EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201403402

Variations in the Blaise Reaction: Conceptually New Synthesis of 3-Amino Enones and 1,3-Diketones

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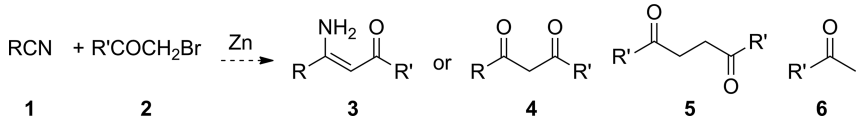
Keywords: Zinc / Cyanides / Halides / Ketones / Condensation reactions

Organic compounds with 3-amino enone or 1,3-diketone functional groups are extremely important, as they can be converted into a plethora of heterocyclic or carbocyclic compounds, or can be used as ligands in metal complexes. We have achieved a new, easy, straightforward and convenient synthesis of 3-amino enones and 1,3-diketones starting from aryl/heteroaryl/alkyl nitriles and 1-aryl/alkyl 2-bromoethanones. The reaction is a variation of the classical Blaise reaction, and it works with zinc and trimethylsilyl chloride as an activator. By running the hydrolysis of the reaction intermediate with HCl (3 N aq.) at 0–30 °C or at 100 °C, it is possible to form either 3-amino enones or 1,3-diketones, respectively. The newly developed method was used for the synthesis of avobenzone, an ingredient of sun-screen lotions. Furthermore, an easy synthesis of (Z)-3-amino-1-[4-(*tert*-butyl)phenyl]-3-(4-methoxyphenyl)prop-2-en-1-one, with UV/Vis absorption characteristics similar to those of avobenzone, was also achieved.

Introduction

The Blaise reaction is a classical reaction for the zinc-mediated transformation of nitriles and ethyl bromoacetate into the corresponding β-keto esters.[1] Zinc-bound β-amino α,β-unsaturated esters are intermediates in the reaction.[2] Even though the Blaise reaction is contemporary with its more famous sibling, the Reformatsky reaction,[3] it did not enter mainstream synthetic planning for a long time, mainly due to the poor yields of the β-keto ester products. In recent years, however, developments in methods for the pre-activation of zinc have led to improvements in the yields of the β-keto esters.[4] The versatility of the Blaise reaction lies in the fact that by simple variation of the processing of the reaction mixture one can easily generate β-keto esters or β-amino α,β-unsaturated esters. Since compounds bearing such functional groups are starting materials for the synthesis of a large variety of carbocylic and heterocyclic compounds, the Blaise reaction could be very useful in organic synthesis. Furthermore, the Blaise reaction has enormous potential in organic synthesis[5] as there are many possibilities for the modification of α-bromoacetates or nitriles. We reasoned that by using 2-bromoethan-1-ones (acylmethyl bromides) **2** as one of the reacting partners instead of the traditional α-bromoacetate, it should be possible convert nitriles **1** directly into 3-amino enones (enamino ketones or β-amino enones) **3** or 1,3-diketones (β-diketones) **4**. In this paper, we describe the realization of this concept for the zinc-mediated synthesis of a variety of 3-amino enones **3** and 1,3-diketones **4** from nitriles **1** and 2-bromoethanones **2** (Scheme 1). To achieve the synthesis of 3-amino enones or 1,3-diketones and avoid the formation of reductive debromination products such as **5** and **6** it was important to optimize the reaction conditions and the processing of the reaction mixture (Scheme 1).

3-Amino enones **3** are versatile synthetic intermediates that are used for the synthesis of a wide variety of heterocyclic compounds.[6] Generally, they are synthesized from 1,3-diketones by reaction with alkylamines or arylamines. However, the generation of 3-amino enones **3** with primary amino groups by this route is difficult. Recently, Yu and coworkers reported a CuI-catalysed and strong base (*t*BuONa) mediated Aldol-type reaction of aryl methyl ketones with aryl nitriles to give 3-amino enones in moderate yield.[7] Although this reaction is a straightforward



Scheme 1. Zinc-mediated transformation of nitriles **1** and 2-bromoethanones **2** into 3-amino enones **3** or 1,3-diketones **4**.

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201403402.

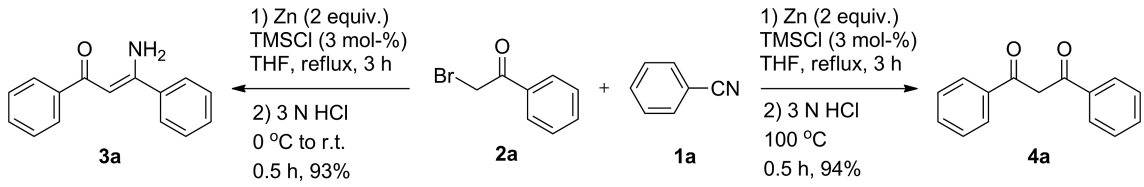
method for the conversion of nitriles into 3-amino enones, it has several limitations, including: (i) the requirement for a strong base; (ii) the need for a ligand to complex with the CuI; (iii) moderate yields, which limits scaling up; (iv) the substrate selectivity is restricted to aryl nitriles and methyl ketones; and (v) strictly anhydrous reaction conditions. Alternatively, 3-amino enones **3** can be prepared by reductive ring cleavage of isoxazoles[8] or through electron transfer from reducing agents like SmI_2.[9]

Similarly to 3-amino enones **3**, 1,3-diketones **4** are extremely useful starting materials for both carbon–carbon and carbon–heteroatom bond-forming reactions to form carbocycles and heterocycles, respectively.[10] The 1,3-diketones themselves are target compounds in synthesis as some of them have found technological applications. For example, avobenzone **7** (vide infra) is the main ingredient in sunscreen lotions.[11] The 1,3-diketone functional group appears in some natural products, and such natural products show antioxidant, antitumor, antimicrobial, antiviral and antifungal activities.[10] The extremely popular Claisen condensation between aryl methyl ketones and esters under basic conditions is a general method for synthesis of 1,3-diketones.[12] However, the method demands strictly anhydrous reaction conditions, the use of excess acylating agent, and the removal of the alcohol by-product. Moreover, *O*-alkylation is possible under Claisen conditions. The soft enolization of ketones with $MgBr_2{\cdot}OEt_2$ and subsequent treatment with acylating agents like acyl chlorides in the presence of Hunig's base (iPr$_2$NEt) is among the recent developments in this area.[13] Overall, there is a need for the development of easy methods for the synthesis of both 3-amino enones and 1,3-diketones from common starting materials (e.g., nitriles). We have accomplished this by modifying the Blaise reaction.

Results and Discussion

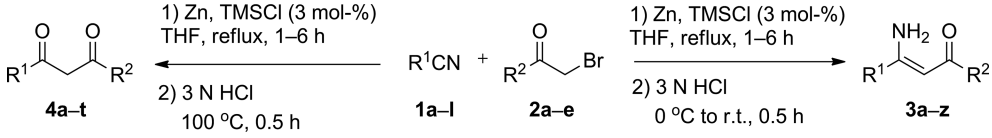
We concentrated our initial efforts on the development of appropriate conditions for engineering the Blaise reaction of nitriles **1** and 2-bromoethanones **2** towards the formation of 3-amino enones or 1,3-diketones, as the reaction could also give 1,4-diketones **5** or methyl ketones **6** as side-products (Scheme 1). The 1,4-diketones (i.e., **5**) and methyl ketones (i.e., **6**) are generated by zinc-mediated reductive removal of the bromine from **2**. We chose the reaction of benzonitrile (**1a**) and 2-bromo-1-phenylethanone (phenacyl bromide or benzoylmethyl bromide; **2a**) to optimize the reaction conditions (Scheme 2). Preactivation of table-top zinc dust was carried out with trimethylsilyl chloride (TMSCl; 3 mol-%).[4c] The reaction was carried out on a 1 mmol scale (both the reactants) in reagent-grade tetrahydrofuran (THF) at reflux for 3 h. This was followed by hydrolysis of the reaction mixture with HCl (3 N aq.) at 0 °C→room temp. to give 3-amino-1,3-diphenylprop-2-en-1-one (**3a**) exclusively in nearly quantitative yield. On the other hand, hydrolysis with HCl (3 N aq.) at 100 °C for 30 min provided 1,3-diketone **4a** exclusively in excellent yield. Thus, a marginal change in the processing of the reaction mixture led to the exclusive formation of either 3-amino enone **3a** or 1,3-diketone **4a**. The concentration of the reactants, namely nitrile **1a** and 2-bromoethanone **2a**, in THF appeared to be critical to steer the reaction towards **3a** or **4a** rather than 1,4-diketones **5** or methyl ketones **6**. After careful experimentation, we found that 1 mmol of each of the reactants in 5 mL of the solvent was optimal. At higher dilution (e.g., 10 mL THF), the reaction was slow, and required more than 6 h for completion, and the yield of the desired products fell by 20%. At higher concentrations (e.g., 3 mL THF), 1,4-diphenylbutane-1,4-dione **5** (R, R′ = Ph, Scheme 1) formed to an extent of 10%. The structures of 3-amino enone[7] **3a** and 1,3-diketone[14] **4a** were assigned on the basis of spectroscopic data and by comparison with authentic samples. In a scale-up run, we subjected 50 mmol of each of nitrile **1a** and 2-bromoethanone **2a** to the Blaise reaction under the optimized conditions to give **3a** in 90% yield (Scheme 2).

Having established the conditions for the straightforward and simple conversion of benzonitrile (**1a**) and phenacyl bromide (**2a**) into 3-amino-1,3-diphenylprop-2-en-1-one (**3a**) or to 1,3-diphenylpropane-1,3-dione (**4a**), we went on to explore the generality of the reaction with various nitriles and 2-bromoethanones. Thus, we evaluated the effect of electron-donating and electron-withdrawing groups on the outcome of the reaction. The results of this study are collected in Table 1. We conducted the condensation of four arylnitriles **1a**–**1d** with four 1-aryl-2-bromoethanones **2a**–**2d** in a combinatorial fashion to form sixteen 3-amino enones **3a**–**3p** and ten 1,3-diketones **4a**–**4j** without much difficulty. The substitution in the aromatic ring of arylnitriles **1** and 1-aryl-2-bromoethanones **2** was systematically varied at the C-4 position from H (**1a** and **2a**) to highly electron-withdrawing CF_3 (**1b** and **2b**), moderately electron-withdrawing but *ortho*,*para*-directing Cl (**1c** and **2c**), and highly electron-donating OMe (**1d** and **2d**). The following points emerged from this study: (i) The placement of a highly electron-withdrawing CF_3 group into the nitrile or the 2-bromoethanone promotes the condensation (Table 1, entries 2, 5–8, 10 and 14). (ii) The condensation is not efficient if a strongly elec-



Scheme 2. Optimization of the reaction conditions for the synthesis of 3-amino enone **3a** and 1,3-diketone **4a**.

Table 1. Synthesis of 3-amino enones and 1,3-diketones.

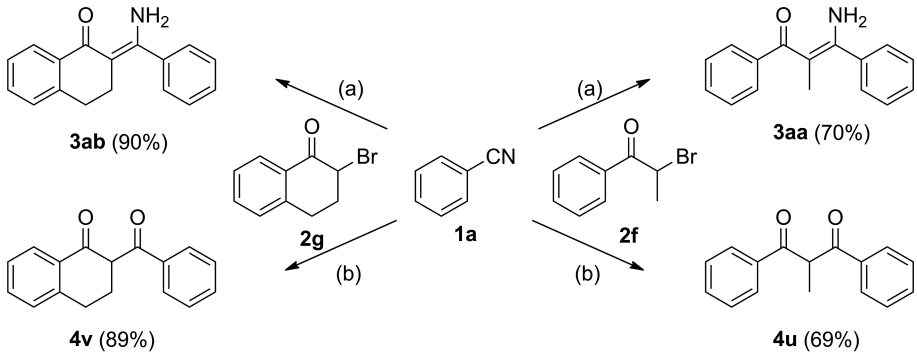


Entry[a]	R^1	R^2	Time [h]	3-amino enone, yield [%]	1,3-Diketone, yield [%]
1	**1a**: C_6H_5	**2a**: C_6H_5	4	**3a**, 93	**4a**, 91
2	**1a**: C_6H_5	**2b**: 4-$CF_3C_6H_4$	3	**3b**, 94	**4b**, 93
3	**1a**: C_6H_5	**2c**: 4-ClC_6H_4	3	**3c**, 87	**4c**, 90
4	**1a**: C_6H_5	**2d**: 4-$OMeC_6H_4$	4	**3d**, 74[b]	**4d**, 70[b]
5	**1b**: 4-$CF_3C_6H_4$	**2a**: C_6H_5	4	**3e**, 97	**4b**, 94
6	**1b**: 4-$CF_3C_6H_4$	**2b**: 4-$CF_3C_6H_4$	3	**3f**, 96	**4e**, 95
7	**1b**: 4-$CF_3C_6H_4$	**2c**: 4-ClC_6H_4	3	**3g**, 89	**4f**, 91
8	**1b**: 4-$CF_3C_6H_4$	**2d**: 4-$OMeC_6H_4$	6	**3h**, 81	**4g**, 80
9	**1c**: 4-ClC_6H_4	**2a**: C_6H_5	4	**3i**, 79	**4c**, 76
10	**1c**: 4-ClC_6H_4	**2b**: 4-$CF_3C_6H_4$	4	**3j**, 82	**4f**, 81
11	**1c**: 4-ClC_6H_4	**2c**: 4-ClC_6H_4	3	**3k**, 87	**4h**, 87
12	**1c**: 4-ClC_6H_4	**2d**: 4-$OMeC_6H_4$	6	**3l**, 77	**4i**, 74
13	**1d**: 4-$OMeC_6H_4$	**2a**: C_6H_5	4	**3m**, 79	**4d**, 78
14	**1d**: 4-$OMeC_6H_4$	**2b**: 4-$CF_3C_6H_4$	4	**3n**, 84	**4g**, 83
15	**1d**: 4-$OMeC_6H_4$	**2c**: 4-ClC_6H_4	4	**3o**, 81	**4i**, 80
16	**1d**: 4-$OMeC_6H_4$	**2d**: 4-$OMeC_6H_4$	5	**3p**, 64[b]	**4j**, 63[b]
17	**1e**: 1-naphthyl	**2a**: C_6H_5	6	**3q**, 77[b]	**4k**, 73[b]
18	**1f**: 2-furyl	**2a**: C_6H_5	1	**3r**, 85	**4l**, 82
19	**1g**: 2-thiophenyl	**2a**: C_6H_5	1	**3s**, 87	**4m**, 84
20	**1h**: *N*-tosyl-3-indolyl	**2a**: C_6H_5	3	**3t**, 80	**4n**, 80
21	**1i**: 3-pyridyl	**2a**: C_6H_5	3	**3u**, 78	**4o**, 80
22	**1j**: benzyl	**2a**: C_6H_5	6	**3v**, 81	**4p**, 83
23	**1k**: *n*-propyl	**2a**: C_6H_5	3	**3w**, 78	**4q**, 75
24	**1a**: C_6H_5	**2e**: *tert*-butyl	4	**3x**, 81	**4r**, 80
25	**1k**: *n*-propyl	**2e**: *tert*-butyl	4	**3y**, 75	**4s**, 76
26	**1l**: 4-*t*BuC_6H_4	**2a**: C_6H_5	6	**3z**, 72	**4t**, 74

[a] See Figures S1 and S2 in the Supporting Information for the structures of the products. [b] 1,4-dioxane used as the solvent; for all other examples, THF was used as the solvent.

tron-donating OMe group is present in one or both the components (Table 1, entries 4, 12 and 13–16). To force such condensations to take place, the higher-boiling solvent dioxane must be used. (iii) When a moderately electron-withdrawing but *ortho*,*para*-directing C-4–Cl group is present, the reaction is efficient if the other reacting partner also has an electron-withdrawing group (Table 1, entries 9–11). The electron-withdrawing C-4-substitution on the aromatic ring promotes the reaction by making the nitrile and the zinc enolates more reactive. The reaction of 1-naphthonitrile (**1e**) with phenacyl bromide (**2a**) (Table 1, entry 17), however, required the higher-boiling solvent dioxane, possibly due to the electron-rich nature of the aromatic ring and steric hindrance by the *peri* hydrogen to the approach of the Blaise reagent. The reactions of 2-bromoethanone **2a** with heteroaromatic nitriles, such as furan-2-carbonitrile (**1f**; Table 1, entry 18), thiophene-2-carbonitrile (**1g**; Table 1, entry 19), 1-tosyl-1*H*-indole-3-carbonitrile (**1h**; Table 1, entry 20), and nicotinonitrile (**1i**; Table 1, entry 21) worked without much difficulty. The reaction of nitriles on aliphatic carbons, e.g., 2-phenylacetonitrile (**1j**; Table 1, entry 22) and butyronitrile (**1k**; Table 1, entry 23), with 2-bromo-1-phenylethan-1-one **2a** worked without any problem. The reaction of alkyl bromomethyl ketones, represented by 1-bromo-3,3-dimethylbutan-2-one (**2e**), with benzonitrile (**1a**; Table 1, entry 24) or with butyronitrile (**1k**; Table 1, entry 25) provided the corresponding 3-amino enones **3x**–**3y** and 1,3-diketones **4r**–**4s** in good yield. However, the Blaise conversion did not take place between benzonitrile and simple alkyl bromomethyl ketones like 1-bromo-2-propanone and 2-bromocyclohexanone. These reactions gave the corresponding 1,4-diketones (i.e., **5**) as the only products. Out of the group of 3-amino enones and 1,3-diketones prepared in this study, the structure of 1,3-diketone **4n** was confirmed by single-crystal X-ray structure determination.[15]

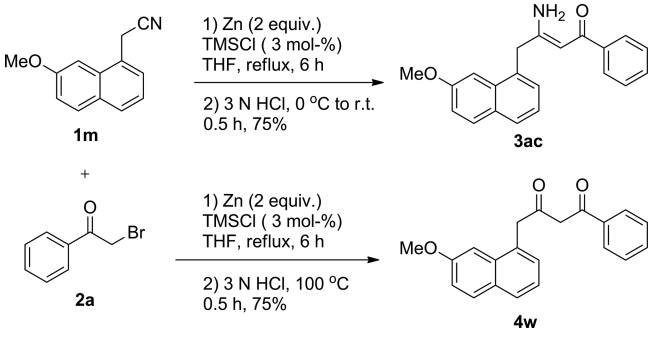
After demonstrating the easy synthesis of 3-amino enones **3a**–**3z** and 1,3-diketones **4a**–**4t** (Table 1), we conducted the reactions of 2-bromo-1-phenylpropan-1-one (2-bromopropiophenone; **2f**) and 2-bromo-3,4-dihydronaphthalen-1(2*H*)-one (2-bromo-α-tetralone; **2g**), independently with benzonitrile (**1a**) to enhance the versatility of our method (Scheme 3). Under Yu's conditions, although **2f** did not react with benzonitrile (**1a**), **2g** did react to give 3-amino enone **3aa**, albeit in moderate yield.[7] However, under our newly developed conditions, both reactions progressed successfully to give 3-amino enones **3aa** and **3ab**, respectively, in very good to excellent yield (Scheme 3). In addition, hydrolysis of the reaction intermediate with HCl (3 N) at 100 °C provided 1,3-diketones **4u** and **4v**, respectively.



Reagents and conditions: (a) i. Zn, TMSCl (3 mol-%), THF reflux, 6 h.; ii. 3 N, HCl, 0 °C to r.t., 0.5 h.
(b) i. Zn, TMSCl (3 mol-%), THF reflux, 6 h.; ii. 3 N, HCl, 100 °C, 0.5 h.

Scheme 3. Synthesis of 3-amino enones **3aa**–**3ab** and 1,3-diketones **4u**–**4v**.

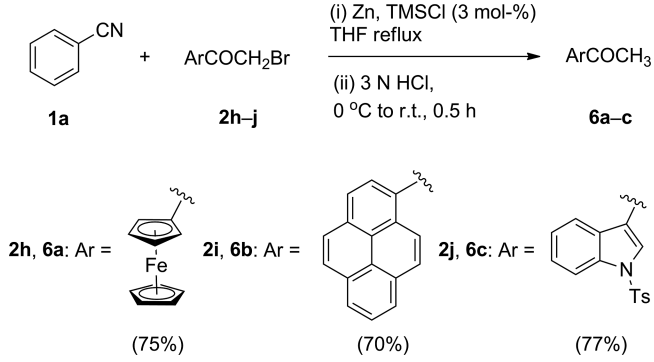
As an extension of this work, we carried out the reaction of phenacyl bromide (**2a**) with nitrile **1m**, which is a precursor for the antidepressant drug agomelatine.[16] This gave 3-amino enone **3ac** or 1,3-diektone **4w** in good yield (Scheme 4). The structure of **3ac** was confirmed on the basis of single-crystal X-ray crystallographic data.[17]



Scheme 4. Synthesis of 3-amino enone **3ac** or 1,3-diektone **4w** from nitrile **1m**, an agomelatine precursor.

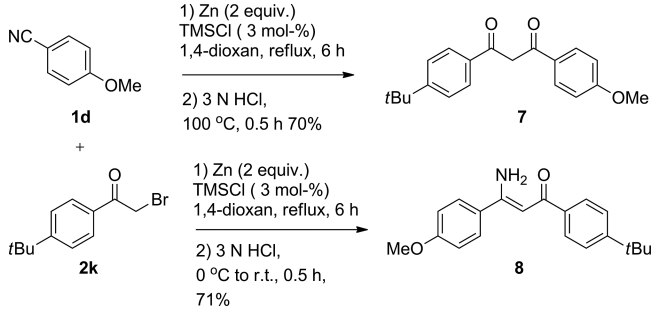
In search of the limits of the Zn-mediated condensation of 2-bromoketones with nitriles, we studied the reactions of 2-bromoketones located on extremely electron-rich aromatic rings such as 2-bromo-1-(ferrocen-1-yl)ethan-1-one (**2h**), 2-bromo-1-(pyren-1-yl)ethan-1-one (**2i**), and 2-bromo-1-(1*H*-indol-3-yl)ethan-1-one (**2j**) with benzonitrile (**1a**). The reactions gave the corresponding methyl ketones (i.e., **6a**–**6c**) exclusively (Scheme 5) as a result of zinc-mediated reductive debromination.[18] In all three of these cases, the products arose from the bromides without the involvement of the nitriles, which indicates that the organozinc intermediates generated in these reactions proceed towards the reductive debromination pathway rather than reacting with benzonitrile.

Next, we designed a new synthesis of avobenzone **7**, which shows strong absorption of UV/Vis light of 320–400 nm wavelength.[19] As a prelude to avobenzone synthesis, we carried out the condensation of 4-*tert*-butylbenzonitrile (**1l**) with phenacyl bromide (**2a**) to give the corresponding 3-amino enone (i.e., **3z**) and 1,3-diketone (i.e., **4t**) in good yields (Table 1, entry 26).



Scheme 5. Zn-mediated reaction of 2-bromoketones located on electron-rich aromatic rings.

From the different possible combinatorial options, avobenzone synthesis worked best when 4-methoxybenzonitrile (**1d**) was treated with 4-*tert*-butylphenacyl bromide (**2k**) (Scheme 6). This reaction gave the enamine analogue of avobenzone **8** under slightly changed conditions (Scheme 6). The UV spectrum of 3-amino enone **8** showed an absorption maximum λ_{max} at 356 nm ($\log\varepsilon$ = 4.14) with absorption range from 300 nm to 400 nm, similar to that



Scheme 6. Synthesis of avobenzone **7** and 3-amino enone **8**, an avobenzone analogue.

of avobenzone (λ_{max} = 357 nm; log ε = 4.41; range = 320–400 nm).[19] Thus, it should be possible to replace avobenzone in sun-screen lotions with 3-amino enone **8** or its derivatives.

Conclusions

In summary, we have demonstrated a conceptually new synthesis of extremely useful 3-amino enones and 1,3-diketones from readily available nitriles and acylmethyl bromides mediated by activated zinc. The condensation is a useful variation of the Blaise reaction. As an application of the new method, we demonstrated a new synthesis of avobenzone and its 3-amino enone analogue, which shows similar absorption characteristics.

Experimental Section

General Remarks: All reactions were carried out under a nitrogen atmosphere. Solvents were dried before use according to standard procedures. All reactions and chromatographic separations were monitored by thin-layer chromatography (TLC). Glass plates coated with silica gel G was used for TLC. Column chromatography was carried on silica gel (100–200 mesh AVRA Synthesis) using increasing percentages of ethyl acetate in hexanes. Centrifugation was done with a REMI centrifuge at 700 rpm. Melting points were determined using open-ended capillary tubes with a VEEGO VMP-DS instrument. UV/Vis spectra were recorded as dilute solutions in MeOH with a Shimadzu UV 2450 double-beam spectrometer. IR spectra were recorded as KBr pellets with a Nicolet-6700 spectrometer. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and DEPT-135 spectra were recorded as solutions in $CDCl_3$ or $CDCl_3$ + CCl_4 (1:1) with a Bruker Avance 400 spectrometer. Tetramethylsilane was used as internal standard. ^{1}H NMR spectroscopic data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q, = quartet, m = multiplet, dd = doublet of doublets, and br. s = broad singlet), coupling constant (*J*), and integration]. *J* values are given in Hz. ^{13}C NMR spectra were recorded with broadband ^{1}H decoupling. DEPT-135 NMR spectra were recorded for each sample to support the assigned structure. High-resolution mass spectra were recorded with a Waters Q-TOF micro mass spectrometer using the electrospray ionization mode. X-ray diffraction measurements were carried out at 298 K with an Oxford CrysAlis CCD area detector system equipped with a graphite monochromator and a Mo-K_α fine-focus sealed tube (λ = 0.71073 Å). Nitriles were purchased from Sigma–Aldrich, Zn powder from Spectrum Chemicals, and phenacyl bromide and TMSCl from AVRA Synthesis. Phenacyl bromides (**2b**–**2k**) were prepared from the corresponding aryl/alkylmethyl ketones.[20] Some of the 3-amino enones and 1,3-diketones are known compounds, as indicated by an appropriate reference in the Supporting Information. Since characterization data have not been completely reported for all of them, full spectroscopic data of the known compounds are given in the Supporting Information. Experimental details and spectroscopic data for the unknown compounds are given below. In the cases of reactions providing **3p** [yield 576 mg (64%); 75 mg of **1d** recovered], **3q** [yield 531 mg (77%); 112 mg of **1e** recovered], **4j** [yield 572 mg (63%); 74 mg of **1d** recovered], and **4k** [yield 509 mg (73%); 109 mg of **1e** recovered], yields were calculated by taking into account the amount of recovered starting nitriles.

General Procedure for the Synthesis of 3-Amino Enones (Method A): A solution of TMSCl (3 mol-%) in THF (1 mL) was added to a suspension of Zn (2 equiv.) in THF (12 mL). The resulting suspension was heated to reflux with vigorous stirring for 25 min. A solution of the nitrile (4 mmol) in THF (2 mL) and a solution of the α-bromoketone (1 equiv.) in THF (2 mL) were added simultaneously to the resulting suspension dropwise using two syringes over a period of 30 min. After the addition was complete, the reaction mixture, which was pale green in colour, was heated at reflux until all the nitrile had been consumed and the colour had changed to brown (TLC; 1–6 h). Then the reaction mixture was cooled to room temperature, it was centrifuged at 700 rpm, and the upper solution was decanted. The residual solid was washed with THF (2 × 2 mL). The combined washings were cooled and treated with HCl (3 N) until the pH of the solution reached 2 (about 0.1 mL). The resulting solution was stirred for 30 min at room temp., then the THF was removed using a rotator evaporator at room temp. and reduced pressure. CH_2Cl_2 (20 mL) and water (20 mL) were added to the residue. The organic layer was separated, and washed with water (2 × 20 mL) and brine (10 mL). The CH_2Cl_2 solution was dried with anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography using silica gel (100–200 mesh) and 15% ethyl acetate in hexane as eluent.

(*Z*)-3-Amino-1,3-diphenylprop-2-en-1-one (3a): Following the general procedure (Method A), the reaction of Zn (633 mg, 9.7 mmol), benzonitrile (**1a**; 501 mg, 4.85 mmol), 2-bromo-1-phenylethanone (**2a**; 1.93 g, 4.85 mmol), trimethylsilyl chloride (15 mg, 3 mol-%), THF (15 mL), 4 h, and HCl (3 N, 0.5 mL) gave compound **3a** (93%) as a pale yellow liquid. IR: $\tilde{\nu}$ = 3072, 2985, 2932, 1610, 1512, 1438, 1231, 1082, 841, 762 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 10.41 (br. s, 1 H), 7.92 (dd, *J* = 8.1, 1.6 Hz, 2 H), 7.61 (dd, *J* = 8.1, 1.5 Hz, 2 H), 7.51–7.34 (m, 6 H), 6.11 (s, 1 H), 5.86 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 189.8, 163.0, 140.4, 137.5, 130.9, 130.6, 128.9, 128.2, 127.2, 126.4, 91.7 ppm.

(*Z*)-3-Amino-3-phenyl-1-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (3b): Following the general procedure (Method A), the reaction of Zn (631 mg, 9.7 mmol), benzonitrile (**1a**; 502 mg, 4.85 mmol), 2-bromo-1-[4-(trifluoromethyl)phenyl]ethanone (**2b**; 1.29 g, 4.85 mmol), trimethylsilyl chloride (15 mg, 3 mol-%), THF (15 mL), 4 h, and HCl (3 N, 0.5 mL) gave compound **3b** (94%) as a pale yellow liquid. IR: $\tilde{\nu}$ = 1597, 1527, 1508, 1327, 1166, 1122, 1072, 860, 773, 744 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 10.50 (br. s, 1 H), 8.02 (d, *J* = 8.0 Hz, 2 H), 7.68 (d, *J* = 8.1 Hz, 2 H), 7.63 (dd, *J* = 8.0, 1.6 Hz, 2 H), 7.55–7.43 (m, 3 H), 6.10 (s, 1 H), 5.56 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 188.4, 163.8, 143.5, 137.5, 132.8 (q, *J* = 32.5 Hz), 131.1, 129.3, 127.7, 126.5, 125.5 (q, *J* = 3.7 Hz), 124.5 (d, *J* = 210.4 Hz), 91.9 ppm. HRMS (ESI): calcd. for $C_{16}H_{12}F_3NOH$ [M + H] 292.0949; found 292.0943.

(*Z*)-3-Amino-1,3-bis[4-(trifluoromethyl)phenyl]prop-2-en-1-one (3f): Following the general procedure (Method A), the reaction of Zn (381 mg, 5.84 mmol), 4-(trifluoromethyl)benzonitrile (**1b**; 503 mg, 2.92 mmol), 2-bromo-1-[4-(trifluoromethyl)phenyl]ethanone (**2b**; 781 mg, 2.92 mmol), trimethylsilyl chloride (10 mg, 3 mol-%), THF (15 mL), 4 h, and HCl (3 N, 0.5 mL) gave compound **3f** (96%) as a colourless solid, m.p. 137–139 °C. IR: $\tilde{\nu}$ = 3338, 3157, 1624, 1560, 1537, 1502, 1321, 1296, 1166, 1116, 1066 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 10.42 (br. s, 1 H), 8.00 (d, *J* = 8.1 Hz, 2 H), 7.74 (s, 4 H), 7.69 (d, *J* = 8.2 Hz, 2 H), 6.08 (s, 1 H), 5.60 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + CCl_4, 1:1):

δ = 188.9, 162.0, 143.1, 141.0, 133.1 (q, J = 33.1 Hz), 127.7, 127.1, 126.4, 126.3–126.3 (m), 125.6–125.3 (m), 125.2 (d, J = 27.7 Hz), 122.5 (d, J = 27.9 Hz), 92.6 ppm. HRMS (ESI): calcd. for $C_{17}H_{11}F_6NOH$ [M + H] 360.0823; found 360.0821.

(*Z*)-3-Amino-1-(4-chlorophenyl)-3-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (3g): Following the general procedure (Method A), the reaction of Zn (382 mg, 5.84 mmol), 4-(trifluoromethyl)benzonitrile (**1b**; 503 mg, 2.92 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (**2c**; 684 mg, 2.92 mmol), trimethylsilyl chloride (10 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 0.5 mL) gave compound **3g** (89%) as a pale yellow oil. IR: $\tilde{\nu}$ = 3308, 3158, 1614, 1601, 1534, 1324, 1014, 783 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.31 (br. s, 1 H), 7.86–7.77 (m, 2 H), 7.71 (d, J = 3.5 Hz, 4 H), 7.44–7.30 (m, 2 H), 6.02 (s, 1 H), 5.67 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.9, 161.6, 141.1, 138.3, 137.7, 132.8 (q, J = 32.8 Hz), 128.8, 128.7, 127.7, 126.2 (q, J = 3.7 Hz), 123.8 (d, J = 272.5 Hz), 92.2 ppm. HRMS (ESI): calcd. for $C_{16}H_{11}ClF_3NONa$ [M + Na] 348.0379; found 348.0380.

(*Z*)-3-Amino-1-(4-methoxyphenyl)-3-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (3h): Following the general procedure (Method A), the reaction of Zn (379 mg, 5.84 mmol), 4-(trifluoromethyl)benzonitrile (**1b**; 502 mg, 2.92 mmol), 2-bromo-1-(4-methoxyphenyl)ethanone (**2d**; 651 mg, 2.92 mmol), trimethylsilyl chloride (10 mg, 3 mol-%), THF (15 mL), 6 h, and HCl (3 N, 0.5 mL) gave compound **3h** (81%) as a pale yellow oil. IR: $\tilde{\nu}$ = 3308, 3155, 1597, 1556, 1498, 1323, 1303, 1259, 1168, 1138, 848, 785 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 10.24 (br. s, 1 H), 7.88 (d, J = 8.9 Hz, 2 H), 7.70 (d, J = 5.6 Hz, 4 H), 6.90 (d, J = 8.9 Hz, 2 H), 6.05 (s, 1 H), 5.43 (br. s, 1 H), 3.85 (s, 3 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 189.4, 162.4, 160.5, 141.6, 133.6 (q, J = 32.7 Hz), 129.4, 127.0, 126.1, 125.7 (q, J = 3.7 Hz), 123.9 (d, J = 272.5 Hz), 122.5, 113.7, 92.3, 55.4 ppm. HRMS (ESI): calcd. for $C_{17}H_{14}F_3NO_2Na$ [M + Na] 344.0874; found 344.0875.

(*Z*)-3-Amino-3-(4-chlorophenyl)-1-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (3j): Following the general procedure (Method A), the reaction of Zn (474 mg, 7.29 mmol), 4-chlorobenzonitrile (**1c**; 502 mg, 3.62 mmol), 2-bromo-1-[4-(trifluoromethyl)phenyl]ethanone (**2b**; 974 mg, 3.62 mmol), trimethylsilyl chloride (11 mg, 3 mol-%), THF (15 mL), 4 h, and HCl (3 N, 0.5 mL) gave compound **3j** (82%) as a colourless solid, m.p. 145–147 °C. IR: $\tilde{\nu}$ = 3302, 3155, 1618, 1600, 1537, 1323, 1014, 783 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.45 (br. s, 1 H), 8.01 (d, J = 8.1 Hz, 2 H), 7.69 (d, J = 8.2 Hz, 2 H), 7.63–7.52 (m, 2 H), 7.53–7.39 (m, 2 H), 6.07 (s, 1 H), 5.59 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.6, 162.4, 143.1, 137.1, 135.5, 132.5 (q, J = 32.4 Hz), 129.4, 127.9, 127.7, 127.5, 125.3 (q, J = 7.6 Hz), 123.9 (d, J = 272.4 Hz), 91.8 ppm. HRMS (ESI): calcd. for $C_{16}H_{11}ClF_3NONa$ [M + Na] 348.0379; found 348.0378.

(*Z*)-3-Amino-1,3-bis(4-chlorophenyl)prop-2-en-1-one (3k): Following the general procedure (Method A), the reaction of Zn (472 mg, 7.29 mmol), 4-chlorobenzonitrile (**1c**; 503 mg, 3.64 mmol), 4-chlorophenacyl bromide (**2c**; 847 mg, 3.64 mmol), trimethylsilyl chloride (12 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 0.5 mL) gave compound **3k** (87%) as a colourless solid, m.p. 96 °C. IR: $\tilde{\nu}$ = 3479, 3358, 3170, 1595, 1556, 1530, 1479, 1325, 1092, 1012, 841, 777 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.36 (br. s, 1 H), 7.86 (d, J = 8.7 Hz, 2 H), 7.55 (d, J = 8.7 Hz, 2 H), 7.41 (dd, J = 17.5, 8.7 Hz, 4 H), 6.03 (s, 1 H), 5.52 (br. s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.7, 161.9, 138.4, 137.3, 136.9, 135.8, 129.3, 128.6, 128.5, 127.7, 91.6 ppm. HRMS (ESI): calcd. for $C_{15}H_{11}Cl_2NONa$ [M + Na] 314.0114; found 314.0115.

(*Z*)-3-Amino-3-(4-methoxyphenyl)-1-[4-(trifluoromethyl)phenyl]prop-2-en-1-one (3n): Following the general procedure (Method A), the reaction of Zn (488 mg, 7.52 mmol), 4-methoxybenzonitrile (**1d**; 501 mg, 3.76 mmol), 2-bromo-1-[4-(trifluoromethyl)phenyl]ethanone (**2b**; 1.004 g, 3.76 mmol), trimethylsilyl chloride (12 mg, 3 mol-%), THF (15 mL), 4 h, and HCl (3 N, 0.5 mL) gave compound **3n** (84%) as a pale yellow solid, m.p. 115–117 °C. IR: $\tilde{\nu}$ = 3362, 3155, 1618, 1600, 1537, 1323, 1014, 783 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 10.55 (br. s, 1 H), 8.01 (d, J = 8.0 Hz, 2 H), 7.68 (d, J = 8.1 Hz, 2 H), 7.58 (d, J = 8.9 Hz, 2 H), 6.97 (d, J = 8.9 Hz, 2 H), 6.07 (s, 1 H), 3.88 (br. s, 3 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 188.1, 163.6, 162.1, 143.8, 135.4, 132.3 (q, J = 34.8 Hz), 129.5, 127.9, 127.6 (q, J = 7.7 Hz), 124.0 (d, J = 240.3 Hz), 114.6, 91.3, 55.5 ppm. HRMS (ESI): calcd. for $C_{17}H_{14}F_3NO_2Na$ [M + Na] 344.0874; found 344.0875.

(*Z*)-3-Amino-1-phenyl-3-(1-tosyl-1*H*-indol-3-yl)prop-2-en-1-one (3t): Following the general procedure (Method A), the reaction of Zn (219 mg, 3.36 mmol), 1-tosyl-1*H*-indole-3-carbonitrile (**1h**; 503 mg, 1.68 mmol), 2-bromo-1-phenylethanone (**2a**; 336 mg, 1.68 mmol), trimethylsilyl chloride (6 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 0.5 mL) gave compound **3t** (80%) as a pale yellow solid, m.p. 160 °C. IR: $\tilde{\nu}$ = 3443, 3379, 3059, 2926, 1732, 1601, 1571, 1516, 1446, 1373, 1173, 959, 744, 683, 664 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.34 (br. s, 1 H), 8.23–7.69 (m, 7 H), 7.53–7.05 (m, 7 H), 6.21 (s, 1 H), 5.59 (br. s, 1 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.3, 155.8, 145.7, 140.2, 135.3, 134.7, 131.2, 130.2, 128.4, 127.5, 127.2, 127.1, 125.7, 125.6, 124.2, 120.7, 120.2, 114.0, 92.7, 21.7 ppm. HRMS (ESI): calcd. for $C_{24}H_{20}N_2O_3SNa$ [M + Na] 439.1092; found 439.1094.

(*Z*)-3-Amino-1-phenyl-3-(pyridin-3-yl)prop-2-en-1-one (3u): Following the general procedure (Method A), the reaction of Zn (624 mg, 9.6 mmol), pyridine-3-carbonitrile (**1i**; 504 mg, 4.80 mmol), 2-bromo-1-phenylethanone (**2a**; 956 mg, 4.80 mmol), trimethylsilyl chloride (15 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 0.5 mL) gave compound **3u** (78%) as a colourless solid, m.p. 76 °C. IR: $\tilde{\nu}$ = 3351, 3154, 3058, 1604, 1562, 1529, 1474, 1328, 1230, 1021, 749, 693 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.28 (br. s, 1 H), 8.86 (d, J = 1.8 Hz, 1 H), 8.66 (dd, J = 4.9, 1.6 Hz, 1 H), 7.95–7.86 (m, 3 H), 7.50–7.35 (m, 4 H), 6.07 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 190.4, 159.8, 151.3, 147.5, 139.9, 134.3, 133.5, 131.4, 128.4, 127.2, 123.8, 92.5 ppm. HRMS (ESI): calcd. for $C_{14}H_{12}N_2ONa$ [M + Na] 247.0847; found 247.0841.

(*Z*)-3-Amino-1,4-diphenylbut-2-en-1-one (3v): Following the general procedure (Method A), the reaction of Zn (556 mg, 8.54 mmol), 2-phenylacetonitrile (**1j**; 505 mg, 4.27 mmol), 2-bromo-1-phenylethanone (**2a**; 850 mg, 4.27 mmol), trimethylsilyl chloride (13 mg, 3 mol-%), THF (15 mL), 6 h, and HCl (3 N, 0.5 mL) gave compound **3v** (67%) as a colourless solid, m.p. 81 °C. IR: $\tilde{\nu}$ = 3165, 3060, 2926, 1601, 1566, 1485, 1328, 1226, 742, 695 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.19 (br. s, 1 H), 7.85 (dd, J = 8.0, 1.5 Hz, 2 H), 7.44–7.34 (m, 3 H), 7.33–7.28 (m, 2 H), 7.27–7.21 (m, 3 H), 5.80 (s, 1 H), 5.33 (br. s, 1 H), 3.56 (s, 2 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.7, 164.9, 140.2, 135.7, 130.9, 129.2, 128.9, 128.2, 127.4, 127.1, 92.5, 42.5 ppm. HRMS (ESI): calcd. for $C_{16}H_{15}NONa$ [M + Na] 260.1051; found 260.1054.

(*Z*)-5-Amino-2,2-dimethyloct-4-en-3-one (3y): Following the general procedure (Method A), the reaction of Zn (942 mg, 14.28 mmol), butyronitrile (**1k**; 502 mg, 7.24 mmol), 1-bromo-3,3-dimethylbutan-2-one (**2e**; 1278 mg, 7.24 mmol), trimethylsilyl chloride (24 mg, 3 mol-%), THF (15 mL), 4 h, and HCl (3 N, 0.5 mL) gave compound **3y** (75%) as a colourless oil. IR: $\tilde{\nu}$ = 2962, 2866, 1618, 1525, 1351, 1148 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ =

9.77 (br. s, 1 H), 5.18 (br. s, 1 H), 5.12 (s, 1 H), 2.07 (d, J = 8 Hz, 2 H), 1.62–1.50 (m, 2 H), 1.08 (s, 9 H), 0.92 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 205.2, 165.4, 90.2, 41.8, 38.9, 27.9, 21.5, 13.8 ppm. HRMS (ESI): calcd. for $C_{10}H_{19}NOH$ [M + H] 170.1535; found 170.1539.

(*Z*)-3-Amino-4-(7-methoxynaphthalen-1-yl)-1-phenylbut-2-en-1-one (3ac): Following the general procedure (Method A), the reaction of Zn (329 mg, 5.06 mmol), 7-methoxy-1-naphthylacetonitrile (**1m**; 504 mg, 2.53 mmol), 2-bromo-1-phenylethanone (**2a**; 505 mg, 2.53 mmol), trimethylsilyl chloride (8 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 0.5 mL) gave compound **3ac** (75%) as a pale yellow solid, m.p. 98–99 °C. IR: $\tilde{\nu}$ = 3450, 3057, 2928, 2834, 1601, 1517, 1469, 1259, 1273, 1029, 831, 731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.27 (br. s, 1 H), 7.89 (d, J = 6.7 Hz, 2 H), 7.77 (dd, J = 8.4, 5.3 Hz, 2 H), 7.49–7.37 (m, 4 H), 7.35–7.29 (m, 1 H), 7.28–7.23 (m, 1 H), 7.17 (dd, J = 9.0, 2.4 Hz, 1 H), 6.03 (s, 1 H), 5.16 (br. s, 1 H), 4.05 (s, 2 H), 3.83 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.6, 164.8, 158.3, 140.2, 133.4, 131.0, 130.4, 129.9, 129.4, 129.1, 128.4, 128.4, 127.2, 123.2, 118.7, 102.4, 92.1, 55.3, 40.7 ppm. HRMS (ESI): calcd. for $C_{21}H_{19}NO_2Na$ [M + Na] 340.1313; found 340.1313.

(*Z*)-3-Amino-1-[4-(*tert*-butyl)phenyl]-3-(4-methoxyphenyl)prop-2-en-1-one (8): Following the general procedure (Method A), the reaction of Zn (489 mg, 7.5 mmol), 4-methoxybenzonitrile (**1d**; 502 mg, 3.75 mmol), 2-bromo-1-[4-(*tert*-butyl)phenyl]ethan-1-one (**2k**; 962 mg, 3.75 mmol), trimethylsilyl chloride (12 mg, 3 mol-%), 1,4-dioxane (15 mL), 6 h, and HCl (3 N, 0.5 mL) gave compound **8** (71%) as a pale yellow oil. IR: $\tilde{\nu}$ = 3393, 2961, 1606, 1554, 1494, 1256, 1182, 1030, 840, 785 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.44 (s, 1 H), 7.88 (d, J = 8.4 Hz, 2 H), 7.59 (d, J = 8.8 Hz, 2 H), 7.45 (d, J = 8.4 Hz, 2 H), 7.26 (s, 1 H), 6.97 (d, J = 8.8 Hz, 2 H), 6.12 (s, 1 H), 3.86 (s, 3 H), 1.35 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.9, 162.4, 161.7, 154.4, 137.9, 129.9, 127.9, 127.1, 125.5, 125.3, 114.4, 9.4, 55.5, 35.0, 31.3 ppm. HRMS (ESI): calcd. for $C_{20}H_{23}NO_2Na$ [M + Na] 332.1626; found 332.1631.

General Procedure for Synthesis of 1,3-Diketones (Method B)

The general procedure described previously was followed for synthesis of the 1,3-diketones. But the zinc complex obtained from the reaction was treated with HCl (3 N) until the pH was 1 (1 mL), followed by heating to 100 °C for 30 min.

1-(4-Chlorophenyl)-3-[4-(trifluoromethyl)phenyl]propane-1,3-dione (4f): Following the general procedure (Method B), the reaction of Zn (381 mg, 5.84 mmol), 4-(trifluoromethyl)benzonitrile (**1b**; 502 mg, 2.92 mmol), 2-bromo-1-(4-chlorophenyl)ethanone (**2c**; 685 mg, 2.92 mmol), trimethylsilyl chloride (10 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 1 mL) gave compound **4f** (81%) as a colourless solid, m.p. 137–139 °C. IR: $\tilde{\nu}$ = 1593, 1487, 1323, 1182, 1145, 1072, 1012, 862, 790 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 16.70 (s, 1 H), 8.05 (d, J = 8.2 Hz, 2 H), 7.92 (d, J = 8.6 Hz, 2 H), 7.73 (d, J = 8.3 Hz, 2 H), 7.46 (d, J = 8.6 Hz, 2 H), 6.79 (s, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 185.8, 183.4, 139.4, 138.6, 134.13 (q, J = 32.8 Hz), 133.8, 129.2, 128.8, 127.6, 125.8 (q, J = 3.7 Hz), 123.8 (d, J = 272.6 Hz), 93.4 ppm. HRMS (ESI): calcd. for $C_{16}H_{10}ClF_3O_2H$ [M + H] 327.0386; found, 327.0383.

Alternatively, **4f** was synthesized by the reaction of 4-chlorobenzonitrile (**1c**) with 2-bromo-1-[4-(trifluoromethyl)phenyl]ethanone (**2b**) by following Method B. The reaction of Zn (474 mg, 7.29 mmol), 4-chlorobenzonitrile (**1c**; 502 mg, 3.62 mmol), 2-bromo-1-[4-(trifluoromethyl)phenyl]ethanone (**2b**; 974 mg, 3.62 mmol), trimethylsilyl chloride (11 mg, 3 mol-%), THF (15 mL), 4 h, and HCl (3 N, 1 mL) gave compound **4f** (81%) as a colourless solid.

1-Phenyl-3-(1-tosyl-1*H*-indol-3-yl)propane-1,3-dione (4n): Following the general procedure (Method B), the reaction of Zn (220 mg, 3.36 mmol), 1-tosyl-1*H*-indole-3-carbonitrile (**1h**; 502 mg, 1.68 mmol), 2-bromo-1-phenylethanone (**2a**; 330 mg, 1.68 mmol), trimethylsilyl chloride (6 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 1 mL) gave compound **4n** (80%) as a pale yellow solid, m.p. 178 °C. IR: $\tilde{\nu}$ = 3128, 2924, 1597, 1567, 1537, 1493, 1446, 1376, 1172, 1141, 1110, 1088, 1034, 1021, 1000, 961, 774, 749, 663, 576 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 16.87 (s, 1 H), 8.34–8.23 (m, 2 H), 7.98–7.95 (m, 3 H), 7.83 (d, J = 8.4 Hz, 2 H), 7.55–7.45 (m, 3 H), 7.38–7.34 (m, 2 H), 7.26–7.21 (m, 2 H), 6.72 (s, 1 H), 2.32 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 184.9, 181.5, 146.0, 135.2, 134.8, 134.5, 132.3, 130.3, 129.7, 128.8, 127.6, 127.2, 126.9, 125.7, 124.7, 122.8, 120.0, 113.4, 94.4, 21.7 ppm. HRMS (ESI): calcd. for $C_{24}H_{19}NO_4SNa$ [M + Na] 440.0932; found, 440.0934.

4-(7-Methoxynaphthalen-1-yl)-1-phenylbutane-1,3-dione (4w): Following the general procedure (Method B), the reaction of Zn (329 mg, 5.06 mmol), 7-methoxy-1-naphthylacetonitrile (**1m**; 502 mg, 2.53 mmol), 2-bromo-1-phenylethanone (**2a**; 505 mg, 2.53 mmol), trimethylsilyl chloride (8 mg, 3 mol-%), THF (15 mL), 3 h, and HCl (3 N, 1 mL) gave compound **4w** (75%) as a yellow oil. IR: $\tilde{\nu}$ = 3057, 3005, 2935, 2834, 1626, 1601, 1555, 1512, 1469, 1264, 1033, 831, 764, 695 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 16.14 (s, 1 H), 7.78–7.68 (m, 4 H), 7.45–7.40 (m, 2 H), 7.36–7.30 (m, 3 H), 7.15 (dd, J = 8.9, 2.5 Hz, 1 H), 6.07 (s, 1 H), 4.12 (s, 2 H), 3.89 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 196.5, 182.3, 158.2, 134.4, 133.5, 132.4, 130.3, 130.3, 129.4, 128.8, 128.7, 128.6, 128.5, 127.9, 127.0, 123.4, 118.5, 102.7, 96.1, 55.4, 44.7 ppm. HRMS (ESI): calcd. for $C_{21}H_{18}O_3Na$ [M + Na] 341.1154; found, 341.1158.

1-[4-(*tert*-Butyl)phenyl]-3-(4-methoxyphenyl)propane-1,3-dione (7): Following the general procedure (Method B), the reaction of Zn (490 mg, 7.5 mmol), 4-methoxybenzonitrile (**1d**; 506 mg, 3.75 mmol), 2-bromo-1-[4-(*tert*-butyl)phenyl]ethan-1-one (**2k**; 962 mg, 3.75 mmol), trimethylsilyl chloride (12 mg, 3 mol-%), 1,4-dioxane (15 mL), 6 h, and HCl (3 N, 1 mL) gave compound **7** (70%) as a white solid, m.p. 82 °C. IR: $\tilde{\nu}$ = 2963, 2869, 1603, 1507, 1365, 1306, 1261, 1231, 1175, 1111, 1029, 846, 792 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 17.03 (s, 1 H), 8.00–7.86 (m, 4 H), 7.53–7.44 (m, 2 H), 7.00–6.93 (m, 2 H), 6.76 (s, 1 H), 3.89 (s, 3 H), 1.37 (s, 9 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$ + CCl_4, 1:1): δ = 185.9, 184.3, 163.2, 155.9, 133.0, 129.4, 128.5, 127.1, 125.7, 114.1, 92.1, 55.5, 35.2, 31.4 ppm.

Acknowledgments

H. S. P. thanks the University Grants Commission (UGC), New Delhi for UGC-SAP and UGC-MRP grants and a junior research fellowship to N. M., the Department of Science and Technology (DST), Fund for Improvement of Science and Technology Infrastructure in Higher Educational Institutions (FIST), the Council of Scientific and Industrial Research (CSIR), Open Source Drug Discovery (OSDD) programme and the Department of Biotechnology, Interdisciplinary Program in Life Sciences (DBT-IPLS) for financial support. The authors thank the Central Instrumentation Facility (CIF), Pondicherry University (PU) for spectroscopic facilities, and the Department of Organic Chemistry, Indian Institute of Science (IISc), Bangalore for HRMS data.

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Received: October 29, 2014
Published Online:
Published Online: ■

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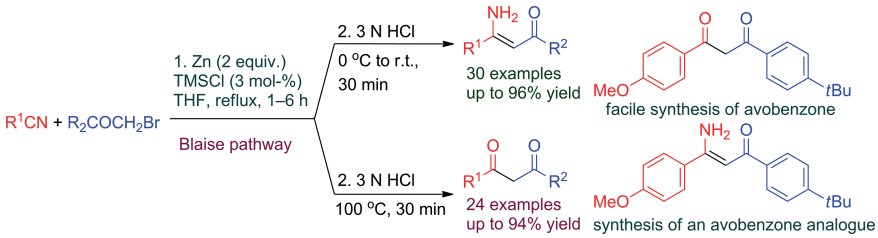

A variety of aryl/heteroaryl/alkyl nitriles were converted into 3-amino enones or 1,3-diketones by reaction with 2-bromoethanones in the presence of zinc under Blaise reaction conditions. The commercially important product avobenzone was synthesized.

Keywords: Zinc / Cyanides / Halides / Ketones / Condensation reactions

