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Unexpected cyclization of *ortho*-nitrochalcones into 2-alkylideneindolin-3-ones†

Nicolai A. Aksenov, *[a] Dmitrii A. Aksenov, [a] Nikolai A. Arutiunov,[a] Daria S. Aksenova,[a] Alexander V. Aksenov [a] and Michael Rubin *[ab]

An original, facile, and highly efficient method for the preparation of 2-(3-oxoindolin-2-ylidene) acetonitriles from *ortho*-nitrochalcones is described. The featured transformation is a triggered Michael addition of the cyanide anion to the chalcone followed by a cascade cyclization mechanistically related to the Baeyer–Drewson reaction.

Introduction

It would be hard to overstate the importance of 2-alkylideneindolin-3-one derivatives in modern medicinal chemistry. The bis-indole indirubin, a main component of "Tyrian purple" dye, is also a known active component of a traditional Chinese herbal medicine, while its numerous synthetic derivatives show potent and highly selective pharmacological inhibition of glycogen synthase kinases and cyclin-dependent kinases.[1–6] These molecules induce apoptosis of human cancer cells and have promising potential for applications in the treatment of several neurodegenerative conditions, such as Alzheimer's disease.[1–6] Indirubin, as well as other related dyes, can be easily prepared *via* base-assisted condensation of *ortho*-nitrobenzaldehydes with acetone according to the classical Baeyer–Drewson reaction.[7–9] 2-Alkylideneindolin-3-one derivatives possessing a single indoline subunit (or two remotely positioned subunits) also occur in nature and also exhibit a wide spectrum of important biological properties (Fig. 1).[10–17] Normally, preparation of such compounds relies heavily on the chemistry of isatins, which makes synthetic approaches to certain substitution patterns hardly accessible. An alternative synthetic platform for assembling indoline alkaloids and related non-natural, biologically active target molecules has also emerged, relying on the chemistry of 2-alkylidene-3-oxindoles.[18–23] Various synthetic approaches to these synthons have been developed based on the aldol condensation of 3*H*-indol-3-ones with carbonyl compounds (path A, Scheme 1),[24–28] transition metal-catalyzed carbonylative coupling of *ortho*-iodoanilines to acetylenes (path B, Scheme 1),[29–32] and cascade reactions of anilines with α-ketoesters involving an electrophilic aromatic substitution step (path C, Scheme 1)[10,33] Herein we wish to report on our recent serendipitous discovery of the unexpected one-pot cascade transformation of *ortho*-nitrochalcones **1** *via* a Baeyer–Drewson-like pathway, but affording 2-alkylideneindolin-3-ones **2** rather than indigo-like dimers (Scheme 1).

Results and discussion

In the frame of our ongoing project dealing with the synthesis of nitrogen-based heterocyclic compounds and evaluation of their biological activity, we were interested in the preparation of a series of minaprine analogs **4**,[34–37] possessing an additional amino-group handle at C-2′.[38,39] To tackle this task, we decided to employ a routine cyclocondensation of hydrazine with 3-cyanoketone **3** bearing an *ortho*-nitro group, which was supposed to be routinely reduced and properly modified in subsequent steps (Scheme 2). We planned to access precursor **3** *via* conjugate addition of hydrogen cyanide to α,β-unsaturated

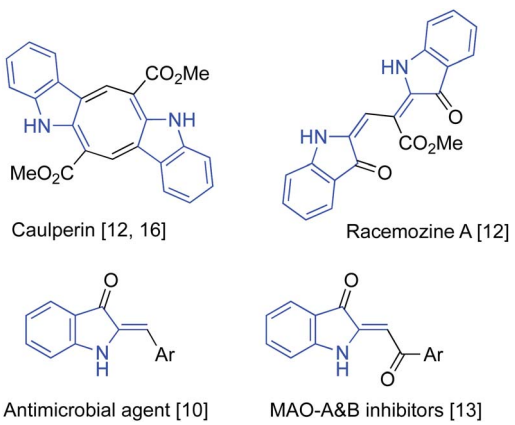

Fig. 1 Biologically active 2-alkylideneindolin-3-ones.

[a]*Department of Chemistry, North Caucasus Federal University, 1a Pushkin St., Stavropol 355009, Russian Federation*

[b]*Department of Chemistry, University of Kansas, 1567 Irving Hill Rd., Lawrence, KS 66045-7582, USA. E-mail: mrubin@ku.edu; Tel: +1-785-864-5071*

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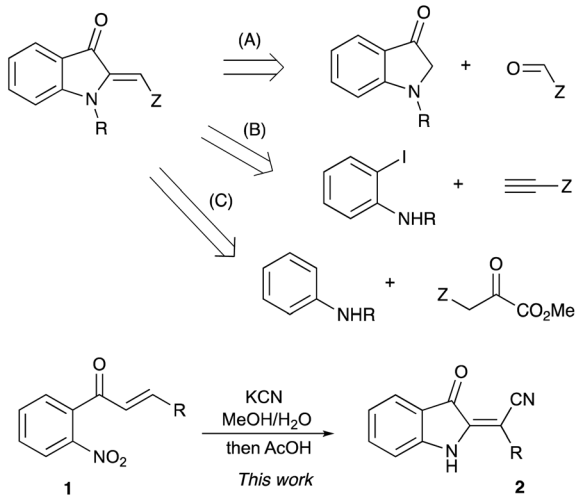
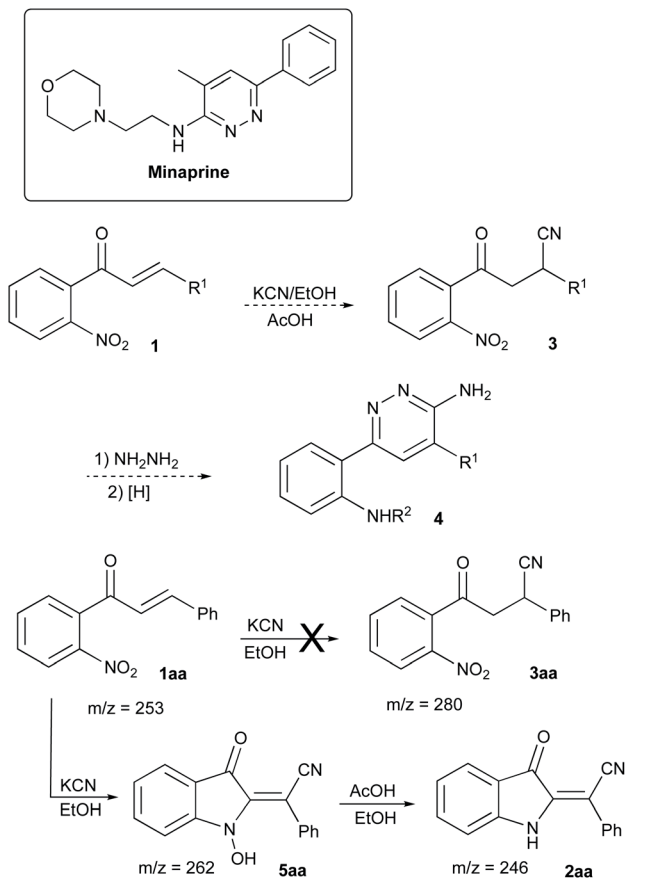


Scheme 1 Synthetic approaches to 2-alkylideneindolin-3-ones.



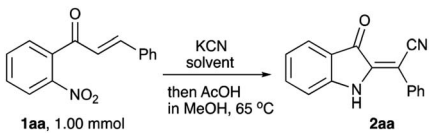
Scheme 2 Unexpected assembly of 2-benzylideneindolin-3-one **2a**.

ketones **1**.[40–43] Although hydrocyanation of conjugate carbonyl compounds is unknown for specific substrates of type **1**, possessing *ortho*-nitro functionality, we did not initially expect any problems with this well-established chemistry.

To evaluate the planned synthetic route, chalcone **1aa** – prepared by aldol condensation of *ortho*-nitroacetophenone (**6a**) with benzaldehyde (**7a**) – was treated with KCN in EtOH in the presence of acetic acid (1.3 equiv.) at room temperature. Unexpectedly, this reaction provided only marginal yields, which was initially attributed to poor solubility of **1aa** in ethanol. To address this situation, we tried to perform this reaction in methanol at elevated temperature, which also failed (Table 1, entry 1). In one of the trial experiments, a mixture of chalcone **1aa** and KCN was pre-heated in MeOH to reflux prior to addition of the acetic acid. To our great surprise, within 15 min the reaction mixture turned emerald green. The starting material (*m*/*z* 276, M + Na) disappeared, but the expected product **3aa** (*m*/*z* 303, M + Na) did not form, while cyclic hydroxylamine product **5aa** was detected in MS (*m*/*z* 285, M + Na) and NMR spectra of the crude reaction mixture instead. The following treatment with acetic acid in boiling methanol led to the conversion of **5aa** into indoline **2aa** (*m*/*z* 269, M + Na), which was isolated in 57% yield (entry 2) as a yellowish-orange crystalline solid with properties identical to those reported in the literature.[44] Next, we attempted to increase the loading of KCN, which had a significant positive effect – although not dramatic (entry 3). Nearly the same efficiency was achieved in a test in which the second stage of the reaction was carried out at room temperature for 12 h (entry 4). The best results were obtained in the experiment involving the initial treatment of chalcone **1aa** with KCN in methanol in the presence of water (entry 5), which improves the solubility of cyanide. It is important to mention, that ideal homogenization of the reaction mixture seems to be crucial for achieving good yields of **2aa**. Indeed, KCN reagent did not dissolve in the mixtures when the test reactions were carried out in THF or acetone even in the presence of additional water. In these cases, product **2aa** did not form at all (Table 1, entries 6–9). The reaction in polar aprotic solvents, such as DMSO and DMF, was also tested. It was found that the outcome of these reactions also improves in the presence of water, but the overall performance in these solvents remains relatively poor (entries 10–13).

With optimized conditions in hand we decided to evaluate the scope of the reaction of various chalcones and with respect to the nature of substituent R^1 (originated from an aldehyde precursor). To this end, a series of chalcones **1** were prepared from *o*-nitroacetophenones **6** and aldehydes **7**. These chalcones were subjected to the reaction with KCN under the optimized reaction conditions. The results are presented in Scheme 3. The preparative reaction of chalcone **1aa** proceeded uneventfully affording product **1aa** in 76% isolated yield (entry 1). Reactions of chalcones **1ab–1ae**, derived from benzaldehydes **7b–e** bearing alkyl substituents also proceeded smoothly to yield the corresponding indolines **2ab–2ae** in good yields (Scheme 3, entries 2–5). Next, the tolerance to substitution with halogenes was tested. We were pleased to find that the corresponding products **2af–2aj** formed in good to high yields (entries 6–10). The reactivity of chalcones **1ak** and **2ak** derived from electron-rich benzaldehydes **7k,l** was also examined (entries 11 and 12). These materials also reacted smoothly, although isolation of product **2al** bearing NMe_2 substituent proved to be more challenging due to the partial decomposition, which reduced the overall efficiency of the process (entry 12). The same problem

Table 1 Optimization of the reaction condition towards formation of product **2aa**



1aa, 1.00 mmol **2aa**

#	KCN, mg	Solvent, 1.5 mL	H_2O, mg	Yield of **2aa**[a], %
1	65	MeOH	0	0[b]
2	40	MeOH	0	57
3	65	MeOH	0	65
4	40	MeOH	0	62[c]
5	**40**	**MeOH**	**200**	**78**
6	40	THF	0	0[d]
7	40	THF	200	0[d]
8	40	Acetone	0	0[d]
9	40	Acetone	200	0[d]
10	40	DMSO	0	24
11	40	DMSO	200	50
12	40	DMF	0	0[d]
13	40	DMF	200	44

[a] NMR yields are reported. [b] All reagents were mixed in one pot and the reaction was carried out at reflux for 1 h. [c] The second stage of the reaction was carried out at RT for 12 h. [d] KCN is insoluble in this reaction mixture.

was encountered in the attempt to employ pyridine carboxaldehyde derivatives **1am–1ao**. The corresponding indolines **2am–2ao** formed smoothly, but were isolated in moderate yields (entries 13–15). Reaction of piperonal derivative **1ap** was accompanied by a notable decomposition of the target product **2ap**, which was isolated in quite marginal yield (entry 16). Such decomposition became much greater issue in the experiments involving chalcones **1aq** and **1ar**, derived from thiophene-2-carbaldehyde and hydrocinnamic aldehyde, respectively. The corresponding products **2aq** and **2ar** were not isolated (entries 17 and 18). Finally, the reaction of chalcone **1ba**, derived from 1-(4,5-dimethoxy-2-nitrophenyl)ethan-1-one (**6b**) and benzaldehyde (**7a**), was also tested. The corresponding product **2ba** was isolated in 51% yield (Scheme 3, entry 19), thus confirming the possibility for the installation of additional substituents onto the aromatic ring of the indoline. Formation of the (*E*)-2-(3-oxoindolin-2-ylidene)-2-arylacetonitrile moiety was unambiguously confirmed by single crystal X-ray diffraction of compound **2ad** (CCDC #1992506, Fig. 2).

The putative mechanistic rationale proposed for the featured transformation is shown in Scheme 4. It is assumed that the reaction begins with the Michael-type addition of the CN-anion across the conjugate C=C bond of chalcone **1** to afford enolate **8**. This enolate triggers a 5-*exo*-trig cyclization involving the *ortho*-nitro group in the substrate molecule. Mechanistically related to the Baeyer–Drewson reaction, this step affords cyclic nitronate **9**, which should exist in equilibrium with tautomeric cyclic enolate form **10**. Subsequent elimination of water would afford 3-oxo-3*H*-indole *N*-oxide **11**, which should quickly transform into the thermodynamically more stable 1-hydroxy-2-methyleneindolin-3-one form **5**. It should be pointed out, that this intermediate was detected in MS and ^{1}H NMR spectra of the crude reaction mixture involving chalcone **1aa** (R = Ph). Evidently, the formation of this structure is responsible for the intense color of the reaction mixtures. Finally, upon acidification with acetic acid, emerald-green **5** is reduced into orange-red product **2**. Although the precise mechanism of this reduction was not elucidated, we believe it could involve the methanol used as a solvent. Since the product **2** is an enamine, it should exist in tautomeric equilibrium between *E* and *Z* forms. Only *E*-tautomers were observed, suggesting that they are thermodynamically much more favored. This stereochemical outcome could be easily rationalized taking into account greater steric hindrance provided by aryl substituent as compared to nitrile functional group.

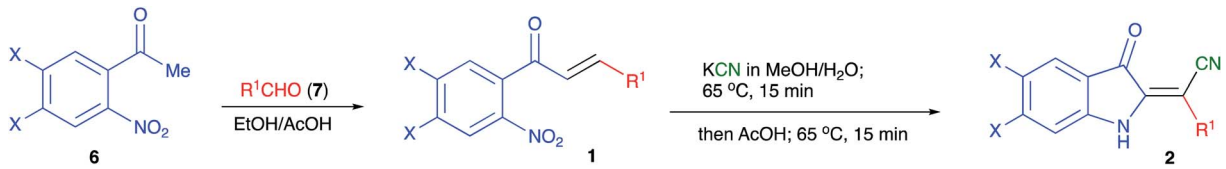
In order to avoid utilization of highly toxic KCN reagent, other cyanide ion sources were also tested, such as Me_3SiCN and $K_4[Fe(CN)_6]$. In both cases, however, formation of the (*E*)-2-(3-oxoindolin-2-ylidene)-2-arylacetonitrile products was not detected. Evidently, the reaction requires a high concentration of nucleophile, which cannot be achieved in the presence of reagents, slowly releasing free cyanide.

Conclusion

In conclusion, an unusual cascade cyclization triggered by the conjugate addition of the cyanide anion to *ortho*-nitro-substituted chalcones was unexpectedly discovered. This novel transformation involves an intramolecular 5-*exo*-trig attack of an enolate on the electrophilic nitro-group, which is mechanistically related to the Baeyer–Drewson reaction. A series of (*E*)-2-(3-oxoindolin-2-ylidene)-2-arylacetonitriles was efficiently, obtained in good to excellent yield.

Experimental part

General information. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-III spectrometer (400 or 100 MHz, respectively) equipped with a BBO probe in $CDCl_3$ or DMSO-d_6 using TMS as an internal standard. High-resolution mass spectra were registered with a Bruker Maxis spectrometer (electrospray ionization, in MeCN solution, using HCO_2Na–HCO_2H for calibration). Melting points were measured with a Stuart smp30 apparatus. Unless specified otherwise, all reactions were performed in 5 mL round-bottomed flasks equipped with reflux condensers. The reaction progress and purity of isolated compounds were controlled by TLC on Silufol UV-254 plates, with hexanes/EtOAc mixtures used as eluents. 1-(4,5-Dimethoxy-2-nitrophenyl)ethan-1-one was prepared according to the known procedure[45] and had physical and spectral properties identical to those reported in literature. (*E*)-1-(2-Nitrophenyl)-5-phenylpent-2-en-1-one was obtained according to the known procedure and was identical to the material described in literature.[46] All other reagents and solvents were purchased from commercial vendors and used as received.

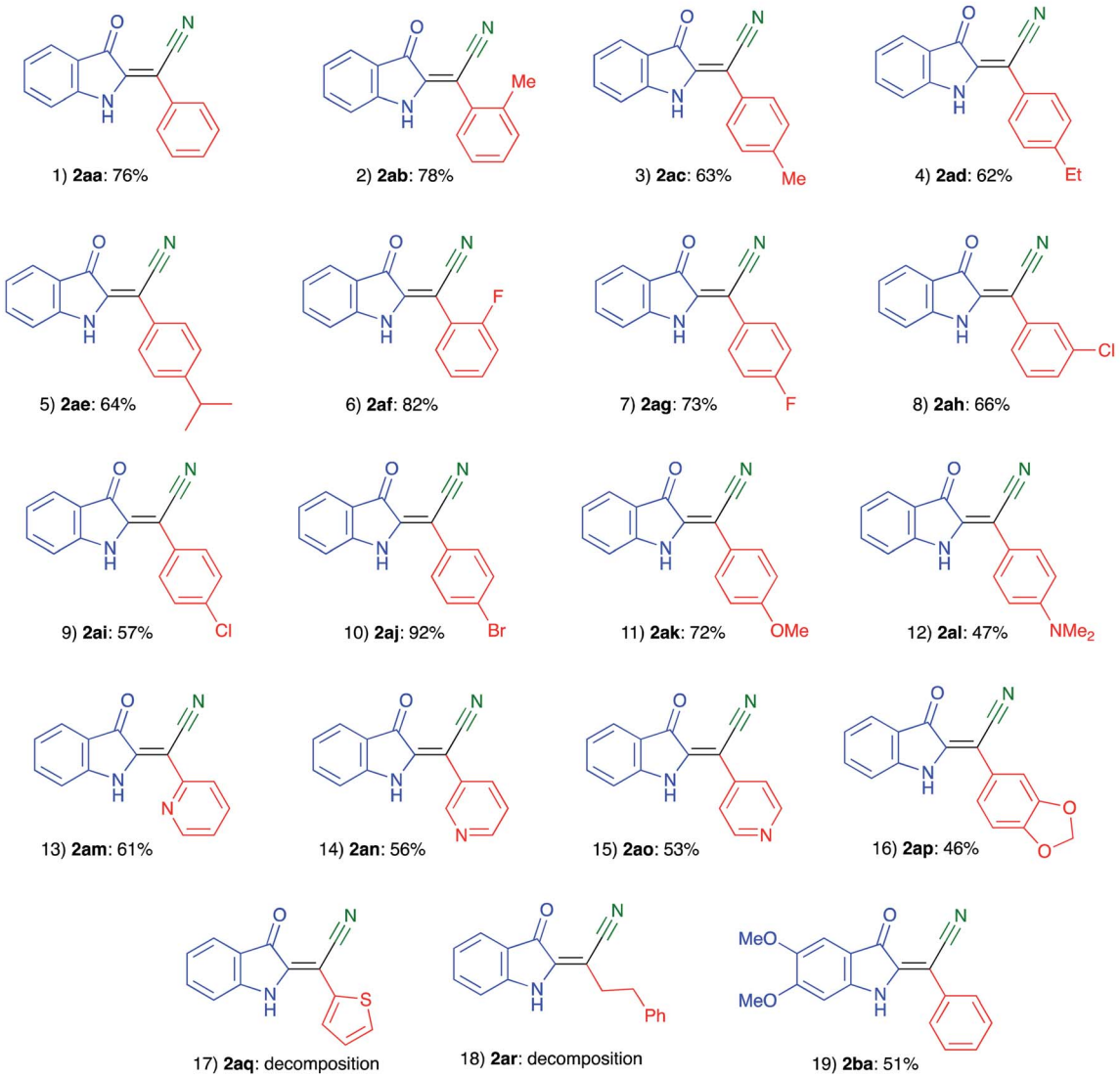


6 1 2

6a: X = H;
6b: X = OMe.

7a: R^1 = Ph; **7b**: R^1 = 2-MeC_6H_4; **7c**: R^1 = 4-MeC_6H_4; **7d**: R^1 = 4-EtC_6H_4; **7e**: R^1 = 4-*i*-PrC_6H_4;
7f: R^1 = 2-FC_6H_4; **7g**: R^1 = 4-FC_6H_4; **7h**: R^1 = 3-ClC_6H_4; **7i**: R^1 = 4-ClC_6H_4; **7j**: R^1 = 4-BrC_6H_4;
7k: R^1 = 4-$MeOC_6H_4$; **7l**: R^1 = 4-$Me_2NC_6H_4$; **7m**: R^1 = 2-Py; **7n**: R^1 = 3-Py; **7o**: R^1 = 4-Py;
7p: R^1 = 3,4-$(OCH_2O)C_6H_3$; **7q**: R^1 = CH_2CH_2Ph; **7q**: R^1 = 2-thienyl

1aa: X = H, R^1 = Ph; **1ab**: X = H, R^1 = 2-MeC_6H_4; **1ac**: X = H, R^1 = 4-MeC_6H_4; **1ad**: X = H, R^1 = 4-EtC_6H_4;
1ae: X = H, R^1 = 4-*i*-PrC_6H_4; **1af**: X = H, R^1 = 2-FC_6H_4; **1ag**: X = H, R^1 = 4-FC_6H_4; **1ah**: X = H, R^1 = 3-ClC_6H_4;
1ai: X = H, R^1 = 4-ClC_6H_4; **1aj**: X = H, R^1 = 4-BrC_6H_4; **1ak**: X = H, R^1 = 4-$MeOC_6H_4$; **1al**: X = H, R^1 = 4-$Me_2NC_6H_4$;
1am: X = H, R^1 = 2-Py; **1an**: X = H, R^1 = 3-Py; **1ao**: X = H, R^1 = 4-Py;
11ap: R^1 = 3,4-$(OCH_2O)C_6H_3$; **11aq**: R^1 = 2-thienyl; **1ba**: X = OMe, R^1 = Ph.



Scheme 3 Preparation of (*E*)-2-(3-oxoindolin-2-ylidene)-2-arylacetonitriles *via* featured cyanide-induced cyclization of chalcones.

Preparation of chalcones

(*E*)-1-(2-Nitrophenyl)-3-phenylprop-2-en-1-one (1aa). This compound was prepared according to the known procedure[46] employing benzaldehyde (**1a**) (825 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.214 g (4.80 mmol, 96%), colorless solid, mp 124.1–126.0 °C, lit.[47] 130 °C, R_f 0.40 (EtOAc/Hex, 1 : 4). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 8.1 Hz, 1H), 7.77 (t, J = 7.3 Hz, 1H), 7.66 (t, J =

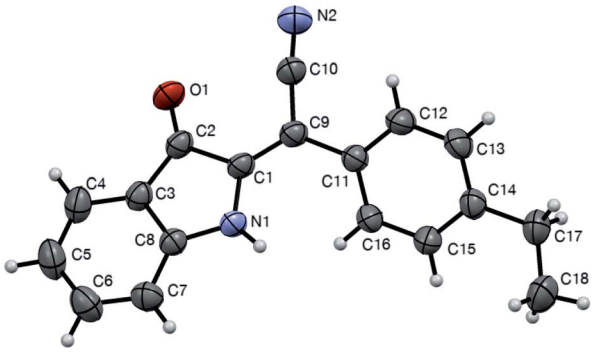
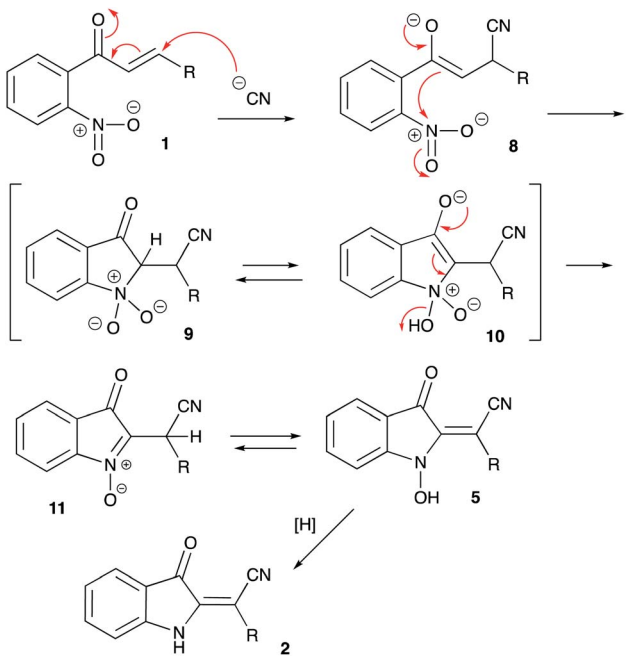


Fig. 2 ORTEP drawing of crystal structure of compound **2ad** (CCDC #1992506) showing 50% probability thermal ellipsoids and atom numbering scheme.



Scheme 4 Proposed mechanistic rationale.

7.4 Hz, 1H), 7.50 (dd, J = 7.7, 4.2 Hz, 3H), 7.39 (d, J = 6.5 Hz, 3H), 7.24 (d, J = 15.9 Hz, 1H), 7.01 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 146.9, 146.5, 136.5, 134.2, 134.1, 131.2, 130.7, 129.2 (2C), 129.0, 128.7 (2C), 126.4, 124.7; FTIR (KBr, cm^{-1}): 3741, 3298, 3092, 1647, 1531, 1340, 1277, 1107; HRMS (ES TOF) calc'd for $C_{15}H_{11}NNaO_3$ (M + Na)$^+$ 276.0631, found 276.0634 (1.0 ppm).

(*E*)-1-(2-Nitrophenyl)-3-(*o*-tolyl)prop-2-en-1-one (1ab). This compound was prepared according to the known procedure[46] employing 2-methylbenzaldehyde (**7b**) (600 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.255 g (4.70 mmol, 94%), light yellow crystals, mp 95.0–96.2 °C. R_f 0.53 (EtOAc/Hex, 1 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 7.7 Hz, 1H), 7.82–7.72 (m, 1H), 7.71–7.63 (m, 1H), 7.61–7.56 (m, 2H), 7.54 (dd, J = 7.5, 1.0 Hz, 1H), 7.33–7.14 (m, 3H), 6.91 (d, J = 16.1 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 147.0, 143.8, 138.2, 136.5, 134.1, 133.0, 131.0, 130.9, 130.8, 129.0, 127.1, 126.8, 126.6, 124.6, 19.7; FTIR (KBr, cm^{-1}): 2931, 2363, 1673, 1561, 1525, 1363, 1327, 1218, 1030; HRMS (ES TOF) calc'd for $C_{16}H_{13}NNaO_3$ (M + Na)$^+$ 290.0788, found 290.0783 (1.6 ppm).

(*E*)-1-(2-Nitrophenyl)-3-(*p*-tolyl)prop-2-en-1-one (1ac). This compound was prepared according to the known procedure[46] employing 4-methylbenzaldehyde (**7c**) (600 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.295 g (4.85 mmol, 97%), colorless solid, mp 130.8–131.6 °C (EtOH), lit.[47] mp 134–135 °C, R_f 0.28 (EtOAc/Hex, 1 : 4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.2 Hz, 1H), 7.76 (t, J = 7.4 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.50 (d, J = 7.4 Hz, 1H), 7.39 (d, J = 7.9 Hz, 2H), 7.24–7.16 (m, 3H), 6.97 (d, J = 16.2 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.2, 146.9, 146.7, 141.9, 136.6, 134.1, 131.3, 130.6, 129.9 (2C), 129.0, 128.7 (2C), 125.5, 124.7, 21.7; FTIR (KBr, cm^{-1}): 3067, 1668, 1591, 1524, 1364, 1320, 1230, 1210, 1029; HRMS (ES TOF) calc'd for $C_{16}H_{13}N_1NaO_3$ (M + Na)$^+$ 290.0788, found 290.0790 (0.8 ppm).

3-(2-Fluorophenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1af). This compound was prepared according to the known procedure[46] employing 2-fluorobenzaldehyde (**7f**) (620 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.246 g (4.60 mmol, 92%), colorless crystals, mp 97.3–97.9 °C, R_f 0.46 (EtOAc/Hex, 1 : 4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.1 Hz, 1H), 7.77 (dd, J = 7.4, 6.8 Hz, 1H), 7.72–7.62 (m, 1H), 7.59–7.47 (m, 2H), 7.41–7.33 (m, 2H), 7.16 (t, J = 7.5 Hz, 1H), 7.13–7.00 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 161.5 (d, J = 254.6 Hz), 146.8, 138.5 (d, J = 3.3 Hz), 136.2, 134.2, 132.7 (d, J = 8.9 Hz), 130.8, 129.1 (d, J = 2.5 Hz), 128.9, 128.3 (d, J = 5.9 Hz), 124.72 (d, J = 3.8 Hz), 124.68, 122.2 (d, J = 11.5 Hz), 116.3 (d, J = 21.7 Hz); FTIR (KBr, cm^{-1}): 3289, 3065, 1651, 1603, 1531, 1340, 1290, 1215; HRMS (ES TOF) calc'd for $C_{15}H_{10}FNNaO_3$ (M + Na)$^+$ 294.0537, found 294.0538 (0.4 ppm).

3-(4-Fluorophenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1ag). This compound was prepared according to the known procedure[46] employing 4-fluorobenzaldehyde (**7g**) (620 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.233 g (4.55 mmol, 91%), colorless solid, mp 99.1–100.5 °C, R_f 0.46 (EtOAc/Hex, 1 : 4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.2 Hz, 1H), 7.82–7.72 (m, 1H), 7.70–7.60 (m, 1H), 7.55–7.44 (m, 3H), 7.21 (d, J = 16.3 Hz, 1H), 7.07 (t, J = 8.6 Hz, 2H), 6.92 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.8, 164.4 (d, J = 252.8 Hz), 146.8, 145.0, 136.4, 134.2, 130.8, 130.7 (d, J = 8.7 Hz, 2C), 130.3 (d, J = 3.2 Hz), 128.9, 126.1 (d, J = 2.2 Hz), 124.7, 116.3 (d, J = 22.0 Hz, 2C); FTIR (KBr, cm^{-1}): 3302, 3052, 1651, 1522, 1353, 1286, 1232, 1112; HRMS (ES TOF) calc'd for $C_{15}H_{10}FNNaO_3$ (M + Na)$^+$ 294.0537, found 294.0538 (0.4 ppm).

(*E*)-3-(3-Chlorophenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1ah). This compound was prepared according to the known procedure[46] employing 3-chlorobenzaldehyde (**7h**) (700 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.291 g (4.50 mmol, 90%), light-yellow solid, mp 122.0–124.1 °C (EtOH), R_f 0.27 (EtOAc/Hex, 1 : 4), 0.52 (EtOAc/Hex, 1 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.0 Hz,

1H), 7.82–7.73 (m, 1H), 7.71–7.62 (m, 1H), 7.50 (dd, J = 7.5, 1.0 Hz, 1H), 7.46 (s, 1H), 7.34 (tt, J = 15.2, 7.4 Hz, 3H), 7.18 (d, J = 16.3 Hz, 1H), 6.98 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 146.8, 144.4, 136.2, 135.9, 135.1, 134.3, 130.93, 130.89, 130.4, 128.9, 128.4, 127.5, 126.7, 124.7; FTIR (KBr, cm^{-1}): 3050, 1647, 1514, 1340, 1284, 1254, 1205, 1099; HRMS (ES TOF) calc'd for $C_{15}H_{10}Cl_1N_1Na_1O_3$ $(M + Na)^+$ 310.0241, found 310.0246 (−1.5 ppm).

(*E*)-3-(4-Chlorophenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1ai). This compound was prepared according to the known procedure[46] employing 4-chlorobenzaldehyde (**7i**) (700 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.409 g (4.90 mmol, 98%), white solid, mp 120.4–121.4 °C, lit.[48] mp 123–124 °C. R_f 0.35 (EtOAc/Hex, 1 : 4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28–8.14 (m, 1H), 7.77 (t, J = 7.1 Hz, 1H), 7.70–7.63 (m, 1H), 7.50 (dd, J = 7.6, 1.5 Hz, 1H), 7.43 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.20 (d, J = 16.3 Hz, 1H), 6.96 (d, J = 16.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.7, 146.8, 144.7, 137.1, 136.3, 134.3, 132.6, 130.8, 129.8 (2C), 129.4 (2C), 128.9, 126.7, 124.7; FTIR (KBr, cm^{-1}): 3258, 3056, 2868, 1906, 1638, 1527, 1343; HRMS (ES TOF) calc'd for $C_{15}H_{10}ClNNaO_3$ $(M + Na)^+$ 310.0241, found 310.0246 (1.5 ppm).

(*E*)-3-(4-Bromophenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1aj). This compound was prepared according to the known procedure[46] employing 4-bromobenzaldehyde (**7j**) (920 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.572 g (4.75 mmol, 95%), colorless solid, mp 130.4–132.1 °C (EtOH), lit.[49] mp 145–147 °C, R_f 0.25 (EtOAc/hexanes 1 : 4); ^{1}H NMR (400 MHz, DMSO) δ 8.21 (d, J = 8.0 Hz, 1H), 7.91 (t, J = 7.3 Hz, 1H), 7.81 (t, J = 7.4 Hz, 1H), 7.76–7.68 (m, 3H), 7.62 (d, J = 8.3 Hz, 2H), 7.44–7.27 (m, 2H); ^{13}C NMR (101 MHz, DMSO) δ 192.2, 146.7, 144.6, 135.3, 134.5, 133.3, 132.0 (2C), 131.5, 130.8 (2C), 129.1, 126.4, 124.6, 124.6; FTIR (KBr, cm^{-1}): 3255, 3061, 1638, 1584, 1527, 1487, 1347, 1307, 1290; HRMS (ES TOF) calc'd for $C_{15}H_{10}BrNNaO_3$ $(M + Na)^+$ 353.9736, found 353.9739 (0.9 ppm).

(*E*)-3-(4-Methoxyphenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1ak). This compound was prepared according to the known procedure[46] employing anisaldehyde (**7k**) (680 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.316 g (4.65 mmol, 93%), white solid, mp 97.0–97.5 °C, lit.[50] mp 101–103 °C, R_f 0.13 (EtOAc/Hex, 1 : 4), 0.56 (EtOAc/Hex, 1 : 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J = 8.2 Hz, 1H), 7.79–7.71 (m, 1H), 7.69–7.60 (m, 1H), 7.50 (dd, J = 7.5, 1.1 Hz, 1H), 7.45 (d, J = 8.7 Hz, 2H), 7.20 (d, J = 16.2 Hz, 1H), 6.94–6.82 (m, 3H), 3.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 162.2, 146.9, 146.5, 136.7, 134.1, 130.6 (2C), 130.5, 129.0, 126.8, 124.7, 124.1, 114.6 (2C), 55.6; FTIR (KBr, cm^{-1}): 3288, 2939, 1654, 1521, 1347, 1251, 1172, 1026; HRMS (ES TOF) calc'd for $C_{16}H_{13}NNaO_4$ $(M + Na)^+$ 306.0737, found 306.0730 (2.3 ppm).

3-(4-(Dimethylamino)phenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1al). This compound was prepared according to the known procedure[46] employing 4-(dimethylamino)benzaldehyde (**7l**) (745 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.391 g (4.70 mmol, 94%), orange solid, 101.4–102.6 °C, lit.[51] mp 157 °C. R_f 0.27 (EtOAc/Hex, 1 : 4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.1 Hz, 1H), 7.71 (t, J = 7.1 Hz, 1H), 7.63–7.54 (m, 1H), 7.53–7.43 (m, 1H), 7.36 (d, J = 8.8 Hz, 2H), 7.19 (d, J = 16.0 Hz, 1H), 6.80 (d, J = 16.0 Hz, 1H), 6.61 (d, J = 8.8 Hz, 2H), 3.00 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.9, 152.4, 148.0, 146.9, 137.0, 133.8, 130.7, 130.2, 129.0, 124.5, 121.5, 120.8, 111.8 (2C), 40.1 (2C); FTIR (KBr, cm^{-1}): 3096, 3029, 2900, 2820, 1598, 1522, 1433, 1348, 1299, 1237, 1179, 1112; HRMS (ES TOF) calc'd for $C_{17}H_{16}N_2NaO_3$ $(M + Na)^+$ 319.1053, found 319.1053 (0.1 ppm).

(*E*)-1-(4,5-Dimethoxy-2-nitrophenyl)-3-phenylprop-2-en-1-one (1ba). This compound was prepared according to the known procedure[52] employing benzaldehyde (**1a**) (825 mg, 5.00 mmol) and 1-(4,5-dimethoxy-2-nitrophenyl)ethan-1-one[45] (1.126 g, 5.00 mmol). The titled compound was obtained as colorless solid, mp 113.4–116.3 °C (benzene), lit.[52] mp 159–160 °C (EtOH), R_f 0.28 (EtOAc/Hex, 1 : 2). Yield 1.330 g (4.25 mmol, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.52–7.44 (m, 2H), 7.42–7.32 (m, 3H), 7.20 (d, J = 16.2 Hz, 1H), 6.95 (d, J = 16.2 Hz, 1H), 6.85 (s, 1H), 4.01 (s, 3H), 3.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 153.9, 149.7, 145.4, 139.4, 134.1, 131.0, 130.8, 129.1 (2C), 128.6 (2C), 126.7, 110.0, 107.1, 56.8, 56.7; FTIR (KBr, cm^{-1}): 3036, 2977, 1650, 1571, 1514, 1445, 1337, 1287, 1217, 1122; HRMS (ES TOF) calc'd for $C_{17}H_{15}NNaO_5$ $(M + Na)^+$ 336.0842, found 336.0849 (1.9 ppm).

(*E*)-3-(Benzo[*d*][1,3]dioxol-5-yl)-1-(2-nitrophenyl)prop-2-en-1-one (1ap). This compound was prepared according to known procedure,[53] employing piperonal (**7p**) (1.50 g, 10.00 mmol) and 2′-nitroacetophenone (**6a**) (1.65 g, 10.00 mmol). The title compound was obtained as colorless solid, mp 129.2–130.9 °C, lit.[53] mp 126–128 °C, R_f 0.55 (EtOAc/Hex, 1 : 2). Yield 2.525 g (8.5 mmol, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.1 Hz, 1H), 7.75 (t, J = 7.1 Hz, 1H), 7.69–7.61 (m, 1H), 7.49 (dd, J = 7.5, 0.9 Hz, 1H), 7.16 (d, J = 16.1 Hz, 1H), 7.03 (d, J = 1.2 Hz, 1H), 6.95 (dd, J = 8.0, 1.2 Hz, 1H), 6.87–6.75 (m, 2H), 6.01 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.9, 150.5, 148.6, 146.9, 146.4, 136.6, 134.1, 130.6, 128.9, 128.5, 125.7, 124.7, 124.4, 108.8, 106.8, 101.9; FTIR (film, NaCl, cm^{-1}): 3262, 3101, 3014, 2913, 1645, 1524, 1498, 1447, 1337, 1243, 1106; HRMS (ES TOF) calc'd for $C_{16}H_{11}NNaO_5$ $(M + Na)^+$ 320.0529, found 320.0527 (0.7 ppm).

(*E*)-1-(2-Nitrophenyl)-3-(pyridin-2-yl)prop-2-en-1-one (1am). This compound was prepared *via* modified literature protocol[48] (typical procedure A): a 15 mL Erlenmeyer flask equipped with magnetic stirring bar was charged with picolinaldehyde (**7m**) (535 mg, 5.00 mmol), 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol) and EtOH (3 mL). The stirred reaction mixture was cooled in the ice bath, and a solution of KOH (56 mg, 1.00 mmol) in water (300 μL) was added upon stirring maintaining the reaction temperature below +10 °C. After consumption of the starting acetophenone (TLC, EtOAc : Hex 1 : 4) the reaction mixture was diluted with cold water (20 mL) and extracted with EtOAc (4 × 15 mL). Combined organic extracts were washed consecutively with water (3 × 15 mL) and brine (15 mL). After concentration *in vacuo* the crude product was recrystallized from EtOH to afford the titled compound as colorless solid, mp 101.2–103.5 °C (EtOH), lit.[48] mp 102–105 (isopropanol), R_f 0.40 (EtOAc/Hex, 1 : 1). Yield 1.143 g (0.45 mmol, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 4.1 Hz, 1H), 8.18 (d, J =

8.2 Hz, 1H), 7.81–7.69 (m, 2H), 7.69–7.61 (m, 1H), 7.55–7.46 (m, 2H), 7.41 (d, J = 16.1 Hz, 1H), 7.33–7.22 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 152.7, 150.3, 146.7, 144.6, 137.0, 136.4, 134.3, 130.9, 129.7, 128.9, 124.8, 124.7, 124.5; FTIR (KBr, cm^{-1}): 3074, 1752, 1661, 1528, 1431, 1337, 1277, 1247; HRMS (ES TOF) calc'd for $C_{14}H_{10}N_2NaO_3$ (M + Na)$^+$ 277.0584, found 277.0593 (3.4 ppm).

3-(4-Ethylphenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1ad). This compound was prepared according to the typical procedure A employing 4-ethylbenzaldehyde (**7d**) (670 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). The crude product was purified by preparative column chromatography eluting with EtOAc/Hex, 1 : 4. Yield 1.306 g (4.65 mmol, 93%), pale brown oil, R_f 0.51 (EtOAc/Hex, 1 : 4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.2 Hz, 1H), 7.75 (td, J = 7.5, 0.9 Hz, 1H), 7.67–7.61 (m, 1H), 7.49 (dd, J = 7.5, 1.2 Hz, 1H), 7.41 (d, J = 8.1 Hz, 2H), 7.26–7.17 (m, 3H), 6.97 (d, J = 16.3 Hz, 1H), 2.65 (q, J = 7.6 Hz, 2H), 1.22 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 148.1, 146.8, 146.7, 136.4, 134.1, 131.5, 130.6, 128.9, 128.8 (2C), 128.6 (2C), 125.4, 124.6, 28.9, 15.3; FTIR (KBr, cm^{-1}): 3035, 2970, 2873, 1652, 1596, 1531, 1350, 1210; HRMS (ES TOF) calc'd for $C_{17}H_{15}NNaO_3$ (M + Na)$^+$ 304.0944, found 304.0948 (1.1 ppm).

(*E*)-3-(4-Isopropylphenyl)-1-(2-nitrophenyl)prop-2-en-1-one (1ae). This compound was prepared according to the typical procedure A employing 4-isopropylbenzaldehyde (**7e**) (740 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). The crude product was purified by preparative column chromatography eluting with EtOAc/Hex, 1 : 4. Yield 1.292 g (4.4 mmol, 88%), yellow oil, R_f 0.38 (EtOAc/Hex, 1 : 4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.2 Hz, 1H), 7.75 (td, J = 7.5, 0.9 Hz, 1H), 7.67–7.61 (m, 1H), 7.50 (dd, J = 7.5, 1.2 Hz, 1H), 7.44 (d, J = 8.2 Hz, 2H), 7.24 (dd, J = 12.1, 3.8 Hz, 3H), 6.99 (d, J = 16.3 Hz, 1H), 2.92 (septet, J = 6.9 Hz, 1H), 1.24 (d, J = 6.9 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.1, 152.7, 146.8, 146.6, 136.4, 134.1, 131.6, 130.6, 128.9, 128.8 (2C), 127.2 (2C), 125.4, 124.6, 34.2, 23.7 (2C); FTIR (KBr, cm^{-1}): 2958, 1742, 1653, 1591, 151, 1360, 1300, 1280, 1244, 1201, 1109; HRMS (ES TOF) calc'd for $C_{18}H_{17}N_1Na_1O_3$ (M + Na)$^+$ 318.1101, found 318.1101 (0.1 ppm).

(*E*)-1-(2-Nitrophenyl)-3-(pyridin-3-yl)prop-2-en-1-one (1an). This compound was prepared according to typical procedure A employing nicotinaldehyde (**7n**) (535 mg, 5.00 mmol) and 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1.092 g (4.30 mmol, 86%), colorless solid, mp 88.3–89.8 °C (EtOH), R_f 0.25 (EtOAc/hexanes 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (d, J = 1.4 Hz, 1H), 8.60 (dd, J = 4.7, 1.2 Hz, 1H), 8.19 (d, J = 8.2 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.82–7.72 (m, 1H), 7.72–7.58 (m, 1H), 7.55–7.42 (m, 1H), 7.33 (dd, J = 7.9, 4.8 Hz, 1H), 7.24 (d, J = 16.4 Hz, 1H), 7.04 (d, J = 16.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 151.7, 150.3, 146.7, 142.1, 136.1, 134.5, 134.4, 131.0, 129.9, 128.9, 128.1, 124.8, 124.0; FTIR (KBr, cm^{-1}): 3308, 3034, 1661, 1581, 1524, 1350, 1256, 1102; HRMS (ES TOF) calc'd for $C_{14}H_{10}N_2NaO_3$ (M + Na)$^+$ 277.0584, found 277.0585 (−0.6 ppm).

(*E*)-1-(2-Nitrophenyl)-3-(pyridin-4-yl)prop-2-en-1-one (1ao). This compound was prepared according to typical procedure A employing isonicotinaldehyde (**7o**) (535 mg, 5.00 mmol), 1-(2-nitrophenyl)ethan-1-one (**6a**) (825 mg, 5.00 mmol). Yield 1041.4 mg (4.1 mmol, 82%), colorless crystals, mp 140.0–141.6 °C (EtOH), R_f 0.22 (EtOAc/hexanes 1 : 1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 5.1 Hz, 2H), 8.19 (d, J = 8.1 Hz, 1H), 7.78 (t, J = 7.4 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.50 (d, J = 7.3 Hz, 1H), 7.32 (d, J = 5.0 Hz, 2H), 7.13 (q, J = 16.3 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.3, 150.8 (2C), 146.7, 142.4, 141.2, 135.9, 134.5, 131.1, 130.1, 128.8, 124.7, 122.1 (2C); FTIR (KBr, cm^{-1}): 3308, 3060, 1661, 1598, 1524, 1413, 1343, 1286, 1109; HRMS (ES TOF) calc'd for $C_{14}H_{10}N_2NaO_3$ (M + Na)$^+$ 277.0584, found 277.0576 (2.8 ppm).

(*E*)-1-(2-Nitrophenyl)-3-(thiophen-2-yl)prop-2-en-1-one (1aq). This compound was prepared according to the typical procedure A employing thiophene-2-carbaldehyde (**7q**) (560 mg, 5 mmol) and 2′-nitroacetophenone (**6a**) (825 mg, 5.00 mmol). The title compound was obtained as colorless solid, mp 95.0–96.2 °C, lit.[54] mp 94–95 °C, R_f 0.35 (EtOAc/Hex, 1 : 4). Yield 1.062 g (4.1 mmol, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 1H), 7.75 (t, J = 7.3 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.54–7.33 (m, 3H), 7.29–7.17 (m, 1H), 7.12–6.99 (m, 1H), 6.78 (d, J = 15.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 192.4, 146.7, 139.3, 138.8, 136.3, 134.1, 132.5, 130.7, 130.2, 128.8, 128.5, 124.8, 124.7; FTIR (KBr, cm^{-1}): 3107, 2859, 1651, 1604, 1521, 1420, 1343, 1280, 1253, 1193; HRMS (ES TOF) calc'd for $C_{13}H_9N_1Na_1O_3S_1$ (M + Na)$^+$ 282.0195, found 282.0195 (0.0 ppm).

Synthesis of (*E*)-2-(3-oxoindolin-2-ylidene)-2-arylacetonitriles

(*E*)-2-(3-Oxoindolin-2-ylidene)-2-phenylacetonitrile (2aa). Typical procedure B: reaction vessel was charged with (*E*)-1-(2-nitrophenyl)-3-phenylprop-2-en-1-one (**1aa**) (253 mg, 1.00 mmol), KCN (80 mg, 1.23 mmol), water (400 mg), and methanol (3 mL). The mixture was stirred at reflux for 15 min monitoring the reaction by TLC. When the starting chalcon was consumed, the emerald-green mixture was cooled down to room temperature and acetic acid (40 mg, 0.66 mmol) was added slowly (**Caution!** This process is very exothermic and toxic HCN may evolve, use well-ventilated fume hood. Residual materials containing free cyanides should be quenched with KOH and $FeCl_3$ aqueous solutions). The refluxing was continued for additional 15 min. Then, the mixture was diluted with water (10 mL), treated with saturated aqueous solution of sodium bicarbonate (5 mL), and extracted with ethyl acetate (4 × 20 mL). Crude product was purified by preparative column chromatography eluting with a mixture EtOAc/hexanes, gradient 1 : 2–1 : 1. Additional purification can be performed by recrystallization from ethanol. The titled compound was obtained as red crystals, mp 233.1–235.9 °C (EtOH), lit.[44] mp 236–237 °C, R_f 0.32 (EtOAc/hexanes 1 : 2), R_f 0.65 (EtOAc/hexanes 1 : 1). Yield 187 mg (0.76 mmol, 76%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.51 (s, 1H), 7.70–7.43 (m, 7H), 7.09 (d, J = 7.9 Hz, 1H), 7.02 (t, J = 7.2 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.2, 152.5, 142.5, 137.5, 132.1, 129.3 (2C), 129.1, 128.8 (2C), 124.9, 121.5, 119.5, 118.0, 112.7, 88.8; FTIR (KBr, cm^{-1}): 3308, 3060, 2222, 1708, 1601, 1470, 1447, 1391, 1340, 1213; HRMS (ES TOF) calc'd for $C_{16}H_{10}N_2NaO$ (M + Na)$^+$ 269.0685, found 269.0692 (−2.3 ppm).

(*E*)-2-(3-Oxoindolin-2-ylidene)-2-(*o*-tolyl)acetonitrile (2ab). This compound was prepared according to the typical procedure B employing (*E*)-1-(2-nitrophenyl)-3-(*o*-tolyl)prop-2-en-1-one (**1ab**) (267 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 2. Yield 203 mg (0.78 mmol, 78%), red crystals, mp 201.8–203.5 °C (EtOH), R_f 0.29 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.06 (s, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.55 (dd, J = 11.2, 4.1 Hz, 1H), 7.44–7.28 (m, 4H), 7.08–6.87 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.0, 152.5, 143.9, 137.6, 136.9, 131.0, 130.8, 130.0, 129.5, 126.8, 124.9, 121.3, 119.6, 117.6, 112.4, 87.7, 19.3; FTIR (KBr, cm^{-1}): 3336, 2215, 1708, 1598, 1377, 1330, 1220, 1139, 1082, 965; HRMS (ES TOF) calc'd for $C_{17}H_{12}N_2NaO$ (M + Na)$^+$ 283.0842, found 283.0840 (0.5 ppm).

(*E*)-2-(3-Oxoindolin-2-ylidene)-2-(*p*-tolyl)acetonitrile (2ac). This compound was prepared according to the typical procedure B employing (*E*)-1-(2-nitrophenyl)-3-(*p*-tolyl)prop-2-en-1-one (**1ac**) (267 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 3. Yield 164 mg (0.63 mmol, 63%), orange crystals, mp 231–234 °C (EtOH), lit.[44] mp 236–240 °C, R_f 0.46 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.45 (s, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.56 (dd, J = 16.7, 7.8 Hz, 3H), 7.38 (d, J = 7.9 Hz, 2H), 7.09 (d, J = 8.0 Hz, 1H), 7.02 (t, J = 7.4 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 184.2, 152.5, 142.2, 139.0, 137.4, 129.9 (2C), 129.2, 128.8 (2C), 124.9, 121.4, 119.5, 118.0, 112.7, 89.2, 20.9; FTIR (KBr, cm^{-1}): 3296, 2208, 1705, 1591, 1471, 1307, 1243, 811; HRMS (ES TOF) calc'd for $C_{17}H_{12}N_2NaO^+$ (M + Na)$^+$ 283.0842, found 283.0844 (0.8 ppm).

(*E*)-2-(4-Ethylphenyl)-2-(3-oxoindolin-2-ylidene)acetonitrile (2ad). This compound was prepared according to the typical procedure B employing (*E*)-3-(4-ethylphenyl)-1-(2-nitrophenyl) prop-2-en-1-one (**1ad**) (281 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 3. Yield 170 mg (0.62 mmol, 62%), red crystals, mp 223.2–225.7 °C (EtOH), R_f 0.56 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.46 (s, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.60–7.50 (m, 3H), 7.41 (d, J = 8.1 Hz, 2H), 7.09 (d, J = 8.0 Hz, 1H), 7.02 (t, J = 7.4 Hz, 1H), 2.68 (q, J = 7.5 Hz, 2H), 1.22 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.2, 152.5, 145.2, 142.1, 137.4, 129.4, 128.9 (2C), 128.8 (2C), 124.9, 121.4, 119.5, 118.0, 112.7, 89.2, 28.0, 15.4; FTIR (KBr, cm^{-1}): 3429, 2933, 2255, 2134, 1665, 1585, 1461, 1370, 1243, 1022, 998, 828; HRMS (ES TOF) calc'd for $C_{18}H_{14}N_2NaO$ (M + Na)$^+$ 297.0998, found 297.0997 (0.4 ppm).

(*E*)-2-(4-Isopropylphenyl)-2-(3-oxoindolin-2-ylidene) acetonitrile (2ae). This compound was prepared according to the typical procedure B employing (*E*)-3-(4-isopropylphenyl)-1-(2-nitrophenyl)prop-2-en-1-one (**1ae**) (295 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, gradient 1 : 3–1 : 2. Yield 184 mg (0.64 mmol, 64%), red crystals, mp 223.0–226.6 °C (EtOH), lit.[44] mp 228–230 °C, R_f 0.47 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.47 (s, 1H), 7.64 (d, J = 7.4 Hz, 1H), 7.57 (d, J = 7.5 Hz, 3H), 7.44 (d, J = 7.8 Hz, 2H), 7.09 (d, J = 7.9 Hz, 1H), 7.01 (t, J = 7.3 Hz, 1H), 2.96 (septet, J = 6.7 Hz, 1H), 1.24 (d, J = 6.7 Hz, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.2, 152.5, 149.7, 142.1, 137.4, 129.6, 128.9 (2C), 127.4 (2C), 124.9, 121.4, 119.5, 118.0, 112.8, 89.2, 33.4, 23.7 (2C); FTIR (KBr, cm^{-1}): 3349, 2959, 2872, 2208, 1708, 1591, 1524, 1464, 1333, 1210; HRMS (ES TOF) calc'd for $C_{19}H_{16}N_2NaO$ (M + Na)$^+$ 311.1155, found 311.1155 (0.0 ppm).

(*E*)-2-(2-Fluorophenyl)-2-(3-oxoindolin-2-ylidene)acetonitrile (2af). This compound was prepared according to the typical procedure B employing (*E*)-3-(2-fluorophenyl)-1-(2-nitrophenyl) prop-2-en-1-one (**1af**) (271 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 2. Yield 216 mg (0.82 mmol, 82%), red crystals, mp 211.1–212.6 °C (EtOH), lit.[44] mp 215–216 °C, R_f 0.26 (EtOAc/hexanes 1 : 2), R_f 0.63 (EtOAc/hexanes 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.42 (s, 1H), 7.70–7.50 (m, 4H), 7.47–7.33 (m, 2H), 7.12–6.96 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 183.9, 159.4 (d, J = 249.6 Hz), 152.3, 144.2, 137.8, 131.8 (d, J = 8.5 Hz), 131.5 (d, J = 1.8 Hz), 125.4 (d, J = 3.4 Hz), 125.1, 121.6, 119.43 (d, J = 14.7 Hz), 119.40, 117.3, 116.7 (d, J = 20.8 Hz), 112.4, 81.9; FTIR (KBr, cm^{-1}): 3296, 3047, 2222, 1718, 1598, 1454, 1340, 1306; HRMS (ES TOF) calc'd for $C_{16}H_9FN_2NaO$ (M + Na)$^+$ 287.0591, found 287.0597 (1.9 ppm).

(*E*)-2-(4-Fluorophenyl)-2-(3-oxoindolin-2-ylidene)acetonitrile (2ag). This compound was prepared according to the typical procedure B employing (*E*)-3-(4-fluorophenyl)-1-(2-nitrophenyl) prop-2-en-1-one (**1ag**) (271 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 3. Yield 192 mg (0.73 mmol, 73%), orange crystals, mp 281.1–282.8 °C (EtOH), lit.[44] mp 282–284 °C, R_f 0.54 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.50 (s, 1H), 7.78–7.62 (m, 3H), 7.58 (t, J = 7.4 Hz, 1H), 7.42 (t, J = 8.4 Hz, 2H), 7.08 (d, J = 7.9 Hz, 1H), 7.02 (t, J = 7.3 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.2, 162.1 (d, J = 247.8 Hz), 152.5, 142.7, 137.5, 131.3 (d, J = 8.7 Hz, 2C), 128.5 (d, J = 3.1 Hz), 124.9, 121.5, 119.5, 118.0, 116.4 (d, J = 22.0 Hz, 2C), 112.7, 87.8; FTIR (KBr, cm^{-1}): 3302, 2222, 1715, 1608, 1511, 1468, 1330, 1240, 1213, 1103, 965, 844; HRMS (ES TOF) calc'd for $C_{16}H_9FN_2NaO$ (M + Na)$^+$ 287.0591, found 287.0590 (0.5 ppm).

(*E*)-2-(3-Chlorophenyl)-2-(3-oxoindolin-2-ylidene)acetonitrile (2ah). This compound was prepared according to the typical procedure B employing (*E*)-3-(3-chlorophenyl)-1-(2-nitrophenyl) prop-2-en-1-one (**1ah**) (287 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 3. Yield 185 mg (0.66 mmol, 66%), orange solid, mp 267–269 °C (EtOH), R_f 0.57 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 7.66 (d, J = 7.5 Hz, 2H), 7.64–7.51 (m, 4H), 7.09 (d, J = 8.0 Hz, 1H), 7.04 (t, J = 7.4 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) 184.2, 152.4, 143.2, 137.6, 134.2, 133.9, 131.2, 129.0, 128.5, 127.6, 125.0, 121.7, 119.4, 117.7, 112.7, 87.0; FTIR (KBr, cm^{-1}): 3289, 2215, 1709, 1458, 1243, 1096, 1016; HRMS (ES TOF) calc'd for $C_{16}H_9ClN_2NaO^+$ (M + Na)$^+$ 303.0296, found 303.0293 (1.0 ppm).

(*E*)-2-(4-Chlorophenyl)-2-(3-oxoindolin-2-ylidene)acetonitrile (2ai). This compound was prepared according to the typical procedure B employing (*E*)-3-(4-chlorophenyl)-1-(2-nitrophenyl) prop-2-en-1-one (**1ai**) (287 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, gradient 1 : 2–1 : 1. Yield 160 mg (0.57 mmol, 57%), orange crystals, mp 285.9–287.8 °C (EtOH), R_f 0.22 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 7.74–7.51 (m, 6H), 7.13–6.94 (m,

2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.2, 152.4, 142.9, 137.6, 133.7, 131.0, 130.7 (2C), 129.4 (2C), 125.0, 121.6, 119.5, 117.8, 112.7, 87.5; FTIR (KBr, cm^{-1}): 3282, 2222, 1715, 1601, 1468, 1407, 1336, 1250, 1096, 1015, 841; HRMS (ES TOF) calc'd for $C_{16}H_9ClN_2NaO$ (M + Na)$^+$ 303.0296, found 303.0297 (0.5 ppm).

(*E*)-2-(4-Bromophenyl)-2-(3-oxoindolin-2-ylidene)acetonitrile (2aj). This compound was prepared according to the typical procedure employing (*E*)-3-(4-bromophenyl)-1-(2-nitrophenyl) prop-2-en-1-one (**1aj**) (331 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, gradient 1 : 4–1 : 2. Yield 297 mg (0.92 mmol, 92%), red crystals, mp 278.8–282.5 °C (EtOH), R_f 0.66 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.55 (s, 1H), 7.76 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 7.5 Hz, 1H), 7.58 (d, J = 8.1 Hz, 3H), 7.07 (d, J = 8.0 Hz, 1H), 7.03 (t, J = 7.5 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.2, 152.4, 142.9, 137.6, 132.3 (2C), 131.4, 130.9 (2C), 125.0, 122.4, 121.6, 119.4, 117.7, 112.7, 87.5; FTIR (KBr, cm^{-1}): 3282, 3060, 2215, 1712, 1602, 1487, 1464, 1407, 1333, 1243; HRMS (ES TOF) calc'd for $C_{16}H_9BrN_2NaO$ (M + Na)$^+$ 346.9790, found 346.9790 (0.2 ppm).

(*E*)-2-(4-Methoxyphenyl)-2-(3-oxoindolin-2-ylidene) acetonitrile (2ak). This compound was prepared according to the typical procedure B employing (*E*)-3-(4-methoxyphenyl)-1-(2-nitrophenyl)prop-2-en-1-one (**1ak**) (283 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 2–1 : 1. Yield 199 mg (0.72 mmol, 72%), red crystals, mp 250.1–251.1 °C (EtOH), lit.[44] mp 245–247 °C, R_f 0.23 (EtOAc/hexanes 1 : 2), R_f 0.43 (EtOAc/hexanes 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.41 (s, 1H), 7.60 (td, J = 15.9, 7.6 Hz, 4H), 7.11 (dd, J = 14.9, 8.4 Hz, 3H), 7.01 (t, J = 7.4 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.1, 159.8, 152.4, 141.6, 137.3, 130.4 (2C), 124.8, 124.1, 121.3, 119.6, 118.0, 114.8 (2C), 112.7, 89.4, 55.5; FTIR (KBr, cm^{-1}): 3289, 3060, 2208, 1705, 1594, 1300, 1246, 1176; HRMS (ES TOF) calc'd for $C_{17}H_{12}N_2NaO_2$ (M + Na)$^+$ 299.0791, found 299.0794 (1.0 ppm).

(*E*)-2-(4-(Dimethylamino)phenyl)-2-(3-oxoindolin-2-ylidene) acetonitrile (2al). This compound was prepared according to the typical procedure B employing (*E*)-3-(4-(dimethylamino) phenyl)-1-(2-nitrophenyl)prop-2-en-1-one (**1al**) (296 mg, 1.00 mmol). Reaction time was extended to 3 h at the first stage, and to 1 h at the second stage. Eluent for chromatographic purification: EtOAc/hexanes, 1 : 1. Yield 135 mg (0.47 mmol, 47%), violet crystals, mp 234.8–237.6 °C (EtOH), lit.[44] mp 220–225 °C, R_f 0.20 (EtOAc/hexanes 1 : 2), R_f 0.69 (EtOAc/hexanes 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 7.63 (d, J = 7.4 Hz, 1H), 7.55 (t, J = 9.7 Hz, 3H), 7.12 (d, J = 8.0 Hz, 1H), 7.00 (t, J = 7.3 Hz, 1H), 6.87 (d, J = 8.6 Hz, 2H), 3.01 (s, 6H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 183.7, 152.2, 150.5, 139.7, 136.8, 130.0 (2C), 124.5, 121.0, 119.8, 118.6, 118.0, 112.8, 112.3 (2C), 91.4, 39.8 (2C); FTIR (KBr, cm^{-1}): 3315, 2899, 2798, 2201, 1698, 1608, 1521, 1364, 1323, 1199; HRMS (ES TOF) calc'd for $C_{18}H_{15}N_3NaO$ (M + Na)$^+$ 312.1107, found 312.1110 (−0.8 ppm).

(*E*)-2-(3-Oxoindolin-2-ylidene)-2-(pyridin-2-yl)acetonitrile (2am). This compound was prepared according to the typical procedure B employing (*E*)-1-(2-nitrophenyl)-3-(pyridin-2-yl) prop-2-en-1-one (**1am**) (254 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc/hexanes, 1 : 2. Yield 151 mg (0.61 mmol, 61%), purple crystals, mp 202.6–204.9 °C (EtOH), R_f 0.36 (EtOAc/hexanes 1 : 2); ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.69 (s, 1H), 8.76 (d, J = 3.9 Hz, 1H), 8.00 (t, J = 7.2 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.72–7.54 (m, 2H), 7.49–7.28 (m, 2H), 7.05 (t, J = 7.4 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 185.2, 152.4, 151.8, 149.2, 143.2, 138.0, 137.6, 125.0, 122.6, 122.5, 122.2, 119.1, 116.6, 113.5, 85.0; FTIR (KBr, cm^{-1}): 3228, 3121, 2214, 1708, 1591, 1464, 1434, 1343, 1236; HRMS (ES TOF) calc'd for $C_{15}H_9N_3NaO$ (M + Na)$^+$ 270.0638, found 270.0640 (0.9 ppm).

(*E*)-2-(3-Oxoindolin-2-ylidene)-2-(pyridin-3-yl)acetonitrile (2an). This compound was prepared according to the typical procedure B employing (*E*)-1-(2-nitrophenyl)-3-(pyridin-3-yl) prop-2-en-1-one (**1an**) (254 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc. Yield 138 mg (0.56 mmol, 56%), light-brown crystals, mp 208.1–211.1 °C (EtOH), R_f 0.34 (EtOAc); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.71 (s, 1H), 8.83 (d, J = 1.2 Hz, 1H), 8.66 (d, J = 3.9 Hz, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.63–7.54 (m, 2H), 7.21–6.93 (m, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.1, 152.4, 149.6, 149.4, 143.5, 137.7, 136.4, 128.6, 125.1, 124.2, 121.7, 119.4, 117.6, 112.7, 85.2; FTIR (KBr, cm^{-1}): 3557, 2215, 1712, 1622, 1591, 1541, 1467, 1417, 1387, 1337, 1219, 1190, 1136; HRMS (ES TOF) calc'd for $C_{15}H_9N_3NaO$ (M + Na)$^+$ 270.0638, found 270.0635 (1.0 ppm).

(*E*)-2-(3-Oxoindolin-2-ylidene)-2-(pyridin-4-yl)acetonitrile (2ao). This compound was prepared according to the typical procedure B employing (*E*)-1-(2-nitrophenyl)-3-(pyridin-4-yl) prop-2-en-1-one (**1ao**) (254 mg, 1.00 mmol). Eluent for chromatographic purification: EtOAc – EtOH/EtOAc, 1 : 3. Yield 131 mg (0.53 mmol, 53%), red crystals, mp 266.3–268.4 °C (EtOH), R_f 0.17 (EtOAc), 0.65 (EtOH/EtOAc 1 : 3); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.78 (s, 1H), 8.74 (d, J = 5.7 Hz, 2H), 7.67 (d, J = 7.5 Hz, 1H), 7.60 (t, J = 7.1 Hz, 3H), 7.10 (d, J = 8.0 Hz, 1H), 7.06 (t, J = 7.4 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.3, 152.3, 150.5 (2C), 143.8, 140.1, 137.8, 125.2, 122.9 (2C), 122.1, 119.3, 117.2, 112.8, 85.3; FTIR (KBr, cm^{-1}): 2993, 2221, 1742, 1718, 1598, 1557, 1517, 1373, 1250, 1206; HRMS (ES TOF) calc'd for $C_{15}H_9N_3NaO$ (M + Na)$^+$ 270.0638, found 270.0630 (2.7 ppm).

(*E*)-2-(Benzo[*d*][1,3]dioxol-5-yl)-2-(3-oxoindolin-2-ylidene) acetonitrile (2ap). This compound was prepared according to the typical procedure B employing (*E*)-3-(benzo[*d*][1,3]dioxol-5-yl)-1-(2-nitrophenyl)prop-2-en-1-one (**1ap**) (297 mg, 1.00 mmol). The title compound was obtained as red solid, mp 247.9–248.7 °C. R_f 0.62 (EtOAc/Hex, 1 : 2). Yield 133 mg (0.46 mmol, 46%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.41 (s, 1H), 7.64 (d, J = 7.6 Hz, 1H), 7.57 (t, J = 7.6 Hz, 1H), 7.23–7.07 (m, 4H), 7.01 (t, J = 7.4 Hz, 1H), 6.14 (s, 2H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 184.1, 152.4, 148.1, 148.0, 141.9, 137.4, 125.7, 124.8, 123.6, 121.4, 119.6, 118.0, 112.7, 109.2, 108.9, 101.9, 89.2; FTIR (film, NaCl, cm^{-1}): 3316, 2926, 2208, 1712, 1595, 1481, 1350, 1247, 1206, 1046; HRMS (ES TOF) calc'd for $C_{17}H_{10}N_2NaO_3$ (M + Na)$^+$ 313.0584, found 313.0586 (0.8 ppm).

(*E*)-2-(5,6-Dimethoxy-3-oxoindolin-2-ylidene)-2-phenylacetonitrile (2ba). This compound was prepared according to the typical procedure B employing (*E*)-1-(4,5-dimethoxy-2-nitrophenyl)-3-phenylprop-2-en-1-one (**1ba**) (313 mg, 1.00 mmol). Reaction time was extended to 1 h at the

first stage of the reaction. Eluent for chromatographic purification: EtOAc/hexanes, 1 : 1. Yield 156 mg (0.51 mmol, 51%), purple crystals, mp 205.2–207.6 °C (EtOH), R_f 0.47 (EtOAc/hexanes 1 : 1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.13 (s, 1H), 7.62 (d, J = 7.5 Hz, 2H), 7.55 (t, J = 7.5 Hz, 2H), 7.47 (t, J = 7.1 Hz, 1H), 7.07 (s, 1H), 6.62 (s, 1H), 3.85 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 181.9, 157.8, 150.2, 144.9, 143.9, 132.3, 129.3 (2C), 129.0, 128.8 (2C), 118.0, 110.4, 105.8, 95.9, 88.5, 56.1, 55.9; FTIR (KBr, cm^{-1}): 3282, 3000, 2839, 2215, 1682, 1598, 1491, 1441, 1323, 1203, 1172; HRMS (ES TOF) calc'd for $C_{18}H_{14}N_2NaO_3$ (M + Na)$^+$ 329.0897, found 329.0901 (1.3 ppm).

It should be pointed out, that preparation of basic compounds, containing dimethylamine functionality (**2al**) or pyridine ring (**2am–2ao**) requires twice more acetic acid (80 mg) at the second stage of the procedure. It is also worth mentioning that these compounds slowly decompose in solutions of ethyl acetate or acetone, but perfectly shelf-stable in crystalline form.

Conflicts of interest

There are no conflicts to declare.

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