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Efficient Synthesis of β-Acetamido Ketones and Esters Using Aluminum Chloride as an Inexpensive and Green Catalyst

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Aluminum chloride ($AlCl_3$) efficiently catalyzes one-pot multicomponent condensation of enolizable ketones or alkyl acetoacetates with aldehydes, acetonitrile and acetyl chloride to afford β-acetamido ketone or ester derivatives in high to excellent yields and in relatively short reaction times. Moreover, by this synthetic method, some novel β-acetamido ketones and esters (*i.e.* one complex structure) are prepared.

Keywords β-acetamido ketone, β-acetamido ester, aluminum chloride, enolizable ketone, synthetic methods, multicomponent reactions

Introduction

Multicomponent reactions (MCRs) have drawn great interest enjoying an outstanding status in modern organic synthesis and medicinal chemistry because they are one-pot processes bringing together three or more components and show high atom economy and high selectivity.[1-12] MCRs have great contributions in convergent synthesis of complex and important organic molecules from simple and readily available starting materials, and have emerged as powerful tools for drug discovery.[2-12]

β-Acetamido ketone or ester derivatives are useful building blocks for a number of biologically and pharmaceutically valuable compounds.[13-17] They are precursors of molecules such as 1,3-amino alcohols,[13-17] and structural scaffolds found in natural nucleoside peptide antibiotics such as nikkomycins or neopolyoxins. Moreover, recently, it is reported that β-acetamido ketones can act as aglucosidase inhibitors.[18] The structural and bioactive properties of β-acetamido carbonyl compounds led to the generation of some processes employing some catalysts such as montmorillonite K10,[19] $CoCl_2$,[20-22] $H_6P_2W_{18}O_{62}$,[23] $H_3PW_{12}O_{40}$,[24] $Zr(HSO_4)_4$,[25] $Mg(HSO_4)_2$,[25] TMSCl,[26] $BiCl_3$,[27] I_2,[28] silica sulfuric acid,[29] ZnO,[30] selectfluor™,[31] sulfamic acid,[32] and $ZrOCl_2{\bullet}8H_2O$.[33] However, most of the reported methods for the synthesis of these compounds are associated with one or more of the following drawbacks: (i) low yields, (ii) long reaction times, (iii) the use of large amount of catalyst, (iv) the use of toxic or expensive catalysts, (v) tedious work-up procedure, and (vi) performance of the reaction under certain special conditions. Thus, search for an efficient, inexpensive, simple and nonpolluting method for the synthesis of β-acetamido carbonyl compounds is still of practical importance.

In recent decades, the applications of eco-friendly applicable industrial and green catalysts have received considerable interest. In fact, green chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products. Along this line, using aluminum chloride ($AlCl_3$), which is green,[34] inexpensive and low in toxicity, has found more attention. It has been used as an efficient acidic catalyst in organic synthesis, and found several industrial applications.[34-38] For example, $AlCl_3$ has been utilized as effective catalyst for Fries rearrangement,[38] Friedel-Crafts reactions (both acylations and alkylations),[39] Gatterman-Koch reaction,[40] esterification,[41] synthesis of 3,4-disubstituted dihydrocoumarin derivatives,[42] synthesis of multi-walled carbon nanotubes,[43] and [3+2] cycloadditions.[44]

Considering the above subjects, we describe here a simple new procedure for the synthesis of β-acetamido ketones and esters via the one-pot multicomponent condensation reaction between enolizable ketones or alkyl acetoacetates, aldehydes, acetonitrile and acetyl

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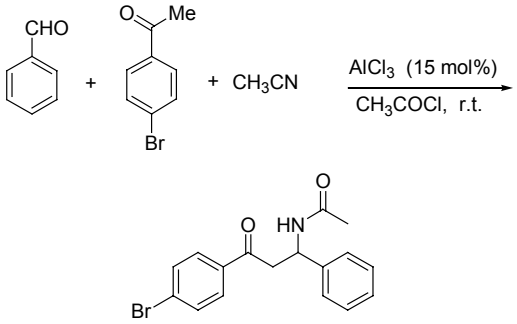
chloride in the presence of $AlCl_3$ as an efficient, green and very cheap catalyst at room temperature (Scheme 1).

Scheme 1 The synthesis of *N*-(3-(4-bromophenyl)-3-oxo-1-phenylpropyl)acetamide (**1l**) via the condensation reaction between 4-bromoacetophenone, benzaldehyde, acetonitrile and acetyl chloride



Results and Discussion

To optimize the reaction conditions for the synthesis of *β*-acetamido carbonyl compounds, the condensation of 4-bromoacetophenone with benzaldehyde, acetonitrile and acetyl chloride was selected as a model reaction to provide compound **1l** (Scheme 1). At first, the reaction was examined in the presence of 15 mol% of some metal salts and oxides such as $AlCl_3$, $MgCl_2$, $Mn(OAc)_2$, $Ni(OAc)_2$, $Cu(OAc)_2$, $Zn(OAc)_2$, $CuCl_2$, $CuSO_4$ and SiO_2 at room temperature. The results are summarized in Figure 1. As Figure 1 indicates, higher yield and shorter reaction time were obtained when $AlCl_3$ was utilized as catalyst.

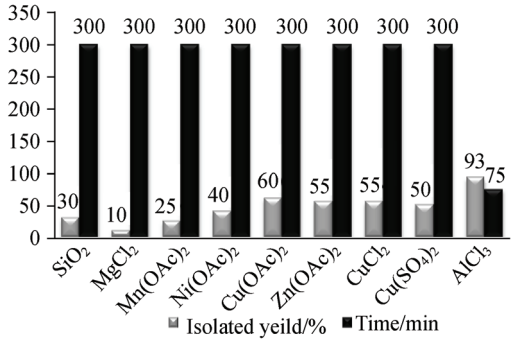


Figure 1 The condensation of 4-bromoacetophenone with benzaldehyde, acetonitrile and acetyl chloride using different catalysts (15 mol%).

In the next step, the reaction of 4-bromoacetophenone with benzaldehyde, acetonitrile and acetyl chloride was tested using different amounts of $AlCl_3$ at room temperature (Figure 2). As it can be seen in Figure 2, the best amount of the catalyst was 15 mol%.

In another study, to choose the appropriate solvent, amount of acetyl chloride and temperature for the reaction, the condensation of 4-bromoacetophenone with benzaldehyde, acetonitrile and acetyl chloride was examined using $AlCl_3$ at range of 30—70 ℃ in various

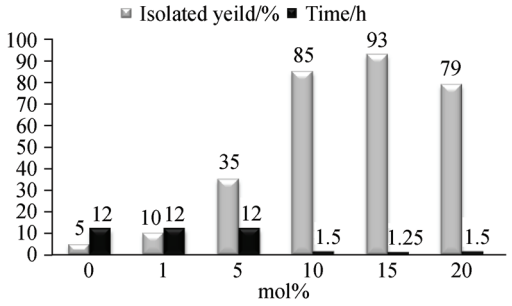


Figure 2 The reaction of 4-bromoacetophenone with benzaldehyde, acetonitrile and acetyl using different amounts of $AlCl_3$.

solvents (6 mL) in the presence of different amounts of acetyl chloride (Table 1). As Table 1 indicates, higher yield and shorter reaction time were obtained when the reaction was performed in acetonitrile as solvent in the presence of 0.6 mL of acetyl chloride at room temperature (Table 1, Entry 6).

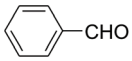
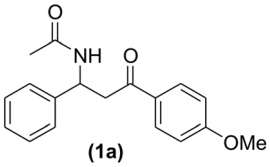
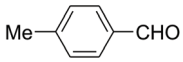
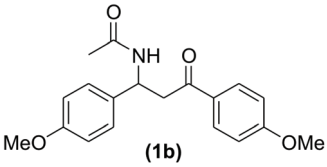
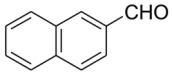
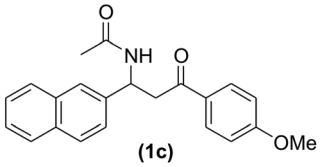
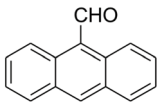
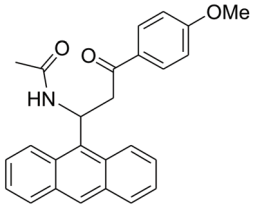
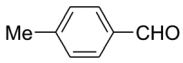
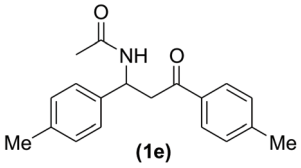
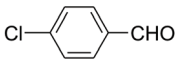
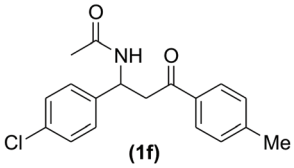
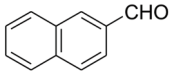
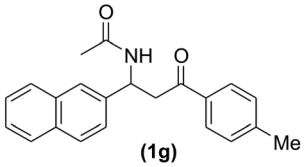
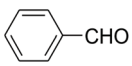
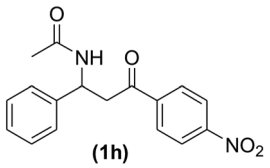
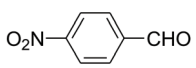
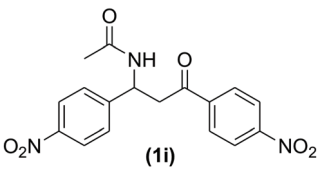
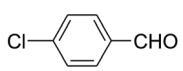
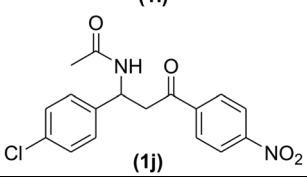
Table 1 Effect of solvent, amount of acetyl chloride and temperature on the reaction of 4-bromoacetophenone with benzaldehyde, acetonitrile and acetyl chloride promoted by $AlCl_3$

Entry[a]	Solvent	CH_3COCl amount/mL	Temperature/℃	Time/h	Yield[b]/%
1	EtOH	0.6	r.t.	5	28
2	MeOH	0.6	r.t.	5	34
3	THF	0.6	r.t.	5	79
4	EtOAc	0.6	r.t.	5	37
5	$CHCl_3$	0.6	r.t.	5	45
6	MeCN	0.6	r.t.	1.25	93
7	MeCN	0.4	r.t.	3	46
8	MeCN	0.8	r.t.	1.25	87
9	MeCN	0.6	45	1.25	41[c]
10	MeCN	0.6	70	1.25	30[c]

[a] The reaction conditions: 4-bromoacetophenone (2 mmol), benzaldehyde (2 mmol), acetonitrile (3 mmol), acetyl chloride (0.4—8 mL), $AlCl_3$ (15 mol%), solvent (6 mL), temperature (30—70 ℃). [b] Isolated yield. [c] In this reaction, some by-products were obtained besides the main product.

To assess the generality and efficacy of the method, different enolizable carbonyl compounds were reacted with structurally and electronically diverse aldehydes, acetonitrile and acetyl chloride under the optimized reaction conditions; the respective results are summarized in Table 1. As it can be seen in Table 1, the protocol was general and efficient; all reactions proceeded efficiently and the desired products were obtained in good to excellent yields in relatively short reaction times. The influence of electron-releasing substituents, electron-withdrawing substituents and halogens on the aromatic ring of the aldehyde was also studied. As Table 2 shows, electron-releasing groups increased the reaction yields (Table 2, compounds **1b** and **1e**); electron-withdrawing substituents slightly decreased the yields (Table 2,

Table 2 The synthesis of β-acetamido ketones and esters via the condensation of enolizable ketones or alkyl acetoacetates with aldehydes, acetonitrile and acetyl chloride

Aldehyde	Product[a]	Time/h	Yield[b]/%	m.p./℃ (lit.)
	 (1a)	1.25	94	127—129 (130—132)[33]
	 (1b)	1.25	96	124—127[c]
	 (1c)	1.25	96	108—110[c]
	 (1d)	3.5	85	138—140[c]
	 (1e)	1	95	118—119[c]
	 (1f)	2	92	130—132[c]
	 (1g)	1.25	92	111—112 (112—114)[26]
	 (1h)	2.5	92	75—77 (74—76)[33]
	 (1i)	3.5	88	185—188 (187—188)[25]
	 (1j)	3	90	114—116 (116—118)[26]

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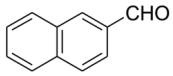
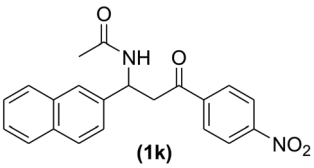
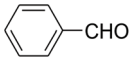
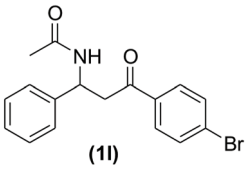
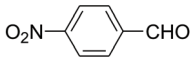
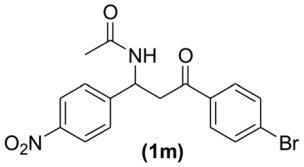
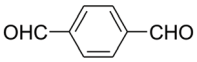
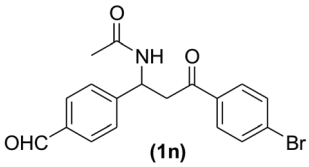
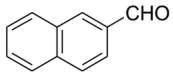
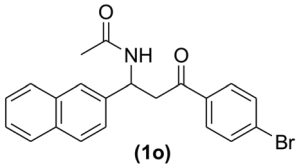
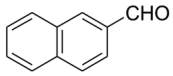
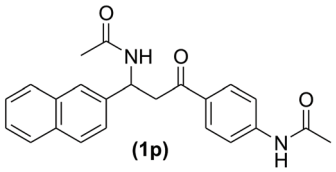
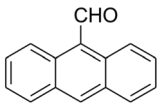
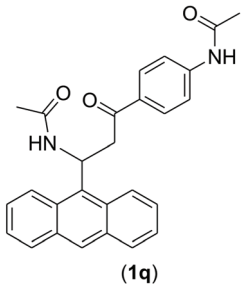
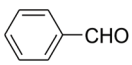
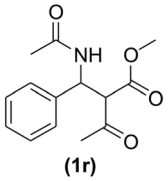
Aldehyde	Product[a]	Time/h	Yield[b]/%	m.p./℃ (lit.)
	 **(1k)**	3	87	165—166[c]
	 **(1l)**	1.25	93	100—101 (98—100)[26]
	 **(1m)**	2.5	88	162—163[d]
	 **(1n)**	2	86	104—105[c]
	 **(1o)**	1.5	90	138—140[c]
	 **(1p)**	1.25	83	168—174[c]
	 **(1q)**	3	86	166—167[c]
	 **(1r)**	1.75	88	140—142 (140—141)[25]

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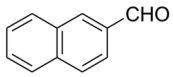
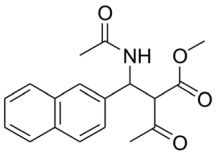
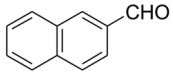
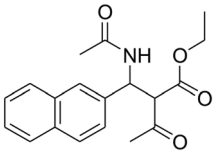
Aldehyde	Product[a]	Time/h	Yield[b]/%	m.p./℃ (lit.)
	 (1s)	1.75	89	138—139[c]
	 (1t)	2.75	90	149—152[c]

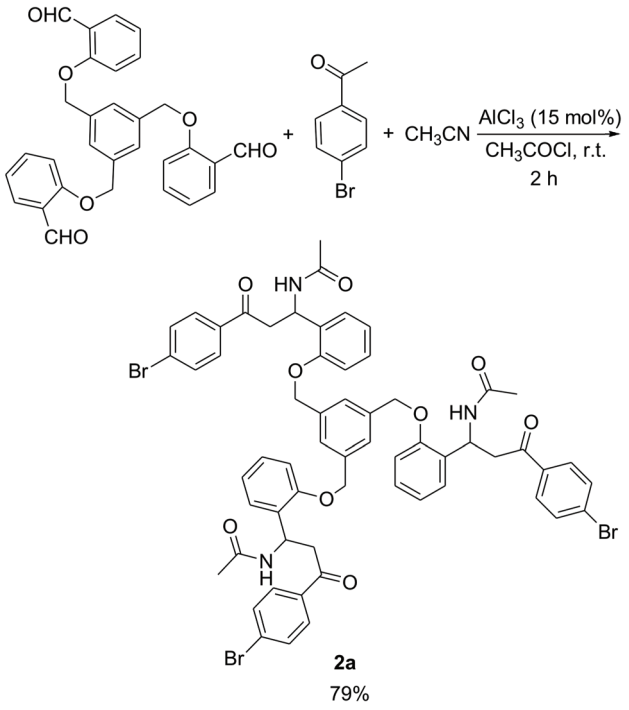
[a] The reaction conditions: enolizable ketone or alkyl acetoacetate (2 mmol), aldehyde (2 mmol), acetonitrile (6 mL), acetyl chloride (0.6 mL), $AlCl_3$ (15 mol%), room temperature. [b] Isolated yield. [c] This compound is new. [d] The melting point of this compound has not been reported.

compounds **1i** and **1m**); and halogens had no significant effect on the yields (Table 2, compounds **1f** and **1j**). Moreover, the method was worked well when 2-naphthaldehyde and anthracene-10-carbaldehyde were used instead of benzaldehydes (Table 2, compounds **1c**, **1d**, **1g**, **1k**, **1o—q**, **1s** and **1t**). Various enolizable ketones including acetophenones bearing electron-releasing substituents, electron-withdrawing substituents and halogens on the aromatic ring, as well as alkyl acetoacetates were also condensed with aldehydes, acetonitrile and acetyl chloride in the presence of $AlCl_3$ to afford the corresponding β-acetamido ketones and esters in high yields within relatively short reaction times.

Interestingly, the condensation of *p*-bromoacetophenone (3.2 equiv.) with a tris-aldehyde (1 equiv.), acetonitrile (6 mL) and acetyl chloride (0.9 mL) in the presence of $AlCl_3$ (15 mol%) at room temperature afforded complex compound **2a** in 79% yield within 2 h (Scheme 2). This is the first report of the synthesis of this class of β-acetamido ketones.

Based on the literature,[45,46] we suggest the following mechanism for our reaction (Scheme 3).

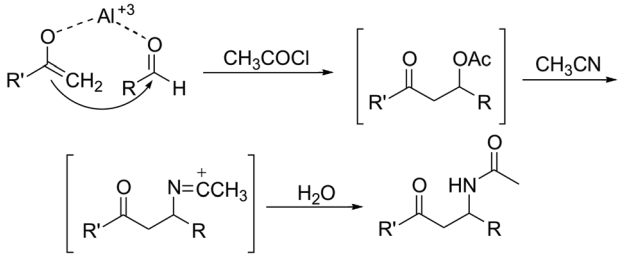
Scheme 2 The synthesis of complex compound **2a**



Conclusions

In conclusion, we have developed a new method for the preparation of β-acetamido ketone/ester derivatives via one-pot multicomponent condensation of enolizable ketones or alkyl acetoacetates with aldehydes, acetonitrile and acetyl chloride using $AlCl_3$ as catalyst. The promising points for the presented methodology are efficiency, generality, high yields, relatively short reaction times, cleaner reaction profile and simplicity.

Scheme 3 The proposed mechanism for the preparation of β-acetamido carbonyl compounds using $AlCl_3$ as catalyst.



Experimental

All chemicals were purchased from Merck or Fluka Chemical Companies. All known compounds were identified by comparison of their melting points and spectral data with those reported in the literature. Pro-

gress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were run on a Bruker Avance DPX-250, FT-NMR spectrometer. Microanalysis was performed on a Perkin-Elmer 240-B microanalyzer. Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

General procedure for the synthesis of *β*-acetamido carbonyl compounds

To a mixture of compounds consisting of enolizable ketone or alkyl acetoacetate (2 mmol), aldehyde (2 mmol), acetonitrile (6 mL) and acetyl chloride (0.6 mL, 8.4 mmol) in a 10 mL round-bottomed flask was added $AlCl_3$ (0.02 g, 0.3 mmol), and the resulting mixture was stirred at room temperature. After completion of the reaction, as monitored with TLC, crushed ice (20 mL) was added to the reaction mixture and stirred thoroughly. On solidification, the crude product was filtered, dried, and purified by short column chromatography on silica gel eluted with EtOAc/*n*-hexane (1/4).

Some selected spectral data of the products

***N*-(3-(4-Methoxyphenyl)-3-oxo-1-phenylpropyl)-acetamide (1a)** Pale yellow solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 2.00 (s, 3H), 3.38 (dd, *J*=5.9, 16.5 Hz, 1H), 3.66 (dd, *J*=5.4, 16.6 Hz, 1H), 3.85 (s, 3H), 5.54 (q, *J*=7.5 Hz, 1H), 6.91 (d, *J*=8.7 Hz, 2H), 7.21—7.35 (m, 6H), 7.88 (d, *J*=9.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 23.3, 42.8, 50.1, 55.5, 113.8, 126.5, 127.3, 128.6, 129.7, 130.5, 141.1, 163.8, 169.6, 196.9; IR (KBr) *v*: 1678, 3268 cm^{-1}; MS *m/z*: 297 (M^+). Anal. calcd for $C_{18}H_{19}NO_3$: C 72.71, H 6.44, N 4.71; found C 72.53, H 6.52, N 4.82.

***N*-(1,3-Bis(4-methoxyphenyl)-3-oxopropyl)acetamide (1b)** Pale yellow solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 2.02 (s, 3H), 3.67 (s, 1H), 3.76 (s, 3H), 3.86 (s, 3H), 5.49 (s, 1H), 6.88 (q, *J*=7.8 Hz, 5H), 7.26 (d, *J*=8.3 Hz, 2H), 7.90 (d, *J*=8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 23.4, 42.8, 49.7, 55.2, 55.5, 113.8, 113.9, 127.7, 129.6, 130.5, 133.1, 158.7, 163.7, 169.6, 197.2; IR (KBr) *v*: 1678, 3273 cm^{-1}; MS *m/z*: 327 (M^+). Anal. calcd for $C_{19}H_{21}NO_4$: C 69.71, H 6.47, N 4.28; found C 69.94, H 6.58, N 4.36.

***N*-(3-(4-Methoxyphenyl)-1-(naphthalen-3-yl)-3-oxopropyl)acetamide (1c)** Pale yellow solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 2.03 (s, 3H), 3.43 (d, *J*=6.6 Hz, 1H), 3.79 (s, 4H), 5.72 (s, 1H), 6.90 (q, *J*=6.8 Hz, 2H), 7.42—7.53 (m, 4H), 7.75—8.10 (m, 5H), 8.23 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 22.6, 43.1, 50.6, 55.5, 113.8, 124.8, 125.4, 126.0, 127.6, 127.9, 128.5, 129.5, 130.5, 132.6, 133.2, 138.4, 163.7, 170.9, 196.4; IR (KBr) *v*: 1671, 3276 cm^{-1}; MS *m/z*: 347 (M^+). Anal. calcd for $C_{22}H_{21}NO_3$ C 76.06, H 6.09, N 4.03; found C 76.27, H 6.19, N 3.95.

***N*-(1-(Anthracen-10-yl)-3-(4-methoxyphenyl)-3-oxopropyl)acetamide (1d)** Deep red solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 2.06 (s, 3H), 3.84 (s, 1H), 4.14 (q, *J*=7.0 Hz, 1H), 5.27 (s, 1H), 6.86 (d, *J*=8.7 Hz, 2H), 7.13 (d, *J*=6.3 Hz, 1H), 7.46 (t, *J*=6.9 Hz, 2H), 7.56 (t, *J*=8.4 Hz, 2H), 7.91 (d, *J*=8.7 Hz, 2H), 8.05 (d, *J*=5.4 Hz, 2H), 8.42 (s, 1H), 8.52 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 23.2, 29.7, 46.1, 55.4, 59.5, 113.7, 124.2, 124.9, 125.4, 126.5, 128.8, 129.1, 129.3, 129.7, 130.5, 131.9, 142.6, 163.5, 195.2; IR (KBr) *v*: 1674, 3184, 3279 cm^{-1}; MS *m/z*: 397 (M^+). Anal. calcd for $C_{26}H_{23}NO_3$: C 78.57, H 5.83, N 3.52; found C 78.77, H 5.94, N 3.59.

***N*-(3-Oxo-1,3-dip-tolylpropyl)acetamide (1e)** Pale yellow solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 1.93 (s, 3H), 2.27 (s, 3H), 2.37 (s, 3H), 3.36 (q, *J*=6.2 Hz, 1H), 3.64 (q, *J*=5.8 Hz, 1H), 5.55 (q, *J*=7.1 Hz, 1H), 7.09 (d, *J*=7.7 Hz, 2H), 7.22 (m, 2H), 7.41 (d, *J*=7.7 Hz, 1H), 7.80 (d, *J*=7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 21.1, 21.7, 23.1, 43.6, 49.8, 126.5, 128.3, 129.2, 129.3, 134.1, 136.9, 138.4, 144.2, 169.8, 197.8; IR (KBr) *v*: 1680, 3257 cm^{-1}; MS *m/z*: 295 (M^+). Anal. calcd for $C_{19}H_{21}NO_2$: C 77.26, H 7.17, N 4.74; found C 77.41, H 7.08, N 4.85.

***N*-(1-(4-Chlorophenyl)-3-oxo-3-p-tolylpropyl)acetamide (1f)** Pale yellow solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 2.02 (s, 3H), 2.40 (s, 3H), 3.35 (dd, *J*=3.8, 17.1 Hz, 1H), 3.68 (dd, *J*=5.3, 17.1 Hz, 1H), 5.5 (q, *J*=5.5 Hz, 1H), 7.26—7.32 (m, 5H), 7.37 (s, 1H), 7.77 (d, *J*=8.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 21.7, 23.1, 42.8, 49.3, 127.9, 128.2, 128.7, 129.4, 133.1, 133.8, 139.6, 144.7, 170.1, 197.8; IR (KBr) *v*: 1689, 3302 cm^{-1}; MS *m/z*: 312 (M^+). Anal. calcd for $C_{18}H_{18}ClNO_2$: C 68.46, H 5.75, N 4.44; found C 68.29, H 5.84; N 4.53.

***N*-(1-(Naphthalen-3-yl)-3-oxo-3-*p*-tolylpropyl)acetamide (1g)** Pale yellow solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 1.96 (s, 3H), 2.39 (s, 3H), 3.46 (q, *J*=8.7 Hz, 1H), 3.78 (q, *J*=5.1 Hz, 1H), 5.73 (d, *J*=6.8 Hz, 1H), 7.16—7.28 (m, 2H), 7.43—7.49 (m, 4H), 7.72—7.78 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 21.7, 23.4, 43.1, 50.1, 124.7, 125.2, 125.9, 126.2, 127.9, 128.2, 128.4, 129.4, 129.6, 132.6, 133.2, 134.1, 138.4, 144.5, 169.7, 198.1; IR (KBr) *v*: 1676, 3280 cm^{-1}; MS *m/z*: 331 (M^+). Anal. calcd for $C_{22}H_{21}NO_2$: C 79.73, H 6.39, N 4.23; found C 79.51, H 6.47, N, 4.11.

***N*-(3-(4-Nitrophenyl)-3-oxo-1-phenylpropyl)acetamide (1h)** White solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 1.95 (s, 3H), 3.43 (dd, *J*=3.5, 16.6 Hz, 1H), 3.78 (dd, *J*=3.5, 14.1 Hz, 1H), 5.53 (q, *J*=3.9 Hz, 1H), 6.95 (d, *J*=6.3 Hz, 1H), 7.31 (s, 5H), 8.03 (d, *J*=6.0 Hz, 2H), 8.23 (d, *J*=5.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 23.1, 44.3, 50.1, 123.8, 126.5, 127.8, 129.2, 140.9, 150.3, 169.9, 196.6; IR (KBr) *v*: 1689, 3302 cm^{-1}; MS *m/z*: 312 (M^+). Anal. calcd for $C_{17}H_{16}N_2O_4$: C 65.38, H 5.16, N 8.97; found C 65.57, H 5.06, N 8.84.

***N*-(1,3-Bis(4-nitrophenyl)-3-oxopropyl)acetamide (1i)** White solid; ^{1}H NMR ($CDCl_3$, 300 MHz) *δ*: 2.10 (s, 3H), 3.61 (dd, *J*=3.5, 14.1 Hz, 1H), 3.88 (dd, *J*=3.8, 13.3 Hz, 1H), 5.69 (s, 1H), 6.73 (s, 1H), 7.27 (s, 1H), 7.54 (s, 1H), 8.09—8.32 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) *δ*: 29.7, 49.1, 59.5, 124.1, 124.1, 124.4, 129.2, 140.3, 147.3, 147.7, 150.7, 169.8, 196.3; IR (KBr) *v*:

1694, 3277 cm^{-1}; MS *m/z*: 357 (M^+). Anal. calcd for $C_{17}H_{15}N_3O_6$: C 57.14, H 4.23, N 11.76; found C 57.36, H 4.11, N, 11.64.

***N*-(1-(4-Chlorophenyl)-3-(4-nitrophenyl)-3-oxopropyl)acetamide (1j)** Pale yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.99 (s, 3H), 3.46 (q, J=6.9 Hz, 1H), 3.84 (s, 1H), 5.52 (s, 1H), 7.11—7.27 (m, 3H), 7.73—7.78 (m, 1H), 8.05—8.31 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 21.1, 22.7, 44.2, 44.4, 49.5, 50.1, 123.9, 126.5, 128.2, 128.9, 129.2, 129.5, 133.5, 137.1, 137.7, 140.8, 150.3, 170.7, 196.1; IR (KBr) *v*: 1695, 3280 cm^{-1}; MS *m/z*: 347 (M^+). Anal. calcd for $C_{17}H_{15}ClN_2O_4$: C 58.88, H 4.36, N 8.08; found C 59.02, H 4.27, N 8.18.

***N*-(1-(Naphthalen-3-yl)-3-(4-nitrophenyl)-3-oxopropyl)acetamide (1k)** Pale yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.08 (s, 3H), 2.85—3.05 (m, 2H), 5.50 (s, 1H), 7.47—8.50 (m, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 29.7, 49.8, 59.5, 124.7, 125.5, 126.4, 126.6, 126.8, 127.1, 127.5, 127.7, 128.1, 129.1, 129.4, 129.5, 130.5, 173.9, 194.1; IR (KBr) *v*: 1665, 3280 cm^{-1}; MS *m/z*: 362 (M^+). Anal. calcd for $C_{21}H_{18}N_2O_4$: C 69.60, H 5.01, N 7.73; found C 69.39, H 5.12, N 7.65.

***N*-(3-(4-Bromophenyl)-3-oxo-1-phenylpropyl)acetamide (1l)** Pale yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.04 (s, 3H), 3.37 (q, J=5.4 Hz, 1H), 3.66 (q, J=5.4 Hz, 1H), 5.54 (q, J=6.6 Hz, 1H), 6.99—7.75 (m, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.2, 29.6, 43.5, 50.0, 126.5, 127.5, 128.6, 129.6, 131.9, 135.3, 140.8, 169.7, 197.2; IR (KBr) *v*: 1685, 3275 cm^{-1}; MS *m/z*: 345 (M^+). Anal. calcd for $C_{17}H_{16}BrNO_2$: C 58.97, H 4.66, N 4.05; found C 58.81, H 4.58, N 4.14.

***N*-(3-(4-Bromophenyl)-1-(4-nitrophenyl)-3-oxopropyl)acetamide (1m)** White solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.05 (s, 3H), 3.47 (q, J=5.6 Hz, 1H), 3.79 (q, J=5.19 Hz, 1H), 5.65 (q, J=5.5 Hz, 1H), 7.02 (d, J=7.9 Hz, 1H), 7.58 (d, J=8.7 Hz, 2H), 7.61 (d, J=8.4 Hz, 2H), 7.76 (d, J=8.4 Hz, 2H), 8.15 (d, J=8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.3, 42.7, 49.1, 113.8, 123.8, 127.4, 129.3, 129.5, 132.2, 134.8, 147.1, 148.4, 169.8, 196.8; IR (KBr) *v*: 1687, 3261 cm^{-1}; MS *m/z*: 390 (M^+). Anal. calcd for $C_{17}H_{15}BrN_2O_4$: C 52.19, H 3.86, N 7.16; found C 52.01, H 3.98, N 7.05.

Compound (1n) Pale yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.07 (s, 3H), 3.46 (d, J=6.8 Hz, 1H), 3.81 (d, J=7.8 Hz, 1H), 5.63 (s, 1H), 7.09 (s, 1H), 7.20—7.60 (m, 3H), 7.70—8.20 (m, 4H), 9.96 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.3, 42.8, 49.5, 127.1, 129.2, 129.6, 130.1, 132.1, 134.9, 135.5, 147.6, 170.01, 191.8, 197.1; IR (KBr) *v*: 1689, 1736, 3286 cm^{-1}; MS *m/z*: 373 (M^+). Anal. calcd for $C_{18}H_{16}BrNO_3$: C 57.77, H 4.31, N 3.74; found C 57.93, H 4.42, N 3.19.

***N*-(3-(4-Bromophenyl)-1-(naphthalen-3-yl)-3-oxopropyl)acetamide (1o)** Pale yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.98 (s, 3H), 3.41 (dd, J=6.4, 12.7 Hz, 1H), 3.76 (dd, J=6.6, 13.2 Hz, 1H), 5.70 (s, 1H), 7.27—7.59 (m, 6H), 7.69—7.92 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.2, 43.5, 50.1, 124.7, 125.3, 126.1, 126.3, 127.6, 128.6, 129.6, 131.9, 132.7, 133.1, 135.1, 138.2, 170.1, 197.1; IR (KBr) *v*: 1682, 3276 cm^{-1}; MS *m/z* : 395 (M^+). Anal. calcd for $C_{21}H_{18}BrNO_2$: C 63.65, H 4.58, N 3.53; found C 63.48, H 4.67, N 3.44.

***N*-(4-(3-Acetamido-3-(naphthalen-2-yl)propanoyl)-phenyl)acetamide (1p)** Brown solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.89 (s, 3H), 2.06 (s, 3H), 3.84 (s, 1H), 4.14 (d, J=7.2 Hz, 1H), 5.23 (s, 1H), 5.75 (s, 2H), 7.41—7.98 (m, 11H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 26.5, 29.7, 42.1, 60.5, 118.8, 119.1, 123.6, 126.1, 127.8, 127.9, 128.6, 129.7, 132.6, 133.1, 142.6, 144.7, 170.1, 172.3, 189.2; IR (KBr) *v*: 1674, 3184, 3279 cm^{-1}; MS *m/z*: 374 (M^+). Anal. calcd for $C_{23}H_{22}N_2O_3$: C 73.78, H 5.92, N 7.48; found C 73.94, H 6.04, N 7.39.

***N*-(4-(3-Acetamido-3-(anthracen-9-yl)propanoyl)-phenyl)acetamide (1q)** Brown solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.88 (s, 3H), 2.00 (s, 3H), 3.75 (dd, J=7.2, 14.1 Hz, 1H), 3.94 (dd, J=7.5, 15.9 Hz, 1H), 6.5 (s, 2H), 7.44—7.60 (m, 7H), 7.74—7.85 (m, 4H), 8.03 (d, J=8.4, 2H); ^{13}C NMR ($CDCl_3$,75 MHz) δ: 23.2, 24.5, 45.4, 58.4, 118.8, 124.1, 124.9, 126.5, 128.8, 129.4, 129.8, 131.7, 142.7, 168.7, 170.2, 196.2; IR (KBr) *v*: 1674, 3184, 3279 cm^{-1}; MS *m/z*: 424 (M^+), 382 (M^+-CH_3CO). Anal. calcd for $C_{27}H_{24}N_2O_3$: C 76.39, H 5.70, N 6.60; found C 76.59, H 5.61, N 6.49.

Methyl 2-(acetamido(phenyl)methyl)-3-oxobutanoate (1r) Yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.95 (s, 3H), 2.16 (s, 3H), 3.64 (s, 3H), 4.10 (s, 1H), 5.75 (s, 1H), 7.29 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.2, 30.6, 52.3, 52.8, 62.8, 126.6, 127.8, 128.7, 139.1, 167.6, 169.8, 203.6; IR (KBr) *v*: 1647, 1720, 1746, 3332 cm^{-1}; MS *m/z*: 263 (M^+). Anal. calcd for $C_{14}H_{17}NO_4$: C 63.87, H 6.51, N 5.32; found C 64.01, H 6.43, N 5.19.

Methyl 2-(acetamido(naphthalen-3-yl)methyl)-3-oxobutanoate (1s) Yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 2.01 (s, 3H), 2.19 (s, 3H), 3.65 (s, 3H), 4.26 (s, 1H), 5.96 (s, 1H), 7.46 (s, 3H), 7.77 (s, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.3, 30.6, 52.6, 52.8, 62.7, 124.5, 125.7, 126.2, 127.6, 128.1, 128.6, 132.8, 133.1, 136.5, 167.6, 169.8, 203.5; IR (KBr) *v*: 1636, 1747, 3347 cm^{-1}; MS *m/z*: 313 (M^+). Anal. calcd for $C_{18}H_{19}NO_4$: C 68.99, H 6.11, N 4.47; found C 69.81, H 6.23, N 4.56.

Ethyl 2-(acetamido(naphthalen-3-yl)methyl)-3-oxobutanoate (1t) Yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.11 (t, J=5.0 Hz, 3H), 2.02 (s, 3H), 2.18 (s, 3H), 4.1 (q, J=6.1 Hz, 2H), 4.17 (q, J=6.3 Hz, 1H), 5.95 (s, 1H), 7.26—7.48 (m, 4H), 7.76 (t, J=7.5 Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.2, 30.6, 52.3, 52.8, 62.8, 126.6, 127.8, 128.7, 139.1, 167.6, 169.8, 203.6; IR (KBr) *v*: 1647, 1720, 1746, 3332 cm^{-1}; MS *m/z*: 327 (M^+). Anal. calcd for $C_{19}H_{21}NO_4$: C 69.71, H 6.47, N 4.28; found C 69.52, H 6.34, N 4.39.

Compound (2a) Yellow solid; ^1H NMR ($CDCl_3$, 300 MHz) δ: 1.86 (s, 9H), 3.36—3.49 (m, 6H), 5.16 (s, 6H), 5.83 (s, 3H), 6.91—7.02 (m, 6H), 7.15—7.38 (m, 11H), 7.51—7.64 (m, 9H), 7.67—7.83 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 23.0, 43.1, 46.8, 69.8 112.3, 121.3, 126.2, 127.9, 128.4, 128.8, 129.7, 129.8, 131.8, 131.9, 135.2, 138.1, 155.4 168.2, 197.4; IR (KBr) *v*:

1674, 3433 cm^{-1}; MS *m/z*: 1197 (M^+). Anal. calcd for $C_{60}H_{54}Br_3N_3O_9$: C 60.01, H 4.53, N 3.50; found C 59.88, H 4.65, N 3.42.

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