

# Facile Baylis-Hillman reaction of substituted 3-isoxazolecarbaldehydes: The impact of proximal heteroatom within a heterocycle on the acceleration of reaction <sup>1</sup>

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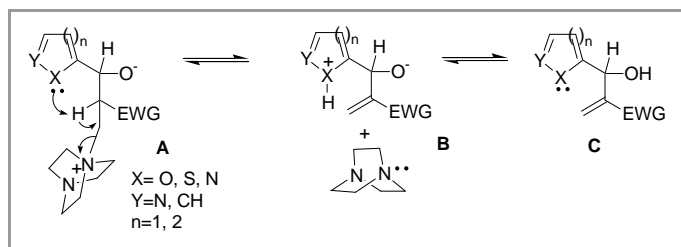
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**Abstract:** The fast and facile Baylis-Hillman reaction in substituted 3-isoxazolecarbaldehydes confirms the impact of the proximal heteroatom within a heterocycle towards enhanced reactivity of the formyl group for this reaction.

**Key words:** Baylis-Hillman reaction, 3-isoxazolecarbaldehyde, DABCO, DMAP.

The Baylis-Hillman reaction has been identified as a novel C-C bond forming reaction for delivering wide array of useful derivatives in solution and solid phase.<sup>2</sup> The fast reacting substrates for Baylis-Hillman reaction is of interest since they help to expedite the process of exploring and studying various synthetic and mechanistic aspects of the reaction. We reported<sup>3</sup> earlier that the substituted 5-isoxazolecarbaldehydes were fast reacting electrophiles for the Baylis-Hillman reaction and the reason ascribed for the fast reactivity was concerned with the proximity of the formyl group with the heteroatom (Fig. 1). On the basis of similar reasoning it was also envisaged in our earlier report<sup>4</sup> that substituted 3-isoxazolecarbaldehydes would also be fast reacting electrophiles in Baylis-Hillman reaction. To substantiate this hypothesis on the basis of experimental evidence, the synthesis and Baylis-Hillman reaction of substituted 3-isoxazolecarbaldehydes were undertaken. As expected, these substrates undergo very fast and facile Baylis-Hillman reaction in solution with variety of alkenes under conventional conditions and their solid phase reactions were also efficient under ordinary conditions. The details of our results are being presented here.



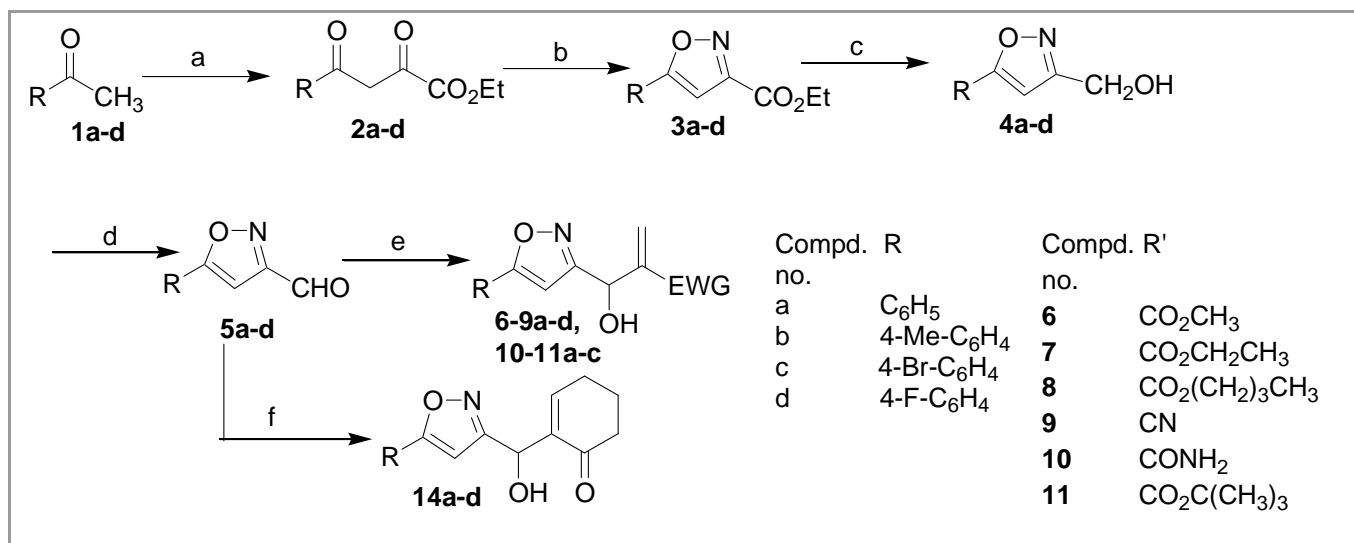
**Figure 1** Proton abstraction is aided by the lone pair of the heteroatom leading to immediate release of the base (published earlier).<sup>4</sup>

The substituted 3-isoxazolecarbaldehydes were prepared by following the synthetic strategy reported earlier.<sup>5</sup> This strategy involved the reaction of various substituted

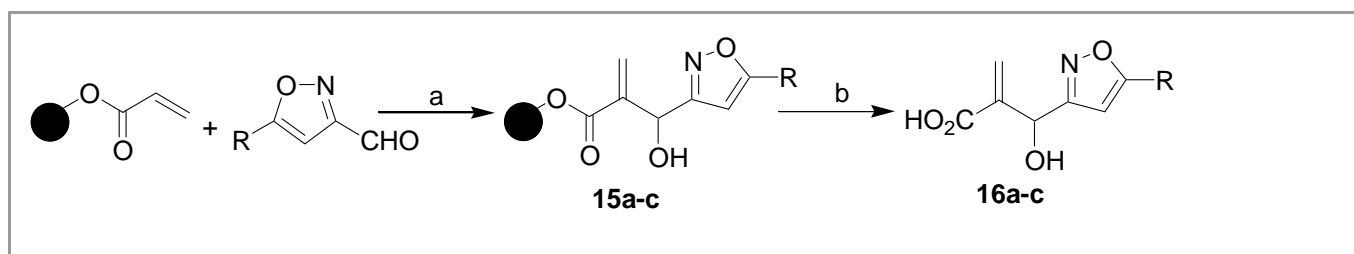
acetophenones (**1a-d**) with diethyl oxalate in the presence of sodium hydride (60% in oil)(Scheme 1). The resulting 2, 4-diketoesters (**2a-d**) on treatment with hydroxylamine hydrochloride furnished substituted 3-isoxazole esters (**3a-d**) in excellent yields. These esters were reduced with lithium aluminum hydride and the resulting alcohols (**4a-d**) were oxidized with pyridinium chlorochromate to yield the desired substituted 3-isoxazolecarbaldehydes (**5a-d**). These aldehydes (**5a-d**) were then treated with various activated alkenes in the presence of DABCO and in the absence of any solvent to furnish the Baylis-Hillman adducts (**6-9a-d**, **10-11a-c**) in excellent yields (Table 1). Contrary to the findings with their corresponding 5-isomer,<sup>7</sup> we failed to isolate ether derivatives in reactions of these aldehydes. The substituted 3-isoxazolecarbaldehydes also undergoes fast reaction with acrylamide in the presence of DABCO and with cyclohexenone in the presence of DMAP (**14a-d**).

Reactions of substituted 3-isoxazolecarbaldehydes (**5a-c**) with the acrylate resins derived from the Wang resins led to the assessment of their reactivity towards Baylis-Hillman reaction on the solid phase. Similar to the reactions in solution phase, these aldehydes undergo fast Baylis-Hillman reaction on solid phase to yield the desired products (**16a-c**) in excellent yields and high purity (Scheme 2).

In an attempt to study the comparative reactivity of 3-, 4- and 5-isoxazolecarbaldehydes the profiling of the progress of the reaction on the basis of the formation of Baylis-Hillman adducts at different time intervals, was carried out with the help of HPLC (Table 2). However, no significant difference was observed for the reactivities of 3- and 5-isoxazolecarbaldehydes towards Baylis-Hillman reaction. Compared to these situations, reaction of substituted 4-isoxazolecarbaldehydes was sluggish and after 45 mins. only small fraction of aldehyde was converted to the adduct. These results provide experimental evidence to support the hypothesis that the presence of proximal heteroatom within a heterocycle does facilitate the elimination of the base from the intermediate (Fig. 1) and accelerates the reaction. However, this study does not provide a clue to comment on the possible contribution of basicity of the heteroatom towards acceleration of the reaction.



**Scheme 1** Reagents and Conditions: a) Diethyl oxalate, NaH, toluene, reflux, 1.5 h. b) NH<sub>2</sub>OH.HCl, EtOH, reflux, 1h. c) LiAlH<sub>4</sub>, diethyl ether, reflux, 30 min. d) PCC, CH<sub>2</sub>Cl<sub>2</sub>, r.t., 5 h. e) CH<sub>2</sub>=CHEWG, DABCO, 15-30 min. f) cyclohexenone, DMAP, dioxane: water (2:1), r.t., 1h.



**Scheme 2** Reagents and Conditions: a) DABCO, DMSO, 3h, rt, 600rpm. b) CH<sub>2</sub>Cl<sub>2</sub>: TFA (1:1), 1h, rt.

In conclusion, we have described the fast and efficient Baylis-Hillman reaction of substituted 3-isoxazolecarbaldehydes with variety of alkenes. The results of the present study support our hypothesis proposed earlier that proximal heteroatom within the heterocycle does contribute towards acceleration of Baylis-Hillman reaction. This may in turn prove important for predicting the reactivity of formyl group for Baylis-Hillman reaction in other heterocyclic systems.

Melting points are uncorrected and were determined in capillary tubes on a hot stage apparatus containing silicon oil. IR spectra were recorded using Perkin Elmer's Spectrum RX I FTIR spectrophotometer as KBr disc or neat. <sup>1</sup>H NMR spectra were recorded either on a Bruker DPX-200 FT or Bruker Avance DRX-300 spectrometers, using TMS as an internal standard (chemical shifts in  $\delta$  values, J in Hz). The ESMS were recorded through direct flow injections in Merck M-8000 LCMS system and FABMS spectra were recorded on JEOL/ SX-102 spectrometer. Elemental analyses were performed on Elementar's Vario EL III microanalyzer. All HPLC were carried out on Agilent 1100 automated system having

DA detector ( $\lambda_{\max}$  = 220nm, 254nm used for this study) using a gradient run of 0-100% acetonitrile in water containing 0.1% TFA in 25 min on a RP-18e column (150 X 4.6 mm) having particle size of 5 $\mu$ m.

**Synthesis of substituted 3-isoxazolecarbaldehyde (5a-d)-General Procedure:** To the solution of appropriately substituted acetophenone (0.083 mol) in anhydrous toluene (200 mL) was added suspension of 60% NaH in oil (6.4g, 0.16 mol) in portions and the mixture was warmed to 45-50 °C under stirring. At this temperature a solution of diethyl oxalate (17 mL, 0.124 mol) in anhydrous toluene (50 mL) was added dropwise under stirring. The reaction mixture was refluxed for another 1.5 h. Thereafter, the reaction mixture was filtered and the filtrate was concentrated and column chromatographed using hexane: ethylacetate (80: 20, v/v) to remove the oil of NaH and obtain the pure 2, 4-diketo ester derivatives (2a-d) in 90-95% yield (column chromatography can be circumvented resulting in decrease of yields of final products by 2-4 %). To the solution of appropriate 2, 4-diketo ester (2a-d) (0.03 mol) in EtOH (75 mL) was added NH<sub>2</sub>OH. HCl (6.25 g, 0.09 mol) and the reaction mixture was refluxed under stirring for 1 h. The reaction mixture was cooled to 10-12 °C and the separated solid product

was filtered. The yield of ester (**3a-d**) ranged between 72-75%. To the solution of appropriate ester (0.019 mol)

Table 1: Characterization data for Baylis-Hillman adducts of substituted 3-isoxazolecarbaldehydes

Compd. no	R	EWG	Yield (%) <sup>a</sup>	Mp (°C)	Mass (ES+) <i>m/z</i>	IR (cm <sup>-1</sup> )
<b>6a</b>	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Me	90	97-99	260 (M <sup>+</sup> +1)	1721 (ester C=O), 3337 (OH)
<b>6b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Me	93	98-100	296.40 (M <sup>+</sup> +Na)	1723 (ester C=O), 3315 (OH)
<b>6c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Me	89	95-96	360.27 (M <sup>+</sup> +Na)	1711 (ester C=O), 3493 (OH)
<b>6d</b>	4-F-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Me	85	103-104	300.47 (M <sup>+</sup> +Na)	1716 (ester C=O), 3473 (OH)
<b>7a</b>	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	89	71-72	296.33 (M <sup>+</sup> +Na)	1715 (ester C=O), 3342 (OH)
<b>7b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	88	81-83	310.33 (M <sup>+</sup> +Na)	1717 (ester C=O), 3497 (OH)
<b>7c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	83	85-86	374.27 (M <sup>+</sup> +Na)	1706 (ester C=O), 3485 (OH)
<b>7d</b>	4-F-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	77	Oil (pale yellow)	314.40 (M <sup>+</sup> +Na)	1712 (ester C=O), 3403 (OH)
<b>8a</b>	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Bu-n	90	67-70	324.33 (M <sup>+</sup> +Na)	1717 (ester C=O), 3345 (OH)
<b>8b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Bu-n	90	77-78	338.27 (M <sup>+</sup> +Na)	1719 (ester C=O), 3305 (OH)
<b>8c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Bu-n	89	81-83	402.20 (M <sup>+</sup> +Na)	1707 (ester C=O), 3496 (OH)
<b>8d</b>	4-F-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Bu-n	81	Oil (pale yellow)	342.40 (M <sup>+</sup> +Na)	1712 (ester C=O), 3419 (OH)
<b>9a</b>	C <sub>6</sub> H <sub>5</sub>	CN	91	135-136	227.07 (M <sup>+</sup> +1)	2226 (C≡N), 3345 (OH)
<b>9b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CN	93	133-134	241.00 (M <sup>+</sup> +Na)	2227 (C≡N), 3273 (OH)
<b>9c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	CN	90	139-140	304.67 (M <sup>+</sup> +1)	2224 (C≡N), 3306 (OH)
<b>9d</b>	4-F-C <sub>6</sub> H <sub>4</sub>	CN	90	105-107	245.22 (M <sup>+</sup> +1)	2232 (C≡N), 3396 (OH)
<b>10a</b>	C <sub>6</sub> H <sub>5</sub>	CONH <sub>2</sub>	79	139-140	267.27 (M <sup>+</sup> +Na)	1660 (amide C=O), 3199 (NH <sub>2</sub> ), 3387 (OH)
<b>10b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CONH <sub>2</sub>	81	163-164	281.40 (M <sup>+</sup> +Na)	1650 (amide C=O), 3199 (NH <sub>2</sub> ), 3392 (OH)
<b>10c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	CONH <sub>2</sub>	77	154-156	324.33 (M <sup>+</sup> +1)	1662 (amide C=O), 3196 (NH <sub>2</sub> ), 3400 (OH)
<b>11a</b>	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Bu-t	88	Oil (pale yellow)	324.23 (M <sup>+</sup> +Na)	17011 (ester C=O), 3308 (OH)
<b>11b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Bu-t	84	85-86	338.13 (M <sup>+</sup> +Na)	1704 (ester C=O), 3349 (OH)
<b>11c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Bu-t	80	82-83	402.20 (M <sup>+</sup> +Na)	1707 (ester C=O), 3371 (C=O)
<b>15a</b>	C <sub>6</sub> H <sub>5</sub>	-	90	96-98	270 (M <sup>+</sup> +1) <sup>b</sup>	1659 (C=O), 3405 (OH)
<b>15b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	-	90	103-104	284 (M <sup>+</sup> +1) <sup>b</sup>	1650 (C=O), 3366 (OH)
<b>15c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	-	84	87-88	370.20 (M <sup>+</sup> +Na)	1623 (C=O), 3417 (OH)
<b>15d</b>	4-F-C <sub>6</sub> H <sub>4</sub>	-	79	Oil (pale yellow)	288 (M <sup>+</sup> +1) <sup>b</sup>	1667 (C=O), 3399 (OH)
<b>16a</b>	C <sub>6</sub> H <sub>5</sub>	-	89 (94)	191-192	268.40 (M <sup>+</sup> +Na)	1690 (acid C=O), 3332 (OH)
<b>16b</b>	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	-	95 (99) <sup>c</sup>	179-181	282.33 (M <sup>+</sup> +Na)	1690 (acid C=O), 3313 (OH)
<b>16c</b>	4-Br-C <sub>6</sub> H <sub>4</sub>	-	93 (99) <sup>c</sup>	139-140	346.33 (M <sup>+</sup> +Na)	1690 (acid C=O), 3387 (OH)

<sup>a</sup>All compounds were obtained as white solids except stated otherwise. <sup>b</sup>FABMS. <sup>c</sup>Analytical HPLC of the crude product show single peak.

Table 2: Evaluation of the reactivities of 3, 4, 5-isoxazolecarbaldehydes (ICD)<sup>a</sup> with the help of analytical HPLC<sup>b</sup>.

Time (min)	% formation of BH products with methyl acrylate						Time (min)	% formation of BH products with acrylonitrile					
	3-ICD		4-ICD		5-ICD			3-ICD		4-ICD		5-ICD	
	H	4-Me	H	4-Me	H	4-Me		H	4-Me	H	4-Me	H	4-Me
5	5:95	9:91	100:0	100:0	4:96	10:90	5	2:98	5:95	100:0	100:0	1:99	1:99
10	C <sup>c</sup>	C	100:0	100:0	C	C	10	C	C	100:0	100:0	C	C
20	-	-	100:0	100:0	-	-	20	-	-	100:0	100:0	-	-
25	-	-	100:0	100:0	-	-	25	-	-	99:1	98:2	-	-
35	-	-	100:0	100:0	-	-	35	-	-	96:4	96:4	-	-
45	-	-	99:1	99:1	-	-	45	-	-	96:4	97:3	-	-

<sup>a</sup>All reactions were performed under neat conditions using same amount of substrates and reactants. The ratios expressed are of starting substrate: product formed. <sup>b</sup>The HPLC were performed at  $\lambda_{\max}$  of 220 and 254nm at a gradient run of 0-100% acetonitrile in water containing 0.1% TFA in 25 min on a RP-18e column (150 X 4.6mm) having particle size of 5 $\mu$ m. <sup>c</sup>Complete. Blank columns indicate no change in HPLC profile after completion.

in anhydrous ether was added  $\text{LiAlH}_4$  (1.13 g, 0.029 mol) and the reaction mixture was stirred for 30 min at 40 °C. The reaction mixture was decomposed with 10% aqueous NaOH solution and the separated solid was filtered and washed with EtOAc. The filtrate was dried and concentrated to obtain alcohols (**4a-d**) (82-87%), which were used without any purification. To the solution of appropriate alcohol (**4a-d**) (0.02 mol) in anhydrous  $\text{CH}_2\text{Cl}_2$  was added PCC (6.4 g, 0.03 mol) and the reaction mixture was stirred at r.t. On completion (approx. 5h) the reaction mixture was passed through a small band of silica gel using hexane: ethyl acetate (85: 15, v/v) as eluent to obtain the pure substituted 3-isoxazolecarbaldehydes (**5a-d**) as solids in 78-81% yields.

**Baylis-Hillman reaction-General Procedure:** To a mixture of DABCO (0.15 g, 0.0013 mol) and appropriate alkene (0.0053 mol) that has been stirred at r.t. for 10 min. was added appropriate aldehyde from **5a-d** (0.0053 mol) under stirring and the reaction was allowed to proceed for a period 10-30 min. Thereafter 5% aq. HCl soln. (50 mL) was added to the reaction mixture to neutralize the base and extracted with ethyl acetate (2x50 mL). The organic layers were combined, washed with brine (75 mL), dried over  $\text{Na}_2\text{SO}_4$  and evaporated under vacuum to yield an oily residue. The residue upon trituration with hexane furnished pure products. However analytically pure samples were obtained by passing through a small band of silica gel (60-120 mesh) using a mixture of hexane: ethyl acetate (75:25, v/v) as eluent.

#### 2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-acrylic acid methyl ester (6a)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz):  $\delta$  = 3.62, 3.65 (d, 1H,  $J$  = 7.2 Hz, OH), 3.80 (s, 3H,  $\text{CO}_2\text{Me}$ ), 5.66, 5.69 (d, 1H,  $J$  = 7.0 Hz, CH), 6.01 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.59 (s, 1H, =CH), 7.43-7.45 (m, 3H, ArH), 7.74-7.79 (m, 2H, ArH).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50.32 MHz):  $\delta$  = 52.57 ( $\text{CH}_3$ ), 67.82 (CH), 98.48 (CH), 126.24 (2 X CH), 127.71 (C), 127.95 ( $\text{CH}_2$ ), 129.34 (2 X CH), 130.65 (CH), 139.67 (C), 165.87 (C), 166.85 (C), 170.72 (C).

Anal. Calcd. for  $\text{C}_{14}\text{H}_{13}\text{NO}_4$ : C, 64.86; H, 5.05; N, 5.40. Found: C, 64.82; H, 5.17; N, 5.13.

#### 2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-acrylic acid methyl ester (6b)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz):  $\delta$  = 2.39 (s, 3H,  $\text{CH}_3$ ), 3.60, 3.64 (d, 1H,  $J$  = 7.2 Hz, OH), 3.80 (s, 3H,  $\text{CO}_2\text{Me}$ ), 5.65, 5.69 (d, 1H,  $J$  = 7.2 Hz, CH), 6.01 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.54 (s, 1H, =CH), 7.23, 7.27 (d, 2H,  $J$  = 8.0 Hz, ArH), 7.63, 7.67 (d, 2H,  $J$  = 8.0 Hz, ArH).

Anal. Calcd. for  $\text{C}_{15}\text{H}_{15}\text{NO}_4$ : C, 65.92; H, 5.53; N, 5.13. Found: C, 66.10; H, 5.52; N, 5.11.

#### 2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid methyl ester (6c)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz):  $\delta$  = 3.60, 3.64 (d, 1H,  $J$  = 7.2 Hz, OH), 3.80 (s, 3H,  $\text{CO}_2\text{Me}$ ), 5.65, 5.69 (d, 1H,  $J$  = 7.2 Hz, CH), 6.01 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.54 (s, 1H, =CH), 7.23, 7.27 (d, 2H,  $J$  = 8.0 Hz, ArH), 7.63, 7.67 (d, 2H,  $J$  = 8.0 Hz, ArH).

Anal. Calcd. for  $\text{C}_{14}\text{H}_{12}\text{BrNO}_4$ : C, 49.73; H, 3.58; N, 4.14. Found: C, 50.06; H, 3.88; N, 4.07.

#### 2-[[5-(4-Fluoro-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid methyl ester (6d)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz):  $\delta$  = 3.59, 3.62 (d, 1H,  $J$  = 7.8 Hz, OH), 3.81 (s, 3H,  $\text{CO}_2\text{Me}$ ), 5.64, 5.68 (d, 1H,  $J$  = 7.4 Hz, CH), 6.01 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.55 (s, 1H, =CH), 7.10-7.19 (m, 2H, ArH), 7.72-7.79 (m, 2H, ArH).

Anal. Calcd. for  $\text{C}_{14}\text{H}_{12}\text{FNO}_4$ : C, 60.65; H, 4.36; N, 5.05. Found: C, 60.36; H, 4.36; N, 4.80.

#### 2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-acrylic acid ethyl ester (7a)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz):  $\delta$  = 1.31 (t, 3H,  $J$  = 7.0 Hz,  $\text{CH}_3$ ), 3.71, 3.74 (d, 1H,  $J$  = 7.0 Hz, OH), 4.25 (q, 2H,  $J$  = 7.0 Hz,  $\text{CO}_2\text{CH}_2$ ), 5.66, 5.69 (d, 1H,  $J$  = 6.0 Hz, CH), 5.99 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.60 (s, 1H, =CH), 7.43-7.48 (m, 3H, ArH), 7.74-7.79 (m, 2H, ArH).

Anal. Calcd. for  $\text{C}_{15}\text{H}_{15}\text{NO}_4$ : C, 65.92; H, 5.53; N, 5.13. Found: C, 66.04; H, 5.61; N, 4.86.

#### 2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-acrylic acid ethyl ester (7b)

$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 200 MHz):  $\delta$  = 1.20 (t, 3H,  $J$  = 7.0 Hz,  $\text{CH}_3$ ), 2.33 (s, 3H,  $\text{CH}_3$ ), 3.71, 3.74 (d, 1H,  $J$  = 7.0 Hz, OH), 4.22 (q, 2H,  $J$  = 7.0 Hz,  $\text{CO}_2\text{CH}_2$ ), 5.72 (s, 1H, CH), 6.03, 6.05 (d, 1H,  $J$  = 3.0 Hz, =CHH), 6.40, 6.41 (s, 1H,  $J$  = 2.8 Hz, =CHH), 6.53 (s, 1H, =CH), 7.20, 7.24 (d, 2H,  $J$  = 8.0 Hz, ArH), 7.58-7.62 (d, 2H,  $J$  = 8.0 Hz, ArH).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 50.32 MHz):  $\delta$  = 14.40 ( $\text{CH}_3$ ), 21.78 ( $\text{CH}_3$ ), 61.56 ( $\text{CH}_2$ ), 67.17 (CH), 97.98 (CH), 125.00 (C), 126.14 (2 X CH), 127.40 ( $\text{CH}_2$ ), 129.98 (2 X CH), 140.24 (C), 140.86 (C), 165.99 (C), 166.32 (C), 170.71 (C).

Anal. Calcd. for  $\text{C}_{16}\text{H}_{17}\text{NO}_4$ : C, 66.89; H, 5.96; N, 4.88. Found: C, 67.15; H, 5.91; N, 4.86.

#### 2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid ethyl ester (7c)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 1.30 (t, 3H, *J* = 7.2 Hz, CH<sub>3</sub>), 3.71, 3.74 (d, 1H, *J* = 5.4 Hz, OH), 4.25 (q, 2H, *J* = 7.2 Hz, CO<sub>2</sub>CH<sub>2</sub>), 5.65, 5.68 (d, 1H, *J* = 5.2 Hz, CH), 6.00 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.61 (s, 1H, =CH), 7.60 (s, 4H, ArH).

Anal. Calcd. for C<sub>15</sub>H<sub>14</sub>BrNO<sub>4</sub>: C, 51.16; H, 4.01; N, 3.98. Found: C, 50.94; H, 4.05; N, 3.91.

#### **2-[[5-(4-Fluoro-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid ethyl ester (7d)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 1.30 (t, 3H, *J* = 7.2 Hz, CH<sub>3</sub>), 3.77 (brs, 1H, OH), 4.25 (q, 2H, *J* = 7.2 Hz, CO<sub>2</sub>CH<sub>2</sub>), 5.66 (s, 1H, CH), 5.99 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.55 (s, 1H, =CH), 7.10-7.19 (m, 2H, ArH), 7.72-7.79 (m, 2H, ArH).

Anal. Calcd. for C<sub>15</sub>H<sub>14</sub>FNO<sub>4</sub>: C, 61.85; H, 4.84; N, 4.81. C, 61.55; H, 5.06; N, 4.73.

#### **2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-acrylic acid butyl ester (8a)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 0.92 (t, 3H, *J* = 7.2 Hz, CH<sub>3</sub>), 1.32-1.43 (m, 2H, CH<sub>2</sub>), 1.58-1.68 (m, 2H, CH<sub>2</sub>), 3.73, 3.76 (d, 1H, *J* = 7.4 Hz, OH), 4.20 (t, 2H, *J* = 6.6 Hz, CO<sub>2</sub>CH<sub>2</sub>), 5.66, 5.69 (d, 1H, *J* = 7.0 Hz, CH), 5.99 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.60 (s, 1H, =CH), 7.43-7.48 (m, 3H, ArH), 7.74-7.79 (m, 2H, ArH).

Anal. Calcd. for C<sub>17</sub>H<sub>19</sub>NO<sub>4</sub>: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.90; H, 6.26; N, 4.39.

#### **2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-acrylic acid butyl ester (8b)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 0.92 (t, 3H, *J* = 7.2 Hz, CH<sub>3</sub>), 1.35-1.47 (m, 2H, CH<sub>2</sub>), 1.57-1.68 (m, 2H, CH<sub>2</sub>), 2.39 (s, 3H, CH<sub>3</sub>), 3.63, 3.66 (d, 1H, *J* = 7.4 Hz, OH), 4.20 (t, 2H, *J* = 6.6 Hz, CO<sub>2</sub>CH<sub>2</sub>), 5.64, 5.68 (d, 1H, *J* = 7.0 Hz, CH), 5.98 (s, 1H, =CHH), 6.42 (s, 1H, =CHH), 6.54 (s, 1H, =CH), 7.23, 7.27 (d, 2H, *J* = 8.0 Hz, ArH), 7.63-7.67 (d, 2H, *J* = 8.0 Hz, ArH).

Anal. Calcd. for C<sub>18</sub>H<sub>21</sub>NO<sub>4</sub>: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.71; H, 6.74; N, 4.44.

#### **2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid butyl ester (8c)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 0.91 (t, 3H, *J* = 7.2 Hz, CH<sub>3</sub>), 1.32-1.38 (m, 2H, CH<sub>2</sub>), 1.61-1.68 (m, 2H, CH<sub>2</sub>), 3.79, 3.82 (d, 1H, *J* = 7.4 Hz, OH), 4.18 (t, 2H, *J* = 6.2 Hz, CO<sub>2</sub>CH<sub>2</sub>), 5.65, 5.68 (d, 1H, *J* = 7.4 Hz, CH), 5.98, 6.00 (d, 1H, *J* = 4.0 Hz, =CHH), 6.41, 6.43 (s, 1H, *J* = 4.0 Hz, =CHH), 6.58, 6.60 (s, 1H, *J* = 4.0 Hz, =CH), 7.57-7.60 (m, 4H, ArH).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 50.32 MHz): δ = 14.03 (CH<sub>3</sub>), 19.50 (CH<sub>2</sub>), 30.91 (CH<sub>3</sub>), 65.57 (CH<sub>2</sub>), 67.79 (CH), 98.95 (CH), 125.03 (C), 126.60 (C), 127.66 (CH<sub>2</sub>), 127.77 (2 X CH), 132.64 (2 X CH), 139.82 (C), 166.14 (C), 166.45 (C), 169.54 (C).

Anal. Calcd. for C<sub>17</sub>H<sub>18</sub>BrNO<sub>4</sub>: C, 53.70; H, 4.77; N, 3.68. Found: C, 53.83; H, 4.72; N, 4.07.

#### **2-[[5-(4-Fluoro-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid butyl ester (8d)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 0.92 (t, 3H, *J* = 6.0 Hz, CH<sub>3</sub>), 1.26-1.44 (m, 2H, CH<sub>2</sub>), 1.60-1.70 (m, 2H, CH<sub>2</sub>), 3.74 (brs, 1H, OH), 4.20 (t, 2H, *J* = 6.6 Hz, CO<sub>2</sub>CH<sub>2</sub>), 5.67 (s, 1H, CH), 6.00 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.55 (s, 1H, =CH), 7.157 (t, 2H, *J* = 6.0 Hz, ArH), 7.73-7.77 (m, 2H, ArH).

Anal. Calcd. for C<sub>17</sub>H<sub>18</sub>FNO<sub>4</sub>: C, 63.94; H, 5.68; N, 4.39. Found: C, 63.88; H, 5.68; N, 4.38.

#### **2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-acrylonitrile (9a)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 3.13 (s, 1H, OH), 5.55, 5.57 (d, 1H, *J* = 4.0 Hz, CH), 6.169, 6.175 (d, 1H, *J* = 1.4 Hz, =CHH), 6.255, 6.262 (d, 1H, *J* = 1.4 Hz, =CHH), 6.60 (s, 1H, =CH), 7.45-7.50 (m, 3H, ArH), 7.76-7.81 (m, 2H, ArH).

Anal. Calcd. for C<sub>13</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub>: C, 69.02; H, 4.46; N, 12.38. Found: C, 68.76; H, 4.52; N, 12.18.

#### **2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-acrylonitrile (9b)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 2.39 (s, 3H, CH<sub>3</sub>), 3.18 (s, 1H, OH), 5.55 (s, 1H, CH), 6.17 (s, 1H, =CHH), 6.248, 6.252 (d, 1H, *J* = 0.8 Hz, =CHH), 6.59 (s, 1H, =CH), 7.25, 7.29 (d, 2H, *J* = 8.0 Hz, ArH), 7.64, 7.68 (d, 2H, *J* = 8.0 Hz, ArH).

Anal. Calcd. for C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: C, 69.99; H, 5.03; N, 11.66. Found: C, 69.84; H, 5.06; N, 11.57.

#### **2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylonitrile (9c)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 3.19 (brs, 1H, OH), 5.56 (s, 1H, CH), 6.18 (s, 1H, =CHH), 6.260, 6.265 (d, 1H, *J* = 1.0 Hz, =CHH), 6.66 (s, 1H, =CH), 7.62 (s, 4H, ArH).

Anal. Calcd. for C<sub>13</sub>H<sub>9</sub>BrN<sub>2</sub>O<sub>2</sub>: C, 51.17; H, 2.97; N, 9.18. Found: C, 51.52; H, 2.95; N, 8.78.

#### **2-[[5-(4-Fluoro-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylonitrile (9d)**

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 3.47 (s, 1H, OH), 5.56 (s, 1H, CH), 6.17 (s, 1H, =CHH), 6.260 (s, 1H, =CHH), 6.61 (s, 1H, =CH), 7.11-7.20 (m, 2H, ArH), 7.73-7.80 (m, 2H, ArH).

Anal. Calcd. for C<sub>13</sub>H<sub>9</sub>FN<sub>2</sub>O<sub>2</sub>: C, 63.93; H, 3.71; N, 11.47. Found: C, 63.85; H, 4.01; N, 11.13.

#### 2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-acrylamide (10a)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 5.66, 5.69 (d, 1H, *J* = 5.8 Hz, OH), 5.75 (s, 1H, =CHH), 5.94, 5.77 (d, 1H, *J* = 6.0 Hz, CH), 6.12 (s, 1H, =CHH), 6.65 (s, 1H, =CH), 7.40-7.49 (m, 4H, Ar-H and NH<sub>2</sub>), 7.73-7.78 (m, 2H, ArH).

Anal. Calcd. for C<sub>13</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>: C, 63.93; H, 4.95; N, 11.47. Found: C, 63.86; H, 5.08; N, 11.64.

#### 2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-acrylamide (10b)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 2.39 (s, 3H, CH<sub>3</sub>), 5.66 (s, 1H, OH), 5.74 (s, 2H, CH and =CHH), 6.12 (s, 1H, =CHH), 6.58 (s, 1H, =CH), 7.24, 7.27 (d, 2H, *J* = 8.0 Hz, ArH), 7.34 (s, 1H, NH<sub>2</sub>), 7.62, 7.66 (d, 2H, *J* = 8.0 Hz, ArH).

Anal. Calcd. for C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.22; H, 5.56; N, 11.01.

#### 2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylamide (10c)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 5.66, 5.69 (d, 1H, *J* = 5.8 Hz, OH), 5.75 (s, 1H, =CHH), 5.92, 5.94 (d, 1H, *J* = 5.2 Hz, CH), 6.12 (s, 1H, =CHH), 6.66 (s, 1H, =CH), 7.39 (s, 1H, NH<sub>2</sub>), 7.61, 7.62 (d, *J* = 2.6 Hz, 3H, Ar-H).

Anal. Calcd. for C<sub>13</sub>H<sub>11</sub>BrN<sub>2</sub>O<sub>3</sub>: C, 48.32; H, 3.43; N, 8.67. Found: C, 48.25; H, 3.59; N, 8.88.

#### 2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-acrylic acid tert-butyl ester (11a)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 1.47 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 3.90 (brs, 1H, OH), 5.65 (s, 1H, CH), 5.92 (s, 1H, =CHH), 6.34 (s, 1H, =CHH), 6.59 (s, 1H, =CH), 7.42-7.45 (m, 3H, ArH), 7.73-7.78 (m, 2H, ArH).

Anal. Calcd. for C<sub>17</sub>H<sub>19</sub>NO<sub>4</sub>: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.71; H, 6.35; N, 4.55

#### 2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-acrylic acid tert-butyl ester (11b)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 1.48 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 2.39 (s, 3H, CH<sub>3</sub>), 3.79, 3.81 (d, 1H, *J* = 7.2 Hz, OH), 5.61, 5.63 (d, 1H, *J* = 6.6 Hz, CH), 5.90 (s, 1H, =CHH), 6.32 (s, 1H, =CHH), 6.53 (s, 1H, =CH), 7.24, 7.26 (d, 2H, *J* = 7.8 Hz, ArH), 7.64-7.66 (d, 2H, *J* = 7.8 Hz, ArH).

Anal. Calcd. for C<sub>18</sub>H<sub>21</sub>NO<sub>4</sub>: C, 68.55; H, 6.71; N, 4.44. Found: 68.40; H, 6.79; N, 4.07.

#### 2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid tert-butyl ester (11c)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 1.48 (s, 9H, C(CH<sub>3</sub>)<sub>3</sub>), 3.89 (brs, 1H, OH), 5.62 (s, 1H, CH), 5.90 (s, 1H, =CHH), 6.33 (s, 1H, =CHH), 6.60 (s, 1H, =CH), 7.58-7.65 (m, 4H, ArH).

Anal. Calcd. for C<sub>17</sub>H<sub>18</sub>BrNO<sub>4</sub>: C, 53.70; H, 4.77; N, 3.68. Found: C, 53.92; H, 4.89; N, 3.40.

**Baylis-Hillman reaction of cyclohexenone- General Procedure:** A mixture of appropriate compound from **5a-d** (0.0035 mol), DMAP (0.084g, 0.0006 mol) and cyclohexenone (0.34 mL, 0.0035 mol) in 5 mL of dioxane: water (3: 2, v/v) mixture was stirred at r.t. for 1h. Thereafter the reaction mixture was extracted with ethyl acetate (2 X 30 mL). The usual work up of the organic layer furnished a residue that upon trituration with hexane furnished pure solid products. For compound **14d**, column chromatography on silica gel using a mixture of hexane: ethyl acetate (85: 15, v/v) as eluent yielded the pure derivative.

#### 2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-cyclohex-2-enone (14a)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 1.99-2.07 (m, 2H, CH<sub>2</sub>), 2.42-2.52 (m, 4H, 2 X CH<sub>2</sub>), 4.10 (brs, 1H, OH), 5.60 (s, 1H, CH), 6.63 (s, 1H, =CH), 7.05 (t, 1H, *J* = 3.0 Hz, =CH), 7.235-7.26 (d, 2H, *J* = 8.0 Hz, ArH), 7.64-7.66 (d, 2H, *J* = 8.0 Hz, ArH).

Anal. Calcd. for C<sub>16</sub>H<sub>15</sub>NO<sub>3</sub>: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.23; H, 5.68; N, 5.30.

#### 2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-cyclohex-2-enone (14b)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 1.99-2.08 (m, 2H, CH<sub>2</sub>), 2.39 (s, 3H, CH<sub>3</sub>), 2.42-2.53 (m, 4H, 2 X CH<sub>2</sub>), 3.97 (brs, 1H, OH), 5.58 (s, 1H, CH), 6.57 (s, 1H, =CH), 7.05 (t, 1H, *J* = 3.9 Hz, =CH), 7.39-7.44 (m, 3H, ArH), 7.74-7.77 (m, 2H, ArH).

<sup>13</sup>C NMR (CDCl<sub>3</sub>, 50.32 MHz): δ = 21.83 (CH<sub>3</sub>), 22.74 (CH<sub>2</sub>), 26.14 (CH<sub>2</sub>), 38.78 (CH<sub>2</sub>), 67.70 (CH), 98.20 (CH), 125.10 (C), 126.15 (2 X CH), 130.00 (2 X CH), 138.68 (C), 140.84 (C), 149.00 (CH), 166.41 (C), 170.67 (C), 200.71 (C).

Anal. Calcd. for C<sub>17</sub>H<sub>17</sub>NO<sub>3</sub>: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.83; H, 5.95; N, 5.04.

#### 2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-cyclohex-2-enone (14c)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz): δ = 2.01-2.09 (m, 2H, CH<sub>2</sub>), 2.43-2.54 (m, 4H, 2 X CH<sub>2</sub>), 4.10, 4.14 (d, 1H, *J* = 7.2 Hz, OH), 5.56 (s, 1H, CH), 6.64 (s, 1H, =CH), 7.04 (t, 1H, *J* = 4.0 Hz, =CH), 7.60-7.66 (m, 4H, ArH).

Anal. Calcd. for C<sub>16</sub>H<sub>14</sub>BrNO<sub>3</sub>·H<sub>2</sub>O: C, 52.48; H, 4.40; N, 3.82. Found: C, 52.72; H, 4.49; N, 3.42.

#### 2-[[5-(4-Fluoro-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-cyclohex-2-enone (14d)

<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ = 1.93-2.08 (m, 2H, CH<sub>2</sub>), 2.44-2.63 (m, 4H, 2 X CH<sub>2</sub>), 4.08 (brs, 1H, OH), 5.57 (s, 1H, CH), 6.54 (s, 1H, =CH), 7.03-7.17 (m, 3H, ArH and =CH), 7.73-7.77 (m, 4H, ArH).

Anal. Calcd. for C<sub>16</sub>H<sub>14</sub>FNO<sub>3</sub>·1/2H<sub>2</sub>O C, 64.85; H, 5.10; N, 4.72. Found: C, 64.69; H, 5.07; N, 4.73.

**Baylis Hillman reaction on solid support-General Procedure:** To Wang acrylate resin (100 mg each in 3 PP syringes) prepared<sup>8</sup> from Wang resin (1.13 mmol/g, Novabiochem) in 800 μL DMSO was added 2 equivalents of DABCO. After 15 mins. of shaking solution of substituted 3-isoxazolecarboxaldehyde (**5a-c**) (4.0 eq.) in 300 μL of DMSO was added to respective reaction vessel. The resulting mixture was shaken at 600rpm for 3 h. Subsequently, the resin was washed with DMF (4 mL X 6), MeOH (4 mL X 6), DCM (4 mL X 3) and diethyl ether (4mL X 2). Finally the resins were cleaved with 50% TFA in DCM for 1h. The filtrate was evaporated and lyophilized using tert-butanol: water (4:1).

#### 2-[Hydroxy-(5-phenyl-isoxazol-3-yl)-methyl]-acrylic acid (16a)

95% purity (R<sub>t</sub> = 13.12 min)

<sup>1</sup>H NMR (CDCl<sub>3</sub>+ DMSOd<sub>6</sub>, 200 MHz): δ = 5.71 (s, 1H, CH), 6.06 (s, 1H, =CHH), 6.44 (s, 1H, =CHH), 6.60 (s, 1H, =CH), 7.41-7.46 (m, 3H, ArH), 7.74-7.77 (m, 2H, ArH).

<sup>13</sup>C NMR (CDCl<sub>3</sub>+ DMSOd<sub>6</sub> (a drop only)), 50.32 MHz): δ = 65.71 (CH), 98.08 (CH), 125.31 (2 X CH), 126.10 (CH<sub>2</sub>), 127.15 (C), 128.65 (2 X CH), 129.72 (CH), 140.32 (C), 165.73 (C), 167.45 (C), 169.32 (C). Anal. Calcd. for C<sub>13</sub>H<sub>11</sub>NO<sub>4</sub> C, 63.67; H, 4.52; N, 5.71. Found: C, 63.70; H, 4.59; N, 5.51.

Anal. Calcd. for C<sub>13</sub>H<sub>11</sub>NO<sub>4</sub>·H<sub>2</sub>O C, 59.31; H, 4.97; N, 5.32. Found: C, 59.59; H, 4.87; N, 5.18.

#### 2-[Hydroxy-(5-p-tolyl-isoxazol-3-yl)-methyl]-acrylic acid (16b)

99% purity (R<sub>t</sub> = 14.95 mins)

<sup>1</sup>H NMR (CDCl<sub>3</sub>+ DMSOd<sub>6</sub>, 300 MHz): δ = 2.39 (s, 3H, CH<sub>3</sub>), 5.69 (s, 1H, CH), 6.02 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.55 (s, 1H, =CH), 7.24, 7.26 (d, 2H, *J* = 8.0 Hz, ArH), 7.63-7.65 (d, 2H, *J* = 8.0 Hz, ArH).

Anal. Calcd. for C<sub>14</sub>H<sub>13</sub>NO<sub>4</sub> C, 64.86; H, 5.05; N, 5.40. Found: C, 64.61; H, 5.03; N, 5.20.

#### 2-[[5-(4-Bromo-phenyl)-isoxazol-3-yl]-hydroxy-methyl]-acrylic acid (16c)

99% (R<sub>t</sub> = 15.45 mins)

<sup>1</sup>H NMR (CDCl<sub>3</sub>+ DMSOd<sub>6</sub>, 300 MHz): δ = 5.70 (s, 1H, CH), 6.07 (s, 1H, =CHH), 6.43 (s, 1H, =CHH), 6.62 (s, 1H, =CH), 7.61 (s, 4H, ArH).

Anal. Calcd. for C<sub>13</sub>H<sub>10</sub>BrNO<sub>4</sub> C, 48.17; H, 3.11; N, 4.32. Found: C, 48.44; H, 3.51; N, 3.99.

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