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PAPER

In Situ Formed Acetal Facilitated Direct Michael Addition of Unactivated Ketones

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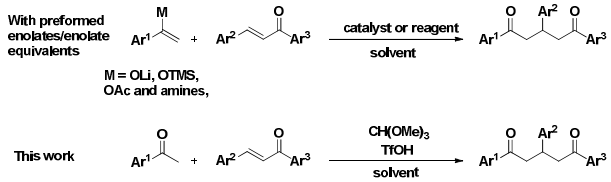
TfOH-promoted synthesis of 1,5-diketones by the Michael reaction of unactivated ketones and chalcones has been described. Acetals formed under $HC(OMe)_3$/TfOH condition generate required enol-equivalent for smooth Michael reaction. A wide array of symmetrical and unsymmetrical 1,5-diketones have been synthesised.

Introduction

Michael reaction plays a significant role in organic synthesis due to the efficient formation of carbon-carbon bond.[1] The broader scope of Michael reaction in organic synthesis is mainly attributed to the possibility of further synthetic manipulation of Michael products.[2,3] 1,5-Diketones have usually been synthesised by Michael reaction of ketone enolates with α,β-unsaturated ketones under basic reaction conditions.[4, 5] Base-mediated one pot aldol/Michael reactions have also been evaluated for making 1,5-diketones by reacting benzaldehydes with excess of acetophenones.[5] These 1,5-diketones are quite useful substrates for the synthesis of carbocyles, nitrogen heterocyles and other important complex molecules.[3] When it comes to direct Michael reaction, 1,3-diketones are widely employed nucleophiles because of their low pK_a values.[6] Since the 1,3-dicarbonyls exist in enolic form, they can be used in Lewis/Brønsted acid-catalyzed/promoted Michael reactions.[7] But, direct utilisation of unactivated ketones such as acetophenones in Michael reaction under acid catalysis is quite challenging owing to the high pK_a values of the α-hydrogens. For the Michael reaction of unactivated ketones, metal/non-metal enolates such as silyl,[8] lithium,[9] few other metal enolates[10] and enamines[11] have been employed (Scheme 1). Some of them such as silyl enol ether have to be pre-formed. Recently, Akio Baba *et al.* reported the Michael reaction of enol acetates with chalcones in the presence of catalytic amount of $InCl_3$ and TMSCl to furnish the enol acetate of Michael adduct.[12] Jung and co-worker have reported the Michael reaction of simple ketones with cyclohexenone by heating the reaction mixture in a microwave reactor in the presence of P_2O_5 and 3 equivalents of TfOH.[13]

Recently, we had shown that unactivated ketones could be alkylated at the α-position using benzylic alcohols *via* in situ formed acetals.[14] Very recently, same reaction following our strategy was reported using a reusable catalyst system, Amberlyst-15/ionic liquid.[15] We anticipated that such vinyl ether generated via in situ formed acetal could be used for the direct Michael addition of unactivated ketones (Scheme 1).

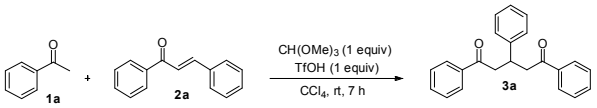


Scheme 1 Approaches for Michael reaction of unactivated ketones

Results and discussion

Preliminary evaluation of Michael addition of unactivated ketones via in situ formed acetals was attempted using acetophenone **1a** and chalcone **2a** using 1 equivalent each of TfOH and trimethyl orthoformate (TMOF). Carbon tetrachloride was chosen as the solvent as it worked better in the alkylation of unactivated

Table 1 Optimization of stoichiometry of reactants for the synthesis of 1,5-diketones



Entry	Ketone (equiv)	Chalcone (equiv)	Yield[a] (%)
1	1.0	1.5	40
2	2.0	1.0	51
3	3.0	1.0	58
4	5.0	1.0	77
5	1.0	5.0	70
6[b]	5.0	1.0	50
7[c]	5.0	1.0	30
8	5.0[d]	1.0	56

[a]Isolated yields. [b]20 mol% of TfOH was used. [c]Without TMOF. [d]5 equiv of acetophenone dimethylacetal was used in the absence of trimethyl orthoformate.

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Electronic Supplementary Information (ESI) available: Copies of the ^1H and ^{13}C spectra of the products.

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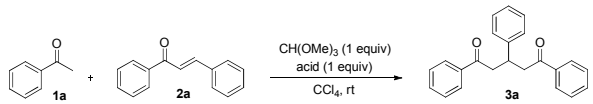
ketones.[14a] The results are given in Table 1. The reaction of 1 equivalent of acetophenone **1a** and 1.5 equivalents of chalcone **2a** resulted in 40% yield of the desired product **3a**. When acetophenone was taken in 2 fold excess with respect to chalcone an improved yield of 51% was observed. This result prompted us to find the apt stoichiometry that favours better yield of **3a**. A maximum of 77% yield of **3a** was obtained when the reaction was carried out using 5 equivalents of acetophenone **1a** with respect to chalcone **2a** (Table 1, entry 4). Reducing the amount of TfOH to 20 mol% reduced the yield of the product to 50% (Table 1, entry 6). In the absence of trimethyl orthoformate the reaction worked, however, yielding only 30% of the product (Table 1, entry 7). Acetophenone dimethylacetal also reacted with chalcone **2a** and furnished **3a** in moderate yield (Table 1, entry 8). The reduction in yield in this case compared to the reaction presented in entry 4 might be due to the conversion of acetal into its corresponding poor reactive ketone under the acidic condition. This experiment indicates that the in situ formed acetal plays a certain role in increasing the yield, perhaps, by generating the enol equivalent methyl vinyl ether from acetophenone. To get more insight into the requirement of 5 equivalents of acetophenone, a reaction was carried out using equimolar amounts of trimethyl orthoforamte and acetophenonone in the presence of 1 equivalent TfOH. This reaction, however, resulted in the formation of aldol self-condensation product of acetophenone in 30% yield after 7 h. Further, the expected acetal was not isolated, indicating a possible equilibrium between the ketone and its corresponding acetal. The same reaction without trimethyl orthoformate resulted in 12% of the aldol self-condensation product. ^{1}H NMR analysis of the reaction of equimolar quantities trimethyl orthoformate and acetophenone in the presence of 50 mol% of triflic acid in $CDCl_3/CCl_4$ in a NMR tube showed the peak corresponding to OMe of acetal but in minor quantity. The other methyl peak of the acetal is merged in the water peak. This experiment supports the formation of acetal intermediate.

Table 2 Results of reaction of direct Michael reaction under different Brønsted/Lewis acid conditions



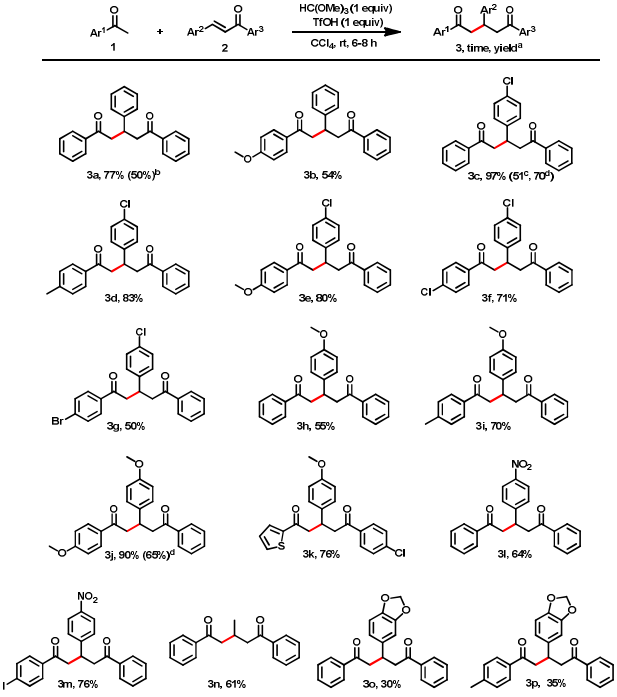
Entry[a]	Acid (1 equiv)	Time (h)	Yield[b] (%)
1	*p*-TSA	24	NR
2	Trifluoroacetic acid	24	NR
3	Acetic acid	12	NR
4	Camphor sulfonic acid	24	NR
5	$HClO_4$	24	10
6	CH_3SO_3H	24	48
7	TfOH	7	77
8	$HSbF_6$[c]	24	NR
9	$Cu(OTf)_2$[c]	24	NR
10	AgOTf[c]	24	NR
11	$AgSbF_6$[c]	24	27

[a]Chalcone (1 equiv) and ketone (5 equiv) was used. [b]Isolated yield. [c]20 mol% of acid was used.

The reaction was then screened using a set of Brønsted and Lewis acids (Table 2). Among the Brønsted acids screened, apart from TfOH, $HClO_4$ and CH_3SO_3H promoted the reaction but resulted in poor yields of **3a** (Table 2, entries 5 and 6). Among the Lewis acids, $AgSbF_6$ resulted in 27% of the expected product (Tabel 2, entry 11). Based on these results, the substrate scope was evaluated using the condition mentioned in the entry 4 of Table 1. While preparing the manuscript Gu and co-workers published the synthesis of benzofurans from unactivated ketones and 1,4-benzoquinones.[16] This reaction involves initial Michael reaction of methyl vinyl ether generated from ketone via in situ formed acetal with 1,4-benzoquinone.

Chalcones **2a-2f** were made by trivial base-promoted aldol condensation of acetophenones with aryl aldehydes. A variety of chalcones with methyl, methoxy, chloro and methylenedioxy substituents thus synthesis
ed were subjected to TfOH-promoted Michael addition. Aryl methyl ketones having electron donating groups such as OMe and Me and accepting groups such as halo on the aryl ring were employed. Overall, there was no substantial effect of the substituents on the yield of the products except few trends. The aryl methyl ketones with electron donating substituents on the aryl ring resulted in better yields than their counterparts having electron withdrawing groups (Table 3, **3c-3g**). Even 2-acetylthiophene underwent Michael addition (Table 3, **3k**). Aliphatic ketones such as acetone and cyclohexanone did not undergo such Michael additions under the present conditions. When the aryl at the β-position of the enone has electron donating groups like OMe, the yields of the products were comparatively less (Table 3, **3h**, **3o** and **3p**) and (Table 4, **5b**), perhaps, due to the reduction of electrophilicity at the β-carbon. The effect was very much seen

Table 3 Results of triflic acid mediated synthesis of 1,5-diketones from unactivated ketones[a]



[a]Reaction conditions: Chalcone (1 equiv), ketone (5 equiv), trimethylorthoformate (1 equiv) and TfOH (1 equiv) in CCl_4, rt. [b]Isolated yield. [c]20 mol% of TfOH was used. [d]50 mol% of TfOH was used.

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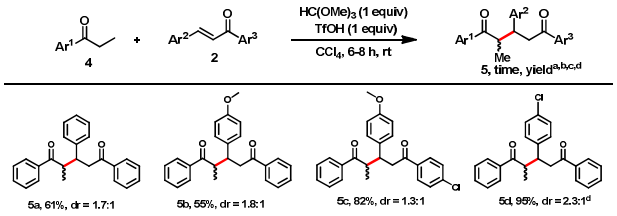
when methylenedioxy substituent was there on the β-aryl (Table 3, **3o** & **3p**). At the same time, prominent electron withdrawing nitro group on β-aryl did not improve the yield significantly either (Table 3, **3l** & **3m**). On the other hand, introducing electron withdrawing groups on the aryl ring of enones did improve the yields (Table 4, compare **5b** and **5c**).

α,β-Unsaturated ketones bearing an alkyl substitution at the β-carbon can also be used. Reaction of (*E*)-1-phenylbut-2-en-1-one with acetophenone resulted **3n** in 61% yield. However, α,β-unsaturated ketones having alkyl group attached at the carbonyl group are not suitable substrates for the present Michael reaction. For example, reaction of (*E*)-4-phenylbut-3-en-2-one resulted in a bicyclo[2.2.2]octane derivative. Formation of such derivative under the acidic condition is known in the literature.[17]

Then, a few reactions were carried out using ethyl phenyl ketone (Table 4, **5a**-**5d**). These reactions resulted in a mixture of diastereomers, marginally favoring the syn diastereomer over the anti diastereomer.

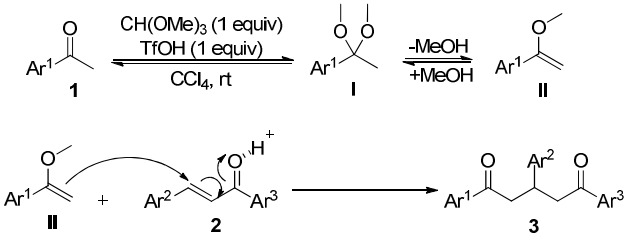
Table 4. Results of triflic acid mediated synthesis of diastereomeric 1,5-diketones from propiophenone[a]



[a]Reaction conditions: Chalcone (1 equiv), ketone (5 equiv), trimethylorthoformate (1 equiv) and TfOH (1 equiv) in CCl_4, rt. [b]Isolated yield. [c]Syn/anti ratio based on ^1H NMR. [d]Syn/anti ratio based on isolated yields of the syn and anti diastereomers.

Although the reaction required 5 equivalents of ketone, the unreacted ketone was recovered in all the reactions without much loss. Also, this reaction works well only when 1 equivalent of TfOH was used. The yield of the product decreased when lesser amount of TfOH (50 mol%) was used (Table 3, **3a**, **3c** and **3j**).

As proposed earlier,[14b] the ketone is expected to form the acetal **I,** which will set up an equilibrium with the enol ether **II**. In the presence of acid, chalcones will be activated for efficient Michael reaction with the enol ether **II** as shown in scheme 2. It is believed that, this methyl vinyl ether **II** under the reaction conditions acts as an enolate equivalent and reacts with the electrophilic chalcone **2** to furnish 1,5-diketone **3** efficiently.



Scheme 2 Plausible mechanism for the Michael addition of unactivated ketones via in situ formed acetals

Conclusions

In summary, acid-promoted Michael addition of unactivated ketones with chalcones proceeds smoothly in the presence of trimethyl orthoformate. It is believed that the acetal formed in situ under the reaction condition facilitate the Micahel addition. The substrate scope was evaluated using different substituted aryl methyl ketones and chalcones and found to result the respective adducts in good yields. Developing asymmetric version of this transformation using chiral Brønsted acid catalysis is currently being pursuaded.

Experimental

General

All reagents were obtained commercially and used without further purification unless otherwise mentioned. TfOH was purchased from Sigma-Aldrich chemical company and used without any further purification. Trimethyl orthoformate was distilled prior to use. HPLC grade CCl_4 procured from MERCK was used as solvent for Michael reaction. Thin-layer chromatography was performed by using Merck silica gel F-254 coated aluminum plates and the visualization of spots were done using UV illumination and charring the TLC plates sprayed with Seebach solution. Column chromatography was performed on silica gel 100-200 mesh, using ethyl acetate and hexane mixture as eluent. ^1H and ^{13}C NMR spectra of the synthesised compounds were recorded in Bruker Avance 400 NMR machine using their solutions in $CDCl_3$. The ^1H NMR and ^{13}C NMR were recorded with TMS as an internal standard. IR spectra were recorded using JASCO FT/IR-5300 spectrometer. High resolution mass spectra (HRMS) were recorded using electrospray ionization technique in Bruker Maxis machine.

Chalcones were made by base-promoted aldol condensation of acetophenones with aryl aldehydes. Methyl, methoxy, chloro, methylenedioxy and nitro substituted chalcones were synthesised and characterised. The ^1H and ^{13}C NMR data of synthesised chalcones were found in agreement with the reported data.[19-22]

Procedure for Michael addition of 1a on 2a

To a solution of chalcone **2a** (50 mg, 0.24 mmol, 1 equiv) and acetophenone **1a** (145 mg, 1.2 mmol, 5 equiv) in carbon tetrachloride (2 mL), trimethylorthoformate (27 µL, 0.24 mmol, 1 equiv) was added. After 5 min., triflic acid (22 µL, 0.24 mmol, 1 equiv) was added to the reaction mixture. The reaction mixture was stirred at room temperature. After completion of the reaction as indicated by TLC, the reaction mixture was concentrated under vaccum and directly loaded onto the silica gel column and purified using ethylacetate and hexane as eluents to get pure **3a** in 77% yield (61 mg)

Same procedure was followed for the preparation of other 1,5-diketones.

1,3,5-Triphenylpentane-1,5-dione[22] 3a

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61 mg, Yield: 77%; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.94 (d, *J* = 8.0 Hz, 4H), 7.56-7.52 (m, 2H), 7.45-7.41 (m, 4H), 7.28-7.25 (m, 4H), 7.20-7.15 (m, 1H), 4.06 (quint, *J* = 7.0 Hz, 1H), 3.49 (dd, *J* = 16.6, 6.9 Hz, 2H), 3.35 (dd, *J* = 16.6, 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.7, 143.9, 136.9, 133.2, 128.7, 128.2, 127.5, 126.8, 45.0, 37.2.

1-(4-Methoxyphenyl)-3,5-diphenylpentane-1,5-dione[23] 3b

47 mg, Yield: 54%; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.95-7.91 (m, 4H), 7.55-7.51 (m, 1H), 7.44-7.41 (m, 2H), 7.29-7.24 (m, 4H), 7.19-7.14 (m, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 4.05 (quint, *J* = 7.0 Hz, 1H), 3.84 (s, 3H), 3.52-3.39 (m, 2H), 3.36-3.26 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.7, 197.2, 163.5, 144.0, 136.9, 133.1, 130.5, 130.0, 128.6, 128.2, 127.5, 126.7, 113.8, 55.5, 45.0, 44.7, 37.4.

3-(4-Chlorophenyl)-1,5-diphenylpentane-1,5-dione[22] 3c

72 mg, Yield: 97%; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.93 (d, *J* = 7.6 Hz, 4H), 7.57-7.53 (m, 2H), 7.46-7.43 (m, 4H), 7.25-7.23 (m, 4H), 4.06 (quint, *J* = 7.0 Hz, 1H), 3.48 (dd, *J* = 16.9, 6.9 Hz, 2H), 3.32 (dd, *J* = 16.7, 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.3, 142.4, 136.8, 133.3, 132.4, 129.0, 128.8, 128.7, 128.2, 44.8, 36.5.

3-(4-Chlorophenyl)-1-phenyl-5-p-tolylpentane-1,5-dione[4a] 3d

65 mg, Yield: 83%; ^{1}H NMR (400 MHz, $CDCl_3$) : 7.92 (d, *J* = 7.8 Hz, 2H), 7.83 (d, *J* = 8.1 Hz, 2H), 7.55-7.52 (m, 1H), 7.45-7.41 (m, 2H), 7.24-7.22 (m, 6H), 4.04 (quint, *J* = 7.1 Hz, 1H), 3.50-3.40 (m, 2H), 3.33-3.25 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.3, 197.9, 144.1, 142.4, 136.8, 134.3, 133.2, 132.2, 129.4, 128.9, 128.7, 128.2, 44.7, 36.6, 21.7.

3-(4-Chlorophenyl)-1-(4-methoxyphenyl)-5-phenylpentane-1,5-dione 3e

65 mg, Yield: 80%; Light brown liquid; R_f = 0.33 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 2367, 1676, 1583, 1068, 986, 542; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.94-7.91 (m, 4H), 7.56-7.52 (m, 1H), 7.45-7.41 (m, 2H), 7.25-7.22 (m, 4H), 6.91 (d, *J* = 8.7 Hz, 2H), 4.03 (quint, *J* = 7.0 Hz, 1H), 3.84 (s, 3H), 3.48 (dd, *J* = 16.8, 6.6 Hz, 1H), 3.41 (dd, *J* = 16.7, 6.7 Hz, 1H), 3.30 (dd, *J* = 16.7, 7.4 Hz, 1H), 3.25 (dd, *J* = 16.4, 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.3, 196.8, 163.6, 142.5, 136.8, 133.2, 132.3, 130.4, 129.9, 129.0, 128.7, 128.6, 128.1, 113.8, 55.5, 44.8, 44.5, 36.7; HRMS (ESI) m/z calcd for $C_{24}H_{21}ClO_3$ $[M+Na]^+$ = 393.1257, found = 393.1260.

1,3-Bis(4-chlorophenyl)-5-phenylpentane-1,5-dione 3f

58 mg, Yield: 71%; Light brown solid; m.p. 54-56 °C; R_f = 0.45 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 3063, 2920, 1682, 1600, 1210, 1084, 810, 690; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.92 (d, *J* = 7.7 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 2H), 7.57-7.53 (m, 1H), 7.45 (d, *J* = 7.7 Hz, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 7.25-7.19 (m, 4H), 4.03 (quint, *J* = 7.0 Hz, 1H), 3.46 (dd, *J* = 16.7, 6.8 Hz, 1H), 3.31 (d, *J* = 17.3, 7.0 Hz, 2H), 3.26 (d, *J* = 14.4, 5.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.2, 197.1, 142.1, 139.6, 135.0, 133.3, 132.4, 129.5, 129.2, 128.9, 128.5, 128.1, 122.4, 44.6, 36.4; HRMS (ESI) m/z calcd for $C_{23}H_{18}Cl_2O_2$ $[M+H]^+$ = 397.0762, found = 397.0761.

1-(4-Bromophenyl)-3-(4-chlorophenyl)-5-phenylpentane-1,5-dione 3g

46 mg, Yield: 50%; Yellow liquid; R_f = 0.4 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 2898, 1676, 1582, 1484, 1232, 985, 547; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.93 (d, *J* = 7.4 Hz, 2H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.59-7.54 (m, 3H), 7.46-7.42 (m, 2H), 7.25-7.19 (m, 4H), 4.02 (quint, *J* = 6.9 Hz, 1H), 3.46 (dd, *J* = 16.8, 6.7 Hz, 2H), 3.34-3.22 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.2, 197.2, 142.1, 136.7, 135.5, 133.4, 132.5, 132.0, 129.7, 128.9, 128.8, 128.7, 128.5, 128.1, 44.7, 44.6, 36.5; HRMS (ESI) m/z calcd for $C_{23}H_{18}BrClO_2$ $[M+Na]^+$ = 441.0257, found = 441.0256.

3-(4-Methoxyphenyl)-1,5-diphenylpentane-1,5-dione[22] 3h

41 mg, Yield: 55%; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.94 (d, *J* = 7.2 Hz, 4H), 7.55-7.52 (m, 2H), 7.45-7.41 (m, 4H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 4.02 (quint, *J* = 7.0 Hz, 1H), 3.74 (s, 3H), 3.46 (dd, *J* = 16.6, 6.8 Hz, 2H), 3.30 (dd, *J* = 16.6, 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.8, 158.2, 136.9, 135.8, 133.1, 128.6, 128.4, 128.2, 114.0, 55.2, 45.2, 36.5.

3-(4-Methoxyphenyl)-1-phenyl-5-p-tolylpentane-1,5-dione 3i

55 mg, Yield: 70%; Colour less liquid; R_f = 0.33 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 3002, 2926, 1676, 1610, 1506, 1243, 1183, 756; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.94 (d, *J* = 7.5 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.55-7.51 (m, 1H), 7.45-7.41 (m, 2H), 7.25-7.17 (m, 4H), 6.80 (d, *J* = 8.8 Hz, 2H), 4.00 (quint, *J* = 7.0 Hz, 1H), 3.74 (s, 3H), 3.49-3.39 (m, 2H), 3.32-3.24 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.8, 198.4, 158.2, 143.9, 137.0, 136.0, 134.5, 133.0, 129.3, 128.6, 128.4, 128.3, 128.2, 114.0, 55.2, 45.1, 36.6, 29.7, 21.7; HRMS (ESI) m/z calcd for $C_{25}H_{24}O_3$ $[M+Na]^+$ = 395.1623, found = 395.1622.

1,3-Bis(4-methoxyphenyl)-5-phenylpentane-1,5-dione 3j

74 mg, Yield: 90%; Yellow liquid; R_f = 0.26 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 2931, 2838, 1676, 1600, 1506, 1249, 1178, 1030, 832; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.92 (m, 4H), 7.55-7.51 (m, 1H), 7.44-7.41 (m, 2H), 7.18 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 4.00 (quint, *J* = 7.0 Hz, 1H), 3.84 (s, 3H), 3.74 (s, 3H), 3.47 (dd, *J* = 16.4, 6.7 Hz, 1H), 3.40 (dd, *J* = 16.0, 7.0 Hz, 1H), 3.29 (dd, *J* = 16.5, 7.5 Hz, 1H), 3.24 (dd, *J* = 16.3, 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 197.4, 163.5, 158.2, 137.0, 135.9, 133.1, 130.5, 130.3, 130.0, 128.6, 128.4, 128.2, 114.0, 113.8, 113.6, 55.5, 55.2, 45.2, 44.9, 36.8, 24.7; HRMS (ESI) m/z calcd for $C_{25}H_{24}O_4$ $[M+Na]^+$ = 411.1572, found = 411.1573.

1-(4-Chlorophenyl)-3-(4-methoxyphenyl)-5-(thiophen-2-yl)pentane-1,5-dione 3k

56 mg, Yield: 76%; White solid; m.p. 116-118 °C; R_f = 0.25 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 2936, 2838, 1676, 1517, 1419, 1243, 1035, 843, 717; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.74 (d, *J* = 3.7 Hz, 1H), 7.61 (m, 1H), 7.41 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 7.12-7.10 (m, 1H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.97 (quint, *J* = 7.0 Hz, 1H), 3.75 (s, 3H), 3.47 (dd, *J* = 16.5, 6.6 Hz, 1H), 3.36 (dd, *J* = 16.0, 7.3 Hz, 1H), 3.29-3.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 191.6, 158.4, 144.3, 139.5, 135.3, 133.8, 132.2, 129.6, 129.0, 128.4, 128.2, 114.1, 55.2, 45.9, 44.9, 37.0; HRMS (ESI) m/z calcd for $C_{22}H_{19}ClO_3S$ $[M+Na]^+$ = 421.0641, found = 421.0642.

3-(4-Nitrophenyl)-1,5-diphenylpentane-1,5-dione[5b] 3l

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47 mg, Yield: 64%; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.14 (d, *J* = 8.2 Hz, 2H), 7.93 (d, *J* = 7.7 Hz, 4H), 7.57 (t, *J* = 7.3 Hz, 2H), 7.50-7.43 (m, 6H), 4.21 (quint, *J* = 6.8 Hz, 1H), 3.55 (dd, *J* = 16.7, 6.5 Hz, 2H), 3.40 (dd, *J* = 16.0, 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.6, 151.7, 136.5, 133.4, 130.1, 128.7, 128.5, 128.0, 123.8, 44.2, 36.7.

1-(4-Iodophenyl)-3-(4-nitrophenyl)-5-phenylpentane-1,5-dione 3m

75 mg, Yield: 76%; White solid; m.p. 90-92 °C; R_f = 0.26 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 1671, 1572, 1512, 1342, 980; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.13 (d, *J* = 8.6 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.59-7.55 (m, 1H), 7.49-7.43 (m, 4H), 4.18 (quint, *J* = 6.7 Hz, 1H), 3.56-3.49 (m, 2H), 3.42-3.31 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 196.9, 151.4, 146.6, 138.0, 136.4, 135.6, 133.5, 129.4, 128.7, 128.5, 128.0, 123.8, 101.5, 44.1, 44.0, 36.5; HRMS (ESI) m/z calcd for $C_{23}H_{18}INO_4$ $[M+Na]^+$ = 522.0178, found = 522.0176.

3-(Benzo[d][1,3]dioxol-5-yl)-1,5-diphenylpentane-1,5-dione 3n

22 mg, Yield: 30%; Light yellow solid; m.p. 112-114 °C; R_f = 0.3 (ethyl acetate/hexane, 1:4); IR (KBr, Cm^{-1}): 2882, 1682, 1490, 1249, 1035, 750, 690; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 7.4 Hz, 4H), 7.57-7.53 (m, 2H), 7.46-7.43 (m, 4H), 6.77 (br s, 1H), 6.73-6.68 (m, 2H), 5.89 (s, 2H), 3.99 (quint, *J* = 7.0 Hz, 1H), 3.44 (dd, *J* = 16.6, 6.9 Hz, 2H), 3.29 (dd, *J* = 16.6, 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.6, 147.8, 146.2, 137.7, 136.9, 133.2, 128.7, 128.2, 120.6, 108.4, 107.9, 101.0, 45.2, 37.1; HRMS (ESI) m/z calcd for $C_{24}H_{20}O_4$ $[M+H]^+$ = 373.1440, found = 373.1439.

3-(Benzo[d][1,3]dioxol-5-yl)-1-phenyl-5-p-tolylpentane-1,5-dione 3o

27 mg, Yield: 35%; Light yellow solid; m.p. 96-98 °C; R_f = 0.3 (ethyl acetate/hexane, 1:4); IR (KBr, Cm^{-1}): 2920, 1682, 1490, 1249, 1035, 805; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.94 (d, *J* = 7.5 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.56-7.52 (m, 1H), 7.46-7.42 (m, 2H), 7.25-7.23 (m, 2H), 6.77 (br s, 1H), 6.72-6.67 (m, 2H), 5.88 (m, 2H), 3.98 (quint, *J* = 6.9 Hz, 1H), 3.47-3.37 (m, 2H), 3.30-3.23 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 198.6, 198.2, 147.7, 146.2, 144.0, 137.8, 136.9, 134.4, 133.1, 129.3, 128.6, 128.3, 128.2, 120.5, 108.4, 107.9, 100.9, 45.2, 45.1, 37.1, 21.7; HRMS (ESI) m/z calcd for $C_{25}H_{22}O_4$ $[M+H]^+$ = 387.1596, found = 387.1596.

3-Methyl-1,5-diphenylpentane-1,5-dione[24] 3p

56 mg, Yield: 61%; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.01-7.99 (m, 4H), 7.58-7.54 (m, 2H), 7.48-7.45 (m, 4H), 3.02-3.15 (m, 2H), 2.90-2.85 (m, 3H), 1.09-1.07 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 137.0, 133.0, 128.6, 128.1, 45.4, 26.6, 20.3.

2-Methyl-1,3,5-triphenylpentane-1,5-dione[25] 5a

50 mg, Yield: 61%; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.04 (d, *J* = 7.8 Hz, 2H), 7.87-7.83 (m, 3.5H), 7.58-7.57 (m, 1H), 7.51-7.47 (m, 3H), 7.42-7.37 (m, 3H), 7.27-7.23 (m, 3H), 7.19-7.17 (m, 3H), 3.95-3.94 (m, 1.5H), 3.84-3.83 (m, 1H), 3.47-3.35 (m, 1.7H), 3.24 (dd, *J* = 16.0, 9.4 Hz, 1H), 1.27 (d, *J* = 6.0 Hz, 1.9H), 1.00 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 203.8, 203.3, 198.6, 198.5, 142.9, 141.5, 137.1, 137.0, 136.9, 133.3, 133.0, 132.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 128.0, 127.9, 126.9, 126.5,46.0, 45.7, 44.4, 43.5, 42.8, 39.9, 16.7, 14.1.

3-(4-Methoxyphenyl)-2-methyl-1,5-diphenylpentane-1,5-dione 5b

43 mg, Yield: 55%; Light brown liquid; R_f = 0.33 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 2958, 2931, 1676, 1512, 1249, 1178, 706; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.04 (d, *J* = 8.3 Hz, 2H), 7.86-7.83 (m, 3.5H), 7.59-7.57 (m, 1H), 7.52-7.48 (m, 4H), 7.42-7.38 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 0.9H), 7.08 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 H, 2H), 6.72 (d, *J* = 8.6 Hz, 0.8H), 3.93-3.85 (m, 1.7H), 3.83-3.78 (m, 1H), 3.75 (s, 3H), 3.70 (s, 1.2H), 3.41-3.34 (m, 2H), 3.18 (dd, *J* = 15.7, 9.3 Hz, 1H), 1.27 (d, *J* = 6.6 Hz, 1.7H), 1.00 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 204.0, 198.8, 158.3, 137.0, 136.9, 133.4, 133.3, 132.9, 129.3, 128.9, 128.8, 128.6, 128.5, 128.4, 128.2, 128.0, 113.8, 55.2, 46.1, 45.9, 43.7, 42.2, 40.2, 16.5, 14.3; HRMS (ESI) m/z calcd for $C_{25}H_{24}O_3$ $[M+Na]^+$ = 395.1623, found = 395.1622.

5-(4-chlorophenyl)-3-(4-methoxyphenyl)-2-methyl-1-phenylpentane-1,5-dione 5c

61 mg, Yield: 82%; Light brown liquid; R_f = 0.33 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 1676, 1506, 1243, 1101, 1030; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.04 (d, *J* = 8.5 Hz, 2H), 7.87-7.82 (m, 3H), 7.61-7.57 (m, 1H), 7.52-7.48 (m, 2H), 7.42-7.39 (m, 1H), 7.27-7.23 (m, 2H), 7.20-7.17 (m, 5H), 6.90-6.85 (m, 2H), 3.96-3.87 (m, 2H), 3.83 (s, 3H), 3.34 (dd, *J* = 14.2, 3.6 Hz, 1H), 3.16 (d, *J* = 15.3, 9.4 Hz, 1H) 1.27 (d, *J* = 6.5 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.9, 197.6, 158.3, 136.7, 135.1, 133.2, 133.0, 129.6, 129.4, 129.1, 128.8, 128.7, 128.5, 128.3, 128.1, 113.8, 113.7, 55.0, 45.9, 43.8, 43.7, 42.1, 40.0, 16.7, 14.1 ; HRMS (ESI) m/z calcd for $C_{25}H_{23}ClO_3$ $[M+H]^+$ = 407.1414, found = 407.1416.

3-(4-Chlorophenyl)-2-methyl-1,5-diphenylpentane-1,5-dione 5d (Syn isomer)

51 mg, Yield: 66%; Light brown liquid; R_f = 0.40 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 3057, 2925, 1681, 1254, 969, 832, 744; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 8.07 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 7.6 Hz, 2H), 7.63 (m, 1H), 7.54 (t, *J* = 6.8 Hz, 3H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.28-7.25 (m, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 3.94-3.83 (m, 2H), 3.41 (dd, *J* = 16.2, 4.0 Hz, 1H), 3.24 (dd, *J* = 16.2, 9.2 Hz, 1H), 1.03 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 203.4, 198.2, 140.0, 136.7, 136.6, 133.3, 133.0, 132.4, 129.7, 128.8, 128.6, 128.5, 128.4, 128.1, 45.5, 43.7, 43.3, 16.6; HRMS (ESI) m/z calcd for $C_{24}H_{21}ClO_2$ $[M+H]^+$ = 377.1308, found = 377.1309.

3-(4-Chlorophenyl)-2-methyl-1,5-diphenylpentane-1,5-dione 5d' (Anti isomer)

22 mg, Yield: 29%; Light brown liquid; R_f = 0.34 (ethyl acetate/hexane, 1:5); IR (KBr, Cm^{-1}): 3062, 2931, 1681, 1489, 1243, 1013, 689; ^{1}H NMR (400 MHz, $CDCl_3$) : δ 7.84 (d, *J* = 7.7 Hz, 4H), 7.56-7.50 (m, 2H), 7.44-7.39 (m, 4H), 7.16 (q, *J* = 14.3, 8.5 Hz, 4H), 3.96-3.87 (m, 2H), 3.42 (d, *J* = 6.3 Hz, 2H), 1.28 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) : δ 202.9, 198.2, 141.3, 136.9, 136.5, 133.1, 129.3, 129.2, 128.7, 128.5, 128.4, 128.1, 128.0, 127.9, 45.7, 42.3, 40.1, 14.6; HRMS (ESI) m/z calcd for $C_{24}H_{21}ClO_2$ $[M+H]^+$ = 377.1308, found = 377.1310.

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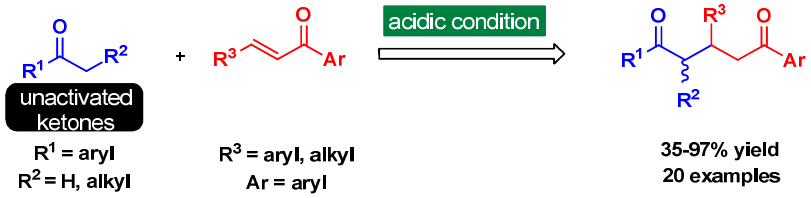
Graphical Abstract



A facile Michael addition of unactivated ketones under Brønsted acid condition for the synthesis of 1,5-diketones.