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Ionic Liquid 3-Methyl-1-sulphonic Acid Imidazolium Chloride {[Msim]Cl}: A Highly Efficient, Mild and Green Catalyst for the Synthesis of β-Acetamido Ketones

Abdolkarim Zare[a,*], Tahereh Hekmat-Zadeh[a], Setareh Mirzaei-Monfared[b], Maria Merajoddin[a], Hossein Torabi-Monfared[a], Mohammad Ali Zolfigol[c,*], Ahmad Reza Moosavi-Zare[c], Esmael Rostami[a], Mohammad Mokhlesi[c], Fatemeh Derakhshan-Panah[c], Saeedeh Porbahi[a] and Samira Balandeh[a]

[a]*Department of Chemistry, Payame Noor University, P.O. Box 19395-4697, Tehran, Iran.*
[b]*Department of Chemistry, Yasouj University, Yasouj, 75914-35, Iran.*
[c]*Faculty of Chemistry, Bu-Ali Sina University, Hamedan, 6517838683, Iran.*

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ABSTRACT

Brønstedacidic ionic liquid 3-methyl-1-sulphonic acid imidazolium chloride {[Msim]Cl} is utilized as a highly efficient, inexpensive, mild and green catalyst for the synthesis of β-acetamido ketones by the one-pot multi-component coupling between acetophenones, arylaldehydes, acetonitrile and acetyl chloride at room temperature. Under these conditions, the title compounds are produced in high to excellent yields and in relatively short reaction times. In addition, this method is superior to reported methods, for the synthesis of β-acetamido ketones and is applicable for the synthesis of tris(β-acetamido ketone).

KEYWORDS

3-Methyl-1-sulphonic acid imidazolium chloride {[Msim]Cl}, β-acetamido ketone, Brønsted acidic catalyst, ionic liquid, one-pot multi-component reaction, acetophenone.

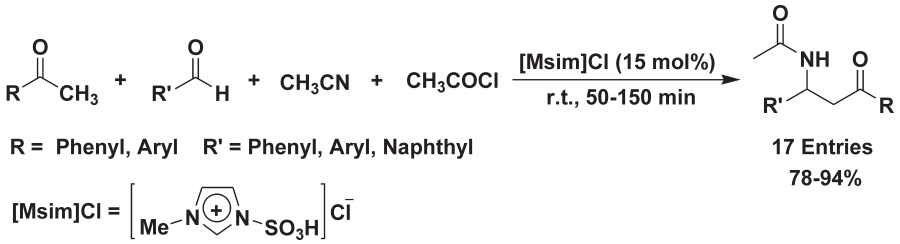
1. Introduction

In the area of sustainable chemistry,[1] the design and development of sequences allowing highly selective access to complex molecular scaffolds while combining structural diversity with the use of eco-friendly and environmentally benign catalysts and reagents are great challenges for organic chemists.[2] Due to these environmental concerns, the investigation of alternatives to toxic and non-green catalysts and reagents has resulted in a highly growing interest in the application of ionic liquids (ILs) as catalysts and reagents.[3–15] In fact, the user-friendly and adjustable physico-chemical properties of ILs such as low volatility, non-flammability, high thermal stability, negligible vapour pressure and the ability to dissolve a wide range of materials, have found numerous applications as environmentally benign catalysts and reagents. ILs also serve to homogenize the reaction media for organic transformations.[3–15] From this point of view, combining synthetic advantages of multi-component reactions with the use of ILs as promoters and homogenizers of the reaction mixture has resulted in several promising routes for the development of important eco-compatible organic synthesis procedures.[15] The most frequently described ILs are quaternary nitrogen compounds, mainly imidazolium salts.[16–22] Among them, the Brønsted acidic ionic liquids, based an imidazolium moiety, was designed to replace solid acids and traditional mineral liquid acids like sulphuric acid and hydrochloric acid in chemical procedures.[18,22] Along this line, more recently, we have synthesized some novel SO_3H-containing ionic liquids, based on the imidazolium moiety, by means of simple and clean procedures. We have also successfully applied them as efficient catalysts, reagents as well as homogenizer of the reaction media in some organic transformations including nitration of phenols,[19] and the synthesis of 1-amidoalkyl-2-naphthols,[20] N-sulphonyl imines[21] and bis(indolyl)methanes.[22]

One-pot transformations, especially multi-component reactions (MCRs), are of current significant interest to organic chemists.[23] Since the first MCRs were reported in 1850 by Strecker,[24] this methodology has been developed as an efficient and powerful tool in modern synthetic organic chemistry. Multi-component reactions are important transformations for the achievement of high levels of diversity, as they allow more than two components to be combined in one step, short reaction times, one-pot reactions and syntheses to yield complex species by simultaneous formation of two or more bonds, according to the domino principle.[25] MCRs are attractive in terms of economic and practical considerations and are acceptable from a green chemistry point of view. They are useful for an environmentally friendly process by reducing the number of synthetic steps, energy consumption and waste generation. This technology is currently employed as one of the most efficient and economic tools for combinatorial chemistry, parallel synthesis, automated synthesis and as a result, the preparation of large arrays of compounds with diverse substitution patterns.[25,26] MCRs are powerful tools in modern drug discovery and allow fast, automated and high throughput synthesis of diverse structural scaffolds required in a search of novel therapeutic molecules.[25–27]

β-Acetamido ketone derivatives are useful intermediates in a series of organic syntheses due to their polyfunctional nature and presence in various bioactive compounds.[28,29] These are precursors of 1,3-amino alcohol derivatives[30,31] present in biologically and pharmaceutically important compounds such as antibiotic nikkomycins or neopolyoxines.[32,33] The conventional route for synthesizing β-acetamido ketones is the Dakin-West reaction[34] which involves the condensation of α-amino acids

* To whom correspondence should be addressed.
E-mail: abdolkarimzare@yahoo.com or mzolfigol@yahoo.com



Scheme 1
Preparation of β-acetamido ketones from acetophenones, arylaldehydes, acetonitrile and acetyl chloride using [Msim]Cl.

with acetic anhydride in the presence of a base. Nevertheless, the current best route for synthesis of these compounds is the one-pot multi-component coupling reaction between acetophenones, arylaldehyde, acetonitrile and acetyl chloride as first reported by Iqbal and co-workers.[35] Some catalysts have been employed to perform this reaction, e.g. $FeCl_3$.polyaniline sulphate salt,[42] selectfluor™, [43]ZnO, [44]$Sc(OTf)_3$, [45]$ZrOCl_2.8H_2O$, [46]$K_5CoW_{12}O_{40}.3H_2O$,[47] and trifluoroacetic acid.[48] These methods, while offering some advantages, also suffer from different drawbacks such as prolonged reaction times, moderate yields, the use of expensive, not readily available and toxic catalysts, the use of large amounts of catalysts, harsh reaction conditions, requiring an inert atmosphere and tedious workup procedures. Hence, development of new catalysts and methods for the preparation of β-acetamido ketones, which are not associated with the above mentioned disadvantages, is of significant interest.

In this paper, we report a new, mild, inexpensive and highly efficient method for the preparation of β-acetamido ketones utilizing a one-pot multi-component condensation of acetophenones with arylaldehydes, acetonitrile and acetyl chloride, catalyzed by 3-methyl-1-sulphonic acid imidazolium chloride {[Msim]Cl} at room temperature (Scheme 1). These catalysts are imidazolium-based ionic liquids with Brønsted acidic properties. This method eliminated all of the above-mentioned drawbacks experienced by other existing methods. Nevertheless, it should be mentioned that the products are a mixture of enantiomers.

2. Results and Discussion

Recently, we have synthesized a range of novel sulphonic acid functionalized imidazolium salts including 3-methyl-1-sulphonic acid imidazolium chloride {[Msim]Cl} (an ionic liquid), 1,3-disulphonic acid imidazolium chloride {[Dsim]Cl} (an ionic liquid) and 3-methyl-1-sulphonic acid imidazolium tetrachloroaluminate {[Msim]$AlCl_4$} (a solid). We have successfully applied them as efficient catalysts and reagents in organic synthesis.[19–22] As part of a project to develop catalytic applications of the imidazolium salts in organic transformations and in light of the importance of β-acetamido ketones, we have examined the efficiency of these catalysts in the preparation of β-acetamido ketone derivatives. For this purpose, as a model reaction, a mixture of benzaldehyde (1 mmol), acetophenone (1 mmol), acetyl chloride (0.3 mL) and acetonitrile (3 mL, as reactant and solvent) was stirred in the presence of a catalytic amount of the imidazolium salts (15 mol%) at room temperature. The results are summarized in Table 1.

Interestingly, all imidazolium salts {[Msim]Cl, [Dsim]Cl and [Msim]$AlCl_4$} catalyzed the reaction efficiently and gave the desired β-acetamido ketone in high yields and in relatively short reaction times. Nevertheless, we selected [Msim]Cl as a catalyst for the reaction, because the preparation of this ionic liquid was easier and faster than [Dsim]Cl and [Msim]$AlCl_4$. [Msim]Cl was prepared by the simple reaction of 1-methylimidazole with chlorosulphonic acid in dichloromethane at room temperature within 25 min; but the time needed for the synthesis of [Dsim]Cl was 12 hours.[20] In the case of [Msim]$AlCl_4$, first, [Msim]Cl was prepared, and subsequently this ionic liquid was reacted with $AlCl_3$ to afford [Msim]$AlCl_4$.[20]

Table 1 The condensation of benzaldehyde (1 mmol) with acetophenone (1 mmol), acetyl chloride (0.3 mL) and acetonitrile (3 mL) using different catalysts (15 mol%).

Entry	Catalyst	Time/min	Yield [a]/%
1	–	600	Trace
2	[Msim]Cl	60	94
3	[Dsim]Cl	60	94
4	[Msim]$AlCl_4$	60	93

[a] Isolated yield.

Next, the one-pot multi-component condensation of benzaldehyde (1 mmol) with acetophenone (1 mmol), acetonitrile (3 mL) and acetyl chloride (0.3 mL) was tested using different molar ratios of [Msim]Cl at room temperature. The results are summarized in Table 2. As it is shown in Table 2, under catalyst-free conditions, the product was obtained in trace yield after 600 min; 10 mol% of the catalyst was not sufficient to promote the reaction effectively; 15 mol% of it efficiently catalyzed the reaction and gave the product in excellent yield (94%) within relatively short reaction time (60 min); any excess amount of [Msim]Cl did not lead to increased yields or reaction times. Thus, the optimized amount of the catalyst was 15 mol%.

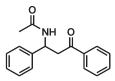
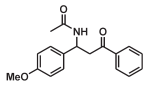
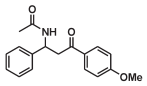
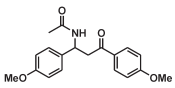
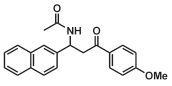
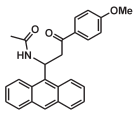
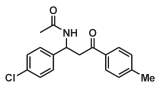
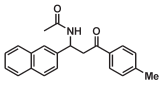
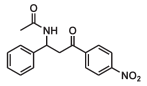
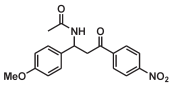
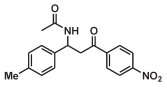
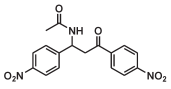
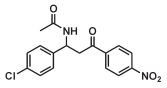
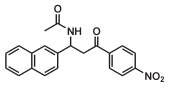
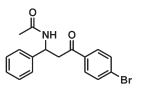
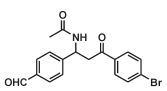
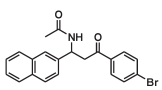
To assess the efficacy and the scope of the method, different acetophenons (containing electron-donating substituents, electron-withdrawing substituents or halogen on their aromatic ring) were reacted with a variety of aromatic aldehydes (possessing electron-donating substituents, electron-withdrawing substituents or halogen on their aromatic ring), acetonitrile and acetyl chloride. The corresponding β-acetamido ketones were obtained in high to excellent yields (78–94 %) and with relatively short reaction times (50–150 min); the respective results are displayed in Table 3. Furthermore, the reaction was successfully achieved when 2-naphthaldehyde or anthracene-10-carbaldehyde instead of benzaldehyde derivatives were used (Table 3, entries 5, 6, 8, 14 and 17).

Table 2 Optimization of the catalyst amount for the reaction of benzaldehyde with acetophenone, acetonitrile and acetyl chloride.

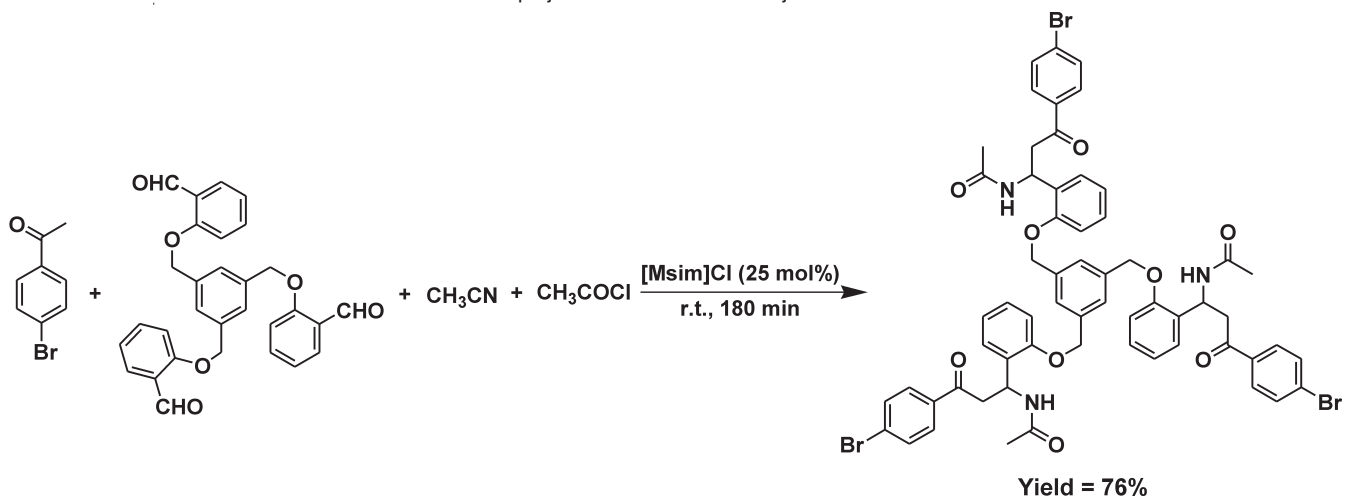
Entry	Catalyst amount/ mol%	Time/min	Yield [a]/%
1	–	600	Trace
2	10	80	89
3	15	60	94
4	20	60	94

[a] Isolated yield.

Table 3 The [Msim]Cl-catalyzed condensation of acetophenones with aldehydes, acetonitrile and acetyl chloride leading to β-acetamido ketones at room temperature.

Entry	Product	Time/min	Yield[a]/%	M.p. °C (lit.)
1		60	94	100–102 (102–104) [44]
2		70	88	109–111 (110–112) [46]
3		50	91	127–129 (130–132) [46]
4		60	93	124–127 (124–127) [38]
5		80	92	107–109 (108–110) [38]
6		150	78	138–140 [38] (138–140)
7		60	93	131–133 (130–132) [38]
8		90	88	113–115 (111–112) [38]
9		75	90	77–79 (74–76) [46]
10		75	94	89–91 (88–90) [49]
11		50	92	80–82 (84–85) [49]
12		70	85	185–188 (187–188) [46]
13		60	92	113–115 (116–118) [49]
14		80	87	165–166 (165–166) [38]
15		70	94	102–104 (98–100) [42]
16		120	85	104–105 (104–105) [38]
17		110	91	137–139 (138–140) [38]

[a] Isolated yield.



Scheme 2
The [Msim]Cl-catalyzed synthesis of tris(*β*-acetamido ketone).

Interestingly, the one-pot multi-component reaction of *p*-bromoacetophenone (3.2 mmol) with a tris(aldehyde) (1 mmol), acetonitrile (10 mL) and acetyl chloride (0.9 mL) in the presence of [Msim]Cl (25 mol%) at room temperature afforded a tris(*β*-acetamido ketone) in 76 % yield within 180 min (Scheme 2).[38] This complex compound was analyzed by HPLC using acetonitrile/H_2O (95/5) as mobile phase with flow rate 1 mL/min. The analysis could identify three diasteromers of the tris(*β*-acetamido ketone). These isomers were separated in retention times 3.2, 6.1 and 7.3 s.

In another study, to compare the efficiency of our method with the previously reported methods for the synthesis of *β*-acetamido ketones, we have tabulated the reaction results related to these methods, for the condensation between acetophenone, benzaldehyde, acetonitrile and acetyl chloride, in Table 4. As Table 4 indicates, our method is superior to the reported methods in terms of reaction times and yields. Moreover, our procedure is more inexpensive in comparison with the reported procedures.

To recognize the applicability of our method in larger scale synthesis, we examined some reactions in scale of 10 mmol (more than 1 g). For this purpose, acetophenone or its derivative (10 mmol) was reacted with arylaldehyde (10 mmol), acetyl chloride (3 mL) and acetonitrile (30 mL) in the presence of [Msim]Cl (1.5 mmol, 0.3 g) at room temperature; the respective results are summarized in Table 5. As it is shown in Table 5, the reactions were successfully performed at the larger scale without significant loss of the yields.

In conclusion, we have introduced a new method for the preparation of *β*-acetamido ketones from acetophenones, arylaldehydes, acetonitrile and acetyl chloride using catalytic amount of [Msim]Cl as a green Brønsted acidic ionic liquid. The major advantages of this method are high yields, relatively short reaction times, generality, efficiency, low cost, mild reaction conditions and easy preparation of the catalyst.

3. Experimental

3.1. General

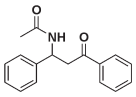
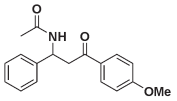
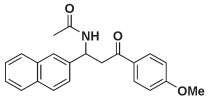
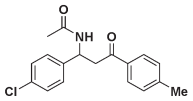
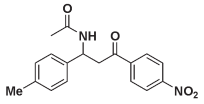
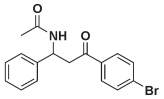
The reactions were carried out in an efficient hood cupboard. All the materials were purchased from Merck, Fluka, Across Organics or Aldrich Chemical Companies. Acetonitrile and dichloromethane were dried, distilled and stored over molecular sieves. [Msim[Cl, [Dsim]Cl and [Msim]$AlCl_4$ were prepared

Table 4 Comparison of the results of the reaction of acetophenone with benzaldehyde, acetonitrile and acetyl chloride using our method with those obtained by the reported methods.

Catalyst	Time/min	Yield/%	Ref.
[Msim]Cl	60	94	Our method
$FeCl_3.6H_2O$	480	88	36
Copper(II) phthalocyanine	210	73	37
Silica-functionalized sulphonic acid	105	91	38
$H_6P_2W_{18}O_{62}$	25	86	39
$Zr(HSO_4)_4/SiO_2$	180	96	40
$Mg(HSO_4)_2$	50	89	41
Polyaniline-supported acid	60	86	42
Selectfluor™	120	74	43
Zinc oxide	360	90	44
$Sc(OTf)_3$	1800	82	45
$ZrOCl_2.8H_2O$	300	90	46
$K_5CoW_{12}O_{40}$ $3H_2O$	60	86	47
CF_3CO_2H	1320	90	48 [a]
$H_3PW_{12}O_{40}$	195	65	49 [b]

[a] In this case, the results of the condensation of benzaldehyde with 4-chloroacetophenone, acetonitrile and acetyl chloride have been shown.
[b] In this method, trimethylsilyl chloride instead of acetyl chloride has been used.

Table 5 The large scale preparation of some β-acetamido ketones using [Msim]Cl at room temperature.

Entry	Product	Time/min	Yield [a]/%
1		75	92
2		60	88
3		100	88
4		70	92
5		70	87
6		80	92

according to reported procedures.[19–22] Merck silica gel 40 was used for column chromatography. Merck silica gel 60 F254 TLC plates were used for thin layer chromatography (TLC). AHPLC apparatus model SCL-10AVP SHIMATZU with RP column (150 × 4.6 mm) was used for analysis. The melting points were recorded on a Büchi B-545 apparatus in open capillary tubes. IR spectra were measured on a Perkin-Elmer model 543 and FT-IR BRUKER spectrometers. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) were run on a Bruker Avance DPX-250 FT-NMR spectrometer (δ in ppm). Mass spectra were obtained with a Shimadzu GC-MS-QP 1100 EX model.

3.2. General Procedure for the Preparation of β -Acetamido Ketone Derivatives

A mixture of acetophenone or its derivative (1 mmol), aromatic aldehyde (1 mmol), acetyl chloride (0.3 mL) and [Msim]Cl (0.15 mmol, 0.03 g) in acetonitrile (3 mL) was stirred at room temperature for the times reported in Table 3. Afterwards, crushed ice (10 mL) was added to the reaction mixture and stirred thoroughly. On solidification, the crude product (solid) was filtered, dried, and purified by short column chromatography on silica gel eluted with EtOAc/*n*-hexane (1/4).

3.3. Some Selected Spectral Data of the Products

***N*-[3-(4-Methoxyphenyl)-3-oxo-1-phenylpropyl]acetamide (Table 3, entry 3)**: R_f (EtOAc/*n*-hexane: 1/1) = 0.33; ^{1}H NMR ($CDCl_3$): 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 ($CDCl_3$): 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.

***N*-[1,3-Bis(4-methoxyphenyl)-3-oxopropyl]acetamide (Table 3, entry 4):** R_f (EtOAc/*n*-hexane: 1/1)= 0.26; IR (KBr): 1678, 3273 cm^{-1}; ^{1}H NMR ($CDCl_3$): 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 ($CDCl_3$): 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; MS (*m*/*z*): 327 (M^+).

***N*-[3-(4-Methoxyphenyl)-1-(naphthalen-3-yl)-3-oxopropyl] acetamide (Table 3, entry 5):** R_f (EtOAc/*n*-hexane: 1/1) = 0.39; IR (KBr): 1671, 3276 cm^{-1}; ^{1}H NMR ($CDCl_3$): 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 ($CDCl_3$): 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; MS (*m*/*z*): 347 (M^+).

***N*-[1-(Anthracen-10-yl)-3-(4-methoxyphenyl)-3-oxopropyl] acetamide (Table 3, entry 6):** R_f (EtOAc/*n*-hexane: 1/1) = 0.41; IR (KBr): 1674, 3184, 3279 cm^{-1}; ^{1}H NMR ($CDCl_3$): 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 ($CDCl_3$): 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; MS (*m*/*z*): 397 (M^+).

***N*-[1-(4-Chlorophenyl)-3-oxo-3-p-tolylpropyl]acetamide (Table 3, entry 7)**: R_f (EtOAc/*n*-hexane: 1/1) = 0.31; ^{1}H NMR ($CDCl_3$): δ 2.02 (s, 3H), 2.40 (s, 3H), 3.35 (dd, J = 3.9, 17.1 Hz, 1H), 3.68 (dd, J = 5.3, 17.1 Hz, 1H), 5.5 (q, J = 5.5 Hz, 1H), 7.26 (m, 5H), 7.37 (s, 1H), 7.79 (d, J = 8.0 Hz, 3H); ^{13}C NMR ($CDCl_3$): 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.

***N*-[3-(4-Nitrophenyl)-3-oxo-1-phenylpropyl]acetamide (Table 3, entry 9):** R_f (EtOAc/*n*-hexane: 1/1) = 0.23;^{1}H NMR ($CDCl_3$): 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 ($CDCl_3$): δ 23.1, 44.3, 50.1, 123.8, 126.5, 127.8, 129.2, 140.9, 150.3, 169.9, 196.6.

***N*-[1,3-Bis(4-nitrophenyl)-3-oxopropyl]acetamide (Table 3, entry 12):** R_f (EtOAc/*n*-hexane: 1/1) = 0.21;^{1}H NMR ($CDCl_3$): δ 2.10 (3H, s, 3H), 3.61 (d, J = 14.1 Hz, 1H), 3.88 (d, J = 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 ($CDCl_3$): 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.

***N*-[1-(Naphthalen-3-yl)-3-(4-nitrophenyl)-3-oxopropyl] acetamide (Table 3, entry 14)**: R_f (EtOAc/*n*-hexane: 1/1) = 0.28;IR (KBr): 1665, 3280 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.08 (s, 3H), 2.87–3.05 (2H, m), 5.50 (s, 1H), 7.47–8.5 (m, 12H); ^{13}C NMR ($CDCl_3$): 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; MS (*m*/*z*): 362 (M^+).

***N*-[1-(4-Formylophenyl)-3-(4-nitrophenyl)-3-oxopropyl] acetamide (Table 3, entry 16)**: R_f (EtOAc/*n*-hexane: 1/1) = 0.20; IR (KBr): 1689, 1736, 3286 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.06 (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), 7.2–7.6 (m, 3H), 7.7–8.2 (m, 4H), 9.96 (s, 1H); ^{13}C NMR ($CDCl_3$): 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; MS (*m*/*z*) 373 (M^+).

***N*-[3-(4-Bromophenyl)-1-(naphthalen-3-yl)-3-oxopropyl] acetamide (Table 3, entry 17):** R_f (EtOAc/*n*-hexane: 1/1) = 0.35; IR (KBr): 1682, 3276 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.98 (s, 3H), 3.38 (d, J = 12.7 Hz, 1H), 3.74 (d, J = 13.2 Hz, 1H), 5.70 (s, 1H), 7.27–7.59 (m, 6H), 7.69–7.92 (m, 6H); ^{13}C NMR ($CDCl_3$): 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; MS (*m*/*z*): 396 (M^+).

Tris(β-acetamido ketone) (Scheme 2): $^{38}R_f$ (EtOAc/*n*-hexane: 1/1) = 0.06; M.p. = 219–223 °C; IR (KBr): 1674, 3433 cm^{-1}; ^1H NMR ($CDCl_3$): 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 ($CDCl_3$): δ 23.0, 43.1, 46.8, 69.8, 112.3, 121.3, 126.2, 127.9, 128.4, 128.8, 129.7, 129.9, 131.8, 135.2, 138.1, 155.4, 168.2, 197.4.

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