Tetrahedron 70 (2014) 3342–3348

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Ruthenium-catalyzed oxidative alkyne annulation by C–H activation on ketimines

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ARTICLE INFO

Article history:
Received 6 September 2013
Accepted 4 October 2013
Available online 10 October 2013

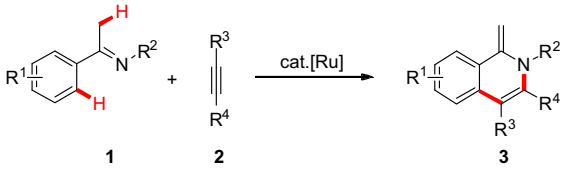
Keywords:
C–H activation
Isoquinolines
Heterocycles
Ketimines
Multicatalysis
Ruthenium

ABSTRACT

Carboxylate assistance allowed for ruthenium(II)-catalyzed oxidative alkyne annulations by ketimines under an ambient atmosphere of air. The ruthenium catalyst outperformed representative rhodium and palladium complexes, and provided versatile access to differently decorated 1-methylene-1,2-dihydroisoquinolines in a highly step- and atom-economical manner. Detailed mechanistic studies provided evidence for an initial reversible C–H bond activation event.

1. Introduction

Isoquinolines are key structural motifs of various heterocyclic[1,2] compounds with inter alia cardiovascular, anti-inflammatory or anti-malarial bioactivities.[3] As a consequence, there is a continued strong demand for methods that allow for the efficient assembly of this heterocycle. For instance, *ortho*-halo-substituted aromatic imines have been utilized for transition-metal-catalyzed annulations to furnish diversely decorated isoquinolines.[4] However, a more step-economical approach is represented by the catalyzed activation of otherwise unreactive C–H bonds, because these reactions avoid the synthesis and use of prefunctionalized starting materials.[5] Thus, in recent years we[5b,6] and others have developed ruthenium-[7] or rhodium-catalyzed[5i,8] isoquinoline syntheses exploiting C–H bond functionalizations.[6d,9] In contrast, we wish to report herein on a novel oxidative alkyne annulation that utilizes easily accessible ketimines **1**[10] and provides an expedient access to *exo*-methylene-1,2-dihydroisoquinolines **3** (Scheme 1). Notably, ruthenium catalyst proved to be optimal for this formal C–H activation process and thus outperformed representative rhodium and palladium catalysts.



1 2 3

Scheme 1. Catalyzed C–H functionalization for the synthesis of dihydroisoquinolines **3**.

2. Results and discussion

2.1. Optimization studies

At the outset of our studies, we probed various reaction conditions for the desired ruthenium(II)-catalyzed oxidative C–H bond functionalization utilizing ketimine **1a**, along with $Cu(OAc)_2 \cdot H_2O$ as the oxidant (Table 1). Preliminary experiments indicated DCE to be the solvent of choice, while significantly lower yields were obtained with *t*-AmOH, MeOH, H_2O, DMF or toluene. As to cocatalytic additives, KPF_6 and KO_2CMes proved to be suitable. Yet, most effective catalysis was accomplished with $AgSbF_6$ (entries 1–4), which is likely due to the in situ formation of a cationic ruthenium catalyst. It is noteworthy that the C–H bond functionalization proceeded efficiently under an ambient atmosphere of air, thereby highlighting the user-friendly nature of our protocol (entry 5). Replacing the oxidant $Cu(OAc)_2 \cdot H_2O$ by $CuBr_2$ did shut down the

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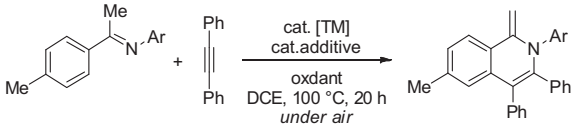
http://dx.doi.org/10.1016/j.tet.2013.10.003

oxidative alkyne annulation (entry 6). Interestingly, the catalytic activity was restored through the addition of metal acetates, indicating carboxylate assistance to be of prime importance for the C–H bond functionalization (entries 7–9).[7b] Notably, we found that the ruthenium(II) catalyst outcompeted typical rhodium or palladium complexes (entries 5, 10, and 11).

Table 1
Optimization of the oxidative annulation with ketimine **1a**[a]



1a **2a** **3a**

Entry	Catalyst	Additive	Oxidant	**3a**
1	—	—	$Cu(OAc)_2 \cdot H_2O$	—
2	$[RuCl_2(p\text{-cymene})]_2$	KPF_6	$Cu(OAc)_2 \cdot H_2O$	51%[b]
3	$[RuCl_2(p\text{-cymene})]_2$	KO_2CMes	$Cu(OAc)_2 \cdot H_2O$	61%[b]
4	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$Cu(OAc)_2 \cdot H_2O$	67%[b]
5	**$[RuCl_2(p\text{-cymene})]_2$**	**$AgSbF_6$**	**$Cu(OAc)_2 \cdot H_2O$**	**71%**
6	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$	—
7	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$/NaOAc[c]	54%
8	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$/KOAc[c]	53%
9	$[RuCl_2(p\text{-cymene})]_2$	$AgSbF_6$	$CuBr_2$/CsOAc[c]	37%
10	$[RhCpCl_2]_2$	$AgSbF_6$	$Cu(OAc)_2 \cdot H_2O$	46%
11	$PdCl_2(PPh_3)_2$	$AgSbF_6$	$Cu(OAc)_2 \cdot H_2O$	—

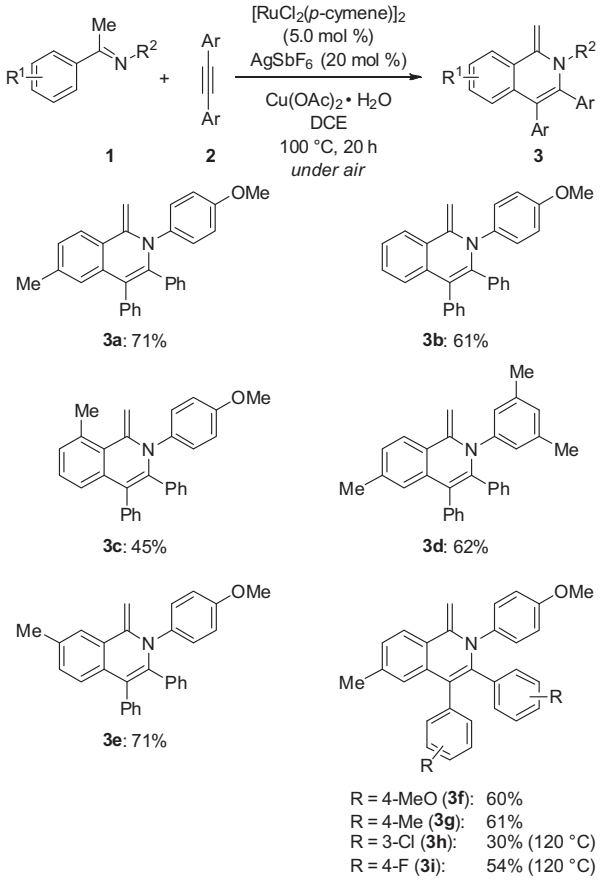
Bold value signifies to highlight the optimal catalytic system.
[a] General reaction conditions: **1a** (0.50 mmol), **2a** (1.00 mmol), catalyst (5.0 mol %), additive (20–30 mol %), oxidant (0.5 mmol); DCE (2.0 mL), under ambient air; 100 °C, 20 h; Ar=4-$MeOC_6H_4$; yields of isolated products.
[b] Under an atmosphere of N_2.
[c] MOAc (1.0 mmol).

2.2. Scope and limitations

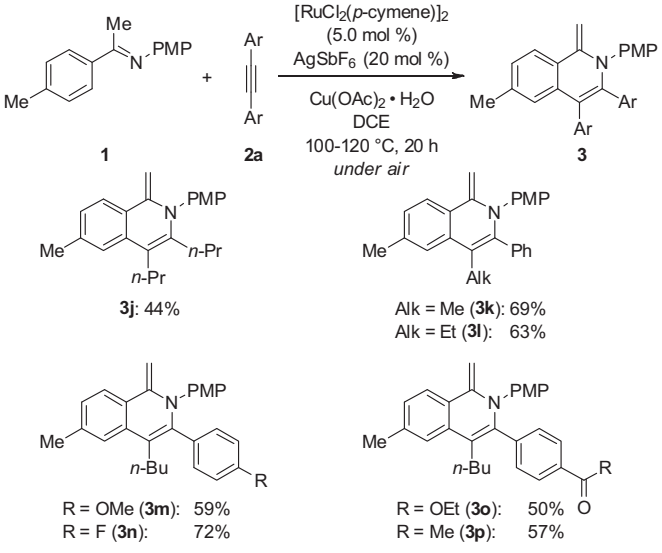
With an optimized catalytic system in hand, we tested its scope and limitations in the oxidative C–H bond functionalization with differently substituted ketimines **1** and alkynes **2** (Scheme 2). Hence, the oxidative annulation efficiently occurred with ketimines **1** displaying substituents on the *N*-aryl moiety. Notably, a more sterically hindered substrate bearing an *ortho*-methyl-substituent was also converted, albeit with a lower isolated yield of the product **3c**. A *meta*-decorated arene led to the site-selective C–H bond activation (**3e**), which can be rationalized in terms of significant steric interactions. Substituted tolane derivatives were found to be viable substrates as well, thereby delivering the desired products **3f**–**i**.

The optimized ruthenium(II) catalyst was not restricted to the use of diarylalkynes **2**, but proved to be applicable to alkyl-substituted starting materials as well (Scheme 3). Here, we particularly focused on the use of unsymmetrical substrates **2** to probe the challenging regiocontrol in the oxidative annulation. We were pleased to observe that the C–H bond functionalizations proceeded with excellent regioselectivities, placing the alkyl group distal to nitrogen. Furthermore, the ruthenium catalyst displayed a high chemoselectivity in which oxidative annulations of alkynes bearing an ester or a ketone group solely took place through chelation assistance by the ketimine moiety to furnish products **3o** and **3p**.

In order to access the corresponding reduced 1,2-dihydroisoquinolines **4** we subsequently devised a two-step reaction sequence consisting of the ruthenium-catalyzed C–H bond functionalization, along with a palladium-catalyzed hydrogenation (Scheme 4). The multicatalytic approach set the stage for the efficient preparation of the decorated products **4**, again occurring with excellent regio- and chemo-selectivities. It is noteworthy that a more sterically congested ketimine gave the ethyl-substituted dihydroisoquinoline **4c** in a comparable yield.



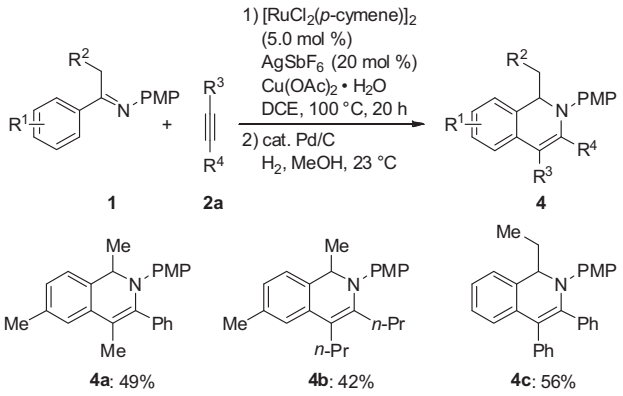
Scheme 2. Oxidative C–H functionalization with aromatic alkynes **2**.



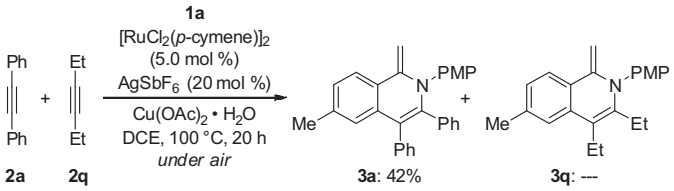
Scheme 3. Oxidative C–H functionalization with aromatic alkynes **2**.

2.3. Mechanistic considerations

Given the unique features of our ruthenium-catalyzed C–H bond functionalization process, we performed mechanistic studies to delineate its mode of action. To this end, we performed competition experiments, which revealed arylalkynes to be preferentially converted (Scheme 5).

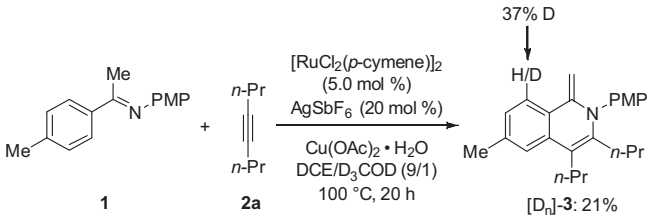


Scheme 4. Multicatalytic synthesis of 1,2-dihydroisoquinolines **4**.



Scheme 5. Competition experiment with alkynes **2**.

Furthermore, reactions in the presence of a deuterated cosolvent indicated the C–H bond activation to be reversible in nature (Scheme 6).

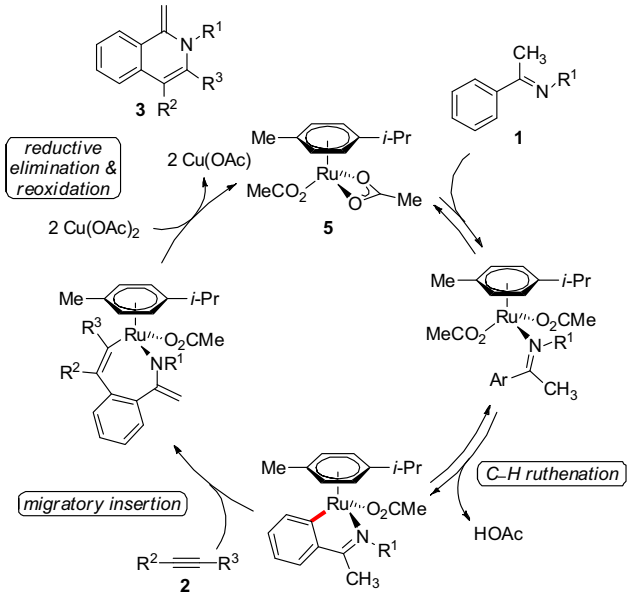


Scheme 6. C–H functionalization with deuterated cosolvent D_3COD.

Based on these mechanistic studies we propose the catalytic cycle to commence with a reversible chelation-assisted C(sp^2)–H bond ruthenation (Scheme 7). Subsequent migratory insertion,[5b] tautomerization,[11] and reductive elimination furnish the desired products **3**, while the catalytically active species **5** is regenerated through oxidation by $Cu(OAc)_2$.

3. Conclusions

In summary, we have developed a novel catalyzed oxidative annulation of alkynes by ketimines to furnish *exo*-methylene-1,2-dihydroisoquinolines. Particularly, carboxylate-assisted ruthenium(II) catalysis proved to be key to success for the synthesis of diversely decorated products in high yields. The ruthenium-catalyzed C–H bond functionalization proceeded with excellent chemo-, site-, and regio-selectivities under an ambient atmosphere of air and mechanistic studies were indicative of a reversible C–H bond metalation step.



Scheme 7. Proposed catalytic cycle.

4. Experimental

4.1. General

All catalytic reactions were carried out under an atmosphere of ambient air using pre-dried glassware. 1,2-Dichloroethane (DCE) was obtained from the VWR and was used without further purification. All ketimines **1** were synthesized from the corresponding ketones and arylamines.[12] Other chemicals were obtained from commercial sources and were used without further purification. Yields refer to isolated compounds, estimated to be >95% pure as determined by ^1H NMR. Chromatography: Merck silica gel 60 (40–63 μm). NMR: Spectra were recorded on Varian Unity 300, Mercury 300 or Inova 600 in the solvent indicated; chemical shifts (δ) are reported in parts per million. All IR spectra were recorded on a Bruker FT-IR Alpha device. MS: EI-MS-spectra were recorded with Finnigan MAT 95, 70 eV; High resolution mass spectrometry (HRMS) with APEX IV 7T FTICR, ESI-MS: Finnigan LCQ, Bruker Daltonic. Mp: Stuart melting point apparatus SMP3, Barlworld Scientific, values are uncorrected.

4.2. General procedure A for the ruthenium-catalyzed oxidative alkyne annulation by ketimines

A suspension of ketimine **1** (0.50 mmol), alkyne **2** (1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20.0 mol %), and $Cu(OAc)_2 \cdot H_2O$ (99.5 mg, 1.00 mmol) in DCE (2.0 mL) was stirred at 100 °C for 20 h under an atmosphere of ambient. At ambient temperature, the reaction mixture was extracted with EtOAc (3×20 mL) and the combined organic layers were washed with brine (20 mL), and dried over Na_2SO_4. The solvent was evaporated and the remaining residue was purified by column chromatography (*n*-hexane/EtOAc/Et_3N) to afford product **3**.

4.3. General procedure B for the multicatalytic reaction sequence

A suspension of ketimine **1** (0.50 mmol), alkyne **2** (1.00 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $AgSbF_6$ (34.4 mg, 20.0 mol %), and $Cu(OAc)_2 \cdot H_2O$ (99.5 mg, 1.00 mmol) in DCE

(2.0 mL) was stirred at 100 °C for 20 h under an ambient atmosphere of air. At ambient temperature, the reaction mixture was concentrated and the remaining residue was quickly purified by a short silica gel column chromatography (*n*-hexane/EtOAc/Et_3N) to afford crude product **3**, which was added to a suspension of anhydrous Pd/C (2 mol %) in MeOH (10 mL). The mixture was stirred at ambient temperature overnight under an atmosphere of H_2, until compound **3** was completely converted, as judged by TLC. The residue mixture was filtered through a Celite column. The organic layers were concentrated and then purified by column chromatography (*n*-hexane/EtOAc) to afford product **4**.

4.4. 2-(4-Methoxyphenyl)-6-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (3a)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and diphenylacetylene (**2a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2/1/0.05) yielded **3a** (147 mg, 71%) as a yellow solid. Mp: 190–192 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.66 (d, J=8.2 Hz, 1H), 7.14 (m, 2H), 7.01–7.04 (m, 6H), 6.84–6.94 (m, 5H), 6.76 (d, J=8.8 Hz, 2H), 6.41 (s, 1H), 4.46 (s, 1H), 3.63 (s, 3H), 3.07 (s, 1H), 2.13 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.5 (C_q), 147.2 (C_q), 142.0 (C_q), 138.0 (C_q), 137.4 (C_q), 135.9 (C_q), 134.8 (C_q), 133.6 (C_q), 131.8 (CH), 131.6 (CH), 130.7 (CH), 127.7 (CH), 127.1 (CH), 126.7 (CH), 126.5 (CH), 125.9 (CH), 124.7 (C_q), 124.0 (CH), 123.8 (CH), 114.3 (CH), 112.1 (C_q), 79.2 (CH_2), 55.0 (CH_3), 20.9 (CH_3). IR (neat): 3024, 1654, 1507, 1245, 1028, 697 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 415 (55) [M^+], 414 (100), 400 (45), 383 (15), 370 (10), 294 (10). HR-MS (ESI) *m*/*z* calcd for $C_{30}H_{25}NO$ [M+H^+] 416.2014, found 416.2009.

4.5. 2-(4-Methoxyphenyl)-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (3b)

The general procedure A was followed using **1b** (113 mg, 0.50 mmol) and diphenylacetylene (**2a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2/1/0.02) yielded **3b** (122 mg, 61%) as an off white solid. Mp: 189–190 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.76 (m, 1H), 6.85–7.20 (m, 14H), 6.77 (d, J=8.7 Hz, 2H), 6.61 (m, 1H), 4.52 (s, 1H), 3.63 (s, 3H), 3.13 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.3 (C_q), 147.0 (C_q), 141.8 (C_q), 137.2 (C_q), 135.5 (C_q), 134.6 (C_q), 133.4 (C_q), 131.6 (CH), 131.4 (CH), 130.5 (CH), 128.7 (CH), 127.6 (CH), 127.0 (C_q), 126.6 (CH), 126.4 (CH), 125.9 (CH), 125.8 (CH), 123.8 (CH), 123.6 (CH), 114.3 (CH), 112.1 (C_q), 80.1 (CH_2), 54.9 (CH_3). IR (neat): 2993, 1621, 1507, 1244, 758, 699 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 401 (50) [M^+], 400 (100), 388 (10), 356 (5), 209 (10). HR-MS (EI) *m*/*z* calcd for $C_{29}H_{23}NO$ [M–H^+] 400.1701, found 400.1699.

4.6. 2-(4-Methoxyphenyl)-8-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (3c)

The general procedure A was followed using **1c** (120 mg, 0.50 mmol) and diphenylacetylene (**2a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3/1/0.02) yielded **3c** (94 mg, 45%) as a yellow solid. Mp: 186–188 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.08–7.18 (m, 5H), 7.02 (d, J=8.7 Hz, 2H), 6.97–7.00 (m, 2H), 6.89–6.91 (m, 5H), 6.75 (d, J=8.7 Hz, 2H), 6.42 (dd, J=7.6, 1.5 Hz, 1H), 4.31 (s, 1H), 3.92 (s, 1H), 3.65 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.1 (C_q), 146.3 (C_q), 142.1 (C_q), 137.9 (C_q), 135.8 (C_q), 135.7 (C_q), 135.1 (C_q), 133.8 (C_q), 131.7 (CH), 131.1 (CH), 130.3 (CH), 129.2 (CH), 127.6 (CH), 127.3 (CH), 126.8 (C_q), 126.6 (CH), 126.3 (CH), 125.7 (CH), 120.7 (CH), 114.1 (CH), 113.7 (C_q), 96.1 (CH_2), 54.9 (CH_3), 22.5 (CH_3). IR (neat): 2959, 1616, 1507, 1239, 1034, 760 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 415 (75) [M^+], 400 (100), 369 (10), 294 (5), 279 (5), 121 (10). HR-MS (EI) *m*/*z* calcd for $C_{30}H_{25}NO$ [M^+] 415.1936, found 415.1927.

4.7. 2-(3,5-Dimethylphenyl)-6-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (3d)

The general procedure A was followed using **1d** (119 mg, 0.50 mmol) and diphenylacetylene (**2a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 5/1/0.01 → 5/1/0.02) yielded **3d** (125 mg, 62%) as an off white solid. Mp: 194–196 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.65 (d, J=8.3 Hz, 1H), 7.00–7.17 (m, 6H), 6.83–6.94 (m, 5H), 6.72 (br s, 3H), 6.41 (s, 1H), 4.45 (s, 1H), 3.12 (s, 1H), 2.14 (s, 3H), 2.10 (s, 6H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=146.6 (C_q), 141.8 (C_q), 141.6 (C_q), 138.0 (C_q), 137.8 (C_q), 137.4 (C_q), 135.7 (C_q), 133.5 (C_q), 131.7 (CH), 130.6 (CH), 128.1 (CH), 127.9 (CH), 127.6 (CH), 127.0 (CH), 126.4 (CH), 126.3 (CH), 125.8 (CH), 124.7 (C_q), 123.9 (CH), 123.6 (CH), 112.1 (C_q), 79.6 (CH_2), 20.7 (CH_3), 20.3 (CH_3). IR (neat): 3011, 1738, 1600, 1481, 1302, 698 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 415 (5) [M^+], 400 (10), 291 (5), 131 (5), 69 (30), 44 (100). HR-MS (EI) *m*/*z* calcd for $C_{31}H_{27}N$ [M–H^+] 412.2065, found 412.2069.

4.8. 2-(4-Methoxyphenyl)-7-methyl-1-methylene-3,4-diphenyl-1,2-dihydroisoquinoline (3e)

The general procedure A was followed using **1e** (120 mg, 0.50 mmol) and diphenylacetylene (**2a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1/1/0.01 → 1/1/0.03) yielded **3e** (148 mg, 71%) as an off white solid. Mp: 148–150 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.60 (s, 1H), 7.12 (d, J=7.3 Hz, 2H), 6.84–7.07 (m, 11H), 6.77 (d, J=8.6 Hz, 2H), 6.53 (d, J=8.0 Hz, 1H), 4.50 (s, 1H), 3.64 (s, 3H), 3.11 (s, 1H), 2.31 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.5 (C_q), 147.1 (C_q), 141.0 (C_q), 137.5 (C_q), 135.9 (C_q), 135.3 (C_q), 134.9 (C_q), 131.7 (CH), 131.6 (CH), 131.1 (C_q), 130.7 (CH), 129.7 (C_q), 127.7 (CH), 127.0 (C_q), 126.7 (CH), 126.4 (CH), 125.9 (CH), 124.0 (CH), 123.8 (CH), 114.4 (CH), 112.1 (C_q), 79.7 (CH_2), 55.0 (CH_3), 20.8 (CH_3). IR (neat): 2997, 1621, 1507, 1244, 1030, 698 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 415 (100) [M^+], 414 (85), 400 (45), 383 (10), 369 (10), 306 (5). HR-MS (ESI) *m*/*z* calcd for $C_{30}H_{25}NO$ [M+H^+] 416.2014, found 416.2009.

4.9. 2,3,4-Tris(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (3f)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and 1,2-bis(4-methoxyphenyl)acetylene (**2f**) (238 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2/1/0 → 2/1/0.05) yielded **3f** (142 mg, 60%) as a yellow solid. Mp: 125–126 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.63 (d, J=8.5 Hz, 1H), 7.01 (d, J=8.9 Hz, 3H), 6.93 (d, J=8.9 Hz, 2H), 6.84 (d, J=8.9 Hz, 2H), 6.78 (d, J=8.9 Hz, 2H), 6.72 (d, J=8.9 Hz, 2H), 6.44 (d, J=8.9 Hz, 2H), 6.42 (s, 1H), 4.42 (s, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 3.52 (s, 3H), 3.01 (s, 1H), 2.14 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.4 (C_q), 157.1 (C_q), 157.0 (C_q), 147.3 (C_q), 141.9 (C_q), 137.9 (C_q), 135.1 (C_q), 134.1 (C_q), 132.7 (CH), 131.8 (CH), 131.5 (CH), 129.7 (C_q), 128.5 (C_q), 126.9 (CH), 124.7 (C_q), 124.0 (CH), 123.7 (CH), 114.4 (CH), 113.2 (CH), 112.2 (CH), 111.8 (C_q), 79.0 (CH_2), 55.0 (CH_3), 54.7 (CH_3), 54.5 (CH_3), 20.9 (CH_3). IR (neat): 2955, 1737, 1605, 1506, 1235, 807 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 475 (65) [M^+], 474 (100), 460 (20), 443 (5), 366 (5), 240 (5). HR-MS (ESI) *m*/*z* calcd for $C_{32}H_{29}NO_3$ [M+H^+] 476.2226, found 476.2220.

4.10. 2-(4-Methoxyphenyl)-6-methyl-1-methylene-3,4-di-*p*-tolyl-1,2-dihydroisoquinoline (3g)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and 1,2-bis(4-methphenyl)acetylene (**2g**) (206 mg,

1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1/1/0→1/1/0.03) yielded **3g** (134 mg, 61%) as a yellow solid. Mp: 163–165 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.63 (d, *J*=8.3 Hz, 1H), 7.01 (d, *J*=8.8 Hz, 2H), 6.96 (m, 1H), 6.95 (d, *J*=8.1 Hz, 2H), 6.90 (d, *J*=8.1 Hz, 2H), 6.81 (d, *J*=7.8 Hz, 2H), 6.76 (d, *J*=8.8 Hz, 2H), 6.68 (d, *J*=8.1 Hz, 2H), 6.41 (s, 1H), 4.43 (s, 1H), 3.63 (s, 3H), 3.03 (s, 1H), 2.18 (s, 3H), 2.12 (s, H), 1.99 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.4 (C_q), 147.3 (C_q), 141.9 (C_q), 137.9 (C_q), 135.2 (C_q), 135.0 (C_q), 134.6 (C_q), 134.5 (C_q), 133.9 (C_q), 133.2 (C_q), 131.6 (CH), 131.5 (CH), 130.5 (CH), 128.4 (CH), 127.4 (CH), 126.9 (CH), 124.7 (C_q), 124.0 (CH), 123.7 (CH), 114.3 (CH), 112.0 (C_q), 79.1 (CH_2), 54.9 (CH_3), 20.9 (CH_3), 20.6 (CH_3), 20.5 (CH_3). IR (neat): 2956, 1606, 1506, 1239, 1033, 804 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 443 (40) [M$^+$], 430 (100), 411 (5), 386 (5), 342 (15), 237 (60). HR-MS (EI) *m*/*z* calcd for $C_{32}H_{29}NO$ [M−H$^+$] 442.2171, found 442.2179.

4.11. 3,4-Bis(3-chlorophenyl)-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (3h)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and 1,2-bis(3-chlorophenyl)acetylene (**2h**) (246 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1/1/0→1/1/0.03) yielded **3h** (72 mg, 30%) as an off white solid. Mp: 192–194 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.67 (d, *J*=8.7 Hz, 1H), 7.03–7.25 (m, 11H), 6.81 (d, *J*=9.0 Hz, 2H), 6.40 (s, 1H), 4.50 (s, 1H), 3.66 (s, 3H), 3.10 (s, 1H), 2.16 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.7 (C_q), 146.8 (C_q), 140.9 (C_q), 139.4 (C_q), 138.3 (C_q), 137.6 (C_q), 134.3 (C_q), 132.9 (C_q), 132.3 (C_q), 131.5 (C_q), 131.5 (CH), 131.5 (CH), 130.5 (CH), 130.5 (CH), 129.6 (CH), 129.3 (CH), 128.6 (CH), 127.5 (CH), 126.8 (CH), 126.3 (CH), 124.7 (C_q), 123.9 (CH), 123.8 (CH), 114.5 (CH), 111.1 (C_q), 79.8 (CH_2), 55.0 (CH_3), 20.8 (CH_3). IR (neat): 2836, 1622, 1506, 1245, 1031, 773 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 483 (50) [M$^+$], 482 (100), 468 (40), 451 (10), 438 (5), 328 (10). HR-MS (EI) *m*/*z* calcd for $C_{30}H_{23}NCl_2O$ [M−H$^+$] 482.1078, found 482.1069.

4.12. 3,4-Bis(4-fluorophenyl)-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (3i)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and 1,2-bis(4-fluorophenyl)ethyne (**2i**) (214 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 2/1/0→2/1/0.05) yielded **3i** (122 mg, 54%) as an off white solid. Mp: 196–198 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.67 (d, *J*=8.1 Hz, 1H), 6.97–7.06 (m, 9H), 6.79 (d, *J*=8.9 Hz, 2H), 6.73 (t, *J*=8.9 Hz, 2H), 6.40 (s, 1H), 4.48 (s, 1H), 3.65 (s, 3H), 3.08 (s, 1H), 2.15 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=160.9 (C_q, J_{C-F}=243.0 Hz), 159.8 (C_q, J_{C-F}=243.0 Hz), 157.6 (C_q), 147.0 (C_q), 141.3 (C_q), 138.2 (C_q), 134.7 (C_q), 133.6 (CH, J_{C-F}=8.2 Hz), 133.5 (C_q), 132.8 (CH, J_{C-F}=8.2 Hz), 132.3 (C_q), 132.3 (C_q), 131.5 (CH), 127.3 (CH), 124.7 (C_q), 123.9 (CH), 123.8 (CH), 114.7 (CH, J_{C-F}=21.1 Hz), 114.5 (CH), 113.7 (CH, J_{C-F}=21.7 Hz), 111.3 (C_q), 79.4 (CH_2), 55.0 (CH_3), 20.8 (CH_3). ^{19}F NMR (282 MHz, DMSO-d_6): δ=−109.9, −111.4. IR (neat): 2971, 1601, 1505, 1213, 828 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 451 (75) [M$^+$], 450 (100), 436 (45), 419 (15), 406 (5), 330 (5). HR-MS (EI) *m*/*z* calcd for $C_{30}H_{23}NOF_2$ [M−H$^+$] 450.1669, found 450.1672.

4.13. 2-(4-Methoxyphenyl)-6-methyl-1-methylene-3,4-di-*n*-propyl-1,2-dihydroisoquinoline (3j)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and oct-4-yne (**2j**) (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3/1/0.01→3/1/0.05) yielded **3j** (77 mg, 44%) as a yellow oil. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.50 (d, *J*=8.1 Hz, 1H), 7.15 (d, *J*=8.9 Hz, 2H), 7.08 (d, *J*=8.9 Hz, 2H), 7.04 (s, 1H), 6.93 (d, *J*=8.1 Hz, 1H), 4.24 (s, 1H), 3.81 (s, 3H), 2.81 (s, 1H), 2.38–2.43 (m, 2H), 2.31 (s, 3H), 2.00–2.06 (m, 2H), 1.44–1.52 (m, 2H), 1.25–1.33 (m, 2H), 1.00 (t, *J*=7.8 Hz, 3H), 0.62 (t, *J*=8.0 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=158.3 (C_q), 147.4 (C_q), 140.4 (C_q), 138.0 (C_q), 134.7 (C_q), 132.7 (C_q), 131.0 (CH), 126.1 (CH), 124.8 (C_q), 132.7 (CH), 121.9 (CH), 115.1 (CH), 106.1 (C_q), 78.1 (CH_2), 55.2 (CH_3), 31.6 (CH_2), 28.9 (CH_2), 22.8 (CH_2), 21.9 (CH_2), 21.1 (CH_3), 14.1 (CH_2), 14.0 (CH_3). IR (neat): 2957, 1650, 1506, 1241, 1031, 827 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 347 (55) [M$^+$], 334 (65), 320 (100), 304 (50), 291 (45), 176 (45). HR-MS (EI) *m*/*z* calcd for $C_{24}H_{29}NO$ [M−H$^+$] 346.2171, found 346.2167.

4.14. 2-(4-Methoxyphenyl)-4,6-dimethyl-1-methylene-3-phenyl-1,2-dihydroisoquinoline (3k)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and prop-1-yn-1-ylbenzene (**2k**) (116 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1/2/0→1/2/0.03) yielded **3k** (125 mg, 69%) as an off white solid. Mp: 121–123 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.62 (d, *J*=8.9 Hz, 1H), 7.05–7.17 (m, 7H), 6.97 (d, *J*=8.9 Hz, 2H), 6.95 (d, *J*=8.9 Hz, 2H), 4.35 (s, 1H), 3.64 (s, 3H), 2.96 (s, 1H), 2.34 (s, 3H), 1.66 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.4 (C_q), 147.1 (C_q), 141.0 (C_q), 138.3 (C_q), 136.6 (C_q), 135.2 (C_q), 133.3 (C_q), 131.7 (CH), 130.1 (CH), 127.5 (CH), 127.0 (CH), 126.9 (CH), 125.2 (C_q), 123.5 (CH), 122.6 (CH), 114.2 (CH), 102.5 (C_q), 78.1 (CH_2), 55.0 (CH_3), 21.0 (CH_3), 14.4 (CH_3). IR (neat): 2920, 1609, 1506, 1298, 1242, 698 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 353 (45) [M$^+$], 352 (100), 340 (40), 321 (10), 244 (15), 217 (15). HR-MS (EI) *m*/*z* calcd for $C_{25}H_{23}NO$ [M−H$^+$] 352.1701, found 352.1741.

4.15. 4-Ethyl-2-(4-methoxyphenyl)-6-methyl-1-methylene-3-phenyl-1,2-dihydroisoquinoline (3l)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and but-1-yn-1-ylbenzene (**2l**) (130 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 1/1/0→1/1/0.03) yielded **3l** (116 mg, 63%) as an off white solid. Mp: 199–201 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.62 (d, *J*=8.5 Hz, 1H), 7.08–7.18 (m, 6H), 7.02 (d, *J*=8.5 Hz, 1H), 6.96 (d, *J*=9.0 Hz, 2H), 6.74 (d, *J*=9.0 Hz, 2H), 4.33 (s, 1H), 3.63 (s, 3H), 2.92 (s, 1H), 2.34 (s, 3H), 2.08 (q, *J*=7.1 Hz, 2H), 0.92 (t, *J*=7.1 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.4 (C_q), 147.2 (C_q), 141.0 (C_q), 138.2 (C_q), 136.3 (C_q), 135.1 (C_q), 132.0 (C_q), 131.7 (CH), 129.9 (CH), 127.5 (CH), 127.1 (CH), 126.8 (CH), 125.5 (C_q), 123.9 (CH), 122.4 (CH), 114.2 (CH), 108.8 (C_q), 78.0 (CH_2), 54.9 (CH_3), 21.0 (CH_3), 20.6 (CH_2), 14.3 (CH_3). IR (neat): 2970, 1737, 1584, 1508, 1229, 1027, 736 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 367 (50) [M$^+$], 366 (100), 352 (25), 336 (5), 320 (5), 244 (5). HR-MS (ESI) *m*/*z* calcd for $C_{26}H_{25}NO$ [M+H$^+$] 368.2014, found 368.2010.

4.16. 4-*n*-Butyl-2,3-bis(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (3m)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and 1-(hex-1-yn-1-yl)-4-methoxybenzene (**2m**) (188 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3/1/0.01→3/1/0.05) yielded **3m** (125 mg, 59%) as an off white solid. Mp: 133–133 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ=7.60 (d, *J*=8.3 Hz, 1H), 7.10 (s, 1H), 6.99 (m, 1H), 6.99 (d, *J*=8.8 Hz, 2H), 6.95 (d, *J*=8.8 Hz, 2H), 6.76 (d, *J*=8.8 Hz, 2H), 6.71 (d, *J*=8.8 Hz, 2H), 4.31 (s, 1H), 3.65 (s, 6H), 2.90 (s, 1H), 2.33 (s, 3H), 2.05 (t, *J*=7.3 Hz, 2H), 1.34 (m, 2H), 1.16 (m, 2H), 0.71 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=157.6 (C_q), 157.1 (C_q), 147.1 (C_q), 140.9 (C_q), 138.0 (C_q), 135.3 (C_q), 132.3 (C_q), 131.5 (CH), 131.1 (CH), 128.5 (C_q), 126.6 (CH), 125.3 (C_q), 123.7 (CH), 122.3 (CH), 114.2 (CH), 112.7 (CH), 108.0 (C_q), 77.9 (CH_2), 54.9

(CH_3), 54.7 (CH_3), 31.6 (CH_2), 27.2 (CH_2), 22.1 (CH_2), 21.1 (CH_3), 13.4 (CH_3). IR (neat): 2928, 1737, 1507, 1240, 1033, 829 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 425 (65) [M^+], 424 (100), 412 (25), 384 (75), 274 (5), 240 (10). HR-MS (EI) *m*/*z* calcd for $C_{29}H_{31}NO_2$ [M^+] 425.2355, found 425.2344.

4.17. 4-*n*-Butyl-3-(4-fluorophenyl)-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinoline (3n)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and 1-fluoro-4-(hex-1-yn-1-yl)benzene (**2n**) (176 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3/1/0→3/1/0.05) yielded **3n** (148 mg, 72%) as an off white solid. Mp: 96–98 °C. ^1H NMR (300 MHz, DMSO-d_6): δ=7.62 (d, *J*=8.4 Hz, 1H), 7.11–7.16 (m, 3H), 6.96–7.02 (m, 5H), 6.77 (d, *J*=8.8 Hz, 2H), 4.34 (s, 1H), 3.65 (s, 3H), 2.93 (s, 1H), 2.34 (s, 3H), 2.04 (t, *J*=7.2 Hz, 2H), 1.34 (m, 2H), 1.15 (m, 2H), 0.70 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=160.6 (C_q J_{C-F}=245 Hz), 157.3 (C_q), 147.0 (C_q), 140.0 (C_q), 138.1 (C_q), 135.0 (C_q), 132.6 (C_q, J_{C-F}=3.5 Hz), 132.4 (C_q), 132.3 (CH, J_{C-F}=8.0 Hz), 131.5 (CH), 126.8 (CH), 125.3 (C_q), 123.7 (CH), 122.4 (CH), 114.3 (CH, J_{C-F}=21.5 Hz), 114.2 (CH), 108.0 (C_q), 78.1 (CH_2), 55.0 (CH_3), 31.5 (CH_2), 27.1 (CH_2), 22.0 (CH_2), 20.9 (CH_3), 13.4 (CH_3). ^{19}F NMR (282 MHz, DMSO-d_6): δ=−114.4. IR (neat): 2954, 1599, 1507, 1243, 1033, 825 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 413 (50) [M^+], 412 (100), 398 (20), 372 (40), 354 (10), 262 (10). HR-MS (ESI) *m*/*z* calcd for $C_{28}H_{28}NOF$ [M+H^+] 414.2233, found 414.2228.

4.18. Ethyl 4-{4-*n*-butyl-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinolin-3-yl}benzoate (3o)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and ethyl 4-(hex-1-ynyl)benzoate (**2o**) (230 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3/1/0→3/1/0.05) yielded **3o** (116 mg, 50%) as an off white solid. Mp: 151–153 °C. ^1H NMR (300 MHz, DMSO-d_6): δ=7.75 (d, *J*=8.5 Hz, 2H), 7.62 (d, *J*=8.4 Hz, 1H), 7.26 (d, *J*=8.4 Hz, 2H), 7.13 (s, 1H), 7.05 (d, *J*=8.5 Hz, 1H), 6.99 (d, *J*=9.0 Hz, 2H), 6.75 (d, *J*=9.0 Hz, 2H), 4.36 (s, 1H), 4.26 (q, *J*=7.2 Hz, 2H), 3.63 (s, 3H), 2.98 (s, 1H), 2.35 (s, 3H), 2.02 (m, 2H), 1.34 (m, 2H), 1.29 (t, *J*=7.2 Hz, 3H), 1.12 (m, 2H), 0.68 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=165.1 (C_q), 157.5 (C_q), 147.0 (C_q), 141.1 (C_q), 140.0 (C_q), 138.1 (C_q), 134.8 (C_q), 132.0 (C_q), 131.6 (CH), 130.5 (CH), 128.3 (C_q), 128.1 (CH), 127.0 (CH), 125.5 (C_q), 123.8 (CH), 122.4 (CH), 114.3 (CH), 107.9 (C_q), 78.3 (CH_2), 60.5 (CH_2), 54.9 (CH_3), 31.4 (CH_2), 26.9 (CH_2), 21.8 (CH_2), 20.9 (CH_3), 13.8 (CH_3), 13.2 (CH_3). IR (neat): 2928, 1718, 1507, 1272, 1098, 747 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 467 (60) [M^+], 466 (100), 452 (20), 438 (20), 424 (10), 394 (10). HR-MS (ESI) *m*/*z* calcd for $C_{31}H_{33}NO_3$ [M+H^+] 468.2539, found 468.2533.

4.19. 1-{4-(4-*n*-Butyl-2-(4-methoxyphenyl)-6-methyl-1-methylene-1,2-dihydroisoquinolin-3-yl)phenyl}ethan-1-one (3p)

The general procedure A was followed using **1a** (120 mg, 0.50 mmol) and 1-(4-(hex-1-ynyl)phenyl)ethanone (**2p**) (200 mg, 1.00 mmol) at 120 °C. Purification by column chromatography (*n*-hexane/EtOAc/Et_3N: 3/1/0.01→3/1/0.03) yielded **3p** (125 mg, 57%) as an off white solid. Mp: 129–131 °C. ^1H NMR (300 MHz, DMSO-d_6): δ=7.75 (d, *J*=8.3 Hz, 2H), 7.56 (s, 1H), 7.27 (d, *J*=8.3 Hz, 2H), 7.26 (d, *J*=8.5 Hz, 1H), 7.22 (d, *J*=8.5 Hz, 1H), 7.01 (d, *J*=8.4 Hz, 2H), 6.76 (d, *J*=8.4 Hz, 2H), 4.41 (s, 1H), 3.63 (s, 3H), 3.00 (s, 1H), 2.49 (s, 3H), 2.33 (s, 3H), 1.98 (m, 2H), 1.33 (m, 2H), 1.11 (m, 2H), 0.68 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ=197.3 (C_q), 157.5 (C_q), 147.1 (C_q), 141.2 (C_q), 139.2 (C_q), 135.3 (C_q), 135.2 (C_q), 135.0 (C_q), 131.7 (CH), 130.6 (CH), 130.0 (CH), 129.6 (C_q), 127.9 (C_q), 127.3 (CH), 124.1 (CH), 122.5 (CH), 114.4 (CH), 108.0 (C_q), 79.0 (CH_2), 55.0 (CH_3), 31.6 (CH_2), 27.2 (CH_2), 26.5 (CH_3), 22.0 (CH_2), 20.8 (CH_2), 13.4 (CH_3). IR (neat): 2929, 1681, 1507, 1243, 1028, 830 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 437 (60) [M^+], 436 (85), 424 (100), 408 (10), 396 (20), 354 (90). HR-MS (EI) *m*/*z* calcd for $C_{30}H_{31}NO_2$ [M−H^+] 436.2277, found 436.2286.

4.20. 2-(4-Methoxyphenyl)-1,4,6-trimethyl-3-phenyl-1,2-dihydroisoquinoline (4a)

The general procedure B was followed using **1a** (120 mg, 0.50 mmol) and prop-1-ynylbenzene (**2k**) (116 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **4a** (87 mg, 49%) as a white solid. Mp: 150–152 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=7.42 (dd, *J*=8.0, 1.5 Hz, 2H), 7.16–7.28 (m, 4H), 7.00 (d, *J*=8.0 Hz, 1H), 6.90 (d, *J*=7.6 Hz, 1H), 6.78 (d, *J*=8.7 Hz, 2H), 6.57 (d, *J*=8.7 Hz, 2H), 4.90 (q, *J*=7.0 Hz, 1H), 3.63 (s, 3H), 2.40 (s, 3H), 2.23 (s, 3H), 1.50 (d, *J*=7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=154.3 (C_q), 141.5 (C_q), 137.9 (C_q), 136.2 (C_q), 136.1 (C_q), 133.7 (C_q), 132.1 (C_q), 130.8 (CH), 127.5 (CH), 127.1 (CH), 126.8 (CH), 124.5 (CH), 123.3 (CH), 122.9 (CH), 113.9 (C_q), 113.6 (CH), 60.1 (CH), 55.3 (CH_3), 22.0 (CH_3), 21.5 (CH_3), 15.3 (CH_3). IR (neat): 2964, 1738, 1505, 1229, 1033, 772 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 355 (15) [M^+], 340 (100), 325 (5), 296 (10), 282 (5). HR-MS (EI) *m*/*z* calcd for $C_{25}H_{25}NO$ [M^+] 355.1936, found 355.1939.

4.21. 2-(4-Methoxyphenyl)-1,6-dimethyl-3,4-di-*n*-propyl-1,2-dihydroisoquinoline (4b)

The general procedure B was followed using **1a** (120 mg, 0.50 mmol) and oct-4-yne (**2j**) (110 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 50/1) yielded **4b** (75 mg, 42%) as a green oil. ^1H NMR (300 MHz, $CDCl_3$): δ=7.08 (s, 1H), 6.91 (d, *J*=7.6 Hz, 1H), 6.87 (d, *J*=9.2 Hz, 2H), 6.78 (d, *J*=7.6 Hz, 1H), 6.75 (d, *J*=9.2 Hz, 2H), 4.60 (q, *J*=6.8 Hz, 1H), 3.74 (s, 3H), 2.47–2.70 (m, 2H), 2.34–2.42 (m, 1H), 2.34 (s, 3H), 2.06–2.16 (m, 1H), 1.41–1.68 (m, 4H), 1.32 (d, *J*=6.8 Hz, 3H), 1.05 (t, *J*=7.4 Hz, 3H), 0.87 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=155.0 (C_q), 141.5 (C_q), 137.6 (C_q), 135.8 (C_q), 132.0 (C_q), 131.7 (C_q), 126.0 (CH), 124.7 (CH), 124.0 (CH), 121.9 (CH), 118.3 (C_q), 113.9 (CH), 60.3 (CH), 55.4 (CH_3), 31.4 (CH_2), 29.8 (CH_2), 23.4 (CH_2), 22.1 (CH_3), 22.1 (CH_2), 21.6 (CH_3), 14.6 (CH_3), 14.2 (CH_3). IR (neat): 2958, 2869, 1505, 1237, 1035, 827 cm^{-1}. MS (EI) *m*/*z* (relative intensity) 349 (10) [M^+], 334 (100), 320 (10), 304 (5), 290 (5), 276 (5). HR-MS (EI) *m*/*z* calcd for $C_{24}H_{31}NO$ [M^+] 349.2406, found 349.2410.

4.22. 1-Ethyl-2-(4-methoxyphenyl)-3,4-diphenyl-1,2-dihydroisoquinoline (4c)

The general procedure B was followed using **1f** (120 mg, 0.50 mmol) and diphenylacetylene (**2a**) (178 mg, 1.00 mmol). Purification by column chromatography (*n*-hexane/EtOAc: 100/1) yielded **4c** (116 mg, 56%) as an off white solid. Mp: 100–103 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=7.27–7.32 (m, 5H), 7.14–7.22 (m, 5H), 6.89–6.99 (m, 6H), 6.60 (dd, *J*=9.0, 1.3 Hz, 2H), 4.68 (dd, *J*=6.9, 6.9 Hz, 1H), 3.65 (d, *J*=1.4 Hz, 3H), 2.08–2.18 (m, 1H), 1.83–1.92 (m, 1H), 1.23 (t, *J*=7.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=154.7 (C_q), 141.2 (C_q), 138.6 (C_q), 138.5 (C_q), 137.6 (C_q), 132.4 (C_q), 131.9 (CH), 131.8 (C_q), 131.3 (CH), 127.8 (CH), 127.0 (CH), 126.7 (CH), 126.7 (CH), 126.1 (CH), 125.8 (CH), 125.8 (CH), 124.1 (CH), 123.2 (CH), 112.7 (C_q), 113.7 (CH), 67.0 (CH), 55.3 (CH_3), 28.6 (CH_2), 11.2 (CH_3). IR (neat): 2953, 1738, 1505, 1229, 1028, 700 cm^{-1}. MS (EI) *m*/*z* (relative

intensity) 417 (65) [M^+], 388 (100), 372 (5), 344 (10), 280 (5), 252 (5). HR-MS (EI) *m*/*z* calcd for $C_{30}H_{27}NO$ [M^+] 417.2093, found 417.2081.

Acknowledgements

Support by the European Research Council under the European Community's Seventh Framework Program (FP7 2007–2013)/ERC Grant agreement no. 307535 and the CSC (fellowship to J.L.) is gratefully acknowledged.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.10.003.

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