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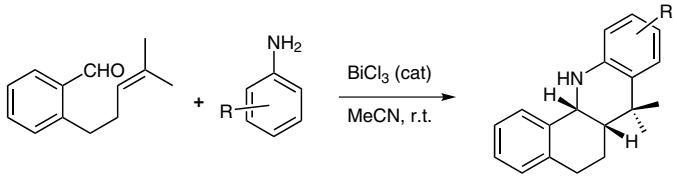
Bismuth(III) Chloride Catalyzed Intramolecular Hetero-Diels–Alder Reaction: Access to *cis*-Fused Angular Hexahydrobenzo[*c*]acridines

Gowravaram Sabitha*
Kontham Shankaraiah
Kancherla Sindhu
Bejawada Madhavi Latha

Natural Products Chemistry Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India
gowravaramsr@yahoo.com
sabitha@iict.res.in



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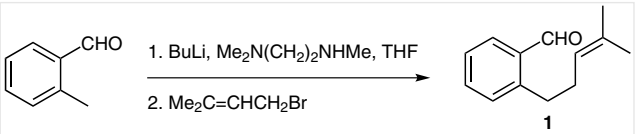
Abstract New polycyclic hexahydrobenzo[*c*]acridines were synthesized in excellent yields by intramolecular [4+2]-cycloaddition reactions of aldimines derived from aromatic amines and 2-(4-methylpent-3-en-1-yl)benzaldehyde in acetonitrile in the presence of 10 mol% of bismuth(III) chloride. The reaction is highly diastereoselective, giving *cis*-fused benzoacridine derivatives preferentially.

Key words hetero-Diels–Alder reactions, catalysis, heterocycles, polycycles, aldimines, aldehydes

The intramolecular hetero-Diels–Alder reaction[1,2] has become an attractive tool for the synthesis of complex molecular structures. Angularly fused polycyclic nitrogen heterocycles[3] are of great importance to chemists and biologists because of the significant role played by such compounds in biological systems and in medicinal chemistry. Heterocyclic systems containing the hexahydrobenzo[*a*]acridine skeleton can be prepared by cascade heterocyclization of cyclic diketones with aromatic amines and vanillyl esters.[4] Benzoacridine derivatives have been reported to possess a significant inhibitory effect on the growth of KB human papilloma cells,[5] an activity that is creating interest in further studies on such derivatives. To the best of our knowledge, there have been no reported syntheses of angularly fused hexahydrobenzoacridine derivatives from 2-(4-methylpent-3-en-1-yl)benzaldehyde (**1**)[6] and aromatic amines. As a continuation of our work on [4+2] cycloaddition chemistry,[7] and on the basis of a report in the literature,[8] we have developed a novel synthesis of angularly fused benzoacridine derivatives by means of the intramolecular hetero-Diels–Alder reaction of 2-(4-methylpent-3-en-1-yl)benzaldehyde with aromatic amines in the presence of bismuth(III) chloride. Aldehyde **1** was prepared in 88% yield from 2-methylbenzaldehyde and 1-bromo-3-methylbut-2-ene (prenyl bromide) in the presence of *N*,*N*,*N*′-trimethylethane-1,2-diamine[6] (Scheme 1).

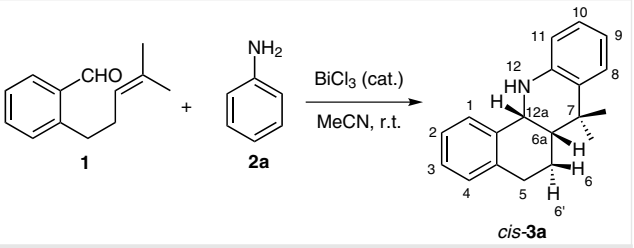


Scheme 1 Preparation of 2-(4-methylpent-3-en-1-yl)benzaldehyde (**1**)

The use of bismuth trichloride in the cyclization of aldehyde **1** with amines has several advantages. Bismuth is the least toxic of the heavy elements[9a,b] and the biochemistry,[9c] toxicology,[9d] and environmental effects[9e] of bismuth compounds have been reviewed. Moreover, bismuth compounds are employed as catalysts in industry for the manufacture of acrolein and acrylonitrile, and they are also used in pharmaceutical products.

Having prepared aldehyde **1**, we examined its intramolecular [4+2]-cycloaddition reactions. Initially, we studied the reaction of aldehyde **1** with aniline (**2a**) in the presence of 10 mol% bismuth(III) chloride in acetonitrile at 85 °C, and we obtained 7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (**3a**) in 82% yield (Scheme 2). The reaction was complete in one hour, as indicated by thin-layer chromatography. The reaction proceeds by generation of an imine that undergoes an intramolecular hetero-Diels–Alder reaction to give the product **3a** as a mixture of *cis*- and *trans*-diastereomers with the former as the predominant product. The ratio of the *cis*- and *trans*-isomers of **3a** was determined by NMR spectroscopic studies on the crude product. In compound **3a**, the H-6a proton appears as a doublet of triplets at δ = 1.83. This is the result of coupling of the H-6a proton with the H-6′ proton, resulting in a doublet with a large *J* value ($J_{6a,6'}$ = 12.3 Hz) that is split into a triplet with a small *J*

value (3.4 Hz) by coupling with the equatorial H-12a and H-6 protons. This corresponds to a *cis*-fusion at the junction. The doublet for the H-12a proton appears at δ = 4.65 with a small *J* value as a result of vicinal coupling with an equatorial H-6a proton ($J_{12a,6a}$ = 3.2 Hz). The *cis*-configuration of H-6a and H-12a in compound **3** was confirmed by the strong NOE peaks. Confirmation of the *cis*-fusion of **3a** was also obtained by direct comparison with data reported in the literature,[7b,d,f] in addition to the ^{1}H NMR spectral data.



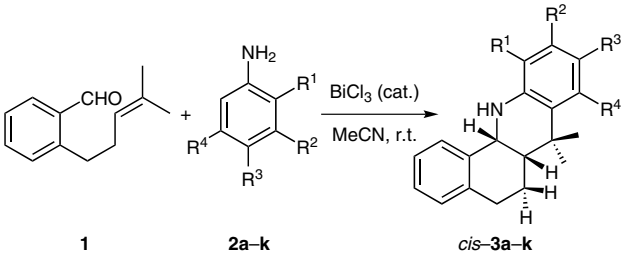
Scheme 2 Preparation of 7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (**3a**)

In an effort to demonstrate the scope of the bismuth(III) chloride-catalyzed hetero-Diels–Alder reaction, we examined the reactions of aldehyde **1** with several anilines **2b**–**k** bearing various substituents (Table 1). Amines bearing electron-donating groups and those bearing electron-withdrawing groups both gave the corresponding products **3** in high yields under similar reaction conditions to those used for aniline (**2a**); the substituents had no obvious effect on the yield or the reaction time under optimized conditions. In all cases, the *cis*-annulated products were formed predominantly. The products were characterized by means of IR, ^{1}H and ^{13}C NMR, and mass spectroscopy. Acetonitrile was selected as the optimal solvent, as it gave better results than other solvents tested such as methanol, tetrahydrofuran, diethyl ether, dichloromethane, or 1,2-dichloroethane.

Mechanistically, the reaction proceeds through formation of an imine from the aromatic amine and 2-(4-methylpent-3-en-1-yl)benzaldehyde (**1**). The imine then undergoes a Lewis acid induced intramolecular hetero-Diels–Alder reaction to give the hexahydrobenzo[*c*]acridine (Scheme 3).

In conclusion, we have demonstrated a convenient synthesis of *cis*-fused hexahydrobenzo[*c*]acridines derivatives in good yields in a one-pot operation using bismuth(III) chloride. The advantages of the present protocol are mild

Table 1 Synthesis of Angular Hexahydrobenzo[*c*]acridines **3a**–**k**

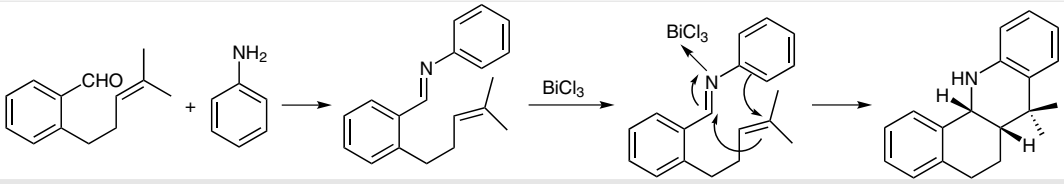


Entry	R^1	R^2	R^3	R^4	Product[a]	Yield[b] (%)	*cis*/*trans*[c]
1	H	H	H	H	**3a**	82	96:4
2	H	H	Me	H	**3b**	80	95:5
3	H	H	OMe	H	**3c**	85	96:4
4	Cl	H	H	H	**3d**	82	95:5
5	H	H	F	H	**3e**	75	96:4
6	OH	H	H	H	**3f**	77	95:5
7	H	H	NO_2	H	**3g**	74	93:7
8	Br	H	H	Br	**3h**	86	96:4
9	H	Br	H	Br	**3i**	82	93:7
10	CO_2H	H	OMe	H	**3j**	87	97:3
11	H	OMe	OMe	OMe	**3k**	80	94:6

[a] All products were characterized by NMR and IR spectroscopy, and mass spectrometry.
[b] Yield of pure product after chromatography.
[c] Ratio determined by ^{1}H NMR spectroscopy on crude product.

conditions, short reaction times, and the use of a soft Lewis acid catalyst that is commercially available. The method is therefore highly practical and might find wide applicability in organic synthesis.

All reagents and catalysts were purchased from Sigma-Aldrich. Reactions were conducted under N_2 in anhydrous solvents such as THF or MeCN. All reactions were monitored by TLC on Merck 60 F-254 silica gel plates visualized under UV radiation. Hexanes (bp 60–80 °C) and EtOAc were used for silica gel column chromatography. Yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) homogeneous materials. Air-sensitive reagents were transferred by syringe. Evaporation of solvents was performed at reduced pressure on a Buchi rotary evaporator. ^{1}H and ^{13}C NMR spectra of samples in $CDCl_3$ were recorded on Bruker UXNMR FT-300 MHz (Avance) spectrometers with TMS as an internal standard. Mass spectra were recorded on



Scheme 3 A plausible reaction mechanism

a Finnigan MAT 1020B or a Micromass VG 70–70 H spectrometer operated at 70 eV with a direct inlet system. Column chromatography was performed on silica gel (60–20 mesh; ACME Chemicals, Mumbai).

2-(4-Methylpent-3-en-1-yl)benzaldehyde (1)[6]

A solution of $Me_2N(CH_2)_2NHMe$ (1.1 mL, 9.8 mmol, 1.1 equiv) in THF (20 mL) at –20 °C was sequentially treated with a 1.6 M solution of BuLi in hexanes (5.89 mL, 9.43 mmol, 1.05 equiv) and 2-MeC_6H_4CHO (1.08 g, 8.98 mmol). After 15 min, a further 3 equivalents of BuLi were added at –20 °C, $Me_2C{=}CH_2Br$ (5.4 mL, 35.95 mmol, 4 equiv) was added at –78 °C, and the mixture was stirred for 30 min. The resulting mixture was then poured into cold sat. aq NH_4Cl (10 mL) and extracted with EtOAc (3 × 20 mL). The extracts were combined, washed with brine (2 × 10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by flash column chromatography [silica gel, hexane–EtOAc (15:1)] to give a colorless oil; yield: 1.48 g (88%).

IR (neat): 3447, 2961, 2927, 2860, 1696, 1600, 1450, 1207, 757 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 10.27 (s, 1 H), 7.83 (dd, *J* = 7.7, 1.3 Hz, 1 H), 7.50 (td, *J* = 7.6, 1.3 Hz, 1 H), 7.36 (td, *J* = 7.6, 1.0 Hz, 1 H), 7.27 (d, *J* = 8.2 Hz, 1 H), 5.20–5.15 (m, 1 H), 3.08–3.01 (m, 2 H), 2.30 (qt, *J* = 15.1, 7.5 Hz, 2 H), 1.66 (s, 3 H), 1.45 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.9, 145.0, 133.6 (2 C), 131.1, 130.9, 126.4, 122.7, 32.3, 30.5, 25.6, 17.4. .

ESI-MS: *m/z* = 211 [M^+ + Na].

7,7-Dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridines 3a–k; General Procedure

$BiCl_3$ (10 mol%) was added to a mixture of the appropriate aromatic amine **2a–k** (1 mmol) and aldehyde **1** (1.1 mmol) in anhyd MeCN (5 mL), and the mixture was refluxed at 85 °C for 1 h. When the reaction was complete (TLC), the mixture was filtered through Celite. The filtrate was extracted with EtOAc (3 × 20 mL), and the extracts were combined, washed with brine (2 × 10 mL), dried (Na_2SO_4), and concentrated. The crude product was purified by chromatography [silica gel, hexanes–EtOAc (16:1)].

7,7-Dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3a)

Pale yellow viscous liquid; yield: 251 mg (82%).

IR (neat): 3445, 3062, 2961, 2926, 1603, 1562, 1474, 1216, 758 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.30 (m, 5 H), 6.67–6.61 (m, 1 H), 6.37 (d, *J* = 7.7 Hz, 1 H), 5.69 (dt, *J* = 7.3, 1.3 Hz, 1 H), 4.65 (d, *J* = 3.2 Hz, 1 H), 4.29 (s, 1 H), 2.93–2.87 (m, 1 H), 2.82 (dd, *J* = 12.0, 6.1 Hz, 1 H), 2.68–2.64 (m, 1 H), 1.83 (dt, *J* = 12.3, 3.4 Hz, 1 H), 1.70–1.65 (m, 1 H), 1.45 (s, 3 H), 1.36 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.4, 130.7, 129.2, 128.2, 128.1, 127.9, 127.6, 126.7, 126.6, 124.9, 117.3, 112.6, 45.8, 40.5, 32.3, 28.3, 25.6, 25.0, 17.6.

ESI-MS: *m/z* = 265 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{22}N$: 264.1752; found: 264.1761.

7,7,9-Trimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3b)

Pale yellow viscous liquid; yield: 221 mg (80%).

IR (neat): 3449, 2924, 2854, 1634, 1459, 1217, 765 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 7.6 Hz, 1 H), 7.38–7.28 (m, 1 H), 7.20 (dt, *J* = 7.9, 0.6 Hz, 1 H), 7.17–7.14 (m, 1 H), 7.11 (d, *J* = 1.3 Hz, 1 H), 6.85–6.83 (m, 1 H), 6.59 (d, *J* = 7.9 Hz, 1 H), 4.30 (d, *J* = 10.3 Hz, 1 H), 4.22–4.11 (br s, 1 H), 2.93–2.89 (m, 1 H), 2.27 (s, 3 H), 2.08–2.03 (m, 1 H), 1.79–1.73 (m, 1 H), 1.59–1.50 (m, 2 H), 1.40 (s, 3 H), 1.23 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.7, 135.7, 132.2, 130.5, 129.1, 128.3, 128.2, 127.3, 126.6, 126.3, 125.7, 116.0, 51.4, 46.9, 35.9, 30.9, 28.3, 27.9, 21.9, 17.6.

ESI-MS: *m/z* = 278 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{20}H_{24}N$: 278.1908; found: 278.1902.

9-Methoxy-7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3c)

Colorless viscous liquid; yield: 249 mg (85%).

IR (neat): 3423, 3063, 2959, 2933, 1612, 1512, 1474, 1228, 1037, 819 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.13 (m, 4 H), 6.84–6.77 (m, 1 H), 6.64–6.55 (m, 1 H), 6.34 (d, *J* = 8.3 Hz, 1 H), 4.60 (d, *J* = 3.0 Hz, 1 H), 4.24 (s, 1 H), 3.75 (s, 3 H), 2.91–2.79 (m, 1 H), 2.68 (dd, *J* = 15.1, 7.5 Hz, 1 H), 1.87–1.78 (m, 1 H), 1.71–1.46 (m, 2 H), 1.43 (m, 3 H), 1.37 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 141.0, 137.9, 130.4, 129.3, 128.1, 126.6, 126.5, 126.0, 114.8, 111.7, 111.3, 70.8, 55.7, 55.3, 40.8, 28.3, 25.6, 25.1, 17.6. 6.

ESI-MS: *m/z* = 294 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{20}H_{24}NO$: 294.1857; found: 294.1859.

11-Chloro-7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3d)

Pale yellow viscous liquid; yield: 243 mg (82%).

IR (neat): 3436, 3063, 2961, 2929, 2869, 1696, 1496, 1303, 1240, 771, 731 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 7.7 Hz, 1 H), 7.33–7.27 (m, 1 H), 7.24–7.20 (m, 2 H), 7.17 (d, *J* = 7.5 Hz, 1 H), 7.12 (dd, *J* = 7.7, 1.2 Hz, 1 H), 6.6 (t, *J* = 7.7 Hz, 1 H), 5.01–4.96 (br s, 1 H), 4.36 (d, *J* = 10.5 Hz, 1 H), 2.73 (dd, *J* = 7.7, 2.8 Hz, 2 H), 2.09–2.03 (m, 1 H), 1.80–1.74 (m, 1 H), 1.62–1.55 (m, 1 H), 1.41 (s, 3 H), 1.23 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8, 131.2, 129.2, 128.1, 126.8, 126.5, 125.5 (2 C), 125.0, 123.5, 120.8, 117.3, 51.0, 46.0, 30.3, 27.6, 26.9, 21.7, 17.8.

ESI-MS: *m/z* = 298 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{21}ClN$: 298.1362; found: 298.1354.

9-Fluoro-7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3e)

Colorless viscous liquid; yield: 210 mg (75%).

IR (neat): 3420, 2925, 2854, 1615, 1470, 1275, 1187, 769 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 7.5 Hz, 1 H), 7.27–7.14 (m, 3 H), 7.00 (dd, *J* = 10.6, 3.0 Hz, 1 H), 6.75 (dt, *J* = 8.3, 2.2 Hz, 1 H), 6.61 (dd, *J* = 8.3, 5.3 Hz, 1 H), 4.29 (d, *J* = 10.6 Hz, 1 H), 4.29–4.26 (br s, 1 H), 2.92 (dd, *J* = 8.3, 3.0 Hz, 2 H), 2.09–2.01 (m, 1 H), 1.77–1.65 (m, 1 H), 1.62–1.53 (m, 1 H), 1.39 (s, 3 H), 1.23 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.2, 139.3, 130.7, 129.8, 129.7, 128.2, 126.7, 126.6, 114.2, 114.0, 112.3, 112.1, 70.5, 40.9, 29.7, 28.3, 25.5, 25.0, 17.6.

ESI-MS: *m/z* = 282 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{21}FN$: 282.1658; found: 282.1668.

7,7-Dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridin-11-ol (3f)

Colorless liquid; yield: 214 mg (77%).

IR (neat): 3422, 3066, 2966, 2928, 1617, 1452, 1216, 751 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.30 (m, 2 H), 7.28–7.19 (m, 3 H), 7.19–7.12 (m, 1 H), 6.95–6.91 (m, 1 H), 6.70–6.42 (br s, 1 H), 4.81–4.46 (m, 2 H), 2.91 (dd, *J* = 17.0, 5.1 Hz, 1 H), 2.86–2.79 (m, 1 H), 2.32–1.99 (m, 1 H), 1.88–1.81 (m, 1 H), 1.74–1.59 (m, 1 H), 1.40 (s, 3 H), 1.36 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.2, 130.9, 129.3, 129.1, 129.0, 128.4, 127.7, 126.6, 126.5, 126.0, 116.0, 113.1, 71.4, 40.7, 29.3, 28.2, 25.5, 25.1, 17.4.

ESI-MS: *m/z* = 280 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{22}NO$: 280.1701; found: 282.1707.

7,7-Dimethyl-9-nitro-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3g)

Yellow viscous liquid; yield: 228 mg (74%).

IR (KBr): 3402, 2953, 2865, 1603, 1510, 1318, 1279, 737 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 2.3 Hz, 1 H), 7.91 (dt, *J* = 9.1, 2.3 Hz, 1 H), 7.33–7.23 (m, 4 H), 6.30 (d, *J* = 9.1 Hz, 1 H), 4.74 (d, *J* = 3.8 Hz, 1 H), 4.55–4.50 (br s, 1 H), 2.98–2.91 (m, 1 H), 2.89–2.84 (m, 1 H), 1.91–1.79 (m, 1 H), 1.78–1.61 (m, 1 H), 1.64–1.56 (m, 1 H), 1.53 (s, 3 H), 1.35 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.6, 137.6, 136.8, 136.2, 129.3, 128.8, 128.3, 126.7, 126.5, 124.2, 123.0, 111.8, 50.2, 41.9, 35.4, 32.4, 29.0, 25.4, 19.2.

ESI-MS: *m/z* = 309 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{21}N_2O_2$: 309.1603; found: 309.1595.

8,11-Dibromo-7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3h)

Brown viscous liquid; yield: 359 mg (86%).

IR (neat): 3414, 3015, 2960, 2927, 1577, 1483, 1442, 1292, 742 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.22 (m, 3 H), 7.18 (d, *J* = 7.3 Hz, 1 H), 7.04 (d, *J* = 8.4 Hz, 1 H), 6.75 (d, *J* = 8.4 Hz, 1 H), 4.60 (d, *J* = 2.7 Hz, 1 H), 4.53–4.47 (br s, 1 H), 2.95–2.90 (m, 1 H), 2.83 (dd, *J* = 11.7, 6.2 Hz, 1 H), 1.97–1.90 (m, 1 H), 1.80 (s, 3 H), 1.69–1.64 (m, 1 H), 1.58 (dd, *J* = 12.6, 5.9 Hz, 1 H), 1.53 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 41.5, 137.1, 136.9, 130.6, 129.2, 129.0, 128.1, 127.2, 126.3, 123.6, 122.2, 107.7, 49.8, 46.8, 37.9, 29.8, 29.3, 27.4, 18.9.

ESI-MS: *m/z* = 422 [M + 2]$^+$, 424 [M + 4]$^+$.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{20}Br_2N$: 419.9962; found: 419.9954.

8,10-Dibromo-7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3i)

Brown viscous liquid; yield: 342 mg (82%).

IR (neat): 3412, 3015, 2961, 2927, 1577, 1443, 1293, 755 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.25 (m, 1 H), 7.24–7.22 (m, 2 H), 7.17 (d, *J* = 7.3 Hz, 1 H), 7.00 (d, *J* = 2.0 Hz, 1 H), 6.45 (d, *J* = 2.0 Hz, 1 H), 4.54 (d, *J* = 2.3 Hz, 1 H), 3.92–3.86 (br s, 1 H), 2.95–2.90 (m, 1 H), 2.83 (dd, *J* = 11.7, 6.8 Hz, 1 H), 1.96–1.90 (m, 1 H), 1.77 (s, 3 H), 1.63–1.54 (m, 2 H), 1.49 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.6, 137.0, 136.2, 130.9, 129.2, 128.9, 128.1, 126.3, 125.4, 119.9, 115.5, 114.0, 49.3, 46.5, 37.2, 29.3, 29.6, 27.6, 19.0.

ESI-MS: *m/z* = 422 [M + 2]$^+$, 424 [M + 4]$^+$.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{20}Br_2N$: 419.9962; found: 419.9976.

9-Methoxy-7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine-11-carboxylic Acid (3j)

Colorless gummy liquid; yield: 293 mg (87%).

IR (KBr): 3450, 2960, 1652, 1583, 1497, 1426, 1217 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 3.0 Hz, 1 H), 7.34–7.12 (m, 3 H), 7.08–7.01 (m, 1 H), 6.59 (d, *J* = 9.0 Hz, 1 H), 4.75 (d, *J* = 3.0 Hz, 1 H), 4.42 (s, 1 H), 3.77 (s, 3 H), 2.92–2.77 (m, 1 H), 2.73–2.61 (m, 1 H), 2.31–2.00 (m, 1 H), 1.75–1.57 (m, 2 H), 1.46 (s, 3 H), 1.34 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.2, 149.3, 146.9, 135.8, 129.3, 129.1, 127.6, 127.2, 126.1, 124.8, 122.2, 114.4, 113.3, 55.8, 49.4, 44.9, 32.4, 31.8, 30.5, 22.5, 19.3.

ESI-MS: *m/z* = 338 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{21}H_{24}NO_3$: 338.1756; found: 338.1761.

8,9,10-Trimethoxy-7,7-dimethyl-5,6,6a,7,12,12a-hexahydrobenzo[*c*]acridine (3k)

Colorless gummy liquid; yield: 282 mg (80%).

IR (neat): 3387, 2962, 2932, 1605, 1481, 1456, 1106, 752 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.15 (m, 4 H), 5.76 (s, 1 H), 4.49 (d, *J* = 2.6 Hz, 1 H), 3.92 (s, 3 H), 3.77 (s, 3 H), 3.72 (s, 3 H), 3.59–3.53 (br s, 1 H), 2.98–2.91 (m, 1 H), 2.87–2.79 (m, 1 H), 1.96–1.90 (m, 1 H), 1.73–1.64 (m, 1 H), 1.57 (m, 4 H), 1.42 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.7, 154.4, 152.0, 138.1, 137.2, 132.9, 129.1, 128.9 (2 C), 127.7, 125.9, 93.1, 60.6, 60.5, 55.5, 50.1, 46.1, 32.3, 29.4, 27.1, 24.6, 19.1.

ESI-MS: *m/z* = 354 [M^+ + H].

HRMS: *m/z* [M + H]$^+$ calcd for $C_{22}H_{28}NO_3$: 354.2069; found: 354.2058.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1379022.

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