Activation of the *N*C–H bond of Morita–Baylis–Hillman adducts of *N*-substituted isatins with cerium ammonium nitrate (CAN) and alcohol (ROH)

Ponnusamy Shanmugam and Vadivel Vaithiyanathan

Abstract: A study on the activation of the *N*C–H bond of Morita–Baylis–Hillman adducts of *N*-substituted isatin with cerium ammonium nitrate (CAN) and saturated and unsaturated alcohols have been carried out. The choice of a Morita–Baylis–Hillman adduct for this study is screened with a number of adducts. A comparative and reactivity pattern study on *N*C-H activation of Morita–Baylis–Hillman adducts of *N*-substituted isatin derivatives viz. *N*-methyl, *N*-ethyl, *N*-methyl acetate, *N*-benzyl, *N*-propargyl, and *N*-isopropyl isatins have been carried out. Effect of aryl ring substitution has also been investigated. A plausible mechanism for the formation of the ether products has been outlined.

Key words: cerium ammonium nitrate (CAN), Morita–Baylis–Hillman adduct, *N*-CH activation, functionalised ethers, nitration.

Résumé : On a effectué une étude sur l'activation, par le nitrate d'ammonium cérique (NAC), de la liaison *N*C-H d'adduits Morita–Baylis–Hillman d'isatine *N*-substituée et d'alcools saturés et non saturés. Le choix de l'adduit Morita–Baylis–Hillman pour cette étude est évalué avec un certain nombre d'adduits. On a aussi réalisé une étude comparative et une étude de patron de réactivité sur l'activation *N*C-H d'adduits Morita–Baylis–Hillman d'isatines *N*-substituées, entre autre par des groupes *N*-méthyle, *N*-éthyle, *N*-méthylacétate, *N*-benzyle, *N*-propargyle et *N*-isopropyle. On a aussi étudié l'effet de la substitution sur les groupes aryles. On propose un mécanisme plausible pour la formation d'éthers comme produits.

Mots-clés : NAC, adduit de Morita–Baylis–Hillman, activation *N*C-H, éthers fonctionnalisés, nitration.

[Traduit par la Rédaction]

Introduction

The C–H bond activation method is one of the challenging synthetic routes in organic synthesis.[1–12] Activation of C–H bonds particularly by oxidative processes[1–5] and by organometallic reagents[6–12] has been of great interest to organic chemists in recent years. Cerium(IV) ammonium nitrate (CAN) has emerged as a versatile reagent for a number of synthetic transformations.[13,14] The synthetic flexibility of isatin and its derivatives has led to the extensive use of this compound in synthetic organic chemistry.[15] Recently, the Morita–Baylis–Hillman (MBH) reaction has emerged as an important carbon–carbon bond, forming reactions that, in general, afford densely functionalized molecular frame works and the reaction is considered as atom economic.[16–19] As part of our ongoing research in the area of novel synthetic methodologies based on MBH adducts,[20–26] we have reported the preliminary results on activation of the *N*C–H bond of MBH adducts of *N*-methylisatin with CAN/ROH (alcohol).[27] In continuation of the work, a detailed study on *N*C-H activation of various MBH derivatives of *N*-substituted isatins with CAN as a one electron oxidant and with a number of alcohols as reagents was carried out. The details of this study are the subject matter of this paper.

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Results and discussion

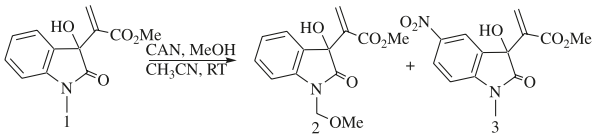
Optimization of the *N*C-H activation and choice of MBH adducts of isatin

The optimization studies were initiated using the MBH adduct of *N*-methylisatin (**1**) as a model substrate. The preliminary study and results are shown in Table 1. Initially, adduct **1** was treated with 2 equiv. of CAN and excess methanol (10 mL) to afford the *N*C-H activated product **2** in trace amount (5%) (Table 1, entry 1). Repeating the reaction with 3 equiv. of CAN and MeOH (5 mL) for 12 h afforded **2** in a slightly improved yield (10%, Table 1, entry 2). Fine-tuning of the reaction conditions is shown in Table 1. Thus, the optimum condition was found as 4 equiv. of CAN and MeOH (1.6 mL, 40 equiv.) and CH_3CN (0.5 mL) and at room temperature (RT) for 24 h (Table 1, entry 4).

Further, to examine the selectivity and structural requirements of *N*-methyl isatin derivatives for *N*C-H activation, we chose different isatin derivatives (**1, 4–9**), as shown in Fig. 1.

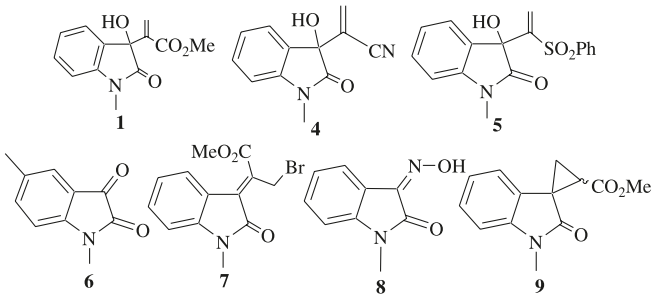
Under the optimized condition, MBH adducts **1, 4**, and **5** of *N*-methyl isatin afforded the ether products **2, 10**, and **12** in 24%–66% yields and the nitrated compound **3, 11**, and **13** in trace-30% yields, respectively (Table 2, entries 1–3). In-

Table 1. Optimization of the *N*C-H activation of 1 with CAN/MeOH.



					Yield (%)	
Entry	MeOH (mL)	CH_3CN (mL)	CAN (equiv.)	Time (h)	**2**	**3**
1	10.0	—	2.0	12	5	—
2	5.0	—	3.0	12	10	—
3	3.0	3.0	4.0	24	20	35
4	1.6	0.5	4.0	24	66	30

Fig. 1. A Choice of different isatin derivatives (1, 4–9) for C-H activation.



terestingly, the simple *N*-methyl isatin **6** yielded only the nitrated product **14** in 15% yields. Other *N*-methylisatin derivatives such as the bromo-derived adduct (**7**), oxime derivative of *N*-methyl isatin (**8**), and *N*-methyl-3-spirocyclopropyl-2-indolone (**9**) did not yield any *N*C-H activated ether product or nitrated product. The results of the preliminary investigation are summarized in Table 2. Hence, the study showed that the MBH adduct of *N*-methyl isatin was the most suitable substrate for *N*C-H activation reaction.

Excellent preliminary results on *N*C-H activation of MBH adduct of *N*-methyl isatin prompted us to investigate a systematic activation study of various *N*-substituted MBH adducts of isatin derivatives. Thus, we chose various MBH adducts with different *N*-alkyl substitutions such as methyl, methylene, and methine, which in principle generate 1•, 2•, and 3• radical cation intermediates during the *N*C-H activation process (Fig. 2).

*N*C-H activation study of primary methyl radical sources

To investigate the *N*C-H activation via primary radical cation intermediates, MBH adducts **1, 3, 4**, and **15** were chosen (Fig. 3.) and the details are discussed in the following section.

NC-*H activation of MBH adducts of* N-*methyl isatin 1 and 4*

As discussed earlier, during the optimization study the MBH adduct **1** with CAN/MeOH afforded the products **2** (ether) and **3** (nitrate). This observation prompted us to further explore the study using adducts **1** and **4** with various saturated and unsaturated 1• alcohols (R^4OH)/CAN. The reactions afforded the *N*C-H activated ethers **10** and **16–23** along with nitrated products **3** and **11** in moderate yield (Table 3, entries 1–9). Notably, the reaction of MBH adduct **1** with 2•- and 3•-alcohols (isopropanol and *t*-butanol) did not yield any *N*C-H activated product and only the nitrated product **3** was obtained in good yields (Table 3, entries 10 and 11). However, the reactions with allyl alcohol/CAN and cinnamyl alcohol/CAN did not afford the *N*C-H activated product. Only alcohol oxidation was observed during the course of the reaction (Table 3, entries 12 and 13). All the new compounds were characterized by spectroscopic (IR, ^1H, and ^{13}C NMR) and HRMS data. The results are summarized in Table 3.

Table 2. *N*C-H activation reactions of isatin derivatives.

		Products		Yield (%)	
Entry	Substrate	Ether (A)	Nitrates (B)	A	B
1	**1**	**2**	**3**	66	30
2	**4**	**10**	**11**	50	30
3	**5**	**12**	**13**	24	Trace
4	**6**	—	**14**	—	15
5	**7**	—	—	—	—
6	**8**	—	—	—	—
7	**9**	—	—	—	—

Fig. 2. Choice of different sources of MBH adduct of isatin derivatives for *N*C-H activation.

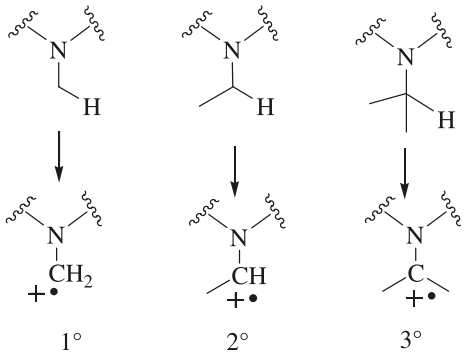
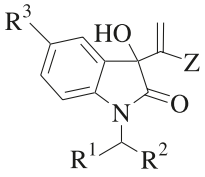


Fig. 3. Choice of different MBH adducts having a methyl *N*C-H source.

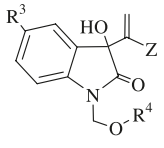


R^1 = H; R^2 =H; R^3=H; Z =CO_2Me **1**
R^1 = H; R^2 =H; R^3 =NO_2; Z =CO_2Me **3**
R^1 = H; R^2 =H; R^3 =H; Z =CN **4**
R^1 = H; R^2 =H; R^3 =Br; Z =CO_2Me **15**

Effect of aryl ring substitution on NC-*H activation of MBH adducts 15 and 3*

To circumvent nitration and to check the effect of substitution at the aryl ring, we examined the activation study with MBH adduct **15** with CAN and alcohols such as methanol, ethanol, homopropargyl alcohol, and *t*-butanol. The reactions underwent smoothly at an enhanced rate (1.5–2 h) and afforded the *N*C-H activated compounds (**24–27**) in good yields (Table 3, entries 14–17). Investigation on the effect of substitution and to understand the reactivity pattern

Table 3. Results of *N*C-H activation study of primary methyl radical sources.



R^3 = H; R^4 = Et; Z = CO_2Me **16**
R^3 = H; R^4 = H_2C—≡; Z = CO_2Me **17**
R^3 = H; R^4 = H_2C (propargyl); Z = CO_2Me **18**
R^3 = H; R^4 = H_2C—OH; Z = CO_2Me **19**
R^3 = H; R^4 = H_2C—OH; Z = CO_2Me **20**
R^3 = H; R^4 = CH_2Ph; Z = CO_2Me **21**
R^3 = H; R^4 = Me; Z = CN **10**
R^3 = H; R^4 = Et; Z = CN **22**
R^3 = H; R^4 = H_2C—≡; Z = CN **23**
R^3 = Br; R^4 = Me; Z = CO_2Me **24**
R^3 = Br; R^4 = Et; Z = CO_2Me **25**
R^3 = Br; R^4 = H_2C (propargyl); Z = CO_2Me **26**
R^3 = Br; R^4 = ^{t}Bu; Z = CO_2Me **27**

				Products		Yield (%)	
Entry	MBHA	Alcohol (R^4)	Time (h)	*N*C-H activation (A)	Nitration (B)	A	B
1	**1**	EtOH	24	**16**	—	52	—
2	**1**	Propargyl	24	**17**	—	51	—
3	**1**	Homopropargyl	24	**18**	**3**	58	25
4	**1**	Ethane-1,2-diol	24	**19**	—	55	—
5	**1**	Propane-1,3-diol	24	**20**	—	67	—
6	**1**	Benzyl alcohol	24	**21**	—	59	—
7	**4**	MeOH	24	**10**	**11**	50	30
8	**4**	EtOH	24	**22**	**11**	53	27
9	**4**	Propargyl	24	**23**	**11**	57	35
10	**1**	Isopropanol	24	—	**3**	—	54
11	**1**	*t*-Butanol	24	—	**3**	—	65
12	**1**	Allyl alcohol	24	—	—	—	—
13	**1**	Cinnamyl	24	—	—	—	—
14	**15**	MeOH	2.0	**24**	—	52	—
15	**15**	EtOH	2.0	**25**	—	51	—
16	**15**	Homopropargyl	1.0	**26**	—	58	—
17	**15**	*t*-BuOH	1.5	**27**	—	55	—
18	**3**	EtOH	48	—	—	—	—
19	**3**	MeOH	48	—	—	—	—

of adducts due to electron withdrawing substitution, the reactions with 5-nitro substituted adduct **3** in methanol and ethanol were tested (Table 3, entries 18 and 19). No *N*C-H activation was found even after allowing the reaction to proceed for a longer period of time (48 h) and with an excess of CAN (6 equiv.); only starting material was recovered quantitatively.

*N*C-H activation study of secondary methylene radical sources

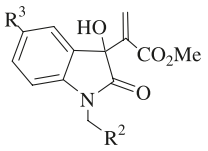
To inspect and understand the *N*C-H activation reaction, which proceeded through a secondary radical intermediate, MBH adducts **28**–**35** were chosen (Fig. 4).

A general synthesis of MBH adducts **28–35** is shown in Scheme 1. Accordingly, *N*-alkylation of isatin was carried out with CaH_2 and alkyl halide in DMF at 60 °C to afford *N*-alkyl isatins in excellent yield. The MBH adducts formation of *N*-alkyl isatins with methyl acrylate and DABCO (1,4-diazabicyclo[2.2.2]octane) in methanol afforded the desired MBH adducts (**28–35**) in excellent yield.

Activation study of MBH adducts 28 and 29 of N-*ethyl isatin*

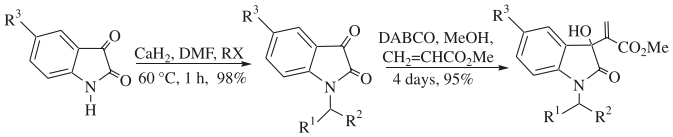
Activation reaction of adduct **28** with CAN/MeOH in CH_3CN for 24 h provided only the nitrated compound **36**

Fig. 4. Choice of different MBH adducts having a methylene *N*C-H source.



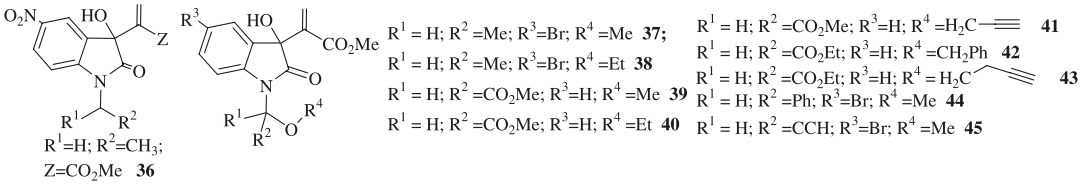
R^2 = CH_3; R^3 = H **28;** R^2 = CH_3; R^3 = Br **29;**
R^2 = CO_2Me; R^3 = H **30;** R^2 = CO_2Et; R^3 = H **31;**
R^2 = Ph; R^3 = H **32;** R^2 = Ph; R^3 = Br **33;**
R^2 = CCH; R^3 = H **34;** R^2 = CCH; R^3 = Br **35**

Scheme 1. Synthesis of MBH adducts 28–35.



and no *N*C-H activated product was observed (Table 4, entry 1). Experiments with other alcohols such as ethanol, propargyl alcohol, and propane-1,3-diol provided only nitrated compound **36** and no *N*C-H activated product was observed in all the cases (Table 4, entries 2–4). The structure of nitrated compound **36** was analyzed by spectroscopic studies. The number of aromatic protons and chemical shifts were the tool for detection of nitration. Accordingly, in the aromatic region, a doublet at δ 6.97 due to ortho coupling (J = 8.6 Hz, 1H), meta coupled doublet at δ 8.04 (J =

Table 4. Results of the *N*C-H activation study of secondary methylene radical sources.



				Products		Yield (%)	
Entry	MBHA	Alcohol (R^4)	Time (h)	*N*C-H activation (A)	Nitration (B)	A	B
1	**28**	MeOH	24	—	**3**	—	56
2	**28**	EtOH	24	—	**36**	—	49
3	**28**	Propargyl alcohol	24	—	**36**	—	45
4	**28**	Propane-1,3-diol	24	—	**36**	—	55
5	**29**	MeOH	48	**37**	—	Trace	—
6	**29**	EtOH	48	**38**	—	Trace	—
7	**30**	MeOH	24	**39**	—	58	—
8	**30**	EtOH	24	**40**	—	49	—
9	**30**	Propargylol	24	**41**	—	55	—
10	**31**	Benzylol	24	**42**	—	47	—
11	**31**	Homopropargylol	24	**43**	—	54	—
12	**32**	MeOH	24	—	—	—	—
13	**32**	EtOH	24	—	—	—	—
14	**33**	MeOH	24	**44**	—	47	—
15	**34**	EtOH	24	—	—	—	—
16	**34**	MeOH	24	—	—	—	—
17	**35**	MeOH	2	**45**	—	85	—

2.3 Hz, 1H), and one doublet of doublet at δ 8.31 (J = 8.6, 2.3 Hz, 1H) due to ortho and meta couplings appeared. The alkyl and olefin region were similar to that of starting material **28**. To demonstrate and to check the effect of electron donating substitution at the aryl ring on *N*C-H activation, another adduct (**29**) was selected. Reactions in methanol and ethanol were carried out (Table 4, entries 5 and 6). To our surprise, we found only a trace of *N*C-H activated product formation (**37**, **38**) as evidenced from its ^{1}H NMR of crude reaction mixture at regular intervals for 48 h.

Activation study of MBH adduct of N-*methyl/ethyl acetate isatin 30 and 31*

Since, the compound **28** with electron releasing substitution at α to the *N*C-H bond did not yield any C-H activation products, we considered checking electron withdrawing substitution at α to the *N*C-H bond for *N*C-H activation of MBH adduct such as **30**. In contrast to the substrates **28** and **29**, activation of adduct **30** with CAN/methanol under optimized reaction condition provided a good yield of *N*C-H activated product **39** (Table 4, entry 7). The presence of -OMe group due to *N*C-H activation in the product **39** was confirmed from its ^{1}H NMR spectrum. Thus, the methoxy protons were observed at δ 3.63 as a singlet and the methine proton was observed as a singlet at δ 5.96. The reactions with ethanol and propargyl alcohol were also tested and the respective *N*C-H activated products (**40** and **41**) were isolated in moderate to good yields (Table 4, entries 8 and 9). Similarly, reactions of adduct **31** with benzyl alcohol and homopropargyl alcohol afforded the corresponding *N*C-H activated products **42** and **43**, respectively (Table 4, entries 10 and 11).

Activation study on MBH adduct of N-*benzyl and propargyl derivatives of isatin 32–35*

Having surprising results obtained from adducts **30** and **31**, we were interested in surveying the *N*C-H activation of highly functionalized MBH adducts **32–33** and **34–35** of *N*-benzyl and *N*-propargyl isatins, respectively. The desired adducts **32–33** and **34–35** were synthesized using standard procedure described earlier (Scheme 1).

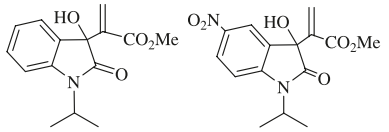
The adduct **32** with CAN/methanol and CAN/ethanol under optimized reaction conditions yielded neither *N*C-H activated product nor nitrated derivative and the starting material was recovered quantitatively (Table 4, entries 12 and 13). However, the 5-bromo MBH adduct **33** afforded the desired *N*C-H activated product (**44**) in good yield (Table 4, entry 14). In the case of adduct (**34**), the reaction mixture became complex (TLC) with CAN/methanol and CAN/ethanol mixture and no *N*C-H activated and nitrated product was obtained (Table 4, entries 15 and 16), while the adduct **35** provided an excellent yield of *N*C-H activated product **45** in 2 h (Table 4, entry 17).

*N*C-H activation study of tertiary methine radical source *N*-isopropyl isatin (46)

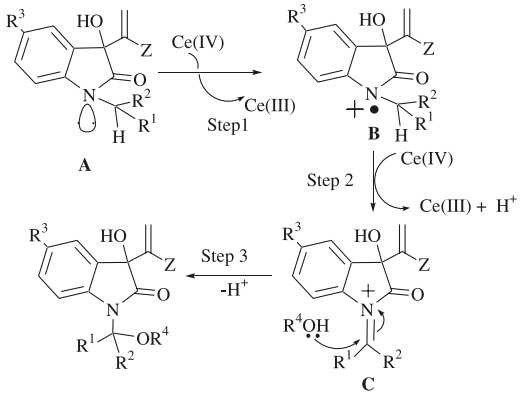
For a comparative study on *N*-alkyl series of isatin derivatives, we chose the MBH adduct of *N*-isopropyl isatin (**46**) as substrate, which is believed to precede the *N*C-H activation via a tertiary radical intermediate (Fig. 5). Adduct **46** was prepared under standard procedure described earlier.

The *N*C-H activation of adduct **46** with CAN/MeOH, under optimized condition did not yield any *N*C-H activated product, instead only a moderate yield of nitrated product **47**

Fig. 5. Choice of MBH adducts having methine *N*C-H source.



Scheme 2. A plausible mechanism for ether formation.



was obtained. Similarly, reactions with ethanol, propargyl alcohol, and propane-1,3-diol furnished only nitrated compound **47**. The results are collected in Tables 2 and 3. The structure of nitrated compound **47** was confirmed from its proton NMR data. Thus, the aromatic protons in **47** showed an ortho coupled doublet at δ 7.10 (J = 8.7 Hz, 1H), a meta coupled doublet at δ 8.03 (J = 2.3 Hz, 1H), and ortho-meta coupled doublet of doublet at δ 8.28 (J = 2.3, 8.7 Hz, 1H). The alkyl and olefin region were similar to that of starting material **46**.

A plausible mechanism of *N*-CH activation/nitration

A plausible mechanism for the formation of the ether products is delineated in Scheme 2. In the first step, the MBH adduct **A** is oxidized by CAN to form a radical cation[28–30] **B**. Further oxidation of radical cation **B** and liberation of H^+ by CAN produce a cation intermediate **C**, which is quenched by alcohol to afford the *N*C-H activated ether product. The proposed mechanism is supported from the results obtained in the studies. It should be noted that for comparison among MBH adducts **1**, **15**, and **3,** only adduct **15** underwent *N*C-H activation in 1.5–2.0 h whilst adduct **1** took 24 h for *N*C-H activation and adduct **3** did not provide any *N*C-H activation product with a clear indication of direct involvement of the nitrogen lone pair in the reaction mechanism.

The reactivity nature of MBH adducts **28**–**35** and **46** towards *N*C-H activation can be explained based on the effect of bulky substitution, which reduces the availability of lone pair on the nitrogen atom, which prevents the first step oxidation and less approach possibility by bulky reagent Ce(IV) towards nitrogen in adducts **28**, **32**, **34**, and **46**. The 5-bromo substitution, which increases the electron density on nitrogen, is clearly found from the reactivity of adducts **29** (trace of *N*C-H activation, 48 h), **33** (47% *N*C-H activation, 24 h), and **35** (85% *N*C-H activation, 2 h). However, quite the opposite occurs; the nitro substituent, having direct resonance

Fig. 6. Effect of substitution and magnitude of lone pair availability on nitrogen.

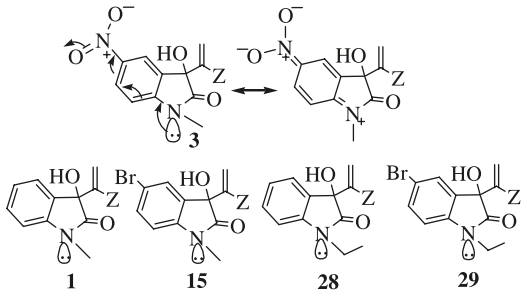
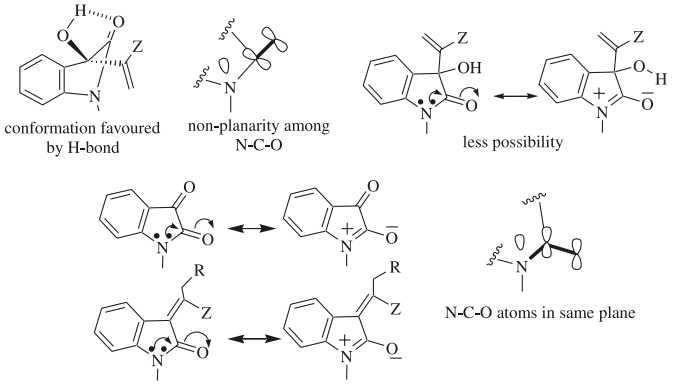


Fig. 7. Selectivity reason for *N*C-H activation towards MBH adducts alone.



with nitrogen lone pair, averts the reactivity of the adduct **3**. A pictorial representation for substitution effect and magnitude of nitrogen lone pair is shown in Fig. 6. The nitration mechanism of the aromatic ring with CAN is well known in the literature.[31]

The selectivity reason for *N*C-H activation towards MBH adducts alone may be due to the conformation favoured by H-bonding in the adduct structure, which brings more availability of lone pair on nitrogen atom and avoids resonance with the adjacent carbonyl group. However, the highly planar structure in the compounds **6**–**9** allows the nitrogen lone pair to be in resonance with the adjacent carbonyl group. Hence, no *N*C-H activation happened with simple isatin derivatives (Fig. 7).

Conclusion

In conclusion, we have carried out a novel study on *N*C-H activation of various Morita–Baylis–Hillman adducts of *N*-substituted isatin with a number of alcohols using CAN as a single electron oxidizing agent. A plausible mechanism of the reaction is proposed. It is noteworthy that the compounds obtained here are highly functionalized and can be used for further synthetic manipulations. Further studies using the reagent system for novel synthetic methods are in progress in our laboratory.

Experimental

General consideration

Analytical thin layer chromatography was performed on silica gel TLC plates. Purification by gravity column chro-

matography was carried out using silica gel (100–200 mesh). Mixture of ethyl acetate and hexane and pure ethyl acetate were used as eluent as required. IR spectra were run on a Nicolet (impact 400D FT-IR) spectrophotometer. NMR spectra were obtained using chloroform-d as solvent on Bruker DPX 300 MHz NMR spectrometer. Chemical shifts are given in δ scale with TMS as the internal reference. HRMS were measured on the JMS 600 JEOL mass spectrometer. Yields refer to quantities obtained after chromatography. Solvents used are reagent grade and were purified before use according to the literature procedure.[32]

General experimental procedure for alkylation of isatin

A mixture of isatin (1 mmol), alkyl bromide/iodide (1.5 mmol), and calcium hydride (3 mmol) in DMF was stirred at 60 °C for 1 h. After completion of the reaction (monitored by TLC), the crude mixture was diluted with water, neutralized with 2 N HCl and extracted using ethyl acetate. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The crude product obtained was purified by silica gel chromatography using EtOAc–hexane (20:80) as eluent to afford the desired *N*-alkylisatin derivatives.

General procedure for the preparation of MBH adducts

A mixture of *N*-alkyl isatin (1 mmol), methyl acrylate (1.5 mmol), and DABCO (0.02 mmol) in MeOH (5 mL) was stirred at RT for 3–4 d. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with ethyl acetate. The organic layer was washed successively with 0.2 N HCl, water, and brine. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The crude product obtained was purified by silica gel column chromatography using EtOAc–hexane (20:80) as eluent to afford the desired MBH adducts of *N*-alkyl isatin.

Spectral data of MBH adducts 28, 30, 34, and 46

Methyl 2-(1-ethyl-3-hydroxy-2-oxoindolin-3-yl)acrylate (28)

Colourless solid. Mp 148–150 °C. R_f = 0.48 (25% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3341, 1723, 1615. ^1H NMR ($CDCl_3$) δ_H: 1.32 (3H, t, J = 7.2 Hz), 2.45 (1H, brs), 3.62 (3H, s), 3.74 (2H, q, J = 7.2 Hz), 6.41 (1H, s), 6.56 (1H, s), 6.88 (1H, d, J = 7.8 Hz), 7.05 (1H, t, J = 6.7 Hz), 7.19 (1H, d, J = 6.4 Hz), 7.32 (1H, t, J = 7.7 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 12.4, 52.3, 64.5, 70.5, 110.4, 123.6, 124.1, 128.0, 129.1, 130.72, 139.2, 143.3, 165.3, 176.5. Anal. calcd. for $C_{14}H_{15}NO_4$: 261.1001; found: 261.1000.

Methyl 2-(1-methylene carbomethoxy-3-hydroxy-2-oxoindolin-3-yl)acrylate (30)

Colourless waxy solid. R_f = 0.29 (25% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3350, 1716, 1615, 1087, 1063. ^1H NMR ($CDCl_3$) δ_H: 3.64 (3H, s), 3.78 (3H, s), 4.41 (1H, brs), 4. 41 (1H, d, J = 17.6 Hz), 4.61 (1H, d, J = 17.6 Hz), 6.44 (1H, s), 6.59 (1H, s), 6.74 (1H, d, J = 7.8 Hz), 7.06 (1H, t, J = 7.4 Hz), 7.06–7.34 (2H, m). ^{13}C NMR ($CDCl_3$) δ_C: 41.4, 52.1, 52.7, 76.0, 108.6, 123.4, 124.1, 128.3, 129.4, 130.3, 138.5, 142.9, 165.2, 168.2, 176.0. Anal calcd. for $C_{15}H_{15}NO_6$: 305.0899; found: 305.0896.

Methyl 2-(3-hydroxy-2-oxo-1-(prop-2-ynyl) indolin-3-yl)acrylate (34)

Colourless waxy solid. R_f = 0.34 (25% EtOAc–Hexanes). ν_{max}(CH_2Cl_2, cm^{-1}): 3425, 2131, 1718, 1611. ^1H NMR ($CDCl_3$) δ_H: 2.28 (1H, t, J = 2.2 Hz), 3.59 (3H, s), 4.07 (1H, s), 4.51–4.58 (2H, m), 6.44 (1H, s), 6.57 (1H, s), 7.04–7.09 (2H, m), 7.18 (1H, d, J = 6.48 Hz), 7.35 (1H, t, J = 7.6 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 29.5, 52.1, 72.6, 76.1, 76.6, 109.6, 123.3, 123.9, 128.1, 129.2, 130.2, 138.9, 142.5, 164.9, 175.4. Anal. calcd. for $C_{15}H_{13}NO_4$: 271.0845; found: 271.0841.

Methyl 2-(3-hydroxy-1-isopropyl-2-oxoindolin-3-yl)acrylate (46)

Colourless waxy solid. R_f = 0.42 (25% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3353, 1699, 1611. ^1H NMR ($CDCl_3$) δ_H: 1.52 (6H, d, J = 8.15 Hz), 3.55 (1H, br s), 3.61 (3H, s), 4.58 (1H, sept, J = 7.0 Hz), 6.42 (1H, s), 6.56 (1H, s), 7.02 (2H, d, J = 7.7 Hz), 7.17 (1H, d, J = 6.6 Hz), 7.30 (1H, t, J = 6.8 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 19.1 (2C), 43.3, 51.8, 75.8, 109.7, 122.3, 124.0, 127.6, 129.8 (2C), 139.3, 143.1, 164.8, 176.1. Anal. calcd. for $C_{15}H_{17}NO_4$: 275.1158; found: 275.1152.

General experimental procedure for *N*C-H activation

A mixture of MBH adduct (1 mmol), 4 equiv. of cerium ammonium nitrate (4 mmol), and 40 equiv. of ROH (1.6 mL) in CH_3CN (0.5 mL) was allowed to stir at RT for 2–48 h. The progress of reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure. The crude reaction mixture was extracted with dichloromethane and washed with water and brine. The organic layer was separated, dried (Na_2SO_4), and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography using gradient elution with hexane and hexane and EtOAc to afford pure functionalized ethers and aromatic nitrated products.

Spectral data for *N*C-H activated compounds

Methyl 2-(3-hydroxy-1-(methoxy methyl)-2-oxoindolin-3-yl)acrylate (2)

Waxy solid. R_f = 0.35 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3386, 1716, 1085, 1063. ^1H NMR ($CDCl_3$) δ_H: 2.57 (1H, bs), 3.41 (3H, s), 3.65 (3H, s), 5.13 (1H, d, J = 11.1 Hz), 5.17 (1H, d, J = 11.1 Hz), 6.42 (1H, s), 6.59 (1H, s), 7.06–7.10 (2H, m), 7.20 (1H, d, J = 7.5 Hz), 7.32 (1H, t, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 52.5, 53.2, 70.5, 76.6, 110.4, 123.7, 124.1, 127.8, 129.1, 130.6, 139.5, 143.3, 164.8, 176.9. Anal. calcd. for $C_{14}H_{15}NO_5$: 277.0950; found: 277.0947.

2-(3-Hydroxy-1-(methoxymethyl)-2-oxoindolin-3-yl)acrylonitrile (10)

Waxy solid. R_f = 0.44 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3376, 2209, 1726, 1614, 1087. ^1H NMR ($CDCl_3$) δ_H: 3.36 (3H, s), 4.07 (1H, s), 5.10 (1H, d, J = 10.9 Hz), 5.19 (1H, d, J = 10.9 Hz), 6.21 (1H, s), 6.39 (1H, s), 7.12 (1H, d, J = 7.7 Hz), 7.17 (1H, t, J = 8.1 Hz), 7.41 (2H, d, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 52.1, 70.7, 76.7, 110.8,

115.5, 123.2, 123.9, 124.8, 126.8, 128.1, 131.5, 142.5, 176.3. Anal. calcd. for $C_{13}H_{12}N_2O_3$: 244.0848; found: 244.0836.

Methyl 2-(1-(ethoxymethyl)-3-hydroxy-2-oxoindolin-3-yl)acrylate (16)

Waxy solid. R_f = 0.43 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3382, 1716, 1089, 1053. ^1H NMR ($CDCl_3$) δ_H: 1.20 (3H, t, J = 6.9 Hz), 2.67 (1H, bs), 3.65 (5H, m), 5.17 (1H, d, J = 11.1 Hz), 5.22 (1H, d, J = 11.1 Hz), 6.43 (1H, s), 6.58 (1H, s), 7.05–7.13 (2H, m), 7.20 (1H, d, J = 7.2 Hz), 7.35 (1H, t, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 15.1, 52.3, 64.6, 70.5, 76.6, 110.4, 123.6, 124.1, 128.0, 128.9, 130.6, 139.2, 143.2, 165.2, 176.9. Anal. calcd. for $C_{15}H_{17}NO_5$: 291.1107; found: 291.1088.

Methyl 2-(3-hydroxy-2-oxo-1-((prop-2-ynyloxy)methyl) indolin-3-yl)acrylate (17)

Waxy solid. R_f = 0.37 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3390, 2210, 1716, 1615, 1087, 1064. ^1H NMR ($CDCl_3$) δ_H: 2.48 (1H, t, J = 2.4 Hz), 2.67 (1H, bs), 3.63 (3H, s), 4.28 (2H, d, J = 2.4 Hz), 5.20 (1H, d, J = 11.2 Hz), 5.37 (1H, d, J = 11.2 Hz), 6.48 (1H, s), 6.59 (1H, s), 7.05–7.20 (3H, m), 7.35 (1H, t, J = 7.6 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 30.5, 52.3, 56.3, 70.3, 75.5, 78.6, 110.7, 123.6, 124.2, 128.1, 129.1, 130.5, 139.3, 143.2, 165.3, 176.9. Anal. calcd. for $C_{16}H_{15}NO_5$: 301.0950; found: 301.0941.

Methyl 2-(1-[(but-3-ynyloxy)methyl]-3-hydroxy-2-oxoindolin-3-yl)acrylate (18)

Waxy solid. R_f = 0.47 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3406, 1716, 1614, 1089, 1050. ^1H NMR ($CDCl_3$) δ_H: 1.80 (1H, bs), 1.95 (1H, t, J = 2.4 Hz), 2.46 (2H, td, J = 6.6, 2.4 Hz), 3.63 (3H, s), 3.66 (2H, t, J = 6.6 Hz), 5.20 (1H, d, J = 11.1 Hz), 5.28 (1H, d, J = 11.1 Hz), 6.46 (1H, s), 6.59 (1H, s), 7.05–7.20 (3H, m), 7.35 (1H, t, J = 7.8 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 19.8, 30.4, 52.3, 66.9, 69.5, 70.6, 81.3, 110.5, 123.7, 124.1, 126.2, 127.9, 130.7, 139.2, 143.1, 165.2, 176.9. Anal. calcd. for $C_{17}H_{17}NO_5$:315.1107; found: 315.1101.

Methyl 2-(1-((2-hydroxyethoxy)methyl)-3-hydroxy-2-oxoindolin-3-yl)acrylate (19)

Waxy solid. R_f = 0.23 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3416, 1716, 1614, 1085, 1065. ^1H NMR ($CDCl_3$) δ_H: 2.67 (2H, bs), 3.62 (3H, s), 3.69–3.75 (4H, m), 5.21 (1H, d, J = 11.1 Hz), 5.28 (1H, d, J = 11.1 Hz), 6.50 (1H, s), 6.60 (1H, s), 7.05–7.26 (3H, m), 7.34 (1H, t, J = 6.6 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 52.4, 59.7, 66.1, 70.5, 76.3, 110.1, 123.5, 123.9, 128.3, 129.4, 130.6, 139.0, 143.2, 165.3, 175.6. Anal. calcd. for $C_{15}H_{17}NO_6$: 307.1056; found: 307.1047.

Methyl 2-(1-[(3-hydroxypropoxy)methyl]-3-hydroxy-2-oxoindolin-3-yl)acrylate (20)

Waxy solid. R_f = 0.28 (20% EtOAc-Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3418, 1716, 1613, 1086, 1055. ^1H NMR ($CDCl_3$) δ_H: 1.73 (2H, quintet, J = 7.2 Hz), 3.11 (2H, bs), 3.48–3.80 (7H, m), 5.14 (1H, d, J = 11.4 Hz), 5.21 (1H, d, J = 11.4 Hz), 6.55 (1H, s), 6.60 (1H, s), 7.03–7.16 (3H, m),7.33 (1H, t, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 32.6, 52.4, 59.8, 66.2, 70.5, 76.3, 110.1, 123.6, 123.9, 128.4, 129.4, 130.5, 139.0, 143.1, 165.4, 177.2. Anal. calcd. for $C_{16}H_{19}NO_6$: 321.1212; found: 321.1205.

Methyl 2-(1-((benzyloxy)methyl)-3-hydroxy-2-oxoindolin-3-yl)acrylate (21)

Waxy solid. R_f = 0.29 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3314, 1716, 1617, 1083, 1055. ^1H NMR ($CDCl_3$) δ_H: 2.67 (1H, bs), 3.62 (3H, s), 4.36 (1H, d, J = 11.6 Hz), 4.72 (1H, d, J = 11.6 Hz), 5.24 (1H, d, J = 11.1 Hz), 5.32 (1H, d, J = 11.1 Hz), 6.47 (1H, s), 6.59 (1H, s), 7.08–7.35 (9H, m). ^{13}C NMR ($CDCl_3$) δ_C: 52.1, 70.1, 70.7, 76.4, 110.3, 123.5, 123.8, 127.8 (2C), 128.2(2C), 128.3 (2C), 128.7, 130.5, 137.5, 138.9, 143.0, 165.0, 176.6. Anal. calcd. for $C_{20}H_{19}NO_5$: 353.1263; found: 353.1254.

2-(1-(Ethoxymethyl)-3-hydroxy-2-oxoindolin-3-yl) acrylonitrile (22)

Waxy solid. R_f = 0.34 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3378, 2917, 2185, 1732, 1613, 1487, 1097. ^1H NMR ($CDCl_3$) δ_H: 1.19 (3H, t, J = 7.2 Hz), 1.90 (1H, bs), 3.57 (2H, q, J = 7.2 Hz), 5.15 (1H, d, J = 11.1 Hz), 5.25 (1H, d, J = 11.1 Hz), 6.21 (1H, s), 6.36 (1H, s), 7.14–7.22 (2H, m), 7.40–7.45 (2H, m). ^{13}C NMR ($CDCl_3$) δ_C: 15.0, 64.8, 70.7, 76.8, 111.1, 115. 6, 123.3, 124.6, 124.9, 126.5, 128.6, 131.6, 142.0, 175.5. Anal. calcd. for $C_{14}H_{14}N_2O_3$: 258.1004; found: 258.0992.

2-(3-Hydroxy-2-oxo-1-[(prop-2-yloxy)methyl] indolin-3-yl)acrylonitrile (23)

Waxy solid. R_f 0.42 = (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3390, 2305, 1733, 1614, 1073. ^1H NMR ($CDCl_3$) δ_H: 1.80 (1H, bs), 2.48 (1H, t, J = 2.4 Hz), 4.21 (2H, d, J = 2.4 Hz), 5.24 (1H, d, J = 11.1 Hz), 5.36 (1H, d, J = 11.1 Hz), 6.21 (1H, s), 6.37 (1H, s), 7.10–7.29 (2H, m), 7.42 (2H, d, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 30.6, 56.4, 69.5, 75.8, 78.7, 110.9, 115.7, 123.1, 125.0, 126.9, 128.8, 131.6, 132.6, 141.9, 174.9. Anal. calcd. for $C_{15}H_{12}N_2O_3$: 268.0848; found: 268.0840.

Methyl 2-(5-bromo-3-hydroxy-1-(methoxymethyl)-2-oxoindolin-3-yl)acrylate (24)

Waxy solid. R_f = 0.47 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3376, 1710, 1079, 1060. ^1H NMR ($CDCl_3$) δ_H: 3.40 (3H, s), 3.58 (1H, s), 3.65 (3H, s), 5.09 (1H, d, J = 11.0 Hz), 5.16 (1H, d, J = 11.0 Hz), 6.47 (1H, s), 6.62 (1H, s), 6.97 (1H, d, J = 8.3 Hz), 7.30 (1H, d, J = 1.8 Hz), 7.46 (1H, dd, J = 8.3, 1.8 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 52.5, 53.1, 70.6, 76.7, 111.8, 116.1, 126.8, 128.3, 130.8, 133.2, 138.6, 142.1, 164.7, 174.4. Anal. calcd. for $C_{14}H_{14}BrNO_5$: 355.0055; found: 355.0051.

Methyl 2-(5-bromo-1-(ethoxymethyl)-3-hydroxy-2-oxoindolin-3-yl)acrylate (25)

Waxy solid. R_f = 0.45 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3379, 1715, 1084, 1062. ^1H NMR ($CDCl_3$) δ_H: 1.19 (3H, t, J = 7.8 Hz), 1.89 (1H, bs), 3.45–3.63 (5H, m), 5.13 (1H, d, J = 11.1 Hz), 5.19 (1H, d, J = 11.1 Hz), 6.47 (1H, s), 6.60 (1H, s), 7.00 (1H, d, J = 8.3 Hz), 7.28 (1H, d, J = 1.9 Hz), 7.46 (1H, dd, J = 8.3, 1.9 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 14.8, 52.1, 64.4, 70.4, 76.2, 111.8, 116.0, 127.1, 128.3, 130.8, 133.2, 138.6, 142.1, 164.7, 174.3. Anal. calcd. for $C_{15}H_{16}BrNO_5$: 369.0212; found: 369.0201.

Methyl 2-(5-bromo-1-((but-3-ynyloxy)methyl)-3-hydroxy-2-oxoindolin-3-yl)acrylate (26)

Waxy solid. R_f = 0.39 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3390, 2210, 1716, 1085, 1063. ^1H NMR ($CDCl_3$) δ_H: 1.94 (1H, t, J = 2.4 Hz), 2.46 (2H, td, J = 6.7, 2.4 Hz), 3.61–3.76 (5H, m), 5.18 (1H, d, J = 11.2 Hz), 5.18 (1H, d, J = 11.2 Hz), 5.25 (1H, d, J = 11.2 Hz), 6.48 (1H, s), 6.62 (1H, s), 7.01 (1H, d, J = 8.3 Hz), 7.29 (1H, d, J = 1.7 Hz), 7.46 (1H, dd, J = 8.3, 1.7 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 19.3, 30.4, 52.5, 67.3, 69.5, 70.5, 81.1, 110.9, 116.2, 127.1, 128.3, 130.7, 133.2, 138.5, 143.0, 164.8, 176.3. Anal. calcd. for $C_{17}H_{16}BrNO_5$: 393.0212; found: 393.0203.

Methyl 2-(1-(t-butoxymethyl)-5-bromo-3-hydroxy-2-oxoindolin-3-yl)acrylate (27)

Waxy solid. R_f = 0.47 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3376, 1710, 1079, 1060. ^1H NMR ($CDCl_3$) δ_H: 1.23 (9H, s), 3.58 (1H s), 3.65 (3H, s), 5.07 (1H, d, J = 10.8 Hz), 5.30 (1H, d, J = 10.8 Hz), 6.38 (1H, s), 6.58 (1H, s), 7.02 (1H, d, J = 8.3 Hz), 7.29 (1H, d, J = 1.9 Hz), 7.46 (1H, dd, J = 8.3, 1.9 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 28.4, 29.7, 65.3, 75.1, 76.3, 109.8, 114.3, 117.1, 121.5, 127.1, 128.3, 133.1, 138.4, 159.0, 164.9. Anal. calcd. for $C_{17}H_{20}BrNO_5$: 397.0525; found: 397.0523.

Methyl 2-(3-hydroxy-1-(methyl 2-methoxyacetate)-2-oxoindolin-3-yl)acrylate (39)

Waxy solid. R_f = 0.44 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3420, 1718, 1606, 1051. ^1H NMR ($CDCl_3$) δ_H: 1.90 (1H, bs), 3.59 (3H, s), 3.63 (3H, s), 3.79 (3H, s), 5.96 (1H, s), 6.55 (1H, s), 6.63 (1H, s), 7.04–7.10 (2H, m), 7.17–7.32 (2H, m). ^{13}C NMR ($CDCl_3$) δ_C: 46.9, 52.1, 56.9, 76.0, 79.7, 111.4, 123.6, 123.8, 128.1, 128.7, 130.5, 138.6, 140.8, 164.7, 166.9, 176.3. Anal. calcd. for $C_{16}H_{17}NO_7$: 335.1005; found: 335.1001.

Methyl 2-(3-hydroxy-1-(methyl 2-ethoxyacetate)-2-oxoindolin-3-yl)acrylate (40)

Waxy solid. R_f = 0.42 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3421, 1727, 1615, 1056. ^1H NMR ($CDCl_3$) δ_H: 1.28 (3H, t, J = 7.2 Hz), 3.97 (1H, bs), 3.65 (3H, s), 3.79 (3H, s), 4.25 (2H, q, J = 7.2 Hz), 6.02 (1H, s), 6.44(1H, s), 6.59 (1H, s), 7.06–7.31 (4H, m). ^{13}C NMR ($CDCl_3$) δ_C: 14.8, 52.1, 53.7, 62.4, 76.0, 79.7, 110.6, 123.6, 123.8, 127.8, 128.7, 130.4, 137.9, 141.5, 165.5, 166.9, 176.2. Anal. calcd. for $C_{17}H_{19}NO_7$: 349.1162; found: 349.1155.

Methyl 2-(3-hydroxy-1-(methyl 2-(prop-2-ynyloxy)acetate)-2-oxoindolin-3-yl)acrylate (41)

Waxy solid. R_f = 0.48 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3294, 2120, 1712, 1610, 1051. ^1H NMR ($CDCl_3$) δ_H: 2.54 (1H, t, J = 2.4 Hz), 3.57 (1H, bs), 3.63 (3H, s), 3.81 (3H, s), 4.46 (2H, d, J = 2.4 Hz), 6.24 (1H, s), 6.57 (1H, s), 6.62 (1H, s), 7.07–7.13 (2H, m), 7.19–7.34 (2H, m). ^{13}C NMR ($CDCl_3$) δ_C: 22.3, 41.5, 52.2, 55.9, 62.7, 75.9, 77.9, 109.3, 111.5, 123.7, 124.1, 128.1, 130.3, 138.7, 140.8, 165.9, 176.1, 176.5. Anal. calcd. for $C_{18}H_{17}NO_7$: 359.1005; found: 359.0996.

Methyl 2-(3-hydroxy-1-(methyl 2-(benzyloxy)acetate)-2-oxoindolin-3-yl)acrylate (42)

Waxy solid. R_f = 0.43 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3396, 1717, 1084, 1065. ^1H NMR ($CDCl_3$) δ_H: 1.19 (3H, t, J = 7.17 Hz), 3.51 (1H, s), 3.64 (3H, s), 4.24 (2H, q, J = 7.17 Hz), 4.72 (1H, d, J = 11.8 Hz), 4.91 (1H, d, J = 11.8 Hz), 6.03 (1H, s), 6.44 (1H, s), 6.64 (1H, s), 7.01 (1H, t, J = 7.5 Hz), 7.18 (2H, t, J = 7.6 Hz), 7.27–7.39 (6H, m). ^{13}C NMR ($CDCl_3$) δ_C: 14.4, 52.6, 62.9, 70.7, 76.5, 112.3, 114.6, 124.4, 128.7 (2C), 128.8 (2C), 129.3 (2C), 130.7 (2C), 136.7, 141.5, 165.6, 167.2, 177.8. Anal. calcd. for $C_{21}H_{20}NO_5$: 366.1341; found: 366.1326.

Methyl 2-(3-hydroxy-1-(methyl 2-(but-3-ynyloxy)acetate)-2-oxoindolin-3-yl)acrylate (43)

Waxy solid. R_f = 0.46 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3388, 2210, 1718, 1615, 1087, 1064. ^1H NMR ($CDCl_3$) δ_H: 1.24 (3H, t, J = 7.20 Hz), 1.90 (1H, t, J = 2.5 Hz), 3.56 (1H, s), 3.63 (3H, s), 4.13–4.28 (4H, m), 6.01 (1H, s), 6.54 (1H, s), 6.62 (1H, s), 7.06–7.29 (4H, m). ^{13}C NMR ($CDCl_3$) δ_C: 13.9, 19.3, 31.6, 62.5, 66.9, 69.7, 76.0, 78.2, 80.2, 111.7, 123.6, 124.0, 128.1, 128.8, 130.3, 138.4, 140.9, 164.7, 165.9, 176.2. Anal. calcd. for $C_{18}H_{18}NO_5$: 328.1185; found: 328.1183.

Methyl 2-(5-bromo-3-hydroxy-1-(methoxy(phenyl) methyl)-2-oxoindolin-3-yl)acrylate (44)

Waxy solid. R_f = 0.39 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3382, 1717, 1085, 1057. ^1H NMR ($CDCl_3$) δ_H: 2.15 (1H, s), 3.45 (3H, s), 3.66 (3H, s), 6.48 (1H, s), 6.53 (1H, s), 6.58 (1H, s), 7.19–7.45 (8H, m). ^{13}C NMR ($CDCl_3$) δ_C: 52.1, 53.4, 65.4, 76.4, 110.3, 123.5, 124.3, 127.8 (2C), 128.1 (2C), 128.2 (2C), 128.7, 131.3, 137.4, 139.0, 143.0, 164.5, 175.5. Anal. calcd. for $C_{20}H_{18}BrNO_5$: 431.0368; found: 431.0357.

Methyl 2-(5-bromo-3-hydroxy-1-(1-methoxyprop-2-ynyl)-2-oxoindolin-3-yl)acrylate (45)

Waxy solid. R_f = 0.48 (20% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3396, 2212, 1714, 1089, 1055. ^1H NMR ($CDCl_3$) δ_H: 2.61 (1H, d, J = 2.1 Hz), 3.48 (3H, s), 3.61 (3H, s), 3.79 (1H, s), 6.12 (1H, d, J = 2.1 Hz), 6.38 (1H, s), 6.43(1H, s), 7.27 (1H, d, J = 8.3 Hz), 7.32 (1H, d, J = 1.9 Hz), 7.46 (1H, dd, J = 8.3, 1.9 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 52.3, 55.9, 56.4, 72.3, 75.1, 75.8, 114.1, 116.4, 126.9, 128.6, 130.9, 132.9, 138.3, 139.5, 164.5, 175.3. Anal. calcd. for $C_{16}H_{14}BrNO_5$: 379.0055; found: 379.0043.

Spectral data for nitrated derivatives

Methyl 2-(1-ethyl-3-hydroxy-5-nitro-2-oxoindolin-3-yl)acrylate (36)

Waxy solid. R_f = 0.48 (25% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3348, 1706, 1611. ^1H NMR ($CDCl_3$) δ_H: 1.32 (3H, t, J = 7.23 Hz), 2.2 (1H, bs), 3.62 (3H, s), 3.77–3.9 (2H, m), 6.58 (1H, s), 6.67 (1H, s), 6.97 (1H, d, J = 8.6 Hz), 8.04 (1H, d, J = 2.3 Hz), 8.31 (1H, dd, J = 2.3 Hz, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 12.1, 43.6, 52.3, 76.1, 109.6, 120.32, 122.3, 123.1, 128.7, 129.9, 144.4, 144.7, 164.8, 176.1. Anal. calcd. for $C_{14}H_{14}N_2O_6$: 306.0852; found: 306.0841.

Methyl 2-(3-hydroxy-1-isopropyl-5-nitro-2-oxoindolin-3-yl)acrylate (47)

Waxy solid. R_f = 0.49 (25% EtOAc–Hexanes). ν_{max} (CH_2Cl_2, cm^{-1}): 3351, 1709, 1612. ^1H NMR ($CDCl_3$) δ_H:

1.55 (6H, d, J = 8.1 Hz), 3.47 (1H, s), 3.63 (3H, s), 4.58–4.63 (1H, m), 6.56 (1H, s), 6.67 (1H, s), 7.1 (1H, d, J = 8.7 Hz), 8.03 (1H, d, J = 2.3 Hz), 8.28 (1H, dd, J = 2.3, J = 8.7 Hz). ^{13}C NMR ($CDCl_3$) δ_C: 19.1 (2C), 43.3, 51.8, 75.8, 109.7, 122.3, 124.0, 127.6, 129.8 (2C), 140.4, 143.2, 164.8, 176.1. Anal. calcd. for $C_{15}H_{16}N_2O_6$: 320.1008; found: 320.1008.

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