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Regio- and diastereoselective synthesis of (*E*)-3-(2-aminochromen-4-yl)-6-aryl-substituted fulvenes

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Abstract: A practical base-catalyzed route was developed for the regio- and diastereoselective synthesis of (*E*)-3-aminochromene-6-aryl-disubstituted fulvenes in high yields up to 94% starting with the Michael addition of cyclopentadiene to 2-iminochromenes in the key step.

Keywords: aminochromene; base catalysis; cyclopentadiene; fulvene; Michael addition.

1 Introduction

Fulvenes are an interesting class of cyclic cross-conjugated molecules that display a wide range of reactions with nucleophiles, electrophiles, and various cycloaddition partners [1–3]. Pentafulvenes serve as activated dienes in Diels-Alder reactions and as synthetic precursors to several biologically occurring compounds [4–6], whereas 6-substituted fulvenes (Fig. 1) are particularly interesting and easily accessible starting materials for the synthesis of novel substituted metallocenes [7–10].

These fulvene-derived metallocenes have been proven to be bio-organometallic anticancer drugs that offer a significant potential against a variety of cancer cell lines. However, the diversity of fulvene precursors of such metallocenes is quite limited [11–15]. As a result, we have become interested in the synthesis of new and more functionalized fulvenes, which may find further application in both metallocene and chromene chemistry. It is well known that chromene frameworks also have a wide application area where they are used as mitogen-activated protein kinase inhibitors, tumor antagonists, and anticancer drugs [16–19].

We now report a new practical route to (*E*)-3-(2-aminochromen-4-yl)-6-aryl-substituted fulvenes in which we use cyclopentadiene as a Michael donor in conjugate addition reactions to 2-iminochromenes and convert these isomeric Michael adducts into (*E*)-3,6-disubstituted fulvenes regio- and diastereoselectively using a modified pyrrolidine-H_2O catalytic system [20, 21].

2 Results and discussion

First, we synthesized 2-iminochromenes (**1a**, **b**) according to the previously reported methods, using malononitrile and salicylaldehyde for **1a**, and 2-hydroxy-1-naphtaldehyde for **1b** in 86% and 99% yield, respectively. The 2-iminochromenes were characterized using reported spectroscopic data and melting points [22].

The conjugate addition of cyclopentadiene (CpH) to electrophilic 2-iminochromenes was the next key step in our strategy. Although several nucleophiles such as indole, nitromethane, or ethyl cyanoacetate were reported in Michael additions to 2-iminochromenes [23, 24], CpH was used for the first time in this manner. A series of organocatalysts were investigated for this addition step, and we obtained the best results using 10 mol% DBU in methanol-water mixture (Table 1).

We obtained **2a** and **2b** as inseparable isomeric mixtures using the DBU-catalyzed conjugate addition reaction (Fig. 2). The isomeric mixtures of **2a** and **2b** were easily obtained by filtration and characterized by spectroscopic methods and elemental analysis. The isomeric ratios were determined by ^{1}H NMR as 1:5 in the case of **2a**, whereas it was 1:1 in the case of **2b**.

Finally, **2a** and **2b** were reacted with a series of aromatic aldehyde and cyclobutanone in MeOH-H_2O (4:1) using 40 mol% of pyrrolidine at 55°C (Fig. 3) to obtain the targeted functionalized fulvenes. The products were easily obtained by filtration without any further purification. The reaction proceeded smoothly and in high yields in

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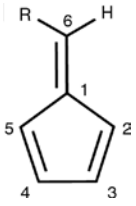
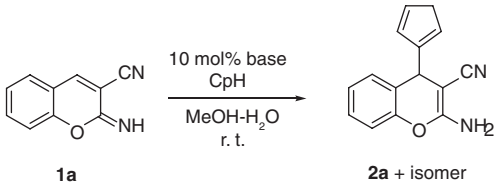


Fig. 1: Atom numbering scheme in pentafulvene.

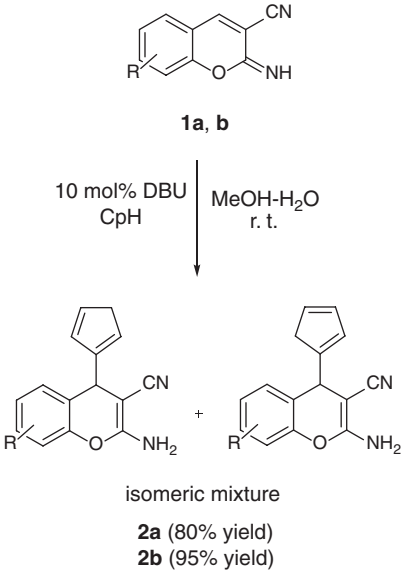
Table 1: The organocatalysts investigated in conjugate addition of CpH to **1a**.



1a **2a** + isomer

Base	Time (min)	Yield (%)[a]
Pyrrolidine	60	64
Piperidine	60	76
DBU	30	80
Triethylamine[b]	60	67

[a]All reactions were performed in MeOH-H_2O (3:1) at room temperature.
[b]A sticky precipitate was obtained.



1a, **b**

isomeric mixture

2a (80% yield)
2b (95% yield)

Fig. 2: DBU-catalyzed conjugate addition of CpH to 2-iminochromenes.

the cases of aromatic aldehydes having electron-donating groups. As expected, aldehydes containing electron-withdrawing groups did not give the corresponding fulvenes. In addition, cyclic ketones such as cyclopentanone and cyclohexanone failed to give fulvenes, whereas cyclobutanone reacted to give **3e** and **3l** in 63% and 77% yield, respectively.

The fulvenes **3a–l** were characterized by elemental analysis and spectroscopic methods (^{1}H NMR, ^{13}C NMR, and NOESY). The only product of the reactions were 3,6-disubstituted fulvenes, and the formation of a 2,6-disubstituted product was not observed in any case.

The exocyclic fulvene double bond had *E* geometry in all of the products except for **3a** according to spectroscopic data. In the ^{1}H NMR spectra, 2-H proton in the Cp ring of the compound (*Z*)-**3a** has a broad singlet at 6.55 ppm, whereas the signals of 4-H and 5-H appear as a 2H ddd (J = 11.8, 5.2, 1.7 Hz) at 6.27 ppm. The fulvenes proton 6-H appears at 7.07 ppm also as a broad singlet. The irradiation of the broad singlet at 6.55 ppm enhanced the doublet of the 4-methoxyphenyl ring at 7.56 ppm by 4% but not the signals of 5-H and 6-H. This confirmed the assigned *Z* geometry as well as the 3,6-disubstitution of compound **3a**. On the other hand, the ^{1}H NMR spectra of compounds **3b–l** have two characteristic doublets at 6.59–6.77 ppm for 4-H and 5-H and a broad singlet at 6.36–6.48 ppm for 2-H, which is indicative of (*E*)-3,6-disubstituted fulvene structures. The structure of **3f** was ascertained by a crystal structure determination but a poor data set made a satisfactory refinement impossible.

3 Conclusion

We have developed a practical base-catalyzed method for the regio- and diastereoselective synthesis of (*E*)-3-(2-aminochromen-4-yl)-6-aryl-disubstituted fulvenes in high yields up to 94%. We used CpH for the first time as a Michael donor in conjugate addition reactions to 2-iminochromenes in the key step of our method. The isomeric mixtures of the CpH Michael adducts were successfully converted to the functionalized fulvenes using catalytic amounts of pyrrolidine at 55°C in MeOH-H_2O. A set of 12 different 3,6-disubstituted fulvenes was prepared, and all except one was determined to have *E* configuration in the exocyclic fulvene double bond.

4 Experimental section

All chemicals and solvents were used as received from commercial suppliers and used without any purification. Silica gel F_{254} (Merck 5554) precoated plates were

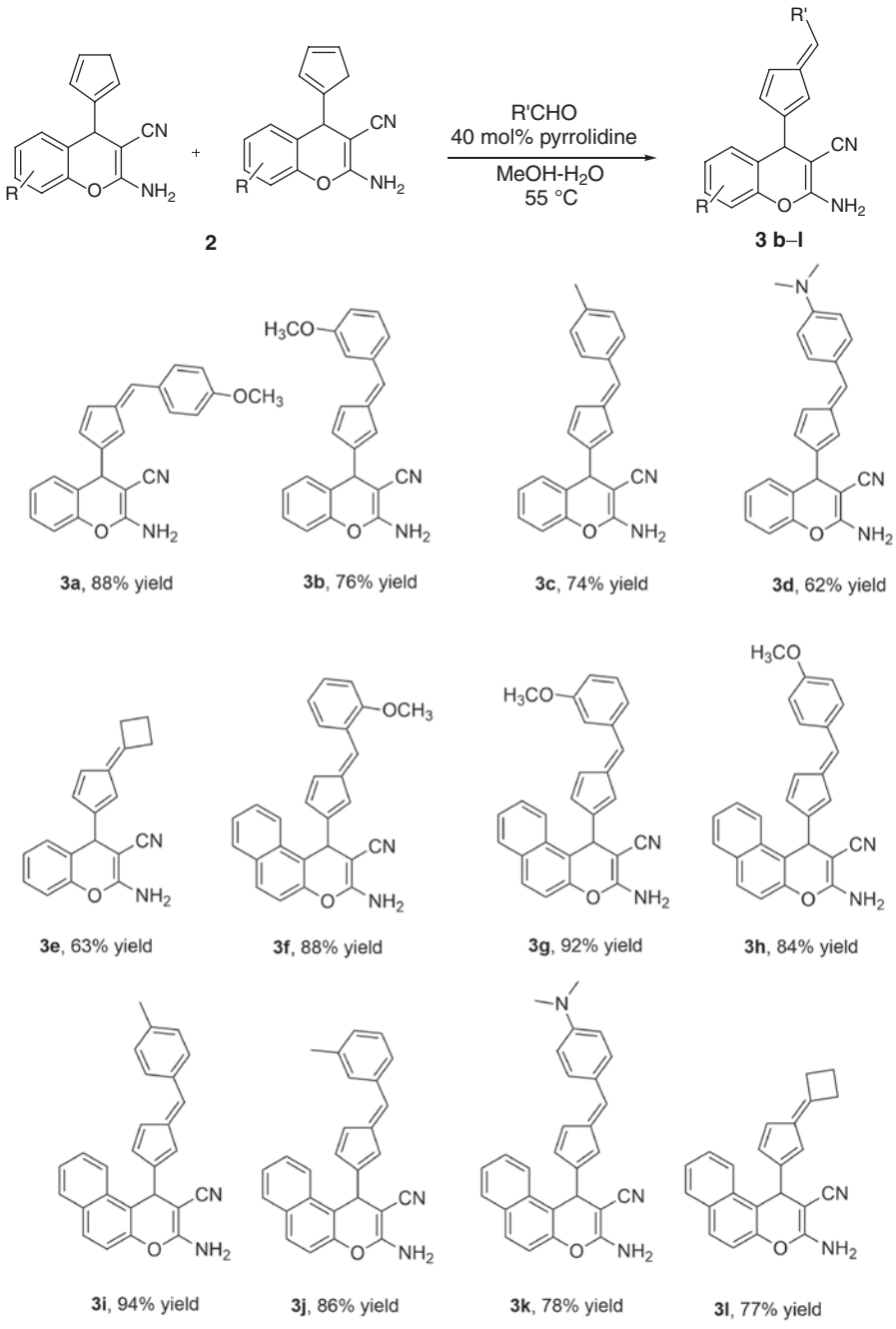


Fig. 3: Regio- and diastereoselective fulvene synthesis with a series of aromatic aldehydes and cyclobutanone.

used for thin layer chromatography. Infrared spectra were recorded on a Thermo-Nicolet 6700 FTIR. UV/Vis spectra were recorded at room temperature with a Cary 60 2.00 spectrometer. NMR experiments were performed on a Varian Mercury Plus 400 MHz spectrometer at ambient temperature using TMS as internal standard. The elemental analyses were performed on a Costech ECS 4010 analyzer. Melting points were determined in open glass capillary tubes with an electrothermal digital melting point apparatus.

4.1 Synthesis of iminochromene Michael adducts (2a, b)

Pyrrolidine (15 mol%) was added to a suspension of aldehyde (5 mmol) and malononitrile (5 mmol) in MeOH-H_2O (3:1, 5 mL). The reaction mixture was stirred at room temperature for the specified time and checked with TLC. The precipitated iminochromenes (**1a**, **b**) were filtered, washed with cold MeOH-H_2O (3:1), and dried in a vacuum oven. 2-Iminochromenes were characterized using

reported spectroscopic data and melting points [19]. DBU (10 mol%) was added to a suspension of iminochromene (5 mmol) and freshly cracked cyclopentadiene (5 mmol) in MeOH-H_2O (3:1, 30 mL). The reaction mixture was stirred at room temperature for 30 min and checked with TLC. The precipitated products were filtered, washed with cold MeOH-H_2O (3:1), and dried in a vacuum oven. The products were obtained as a mixture of isomers forming a yellow precipitate.

4.1.1 2-Imino-2*H*-chromene-3-carbonitrile (1a)

Yellow solid, 86% yield, m.p. 163–165°C (decomp). – ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 7.77 (s, 1H), 7.53 (td, J = 1.6, 8.0 Hz, 1H), 7.39 (dd, J = 1.6, 8.0 Hz, 1H), 7.22 (td, J = 0.8, 8.0 Hz, 1H), 7.16 (d, J = 8.4 Hz, 1H).

4.1.2 3-Imino-3*H*-benzo[*f*]chromene-2-carbonitrile (1b)

Green solid, 99% yield, m.p. 218–220°C (decomp). – ^{1}H NMR (400 MHz, [D_6]DMSO, 25°C, TMS): δ = 9.11 (s, 1H), 8.76 (s, 1H), 8.42 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 9.2 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.69 (t, J = 7.2 Hz, 1H), 7.54 (t, J = 7.6 Hz, 1H), 7.33 (d, J = 8.8 Hz, 1H).

4.1.3 2-Amino-4-(cyclopenta-1,4-dien-1-yl)-4*H*-chromene-3-carbonitriles (2a)

Yellow solid, 80% yield, m.p. 160°C (decomp). – IR (ATR): ν = 3426, 3328, 2190, 1651, 1613, 1581, 1531, 1488, 1406, 1326, 1288, 1266, 1222, 1043 cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS; 5:1 mixture of two isomers): δ = 7.23–7.18 (m, 1H), 7.11–7.05 (m, 2H), 6.99–6.94 (m, 1H), 6.42–6.30 (m, 2H), 6.19 (bs, 0.75H), 4.65 (bs, 0.4H), 4.62 (bs, 2H), 3.02 (d, J = 2.8 Hz, 2H), 3.01–2.68 (m, 0.4H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 159.7, 159.5, 150.3, 148.8, 148.5, 148.3, 135.1, 132.9, 131.9, 131.7, 129.2, 129.0, 128.2, 128.1, 127.9, 125.4, 124.9, 124,8, 122.6, 121.9, 120.0, 116.3, 116.3, 109.9, 59.9, 59.2, 41.2, 40.2, 36.5, 35.6. – $C_{15}H_{12}N_2O$ (236.3): calcd. C 76.25, H 5.12, N 11.86; found C 76.11, H 5.09, N 11.84.

4.1.4 3-Amino-1-(cyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitriles (2b)

Light yellow solid, 95% yield, m.p. 195–197°C. – IR (ATR): ν = 3427, 3331, 2185, 1648, 1590, 1407, 1232, 1178, 1080, 1028 cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS; 1:1 mixture of two isomers): δ = 7.91–7.76 (m, 6H), 7.52–7.41 (m, 4H), 7.21–7.18 (m, 2H), 6.35–6.10 (m, 6H), 5.17 (s, 1H), 5.13 (s, 1H), 4.61 (bs, 4H), 2.96–2.62 (m, 4H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 159.6, 159.3, 150.1, 148.2, 146.8, 146.6, 134.9, 132.2, 131.99, 131.92, 131.22, 131.21, 130.9, 130.8, 129.3, 129.2, 128.43, 128.41, 128.3, 127.2, 127.1, 125.12, 125.10, 123.5, 123.4, 120.1, 116.7, 116.6, 115.6, 114.9, 77.3, 77.2, 61.2, 60.4, 41.2, 40.7, 34.1, 33.4. $C_{19}H_{14}N_2O$ (286.3): calcd. C 79.70, H 4.93, N 9.78; found C 79.67, H 4.90, N 9.76.

4.2 Synthesis of fulvenes 3a–l

Aldehyde (0.15 mmol) and pyrrolidine (40 mol%) was added to a suspension of iminochromene Michael adduct (0.15 mmol) in MeOH-H_2O (4:1, 2 mL). The reaction mixture was stirred at 55°C for the specified time and checked with TLC. The precipitated products were filtered, washed with cold MeOH-H_2O (3:1), and dried in a vacuum oven.

4.2.1 (*Z*)-2-Amino-4-(3-(4-methoxybenzylidene)-cyclopenta-1,4-dien-1-yl)-4*H*-chromene-3-carbonitrile (3a)

Yellow solid, 88% yield, 48 h, m.p. 147–149°C. – UV/Vis (CH_2Cl_2): λ_{max} = 335 nm. – IR (ATR): ν = 3457, 3332, 2189, 1648, 1599, 1512, 1401, 1256, 1175 cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 7.57 (d, J = 8.8 Hz, 2H), 7.21 (td, J = 1.6, 8.8 Hz, 1H), 7.15 (dd, J = 1.2, 7.6 Hz, 1H), 7.09 (d, J = 1.2 Hz, 1H), 7.07 (s, 1H), 6.98 (dd, J = 0.8, 8.4 Hz, 1H), 6.94 (d, J = 8.8 Hz, 2H), 6.55 (s, 1H), 6.27 (ddd, J = 11.8, 5.2, 1.7 Hz, 2H), 4.67 (bs, 3H), 3.86 (s, 3H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 160.5, 159.8, 151.4, 148.7, 142.8, 138.3, 136.6, 132.3, 129.5, 129.4, 128.9, 128.3, 125.0, 121.5, 120.0, 116.3, 115.6, 114.3, 58.7, 55.4, 35.9. – $C_{23}H_{18}N_2O_2$ (354.4): calcd. C 77.95, H 5.12, N 7.90; found C 77.92, H 5.10, N 7.89.

4.2.2 (*E*)-2-Amino-4-(3-(3-methoxybenzylidene)-cyclopenta-1,4-dien-1-yl)-4*H*-chromene-3-carbonitrile (3b)

Orange solid, 76% yield, 48 h, m.p. 176–178°C (decomp.). – IR (ATR): ν = 3451, 3334, 2194, 1657, 1602, 1577, 1512, 1487, 1405, 1251, 1177, 1026 cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 7.51 (d, J = 8.8 Hz, 2H), 7.23–7.17 (m, 2H), 7.11–7.07 (m, 2H), 6.99 (d, J = 8.0 Hz, 1H), 6.91 (d, J = 8.8 Hz, 2H), 6.69 (d, J = 4.0 Hz, 1H), 6.48 (d, J = 5.2 Hz, 1H), 6.09 (s, 1H), 4.64 (s, 1H), 4.61 (bs, 2H), 3.84 (s, 3H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 160.5, 159.7, 148.8, 146.4, 142.8, 138.2,

133.9, 132.2, 129.6, 129.4, 128.2, 124.9, 122.6, 121.9, 121.8, 119.9, 116.3, 115.6, 114.2, 109.9, 59.1, 55.3, 35,5. – $C_{23}H_{18}N_2O_2$ (354.4): calcd. C 77.95, H 5.12, N 7.90; found C 77.95, H 5.10, N 7.88.

4.2.3 (*E*)-2-Amino-4-(3-(4-methylbenzylidene)-cyclopenta-1,4-dien-1-yl)-4*H*-chromene-3-carbonitrile (3c)

Orange solid, 74% yield, 24 h, m.p. 185°C (decomp.). – IR (ATR): ν = 3458, 3347, 2189, 1655, 1605, 1575, 1404 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 7.44 (d, J = 8.0 Hz, 2H), 7.24–7.08 (m, 6H), 6.99 (d, J = 8.0 Hz, 1H), 6.69 (d, J = 4 Hz, 1H), 6.47 (d, J = 5.6 Hz, 1H), 6.09 (s, 1H), 4.64 (s, 1H), 4.61 (bs, 2H), 2.37 (s, 3H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 159.8, 148.9, 146.9, 143.9, 139.3, 138.4, 134.1, 133.9, 130.5, 129.4, 129.3, 128.2, 124.9, 122.5, 122.2, 121.7, 119.9, 116.3, 58.9, 35.5, 21.4. – $C_{23}H_{18}N_2O$ (338.4): calcd. C 81.63, H 5.36, N 8.28; found C 81.59, H 5.29, N 8.21.

4.2.4 (*E*)-2-Amino-4-(3-(4-(dimethylamino)benzylidene)-cyclopenta-1,4-dien-1-yl)-4*H*-chromene-3-carbonitrile (3d)

Orange solid, 62% yield, 24 h, m.p. 203°C (decomp.). – IR (ATR): ν = 3329, 2923, 2189, 1643, 1595, 1528, 1373, 1192 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 7.51 (d, J = 8.8 Hz, 2H), 7.20 (m, 2H), 7.10 (d, J = 7.6 Hz, 1H), 7.05 (s, 1H), 6.98 (d, J = 8.4 Hz, 1H), 6.77 (dd, J = 2.0, 5.2 Hz, 1H), 6.67 (d, J = 9.2 Hz, 2H), 6.45 (d, J = 5.2 Hz, 1H), 6.07 (s, 1H), 4.64 (s, 1H), 4.56 (bs, 2H), 3.03 (s, 6H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 140.3, 139.7, 132.7, 132.6, 132.4, 129.4, 128.0, 124.9, 123.2, 122.9, 121.4, 120.1, 116.2, 111.9, 77.5, 77.4, 77.2, 59.6, 59.1, 40.1, 35.46. – $C_{24}H_{21}N_3O$ (367.2): calcd. C 78.45, H 5.76, N 11.44; found C 78.40, H 5.72, N 11.39.

4.2.5 2-Amino-4-(3-cyclobutylidenecyclopenta-1,4-dien-1-yl)-4*H*-chromene-3-carbonitrile (3e)

Yellow solid, 63% yield, 24 h, m.p. 188°C (decomp.). – IR (ATR): ν = 3456, 3346, 2189, 1654, 1605, 1575, 1485, 1401, 1230 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 7.19 (t, J = 7.2 Hz, 1H), 7.13 (d, J = 7.2 Hz, 1H), 7.07 (t, J = 7.2 Hz, 1H), 6.97 (d, J = 8.0 Hz, 1H), 6.26 (s, 2H), 6.06 (s, 1H), 4.59 (bs, 3H), 3.08 (d, J = 4.8 Hz, 4H), 2.14 (p, J = 7.6 Hz, 2H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 160.1, 159.6, 148.8, 146.9, 138.2, 129.4, 129.3, 128.1, 124.9, 122.0, 121.8, 120.0, 116.3, 115.6, 59.3, 35.7, 32.3, 32.2, 16.9. – $C_{19}H_{16}N_2O$ (288.3): calcd. C 79.14, H 5.59, N 9.72; found C 79.11, H 5.56, N 9.71.

4.2.6 (*E*)-3-Amino-1-(3-(2-methoxybenzylidene)-cyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitrile (3f)

Orange solid, 88% yield, 24 h, m.p. 187°C (decomp.). – IR (ATR): ν = 3464, 3333, 2187, 1652, 1588, 1404, 1232 cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$, 25°C, TMS): δ = 7.94 (d, J = 8.4 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.8 Hz, 1H), 7.53–7.42 (m, 3H), 7.39 (s, 1H), 7.30 (t, J = 7.2 Hz, 1H), 7.20 (m, 1H), 6.95 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.53 (d, J = 5.2 Hz, 1H), 6.47 (d, J = 5.6 Hz, 1H), 6.01 (s, 1H), 5.16 (s, 1H), 4.64 (s, 2H), 3.83 (s, 3H). – ^{13}C NMR (400 MHz, $CDCl_3$): δ = 159.7, 158.3, 147.0, 146.9, 144.6, 133.9, 133.7, 132.2, 131.2, 131.1, 130.4, 129.3, 128.4, 127.2, 125.9, 125.2, 123.6, 122.4, 121.4, 120.5, 120.2, 116.7, 114.8, 110.5, 59.9, 55.5, 33.3. – $C_{27}H_{20}N_2O_2$ (404.5): calcd. C 80.18, H 4.98, N 6.93; found C 79.99, H 4.96, N 6.87.

4.2.7 (*E*)-3-Amino-1-(3-(3-methoxybenzylidene)-cyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitrile (3g)

Orange solid, 92% yield, 48 h, m.p. 195°C (decomp.). – IR (KBr): ν = 3451, 3332, 2186, 1657, 1619, 1592, 1407, 1237 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO, 25°C, TMS): δ = 8.04 (d, J = 8.8 Hz, 1H), 7.91 (m, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.34–7.29 (m, 2H), 7.21 (s, 1H), 7.11 (d, J = 7.6 Hz, 1H), 7.05 (bs, 3H), 6.93 (d, J = 8.0 Hz, 1H), 6.57 (d, J = 4.4 Hz, 1H), 6.35 (d, J = 5.2 Hz, 1H), 6.08 (s, 1H), 5.17 (s, 1H), 3.74 (s, 3H). – ^{13}C NMR (400 MHz, [D_6]DMSO): δ = 161.3, 159.8, 148.3, 147.2, 144.8, 138.5, 137.9, 135.4, 131.1, 130.8, 130.4, 129.8, 128.9, 127.6, 125.5, 123.8, 123.1, 122.2, 121.2, 121.1, 117.3, 115.6, 115.5, 115.3, 55.5, 55.3, 33.1. – $C_{27}H_{20}N_2O_2$ (404.5): calcd. C 80.18, H 4.98, N 6.93; found C 80.08, H 4.95, N 6.90.

4.2.8 (*E*)-3-Amino-1-(3-(4-methoxybenzylidene)-cyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitrile (3h)

Orange solid, 84% yield, 30 h, m.p. 206°C (decomp.). – IR (KBr): ν = 3451, 3332, 2186, 1657, 1619, 1592, 1407, 1237 cm^{-1}. – ^1H NMR (400 MHz, [D_6]DMSO, 25°C, TMS): δ = 8.04 (d, J = 8.4 Hz, 1H), 7.92–7.89 (m, 2H), 7.55–7.51 (m, 3H), 7.45 (t, J = 7.6 Hz, 1H), 7.29 (d, J = 9.2 Hz, 1H), 7.15 (s, 1H), 7.03 (s, 2H), 6.96 (d, J = 8.8 Hz, 2H), 6.61 (d, J = 4.4 Hz, 1H), 6.32

(d, *J* = 5.2 Hz, 1H), 6.04 (s, 1H), 5.14 (s, 1H), 3.76 (s, 3H). – ^{13}C NMR (400 MHz, [D$_6$]DMSO): δ = 160.9, 160.5, 146.8, 146.7, 142.1, 138.4, 134.3, 132.4, 130.7, 130.5, 129.3, 128.9, 128.5, 127.2, 125.1, 123.6, 121.4, 121.2, 120.9, 116.9, 115.3, 114.6, 55.4, 55.2, 32.8. – $C_{27}H_{20}N_2O_2$ (404.5): calcd. C 80.18, H 4.98, N 6.93; found C 80.12, H 4.96, N 6.91.

4.2.9 (*E*)-3-Amino-1-(3-(4-methylbenzylidene)-cyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitrile (3i)

Yellow solid, 94% yield, 30 h, m.p. 238°C (decomp.). – UV/Vis (CH_2Cl_2): λ_{max} = 210 nm. IR (KBr): ν = 3435, 3327, 2187, 1658, 1621, 1594, 1409, 1236 cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25°C, TMS): δ = 8.04 (d, *J* = 8.4 Hz, 1H), 7.92–7.89 (m, 2H), 7.55–7.44 (m, 4H), 7.29 (d, *J* = 9.2 Hz, 1H), 7.22–7.18 (m, 3H), 7.04 (s, 2H), 6.60 (d, *J* = 4.8 Hz, 1H), 6.33 (d, *J* = 4.8 Hz, 1H), 6.06 (s, 1H), 5.15 (s, 1H), 2.29 (s, 3H). – ^{13}C NMR (400 MHz, [D$_6$]DMSO): δ = 160.9, 147.4, 146.8, 146.7, 143.4, 139.4, 138.5, 134.7, 133.6, 130.7, 130.5, 129.7, 129.4, 128.5, 127.2, 125.1, 123.5, 121.6, 121.0, 120.9, 116.9, 115.1, 55.1, 32.7, 21.0. – $C_{27}H_{20}N_2O$ (388.5): calcd. C 83.48, H 5.19, N 7.21; found C 83.42, H 5.15, N 7.19.

4.2.10 (*E*)-3-Amino-1-(3-(3-methylbenzylidene)-cyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitrile (3j)

Yellow solid, 86% yield, 24 h, m.p. 215°C (decomp.). – IR (KBr): ν = 3426, 3334, 2186, 1642, 1621, 1593, 1407, 1235 cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25°C, TMS): δ = 8.04 (d, *J* = 8.4 Hz, 1H), 7.93–7.90 (m, 2H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.33–7.26 (m, 4H), 7.19–7.16 (m, 2H), 7.05 (s, 2H), 6.59 (d, *J* = 5.2 Hz, 1H), 6.35 (d, *J* = 4.8 Hz, 1H), 6.07 (s, 1H), 5.16 (s, 1H), 2.29 (s, 3H). – ^{13}C NMR (400 MHz, [D$_6$]DMSO): δ = 160.9, 147.7, 146.8, 144.1, 138.5, 138.2, 136.3, 134.8, 130.9, 130.8, 130.5, 130.1, 129.4, 128.9, 128.5, 127.6, 127.3, 125.2, 123.5, 121.9, 120.9, 116.9, 115.0, 109.7, 55.0, 32.7, 20.9. – $C_{27}H_{20}N_2O$ (388.5): calcd. C 83.48, H 5.19, N 7.21; found C 83.40, H 5.11, N 7.19.

4.2.11 (*E*)-3-amino-1-(3-(4-(dimethylamino)benzylidene)-cyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitrile (3k)

Orange solid, 78% yield, 48 h, m.p. 234°C (decomp.). – IR (KBr): ν = 3432, 3334, 2186, 1657, 1592, 1529, 1403 cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25°C, TMS): δ = 8.04 (d, *J* = 8.4 Hz, 1H), 7.92–7.89 (m, 2H), 7.54–7.43 (m, 4H), 7.28 (d, *J* = 9.2 Hz, 1H), 7.04 (s, 1H), 6.96 (s, 2H), 6.70 (d, *J* = 8.8 Hz, 2H), 6.64 (dd, *J* = 1.6, 4.8 Hz, 1H), 6.27 (d, *J* = 5.2 Hz, 1H), 5.99 (s, 1H), 5.11 (s, 1H), 2.96 (s, 6H). – ^{13}C NMR (400 MHz, [D$_6$]DMSO): δ = 160.7, 151.2, 146.7, 145.1, 139.8, 139.2, 132.8, 132.5, 130.7, 130.5, 129.2, 128.5, 127.1, 125.2, 125.1, 123.8, 123.6, 123.5, 121.4, 120.7, 120.6, 116.8, 56.1, 55.7, 32.8. – $C_{28}H_{23}N_3O$ (417.5): calcd. C 80.55, H 5.55, N 10.06; found C 80.49, H 5.51, N 10.01.

4.2.12 3-Amino-1-(3-cyclobutylidenecyclopenta-1,4-dien-1-yl)-1*H*-benzo[*f*]chromene-2-carbonitrile (3l)

Yellow solid, 77% yield, 24 h, m.p. 218–220°C (decomp.). – IR (KBr): ν = 3456, 3351, 2186, 1658, 1591, 1405, 1230 cm^{-1}. – ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25°C, TMS): δ = 7.98 (d, *J* = 8.4 Hz, 1H), 7.91–7.87 (m, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.27 (d, *J* = 8.8 Hz, 1H), 6.97 (s, 2H), 6.14 (dd, *J*= 0.8, 4.8 Hz, 1H), 6.07 (d, *J*= 4.4 Hz, 1H), 5.93 (s, 1H), 5.07 (s, 1H), 2.97 (bs, 4H), 2.02 (p, *J* = 7.6 Hz, 2H). – ^{13}C NMR (400 MHz, [D$_6$]DMSO): δ = 160.7, 159.9, 147.8, 146.7, 137.8, 130.7, 130.4, 129.5, 129.2, 128.5, 127.2, 125.1, 123.5, 121.7, 120.9, 116.9, 115.5, 113.9, 55.7, 32.9, 31.9, 31.8, 16.6. – $C_{23}H_{18}N_2O$ (338.4): calcd. C 81.63, H 5.36, N 8.28; found C 81.60, H 5.32, N 8.22.

5 Supporting information

Full experimental details, ^{1}H and ^{13}C NMR spectra of all compounds are given as Supporting Information available online (DOI: 10.1515/znb-2016-0064).

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