JOC The Journal of Organic Chemistry

Note

Indium(III) Triflate-Catalyzed Reactions of Aza-Michael Adducts of Chalcones with Aromatic Amines: Retro-Michael Addition versus Quinoline Formation

Thangavel Selvi, and Sivan Velmathi

J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 02 Mar 2018

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Indium(III) Triflate-Catalyzed Reactions of Aza-Michael Adducts of Chalcones with Aromatic Amines: Retro-Michael Addition versus Quinoline Formation

Thangavel Selvi and Sivan Velmathi*

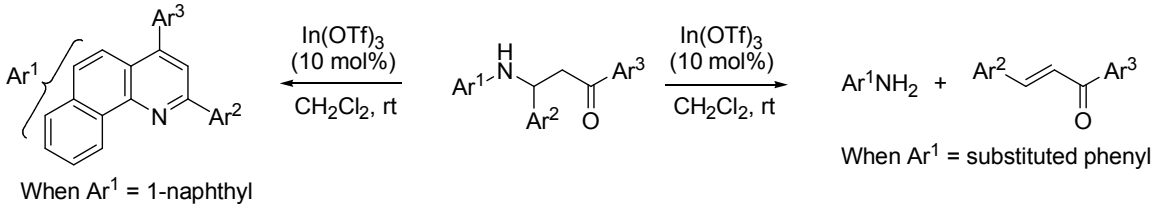
Department of Chemistry, National Institute of Technology,

Tiruchirappalli-620 015, Tamil Nadu, India

*velmathis@nitt.edu

Tel.: +91-431-2503640 & Fax: +91-431-2500133

Abstract:



The indium(III) triflate-catalyzed reaction of aza-Michael adducts of chalcones with aromatic amines has been investigated. The Michael adducts derived from substituted anilines and chalcones underwent retro-Michael addition to give the original starting materials, whereas the adducts derived from 1-naphthylamines and chalcones afforded quinolines. A six-membered cyclic transition state has been proposed to explain the retro-Michael addition, while a Povarov mechanism has been put forward to explain the quinoline formation.

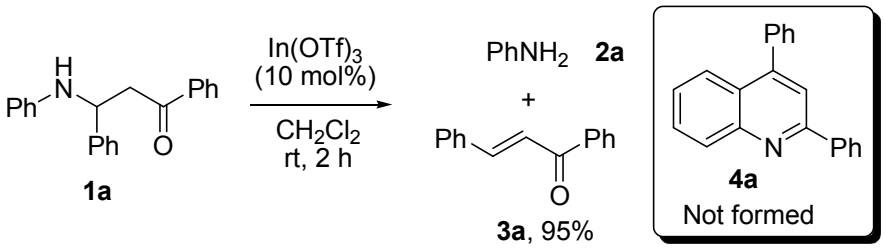
The quinoline structural motif is ubiquitous among bioactive natural products[1] and pharmaceutically important compounds including drugs.[2] This fact has triggered the development of several new methods for the synthesis of quinolines,[3] in addition to traditional

methods.[4] Traditionally, quinolines were synthesized by reacting (1) aromatic amines with α,β-unsaturated carbonyl compounds (the Skraup-Doebner-Miller synthesis[5]), 1,3-diketones (the Combes synthesis[6]) or β-ketoesters (the Conrad-Limpach synthesis[7]), (2) imines derived from aromatic amines and aldehydes with alkenes or alkynes (the Povarov reaction[8]) or (3) *o*-aminobenzaldehydes with carbonyl compounds (the Friedlander synthesis[9]). Among them, the Skraup-Doebner-Miller synthesis has attracted a great deal of attention owing to its simple, yet complex mechanism.[10]

The scope of the Skraup and Doebner-Miller synthesis is somewhat limited with respect to the α,β-unsaturated carbonyl compound used in the reaction.[5] Apart from α,β-unsaturated aldehydes and methyl ketones, no other α,β-unsaturated carbonyl compounds (such as chalcones) could be employed in the synthesis and this surprising fact stimulated us to investigate the reason behind it. As the direct quinoline synthesis from aromatic amines and chalcones at the best stops at the aza-Michael adduct stage, we prepared the aza-Michael adducts independently[11] and subjected them to further cyclization. We found that the Michael adducts derived from substituted anilines and chalcones underwent retro-Michael addition to give the original starting materials, whereas the adducts derived from 1-naphthylamine and chalcones afforded the expected quinoline derivatives in good yields. Further study gave new insights on the mechanism of the transformations and herein the results are presented.

The formation of quinoline from aza-Michael adducts of aromatic amines with chalcones is likely to take place *via* S_EAr cyclization followed by dehydration and aromatization.[5] As Lewis acids are capable of promoting such dehydrative cyclizations, we selected the aza-Michael adduct **1a** as a model substrate and treated with various Lewis/Bronsted acids [10 mol% of

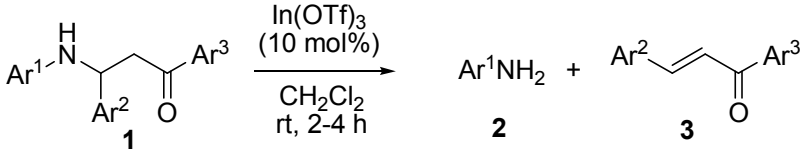
$In(OTf)_3$, $Cu(OTf)_2$, $Sc(OTf)_3$, $Yb(OTf)_3$, $Bi(OTf)_3$, $Zn(OTf)_2$, $InCl_3$, $ZnCl_2$, $AlCl_3$, $FeCl_3$, $BF_3{\cdot}OEt_2$ or TfOH] under different reaction conditions (CH_2Cl_2, 1,2-dichloroethane, THF, EtOH at rt or under reflux) in order to identify optimal catalyst and reaction conditions for the transformation (Scheme 1). Unfortunately, none of the Lewis/Bronsted acids is capable of promoting the desired transformation of **1a** into quinoline **4a**. Instead, **1a** underwent retro-Michael addition to yield aniline (**2a**) and chalcone **3a** with most of the Lewis acids (**1a** was recovered with $FeCl_3$, $BF_3{\cdot}OEt_2$ and TfOH). The best result for retro-Michael addition was obtained when the reaction was carried out with $In(OTf)_3$ in CH_2Cl_2 at rt for 2 h (the yield of isolated chalcone was 95%). It is interesting to note that the retro-Michael addition is essentially dehydroamination which is usually promoted by bases[12] and in the present case, it is catalyzed by a Lewis acid.



Scheme 1. Retro-Michael addition of **1a**.

The retro-Michael addition was not specific to adduct **1a** alone. Similar Michael adducts **1b-q** derived from substituted anilines and chalcones also underwent retro-Michael addition with $In(OTf)_3$ to give the respective parent compounds **2** and **3** (Table 1). Obviously, the presence of electron donating, electron withdrawing and halogen substituents on the phenyl rings of the adducts **1b-p** (entries 1-16) or the placement of a naphthyl ring as Ar^2 as in **1q** did not have any influence on the reaction outcome (entry 17).

Table 1. The scope of retro-Michael addition for various aza-Michael adducts

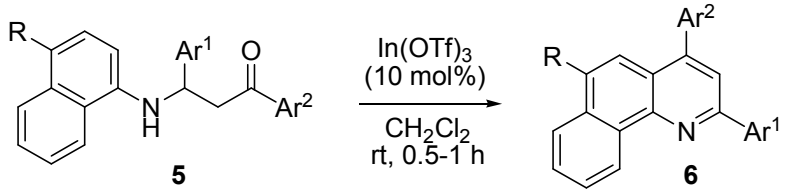


Entry	Ar^1, Ar^2, Ar^3	Time (h)	Yield of **3** (%)[a,b]
1	Ph, Ph, Ph (**1a**)	2	**3a**, 95
2	4-MeC_6H_4, Ph, Ph (**1b**)	3	**3a**, 82
3	4-$MeOC_6H_4$, Ph, Ph (**1c**)	4	**3a**, 86
4	4-ClC_6H_4, Ph, Ph(**1d**)	2	**3a**, 92
5	4-$O_2NC_6H_4$, Ph, Ph (**1e**)	2.5	**3a**, 89
6	Ph, 4-MeC_6H_4, Ph (**1f**)	3	**3b**, 81
7	Ph, 4-$MeOC_6H_4$, Ph (**1g**)	4	**3c**, 89
8	Ph, 4-BrC_6H_4, Ph (**1h**)	2	**3d**, 87
9	Ph, 4-ClC_6H_4, Ph (**1i**)	2	**3e**, 90
10	4-MeC_6H_4, 4-ClC_6H_4, Ph (**1j**)	2	**3e**, 89
11	4-$MeOC_6H_4$, 4-ClC_6H_4, Ph (**1k**)	2.5	**3e**, 87
12	4-ClC_6H_4, 4-ClC_6H_4, Ph(**1l**)	2	**3e**, 91
13	Ph, 4-$(O_2N)C_6H_4$, Ph (**1m**)	3	**3f**, 79
14	Ph, 3,4-$(MeO)_2C_6H_3$, Ph (**1n**)	3	**3g**, 87
15	Ph, 2,4-$Cl_2C_6H_3$, Ph (**1o**)	3	**3h**, 87
16	Ph, 4-ClC_6H_4, 4-$O_2NC_6H_4$ (**1p**)	4	**3i**, 88
17	Ph, 1-naphthyl, Ph (**1q**)	4	**3j**, 83

[a]Isolated yield; [b]The yield of anilines **2** could not be calculated reliably as we used silica gel for column chromatography.

In contrast to the above findings, the Michael adducts **5a-h** derived from 1-naphthylamines and chalcones afforded benzo-fused quinolines **6a-h** under similar reaction conditions (Table 2). The reaction tolerated the presence of different substituents on the chalcone phenyl rings and also the replacement of a phenyl ring by a naphthyl ring in the chalcone unit (entries 1-8).

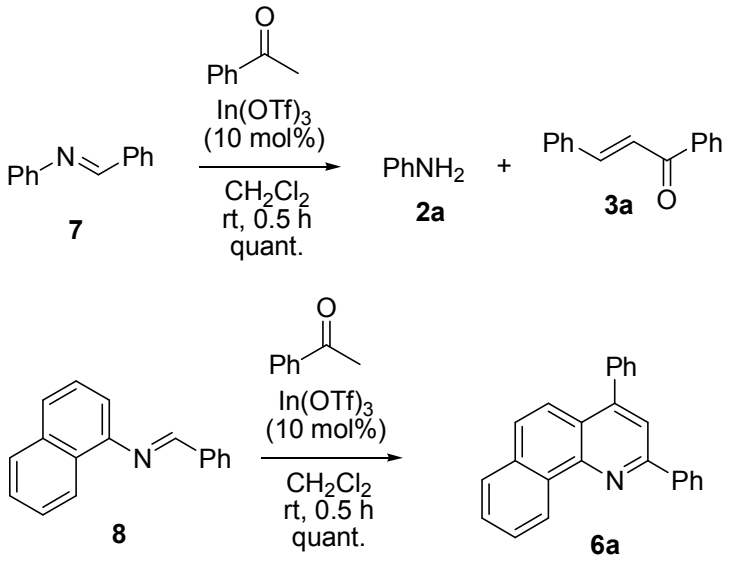
Table 2. Synthesis of benzo-fused quinolines from Michael adducts derived from 1-naphthylamine and chalcones



Entry	Ar^1, Ar^2, R	Time (min)	Yield of **6** (%)[a]
1	Ph, Ph, H (**5a**)	30	**6a**, 90
2	4-MeC_6H_4, Ph, H (**5b**)	30	**6b**, 89
3	4-$MeOC_6H_4$, Ph, H (**5c**)	30	**6c**, 87
4	4-ClC_6H_4, Ph, H (**5d**)	15	**6d**, 92
5	2,4-$(MeO)_2C_6H_3$, Ph, H (**5e**)	60	**6e**, 90
6	4-ClC_6H_4, 4-$O_2NC_6H_4$, H (**5f**)	30	**6f**, 92
7	1-Naphthyl, Ph, H (**5g**)	60	**6g**, 88
8	Ph, Ph, Br (**5h**)	60	**6h**, 84

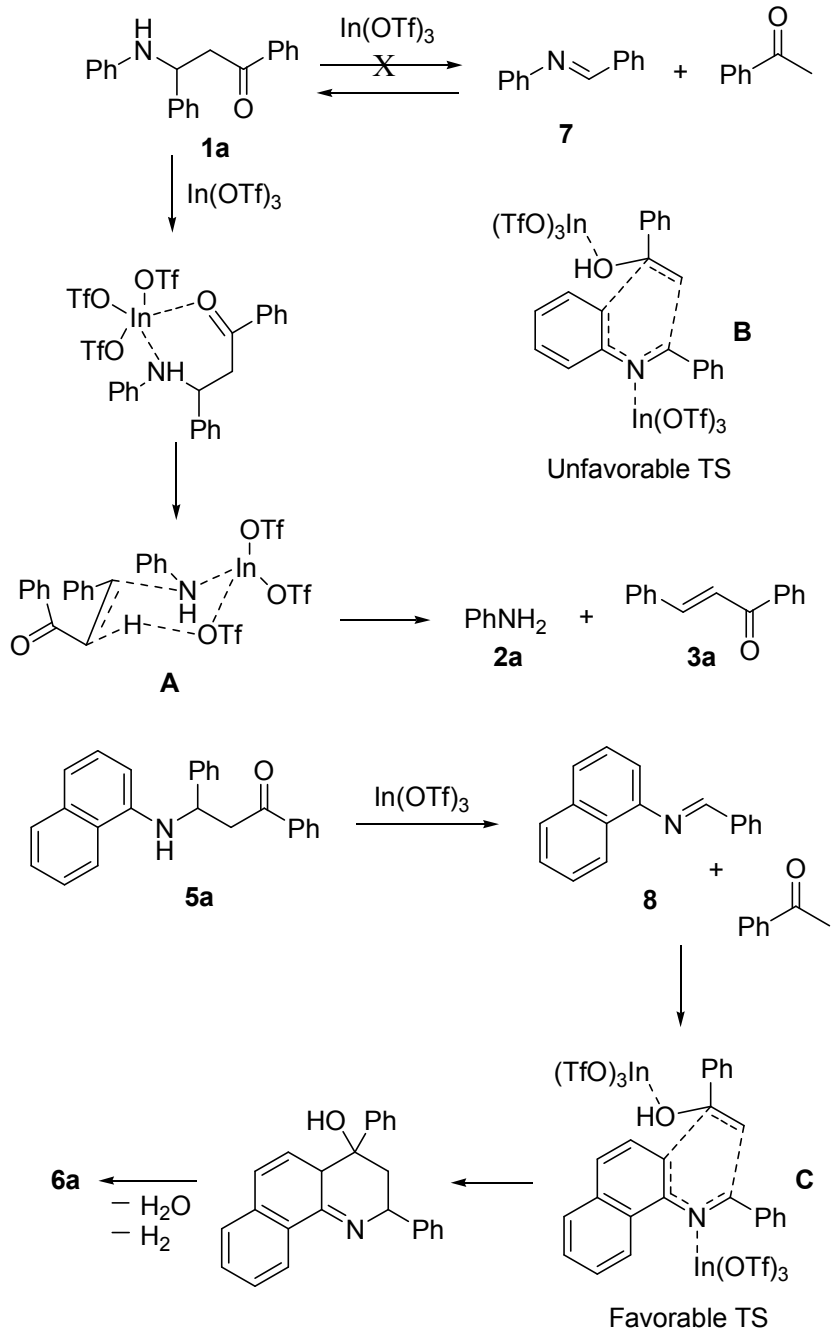
[a]Isolated yield

Denmark and Venkatraman have reported that the aza-Michael adduct formed in the Skraup-Doebner-Miller synthesis undergoes fragmentation to give an imine before undergoing further changes. We conducted few control experiments in order to include or exclude the involvement of imine intermediates in our transformations (Scheme 2). Accordingly, we prepared imines **7** and **8** independently and reacted with acetophenone under similar reactions conditions. The reaction between **7** and acetophenone gave aniline and chalcone **3a** through the Aza-Michael adduct **1a**. On the other hand, the reaction between **8** and acetophenone gave quinoline **6a** readily.



Scheme 2. Control experiments

Based on the above observations, we envisage that the aza-Michael adduct **1a** probably undergoes retro-Michael addition without the formation of the imine intermediate **7** (even if the imine intermediate **7** is formed, it goes back to the aza-Michael adduct **1a** immediately). We propose a six-membered cyclic transition state[13] **A** for the retro-Michael addition step as shown in Scheme 3. In contrast, the aza-Michael adduct **5a** undergoes fragmentation to give imine **8** and acetophenone and the subsequent Povarov [4+2] cycloaddition between **8** and enol form of acetophenone *via* transition state **C** leads to **6a** after dehydration and aromatization. It may be noted that the transition state **C** is energetically more favorable than a similar (unlikely) transition state **B** that could be written for imine **7** and acetophenone enol due to partial bond fixation in the naphthyl ring.[14]



Scheme 3. Mechanisms for the retro-Michael addition and quinoline formation

In summary, the aza-Michael adducts derived from chalcones and aromatic amines show distinct reactivity patterns depending on the nature of the aromatic amines employed. The Michael adducts derived from substituted anilines and chalcones preferentially undergo retro-

Michael addition *via* six-membered cyclic transition state rather than Povarov reaction. On the other hand, the adducts derived from 1-naphthylamines and chalcones prefer Povarov pathway owing to partial bond fixation in the naphthyl ring to afford quinolines.

EXPERIMENTAL SECTION

General remarks: Melting points were determined by the open capillary tube method and are uncorrected. The ^{1}H and ^{13}C NMR spectra were recorded on a *Bruker 500 MHz* NMR spectrometer. High resolution mass spectra were recorded on *Exactive Plus EMR Orbitrap* mass spectrometer. Low resolution mass spectra was recorded on *Thermo Fisher Q-trap* mass spectrometer. Elemental analyses was performed on a CHN analyzer. Thin layer chromatography (TLC) was performed on pre-coated alumina sheets and detected under UV light. *S*ilica gel (100-200 mesh) was used for column chromatography.

General procedure for the retro-Michael addition/synthesis of quinolines 6: To a solution of aza-Michal adduct (1.0 mmol) in dichloromethane (5 mL) was added indium(III) triflate (56 mg, 0.1 mmol) and stirred at room temperature. After the reaction was complete, the reaction mixture was mixed with water and the organic layer was separated. The layer was washed with water and dried (anhydrous Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was purified by column chromatography using hexane-ethylacetate (95:5) as the eluent to afford chalcones **3** (and also anilines **2**) or quinolines **6**.

(*E*)-1,3-Diphenylprop-2-en-1-one (3a): White solid; M.p.: 55-57 °C (lit.[15] 56-57 °C); Yield: 198 mg, 95% (Table 1, entry 1); 170 mg, 82% (Table 1, entry 2); 179 mg, 86% (Table 1, entry 3); 191 mg, 92%, (Table 1, entry 4); 185 mg, 89%, (Table 1, entry 5); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41-7.40 (m, 3H), 7.52-7.48 (m, 2H), 7.59-7.55 (m, 2H), 7.65-7.63 (m, 2H), 7.81 (d,

J = 15.5 Hz, 1H), 8.02 (d, *J* = 7.5 Hz, 2 H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 122.1, 128.49, 128.54, 128.7, 129.0, 130.6, 132.8, 134.9, 138.2, 144.9, 190.6 ppm.

(*E*)-1-Phenyl-3-*p*-tolylprop-2-en-1-one (3b)[15]: Yellow solid; M.p.: 94-96 °C; Yield: 180 mg, 81%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.40 (s, 3H), 7.23 (d, *J* = 7.5 Hz, 2H), 7.60-7.48 (m, 6H), 7.80 (d, *J* = 16.0 Hz, 1H), 8.02 (d, *J* = 7.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.6, 121.1, 128.50, 128.51, 128.6, 129.7, 132.2, 132.7, 138.4, 141.1, 145.0, 190.7 ppm.

(*E*)-3-(4-Methoxyphenyl)-1-phenylprop-2-en-1-one (3c): Yellow solid; M.p.: 118-120 °C (lit.[15,16] 73-75 °C); Yield: 212 mg, 89%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.85 (s, 3H), 6.93 (d, *J* = 8.5 Hz, 2H), 7.41 (d, *J* = 15.5 Hz, 1H), 7.51-7.48 (m, 3H), 7.61-7.55 (m, 2H), 7.79 (d, *J* = 15.5 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.4, 114.5, 119.8, 127.6, 128.4, 128.6, 130.3, 132.6, 138.5, 144.7, 161.7, 190.6 ppm.

(*E*)-3-(4-Bromophenyl)-1-phenylprop-2-en-1-one (3d)[16]: Yellow powder; M.p.: 117-119 °C; Yield: 249 mg, 87%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.49-7.42 (m, 4H), 7.64 (d, *J* = 8.0 Hz, 4H), 7.81 (d, *J* = 15.5 Hz, 1H), 7.89 (d, *J* = 8.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 121.5, 127.9, 128.5, 129.0, 130.0, 130.8, 132.0, 134.7, 137.0, 145.4, 189.4 ppm.

(*E*)-3-(4-Chlorophenyl)-1-phenylprop-2-en-1-one (3e)[16]: Pale yellow solid; M.p.: 113-115 °C (lit.[16] 111-113 °C); Yield: 218 mg, 90% (Table 1, entry 9); 215 mg, 89% (Table 1, entry 10); 210 mg, 87% (Table 1, entry 11); 220 mg, 91%, (Table 1, entry 12); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.5 Hz, 2H), 7.51-7.48 (m, 3H), 7.60-7.55 (m, 3H), 7.75 (d, *J* = 16.0 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 122.5, 128.5, 128.7, 129.3, 129.6, 133.0, 133.4, 136.4, 138.1, 143.3, 190.2 ppm.

(*E*)-3-(4-Nitrophenyl)-1-phenylprop-2-en-1-one (3f)[16]**:** Yellow solid; M.p.: 164-166 °C; Yield: 200 mg, 79%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66-7.46 (m, 6H), 7.84 (d, *J* = 16.0 Hz, 1H), 8.14 (d, *J* = 8.0 Hz, 2H), 8.35 (d, *J* = 8.0 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 121.3, 123.9, 128.7, 129.1, 129.4, 131.3, 134.3, 143.1, 146.8, 150.1, 189.0 ppm.

(*E*)-3-(3,4-Dimethoxyphenyl)-1-phenylprop-2-en-1-one (3g)[16,17]**:** Yellow solid; M.p.: 88-90 °C; Yield: 233 mg, 87%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.92 (s, 3H), 3.95 (s, 3H), 6.90 d, *J* = 8.0 Hz, 1H), 7.16 (s, 1H), 7.23 (d, *J* = 9.5 Hz, 1H), 7.39 (d, *J* = 15.5 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 15.5 Hz, 1H), 8.01 (d, *J* = 7.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.99, 56.01, 110.2, 111.2, 120.1, 123.2, 127.9, 128.4, 128.6, 132.6, 138.5, 145.0, 149.3, 151.5, 190.6 ppm.

(*E*)-3-(2,4-Dichlorophenyl)-1-phenylprop-2-en-1-one (3h)[18]**:** Yellow solid; M.p.: 78-80 °C; Yield: 240 mg, 87%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (d, *J* = 5.5 Hz, 1H), 7.59-7.45 (m, 5H), 7.67 (d, *J* = 7.0 Hz, 1H), 8.00 (d, *J* = 6.5 Hz, 2H), 8.09 (d, *J* = 15.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 125.0, 127.6, 128.5, 128.6, 128.7, 130.1, 131.9, 133.1, 136.1, 136.5, 137.8, 139.3, 190.0 ppm.

(*E*)-3-(4-Chlorophenyl)-1-(4-nitrophenyl)prop-2-en-1-one (3i)[19]**:** Light yellow solid; M.p.:150-152 °C; Yield: 252 mg, 88%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47-7.41 (m, 3H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.79 (d, *J* = 16.0 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 2H), 8.35 (d, *J* = 8.5 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 121.7, 123.9, 129.4, 129.5, 129.8, 132.8, 137.2, 142.8, 145.3, 150.2, 188.7 ppm.

(*E*)-3-(Naphthalen-4-yl)-1-phenylprop-2-en-1-one (3j)[16]: Yellow solid; M.p.: 61-63 °C; Yield: 214 mg, 83%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65-7.51 (m, 7H), 7.94-7.89 (m, 3H), 8.08 (d, *J* = 8.0 Hz, 2H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.67 (d, *J* = 15.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 123.5, 124.8, 125.1, 125.5, 126.3, 127.0, 128.6, 128.7, 128.8, 130.8, 131.8, 132.4, 132.9, 133.8, 138.2, 141.8, 190.4 ppm.

2,4-Diphenylbenzo[*h*]quinoline (6a): White solid; M.p.: 163-165 °C; (lit.[20] 163-165 °C);Yield: 298 mg, 90%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60-7.47 (m, 8H), 7.81-7.70 (m, 4H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.97 (s, 1H), 8.38 (d, *J* = 7.5 Hz, 2H), 9.58 (d, *J* = 8.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 119.5, 122.9, 123.4, 125.2, 126.9, 127.3, 127.5, 127.6, 128.25, 128.31, 128.6, 128.8, 129.3, 129.7, 132.0, 133.6, 138.9, 139.7, 146.8, 149.1, 154.9 ppm.; HRMS (ESI-ion trap) m/z: $[M + H]^+$ Calcd for $C_{25}H_{18}N$ 332.1434; found: 332.1434.

4-Phenyl-2-p-tolylbenzo[*h*]quinoline (6b): White semisolid; M.p.: 70-72 °C; Yield: 307 mg, 89%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.50 (s, 3H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.58-7.52 (m, 5H), 7.79-7.69 (m, 4H), 7.89 (d, *J* = 7.5 Hz, 1H), 7.93 (s, 1H), 8.28 (d, *J* = 8.0 Hz, 2H), 9.58 (d, *J* = 8.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.4, 119.3, 123.0, 123.2, 125.2, 126.8, 127.1, 127.4, 127.6, 128.2, 128.3, 128.6, 129.6, 129.7, 132.1, 133.6, 137.0, 138.9, 139.3, 146.7, 149.0, 154.9 ppm.; HRMS (ESI-ion trap) m/z: $[M + H]^+$ Calcd for $C_{26}H_{20}N$ 346.1590; found: 346.1590.

2-(4-Methoxyphenyl)-4-phenylbenzo[*h*]quinoline (6c): Yellow solid; M.p.: 167-169 °C; Yield: 314 mg, 87%; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.87 (s, 3H), 7.05 (d, *J* = 8.5 Hz, 2H), 7.55-7.49 (m, 5H), 7.76-7.66 (m, 4H), 7.86 (d, *J* = 11.5 Hz, 2H), 8.32 (d, *J* = 8.5 Hz, 2H), 9.55 (d, *J* = 8.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 55.4, 114.2, 118.9, 122.95, 122.97, 125.2, 126.8,

126.9, 127.6, 128.2, 128.3, 128.6, 128.8, 129.7, 132.0, 132.4, 133.7, 139.0, 146.7, 149.0, 154.9, 160.8 ppm.; HRMS (ESI-ion trap) m/z: $[M + H]^+$ Calcd for $C_{26}H_{20}NO$ 362.1539; found: 362.1539.

2-(4-Chlorophenyl)-4-phenylbenzo[*h*]quinoline (6d): White crystalline solid; M.p.: 173-175 °C; Yield: 336 mg, 92%; ^1H NMR (500 MHz, $CDCl_3$): δ 7.58-7.52 (m, 7H), 7.80-7.71 (m, 4H), 7.90 (d, *J* = 9.5 Hz, 2H), 8.32 (d, *J* = 8.5 Hz, 2H), 9.55 (d, *J* = 8.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 119.1, 122.9, 123.5, 125.1, 127.0, 127.6, 127.7, 128.38, 128.41, 128.65, 128.71, 129.0, 129.7, 131.9, 133.7, 135.4, 138.2, 138.7, 146.8, 149.3, 153.6 ppm.; HRMS (ESI-ion trap) m/z: $[M + H]^+$ Calcd for $C_{25}H_{17}ClN$ 366.1044; found: 366.1044.

2-(3,4-Dimethoxyphenyl)-4-phenylbenzo[*h*]quinoline (6e): Semi solid; Yield: 352 mg, 90%; ^1H NMR (500 MHz, $CDCl_3$): δ 3.96 (s, 3H), 3.98 (s, 3H), 6.96 (d, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 1H), 7.47-7.42 (m, 2H), 7.75-7.67 (m, 2H), 7.82-7.79 (m, 3H), 7.91-7.89 (m, 2H), 8.04 (s, 1H), 8.09 (d, *J* = 8.5 Hz, 1H), 8.30 (d, *J* = 9.0 Hz, 1H), 9.48 (d, *J* = 8.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 56.0, 56.2, 109.0, 110.4, 110.5, 111.1, 119.6, 120.0, 121.3, 123.9, 125.0, 126.7, 126.8, 126.9, 127.7, 127.9, 129.3, 132.1, 132.9, 133.6, 144.5, 145.9, 149.7, 150.3, 154.6 ppm.; HRMS (ESI-ion trap) m/z: $[M + H]^+$ Calcd for $C_{27}H_{22}NO_2$ 392.1645; found: 392.1646.

2-(4-Chlorophenyl)-4-(4-nitrophenyl)benzo[*h*]quinoline (6f): Semi solid; Yield: 377 mg, 92%; ^1H NMR (500 MHz, $CDCl_3$): δ 7.59-7.52 (m, 4H), 7.83-7.74 (m, 4H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.97 (s, 1H), 8.41 (d, *J* = 8.0 Hz, 2H), 8.54 (d, *J* = 8.5 Hz, 2H), 9.53 (d, *J* = 8.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 119.5, 122.3, 123.9, 124.1, 125.1, 127.5, 127.9, 128.2,

128.77, 128.83, 129.0, 130.9, 131.8, 133.7, 134.9, 136.7, 145.4, 147.1, 148.4, 152.2 ppm.; HRMS (ESI-ion trap) m/z: $[M + H]^+$ Calcd for $C_{25}H_{16}{}^{35}ClN_2O_2$ 411.0895; found: 411.0896.

2-(Naphthalen-1-yl)-4-phenylbenzo[*h*]quinoline (6g): Colourless liquid; Yield: 335 mg, 88%; ^1H NMR (500 MHz, $CDCl_3$): δ 7.65-7.52 (m, 7H), 7.77-7.71 (m, 3H), 7.89-7.80 (m, 4H), 8.05-7.95 (m, 2H), 8.50 (d, *J* = 7.5 Hz, 1H), 8.71 (d, *J* = 8.0 Hz, 1H), 9.64 (d, *J* = 8.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 110.8, 122.4, 122.9, 124.0, 125.0, 125.4, 125.9, 126.2, 126.46, 126.52, 126.6, 127.1, 127.6, 127.9, 128.3, 128.6, 128.7, 129.0, 129.2, 129.8, 130.7, 131.3, 131.9, 134.1, 137.8, 147.6, 157.3 ppm.; HRMS (ESI-ion trap) m/z: $[M + H]^+$ Calcd for $C_{29}H_{20}N$ 382.1590; found: 382.1593.

6-Bromo-2,4-diphenylbenzo[*h*]quinoline (6h): Yellow semisolid; Yield: 344 mg, 84%; ^1H NMR (500 MHz, $CDCl_3$): δ 7.47 (d, *J* = 6.5 Hz, 2H), 7.52 (d, *J* = 9.0 Hz, 1H), 7.71-7.62 (m, 4H), 7.79-7.76 (m, 1H), 7.91-7.84 (m, 5H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.71 (d, *J* = 8.0 Hz, 1H), 9.64 (d, *J* = 8.5 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 122.6, 123.8, 124.0, 125.5, 125.7, 127.3, 127.5, 127.6, 127.8, 128.0, 128.5, 128.7, 128.9, 129.5, 130.5, 133.0, 133.6, 135.9, 144.7, 145.1, 145.8 ppm. MS (ESI-ion trap) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{18}{}^{81}BrNaN$ 434.04; found: 434.17: C 73.18, H 3.93, N 3.41; found: C 73.30, H 4.05, N 3.53.

ACKNOWLEDGMENTS

T.S. thanks Science and Engineering Research Board (SERB), India for a National Post-Doctoral Fellowship (Project No.: PDF/2015/000012/CS). The authors thank the Director, National Institute of Technology Tiruchirappalli for providing infrastructure and instrumentation facilities.

Supporting Information.

^{1}H and ^{13}C NMR spectra of products. This material is available free of charge *via* the Internet at http://pubs.acs.org.

References:

1. (a) Michael, J. P. *Nat. Prod. Rep.* **2001**, *18*, 543. (b) Michael, J. P. *Nat. Prod. Rep.* **2005**, *22*, 627. (c) Michal, J. P. *Nat. Prod. Rep.* **2008**, *25*, 166.

2. (a) Ridley, R. G. *Nature* **2002**, *415*, 686. (b) Natarajan, J. K.; Alumasa, J. N.; Yearick, K.; Ekoue-Kovi, K. A.; Casabianca, L. B.; de Dios, A. C.; Wolf, C.; Roepe, P. D. *J. Med. Chem.* **2008**, *51*, 3466. (c) Andrews, S.; Burgess, S. J.; Skaalrud, D.; Xu Kelly, J,; Peyton, D. H. *J. Med. Chem.* **2010**, *53*, 916. (d) Solomon, V. R.; Lee, H. *Curr. Med. Chem.* **2011**, *18*, 1488. (e) Teguh, S.; Klonis, N.; Duffy, S.; Lucantoni, L.; Avery, V. M.; Hutton, C. A.; Baell, J. B.; Tilley, L. *J. Med. Chem.* **2013**, *56*, 6200. (f) Holden, J. K.; Lewis, M. C.; Cinelli, M. A.; Abdullatif, Z.; Pensa, A. V.; Silverman, R. B.; Poulos, T. L. *Biochem.* **2016**, *55*, 5587.

3. (a) Liu, B.; Gao, H.; Yu, Y.; Wu, W.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 10319. (b) Rehan, M.; Hazra, G.; Ghorai, P. *Org. Lett.* **2015**, *17*, 1668. (c) Saunthwal, R. K.; Patel, M.; Verma, A. K. *J. Org. Chem.* **2016**, *81*, 6563.

4. (a) Bergstrom, F. W. *Chem. Rev.* **1944**, *35*, 77. (b) Balasubramanian, M.; Keay, J. G. Isoquinoline Synthesis. *In Comprehensive Heterocyclic Chemistry II*; McKillop, A. E.; Katrizky, A. R.; Rees, C. W.; Scrivem, E. F. V. Eds.; Elsevier: Oxford, UK, 1996; *Vol. 5*, p 245.

5. (a) Manske, R. H. F.; Kulka, M. *Org. React.* **1953**, *7*, 59. (b) Yamashkin, S. A.; Oreshkina, E. A.; *Chem. Heterocycl. Comp.* **2006**, *42*, 701. (c) Ramann, G. A.; Cowen, B. J. *Tetrahedron Lett.* **2015**, *56*, 6436.

6. (a) Born, J. L. *J. Org. Chem*. **1972**, *37*, 3952. (b) Sloop, J. C. *J. Phy. Org. Chem.* **2009**, *22*, 110.

7. Wang, Z. In *Comprehensive Organic Name Reactions and Reagents*; Wiley: Hoboken, NJ, 2009; *Vol.1*, p 692.

8. (a) Kouznetsov, V. V. *Tetrahedron* **2009**, *65*, 2721. (b) Masson, G.; Lalli, C.; Benohoud, M.; Dagousset, G. *Chem. Soc. Rev*. **2013**, *42*, 902. (c) Fochi, M.; Caruana, L.; Bernardi, L. *Synthesis* **2014**, *46*, 135.

9. (a) Dormer, P. G.; Eng, K. K.; Farr, R. N.; Humphrey, G. R.; McWilliams, J. C.; Reider, P. J.; Sager, J. W.; Volante, R. P. *J. Org. Chem*. **2003**, *68*, 467. (b) Wu, J.; Xia, H.-G.; Gao, K. *Org. Biomol. Chem.* **2006**, *4*, 126. (c) Bañón-Caballero, A.; Guillena, G.; Nájera, C. *J. Org. Chem.* **2013**, *78*, 5349.

10. (a) Forrest, T. P.; Dauphinee, G. A.; Miles, W. F. *Can. J. Chem.* **1969**, *47*, 2121. (b) Eisch, J. J.; Dluzniewski, T. *J. Org. Chem.* **1989**, *54*, 1269. (c) Denmark, S. E.; Venkatraman, S. *J. Org. Chem.* **2006**, *71*, 1668. (d) Denisov, V. Y.; Grishchenkova, T. N.; Tkachenko, T. B.; Luzgarev, S. V. *Russ. J. Org. Chem.* **2016**, *52*, 1797.

11. (a) Shou, W.-G.; Yang, Y.-Y.; Wang, Y.-G. *Tetrahedron Lett.* **2006**, *47*, 1845. (b) Jiang, J.; Cai, Y.; Chen, W.; Lin, L.; Liu, X.; Feng, X. *Chem. Commun*. **2011**, *47*, 4016. (c) Wang, J.; Wang, W.; Liu, X.; Hou, Z.; Lin, L.; Feng, X. *Eur. J. Org. Chem.* **2011**, 2039.

12. (a) Cai, Y.-F.; Li, L.; Luo, M.-X.; Yang, K.-F.; Lai, G.-Q.; Jiang, J.-X.; Xu, L.-W. *Chirality* **2011**, *23*, 397. (b) Bradshaw, B.; Luque-Corredera, C.; Bonjoch, J. *Chem. Commun.* **2014**, *50*, 7099.

13. Yang, J. *Six-Membered Transition States in Organic Synthesis*; Wiley: Hoboken, NJ, 2008.

14. Efros, L. S. *Russ. Chem. Rev.* **1960**, *29*, 66.

15. Santos, L, Pedrosa, R. C.; Correa, T.-R.; Filho, V. C.; Jos-Nunes, R.; Yunes, R. A. *Arch. Pharm. Chem. Life Sci.* **2006**, *339*, 541.

16. Singh, J. V.; Sharma, S.; Rahar, S. *Der Pharma Chem.* **2015**, *7*, 93.

17. Bui, T. H.; Nguyen, N. T.; Dang, P. H.; Nguyen, H. X.; Nguyen, M. T. T. *Springer Plus* **2016**, *5*, 789.

18. Lopez, S. N.; Castelli, M. V.; Zacchino, S. A.; Domınguez, J. N.; Lobo, G.; Charris-Charris, J.; Cortes, J. C. G.; Ribas, J. C. Devia, C.; Rodrıguez, A. M.; Enriz, R. D. *Bioorg. Med. Chem.* **2001**, *9*, 1999.

19. Yamuna, T. S.; Yathirajan, H. S.; Jasinski, J. P.; Keeley, A. C.; Narayana, B.; Sarojini , B. K. *Acta Cryst.* **2013**, *E69*, o790.

20. Yao, C.; Qin, B.; Zhang, H.; Lu, J.; Wang, D.; Tu, S. *RSC Adv.* **2012**, *2*, 3759.