Nucleophilic Addition of Lewis Acid Complexed α-Amino Carbanions to Arynes: Synthesis of 1-Aryl-*N*-methyl-1,2,3,4-tetrahydroisoquinolines

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Abstract: The direct C-1 arylation of *N*-methyl-1,2,3,4-tetrahydroisoquinolines via coupling of α-amino carbanions derived from Lewis acid complexed tetrahydroisoquinolines and in situ generated arynes is described. This process provides an easy access to the title compounds and a new synthetic route to (±)-cryptostyline alkaloids.

Key words: arylation, arynes, tetrahydroisoquinolines, cryptostyline alkaloids, Lewis acid complexation

The 1-aryltetrahydroisoquinoline moiety is an important structural motif present in many alkaloids and compounds of pharmaceutical interest. A variety of these compounds show potent anti-HIV,[1] antibacterial,[2] and antitumor activities.[3] Various 1-aryl-THIQ (THIQ: tetrahydroisoquinoline) antagonists[4] have been studied as neuroprotective agents, which can be useful in treating ischemia, epilepsy, Huntington, Alzheimer, and Parkinson type diseases. The 1-aryl-*N*-methyl-1,2,3,4-tetrahydroisoquinolines **1** (Figure 1) are also known to modulate glutamate neurotransmission in the CNS.[5] Cryptostyline I–III (**2f**, **2d**, **2e**) (Figure 2) have been isolated from *Cryptostylis fulva*[6] and belong to 1-aryl-*N*-methyl-THIQ alkaloids. These have been studied as pharmacological probes for the D_1 dopamine receptor,[5b] and other analogues of the cryptostylines act as bladder-selective muscarinic M_3 receptor antagonists.[7]

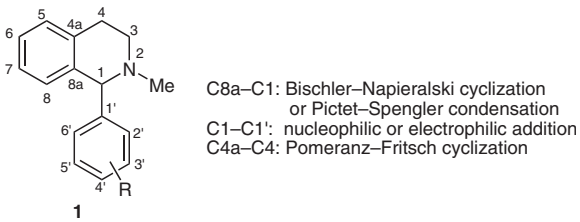

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Figure 1 The disconnection approaches to the synthesis of 1-aryl-*N*-methyl-THIQs

Many reports on the syntheses of 1-aryl-*N*-methyl-THIQs including cryptostylines I–III are available in the literature.[8] Most commonly employed procedures are the Bischler–Napieralski cyclization of amides derived by condensation of acid chlorides with 2-arylethylamines and subsequent reduction of 3,4-dihydroisoquinoline imines[9] and the Pictet–Spengler condensation[2,10] of electron-rich phenethylamines with aldehydes. Methods utilizing addition of carbon nucleophiles to iminium ions generated via Bischler–Napieralski cyclization[9a,11] and addition of Grignard reagents to 3,4-dihydroisoquinolinium tetrafluoroborate salt[12] have also been reported.

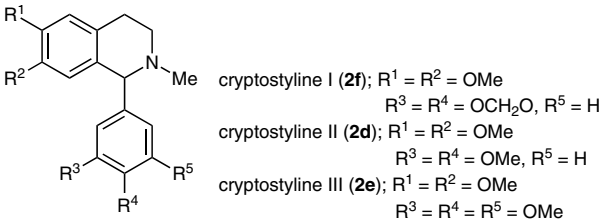

Figure 2 Cryptostyline alkaloids

Furthermore, Saitoh et al. reported the synthesis of 1-aryl-*N*-methyl-THIQs using sulfoxide-mediated electrophilic cyclization via modified Pummerer reaction.[13] Other methods include double cyclization process using *o*-vinylbenzaldehyde and amino alcohols,[14] reaction of various nucleophiles with α-siloxyamines prepared by Polonovsky reaction of tertiary amine *N*-oxides with trialkylsilyltrifluoromethane sulfonates,[15] and radical cyclization method.[16] Recently, Miyaura and co-workers reported rhodium-catalyzed asymmetric addition of aryl boronic acids to *N*-sulfonylarylaldimines for the synthesis of cryptostyline alkaloids.[17]

Lewis acid ($BF_3{\cdot}OEt_2$) complexation of tertiary amines followed by treatment with *sec*-butyllithium in tetrahydrofuran at –78 °C has been established as an effective method for the generation of α-amino carbanions **5** by our research group.[18] The α-amino carbanions can be subsequently reacted with various electrophiles to give α-substituted products[19] (Scheme 1, equation 1). Using this procedure, many *N*-methyltetrahydroisoquinoline alkaloids were synthesized.[19] Recently, we reported our findings involving reactions of β-amino carbanions **6** and arynes, which led to the synthesis of 4-aryl-*N*-methyl-1,2,3,4-tetrahydroisoquinolines[20] (Scheme 1, equation 2). It was of obvious interest to investigate whether the Lewis acid complexed α-amino carbanions **5** can also participate in a similar manner with the in situ generated aryne. If successful, it can lead to a direct one-pot synthesis of 1-aryl-*N*-methyl-1,2,3,4-tetrahydroisoquinolines (Scheme 2).

As outlined in our earlier publication,[20] many methods are available for aryne generation.[21] Further, intermolecu-

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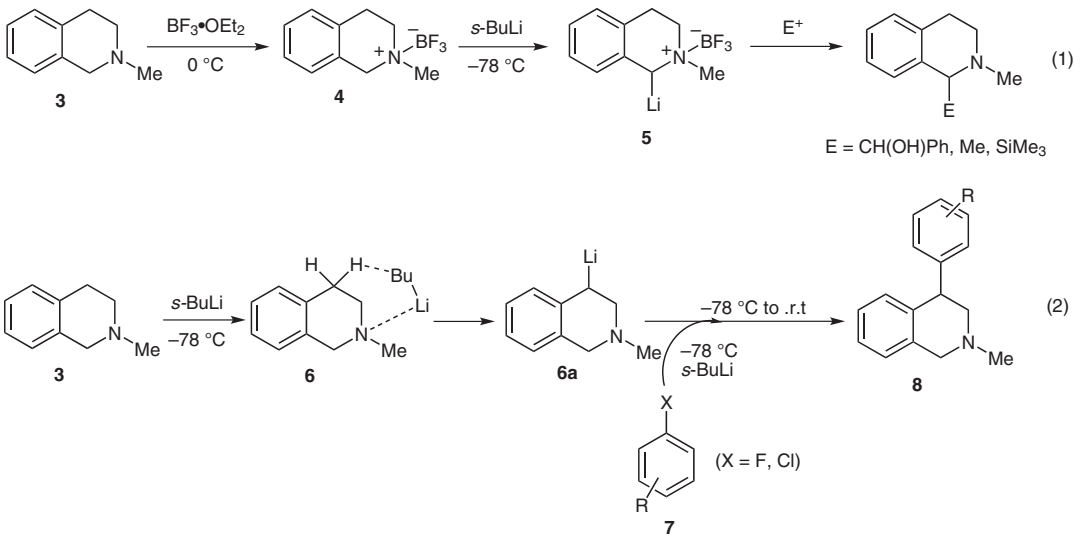
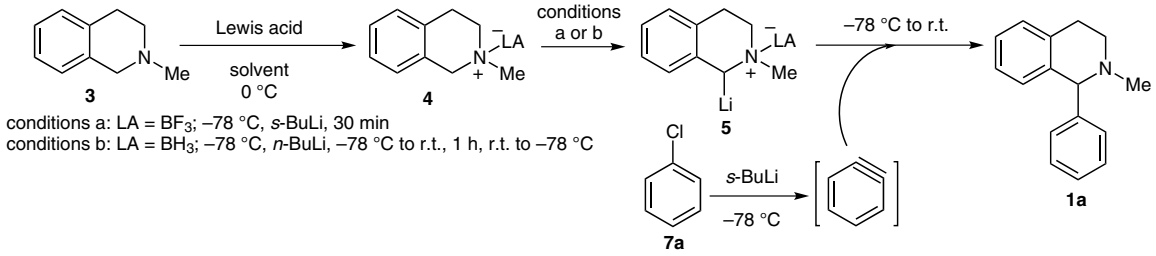


Scheme 1 Lithiation substitution of *N*-methyl-1,2,3,4-THIQ **3**



Scheme 2 Aryne-mediated arylation at C-1 position in **3**

lar/intramolecular reactions of these intermediates are known with a variety of nucleophiles including carbanions.[22] In the present work also we chose *ortho*-lithiation of aryl chlorides or fluorides with alkyllithium at low temperature followed by elimination of lithium halide for aryne generation[23] as the temperature required for this process is compatible with generation and reactions of α-lithiated species **5**.

In a model reaction, the amine-BF_3 complex **4** was generated by taking THIQ **3** (1.36 mmol) in tetrahydrofuran (10 mL) and adding $BF_3{\cdot}OEt_2$ (1.63 mmol) at 0 °C. After an interval of 30 minutes, the reaction mixture was cooled to –78 °C and *sec*-butyllithium (1.36 mmol) was added. It was then stirred for 30 minutes at the same temperature and *sec*-butyllithium (1.63 mmol) was added once again followed by chlorobenzene (**7a**) (1.36 mmol). The reaction mixture was stirred at –78 °C for another 45 minutes and then allowed to warm to room temperature where it was quenched with aqueous 10% HCl. Workup and purification by column chromatography afforded the C-1 arylated product **1a** in a low yield of 28% (Table 1, entry 1).[24] For optimization of the yield, the reaction was carried out by changing various parameters like solvent, amount of the base or of the aryl halide, Lewis acid (BH_3)[25] (Table 1, entries 2–9). Best result was obtained with tetrahydrofuran as solvent, $BF_3{\cdot}OEt_2$ as the Lewis acid and using 3 equivalents of base (second instalment) and 3 equivalents of aryl halide (Table 1, entry 7). Use of a different base, lithium tetramethylpiperidide, instead of *sec*-butyllithium, in the first addition also resulted in a lower yield of the product (Table 1, entry 10). When a solution of 4- bromoanisole and lithium diisopropylamide was used for benzyne generation and subsequently transferred to **5** via cannula, only the starting amine was recovered (Table1, entry 11). Thus, the yield of the product **1a** could not be increased beyond 40%.

After establishing the optimized reaction conditions, various substituted aryne precursors were used to check the scope of aryne mediated C-1 arylation of *N*-methyl-1,2,3,4-THIQ (**3**) and the results are summarized in Table 2. All the selected aryne precursors **7a**–**f**[20] underwent smooth reaction with **3** to furnish products **1a**–**f** in moderate yields (Table 2).

To explore the substrate scope with respect to the starting amine, differently substituted tetrahydroisoquinolines **9a**–**d** were synthesized according to the known procedures.[26] These were reacted with aryne precursors **7a**–**f** using similar conditions as for the reactions with **3** to give the corresponding C-1 arylated products **2a**–**x** (Table 3, entries 1–24), which were obtained in moderate yields. All three

Table 1 Optimizaton of Reaction Conditions for C-1 Arylation of **3**

Entry	Solvent	Base (equiv)		**7a** (equiv)	**1a** (yield %)[a]	
		1st addition (*n*-BuLi or *s*-BuLi)	2nd addition (*s*-BuLi)		LA = BF_3 conditions a	LA = BH_3 conditions b
1	THF	1	1.2	1	28[b]	22[c]
2	Et_2O	1	1.2	1	–	–
3	toluene–Et_2O (1:1)	1	1.2	1	20	–
4	THF–pentane (6:4)	1	1.2	1	19	–
5	THF	2	1.2	1	32	27
6	THF	2	2	2	35	29
7	**THF**	**2.2**	**3**	**3**	**40**	**31**
8	THF	2.2	4	4	36	30
9	THF	2.2	6	6	35	–
10	THF	2.2[d]	3	3	30	
11	THF	2.2	3[e]	3[e]	–	–

[a] Isolated yield.
[b] Reaction conditions: **3** (1.36 mmol), 0 °C, $BF_3{\cdot}OEt_2$ (1.63 mmol), 30 min, 0 °C to –78 °C, *s*-BuLi (1.36 mmol), 30 min, *s*-BuLi (1.63 mmol), **7a** (1.36 mmol), –78 °C (45 min), –78 °C to r.t.
[c] Reaction conditions: **3** (1.36 mmol), 0 °C, $BH_3{\cdot}SMe_2$ (1.63 mmol), –78 °C, *n*-BuLi (1.36 mmol), –78 °C to r.t., 1 h, r.t. to –78 °C, *s*-BuLi (1.63 mmol), **7a** (1.36 mmol), –78 °C (45 min), –78 °C to r.t.
[d] LTMP was used as base instead of *s*-BuLi.
[e] Reaction conditions: {**3** (1.36 mmol), 0 °C, $BF_3{\cdot}OEt_2$ (1.63 mmol), 30 min, 0 °C to –78 °C, *s*-BuLi (2.99 mmol), 30 min} + {4-bromoanisole (4.08 mmol), –78 °C, LDA (4.08 mmol), 30 min}, transferred via cannula, –78 °C to r.t.

alkaloids of *Cryptostylis fulva*, namely cryptostyline I (**2f**), cryptostyline II (**2d**), and cryptostyline III (**2e**) were synthesized in yields of 41, 39 and 45%, respectively (Table 3, entries 6, 4, and 5).

In all the above reactions, some unreacted starting amine **3** or **9** was always recovered. This could be due to (i) incomplete formation of the lithiated intermediate **5** or **11**, or (ii) because the lithiated intermediate gets partially quenched by another proton source (e.g., C-1 benzylic proton of arylated products **1** or **2**, or from the solvent), or (iii) the generated aryne intermediate is partially consumed by other side reactions. To get some insight on these aspects, two experiments were carried out: (1) To a solution of the amine-BF_3 complex **4** (1.36 mmol) in tetrahydrofuran (10 mL) at –78 °C, containing *sec*-butyllithium (2.99 mmol), was added acetic acid-d_1 (2.99 mmol) in tetrahydrofuran (2 mL) at the same temperature. The reaction mixture was allowed to come to room temperature and aqueous 10% HCl was added. The ^{1}H NMR spectrum of the material obtained after workup revealed 100% deuterium incorporation at C-1 (**12**) (Figure 3). (2) The reaction of **4** and **7a** was carried out in the normal manner, but after allowing the reaction mixture to warm from –78 °C to –10 °C, acetic acid-d_1 (in THF) was added. It was further allowed to come to room temperature and aqueous 10% HCl was added. Usual workup and chromatographic separation afforded products **12** (14%) and **13** (41%) (Figure 3) indicating that once the phenylated product **1a** is formed in the reaction, it does not transfer a proton to **5**. In the above reaction, when acetic acid-d_1 was added at room temperature, instead of –10 °C, the products **12** and **13** were obtained in 15% and 39% yield, respectively. Formation of product **13** can be rationalized as shown in Scheme 3.[27] Addition of **5** to the benzyne generates an intermediate carbanion **16** in which the negative charge is located at *ortho*-position of the introduced phenyl substituent. Intramolecular benzylic proton abstraction in **16** gives the rearranged carbanion **17** which upon reaction with acetic acid-d_1 furnishes **13**.

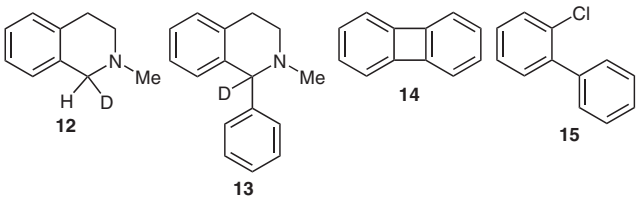
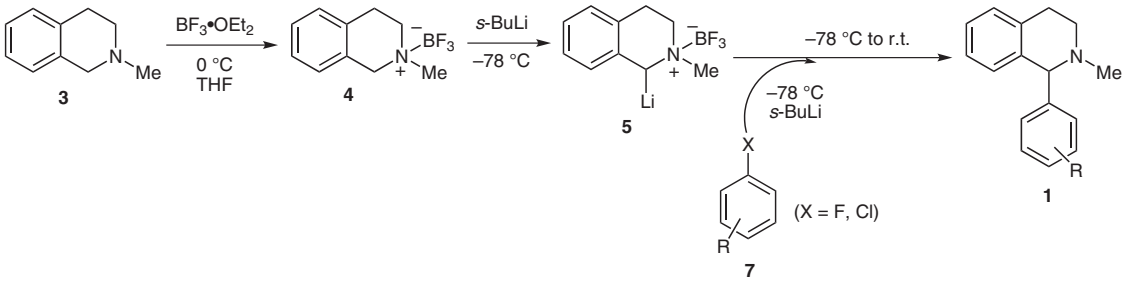
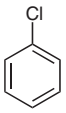
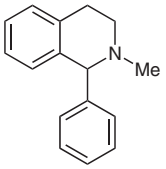
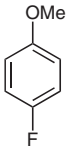
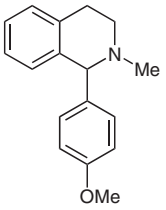
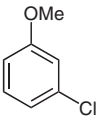
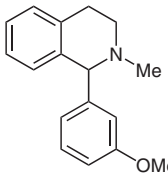
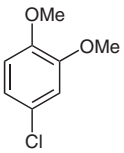
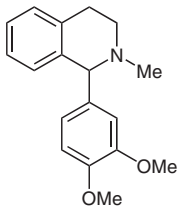
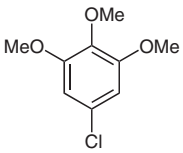
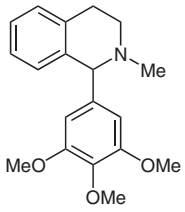
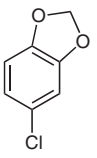
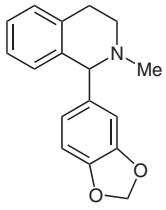


Figure 3 Results of deuterium labeling experiments

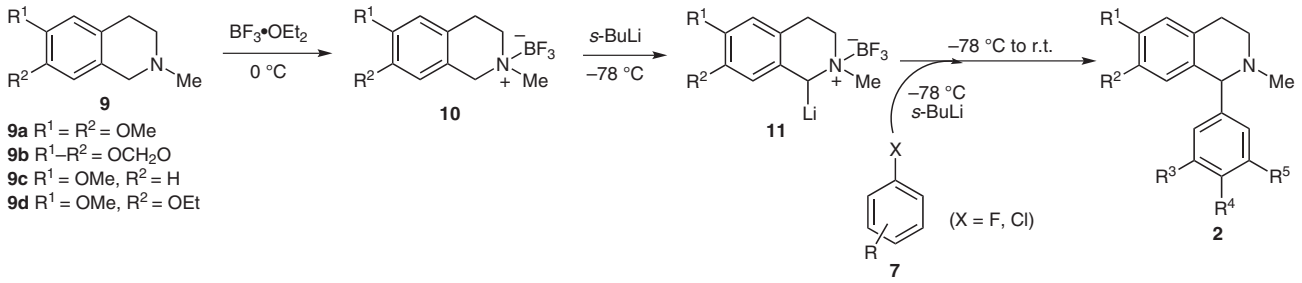
Table 2 Synthesis of **1** Using Different Aryne Substrates[a]



Entry	7		1		Yield (%)[b,c]
1	**7a**		**1a**		40 (50)
2	**7b**		**1b**		35 (47)
3	**7c**		**1c**		50 (61)
4	**7d**		**1d**		32 (45)
5	**7e**		**1e**		45 (56)
6	**7f**		**1f**		40 (52)

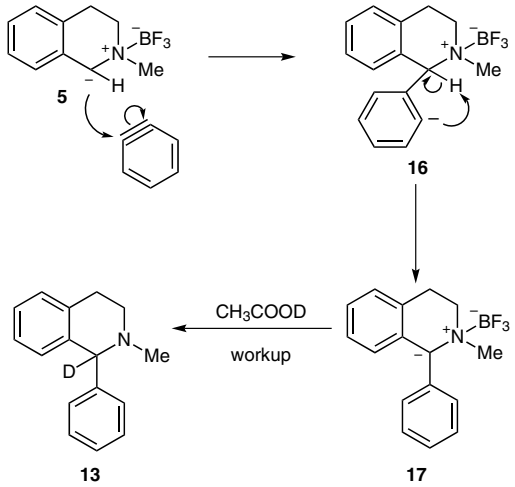
[a] Reaction conditions: *N*-methyl-1,2,3,4-tetrahydroisoquinoline (1 equiv), $BF_3{\cdot}OEt_2$ (1.2 equiv), *s*-BuLi (2.2 equiv, 1st addition), *s*-BuLi (3 equiv, 2nd addition), aryl halide (3 equiv), and THF (4 mL/mmol).
[b] Isolated yield.
[c] Yields shown in parentheses are calculated on the basis of recovered starting amine.

Table 3 C-1 Arylation of Tetrahydroisoquinolines **9**[a]



Entry	9	7	2	Yield (%)[b,c]
1	**9a**	**7a**	**2a** ($R^1 = R^2 = OMe$; $R^3 = R^4 = R^5 = H$)	35 (49)
2	**9a**	**7b**	**2b** ($R^1 = R^2 = OMe$; $R^3 = R^5 = H$, $R^4 = OMe$)	32 (47)
3	**9a**	**7c**	**2c** ($R^1 = R^2 = OMe$; $R^3 = R^4 = H$, $R^5 = OMe$)	45 (59)
4	**9a**	**7d**	**2d** ($R^1 = R^2 = OMe$; $R^3 = H$, $R^4 = R^5 = OMe$)	39 (58)
5	**9a**	**7e**	**2e** ($R^1 = R^2 = OMe$; $R^3 = R^4 = R^5 = OMe$)	45 (52)
6	**9a**	**7f**	**2f** ($R^1 = R^2 = OMe$; $R^3 = H$, $R^4 = R^5 = OCH_2O$)	41 (50)
7	**9b**	**7a**	**2g** ($R^1 + R^2 = OCH_2O$; $R^3 = R^4 = R^5 = H$)	39 (56)
8	**9b**	**7b**	**2h** ($R^1 + R^2 = OCH_2O$; $R^3 = R^5 = H$, $R^4 = OMe$)	33 (49)
9	**9b**	**7c**	**2i** ($R^1 + R^2 = OCH_2O$; $R^3 = R^4 = H$, $R^5 = OMe$)	41 (55)
10	**9b**	**7d**	**2j** ($R^1 + R^2 = OCH_2O$; $R^3 = H$, $R^4 = R^5 = OMe$)	35 (50)
11	**9b**	**7e**	**2k** ($R^1 + R^2 = OCH_2O$; $R^3 = R^4 = R^5 = OMe$)	44 (59)
12	**9b**	**7f**	**2l** ($R^1 + R^2 = OCH_2O$; $R^3 = H$, $R^4 = R^5 = OCH_2O$)	32 (46)
13	**9c**	**7a**	**2m** ($R^1 = OMe$, $R^2 = H$; $R^3 = R^4 = R^5 = H$)	32 (48)
14	**9c**	**7b**	**2n** ($R^1 = OMe$, $R^2 = H$; $R^3 = R^5 = H$, $R^4 = OMe$)	33 (50)
15	**9c**	**7c**	**2o** ($R^1 = OMe$, $R^2 = H$; $R^3 = R^4 = H$, $R^5 = OMe$)	45 (59)
16	**9c**	**7d**	**2p** ($R^1 = OMe$, $R^2 = H$; $R^3 = H$, $R^4 = R^5 = OMe$)	36 (48)
17	**9c**	**7e**	**2q** ($R^1 = OMe$, $R^2 = H$; $R^3 = R^4 = R^5 = OMe$)	41 (57)
18	**9c**	**7f**	**2r** ($R^1 = OMe$, $R^2 = H$; $R^3 = H$, $R^4 = R^5 = OCH_2O$)	40 (52)
19	**9d**	**7a**	**2s** ($R^1 = OMe$, $R^2 = OEt$; $R^3 = R^4 = R^5 = H$)	36 (48)
20	**9d**	**7b**	**2t** ($R^1 = OMe$, $R^2 = OEt$; $R^3 = R^5 = H$, $R^4 = OMe$)	32 (49)
21	**9d**	**7c**	**2u** ($R^1 = OMe$, $R^2 = OEt$; $R^3 = R^4 = H$, $R^5 = OMe$)	47 (61)
22	**9d**	**7d**	**2v** ($R^1 = OMe$, $R^2 = OEt$; $R^3 = H$, $R^4 = R^5 = OMe$)	39 (52)
23	**9d**	**7e**	**2w** ($R^1 = OMe$, $R^2 = OEt$; $R^3 = R^4 = R^5 = OMe$)	43 (58)
24	**9d**	**7f**	**2x** ($R^1 = OMe$, $R^2 = OEt$; $R^3 = H$, $R^4 = R^5 = OCH_2O$)	39 (54)

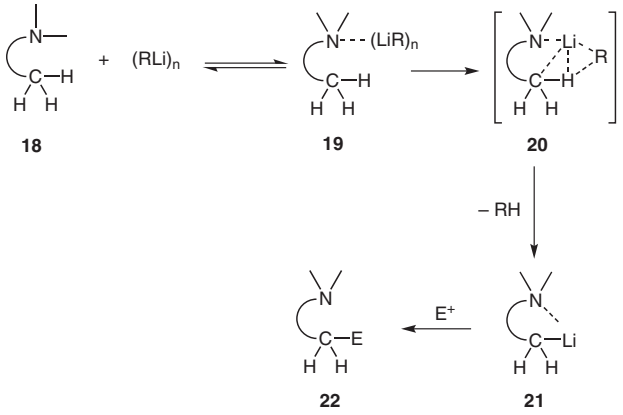
[a] Reaction conditions: **9** (1 equiv), $BF_3 \cdot OEt_2$ (1.2 equiv), *s*-BuLi (2.2 equiv, 1st addition), *s*-BuLi (3 equiv, 2nd addition), aryl halide (3 equiv), and THF (4 mL/mmol).
[b] Isolated yield.
[c] Yields shown in parentheses are calculated on the basis of recovered starting amine.



Scheme 3 Proposed mechanism

In this reaction, the nonbasic material, obtained after workup, was also investigated and found to contain **14** (7%), which results from the dimerization of the benzyne intermediate,[28] and **15** (9%) which is a result of reaction of the *ortho*-anion of chlorobenzene with benzyne (Figure 3).[29] Thus, it may be possible that side reactions of aryne intermediates occur at about the same temperature range where the lithiated intermediates **5** or **11** react with arynes.

As far as the difference in regioselectivity in lithiation/substitution reactions of *N*-methyl-1,2,3,4-tetrahydroisoquinoline – at C-4 position (using strong basic conditions) and at C-1 position (under Lewis acid complexation) – is concerned it has been shown earlier that the heteroatom plays a pivotal role. In the case of the uncomplexed amine, the nitrogen atom coordinates with lithium in the transition state **20** or in a prelithiation complex **19** and promotes 'distal lithiation' through space (Scheme 1, 6, and Scheme 4).[30]



Scheme 4 Nitrogen-assisted deprotonation, E^+ = electrophile

On the other hand, the nitrogen lone pair, unlike P, O, or S, is also known to generate a relatively strong repulsive interaction with an adjoining negative charge thus preventing α-deprotonation.[31] Prior complexation of the nitrogen atom with a strong Lewis acid (Scheme 1, 4) prevents its coordination with lithium atom of the base. Furthermore, the positive charge on the nitrogen atom now inductively facilitates α-deprotonation (Scheme 1, 5).[18,19]

In conclusion, direct C-1 arylation of *N*-methyl-1,2,3,4-tetrahydroisoquinolines involving nucleophilic addition of α-amino carbanions derived from Lewis acid complexed THIQ to arynes has been demonstrated with applications in synthesis of cryptostyline alkaloids. The modest yields of the products are counter-balanced by the fact that this one-pot arylation procedure does not involve the use of any transition metal[32] and has good substrate generality. Further applications of this procedure for the synthesis of 1-aryl-2-methylisoindolines[33] and 1-aryl-2-methyl-2,3,4,5-tetrahydro-2-benz[*c*]azepines[34] are being explored.

^{1}H NMR spectra were recorded on a 400 MHz NMR spectrometer. Chemical shifts δ are reported in ppm using TMS as an internal standard. Data are reported as follows: chemical shift, multiplicity (standard abbreviations), coupling constant (*J*), and integration. ^{13}C NMR spectra were recorded on 75 MHz NMR spectrometer. The chemical shifts are reported on the δ-scale relative to $CDCl_3$ (δ = 77.0 ppm). IR spectra were carried out on neat samples using a Nicolet iS50 FT-IR. The wavenumbers of maximum absorption peaks of IR spectroscopy are presented in cm^{-1}. MS data (APCI) was obtained on Q-Tof Micro™ mass spectrometer. Elemental analyses were performed with a Flash 2000 (organic elemental analyzer). Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected. Flash column chromatography was performed using 230–400 mesh silica gel and hexane–EtOAc or MeOH–$CHCl_3$ mixture as an eluent.

All lithiation reactions were carried out under N_2 atmosphere. Anhydrous solvents were transferred via syringe to flame-dried glassware. THF, Et_2O, and toluene were dried and distilled from sodium benzophenone ketyl. $BF_3{\cdot}OEt_2$ was freshly distilled from CaH_2 under reduced pressure. Pentane was purified and dried according to a known procedure.[35] Alkyllithiums were estimated by using 1,10-phenanthroline as an indicator according to a reported procedure.[36] *n*-BuLi was used as a 1.9 M solution in hexane. *s*-BuLi was used as a 2.6 M solution in pentane. Amine **3** was prepared from isoquinoline according to the reported procedure.[37] Amine **9a** was prepared from homoveratrylamine by a known procedure.[26a] Tetrahydroisoquinoline **9b** was synthesized starting from homopiperonylamine.[26b] Amine **9c** was prepared from 3-methoxybenzaldehyde via a known route.[26b,c] Tetrahydroisoquinoline **9d** was synthesized from vanillin according to a reported procedure.[26c] Chlorobenzene (**7a**) was commercially available. Substrate **7d**,[38a] **7e**,[38b] and **7f**[38c] were prepared according to known procedures. Substrate **7b** and **7c** were prepared from *p*-fluorophenol and *m*-chlorophenol, respectively.[39] All aryne precursors and starting THIQs were dried and distilled from CaH_2, under reduced pressure, before use.

1-Aryl-*N*-methyl-1,2,3,4-tetrahydroisoquinolines; General Procedure

Into a flame-dried two-necked round-bottomed flask, equipped with a magnetic stirrer bar, septum cap and a bubbler, was taken a solution of *N*-methyl-1,2,3,4-tetrahydroisoquinoline (**3**; 200 mg, 1.36 mmol, 1 equiv) or the substituted analogue **9** (1.36 mmol, 1 equiv) in anhydrous THF (10 mL) under an inert N_2 atmosphere. It was cooled to 0 °C and $BF_3{\cdot}OEt_2$ (0.25 mL, 1.63 mmol, 1.2 equiv) was added dropwise. The turbid white solution was stirred at 0 °C for 30 min. It was then cooled to –78 °C and *s*-BuLi [1.43 mL (2.6 M in pentane), 2.99 mmol, 2.2 equiv] was added dropwise. A deep red color (indicative of benzylic carbanion formation) appeared imme-

diately. The solution was stirred at the same temperature for 30 min. The second instalment of *s*-BuLi [1.96 mL (2.6 M in pentane), 4.08 mmol, 3 equiv] was added followed by the addition of a solution of aryl halide **7** (4.08 mmol, 3 equiv) in THF (1–2 mL). The reaction mixture was stirred at –78 °C for 45 min and was allowed to warm to r.t. slowly over a period of 4–5 h. The reaction was quenched with aq 10% HCl (15 mL) and the contents were poured into Et_2O (25 mL). The aqueous layer was separated and the organic layer was further extracted with aq 10% HCl (2 × 15 mL). The combined aqueous layers were washed with Et_2O (2 × 20 mL) to remove non-basic impurities, made alkaline with solid Na_2CO_3, and extracted with $CHCl_3$ (4 × 15 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The solvent was evaporated in vacuo to afford the crude product, which was purified by flash column chromatography using 230–400 mesh silica gel. Elution with EtOAc–hexane (3:7) or MeOH–$CHCl_3$ (2:98) afforded the 1-aryl substituted product. Further elution of the column with same solvent afforded the unreacted starting material (Tables 2 and 3).

2-Methyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline (1a)[40]
Yield: 121 mg (40%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.10 (m, 5 H, ArH), 6.97–6.91 (m, 2 H, ArH), 6.81 (t, *J* = 8.1 Hz, 1 H, ArH), 6.48 (d, *J* = 7.8 Hz, 1 H, ArH), 4.09 (s, 1 H, C_1-H), 3.18–3.12 (m, 1 H, C_3-H), 3.02–2.97 (m, 1 H, C_3-H), 2.66 (dt, *J* = 16.1, 3.1 Hz, 1 H, C_4-H), 2.48 (td, *J* = 11.3, 3.7 Hz, 1 H, C_4-H), 2.11 (s, 3 H, NCH_3).

1-(4-Methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (1b)
Yield: 119 mg (35%); yellow solid; mp 78–80 °C.

IR (neat): 2935, 2840, 1497, 1263, 1028 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (d, *J* = 8.6 Hz, 2 H, ArH), 6.97–6.92 (m, 2 H, ArH), 6.82 (t, *J* = 8.1 Hz, 1 H, ArH), 6.69 (d, *J* = 8.6 Hz, 2 H, ArH), 6.49 (d, *J* = 7.8 Hz, 1 H, ArH), 4.04 (s, 1 H, C_1-H), 3.69 (s, 3 H, OCH_3), 3.15–3.11 (m, 1 H, C_3-H), 3.02–2.97 (m, 1 H, C_3-H), 2.66 (dt, *J* = 16.0, 3.0 Hz, 1 H, C_4-H), 2.47 (td, *J* = 11.2, 3.7 Hz, 1 H, C_4-H), 2.11 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 138.9, 136.1, 134.1, 130.5, 128.6, 128.2, 125.8, 125.6, 113.6, 70.9, 54.9, 52.4, 44.4, 29.6.

MS (APCI): *m*/*z* = 254.08 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{20}NO$: 254.1539; found: 254.1543.

1-(3-Methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (1c)[41]
Yield: 172 mg (50%); light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08 (t, *J* = 7.8 Hz, 1 H, ArH), 6.99–6.93 (m, 2 H, ArH), 6.84 (t, *J* = 8.1 Hz, 1 H, ArH), 6.76 (d, *J* = 7.5 Hz, 1 H, ArH), 6.71–6.66 (m, 2 H, ArH), 6.53 (d, *J* = 7.8 Hz, 1 H, ArH), 4.07 (s, 1 H, C_1-H), 3.67 (s, 3 H, OCH_3), 3.20–3.13 (m, 1 H, C_3-H), 3.04–2.99 (m, 1 H, C_3-H), 2.67 (dt, *J* = 16.1, 2.9 Hz, 1 H, C_4-H), 2.49 (td, *J* = 11.3, 3.7 Hz, 1 H, C_4-H), 2.14 (s, 3 H, NCH_3).

1-(3,4-Dimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (1d)
Yield: 123 mg (32%); white solid; mp 86–87 °C.

IR (neat): 2940, 2843, 1505, 1253, 1028 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.99–6.94 (m, 2 H, ArH), 6.83 (t, *J* = 8.1 Hz, 1 H, ArH), 6.72 (dd, *J* = 8.1, 1.8 Hz, 1 H, ArH), 6.67 (d, *J* = 8.1 Hz, 1 H, ArH), 6.63 (d, *J* = 1.8 Hz, 1 H, ArH), 6.52 (d, *J* = 7.8 Hz, 1 H, ArH), 4.01 (s, 1 H, C_1-H), 3.78 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 3.21–3.13 (m, 1 H, C_3-H), 3.05–3.00 (m, 1 H, C_3-H), 2.67 (br d, *J* = 16.0 Hz, 1 H, C_4-H), 2.48 (td, *J* = 11.4, 3.68 Hz, 1 H, C_4-H), 2.12 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.4, 148.5, 138.6, 136.5, 133.9, 128.4, 128.2, 125.8, 125.6, 122.1, 112.0, 110.5, 71.5, 55.7, 52.7, 44.5, 29.5.

MS (APCI): *m*/*z* = 284.17 [M + H]$^+$.

Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.34; H, 7.38; N, 4.93.

1-(3,4,5-Trimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (1e)
Yield: 191 mg (45%); pale yellow solid; mp 135–138 °C.

IR (neat): 2939, 2836, 1478, 1254, 1008 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98–6.97 (m, 2 H, ArH), 6.90–6.86 (m, 1 H, Ar–H), 6.56 (d, *J* = 7.8 Hz, 1 H, ArH), 6.39 (s, 2 H, ArH), 3.98 (s, 1 H, C_1-H), 3.75 (s, 3 H, OCH_3), 3.74 (s, 6 H, 2 × OCH_3), 3.17–3.13 (m, 1 H, C_3-H), 3.06–3.01 (m, 1 H, C_3-H), 2.67 (br d, *J* = 16.0 Hz, 1 H, C_4-H), 2.48 (td, *J* = 11.4, 3.6 Hz, 1 H, C_4-H), 2.14 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.2, 139.4, 138.3, 133.8, 131.3, 128.2, 128.2, 126.0, 125.7, 106.5, 72.2, 60.5, 56.0, 52.8, 44.6, 29.5.

MS (APCI): *m*/*z* = 314.13 [M + H]$^+$.

Anal. Calcd for $C_{19}H_{23}NO_3$: C, 72.82; H, 7.40; N, 4.47. Found: C, 72.54; H, 7.34; N, 4.53.

2-Methyl-1-(3,4-methylenedioxyphenyl)-1,2,3,4-tetrahydroisoquinoline (1f)
Yield: 145 mg (40%); colorless oil.

IR (neat): 2904, 2843, 1550, 1235, 1082 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98–6.93 (m, 2 H, ArH), 6.88–6.84 (m, 1 H, ArH), 6.66 (dd, *J* = 7.8, 1.4 Hz, 1 H, ArH), 6.63–6.61 (m, 2 H, ArH), 6.55 (d, *J* = 7.8 Hz, 1 H, ArH), 5.83 (d, *J* = 1.4 Hz, 1 H, OCH_2O), 5.81 (d, *J* = 1.4 Hz, 1 H, OCH_2O), 4.01 (s, 1 H, C_1-H), 3.18–3.10 (m, 1 H, C_3-H), 3.02–2.97 (m, 1 H, C_3-H), 2.65 (dt, *J* = 15.8, 2.8 Hz, 1 H, C_4-H), 2.47 (td, *J* = 11.3, 3.7 Hz, 1 H, C_4-H), 2.13 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.9, 146.9, 138.1, 138.1, 134.0, 128.0, 127.9, 126.0, 125.9, 122.9, 109.8, 107.4, 100.7, 71.3, 52.5, 44.4, 29.8.

MS (APCI): *m*/*z* = 268.44 [M + H]$^+$.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}NO_2$: 268.1332; found: 268.1331.

6,7-Dimethoxy-2-methyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline (2a)[42]
Yield: 96 mg (35%); light yellow solid; mp 76–78 °C (Lit.[42] mp 77–79 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.13 (m, 5 H, ArH), 6.48 (s, 1 H, ArH), 5.97 (s, 1 H, ArH), 4.06 (s, 1 H, C_1-H), 3.75 (s, 3 H, OCH_3), 3.47 (s, 3 H, OCH_3), 3.12–3.05 (m, 1 H, C_3-H), 3.02–2.97 (m, 1 H, C_3-H), 2.60 (dt, *J* = 15.7, 3.3 Hz, 1 H, C_4-H), 2.48 (td, *J* = 10.9, 3.7 Hz, 1 H, C_4-H), 2.14 (s, 3 H, NCH_3).

6,7-Dimethoxy-1-(4-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2b)[43]
Yield: 97 mg (32%); light brown solid; mp 93–95 °C (Lit.[43] mp 96–97 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.05 (d, *J* = 8.7 Hz, 2 H, ArH), 6.71 (d, *J* = 8.6 Hz, 2 H, ArH), 6.46 (s, 1 H, ArH), 5.98 (s, 1 H, ArH), 4.02 (s, 1 H, C_1-H), 3.74 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 3.49 (s, 3 H, OCH_3), 3.09–3.02 (m, 1 H, C_3-H), 3.00–2.96 (m, 1 H, C_3-H), 2.59 (dt, *J* = 15.7, 3.4 Hz, 1 H, C_4-H), 2.46 (td, *J* = 10.7, 3.7 Hz, 1 H, C_4-H), 2.12 (s, 3 H, NCH_3).

6,7-Dimethoxy-1-(3-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2c)
Yield: 136 mg (45%); yellow pasty mass.

IR (neat): 2946, 2849, 1504, 1260, 1037 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.09 (t, *J* = 7.6 Hz, 1 H, ArH), 6.75 (d, *J* = 7.6 Hz, 1 H, ArH), 6.70–6.67 (m, 2 H, ArH), 6.47 (s, 1 H,

ArH), 6.01 (s, 1 H, ArH), 4.02 (s, 1 H, C_1-H), 3.76 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 3.50 (s, 3 H, OCH_3), 3.08–3.01 (m, 1 H, C_3-H), 3.00–2.97 (m, 1 H, C_3-H), 2.59 (dd, J = 15.8, 3.1 Hz, 1 H, C_4-H), 2.46 (td, J = 10.9, 3.6 Hz, 1 H, C_4-H), 2.14 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 147.5, 147.2, 145.5, 130.3, 128.9, 126.2, 122.0, 114.6, 112.9, 111.5, 110.8, 71.1, 55.7, 55.6, 54.9, 52.4, 44.4, 29.0.

MS (APCI): m/z = 314.10 $[M + H]^+$.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{19}H_{24}NO_3$: 314.1750; found: 314.1754.

6,7-Dimethoxy-1-(3,4-dimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline [(±)-Cryptostyline II, 2d][14]
Yield: 129 mg (39%); pale yellow solid; mp 95–96 °C (Lit.[14] mp 94 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.73 (dd, J = 8.1, 1.8 Hz, 1 H, ArH), 6.69 (d, J = 8.1 Hz, 1 H, ArH), 6.65 (d, J = 1.6 Hz, 1 H, ArH), 6.48 (s, 1 H, ArH), 6.02 (s, 1 H, ArH), 3.97 (s, 1 H, C_1-H), 3.81 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.50 (s, 3 H, OCH_3), 3.09–3.03 (m, 1 H, C_3-H), 3.02–2.99 (m, 1 H, C_3-H), 2.60 (br d, J = 15.6 Hz, 1 H, C_4-H), 2.47 (td, J = 10.8, 3.5 Hz, 1 H, C_4-H), 2.13 (s, 3 H, NCH_3).

6,7-Dimethoxy-1-(3,4,5-trimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline [(±)-Cryptostyline III, 2e][44]
Yield: 162 mg (45%); light brown solid; mp 138–140 °C (Lit.[44] mp 140–141 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.47 (s, 1 H, ArH), 6.40 (s, 2 H, ArH), 6.05 (s, 1 H, ArH), 3.93 (s, 1 H, C_1-H), 3.78 (s, 6 H, 2 × OCH_3), 3.76 (s, 6 H, 2 × OCH_3), 3.52 (s, 3 H, OCH_3), 3.07–3.03 (m, 1 H, C_3-H), 3.01–2.98 (m, 1 H, C_3-H), 2.59 (br d, J = 15.6 Hz, 1 H, C_4-H), 2.45 (td, J = 10.5, 3.2 Hz, 1 H, C_4-H), 2.15 (s, 3 H, NCH_3).

6,7-Dimethoxy-2-methyl-1-(3,4-methylenedioxyphenyl)-1,2,3,4-tetrahydroisoquinoline [(±)-Cryptostyline I, 2f][11]
Yield: 129 mg (41%); yellow solid; mp 116–117 °C (Lit.[11] mp 117–118 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.65 (dd, J = 7.9, 1.4 Hz, 1 H, ArH), 6.62 (d, J = 7.8 Hz, 1 H, ArH), 6.61 (d, J = 1.2 Hz, 1 H, ArH), 6.46 (s, 1 H, ArH), 6.04 (s, 1 H, ArH), 5.84 (d, J = 1.1 Hz, 1 H, OCH_2O), 5.83 (d, J = 1.2 Hz, 1 H, OCH_2O), 3.98 (s, 1 H, C_1-H), 3.75 (s, 3 H, OCH_3), 3.53 (s, 3 H, OCH_3), 3.09–3.02 (m, 1 H, C_3-H), 3.00–2.95 (m, 1 H, C_3-H), 2.58 (dd, J = 15.7, 3.0 Hz, 1 H, C_4-H), 2.45 (td, J = 10.8, 3.5 Hz, 1 H, C_4-H), 2.14 (s, 3 H, NCH_3).

2-Methyl-6,7-methylenedioxy-1-phenyl-1,2,3,4-tetrahydroisoquinoline (2g)[45]
Yield: 109 mg (39%); light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.24 (m, 2 H, ArH), 7.22–7.19 (m, 3 H, ArH), 6.51 (s, 1 H, ArH), 6.03 (s, 1 H, ArH), 5.78 (d, J = 1.4 Hz, 1 H, OCH_2O), 5.75 (d, J = 1.4 Hz, 1 H, OCH_2O), 4.07 (s, 1 H, C_1-H), 3.13–3.09 (m, 1 H, C_3-H), 3.05–3.01 (m, 1 H, C_3-H), 2.63 (dt, J = 15.7, 3.2 Hz, 1 H, C_4-H), 2.51 (td, J = 11.0, 3.7 Hz, 1 H, C_4-H), 2.17 (s, 3 H, NCH_3).

1-(4-Methoxyphenyl)-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (2h)
Yield: 102 mg (33%); light brown solid; mp 86–88 °C.

IR (neat): 2943, 2833, 1497, 1247, 1040 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (d, J = 8.6 Hz, 2 H, ArH), 6.79 (d, J = 8.7 Hz, 2 H, ArH), 6.51 (s, 1 H, ArH), 6.04 (s, 1 H, ArH), 5.80 (d, J = 1.48 Hz, 1 H, OCH_2O), 5.78 (d, J = 1.4 Hz, 1 H, OCH_2O), 4.04 (s, 1 H, C_1-H), 3.78 (s, 3 H, OCH_3), 3.17–3.09 (m, 1 H, C_3-H), 3.06–3.01 (m, 1 H, C_3-H), 2.64 (dt, J = 15.8, 2.8 Hz, 1 H, C_4-H), 2.51 (td, J = 10.9, 3.6 Hz, 1 H, C_4-H), 2.18 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.9, 145.8, 145.7, 135.8, 131.7, 130.4, 127.3, 113.6, 108.4, 107.7, 100.4, 70.8, 55.0, 52.3, 44.2, 29.5.

MS (APCI): m/z = 298.11 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.59; H, 6.34; N, 4.70.

1-(3-Methoxyphenyl)-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (2i)
Yield: 127 mg (41%); light brown oil.

IR (neat): 2949, 2841, 1493, 1245, 1040 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (t, J = 7.4 Hz, 1 H, ArH), 6.82 (d, J = 7.6 Hz, 1 H, ArH), 6.77–6.75 (m, 2 H, ArH), 6.52 (s, 1 H, ArH), 6.08 (s, 1 H, ArH), 5.82 (d, J = 1.4 Hz, 1 H, OCH_2O), 5.79 (d, J = 1.4 Hz, 1 H, OCH_2O), 4.06 (s, 1 H, C_1-H), 3.77 (s, 3 H, OCH_3), 3.15–3.07 (m, 1 H, C_3-H), 3.05–3.03 (m, 1 H, C_3-H), 2.65 (br d, J = 15.8 Hz, 1 H, C_4-H), 2.54 (td, J = 11.0, 3.6 Hz, 1 H, C_4-H), 2.20 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8, 145.8, 145.6, 132.9, 131.4, 129.0, 127.1, 122.0, 114.5, 113.1, 108.3, 107.7, 100.3, 71.6, 54.8, 52.5, 44.5, 29.7.

MS (APCI): m/z = 298.13 $[M + H]^+$.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{18}H_{20}NO_3$: 298.1437; found: 298.1437.

1-(3,4-Dimethoxyphenyl)-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (2j)
Yield: 119 mg (35%); pale yellow solid; mp 126–128 °C.

IR (neat): 2945, 2826, 1472, 1253, 1028 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.78 (dd, J = 8.1, 1.7 Hz, 1 H, ArH), 6.75 (d, J = 8.1 Hz, 1 H, ArH), 6.71 (d, J = 1.6 Hz, 1 H, ArH), 6.52 (s, 1 H, ArH), 6.06 (s, 1 H, ArH), 5.81 (d, J = 1.4 Hz, 1 H, OCH_2O), 5.79 (d, J = 1.4 Hz, 1 H, OCH_2O), 4.00 (s, 1 H, C_1-H), 3.86 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.15–3.07 (m, 1 H, C_3-H), 3.06–3.04 (m, 1 H, C_3-H), 2.64 (br d, J = 15.8 Hz, 1 H, C_4-H), 2.51 (td, J = 11.1, 3.6 Hz, 1 H, C_4-H), 2.18 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.2, 148.4, 145.8, 145.6, 135.9, 131.3, 127.0, 121.9, 111.6, 110.3, 108.1, 107.6, 100.3, 71.3, 55.6, 55.6, 52.4, 44.1, 29.2.

MS (APCI): m/z = 328.27 $[M + H]^+$.

Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.69; H, 6.34; N, 4.10.

1-(3,4,5-Trimethoxyphenyl)-2-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline (2k)[9d]
Yield: 164 mg (44%); white solid; mp 130–133 °C (Lit.[9d] mp 133–134 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.53 (s, 1 H, ArH), 6.47 (s, 2 H, ArH), 6.11 (s, 1 H, ArH), 5.84 (d, J = 1.4 Hz, 1 H, OCH_2O), 5.82 (d, J = 1.4 Hz, 1 H, OCH_2O), 3.98 (s, 1 H, C_1-H), 3.83 (s, 6 H, 2 × OCH_3), 3.82 (s, 3 H, OCH_3), 3.17–3.10 (m, 1 H, C_3-H), 3.08–3.07 (m, 1 H, C_3-H), 2.65 (br d, J = 15.8 Hz, 1 H, C_4-H), 2.50 (br t, J = 11.1 Hz, 1 H, C_4-H), 2.21 (s, 3 H, NCH_3).

2-Methyl-6,7-methylenedioxy-1-(3,4-methylenedioxyphenyl)-1,2,3,4- tetrahydroisoquinoline (2l)
Yield: 102 mg (32%); yellow solid; mp 164–165 °C.

IR (neat): 2981, 2896, 1478, 1236, 1039 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.72 (dd, J = 7.9, 1.4 Hz, 1 H, ArH), 6.69 (d, J = 7.7 Hz, 1 H, ArH), 6.67 (d, J = 1.1 Hz, 1 H, ArH), 6.51 (s, 1 H, ArH), 6.09 (s, 1 H, ArH), 5.92 (d, J = 1.5 Hz, 1 H, OCH_2O), 5.90 (d, J = 1.5 Hz, 1 H, OCH_2O), 5.81 (d, J = 1.4 Hz, 1 H, OCH_2O), 5.79 (d, J = 1.4 Hz, 1 H, OCH_2O), 4.00 (s, 1 H, C_1-H), 3.16–3.08 (m, 1 H, C_3-H), 3.05–3.01 (m, 1 H, C_3-H), 2.62 (dt, J =

15.8, 3.1 Hz, 1 H, C_4-H), 2.50 (td, *J* = 11.0, 3.6 Hz, 1 H, C_4-H), 2.19 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.9, 146.9, 145.9, 145.8, 138.0, 131.6, 127.3, 122.8, 109.3, 108.3, 107.8, 107.5, 100.8, 100.5, 71.3, 52.4, 44.3, 29.6.

MS (APCI): *m*/*z* = 312.41 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.12; H, 5.62; N, 4.59.

6-Methoxy-2-methyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline (2m)[5b]
Yield: 91 mg (32%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.13 (m, 5 H, ArH), 6.50 (d, *J* = 2.0 Hz, 1 H, ArH), 6.41 (d, *J* = 2.4 Hz, 1 H, ArH), 6.38 (d, *J* = 8.6 Hz, 1 H, ArH), 4.04 (s, 1 H, C_1-H), 3.65 (s, 3 H, OCH_3), 3.15–2.97 (m, 2 H, C_3-H), 2.65 (br d, *J* = 16.0 Hz, 1 H, C_4-H), 2.48 (td, *J* = 11.3, 3.8 Hz, 1 H, C_4-H), 2.12 (s, 3 H, NCH_3).

6-Methoxy-1-(4-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2n)
Yield: 105 mg (33%); light yellow solid; mp 94–96 °C.

IR (neat): 2941, 2834, 1505, 1253, 1029 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (d, *J* = 8.6 Hz, 2 H, ArH), 6.70 (d, *J* = 8.7 Hz, 2 H, ArH), 6.49 (s, 1 H, ArH), 6.44–6.39 (m, 2 H, ArH), 4.00 (s, 1 H, C_1-H), 3.70 (s, 3 H, OCH_3), 3.64 (s, 3 H, OCH_3), 3.18–3.09 (m, 1 H, C_3-H), 3.01–2.96 (m, 1 H, C_3-H), 2.63 (dt, *J* = 16.1, 3.0 Hz, 1 H, C_4-H), 2.47 (td, *J* = 11.2, 3.8 Hz, 1 H, C_4-H), 2.11 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.8, 157.6, 136.2, 135.2, 131.3, 130.4, 129.6, 113.5, 112.4, 112.1, 70.5, 55.0, 54.9, 52.5, 44.3, 29.8.

MS (APCI): *m*/*z* = 284.09 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.44; H, 7.29; N, 4.88.

6-Methoxy-1-(3-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2o)
Yield: 143 mg (45%); yellow viscous oil.

IR (neat): 2914, 2843, 1550, 1235, 1092 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.08 (t, *J* = 7.7 Hz, 1 H, ArH), 6.75 (d, *J* = 7.6 Hz, 1 H, ArH), 6.70–6.66 (m, 2 H, ArH), 6.49 (s, 1 H, ArH), 6.45–6.43 (m, 2 H, ArH), 4.01 (s, 1 H, C_1-H), 3.67 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 3.18–3.11 (m, 1 H, C_3-H), 3.02–2.97 (m, 1 H, C_3-H), 2.63 (dt, *J* = 16.0, 3.1 Hz, 1 H, C_4-H), 2.47 (td, *J* = 11.3, 3.7 Hz, 1 H, C_4-H), 2.13 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.7, 157.6, 145.8, 135.1, 130.8, 129.5, 129.0, 122.0, 114.6, 112.9, 112.5, 112.2, 71.3, 54.9, 54.9, 52.6, 44.5, 29.9.

MS (APCI): *m*/*z* = 284.21 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{22}NO_2$: 284.1645; found: 284.1645.

6-Methoxy-1-(3,4-dimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2p)[46]
Yield: 127 mg (36%); light brown solid; mp 70–72 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.71 (dd, *J* = 8.1, 1.8 Hz, 1 H, ArH), 6.67 (d, *J* = 8.1 Hz, 1 H, ArH), 6.63 (d, *J* = 1.7 Hz, 1 H, ArH), 6.50 (s, 1 H, ArH), 6.44–6.42 (m, 2 H, ArH), 3.95 (s, 1 H, C_1-H), 3.79 (s, 3 H, OCH_3), 3.72 (s, 3 H, OCH_3), 3.66 (s, 3 H, OCH_3), 3.19–3.11 (m, 1 H, C_3-H), 3.03–2.98 (m, 1 H, C_3-H), 2.64 (br d, *J* = 16.1 Hz, 1 H, C_4-H), 2.46 (td, *J* = 11.4, 3.7 Hz, 1 H, C_4-H), 2.11 (s, 3 H, NCH_3).

6-Methoxy-1-(3,4,5-trimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2q)[47]
Yield: 158 mg (41%); pale brown solid; mp 96–97 °C (Lit.[47] mp 94–95 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.50–6.48 (m, 1 H, ArH), 6.46–6.42 (m, 2 H, ArH), 6.39 (s, 2 H, ArH), 3.92 (s, 1 H, C_1-H), 3.74 (s, 3 H, OCH_3), 3.72 (s, 6 H, 2 × OCH_3), 3.65 (s, 3 H, OCH_3), 3.15–3.11 (m, 1 H, C_3-H), 3.03–2.99 (m, 1 H, C_3-H), 2.63 (br d, *J* = 16.0 Hz, 1 H, C_4-H), 2.46 (td, *J* = 11.4, 3.7 Hz, 1 H, C_4-H), 2.13 (s, 3 H, NCH_3).

6-Methoxy-2-methyl-1-(3,4-methylenedioxyphenyl)-1,2,3,4-tetrahydroisoquinoline (2r)
Yield: 134 mg (40%); white solid; mp 110–113 °C.

IR (neat): 2963, 2810, 1490, 1276, 1079 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.65 (dd, *J* = 7.8, 1.4 Hz, 1 H, ArH), 6.61 (d, *J* = 7.8 Hz, 1 H, ArH), 6.60 (d, *J* = 1.4 Hz, 1 H, ArH), 6.48 (d, *J* = 1.7 Hz, 1 H, ArH), 6.45–6.42 (m, 2 H, ArH), 5.82 (d, *J* = 1.4 Hz, 1 H, OCH_2O), 5.81 (d, *J* = 1.4 Hz, 1 H, OCH_2O), 3.96 (s, 1 H, C_1-H), 3.65 (s, 3 H, OCH_3), 3.15–3.08 (m, 1 H, C_3-H), 3.00–2.95 (m, 1 H, C_3-H), 2.66–2.62 (m, 1 H, C_4-H), 2.45 (td, *J* = 11.3, 3.7 Hz, 1 H, C_4-H), 2.12 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.7, 147.9, 146.8, 138.3, 135.2, 130.9, 129.5, 122.8, 112.5, 112.2, 109.3, 107.4, 100.7, 70.9, 54.8, 52.5, 44.3, 29.9.

MS (APCI): *m*/*z* = 298.53 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.59; H, 6.35; N, 4.65.

7-Ethoxy-6-methoxy-2-methyl-1-phenyl-1,2,3,4-tetrahydroisoquinoline (2s)
Yield: 96 mg (36%); yellow oil.

IR (neat): 2927, 2773, 1476, 1227, 1138 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.19–7.10 (m, 5 H, ArH), 6.44 (s, 1 H, ArH), 5.93 (s, 1 H, ArH), 4.02 (s, 1 H, C_1-H), 3.70 (s, 3 H, OCH_3), 3.69–3.55 (m, 2 H, OCH_2CH_3), 3.10–3.02 (m, 1 H, C_3-H), 2.99–2.94 (m, 1 H, C_3-H), 2.62–2.57 (m, 1 H, C_4-H), 2.45 (td, *J* = 11.0, 3.8 Hz, 1 H, C_4-H), 2.10 (s, 3 H, NCH_3), 1.13 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.7, 146.3, 143.9, 130.3, 129.3, 127.9, 127.1, 126.1, 113.2, 111.0, 70.9, 63.9, 55.5, 52.2, 44.2, 28.9, 14.5.

MS (APCI): *m*/*z* = 298.93 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{24}NO_2$: 298.1801; found: 298.1804.

7-Ethoxy-6-methoxy-1-(4-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2t)
Yield: 94 mg (32%); yellow solid; mp 87–89 °C.

IR (neat): 2945, 2838, 1494, 1247, 1038 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (d, *J* = 8.6 Hz, 2 H, ArH), 6.68 (d, *J* = 8.6 Hz, 2 H, ArH), 6.43 (s, 1 H, ArH), 5.96 (s, 1 H, ArH), 3.98 (s, 1 H, C_1-H), 3.71 (s, 3 H, OCH_3), 3.67 (s, 3 H, OCH_3), 3.66–3.59 (m, 2 H, OCH_2CH_3), 3.07–2.99 (m, 1 H, C_3-H), 2.98–2.93 (m, 1 H, C_3-H), 2.56 (br d, *J* = 15.6 Hz, 1 H, C_4-H), 2.44 (td, *J* = 10.8, 3.7 Hz, 1 H, C_4-H), 2.09 (s, 3 H, NCH_3), 1.16 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.6, 147.7, 146.2, 135.7, 130.6, 130.2, 126.2, 113.3, 111.0, 70.2, 63.9, 55.5, 54.7, 52.1, 44.0, 28.8, 14.6.

MS (APCI): *m*/*z* = 328.24 $[M + H]^+$.

Anal. Calcd for $C_{20}H_{25}NO_3$: C, 73.37; H, 7.70; N, 4.28. Found: C, 73.61; H, 7.52; N, 4.19.

7-Ethoxy-6-methoxy-1-(3-methoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2u)
Yield: 139 mg (47%); colorless oil.

IR (neat): 2944, 2836, 1497, 1247, 1040 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.15 (t, *J* = 7.7 Hz, 1 H, ArH), 6.81 (d, *J* = 7.6 Hz, 1 H, ArH), 6.77–6.74 (m, 2 H, ArH), 6.53 (s, 1 H, ArH), 6.07 (s, 1 H, ArH), 4.08 (s, 1 H, C_1-H), 3.81 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.74–3.68 (m, 2 H, OCH_2CH_3), 3.15–3.09 (m, 1 H, C_3-H), 3.08–3.05 (m, 1 H, C_3-H), 2.66 (br d, *J* = 15.6 Hz, 1 H, C_4-H), 2.54 (td, *J* = 10.9, 3.6 Hz, 1 H, C_4-H), 2.21 (s, 3 H, NCH_3), 1.25 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.6, 146.4, 145.5, 130.2, 128.9, 126.2, 122.0, 114.5, 113.2, 113.0, 111.2, 109.4, 71.1, 64.1, 55.6, 54.9, 52.4, 44.4, 29.0, 14.7.

MS (APCI): *m*/*z* = 328.29 $[M + H]^+$.

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{26}NO_3$: 328.1907; found: 328.1906.

7-Ethoxy-6-methoxy-1-(3,4-dimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2v)
Yield: 126 mg (39%); pale yellow solid; mp 93–95 °C.

IR (neat): 2944, 2835, 1464, 1253, 1028 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.69 (dd, *J* = 8.1, 1.7 Hz, 1 H, ArH), 6.65 (d, *J* = 8.1 Hz, 1 H, ArH), 6.64 (d, *J* = 1.5 Hz, 1 H, ArH), 6.44 (s, 1 H, ArH), 5.98 (s, 1 H, ArH), 3.96 (s, 1 H, C_1-H), 3.76 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 3.68–3.56 (m, 2 H, OCH_2CH_3), 3.10–3.04 (m, 1 H, C_3-H), 3.01–2.96 (m, 1 H, C_3-H), 2.56 (br d, *J* = 15.8 Hz, 1 H, C_4-H), 2.46 (td, *J* = 10.9, 3.6 Hz, 1 H, C_4-H), 2.11 (s, 3 H, NCH_3), 1.17 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.1, 148.2, 147.7, 146.2, 136.1, 130.2, 125.9, 121.7, 113.1, 111.6, 110.9, 110.1, 70.8, 63.8, 55.3, 52.4, 44.1, 28.6, 14.5.

MS (APCI): *m*/*z* = 358.41 $[M + H]^+$.

Anal. Calcd for $C_{21}H_{27}NO_4$: C, 70.56; H, 7.61; N, 3.92. Found: C, 70.24; H, 7.52; N, 3.88.

7-Ethoxy-6-methoxy-1-(3,4,5-trimethoxyphenyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (2w)
Yield: 150 mg (43%); white solid; mp 123–125 °C.

IR (neat): 2939, 2841, 1483, 1236, 1030 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.53 (s, 1 H, ArH), 6.45 (s, 2 H, ArH), 6.09 (s, 1 H, ArH), 3.98 (s, 1 H, C_1-H), 3.81 (s, 3 H, OCH_3), 3.80 (s, 9 H, 3 × OCH_3), 3.79–3.71 (m, 2 H, OCH_2CH_3), 3.14–3.09 (m, 1 H, C_3-H), 3.07–3.04 (m, 1 H, C_3-H), 2.64 (br d, *J* = 15.6 Hz, 1 H, C_4-H), 2.53 (td, *J* = 10.7, 3.3 Hz, 1 H, C_4-H), 2.20 (s, 3 H, NCH_3), 1.26 (t, *J* = 7.0 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9, 147.9, 146.2, 139.2, 137.2, 130.0, 126.1, 113.2, 111.1, 106.3, 71.5, 64.1, 60.4, 55.9, 55.5, 52.5, 44.4, 28.7, 14.6.

MS (APCI): *m*/*z* = 388.74 $[M + H]^+$.

Anal. Calcd for $C_{22}H_{29}NO_5$: C, 68.20; H, 7.54; N, 3.61. Found: C, 68.55; H, 7.42; N, 3.69.

7-Ethoxy-6-methoxy-2-methyl-1-(3,4-methylenedioxyphenyl)-1,2,3,4-tetrahydroisoquinoline (2x)
Yield: 120 mg (39%); white solid; mp 88–90 °C.

IR (neat): 2974, 2899, 1477, 1236, 1039 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.64 (dd, *J* = 7.9, 1.4 Hz, 1 H, ArH), 6.61 (d, *J* = 7.7 Hz, 1 H, ArH), 6.60 (d, *J* = 1.0 Hz, 1 H, ArH), 6.44 (s, 1 H, ArH), 6.02 (s, 1 H, ArH), 5.84 (d, *J* = 1.3 Hz, 1 H, OCH_2O), 5.83 (d, *J* = 1.4 Hz, 1 H, OCH_2O), 3.95 (s, 1 H, C_1-H), 3.73 (s, 3 H, OCH_3), 3.72–3.65 (m, 2 H, OCH_2CH_3), 3.07–3.01 (m, 1 H, C_3-H), 2.99–2.94 (m, 1 H, C_3-H), 2.56 (dd, *J* = 15.7, 3.1 Hz, 1 H, C_4-H), 2.44 (td, *J* = 10.8, 3.5 Hz, 1 H, C_4-H), 2.13 (s, 3 H, NCH_3), 1.21 (t, *J* = 7 Hz, 3 H, OCH_2CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.9, 147.8, 146.8, 146.5, 138.0, 130.4, 126.4, 122.7, 113.3, 111.1, 109.3, 107.3, 100.7, 70.8, 64.2, 55.6, 52.3, 44.3, 29.0, 14.7.

MS (APCI): *m*/*z* = 342.39 $[M + H]^+$.

Anal. Calcd for $C_{20}H_{23}NO_4$: C, 70.36; H, 6.79; N, 4.10. Found: C, 70.59; H, 6.52; N, 4.29.

Deuterium Labeling Experiments
(1) Into a flame-dried two-necked round-bottomed flask, equipped with a magnetic stirrer bar, septum cap and a bubbler, was taken a solution of *N*-methyl-1,2,3,4-tetrahydroisoquinoline (**3**, 200 mg, 1.36 mmol, 1 equiv) in anhydrous THF (10 mL) under an inert N_2 atmosphere. It was cooled to 0 °C and $BF_3{\cdot}OEt_2$ (0.25 mL, 1.63 mmol, 1.2 equiv) was added dropwise. The turbid white solution was stirred at 0 °C for 30 min. It was then cooled to –78 °C and *s*-BuLi [1.43 mL (2.6 M in pentane), 2.99 mmol, 2.2 equiv] was added dropwise. A deep red color (indicative of benzylic carbanion formation) appeared immediately. The solution was stirred at the same temperature for 30 min and then a solution of $MeCO_2D$ (182 mg, 0.2 mL, 2.99 mmol, 2.2 equiv) in THF (2 mL) was added. After the addition, the reaction mixture was stirred and warmed to r.t. over a period of 4–5 h, whence aq 10% HCl (15 mL) was added. The contents were poured into Et_2O (25 mL). The aqueous layer was separated and the organic layer was further extracted with aq 10% HCl (2 × 15 mL). The combined aqueous layers were washed with Et_2O (2 × 20 mL) to remove nonbasic impurities, made alkaline with solid Na_2CO_3, and extracted with $CHCl_3$ (4 × 15 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The solvent was evaporated in vacuo to afford the crude product, which was purified by flash column chromatography using 230–400 mesh silica gel. Elution with EtOAc–hexane (1:1) afforded 2-methyl-1,2,3,4-tetrahydro(1-$^2H_1$)isoquinoline (**12**) as a yellow oil; yield: 184 mg (92%).

(2) Into a flame-dried two-necked round-bottomed flask, equipped with a magnetic stirrer bar, septum cap and a bubbler, was taken a solution of *N*-methyl-1,2,3,4-tetrahydroisoquinoline (**3**; 200 mg, 1.36 mmol, 1 equiv) in anhydrous THF (10 mL) under an inert N_2 atmosphere. It was cooled to 0 °C and $BF_3{\cdot}OEt_2$ (0.25 mL, 1.63 mmol, 1.2 equiv) was added dropwise. The turbid white solution was stirred at 0 °C for 30 min. It was then cooled to –78 °C and *s*-BuLi [1.43 mL (2.6 M in pentane), 2.99 mmol, 2.2 equiv] was added dropwise. A deep red color (indicative of benzylic carbanion formation) appeared immediately. The solution was stirred at the same temperature for 30 min. The second instalment of *s*-BuLi [1.96 mL (2.6 M in pentane), 4.08 mmol, 3 equiv] was added followed by the addition of a solution of chlorobenzene (450 mg, 0.41 mL, 4.08 mmol, 3 equiv) in THF (1–2 mL). The reaction mixture was stirred at –78 °C for 45 min and was allowed to warm to –10 °C over a period of 3–4 h. It was then quenched with a solution of $MeCO_2D$ (430 mg, 0.4 mL, 7.07 mmol, 5.2 equiv) in THF (2 mL). After the addition, the mixture was stirred and warmed to r.t. and aq 10% HCl (15 mL) was added. The contents were poured into Et_2O (25 mL). The aqueous layer was separated and the organic layer was further extracted with aq 10% HCl (2 × 15 mL). The combined aqueous layers were washed with Et_2O (2 × 20 mL) to remove nonbasic impurities, made alkaline with solid Na_2CO_3, and extracted with $CHCl_3$ (4 × 15 mL). The combined organic layers were washed with brine (20 mL) and dried (Na_2SO_4). The solvent was evaporated in vacuo to afford the crude product, which was purified by flash column chromatography using 230–400 mesh silica gel. Elution with EtOAc–hexane (3:7) afforded 2-methyl-1-phenyl-1,2,3,4-tetrahydro(1-$^2H_1$)isoquinoline (**13**) as a light yellow oil (123 mg, 41%). Further elution with same solvent gave **12** as a yellow oil (28 mg, 14%).

The same procedure was repeated, with the only difference that $MeCO_2D$ was added at r.t. instead of –10 °C. Workup and purifica-

tion in the similar fashion as described above gave **13** as a light yellow oil (117 mg, 39%) and **12** as a yellow oil (30 mg, 15%).

To investigate the nonbasic material, the Et_2O layer was washed with brine (20 mL) and dried (Na_2SO_4). The solvent was evaporated in vacuo to afford the crude product, which was again purified by flash column chromatography using 230–400 mesh silica gel. Elution with EtOAc–hexane (2:98) afforded biphenylene (**14**) as a yellow solid; yield: 42 mg (7%). Further elution with the same solvent gave 1-chloro-2-phenylbenzene (**15**) as a white solid; yield: 67 mg (9%).

2-Methyl-1,2,3,4-tetrahydro(1-$^2H_1$)isoquinoline (12)
Yield: 28 mg (14%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.72 (dd, *J* = 8.08, 1.84 Hz, 1 H, ArH), 6.67 (d, *J* = 8.08 Hz, 1 H, ArH), 6.63 (d, *J* = 1.76 Hz, 1 H, ArH), 6.52 (d, *J* = 7.84 Hz, 1 H, ArH), 3.44 (br s, 1 H, C_1-H), 2.80 (t, *J* = 8.28 Hz, 2 H, C_3-H), 2.56 (t, *J* = 7.84 Hz, 2 H, C_4-H), 2.20 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.4, 133.9, 129.0, 128.4, 127.2, 125.9, 68.7, 52.6, 44.6, 29.7.

2-Methyl-1-phenyl-1,2,3,4-tetrahydro(1-$^2H_1$)isoquinoline (13)
Yield: 123 mg (41%); light yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.11 (m, 5 H, ArH), 6.96–6.90 (m, 2 H, ArH), 6.81 (t, *J* = 8.08 Hz, 1 H, ArH), 6.47 (d, *J* = 7.8 Hz, 1 H, ArH), 3.18–3.10 (m, 1 H, C_3-H), 3.02–2.97 (m, 1 H, C_3-H), 2.65 (dt, *J* = 15.84, 2.84 Hz, 1 H, C_4-H), 2.47 (td, *J* = 11.32, 3.68 Hz, 1 H, C_4-H), 2.13 (s, 3 H, NCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.4, 138.4, 134.1, 129.5, 128.6, 128.3, 128.2, 127.3, 125.7, 125.5, 72.2, 52.0, 44.2, 29.4.

Biphenylene (14)[27]
Yield: 42 mg (7%); yellow solid; mp 106–108 °C (Lit.[27] mp 109 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68–6.61 (m, 3 H, ArH), 6.57–6.50 (m, 1 H, ArH), 6.48–6.31 (m, 3 H, ArH), 6.27–6.20 (m, 1 H, ArH).

1-Chloro-2-phenylbenzene (15)[48]
Yield: 67 mg (9%); white solid; mp 33 °C (Lit.[48] mp 35 °C).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78–7.75 (m, 2 H, ArH), 7.69–7.68 (m, 1 H, ArH), 7.57–7.28 (m, 4 H, ArH), 7.27–7.12 (m, 2 H, ArH).

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