Silica Supported Perchloric Acid: A Convenient and Environmentally Friendly Catalyst for the One-pot Multicomponent Synthesis of β-Acetamido Ketones

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A modified Dakin-West one-pot, four-component condensation of an aryl aldehyde, aryl ketone, acetyl chloride and acetonitrile in the presence of silica supported perchloric acid as an active, inexpensive, recoverable and recyclable catalyst is reported for the synthesis of β-acetamido ketones under mechanical stirring and ultrasonic irradiation conditions. This system has advantages of short reaction times, good to excellent yields and the ability to carry out the large scale reactions. The use of ultrasound increases the rate of reactions compared with reactions at reflux conditions.

Keywords silica supported perchloric acid, β-acetamido ketone, Dakin-West reaction, supported catalyst, multicomponent reaction

Introduction

The β-acetamido carbonyl compounds has gained considerable attention in organic synthesis, owing to their importance as valuable building blocks for preparation of β-amino acids,[1] or 1,3-amino alcohols[2] as well as for the synthesis of various antibiotics such as nikkomycins or neopolyoxines[3] and potent molecules in α-glucosidase inhibitory activity.[4]

β-Acetamido ketones were usually prepared through Michael addition to α,β-unsaturated ketones,[5] acylation of β-aminoketones[6] or photoisomerization of phthalimides.[7]

The conventional way for the preparation of these compounds is the Dakin-West reaction involving condensation of an α-amino acid with acetic anhydride in the presence of a base via an intermediate azalactone.[8] Iqbal and coworkers[10] reported the best-known route for the synthesis of β-acetamido carbonyl compounds in the one-pot condensation of aldehyde, enolizable ketone, acetyl chloride, and acetonitrile catalyzed by both $CoCl_2$,[9] and Montmorillonite K-10 clay.

Synthesis of β-acetamido ketones has also been catalyzed using Sn(II),[11] Sc(III) triflates,[12] $InCl_3$,[12] H_2SO_4/SiO_2,[13] zirconia,[14] ZnO,[15] phosphotungstic acid,[16] sulfamic acid,[17a] aluminium hydrogen sulfate,[17b] $CeCl_3$,[18] cerium(IV) sulfate[19] and Nafion-H.[20] These methods are valuable but they suffer from different drawbacks such as hazardous reagents, high temperature, expensive catalysts, long reaction time, tedious workup and low yield. Hence, the development of a simple and new protocol with more efficiency is still in demand. Multicomponent reactions (MCRs) have proved to be remarkably successful in generating molecular complexity in a single synthetic step operation.[21] This process has emerged as an efficient and powerful tool in modern synthetic chemistry allowing the facile creation of several new bonds in a one-pot transformation. The organic chemists have transformed this powerful technology into one of the most efficient and economic tools for combinatorial and parallel synthesis.[22]

In recent years, using of solid supported acids have become more important in synthetic organic chemistry due to some advantages such as enhanced selectivity, reactivity and easy product isolation.[23] Silica supported perchloric acid ($HClO_4$-SiO_2) has received considerable attention for numerous organic transformations, including acylation of alcohols[24] or aldehydes,[25] the Ferrier rearrangement,[26] cleavage of benzylidene acetals,[27] electrophilic substitution of indole with various aldehydes and ketones,[28] synthesis of Hantzsch dihydropyridine,[29] homoallylic amines through a three-component reaction,[30] tetrasubstituted imidazoles under solvent free conditions[31] and 1,8-dioxo-octahydroxanthenes via Knoevenagel condensation.[32] In view of its inherent properties like environmental friendly, greater selectivity, operational simplicity, non-corrosive nature, moisture-insensitive and ease of isolation, it is therefore, interesting to find out the behavior of the catalytic system in the synthesis of β-acetamido ketones.

Ultrasound has been used in organic synthesis in the last decades both in cavitations and per-cavitations regimes.[33] The success and advantages of sonochemical reactions include higher yields, shorter reaction times

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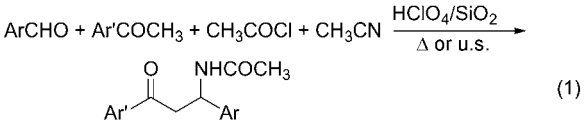
and milder reaction conditions in comparison to classical methods.[34] The mostly important effect of ultrasound by passing its waves through a liquid medium is the generation of many cavities. This leads to development of high temperatures and high pressures within the cavities during their collapse.

Results and discussion

In this work, we wish to report a convenient and efficient procedure for the synthesis of *β*-acetamido ketones using Silica supported perchloric acid as catalyst (Eq. 1).



(1)

Preparation of the supported perchloric acid

Perchloric acid (2.67 g, 18.7 mmol, as a 70% aqueous solution) was added to the suspension of silica gel (23.13 g, 230—400 mesh) in diethyl ether (75 mL). The mixture was concentrated and the residue dried under vacuum at 100 ℃ for 72 h to afford $HClO_4$-SiO_2 (0.75 mmol•g^{-1}) as a free flowing powder.

FT-IR spectra can be used as a powerful technique for the investigation of surface interaction between perchloric acid and inorganic supports. Pure acid display infrared bands at 1089, 1062 [$\nu_{as}(ClO_4)$], 962 [$\nu_s(ClO_4)$], 627 [$\delta_{as}(ClO_4)$] and 467 [$\delta_s(ClO_4)$] cm^{-1}.[35]

However, small shifts of vibrations were registered indicating interactions of the support with the oxygen atoms of acid. In addition, a broad, intense band centered around 3433 cm^{-1} (ν_{O-H} stretching) and a weak absorption at 1630 cm^{-1} [$\delta(H_2O)$ bending] indicate the presence of water (Figure 1).

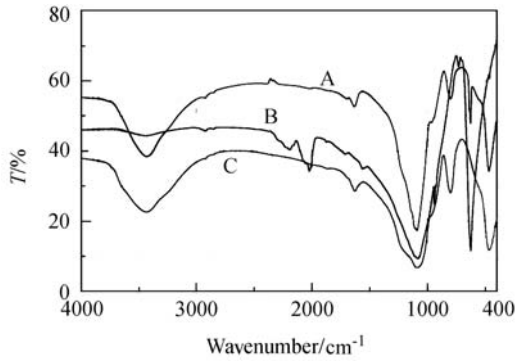


Figure 1 FT-IR spectra of silica supported perchloric acid (A), perchlorate anion (B) and SiO_2 (C).

Effect of perchloric acid loading on SiO_2

For investigation of the effect of different amounts of $HClO_4$ loading on support in the synthesis of *β*-acetamido ketones, various weight percents of acid were used. Table 1 shows differences in catalytic activity among catalysts having 30—60 wt% of $HClO_4$ on silica. Lowering the loading of the deposited perchloric acid causes the reduction of the catalytic activity. No improvements in the reaction rate and yield were observed by increasing the amount of acid on SiO_2 from 30 to 60 wt%. Since 50 wt% of perchloric acid was the best catalyst loading, it was used to study the effect of various parameters on yields.

Table 1 Effect of $HClO_4$-SiO_2 weight ratios in the synthesis of *β*-acetamido ketones from benzaldehyde, acetophenone, acetonitrile and acetyl chloride

Entry	$HClO_4$-SiO_2/wt%	Time/min	Yield[a]/%
1	30	50	68
2	40	35	75
3	50	20	85
4	60	20	86

[a] Isolated yields.

Effect of catalyst concentration

The catalyst concentration was varied over a range of 0.07—0.2 g (0.25—1 mmol of H^+) on the basis of the total volume of the reaction mixture. Table 2 shows the effect of catalyst concentration on the reaction of benzaldehyde, acetophenone, acetonitrile and acetyl chloride. The yield of the corresponding *β*-acetamido ketones increased with increasing catalyst concentration from 0.25 to 0.75 mmol of H^+. Further addition of catalyst had no noticeable effect on the yield. This was due to the fact that beyond a certain concentration, there exists an excess of catalyst sites over what is actually required by the reactant molecules, and hence, the additional catalyst does not increase the rate of the reaction. Therefore, in all further reactions 0.75 mmol of H^+ (equal to 75 mol% of $HClO_4$) were used for 50 wt% of perchloric acid.

Table 2 Investigation of catalyst effects in the synthesis of *β*-acetamido-*β*-phenyl propiophenone from benzaldehyde, acetophenone, acetonitrile and acetyl chloride[a]

Entry	Amount of catalyst/g	H^+/mmol	Time/min	Yield[b]/%
1	0.05	0.25	55	60
2	0.1	0.5	35	78
3	0.15	0.75	20	85
4	0.2	1	20	88

[a] 50% $HClO_4$-SiO_2 were used as catalyst. [b] Isolated yields.

Synthesis of *β*-acetamido ketones catalyzed by supported perchloric acid

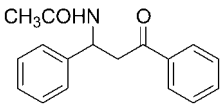
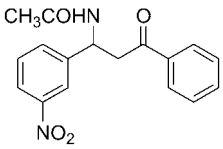
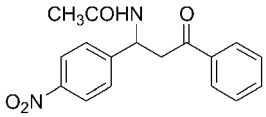
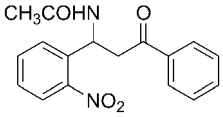
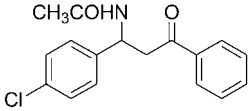
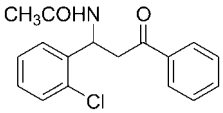
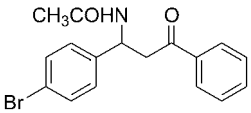
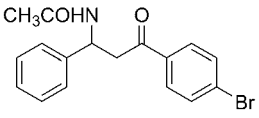
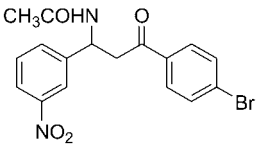
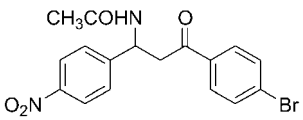
The results from the reactions of aryl aldehydes, aryl methyl ketones and acetyl chloride in the presence of optimized $HClO_4$-SiO_2 in acetonitrile at 80 ℃ and under ultrasonic irradiation are shown in Table 3. The ex-

perimental procedure for this reaction requires no inert atmosphere. Both aromatic aldehydes and acetophenones bearing either activating or deactivating groups underwent transformation well to the corresponding β-acetamido ketones, without the formation of any side products, in high to excellent yields (Entries 1—25).

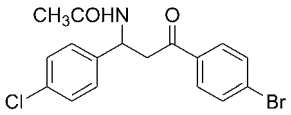
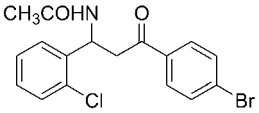
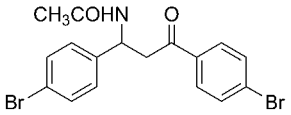
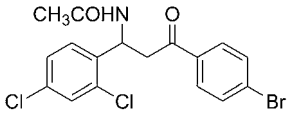
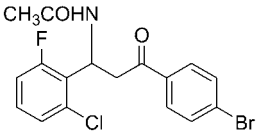
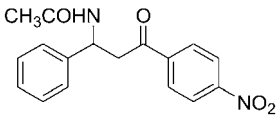
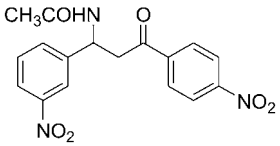
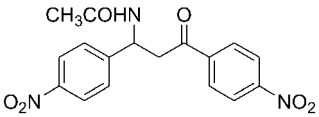
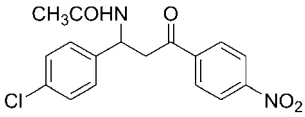
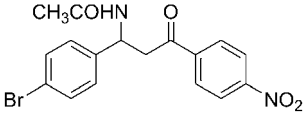
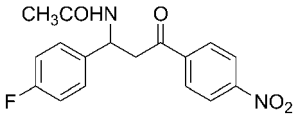
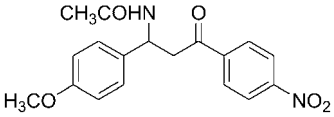
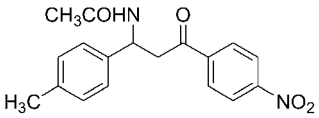
When the reaction mixture was exposed to ultrasonic irradiation, the corresponding β-acetamido ketones derivatives were obtained in 5—15 min. When the same reaction was carried out in the thermal condition, the reaction times were longer (20—65 min).

Interestingly, no acetylation of an aromatic hydroxyl group was observed under the reaction conditions and the corresponding β-acetamido ketone was isolated in an excellent yield (Table 3, Entries 24 and 25). We observed that aliphatic aldehydes react under these conditions, but produce the corresponding product in low yields (Table 3, Entry 26).

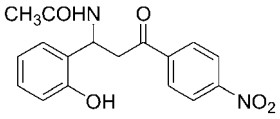
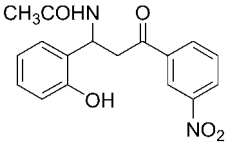
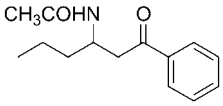
Table 3 Synthesis of β-acetamido ketones in the presence of $HClO_4$-SiO_2 under thermal and ultrasonic conditions

Entry	Ar	Ar'	Product[a]	Thermal		Ultrasonic	
				Time/min	Yield[b]/%	Time/min	Yield/%
1	C_6H_5	C_6H_5		20	85	5	90
2	3-$NO_2C_6H_4$	C_6H_5		65	80	15	84
3	4-$NO_2C_6H_4$	C_6H_5		55	78	10	80
4	2-$NO_2C_6H_4$	C_6H_5		50	85	10	90
5	4-ClC_6H_4	C_6H_5		30	85	6	87
6	2-ClC_6H_4	C_6H_5		25	92	5	92
7	4-BrC_6H_4	C_6H_5		30	87	6	90
8	C_6H_5	4-BrC_6H_4		40	80	10	90
9	3-$NO_2C_6H_4$	4-BrC_6H_4		45	80	10	85
10	4-$NO_2C_6H_4$	4-BrC_6H_4		45	90	10	90

Continuted

Entry	Ar	Ar'	Product[a]	Thermal		Ultrasonic	
				Time/min	Yield[b]/%	Time/min	Yield/%
11	4-ClC_6H_4	4-BrC_6H_4		30	92	6	94
12	2-ClC_6H_4	4-BrC_6H_4		25	90	5	92
13	4-BrC_6H_4	4-BrC_6H_4		35	90	8	90
14	2,4-$Cl_2C_6H_3$	4-BrC_6H_4		40	80	10	85
15	2-Cl-6-FC_6H_3	4-BrC_6H_4		60	87	15	90
16	C_6H_5	4-$NO_2C_6H_4$		40	80	8	86
17	3-$NO_2C_6H_4$	4-$NO_2C_6H_4$		55	75	12	80
18	4-$NO_2C_6H_4$-	4-$NO_2C_6H_4$-		55	85	12	87
19	4-ClC_6H_4	4-$NO_2C_6H_4$		35	90	8	90
20	4-BrC_6H_4	4-$NO_2C_6H_4$		45	90	10	92
21	4-FC_6H_4	4-$NO_2C_6H_4$		45	70	10	78
22	4-$CH_3OC_6H_4$	4-$NO_2C_6H_4$		30	80	5	85
23	4-$CH_3C_6H_4$	4-$NO_2C_6H_4$		55	70	12	74

Continued

Entry	Ar	Ar'	Product[a]	Thermal		Ultrasonic	
				Time/min	Yield[b]/%	Time/min	Yield/%
24	2-OHC_6H_4	4-$NO_2C_6H_4$		40	76	10	80
25	2-OHC_6H_4	3-$NO_2C_6H_4$		35	75	8	80
26	$CH_3CH_2CH_2$	C_6H_5		125	20	30	30

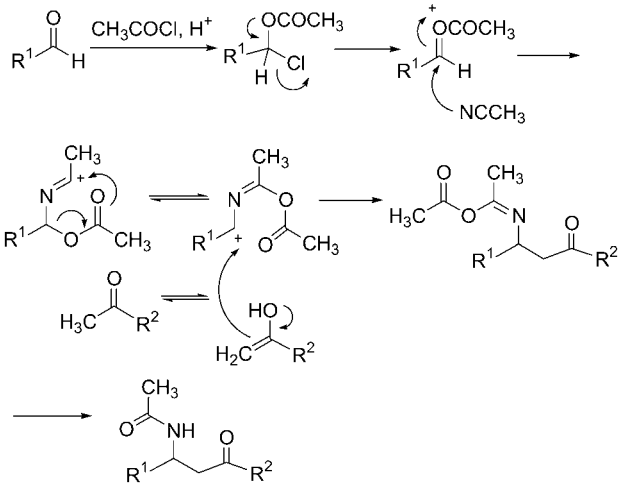
[a] All products were characterized by ^{1}H NMR, ^{13}C NMR and IR spectroscopy and compared with those reported in literatures.[9,19,20] [b] Isolated yields.

To use $HClO_4$-SiO_2 in large scale synthesis especially in chemical laboratory, a typical reaction was performed for synthesis of **1** with tenfold amounts of reactants and catalyst with respect to one mentioned in the experimental section. The result showed that the yield of 80% in these conditions is comparable with one in Table 3.

To achieve the reaction efficiency of recovered catalyst, the reaction mixture of **1** was filtered and washed with hot acetonitrile twice to give silica supported perchloric acid. The recovered acid was used again for synthesis of **1** that led to the yield of 80%. It can also be recovered and reused at least four times without noticeable losing activity.

The plausible mechanism based on Iqbal's suggestion[36] for the formation of β-acetamido ketones is shown in Scheme 1. The presence of acetyl chloride is necessary for the transformation and the desired product in its absence was not prepared even after 3 h.

Scheme 1



Effect of unsupported acid in synthesis of β-acetamido ketones

As shown in Table 4, in the presence of perchloric acid without supporting on SiO_2, the synthesis of β-acetamido ketones were performed in longer time with reduced yields in comparison with supported one. For example, in presence of $HClO_4$-SiO_2, the reaction of benzaldehyde and acetophenone (Entry 1) was completed in 20 min with 85% yield, while by using of unsupported catalyst this reaction was carried out in 100 min with 50% yield. This results show that supporting of perchloric acid on SiO_2 accelerates catalytic strength of this catalyst.

Conclusion

In conclusion, we have found an efficient, inexpensive and straightforward procedure for one-pot synthesis of β-acetamido ketones using $HClO_4$-SiO_2 as catalyst. The catalyst can be easily prepared and can be handled safely. Moreover, nonhygroscopic and inexpensive for this transformation are other advantages of this procedure.

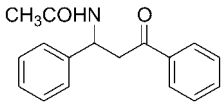
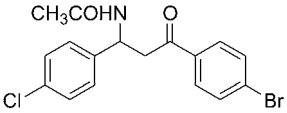
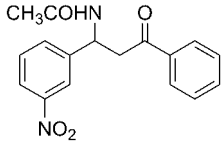
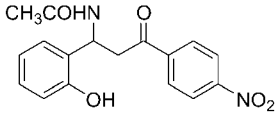
Experimental

Chemicals were purchased from Merck, Fluka and Aldrich chemical companies. All of the products were identified by comparison of their physical and spectral data with those of authentic samples. IR spectra were recorded on a JASCO IR-680 spectrophotometer. ^{1}H NMR spectra were obtained with a Bruker-Arance AQS 300 MHz or a Bruker 400 Ultrasheild (400 MHz) spectrometers. The ultrasonic device used was an UP 400 S instrument.

Preparation of the supported catalyst

The silica gel supported $HClO_4$ was prepared by

Table 4 Synthesis of some imidazolines in the presence of $HClO_4$

Entry	Product	$HClO_4$		$HClO_4$/ SiO_2	
		Time/min	Yield[a]/%	Time/min	Yield/%
1		100	50	20	85
2		150	60	30	92
3		180	45	65	80
4		120	35	40	76

[a] Isolated yield.

mixing silica gel (6 g, Merck grade 40, 0.063—0.2 mm) with 70% aqueous acid solution (0.70 g) in diethyl ether (20 mL). The resulting mixture was stirred for 30 min. After removal of water and ether in a rotary evaporator, the solid powder was dried at 80 ℃ for 4 h followed by 4 h calcinations at 120 ℃.

General procedure for the preparation of *β*-acetamido ketones

A mixture of the aryl aldehyde (1 mmol), aryl ketone (1 mmol), acetyl chloride (0.3 mL) and acetonitrile (2 mL) in the presence of $HClO_4$-SiO_2 (0.15 g, equal to 0.75 mmol H^+) was heated at 80 ℃, with stirring for 20—65 min. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the filtrate poured into 50 mL ice-water. The solid product was filtered, washed with ice-water and recrystallized from ethyl acetate/*n*-heptane to give the pure products in 70%—92% yields based on the starting aldehyde (Table 3).

***N*-(1,3-Diphenyl-3-oxopropyl)acetamide (1)** m.p. 101—103 ℃ (Lit.[19] 102—104 ℃); R_f = 0.48 (*n*-hexane/ethyl acetate, V : V = 1 : 4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.85 (s, 3H), 3.45 (dd, J=6.5, 16.8 Hz, 1H), 3.75 (dd, J=5.5, 16.8 Hz, 1H), 5.50—5.54 (m, 1H), 6.68 (d, J=7.5 Hz, 1H), 7.20—7.28 (m, 5H), 7.49—7.52 (m, 3H), 7.90 (d, J=7.7 Hz, 1H), 8.28 (d, J=7.5 Hz, 1H); IR (KBr) v: 3290, 3093, 1690, 1640, 1543, 1440, 1347, 1295, 1197, 990, 740 cm^{-1}. Anal. calcd for $C_{17}H_{17}NO_2$: C 76.38, H 6.41, N 5.24; found C 76.4, H 6.5, N 5.3.

***N*-[1-(3-Nitrophenyl)-3-phenyl-3-oxopropyl]acetamide(2)** m.p. 112—114 ℃ (Lit.[19] 110—112 ℃); R_f = 0.49 (*n*-hexane/ethyl acetate, V : V = 1 : 4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.02 (s, 3H), 3.47 (dd, J= 5.6, 17.5 Hz, 1H), 3.74 (dd, J=5.2, 17.4 Hz, 1H), 5.56—5.64 (m, 1H), 6.93 (d, J=7.5 Hz, 1H), 7.42—7.47 (m, 3H), 7.54 (t, J=7.5, 1H), 7.68 (d, J=7.4 Hz, 1H), 7.86 (d, J=6.9 Hz, 2H), 8.05 (d, J=6.9 Hz, 1H), 8.17 (s, 1H); R (KBr) v: 3292, 3067, 1687, 1643, 1523, 1350, 1290, 750, 685, 632 cm^{-1}. Anal. calcd for $C_{17}H_{16}N_2O_4$: C 65.38, H 5.16, N 8.97; found C 65.3, H 5.2, N 8.8.

***N*-[1-(4-Chlorophenyl)-3-phenyl-3-oxopropyl]acetamide (5)** m.p. 147—149 ℃ (Lit.[37] 146 ℃); R_f= 0.50 (*n*-hexane/ethyl acetate, V : V=1 : 4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.98 (s, 3H), 3.36 (dd, J=6.2, 17.0 Hz, 1H), 3.71 (dd, J=5.0, 17.2 Hz, 1H), 5.50—5.56 (m, 1H), 6.76 (d, J=7.5 Hz, 1H), 7.17—7.23 (m, 4H), 7.46 (t, J=7.2, 2H), 7.54 (t, J=7.5 Hz, 1H), 7.84 (d, J=7.7 Hz, 2H); IR (KBr) v: 3280, 3085, 1680, 1640, 1545, 1260, 1110, 890, 825, 687 cm^{-1}. Anal. calcd for $C_{17}H_{16}ClNO_2$: C 67.66, H 5.34, N 4.64; found C 67.7, H 5.5, N 3.4.

***N*-[3-(4-Bromophenyl)-1-(4-chlorophenyl)-3-oxopropyl]acetamide (11)** m.p. 141—143 ℃ (Lit.[38] 140—142 ℃); R_f=0.42 (*n*-hexane/ethyl acetate, V : V=1 : 4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.07 (s, 3H), 3.32 (dd, J=7.9, 16.8 Hz, 1H), 3.80 (dd, J=7.8, 16.3 Hz, 1H), 5.59—5.64 (m, 1H), 7.34 (d, J=7.6 Hz, 1H), 7.62 (dd, J=8.2 Hz, 2H), 7.83 (dd, J=8.3 Hz, 2H), 7.92 (d, J=8.5 Hz, 2H), 8.33 (d, J=8.4 Hz, 2H); IR (KBr) v: 3263, 3053, 1680, 1632, 1585, 1293, 1085, 887, 827 cm^{-1}. Anal. calcd for $C_{17}H_{15}BrClNO_2$: C 53.64, H 3.97, N 3.68; found C 53.7, H 4.0, N 3.8.

***N*-[3-(4-Bromophenyl)-1-(2,4-dichlorophenyl)-3-oxopropyl]acetamide (14)** m.p. 192—195 ℃; R_f= 0.53 (*n*-hexane/ethyl acetate, V : V=1 : 4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.72 (s, 3H), 3.36 (dd, J=10.8, 16.8 Hz, 1H), 3.1 (dd, J=9.8, 16.8 Hz, 1H), 5.50—5.54

(m, 1H), 6.98 (d, J=2.1 Hz, 1H), 7.11 (d, J=2.0 Hz, 1H), 7.25 (s, 1H), 7.37 (d, J=6.7 Hz, 2H), 7.58 (d, J=6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 23.24, 42.80, 47.29, 127.53, 128.77, 129.39, 129.60, 129.96, 132.22, 133.47, 135.50, 138.31, 169.89, 196.38; IR (KBr) v: 3288, 3087, 1687, 1656, 1585, 1549, 1474, 1290, 998, 810, 750 cm^{-1}. Anal. calcd for $C_{17}H_{14}BrCl_2NO_2$: C 49.19, H 3.40, N 3.37; found C 49.1, H 3.3, N 3.4.

***N*-[3-(4-Bromophenyl)-1-(2-chloro-6-flourophenyl)-3-oxopropyl]acetamide (15)** m.p. 135—138 ℃; R_f=0.6 (*n*-hexane/ethyl acetate, V∶V=1∶4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.96 (s, 3H), 3.48 (dd, J=8.4, 15.51 Hz, 1H), 3.57 (dd, J=8.1, 15.5 Hz, 1H), 6.17—6.20 (m, 1H), 6.35 (d, J=8.4 Hz, 1H), 6.97—6.99 (m, 1H), 7.18 (d, J=2.4 Hz, 2H), 7.58 (d, J=6.9 Hz, 2H), 7.80 (d, J=7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 23.63, 43.15, 45.47, 115.28, 126.56, 126.58, 129.150, 129.94, 130.03, 130.20, 132.47, 134.65, 134.70, 135.43, 169.62, 196.29; IR (KBr) v: 3291, 3079, 1681, 1650, 1580, 1545, 1425, 1289, 1240, 997, 908, 788, 598 cm^{-1}. Anal. calcd for $C_{17}H_{14}BrClFNO_2$: C 51.22, H 3.54, N 3.51; found C 51.1, H 3.6, N 3.5.

***N*-[3-(4-Nitrophenyl)-1-(3-nitrophenyl)-3-oxopropyl]acetamide (17)** m.p. 155—157 ℃ (Lit.[39] 154—157 ℃); R_f=0.45 (*n*-hexane/ethyl acetate, V∶V=1∶4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.03 (s, 3H), 3.45 (dd, J=7.5, 16.3 Hz, 1H), 3.68 (dd, J=7.9, 16.0 Hz, 1H), 5.82 (s, 1H), 6.85 (d, J=7.1 Hz, 1H), 7.21 (dd, J=7.5 Hz, 2H), 7.32 (dd, J=7.7 Hz, 2H), 7.65—7.83 (m, 4H); IR (KBr) v: 3279, 3075, 1691, 1645, 1512, 1350, 1535, 997, 851, 740 cm^{-1}. Anal. calcd for $C_{17}H_{15}N_3O_6$: C 57.14, H 4.23, N 11.76; found C 57.2, H 4.3, N 12.8.

***N*-[3-(4-Nitrophenyl)-1-(4-nitrophenyl)-3-oxopropyl]acetamide (18)** m.p. 151—153 ℃ (Lit.[4] 150 ℃); R_f=0.43 (*n*-hexane/ethyl acetate, V∶V=1∶4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.05 (s, 3H), 3.52 (dd, J=8.5, 17.2 Hz, 1H), 3.80 (dd, J=8.9, 17.0 Hz, 1H), 5.60—5.64 (m, 1H), 6.67 (d, J=8.0 Hz, 1H), 7.53 (dd, J=8.5 Hz, 2H), 7.74 (dd, J=8.7 Hz, 2H), 8.12 (d, J=8.9 Hz, 2H), 8.28 (d, J=9.0 Hz, 2H); IR (KBr) v: 3271, 3078, 1697, 1663, 1512, 1348, 1111, 999, 855, 740 cm^{-1}. Anal. calcd for $C_{17}H_{15}N_3O_6$: C 57.14, H 4.23, N 11.76; found C 57.2, H 4.3, N 12.8.

***N*-[3-(4-Nitrophenyl)-1-(4-bromophenyl)-3-oxopropyl]acetamide (20)** m.p. 141—143 ℃; R_f=0.36 (*n*-hexane/ethyl acetate, V∶V=1∶4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 2.02 (s, 3H), 3.46 (dd, J=10.5, 17.0 Hz, 1H), 3.80 (dd, J=10.9, 16.9 Hz, 1H), 5.47—5.51 (m, 1H), 6.47 (d, J=7.8 Hz, 1H), 7.21 (dd, J=8.4 Hz, 2H), 7.44 (dd, J=8.5 Hz, 2H), 8.05 (d, J=9.1 Hz, 2H), 8.28 (d, J=9.2 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ: 23.82, 44.15, 49.93, 122.18, 124.41, 128.77, 129.60, 132.37, 139.78, 141.13, 150.99, 170.02, 197.01; IR (KBr) v: 3286, 3082, 1680, 1645, 1590, 1510, 1497, 1328, 998, 842, 740 cm^{-1}. Anal. calcd for $C_{17}H_{15}BrN_2O_4$: C 52.19, H 3.86, N 7.16; found C 52.1, H 3.8, N 7.1.

***N*-[1-(2-Hydroxyphenyl)-3-(3-nitrophenyl)-3-oxopropyl]acetamide (25)** m.p. 131—132 ℃ (Lit.[19] 128—130 ℃); R_f=0.44 (*n*-hexane/ethyl acetate, V∶V=1∶4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 1.97 (s, 3H), 3.42 (dd, J=6.9, 17.5 Hz, 1H), 3.64 (dd, J=7.6, 17.3 Hz, 1H), 5.44—5.50 (m, 1H), 6.89—6.95 (m, 2H), 7.53 (t, J=7.8 Hz, 1H), 7.60—7.68 (m, 1H), 7.76—7.83 (m, 2H), 8.13 (d, J=6.8 Hz, 1H), 8.26 (s, 1H), 8.62 (d, J=7.2 Hz, 1H), 10.96 (s, 1H); IR (KBr) v: 3267, 3054, 1652, 1533, 1348, 1093, 765 cm^{-1}. Anal. calcd for $C_{17}H_{16}N_2O_5$: C 62.19, H 4.91, N 8.53; found C 62.1, H 5.0, N 8.6.

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