Efficient Organocatalytic Dual Activation Strategy for Preparing the Versatile Synthons (2*E*)-1-(Het)Aryl/styryl-3-(dimethylamino)prop-2-en-1-ones and α-(*E*)-[(Dimethylamino)methylene]cycloalkanones

Sachin Bindal, Dinesh Kumar, Damodara N. Kommi, Sonam Bhatiya, Asit K. Chakraborti*

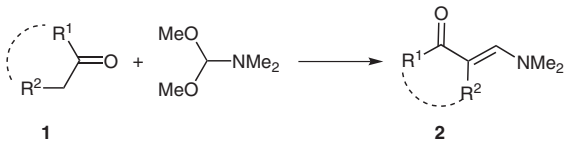
National Institute of Pharmaceutical Education and Research (NIPER), Sector 67, S. A. S. Nagar, Punjab 160062, India
Fax +91(172)2214692; E-mail: akchakraborti@niper.ac.in

Received 30 March 2011

Abstract: A novel organocatalytic dual activation strategy is reported for an efficient synthesis of the versatile synthons (2*E*)-1-aryl/heteroaryl/styryl-3-(dimethylamino)prop-2-en-1-ones and α-(*E*)-[(dimethylamino)methylene]cycloalkanones. 2-Guanidinoacetic acid (10 mol%) serves as an ambifunctional organocatalyst for the reaction of various aryl/heteroaryl/styryl methyl ketones and cyclic ketones having an α-methylene moiety with *N*,*N*-dimethylformamide dimethyl acetal at 100 °C for 1–3 hours under solvent-free conditions to afford the corresponding (2*E*)-3-(dimethylamino)prop-2-en-1-ones in 72–95% yields.

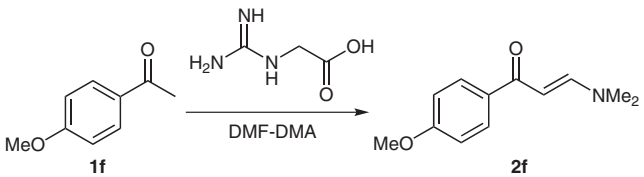
Key words: 2-guanidinoacetic acid, organocatalyst, dual activation, 3-(dimethylamino)propenones, aryl methyl ketone, *N*,*N*-dimethylformamide dimethyl acetal

Enaminones of type **2** are versatile synthons for the construction of diverse heterocycles,[1] the generation of new chemical entities as potential therapeutic agents,[2] and the synthesis of drugs, such as antileukemic agent imatanib.[3] The common strategy for their preparation involves the reaction of the corresponding carbonyl compounds having an α-methylene moiety with *N*,*N*-dimethylformamide dimethyl acetal (DMF-DMA) (Scheme 1).



Scheme 1 Synthetic strategy for enaminones of the type **2**

The various methodologies reported for the synthesis of the enaminones of type **2** are the reaction of the carbonyl substrates **1** with (i) *N*,*N*-dimethylformamide dimethyl acetal,[4,5] *tert*-butoxybis(dimethylamino)methane (Bredereck's reagent),[5] or tris(dimethylamino)methane (neat, 110 °C, 12 h),[5] (ii) *N*,*N*-dimethylformamide diethyl acetal (reflux, 20 h),[6] (iii) *N*,*N*-dimethylformamide dimethyl acetal in anhydrous toluene[7] or xylene[8] (reflux, 8–12 h), (iv) *N*,*N*-dimethylformamide dimethyl acetal under fusion at 180 °C,[9] (v) *N*,*N*-dimethylformamide dimethyl acetal under microwave heating,[10] (vi) *N*,*N*-dimethylformamide dimethyl acetal in anhydrous *N*,*N*-dimethylformamide[11] (reflux, 12–14 h), and (vii) Bredereck's reagent in anhydrous anisole (reflux, 4.5 h).[12] These methodologies suffer from disadvantages such as the use of excess *N*,*N*-dimethylformamide dimethyl acetal,[6,11,13] long reaction times,[4–8,11] the use of high-boiling solvents that are difficult to recover,[11,12] high temperatures,[9,11] the requirement for special apparatus,[10] and moderate yields. Thus, the development of a convenient and improved methodology for the synthesis of these versatile synthons is necessary. A recent effort towards this directive involves performing the condensation reaction at 100 °C for six hours in the presence of stoichiometric amounts of the ionic liquid [bmim][BF_4].[14] Although ionic liquids are used as catalysts for various organic reaction[15] the use of stoichiometric quantities of [bmim][BF_4] for the desired reaction[14] raises the possibility of a general effect of the ionic liquid as a medium. We reasoned that use of a suitable catalytic species that would generate the enolate of the carbonyl substrate and at the same time activate *N*,*N*-dimethylformamide dimethyl acetal for ease of nucleophilic displacement of the OMe group would promote the reaction effectively. To implement such dual activation strategy[16] we chose 4-methoxyacetophenone (**1f**) as the model substrate and treated it with *N*,*N*-dimethylformamide dimethyl acetal under various conditions in the presence of 2-guanidinoacetic acid (glycocyamine) as the guanidine moiety could serve as a base to generate enolate of **1f** while at the same time the carboxylic acid group would activate *N*,*N*-dimethylformamide dimethyl acetal through protonation at one of the OMe groups for nucleophilic displacement by the enolate of **1f** (Scheme 2); the results are summarized in Table 1.



Scheme 2 Reaction of 4-methoxyacetophenone (**1f**) with *N*,*N*-dimethylformamide dimethyl acetal in the presence of 2-guanidinoacetic acid

The desired product 3-(dimethylamino)-1-(4-methoxyphenyl)prop-2-en-1-one (**2f**) was obtained in 88% yield when the reaction was performed in the presence of 2-

SYNTHESIS 2011, No. x, pp 000A–000F
Advanced online publication: xx.xx.2011
DOI: 10.1055/s-0030-1260048; Art ID: C01711SS

guanidinoacetic acid (10 mol%) at 100 °C for three hours (entry 4). The poor yield (25%) obtained in the absence of any catalyst (entry 1) demonstrated the catalytic assistance provided by 2-guanidinoacetic acid. The product yield did not improve significantly when using larger amounts (15 mol%) of 2-guanidinoacetic acid (entry 5), and it decreased when lower amounts of 2-guanidinoacetic acid amounts were used (2.5–5 mol%) (entries 2 and 3). Decreasing the reaction temperature (entries 7–9) and time (entries 12–14) also resulted in inferior yields. No distinct beneficial effect of using a temperature higher than the optimal value (i.e., 100 °C) (entries 10 and 11) or increased reaction time (entries 15 and 16) was observed. The use of solvents (nonpolar, weakly polar, aprotic polar, and protic polar) in general exhibited a detrimental effect (entries 17–26).

Table 1 2-Guanidinoacetic Acid Catalyzed Reaction of 4-Methoxyacetophenone (**1f**) with *N*,*N*-Dimethylformamide Dimethyl Acetal under Different Conditions[a]

Entry	Catalyst[b] (mol%)	Solvent	Temp[c] (°C)	Time (h)	Yield[d] (%)
1	none	neat	100	3	25
2	2.5	neat	100	3	35
3	5	neat	100	3	55
4	10	neat	100	3	88
5	15	neat	100	3	88
6	20	neat	100	3	90
7	10	neat	r.t.	3	0
8	10	neat	50	3	0
9	10	neat	80	3	30
10	10	neat	120	3	89
11	10	neat	140	3	90
12	10	neat	100	0.5	0
13	10	neat	100	1	35
14	10	neat	100	2	60
15	10	neat	100	4	80
16	10	neat	100	5	81
17	10	toluene	100	3	20
18	10	EtOH	reflux	3	30
19	10	MeCN	reflux	3	10
20	10	1,4-dioxane	reflux	3	20
21	10	THF	reflux	3	45
22	10	DMF	100	3	15
23	10	$CHCl_3$	reflux	3	0
24	10	CH_2Cl_2	reflux	3	0
25	10	DCE	reflux	3	0
26	10	H_2O	100	3	0

[a] Reaction conditions: **1f** (0.375 g, 2.5 mmol), DMF-DMA (0.35 g, 3.0 mmol, 1.2 equiv), 2-guanidinoacetic acid.
[b] Amount of 2-guanidinoacetic acid used with respect to the substrate.
[c] Oil bath temperature.
[d] Yield of **2f** obtained after purification.

The role of 2-guanidinoacetic acid is anticipated as that of an ambiphilic dual activating agent due to the ability of the guanidine moiety to act as a base to generate the enolate (nucleophilic activation)[17] of **1f** and simultaneous activation of one of the methoxy groups of *N*,*N*-dimethylformamide dimethyl acetal (electrophilic activation) through the carboxylic acidic site. The requirement of the acid–base dual character of 2-guanidinoacetic acid in affording the desirable yields of **2f** could be demonstrated by selecting other organocatalysts that either contain only an acidic moiety (Table 2, entries 1–13) or the basic moiety (entries 14 and 15). The inferior yields obtained with these organocatalysts clearly indicate the implication of the dual functional character of 2-guanidinoacetic acid. The improved yield obtained in using equimolar (10 mol% each) amounts of pyridine and acetic acid compared (entry 18) to those obtained with acetic acid or pyridine alone further justifies the implication of the dual activation strategy. The use of pyridine-2-, -3-, or -4-carboxylic acids also afforded improved yields (entries 19–21). These further demonstrate the requirement/implication of nucleophile–electrophile dual activation. The improved dual activation ability of pyridine-3-carboxylic acid compared to the 2- or 4-regioisomers is due to the fact that the pyridine nitrogen in the later compounds is less basic as the electron lone pair of the pyridyl nitrogen is in conjugation with the carboxy carbonyl group.

The essential requirement of the bifunctional character of the organocatalyst can be further substantiated by inferior yields obtained using other guanidine derivatives (Table 3) wherein the guanidine moiety remains in the protonated/salt form and hence is not available to generate the enolate of **1f**.

To establish the generality, various aryl/heteroaryl/styryl methyl ketones and cyclic ketones/1,3-diketones **1** having an α-methylene moiety were treated with *N*,*N*-dimethylformamide dimethyl acetal in the presence of 2-guanidinoacetic acid (10 mol%) at 100 °C (oil bath) for 0.5–3 hours (Table 4). The desired enaminones **2** were obtained in 72–95% yields. The reactions were monitored by TLC. However, the progress of the reaction could also be monitored visually. The enaminone **2** formation was indicated by the development of yellowish- to reddish-brown color of the reaction mixture. In some cases, the appearance of a solid precipitate confirmed the completion of the reaction (TLC, GCMS). In most of the cases, a solid mass was obtained after removal of the volatile components (e.g. unreacted DMF-DMA, liberated MeOH etc.) under rotary evaporation of the reaction mixture. Purification was achieved by passing the crude product through a column

Table 2 Reaction of 4-Methoxyacetophenone (**1f**) with *N*,*N*-Dimethylformamide Dimethyl Acetal in the Presence of Various Organocatalysts[a]

Entry	Catalyst	Yield[b] (%)
1	AcOH	25
2	$NCCH_2CO_2H$	27
3	TFA	45
4	Cl_3CCO_2H	25
5	$PhCH_2CO_2H$	55
6	2-naphthylCH_2CO_2H	30
7	$PhOCH_2CO_2H$	50
8	4-$ClC_6H_4CH_2CO_2H$	25
9	$PhSCH_2CO_2H$	60
10	3,4,5-$(MeO)_3C_6H_2CH_2CO_2H$	55
11	Ph_2CHCO_2H	38
12	3,4-$(MeO)_2C_6H_3CH_2CO_2H$	40
13	4-$HOC_6H_4CH_2CO_2H$	37
14	pyridine	35
15	Et_3N	30
16	urea	40
17	thiourea	35
18	pyridine–AcOH	56
19	pyridine-2-carboxylic acid	42
20	pyridine-3-carboxylic acid	51
21	pyridine-4-carboxylic acid	44

[a] Reaction conditions: **1f** (0.375 g, 2.5 mmol), DMF-DMA (0.35 g, 3.0 mmol, 1.2 equiv), organocatalyst (10 mol%), 100 °C (oil bath), 3 h.
[b] Yield of **2f** obtained after purification.

of silica gel (EtOAc–hexane). In some cases the crude solid residue on trituration (Et_2O or EtOAc–hexane) afforded the pure (spectral data) enaminone **2**.

Very good to excellent yields were obtained from substrates **1b–i** bearing various substituents (e.g., Me, OMe, CF_3, NO_2, F, Cl, I) in the aryl moiety. However, no product formation took place in case of 4-hydroxyacetophenone and 4-aminoacetophenone probably due to competitive deprotonation of the hydroxy or amino group, respectively, by 2-guanidinoacetic acid. The reaction was influenced by the electronic effect of the substituent attached to the aromatic ring of the aryl methyl ketones. Substrates with an alkoxy group required a longer time period. Perhaps the electron-donating or -releasing effect of the alkoxy substituent did not permit the abstraction of the α-hydrogen atom of the methyl ketone efficiently. For substrates bearing an electron-withdrawing group, the reaction took place in a shorter time period compared to that for acetophenone. The shorter reaction time required for such substrates could be due to the ease of generation of the corresponding enolate because of lower pK_a values of the corresponding acetophenone derivatives.[18]

Table 3 Reaction of **1f** with *N*,*N*-Dimethylformamide Dimethyl Acetal in the Presence of Different Guanidine Derivatives[a]

Entry	Catalyst	Yield[b] (%)
1	2-guanidinoacetic acid	88
2	guanidine acetate	54
3	guanidine thiocyanate	57
4	guanidine hydrochloride	49

[a] Reaction conditions: **1f** (0.375 g, 2.5 mmol), DMF-DMA (0.35 g, 3.0 mmol, 1.2 equiv), guanidine derivative (10 mol%), 100 °C (oil bath), 3 h.
[b] Yield of **2f** obtained after purification.

Table 4 2-Guanidinoacetic Acid Catalyzed Synthesis of 3-(Dimethylamino)prop-2-enones **2**[a]

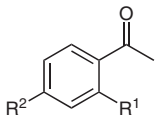
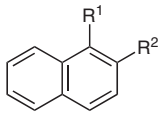
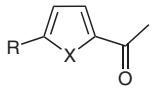
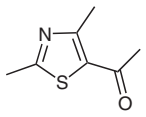
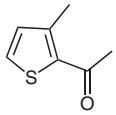
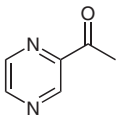
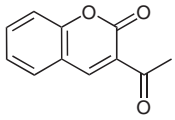
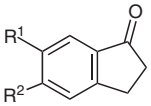
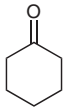
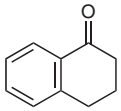
Entry	Substrate	Time (h)	Product	Yield[b,c] (%)
				
1	$R^1 = R^2 = H$	1.5	**2a**	90
2	$R^1 = H$; $R^2 = Me$	2	**2b**	89
3	$R^1 = H$; $R^2 = F$	1	**2c**	90
4	$R^1 = H$; $R^2 = Cl$	1	**2d**	85
5	$R^1 = H$; $R^2 = I$	1.5	**2e**	86
6	$R^1 = H$; $R^2 = OMe$	3	**2f**	88
7	$R^1 = H$; $R^2 = NO_2$	0.5	**2g**	90
8	$R^1 = H$; $R^2 = CF_3$	0.5	**2h**	93
9	$R^1 = R^2 = OMe$	3	**2i**	80
				
10	$R^1 = Ac$, $R^2 = H$	3	**2j**	85
11	$R^1 = H$, $R^2 = Ac$	3	**2k**	90
				
12	R = 2-Ac	1	**2l**	89 (56)[d]
13	R = 3-Ac	1.5	**2m**	91 (72)[d]
14	R = 4-Ac	1	**2n**	95 (51)[d]
				
15	X = NH, R = H	2	**2o**	87 (38)[d]
16	X = NMe, R = H	2	**2p**	72 (12)[d]
17	X = O, R = H	1.5	**2q**	92
18	X = O, R = Me	1.5	**2r**	92
19	X = S, R = H	1.5	**2s**	90

Table 4 2-Guanidinoacetic Acid Catalyzed Synthesis of 3-(Dimethylamino)prop-2-enones **2**[a] (continued)

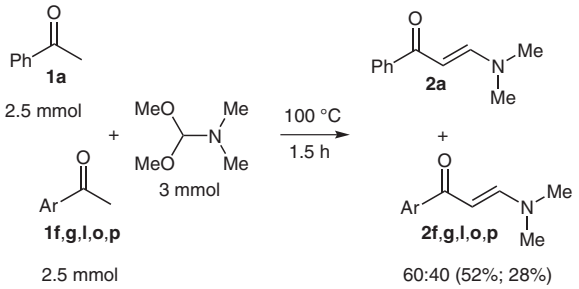
Entry	Substrate	Time (h)	Product	Yield[b,c] (%)
20		1.5	**2t**	93
21		1.5	**2u**	89
22		1	**2v**	91 (75)[d]
23		1.5	**2w**	85
				
24	$R^1 = R^2 = H$	1.5	**2x**	91
25	$R^1 = R^2 = OMe$	1.5	**2y**	83
26		1.5	**2z**	87
27		1.5	**2aa**	90

[a] Reaction conditions: ketone **1** (2.5 mmol), DMF-DMA (3.0 mmol, 1.2 equiv), 2-guanidinoacetic acid (10 mol%), 100 °C (oil bath).
[b] The yield of the corresponding enaminone obtained after purification.
[c] The products were characterized by IR, NMR, and MS.
[d] Yield from the reaction performed under similar conditions in the absence of 2-guanidinoacetic acid.

To find out whether in case of the nitrogen-containing heteroaryl methyl ketones the reactions are self-catalyzed, the reactions of 2- (**1l**), 3- (**1m**), and 4-acetylpyridine (**1n**), 2-acetyl-1*H*-pyrrole (**1o**), 2-acetyl-1-methyl-1*H*-pyrrole (**1p**), and 2-acetylpyrazine (**1v**) were carried out in the absence of 2-guanidinoacetic acid; the corresponding enaminones were formed in 56, 72, 51, 38, 12, and 75% yields, respectively. Thus, the pyridine moiety of 3-acetylpyridine (**1m**) serves as the base catalyst while in case of the 2- (**1l**) and 4-acetylpyridine (**1n**) the 2-guanidinoacetic acid exhibits a distinct catalytic effect as in these cases the pyridine nitrogen is in conjugation with the acetyl group and cannot serve as effectively as a base. The much improved yields obtained with 2-acetylpyrazine (**1v**) in the absence of 2-guanidinoacetic acid was due to the self-catalytic effect as the nitrogen atom at position 4 of the pyrazine moiety serves as a base to abstract the hydrogen atom from the COMe group and generates the corresponding enolate for condensation with *N*,*N*-dimethylformamide dimethyl acetal. The inferior result obtained with 2-acetyl-1-methyl-1*H*-pyrrole (**1p**) is indicative of the importance of the influence of the acidity of the COMe hydrogen atoms on the rate of enaminone formation. In case of the pyrrole derivatives the nitrogen atom does not exhibit an appreciable basic property as its lone pair electrons are engaged in establishing the aromatic sextet of the parent heterocyclic moiety and, hence, in the process increasing the acidic character of the COMe protons. The methyl group attached to the nitrogen atom in 2-acetyl-1-methyl-1*H*-pyrrole (**1p**) decrease the acidity of the COMe hydrogen atoms compared to that of 2-acetyl-1*H*-pyrrole (**1o**) and accounts for the lower yields.

We realized that the influence of the electronic effect on the substrate aryl/heteroaryl methyl ketones **1** resulting in differential reaction time may be used as handle for selective enaminone formation during competitive environments. Thus, we designed intermolecular competition studies involving (a) two aryl methyl ketones with varying electronic factors and (b) an aryl methyl ketone and a heteroaryl methyl ketone. To represent typical examples of aryl methyl ketone with usual electronic factor we considered acetophenone (**1a**) whereas 4-methoxyacetophenone (**1f**) and 4-nitroacetophenone (**1g**) were chosen as representatives of electron-rich and electron-deficient aryl methyl ketones, respectively. When equimolar (2.5 mmol each) amounts of acetophenone (**1a**) and 4-methoxyacetophenone (**1f**) were treated with *N*,*N*-dimethylformamide dimethyl acetal (3 mmol, 1.2 equiv) in the presence of 2-guanidinoacetic acid (0.25 mmol, 10 mol%) (100 °C oil bath, 1.5 h) the isolated product ratio of enaminones **2a/2f** was found to be 60:40 (GCMS), from which the individual pure enaminones **2a** and **2f** were obtained in 52 and 28% yields, respectively, after column chromatographic purification (Table 5). On the other hand performing the reaction under the same conditions with acetophenone (**1a**) and 4-nitroacetophenone (**1g**) afforded a ratio of enaminones **2a/2g** 14:86 (GCMS) and the pure components **2a** and **2g** were obtained in 6 and 74% yields, respectively, after column chromatographic purification. Similarly intermolecular completion studies were performed between aryl methyl ketones, acetophenone (**1a**), and heteroaryl methyl ketones, 2-acetylpyridine (**1l**), 2-acetyl-1*H*-pyrrole (**1o**), and 2-acetyl-1-methyl-1*H*-pyrrole (**1p**) to obtain the corresponding pairs of enaminones with **2a/2l** 30:70, **2a/2o** 85:15, and **2a/2p** 90:10 selectivities (GCMS) reflecting the relative time taken for the individual heteroaryl methyl ketones compared to that of acetophenone. From the respective product mixtures the individual enaminones were obtained in 28 and 56%, 72 and 8%, and 86 and 5% yields, respectively, after purification.

Table 5 Selectivity in Enaminone Formation during Intermolecular Competition between Methyl Ketones with Varying Electronic Requirements



Entry	Ar	Ratio[a]	Yield[b] (%)	
		2a/2f,g,l,o,p	**2a**	**2f,g,l,o,p**
1	4-$MeOC_6H_4$ **2f**	60:40	52	28
2	4-$O_2NC_6H_4$ **2g**	14:86	6	74
3	2-pyridyl **2l**	30:70	24	56
4	1*H*-pyrrol-2-yl **2o**	85:15	72	8
5	1-methyl-1*H*-pyrrol-2-yl **2p**	90:10	86	5

[a] By GCMS.
[b] After column chromatography.

In conclusion, a novel ambifunctional organocatalytic procedure has been developed for a convenient synthesis of acyclic enaminones from the condensation of aryl/heteroaryl/styryl methyl ketones and cyclic ketones having α-methylene group promoted by 2-guanidinoacetic acid under neat conditions in high yields and short reaction times.

^{1}H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker Avance DPX 400 MHz NMR spectrometer in $CDCl_3$ using TMS as an internal standard. IR spectra were recorded either as KBr pellets (for solids) or neat (for liquids) on a Nicolet Impact 410 FTIR spectrophotometer. Mass spectra were recorded on a GCMS-QP 5000 (Shimadzu) [for EI], and Finnigan MAT-LTQ [for APCI] mass spectrometers. The reactions were monitored by TLC (Merck®, Silica gel 60 F_{254}). Evaporation of solvents was performed at reduced pressure, using a Büchi rotary evaporator.

3-(Dimethylamino)-1-(4-methoxyphenyl)prop-2-en-1-one (2f); Typical Procedure

To a magnetically stirred mixture of 4-methoxyacetophenone (**1f**, 375 mg, 2.5 mmol) and DMF-DMA (357 mg, 0.39 mL, 3 mmol, 1.2 equiv) at 100 °C (oil bath) was added 2-guanidinoacetic acid (29 mg, 0.25 mmol, 10 mol%). After completion of the reaction (3 h, TLC) the mixture was subjected to rotary vacuum evaporation to remove the volatile components (excess of DMF-DMA and the liberated MeOH) and the crude product was purified by column chromatography (EtOAc–hexane) to afford **2f** (451 mg, 88%) as a reddish-brown viscous liquid that became solid on standing; mp 90–92 °C.

IR (KBr): 2906, 1639, 1544, 1433, 1358, 1305, 1244, 1172, 1116, 1056, 1026, 899, 774 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.97 (br s, 6 H), 3.84 (s, 3 H), 5.70 (d, *J* = 12.3 Hz, 1 H), 6.88–6.92 (m, 2 H), 7.77 (d, *J* = 12.3 Hz, 1 H), 7.88–7.92 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.41, 161.93, 153.78, 133.13, 129.43, 113.28, 91.72, 55.33, 47.12, 36.52.

MS (APCI): *m/z* = 206.4 (M + 1).

The remaining reactions were performed following this typical procedure and the physical data (mp, IR, NMR, and MS) of all known compounds were identical with those reported in the literature.

Intermolecular Competition Studies; Typical Procedures
Aryl Methyl Ketones with Varying Electronic Factor; Acetophenone (1a) vs 4-Nitroacetophenone (1g)

To a magnetically stirred mixture of acetophenone (**1a**, 300 mg, 2.5 mmol), 4-nitroacetophenone (**1g**, 412 mg, 2.5 mmol), and DMF-DMA (357 mg, 0.39 mL, 3 mmol, 1.2 equiv), 2-guanidinoacetic acid (29 mg, 0.25 mmol, 10 mol% of one of the substrates) was added and the mixture was heated at 100 °C (oil bath) for 1.5 h. The crude mixture on being subjected to GCMS analysis was found to contain 3-(dimethylamino)-1-phenylprop-2-en-1-one (**2a**) and 3-(dimethylamino)-1-(4-nitrophenyl)prop-2-en-1-one (**2g**) in a ratio of 14:86 and afforded the respective enaminones in 26 mg (6%) and 407 mg (74%) yields, respectively, after purification by flash column chromatography (silica gel 230–400 mesh, hexane–EtOAc).

Heteroaryl Methyl Ketones; Acetophenone (1a) vs 2-Acetyl-1*H*-pyrrole (1o)

To a magnetically stirred mixture of acetophenone (**1a**, 300 mg, 2.5 mmol), 2-acetyl-1*H*-pyrrole (**1o**, 272 mg, 2.5 mmol), and DMF-DMA (357 mg, 0.39 mL, 3 mmol, 1.2 equiv), 2-guanidinoacetic acid (29 mg, 0.25 mmol, 10 mol% of one of the substrates) was added and the mixture was heated at 100 °C (oil bath) for 1.5 h. The crude mixture on being subjected to GCMS analysis was found to contain 3-(dimethylamino)-1-phenylprop-2-en-1-one (**2a**) and 3-(dimethylamino)-1-(1*H*-pyrrol-2-yl)prop-2-en-1-one (**2o**) in a ratio of 85:15 and afforded the respective enaminones in 315 mg (72%) and 33 mg (8%) yields, respectively, after purification by flash column chromatography (silica gel 230–400 mesh, hexane–EtOAc).

Acknowledgment

The authors D.K. and D.N.K. thank CSIR, New Delhi, India for award of RA and SRF, respectively.

References

(1) (a) For review see: Elassar, A.-Z. A.; El-Khair, A. A. *Tetrahedron* **2003**, *59*, 8463. (b) Svete, J. *Monatsh. Chem.* **2004**, *135*, 629. (c) Pirc, S.; Bevk, D.; Jakše, R.; Rečnik, S.; Golič, L.; Golobič, A.; Meden, A.; Stanovnik, B.; Svete, J. *Synthesis* **2005**, 2969. (d) Svete, J. *J. Heterocycl Chem.* **2005**, *42*, 361. (e) Valla, A.; Valla, B.; Cartier, D.; Guillou, R. L.; Labia, R.; Florent, L.; Charneau, S.; Schrevel, J.; Potier, P. *Eur. J. Med. Chem.* **2006**, *41*, 142.
(2) (a) Chakraborti, A. K.; Sarin, S.; Rudrawar, S. V.; Kumar, R.; Chankeshwara, S. V.; Dastidar, S.; Ray, A. IN 566/DEL/2006, **2006**. (b) Chakraborti, A. K.; Sarin, S.; Rudrawar, S. V.; Kumar, R.; Chankeshwara, S. V.; Dastidar, S.; Ray, A. IN 565/DEL/2006, **2006**.
(3) Liu, Y. F.; Wang, C. L.; Bai, Y. J.; Han, N.; Jiao, J. P.; Qi, X. L. *Org. Process Res. Dev.* **2008**, *12*, 490.
(4) Abdulla, R. F.; Fuhr, K. H. *J. Org. Chem.* **1978**, *43*, 4248.
(5) Schuda, P. F.; Ebner, C. B.; Morgan, T. M. *Tetrahedron Lett.* **1986**, *27*, 2567.
(6) Lin, Y.-I.; Lang, S. A. *J. Org. Chem.* **1980**, *45*, 4857.
(7) SanMartín, R.; Marigorta, E. M. D.; Domínguez, E. *Tetrahedron* **1994**, *50*, 2255.
(8) Dawood, K. M.; Kandeel, Z. E.; Farag, A. M. *Heteroat. Chem.* **1999**, *10*, 417.

(9) Omran, F. A.; Elassar, A. Z. A.; El-Khair, A. A. *Tetrahedron* **2001**, *57*, 10163.
(10) (a) Pleier, A.-K.; Glas, H.; Grosche, M.; Sirsch, P.; Thiel, W. R. *Synthesis* **2001**, 55. (b) Al-Zaydi, K. M. *Molecules* **2003**, *8*, 541.
(11) (a) Časar, Z.; Bevk, D.; Svete, J.; Stanovnik, B. *Tetrahedron* **2005**, *61*, 7508. (b) Stanovnik, B.; Svete, J. *Mini Rev. Org. Chem.* **2005**, *2*, 211.
(12) Wagger, J.; Bevk, D.; Meden, A.; Svete, J.; Stanovnik, B. *Helv. Chim. Acta* **2006**, *89*, 240.
(13) (a) Brabander, H. J.; Francisco, G. *J. Heterocycl. Chem.* **1987**, *24*, 837. (b) Kepe, V.; Kočevar, M.; Polanc, S. *J. Heterocycl. Chem.* **1996**, *33*, 1707. (c) Čebaek, P.; Wagger, J.; Bevk, D.; Jakše, R.; Svete, J.; Stanovnik, B. *J. Comb. Chem.* **2004**, *6*, 356.
(14) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Rosa, F. A.; Marzari, M. R. B.; Zanatta, N.; Bonacorso, H. G. *Catal. Commun.* **2008**, *9*, 1375.
(15) (a) Sarkar, A.; Raha Roy, S.; Chakraborti, A. K. *Chem. Commun.* **2011**, *47*, 4538. (b) Raha Roy, S.; Chakraborti, A. K. *Org. Lett.* **2010**, *12*, 3866. (c) Chakraborti, A. K.; Raha Roy, S. *J. Am. Chem. Soc.* **2009**, *131*, 6902. (d) Chakraborti, A. K.; Raha Roy, S.; Kumar, D.; Chopra, P. *Green Chem.* **2008**, *10*, 1111.
(16) Dual activation of the nucleophile and electrophile by coordinating alkali metal cation: (a) Basak, A.; Nayak, M. K.; Chakraborti, A. K. *Tetrahedron Lett.* **1998**, *39*, 4883. (b) Chakraborti, A. K.; Basak, A.; Grover, V. *J. Org. Chem.* **1999**, *64*, 8014. (c) Bhagat, S.; Sharma, R.; Sawant, D. M.; Sharma, L.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2006**, *244*, 20. (d) Bhagat, S.; Sharma, R.; Chakraborti, A. K. *J. Mol. Catal. A: Chem.* **2006**, *260*, 235. Hydrogen-bond-assisted dual activation under metal-free condition: (e) Chankeshwara, S. V.; Chakraborti, A. K. *Org. Lett.* **2006**, *8*, 3259. (f) Khatik, G. L.; Kumar, R.; Chakraborti, A. K. *Org. Lett.* **2006**, *8*, 2433. (g) Chakraborti, A. K.; Rudrawar, S.; Jadhav, K. B.; Kaur, G.; Chankeshwara, S. V. *Green Chem.* **2007**, *9*, 1335.
(17) Nucleophilic activation with catalytic amount of base: (a) Chakraborti, A. K.; Sharma, L.; Nayak, M. K. *J. Org. Chem.* **2002**, *67*, 6406. (b) Chakraborti, A. K.; Nayak, M. K.; Sharma, L. *J. Org. Chem.* **1999**, *64*, 8027. (c) Sharma, L.; Nayak, M. K.; Chakraborti, A. K. *Tetrahedron* **1999**, *55*, 9595. (d) Nayak, M. K.; Chakraborti, A. K. *Tetrahedron Lett.* **1997**, *38*, 8749. Hydrogen-bond-assisted catalytic procedure for nucleophilic activation: (e) Chakraborti, A. K.; Sharma, L.; Nayak, M. K. *J. Org. Chem.* **2002**, *67*, 2541. (f) Nayak, M. K.; Chakraborti, A. K. *Chem. Lett.* **1998**, 297.
(18) Guthrie, J. P.; Cossar, J.; Klym, A. *Can. J. Chem.* **1987**, *65*, 2154.