3 Hz, CH), 3.01 (1H, *dd*, *J* = 13.4, 6.5 Hz, CH), 4.33 (1H, *s*, OH), 4.40-5.02 (1H, *m*, CH), 5.47 (1H, *s*, CH), 5.74 (1H, *d*, *J* = 2.4 Hz, CH), 5.79 (1H, *s*, CH), 7.10-7.80 (12H, *m*, Ar), 7.98 (1H, *d*, *J* = 8.6 Hz, Ar), 8.02 (1H, *dd*, *J* = 8.0 7.3 Hz, Ar); EI-MS: *m/e* 378 (M$^+$-37, 0.6), 264 (M$^+$-151, 7.6), 159 (M$^+$-256, 63.5), 105 (M$^+$-310, 100); HRMS: C$_{25}$H$_{21}$NO$_5$ requires 415.1420, found: (EI) *m/z* 415.1233 (M$^+$); *anti*-**4c**: a colorless oil; IR (KBr): v 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 2.99 (2H, *dd*, *J* = 13.7 10.0 Hz, CH$_2$), 4.40-5.02 (1H, *m*, CH), 4.94 (1H, *d*, *J* = 8.5 Hz, OH), 5.61 (1H, *dd*, *J* = 4.3, 3.8 Hz, CH), 5.88 (1H, *s*, CH), 6.20 (1H, *s*, CH), 7.10-7.80 (12H, *m*, Ar), 7.81 (1H, *d*, *J* = 8.6 Hz, Ar), 7.88 (1H, *d*, *J* = 8.6 Hz, Ar); EI-MS: *m/e* 378 (M$^+$-37, 0.6), 264 (M$^+$-151, 7.6), 159 (M$^+$-256, 63.5), 105 (M$^+$-310, 100); HRMS: C$_{25}$H$_{21}$NO$_5$ requires 415.1420, found: (EI) *m/z* 415.1233 (M$^+$).

2-(Hydroxy-pyridin-2-yl-methyl)-4-methylene-1,5-diphenylpentane-1,5-dione (**4d**) (*syn-* and *anti-*mixture= 3:5): *syn*-**4d**: a colorless oil; IR (KBr): v 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 2.90-3.05 (2H, *m*, CH), 4.30-4.41 (1H, *m*, CH), 4.53 (1H, *d*, *J* = 3.2 Hz, OH), 5.02 (1H, *t*, *J* = 4.2 Hz, CH), 5.48 (1H, *s*, CH), 5.83 (1H, *s*, CH), 7.0-7.70 (11H, *m*, Ar), 7.80-7.92 (2H, *m*, Ar), 8.47 (1H, *d*, *J* = 4.7 Hz, Ar); EI-MS: *m/e* 264 (M$^+$-107, 4.8), 159 (M$^+$-212, 67.5), 105 (M$^+$-266, 100); HRMS: C$_{18}$H$_{16}$O$_2$ requires 264.1150, found: (EI) *m/z* 264.1129 (M$^+$-107.0371); *anti*-**4d**: a colorless oil; IR (KBr): v 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 2.90-3.05 (2H, *m*, CH), 4.30-4.41 (1H, *m*, CH), 4.52 (1H, *br.*, *s*, OH), 5.10 (1H, *t*, *J* = 5.1 Hz, CH), 5.67 (1H, *s*, CH), 6.03 (1H, *s*, CH), 7.0-7.70 (11H, *m*, Ar), 7.80-7.92 (2H, *m*, Ar), 8.38 (1H, *d*, *J* = 4.7 Hz, Ar); EI-MS: *m/e* 264 (M$^+$-107, 4.8), 159 (M$^+$-212, 67.5), 105 (M$^+$-266, 100); HRMS: C$_{18}$H$_{16}$O$_2$ requires 264.1150, found: (EI) *m/z* 264.1129 (M$^+$-107.0371).

2-(Hydroxy-pyridin-3-yl-methyl)-4-methylene-1,5-diphenylpentane-1,5-dione (**4e**) (*syn-* and *anti-*mixture = 2:3): *syn*-**4e**: a colorless oil; IR (KBr): v 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 2.70-3.0 (2H, *m*, CH), 4.25-4.37 (1H, *m*, CH), 5.02 (1H, *d*, *J* = 4.3 Hz, CH), 5.12 (1H, *br.*, *s*, OH), 5.53 (1H, *s*, CH), 5.83 (1H, *s*, CH), 7.0-7.50 (10H, *m*, Ar), 7.78 (1H, *d*, *J* = 7.3 Hz, Ar), 7.93 (1H, *d*, *J* = 7.5 Hz, Ar), 8.25 (1H, *dd*, *J* = 7.5 1.9 Hz, Ar), 8.51 (1H, *s*, Ar); EI-MS: *m/e* 264 (M$^+$-107, 1.0), 238 (M$^+$-133, 6.2), 159 (M$^+$-212, 18.1), 105 (M$^+$-266, 36.5), 84 (M$^+$-212, 100); HRMS: C$_{24}$H$_{21}$NO$_3$ requires 371.1521, found: (EI) *m/z* 371.1512 (M$^+$); *anti*-**4e**: a colorless oil; IR (KBr): v 1645, 1675 cm^{-1} (C=O); ^{1}H-NMR: δ 3.07 (2H, *dd*, *J* = 8.0 7.6 Hz, CH$_2$), 4.25-4.37 (1H, *m*, CH), 5.02 (1H, *d*, *J* = 4.3 Hz, CH), 5.18 (1H, *br.*, *s*, OH), 5.59 (1H, *s*, CH), 5.92 (1H, *s*, CH), 7.0-7.50 (10H, *m*, Ar), 7.70 (1H, *d*, *J* = 7.3 Hz, Ar), 7.93 (1H, *d*, *J* = 7.5 Hz, Ar), 8.35 (1H, *dd*, *J* = 7.5 1.9 Hz, Ar), 8.47 (1H, *s*, Ar); EI-MS: *m/e* 264 (M$^+$-107, 1.0), 238 (M$^+$-133, 6.2), 159 (M$^+$-212, 18.1), 105 (M$^+$-266, 36.5), 84 (M$^+$-212, 100); HRMS: C$_{24}$H$_{21}$NO$_3$ requires 371.1521, found: (EI) *m/z* 371.1512 (M$^+$).

2-[Hydroxy-(4-nitrophenyl)methyl]acrylic acid phenyl ester (**5a**): a colorless oil; IR (KBr): v 1723 cm^{-1} (C=O); ^{1}H-NMR: δ 3.27 (1H, *d*, *J* = 5.6 Hz, OH), 5.75 (1H, *d*, *J* = 5.2 Hz, CH), 6.12 (1H, *s*, CH), 6.68 (1H, *s*, CH), 7.03 (2H, *d*, *J* = 7.7 Hz, Ar), 7.25 (1H, *t*, *J* = 7.5 Hz, Ar), 7.36 (2H, *t*, *J* = 7.7 Hz, Ar),

7.63 (2H, *d*, *J* = 8.4 Hz, Ar), 8.23 (2H, *d*, *J* = 8.4 Hz, Ar); EI-MS: *m/e* 205 (M$^+$-94, 1.1), 161 (M$^+$-138, 31.6), 115 (M$^+$-184, 24.4), 94 (M$^+$-205, 100); HRMS: C$_{16}$H$_{13}$NO$_5$ requires 299.0744, found: (EI) *m/z* 299.0733 (M$^+$).

2-[Hydroxy-(3-nitrophenyl)methyl]acrylic acid phenyl ester (**5b**): a colorless oil; IR (KBr): *v* 1724 cm$^-$^{1} (C=O); ^{1}H-NMR: *δ* 3.23 (1H, *d*, *J* = 5.8 Hz, OH), 5.80 (1H, *d*, *J* = 5.8 Hz, CH), 6.16 (1H, *s*, CH), 6.69 (1H, *s*, CH), 7.03 (2H, *dd*, *J* = 8.0, 0.7 Hz, Ar), 7.27 (1H, *t*, *J* = 7.2 Hz, Ar), 7.40 (2H, *t*, *J* = 7.5 Hz, Ar), 7.56 (1H, *t*, *J* = 7.5 Hz, Ar), 7.81 (1H, *d*, *J* = 8.0 Hz, Ar), 8.12 (1H, *d*, *J* = 8.0 Hz, Ar), 8.33 (1H, *s*, Ar); EI-MS: *m/e* 299 (M$^+$, 0.6), 161 (M$^+$-138, 22.7), 115 (M$^+$-184, 19.2), 94 (M$^+$-205, 100); HRMS: C$_{16}$H$_{13}$O$_5$N requires 299.0794, found: (EI) *m/z* 299.0781 (M$^+$).

2-[Hydroxy-(2-nitrophenyl)methyl]acrylic acid phenyl ester (**5c**): a colorless oil; IR (KBr): *v* 1720 cm^{-1} (C=O); ^{1}H-NMR: *δ* 3.58 (1H, *s*, OH), 5.93 (1H, *m*, CH), 6.30 (1H, *s*, CH), 6.62 (1H, *s*, CH), 7.02 (2H, *d*, *J* = 7.7 Hz, Ar), 7.22 (1H, *t*, *J* = 7.5 Hz, Ar), 7.36 (2H, *t*, *J* = 7.7 Hz, Ar), 7.48 (1H, *t*, *J* = 7.5 Hz, Ar), 7.70 (1H, *t*, *J* = 7.5 Hz, Ar), 7.82 (1H, *d*, *J* = 7.7 Hz, Ar), 7.98 (1H, *d*, *J* = 7.7 Hz, Ar); EI-MS: *m/e* 260 (M$^+$-39, 1.4), 206 (M$^+$-93, 21.9), 188 (M$^+$-256, 4.9), 94 (M$^+$-205, 100); HRMS: C$_{10}$H$_8$NO$_4$ requires 206.0453, found: (EI) *m/z* 206.0477 (M$^+$-93.0341).

2-[Hydroxy-(4-bromophenyl)methyl]acrylic acid phenyl ester (**5d**): a colorless oil; IR (KBr): *v* 1731 cm^{-1} (C=O); ^{1}H-NMR: *δ* 3.02 (1H, *s*, OH), 5.52 (1H, *s*, CH), 5.96 (1H, *s*, CH), 6.52 (1H, *s*, CH), 6.97 (2H, *d*, *J* = 7.2 Hz, Ar), 7.10-7.43 (5H, *m*, Ar), 7.40 (2H, *J* = 7.2 Hz, Ar); EI-MS: *m/e* 315 (M$^+$-18, 2.1), 239 (M$^+$-94, 30.9), 160 (M$^+$-173, 72.2), 116 (M$^+$-217, 100); HRMS: C$_{10}$H$_9$BrO$_2$ requires 239.9786, found: (EI) *m/z* 239.9768 (M$^+$-92.0262).

2-[Hydroxy-(4-chlorophenyl)methyl]acrylic acid phenyl ester (**5e**): a colorless oil; IR (KBr): *v* 1730 cm^{-1} (C=O); ^{1}H-NMR: *δ* 2.97 (1H, *s*, OH), 5.53 (1H, *s*, CH), 5.98 (1H, *s*, CH), 6.56 (1H, *s*, CH), 6.94-6.98 (2H, *m*, Ar), 7.10-7.23 (1H, *m*, Ar), 7.20-7.38 (6H, *m*, Ar); EI-MS: *m/e* 288 (M$^+$, 1.1), 271 (M$^+$-17, 10.5), 195 (M$^+$-93, 100), 115 (M$^+$-173, 88.4); HRMS: C$_{16}$H$_{13}$ClO$_3$ requires 288.0553. Found: (EI) *m/z* 288.0572 (M$^+$).

2-(Hydroxy-phenylmethyl)acrylic acid phenyl ester (**5f**): a colorless oil; IR (KBr): *v* 1732 cm^{-1} (C=O); ^{1}H-NMR: *δ* 2.96 (1H, *s*, OH), 5.56 (1H, *s*, CH), 5.97 (1H, *s*, CH), 6.53 (1H, *s*, CH), 6.94-6.98 (2H, *m*, Ar), 7.10-7.23 (1H, *m*, Ar), 7.20-7.42 (7H, *m*, Ar); EI-MS: *m/e* 254 (M$^+$, 1.4), 161 (M$^+$-93, 77.5), 133 (M$^+$-121, 34.1), 115 (M$^+$-139, 100); HRMS: C$_{16}$H$_{14}$O$_3$ requires 254.0943, found: (EI) *m/z* 254.1015 (M$^+$).

3-Hydroxy-2-methylene-5-phenylpent-4-enoic acid phenyl ester (**5g**): a colorless oil; IR (KBr): *v* 1727 cm^{-1} (C=O); ^{1}H-NMR: *δ* 3.04 (1H, *d*, *J* = 5.5 Hz, OH), 5.23 (1H, *t*, *J* = 5.5 Hz, CH), 6.11 (1H, *s*, CH), 6.29 (1H, *dd*, *J* = 15.9 6.3 Hz, CH), 6.54 (1H, *s*, CH), 6.70 (1H, *d*, *J* = 15.9 Hz, CH), 7.02-7.12 (2H, *m*,

Ar), 7.12-7.42 (8H, *m*, Ar); EI-MS: *m/e* 280 (M$^+$, 3.9), 187 (M$^+$-93, 73.1), 169 (M$^+$-111, 39.2), 141 (M$^+$-139, 100); HRMS: C$_{18}$H$_{16}$O$_3$ requires 280.1099, found: (EI) *m/z* 280.1093 (M$^+$).

2-(Hydroxy-pyridin-3-yl-methyl)-acrylic acid phenyl ester (**5h**): a colorless oil; IR (KBr): *v* 1727 cm^{-1} (C=O); ^{1}H-NMR: δ 5.25 (1H, *s*, OH), 5.69 (1H, *s*, CH), 6.27 (1H, *s*, CH), 6.63 (1H, *s*, CH), 7.02 (2H, *d*, *J* = 7.7 Hz, Ar), 7.22 (1H, *t*, *J* = 7.5 Hz, Ar), 7.20 (1H, *dd*, *J* = 2.9 0.82 Hz, Ar), 7.36 (2H, *t*, *J* = 7.7 Hz, Ar), 7.76 (1H, *d*, *J* = 8.0 Hz, Ar), 8.36 (1H, *dd*, *J* = 3.9 0.82 Hz, Ar), 8.48 (1H, *s*, Ar); EI-MS: *m/e* 256 (MH$^+$, 1.0), 162 (M$^+$-93, 100), 144 (M$^+$-112, 17.2), 94 (M$^+$-162, 68.6); HRMS: C$_{15}$H$_{12}$O$_2$N requires 238.0868, found: (EI) *m/z* 238.0871 (M$^+$-17.0027).

2-[(4-Chlorophenyl)-hydroxy-methyl]thioacrylic acid S-phenyl ester (**7**): a colorless oil; IR (KBr): *v* 1674 cm^{-1} (C=O); ^{1}H-NMR: δ 2.98 (1H, *d*, *J* = 4.7 Hz, OH), 5.56 (1H, *d*, *J* = 4.7 Hz, CH), 5.97 (1H, *s*, CH), 6.45 (1H, *s*, CH), 7.20-7.45 (9H, *m*, Ar); EI-MS: *m/e* 304 (M$^+$, 9.0), 195 (M$^+$-109, 100), 167 (M$^+$-137, 45.2), 115 (M$^+$-189, 79.9); HRMS: C$_{16}$H$_{13}$ClO$_2$S requires 304.0325, found: (EI) *m/z* 304.0332 (M$^+$).

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