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Lewis acid catalyzed C-3 alkylidenecyclopentenylolation of indoles: an easy access to functionalized indoles and bisindoles†

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A Lewis acid catalyzed C-3 alkylidenecyclopentenylolation of indoles through the ring opening of pentafulvene derived diazabicyclic olefins has been developed. The present protocol offers an efficient route toward the synthesis of indole and bisindole derivatives. The role of the hydrazine group, as a reaction carrier in the strategy has also been demonstrated by the stepwise synthesis of functionalized bisindole.

Indole, an important nitrogen containing heterocyclic scaffold, is one of the primary building blocks of many natural products, biologically active molecules and functional materials.¹ Moreover, indole is the key component in many pharmaceutical agents such as triptan and its derivatives, a class of psychoactive drugs used in the treatment of 5HT receptor related disorders (Fig. 1).² Owing to the great prevalence of the indole nucleus, enormous research effort has been devoted towards the synthesis and functionalization, especially at the C-3 position, of this privileged core.³ Various synthetic methodologies, involving Lewis and Brønsted acids, organo-catalysts or transition metal catalysts, have been developed by different research groups for the selective C-3 functionalization of indoles.⁴ In 2001, Kobayashi *et al.* achieved the C-3 cyclopentenylolation of indoles through a Lewis acid/surfactant catalyzed Friedel–Crafts type conjugate addition in aqueous medium.⁵ Later, King and coworkers explored the Lewis acid catalyzed Michael addition of indoles to cyclopent-2-enone for the preparation of 3-*cis*-(3-aminocyclopentenyl) indoles as potent inhibitors of hSERT.⁶ Among indole derivatives, bisindole moieties are present in several natural alkaloids⁷ and many of these compounds show promising medicinal properties (Fig. 1).⁸ So the design and development of new atom economic methods for construction of bisindole derivatives remains as a highly demanding strategy in organic synthesis. Herein, we disclose a Lewis acid catalyzed ring-opening of pentafulvene derived bicyclic olefins with *N*-alkyl

as well as free (NH) indoles toward the efficient synthesis of mono and bisindolyl functionalized alkylidenecyclopentenones.

In various cycloaddition reactions, pentafulvenes, a cyclic cross conjugated system, have been well explored as a 2π , 4π or 6π component for the construction of numerous biologically relevant molecules.⁹ Additionally, desymmetrization of diazabicyclic olefins under transition metal catalysis or acid catalysis has been developed as an efficient protocol by several research groups,¹⁰ including our laboratory for the synthesis of highly functionalized cyclopentene derivatives.¹¹

As part of our continuous interest in the chemistry of strained norbornene derivatives, we have utilized diazabicyclic olefins derived from different pentafulvenes as a simple precursor for the synthesis of substituted alkylidenecyclopentenones and complex heterocyclic scaffolds in the presence of a palladium catalyst or Lewis acid. In our previous report we have demonstrated a Lewis acid catalyzed ring-opening of pentafulvene derived diazabicyclic olefins using various *ortho*-functionalized aryl iodides such as 2-iodoanilines, 2-iodophenols and 2-iodobenzene thiols and aliphatic alcohols to access a variety of *trans*-3,4-disubstituted alkylidenecyclopentenones.¹² In

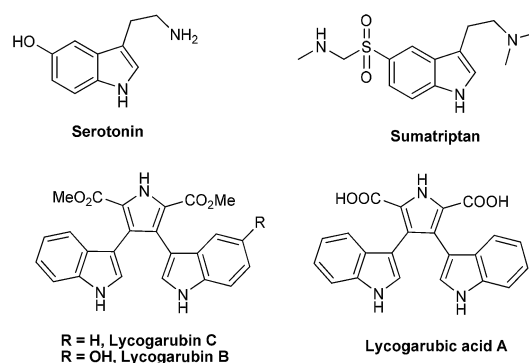


Fig. 1 Bioactive compounds with indole or bisindole scaffolds.

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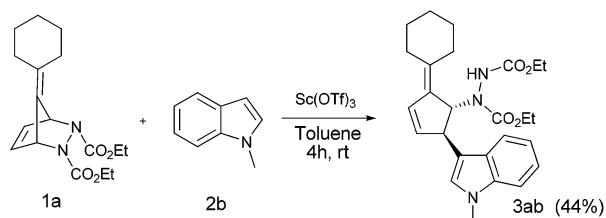
† Electronic supplementary information (ESI) available: ¹H and ¹³C NMR spectra of all new compounds. CCDC 1034718 and 989506. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c5ra01107h

the same report, a palladium/Lewis acid mediated transformation of pentafulvene derived diazabicyclic olefins has also been described for the synthesis of novel spiropentacyclic motifs with indoline/dihydrobenzothiophene and pyrazolidine fused to the cyclopentene core. As a perpetuation of our ongoing investigations in the area of strained bicyclic olefins, we have decided to undertake the Lewis acid catalyzed desymmetrization of pentafulvene derived diazabicyclic olefins by employing biologically significant indoles as nucleophiles. The developed method successfully leads to the C-3 functionalization of indoles with alkylidenecyclopentenyls, along with the formation of bisindole derivatives.

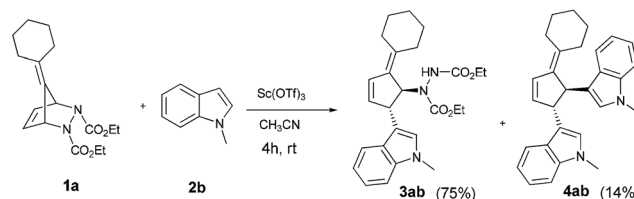
We initiated our investigation by the treatment of pentafulvene derived diazabicyclic olefin **1a** (1.2 equiv.) with *N*-methylindole **2b** (1 equiv.) in the presence of $\text{Sc}(\text{OTf})_3$ (2 mol%) in toluene at room temperature (Scheme 1). After 4 h, the reaction afforded the desired *trans*-3,4-disubstituted alkylidene cyclopentene derivative **3ab** in 44% yield. The structure of **3ab** was established by the usual spectroscopic techniques and also based on comparison with our previous report.¹² Furthermore, the structure and stereochemistry of the product was confirmed by single crystal X-ray analysis of a similar derivative **3eb** (see ESI†).

Further screening of solvents such as DMF, THF, 1,2-dichloroethane, DCM and CH_3CN revealed that CH_3CN was the most favorable medium for the transformation. Astonishingly, when CH_3CN was employed as the solvent, the bisindolyl functionalized alkylidene cyclopentene **4ab** was observed along with the expected 3,4-disubstituted alkylidene cyclopentene **3ab** (Scheme 2). Various Lewis acids were also tested for the ring-opening of **1a** with **2b** in acetonitrile. Among them, $\text{Sn}(\text{OTf})_2$ and $\text{Fe}(\text{OTf})_3$ provided the product **3ab** in comparable yields. During optimization studies, we perceived that the change in equivalents of starting materials **1a** or **2b** played a crucial role in the outcome of the reaction. Use of 2 equiv. of *N*-methylindole **2b** resulted in the formation of bisindole product **4ab** (58% yield) in excess over **3ab** (31% yield) (entry 16). Under optimal conditions (2 mol% $\text{Sc}(\text{OTf})_3$ in CH_3CN), the reaction could be finely tuned towards the formation of alkylidenecyclopentenyl derivative of indole **3ab** or bisindole **4ab** by simply altering the equivalents of starting materials **1a** or **2b**.

Under the optimized catalytic conditions for the preparation of alkylidenecyclopentenyl derivative of indole (Table 1, entry 6) and bisindole (Table 1, entry 16), we examined the scope of different olefins and indoles (Table 2). Diazabicyclic alkenes



Scheme 1 Lewis acid catalyzed C-3 functionalization of *N*-methylindole **2b** with diazabicyclic olefin **1a**.



Scheme 2 $\text{Sc}(\text{OTf})_3$ catalyzed C-3 functionalization of *N*-methylindole **2b** with diazabicyclic olefin **1a** in acetonitrile.

1a–d easily underwent ring opening with *1H*-indole **2a** and gave the corresponding indole derivatives **3aa–da** and bisindole **4aa** in good to moderate yields (entries 1–4). To demonstrate the generality of the reaction, several C-1, C-2 and C-5 substituted indoles **2b–f** were subjected to C-3 alkylidenecyclopentenyl-lation. Reaction was found to be compatible to a variety of indoles having substituents such as $-\text{F}$, $-\text{OH}$, $-\text{NO}_2$ etc. and yielded the C-3 functionalized indoles and bisindoles (entries 5–9).

Next, we turned our attention to explore the scope of C-3 functionalization of indoles with diazabicyclic olefins derived from different pentafulvenes (Table 3). Alkylidenecyclopentenyl-lation of indoles proceeds efficiently through the ring opening of diazabicyclic alkenes **1e–h** to provide the desired indole and bisindole derivatives. In the case of diphenylfulvene derived bicyclic olefin **1h** with indoles **2a** and **2b**, corresponding bisindole derivatives were formed in 84% and 81% yield respectively (entries 7 and 8). Furthermore, the stereochemistry of the bisindole product **4** was unambiguously confirmed by the single crystal X-ray analysis of compound **4ha** (Fig. 2, ESI†).

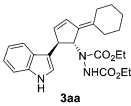
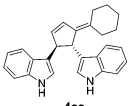
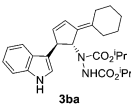
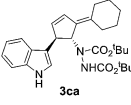
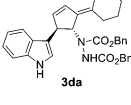
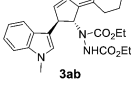
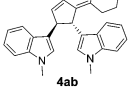
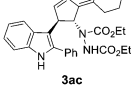
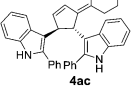
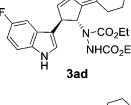
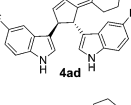
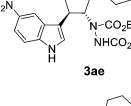
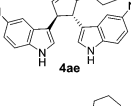
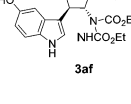
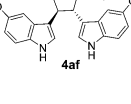
Based on these results we propose a plausible mechanism as shown in Scheme 3. As similar to our previous reports,¹² the

Table 1 Screening of the reactivity of various Lewis acids in different solvents^a

Entry	Lewis acid	Solvent	Yield (%)	
			3ab	4ab
1	$\text{Sc}(\text{OTf})_3$	Toluene	44	—
2	$\text{Sc}(\text{OTf})_3$	DMF	38	—
3	$\text{Sc}(\text{OTf})_3$	THF	30	—
4	$\text{Sc}(\text{OTf})_3$	DCE	65	5
5	$\text{Sc}(\text{OTf})_3$	DCM	58	Trace
6	$\text{Sc}(\text{OTf})_3$	CH_3CN	75	14
7	$\text{Yb}(\text{OTf})_3$	CH_3CN	37	—
8	$\text{Zn}(\text{OTf})_2$	CH_3CN	Trace	—
9	$\text{La}(\text{OTf})_3$	CH_3CN	35	—
10	$\text{Cu}(\text{OTf})_2$	CH_3CN	46	—
11	$\text{Sn}(\text{OTf})_2$	CH_3CN	70	8
12	$\text{Fe}(\text{OTf})_3$	CH_3CN	62	6
13	AgOTf	CH_3CN	Trace	—
14	AlCl_3	CH_3CN	53	Trace
15	BF_3OEt_2	CH_3CN	36	—
16 ^b	$\text{Sc}(\text{OTf})_3$	CH_3CN	31	58

^a Reaction conditions: alkene (1.2 equiv.), *N*-methylindole (1 equiv.), catalyst (2 mol%), solvent (2 mL), at rt. for 4 h. ^b Reaction in the presence of 1.0 equiv. of alkene and 2 equiv. of *N*-methylindole.

Table 2 Substrate scope of indoles with various 6,6-pentamethylene fulvene derived diazabicyclic olefins^a

Entry	Bicyclic olefin	Indole	Product 3	Product 4	Yield (%)	
					3	4
1	1a	2a			73 27 ^b	16 64 ^b
2	1b	2a		4aa	72 14 ^b	16 72 ^b
3	1c	2a		4aa	42 27 ^b	14 28 ^b
4	1d	2a		4aa	39 17 ^b	12 33 ^b
5	1a	2b			75 31 ^b	14 58 ^b
6	1a	2c			78 32 ^b	11 54 ^b
7	1a	2d			61 24 ^b	14 52 ^b
8	1a	2e			59 26 ^b	12 48 ^b
9	1a	2f			56 28 ^b	8 39 ^b

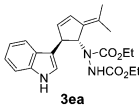
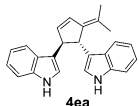
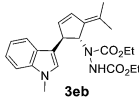
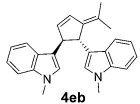
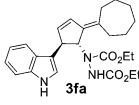
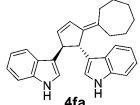
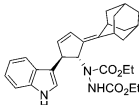
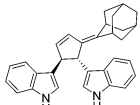
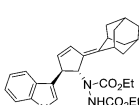
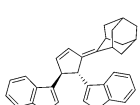
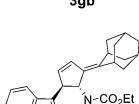
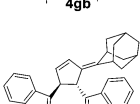
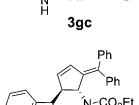
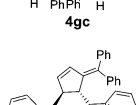
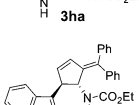
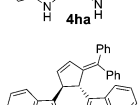
^a Reaction conditions: alkene (1.2 equiv.), indole (1 equiv.), catalyst (2 mol%), solvent (2 mL), at rt. for 4 h. ^b Reaction in presence of 1 equiv. of alkene and 2 equiv. of indole.

catalytic cycle is initiated by coordination of the Lewis acid with the carbonyl oxygen of one of the carbamate groups of diazabicyclic olefin **1** and subsequent cleavage of the C–N bond leads to the generation of a transient allylic cation species **A**. Regioselective nucleophilic attack of indole from the opposite side with respect to the hydrazine moiety of intermediate **A** delivers *trans*-3,4-disubstituted alkylidene cyclopentene **3**. In the next step, the Lewis acid coordinates with the carbonyl group of the hydrazine moiety, followed by the elimination of the hydrazine group through C–N bond cleavage, resulting in the formation of intermediate **D**. Attack of the second molecule of indole to intermediate **D** furnishes the bisindole product **4**. Furthermore, ESI-MS studies

provided strong supporting evidence for the formation of intermediates **C** and **D** (see ESI†).

To confirm the Lewis acid catalyzed generation of an intermediate from **3** by the elimination of hydrazine moiety, we have carried out a reaction with 1 equiv. of 3,4-disubstituted alkylidene cyclopentene **3ha** and 1.2 equiv. of indole **2a** (Scheme 4). As expected, bisindole product **4ha** was obtained in 62% yield, supporting the role of 3,4-disubstituted alkylidene cyclopentene as an intermediate in the course of reaction. It is to be noted that the hydrazine group acts as a key functional moiety in the present atom economic strategy toward the synthesis of functionalized bisindoles. In addition, oxidation of the generated hydrazine could provide the corresponding dialkyl diazene-1,2-

Table 3 Substrate scope of various pentafulvene derived diazabicyclic olefins for the C-3 functionalization of indole^a

Entry	Bicyclic olefin	Indole	Product 3	Product 4	Yield (%)	
					3	4
1	1e	2a			69 24 ^b	18 64 ^b
2	1e	2b			65 27 ^b	15 56 ^b
3	1f	2a			70 25 ^b	9 53 ^b
4	1g	2a			66 30 ^b	24 58 ^b
5	1g	2b			70 32 ^b	16 55 ^b
6	1g	2c			66 13 ^b	14 74 ^b
7	1h	2a			62 8 ^b	28 84 ^b
8	1h	2b			68 10 ^b	24 81 ^b

^a Reaction conditions: alkene (1.2 equiv.), indole (1 equiv.), catalyst (2 mol%), solvent (2 mL), at rt. for 4 h. ^b Reaction in presence of 1 equiv. of alkene and 2 equiv. of indole.

dicarboxylates, which can be reused in the cycloaddition reactions.

In summary, we have developed a Lewis acid catalyzed C-3 alkylidenecyclopentenylolation of indoles through the ring opening of pentafulvene derived diazabicyclic olefins. The developed method provides an efficient synthetic route to furnish pharmaceutically valuable indole and bisindole derivatives of alkylidenecyclopentenones from easily accessible starting materials. While multiple steps are involved in conventional synthetic strategies, this protocol offers a one-pot access to cyclopentene-bisindole hybrids. Moreover, the present strategy is compatible with both *N*-alkyl and free (NH) indoles. Further investigations to elaborate the scope of the reaction on other N-heterocycles and also to explore the

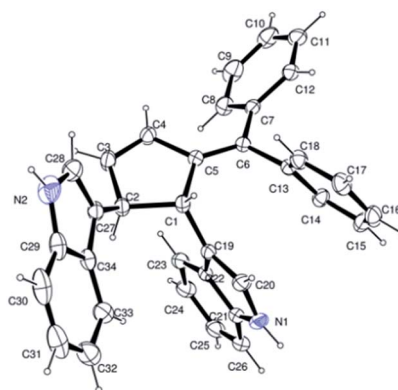
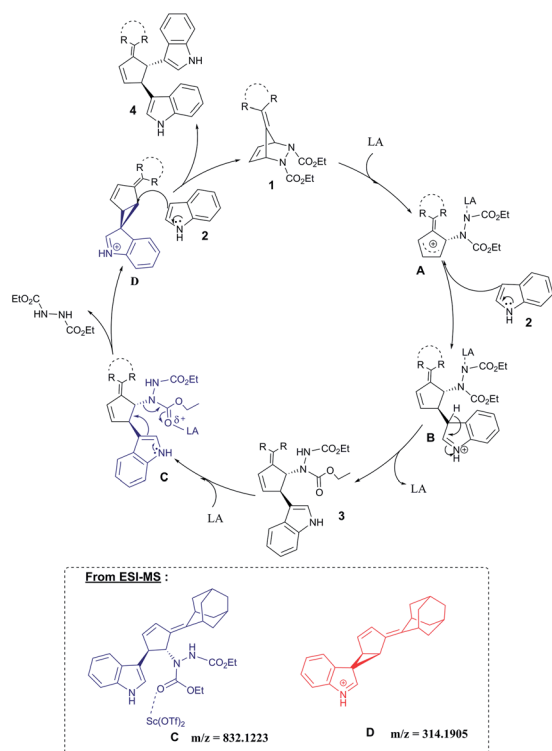
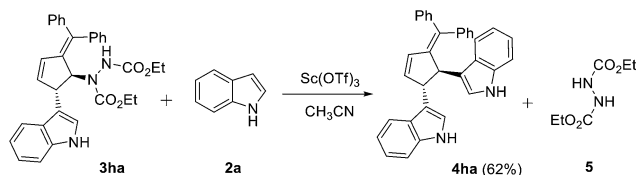


Fig. 2 Single crystal X-ray structure of compound 4ha.



Scheme 3 Plausible mechanism.



Scheme 4 Lewis acid catalyzed synthesis of bisindole derivative.

biological applications of synthesized molecules are currently underway.

Experimental section

General methods

All chemicals were of the best grade commercially available and are used without further purification. All solvents were purified according to standard procedure; dry solvents were obtained according to the literature methods and stored over molecular sieves. Analytical thin layer chromatography was performed on glass plates coated with silica gel containing calcium sulfate binder. Gravity column chromatography was performed using 60–120 or 100–200 mesh silica gel and mixtures of hexane/ethyl acetate were used for elution.

Melting points were determined on a Buchi melting point apparatus and are uncorrected. Proton nuclear magnetic resonance spectra (^1H NMR) were recorded on a Bruker AMX 500 spectrophotometer (CDCl_3 as solvent). Chemical shifts for ^1H NMR spectra are reported as δ in units of parts per million

(ppm) downfield from SiMe_4 (δ 0.0) and relative to the signal of chloroform- d (δ 7.25, singlet). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); dd (double doublet); m (multiplet). Coupling constants are reported as J value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from SiMe_4 (δ 0.0) and relative to the signal of chloroform- d (δ 77.03, triplet). Mass spectra were recorded under EI/HRMS at 60 000 resolution using Thermo Scientific Exactive mass spectrometer. IR spectra were recorded on Bruker FT-IR spectrometer.

General procedure for the Lewis acid catalyzed reaction of pentafulvene derived bicyclic hydrazines towards the synthesis of 3. A mixture of pentafulvene derived bicyclic hydrazine (1.2 equiv.), indole (1.0 equiv.) and $\text{Sc}(\text{OTf})_3$ (2 mol%) were weighed in a Schlenk tube and degassed for 10 minutes. Dry CH_3CN (2 mL) was added and the reaction mixture was purged with argon and allowed to stir at room temperature for 4 hours. The solvent was evaporated *in vacuo* and the residue on silica gel (100–200 mesh) column chromatography yielded *trans*-3,4-disubstituted alkylidene cyclopentene (3) along with minor amount of *trans*-3,4-disubstituted bisindolyl product (4).

General procedure for the Lewis acid catalyzed reaction of pentafulvene derived bicyclic hydrazines towards the synthesis of 4. A mixture of pentafulvene derived bicyclic hydrazine (1.0 equiv.), indole (2.0 equiv.) and $\text{Sc}(\text{OTf})_3$ (2 mol%) were weighed in a Schlenk tube and degassed for 10 minutes. Dry CH_3CN (2 mL) was added and the reaction mixture was purged with argon and allowed to stir at room temperature for 4 hours. The solvent was evaporated *in vacuo* and the residue on silica gel (100–200 mesh) column chromatography yielded *trans*-3,4-disubstituted bisindolyl product (4) along with minor amount of *trans*-3,4-disubstituted alkylidene cyclopentene (3).

Diethyl 1-(2-cyclohexylidene-5-(1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3aa). Yield: 73%; pale yellow solid; M. p. 122–124 °C; R_f : 0.31 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3334, 3054, 2976, 2920, 2853, 1709, 1586, 1458, 1410, 1330, 1220, 1120, 1052, 920, 745 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.10 (brs, 1H), 7.68 (brs, .03) (m, 1H), 6.84 (s, 1H), 6.53 (d, J = 6 Hz, 1H), 6.26 (brs, 1H), 6.04 (brs, 1H), 5.34–5.12 (m, 1H), 4.50–4.40 (m, 1H), 4.24–4.17 (m, 4H), 2.39–2.33 (m, 2H), 2.08–2.07 (m, 2H), 1.66–1.53 (m, 6H), 1.30–1.29 (m, 5H), 1.02 (brs, 1H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.6, 155.1, 136.7, 136.2, 134.0, 129.7, 126.6, 121.9, 120.0, 119.2, 118.1, 110.0, 65.4, 64.1, 62.4, 61.9, 47.4, 32.0, 31.0, 28.4, 28.1, 26.6, 14.5, 14.2. HRMS (ESI): calcd for $\text{C}_{25}\text{H}_{31}\text{N}_3\text{O}_4\text{Na}$: 460.22123; found: 460.22171.

Diethyl 1-(2-cyclohexylidene-5-(1-methyl-1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ab). Yield: 75%; pale yellow solid; M. p. 120–122 °C, R_f : 0.33 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3323, 3055, 2981, 2932, 2855, 1710, 1619, 1583, 1513, 1458, 1415, 1339, 1302, 1227, 1096, 1061, 920, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.68 (brs, 1H), 7.25–7.23 (m, 2H), 7.05 (t, J = 7 Hz, 1H), 6.73 (s, 1H), 6.53 (d, J = 5.5, 1H), 6.23 (brs, 1H), 6.04 (s, 1H), 5.31–5.09 (m, 1H), 4.49–4.39 (m, 1H), 4.24–4.18 (m, 4H), 3.72 (s, 3H), 2.38–2.34 (m, 2H), 2.07–2.03 (m, 2H), 1.61–1.53 (m, 6H), 1.31–1.26 (m,

5H), 1.05–1.04 (brs, 1H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.4, 155.1, 137.4, 133.7, 129.6, 127.0, 125.7, 121.5, 120.1, 118.7, 109.1, 108.8, 65.5, 62.3, 61.8, 47.5, 32.5, 31.9, 28.3, 28.0, 26.5, 14.5. HRMS (ESI): calcd for $\text{C}_{26}\text{H}_{33}\text{N}_3\text{O}_4\text{Na}$: 474.23688; found: 474.23764.

Diethyl 1-(2-cyclohexylidene-5-(2-phenyl-1H-indol-3-yl)-cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ac). Yield: 78%; yellow viscous liquid; R_f : 0.36 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3324, 2980, 2930, 2854, 1701, 1519, 1472, 1420, 1382, 1332, 1261, 1233, 1097, 1060 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.16 (brs, 1H), 7.60–7.25 (m, 6H), 7.19–7.03 (m, 2H), 7.03 (d, J = 7 Hz, 1H), 6.55 (brs, 1H), 6.20–6.03 (m, 1H), 5.91 (brs, 1H), 5.59–5.45 (m, 1H), 4.68–4.53 (m, 1H), 4.16–4.12 (m, 4H), 2.58 (brs, 1H), 2.39–2.12 (m, 3H), 1.75–1.59 (m, 6H), 1.29–0.88 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.2, 155.4, 137.7, 136.3, 134.7, 132.8, 129.0, 128.6, 128.2, 127.6, 125.3, 121.9, 120.3, 119.4, 110.9, 62.4, 61.7, 60.3, 48.3, 34.6, 32.1, 26.9, 26.7, 21.5, 14.5, 14.2. HRMS (ESI): calcd for $\text{C}_{31}\text{H}_{35}\text{N}_3\text{O}_4\text{Na}$: 536.25253; found: 536.25289.

Diethyl 1-(2-cyclohexylidene-5-(5-fluoro-1H-indol-3-yl)-cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ad). Yield: 61%; colourless viscous liquid; R_f : 0.26 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3363, 3277, 3054, 2984, 2931, 2854, 1711, 1582, 1500, 1149, 1411, 1330, 1120, 1050, 1010, 919, 744 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.26 (s, 1H), 7.34 (brs, 1H), 7.27–7.22 (m, 1H), 6.96–6.92 (brs, 1H), 6.65–6.56 (m, 2H), 6.40–6.31 (m, 1H), 6.02 (d, J = 3.5 Hz, 1H), 5.32–5.11 (m, 1H), 4.46–4.18 (m, 5H), 2.41–2.33 (m, 2H), 2.07–2.05 (m, 2H), 1.62–1.45 (m, 6H), 1.35–1.07 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 158.5, 156.8, 155.3, 136.9, 133.3, 130.0, 126.9, 123.1, 118.1, 111.5, 110.3, 104.9, 65.4, 62.6, 62.3, 47.5, 32.0, 31.1, 28.3, 28.0, 26.5, 14.4. HRMS (ESI): calcd for $\text{C}_{25}\text{H}_{30}\text{FN}_3\text{O}_4\text{Na}$: 478.21180; found: 478.21223.

Diethyl 1-(2-cyclohexylidene-5-(5-nitro-1H-indol-3-yl)-cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ae). Yield: 59%; pale yellow solid; M. p. 132–134 °C; R_f : 0.22 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3365, 3071, 2960, 2852, 1712, 1623, 1582, 1469, 1410, 1380, 1318, 1245, 1173, 1115, 1058, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 9.22 (brs, 1H), 8.56 (s, 1H), 7.92 (brs, 1H), 7.17–7.13 (m, 1H), 6.92–6.82 (m, 1H), 6.61 (d, 1H, J = 4.5 Hz), 6.34 (brs, 1H), 5.98 (brs, 1H), 5.39–5.17 (m, 1H), 4.49–4.23 (m, 5H), 2.56–2.06 (m, 4H), 1.76–1.22 (m, 12H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.3, 155.6, 141.3, 139.8, 137.7, 130.1, 129.0, 128.2, 125.5, 125.3, 124.2, 117.6, 117.2, 111.0, 64.3, 62.9, 62.2, 47.5, 32.1, 31.3, 28.2, 26.6, 21.5, 14.5, 14.2. HRMS (ESI): calcd for $\text{C}_{25}\text{H}_{30}\text{N}_4\text{O}_6\text{Na}$: 505.20630; found: 505.20668.

Diethyl 1-(2-cyclohexylidene-5-(5-hydroxy-1H-indol-3-yl)-cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3af). Yield: 56%; pale yellow viscous liquid; R_f : 0.17 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3380, 3280, 3054, 2976, 2928, 2853, 1709, 1586, 1499, 1149, 1410, 1330, 1220, 1120, 1052, 1011, 920, 745 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.89 (brs, 1H), 7.23–7.15 (m, 2H), 6.79–6.77 (m, 1H), 6.56–6.28 (m, 2H), 6.05 (brs, 1H), 5.32–5.09 (m, 1H), 4.45–4.11 (m, 5H), 2.37–2.33 (m, 2H), 2.07–2.06 (m, 2H), 1.60–1.38 (m, 6H), 1.29–1.13 (m, 5H), 0.99 (brs, 1H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 155.2, 154.5, 147.5, 135.8, 135.0, 134.3, 127.2, 126.8, 125.3, 111.9, 111.8, 108.5, 104.5, 64.9, 62.8,

62.2, 41.9, 32.0, 28.2, 26.5, 19.4, 19.2, 14.5. HRMS (ESI): calcd for $\text{C}_{25}\text{H}_{31}\text{N}_3\text{O}_5\text{Na}$: 476.21614; found: 476.21658.

Diisopropyl 1-(2-cyclohexylidene-5-(1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ba). Yield: 72%; pale yellow viscous liquid; R_f : 0.33 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3331, 3068, 2981, 2932, 2857, 1688, 1621, 1583, 1514, 1462, 1380, 1304, 1238, 1108, 1042, 957, 931, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.16 (brs, 1H), 7.75–7.71 (m, 1H), 7.31–7.23 (m, 1H), 7.18–7.05 (m, 2H), 6.88 (brs, 1H), 6.56–6.27 (m, 2H), 6.07 (brs, 1H), 5.34–5.14 (m, 1H), 5.00–4.95 (m, 2H), 4.53–4.43 (m, 1H), 2.36 (brs, 2H), 2.09–1.81 (m, 2H), 1.61–1.51 (m, 6H), 1.44–1.22 (m, 12H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.5, 154.7, 136.8, 133.8, 129.8, 129.0, 128.2, 126.7, 125.3, 121.7, 119.1, 110.9, 69.9, 69.5, 63.9, 47.2, 31.6, 30.8, 29.7, 28.3, 26.9, 22.7, 22.4, 22.1. HRMS (ESI): calcd for $\text{C}_{27}\text{H}_{35}\text{N}_3\text{O}_5\text{Na}$: 488.25253; found: 488.25286.

Di-tert-butyl 1-(2-cyclohexylidene-5-(1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ca). Yield: 42%; pale yellow viscous liquid; R_f : 0.40 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3375, 3078, 2992, 2943, 2836, 1690, 1610, 1583, 1565, 1468, 1462, 1400, 1316, 1238, 1152, 1123, 969, 938, 746 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.00 (d, J = 11 Hz, 1H), 7.99–7.79 (m, 1H), 7.32–7.28 (m, 1H), 7.20–7.06 (m, 2H), 6.87 (s, 1H), 6.55 (d, J = 5.5 Hz, 1H), 6.15–6.00 (m, 2H), 5.30–5.08 (m, 1H), 4.54–4.44 (m, 1H), 2.37 (brs, 2H), 2.12 (brs, 2H), 1.63–1.53 (m, 24H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 155.7, 154.0, 136.7, 136.5, 126.7, 122.1, 121.8, 119.2, 118.2, 111.1, 110.9, 110.7, 81.3, 80.7, 65.5, 44.3, 32.0, 31.1, 28.3, 28.2, 28.0, 26.6. HRMS (ESI): calcd for $\text{C}_{29}\text{H}_{39}\text{N}_3\text{O}_4\text{Na}$: 516.28383; found: 516.28414.

Dibenzyl 1-(2-cyclohexylidene-5-(1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3da). Yield: 39%; yellow viscous liquid; R_f : 0.31 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3358, 3059, 3027, 2920, 2858, 1702, 1580, 1489, 1449, 1400, 1311, 1281, 1050, 1000, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.28 (brs, 1H), 7.66 (brs, 1H), 7.39–6.90 (m, 13H), 6.75 (brs, 2H), 6.46 (s, 1H), 5.98–5.86 (m, 1H), 5.36–5.05 (m, 5H), 4.52–4.29 (m, 1H), 2.36–2.32 (m, 2H), 2.02–1.94 (m, 2H), 1.56–1.26 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.4, 154.8, 136.7, 135.8, 133.4, 128.6, 128.5, 128.3, 128.2, 127.9, 126.6, 122.0, 121.2, 119.9, 119.4, 117.5, 110.9, 68.1, 67.6, 47.5, 32.0, 31.0, 28.3, 28.0, 26.5. HRMS (ESI): calcd for $\text{C}_{35}\text{H}_{35}\text{N}_3\text{O}_4\text{Na}$: 584.25253; found: 584.25288.

Diethyl 1-(2-(1H-indol-3-yl)-5-(propan-2-ylidene)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ea). Yield: 69%; colourless viscous liquid; R_f : 0.29 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3317, 3056, 2982, 2931, 1719, 1620, 1582, 1512, 1415, 1382, 1229, 1096, 1062, 744 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.30 (s, 1H), 7.71 (brs, 1H), 7.34–7.27 (m, 1H), 7.19–7.08 (m, 2H), 6.86–6.78 (m, 2H), 6.52 (d, 1H, J = 5 Hz), 6.05 (s, 1H), 5.35–5.14 (m, 1H), 4.53–4.18 (m, 5H), 1.89 (s, 3H), 1.67 (brs, 3H), 1.29–1.26 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.9, 155.8, 136.8, 136.6, 135.5, 129.0, 126.7, 125.3, 121.7, 119.9, 119.1, 119.0, 117.9, 111.3, 66.0, 62.6, 62.2, 47.6, 21.5, 14.4. HRMS (ESI): calcd for $\text{C}_{22}\text{H}_{27}\text{N}_3\text{O}_4\text{Na}$: 420.18993; found: 420.18866.

Diethyl 1-(2-(1-methyl-1H-indol-3-yl)-5-(propan-2-ylidene)-cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3eb). Yield: 65%;

colourless solid; M. p. 124–126 °C, R_f 0.33 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3385, 3055, 2981, 2924, 1707, 1611, 1474, 1413, 1379, 1321, 1265, 1219, 1163, 1122, 1061, 1021, 933, 739 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.73 (s, 1H), 7.29–7.23 (m, 2H), 7.10 (t, J = 7 Hz, 1H), 6.77 (brs, 1H), 6.53 (d, J = 5 Hz, 1H), 6.39 (brs, 1H), 6.07 (s, 1H), 5.36–5.14 (m, 1H), 4.53–4.20 (m, 5H), 3.73 (s, 3H), 1.90 (s, 3H), 1.69 (s, 3H), 1.31–1.05 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.7, 155.6, 137.5, 136.7, 135.6, 130.5, 128.3, 127.1, 125.9, 121.6, 120.1, 118.8, 116.7, 109.0, 66.2, 62.5, 61.9, 47.5, 32.6, 21.5, 13.8. HRMS (ESI): calcd for $\text{C}_{23}\text{H}_{29}\text{N}_3\text{O}_4\text{Na}$: 434.20588; found: 434.20615.

Diethyl 1-(2-(cycloheptylidene-5-(1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3fa). Yield: 70%; colourless viscous liquid; R_f 0.31 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3348, 3056, 2924, 2853, 1708, 1617, 1458, 1414, 1380, 1226, 1177, 1121, 1061, 741 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.09 (brs, 1H), 7.66 (brs, 1H), 7.28 (brs, 1H), 7.16–7.04 (m, 2H), 6.84 (brs, 1H), 6.51 (d, J = 5.5 Hz, 1H), 6.25–6.21 (m, 1H), 6.04 (brs, 1H), 5.33–5.11 (m, 1H), 4.50–4.18 (m, 5H), 2.50–2.41 (m, 2H), 2.20–2.16 (brs, 2H), 1.71–1.03 (m, 14H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.3, 155.5, 136.8, 129.0, 128.2, 126.6, 125.3, 121.7, 119.0, 119.0, 111.1, 62.4, 61.9, 47.6, 32.7, 32.3, 29.1, 28.2, 27.6, 14.5, 14.2. HRMS (ESI): calcd for $\text{C}_{26}\text{H}_{33}\text{N}_3\text{O}_4\text{Na}$: 474.23688; found: 474.23714.

Compound 3ga. Yield: 66%; colourless viscous liquid; R_f 0.33 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3323, 3057, 2920, 2848, 1713, 1620, 1475, 1413, 1381, 1305, 1294, 1216, 1116, 1085, 1065, 1025, 742 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 8.21 (brs, 1H), 7.70 (brs, 1H), 7.32–7.25 (m, 2H), 7.20–7.05 (m, 3H), 6.86 (brs, 1H), 6.56 (d, J = 5.5 Hz, 1H), 6.29 (brs, 1H), 6.05 (brs, 1H), 5.39–5.16 (m, 1H), 4.53–4.41 (m, 1H), 4.30–4.13 (m, 4H), 3.06 (brs, 1H), 2.59 (brs, 1H), 2.08–1.64 (m, 12H), 1.35–1.08 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.7, 155.2, 144.4, 136.5, 130.2, 129.0, 128.3, 126.6, 125.3, 121.4, 121.1, 119.9, 119.0, 117.1, 111.1, 63.8, 62.5, 62.0, 47.6, 39.9, 39.5, 39.1, 37.0, 35.1, 34.4, 28.1, 28.0, 21.5, 14.6. HRMS (ESI): calcd for $\text{C}_{29}\text{H}_{35}\text{N}_3\text{O}_4$: 512.25253; found: 515.25290.

Compound 3gb. Yield: 70%; pale yellow viscous liquid; R_f 0.36 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3315, 3054, 2910, 2852, 1711, 1612, 1472, 1413, 1379, 1305, 1221, 1124, 1061, 1019, 740 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.71 (brs, 1H), 7.7–7.21 (m, 2H), 7.07 (t, J = 7 Hz, 1H), 6.80 (brs, 1H), 6.55 (d, J = 5.5 Hz, 1H), 6.25 (brs, 1H), 6.05 (s, 1H), 5.35–5.12 (m, 1H), 4.53–4.28 (m, 1H), 4.23–4.13 (m, 4H), 3.75 (s, 3H), 3.05 (s, 1H), 2.58 (brs, 1H), 2.02–1.63 (m, 12H), 1.37–1.09 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.6, 154.9, 137.4, 130.2, 127.1, 125.8, 121.5, 120.2, 118.7, 108.9, 62.3, 61.9, 47.2, 39.6, 37.0, 35.1, 34.7, 32.6, 28.1, 26.9, 25.3, 22.9, 20.8, 14.9. HRMS (ESI): calcd for $\text{C}_{30}\text{H}_{37}\text{N}_3\text{O}_4\text{Na}$: 526.26818; found: 526.26862.

Compound 3gc. Yield: 66%; pale yellow viscous liquid; R_f 0.38 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3378, 3058, 2978, 2908, 2848, 1756, 1704, 1467, 1445, 1409, 1379, 1364, 1338, 1308, 1277, 1248, 1218, 1172, 1157, 1097, 1062, 1022 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.58–7.44 (m, 6H), 7.33–7.19 (m, 3H), 7.04 (brs, 1H), 6.50–6.42 (m, 1H), 6.12–5.81 (m, 2H), 5.45 (brs, 1H), 4.25–4.15 (m, 4H), 3.58 (s, 3H), 3.06 (brs, 1H), 2.65–2.61 (m, 1H), 2.03–1.85 (m, 10H), 1.59–1.25 (m, 2H),

1.01–0.87 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.4, 155.3, 137.4, 131.3, 130.6, 128.1, 128.0, 121.5, 120.2, 119.0, 113.5, 109.3, 65.9, 62.3, 61.7, 47.8, 39.5, 39.4, 37.0, 35.1, 34.6, 30.8, 28.2, 28.1, 14.7. HRMS (ESI): calcd for $\text{C}_{36}\text{H}_{41}\text{N}_3\text{O}_4\text{Na}$: 602.29948; found: 602.29977.

Diethyl 1-(2-(diphenylmethylene)-5-(1-methyl-1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3ha). Yield: 62%; pale yellow solid, M. p. 182–184 °C; R_f 0.24 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3362, 3051, 2968, 2911, 2852, 1736, 1710, 1552, 1514, 1467, 1454, 1411, 1384, 1364, 1308, 1287, 1243, 1231, 1168, 1157, 1069, 1063, 1022, 742 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.85–7.79 (m, 1H), 7.42–7.03 (m, 12H), 6.90–6.59 (m, 3H), 6.32–6.22 (brs, 1H), 6.04–5.91 (m, 2H), 5.08 (brs, 1H), 4.23–4.13 (m, 4H), 3.92–3.73 (m, 1H), 1.35–1.01 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.0, 154.7, 142.5, 142.4, 141.3, 140.8, 137.4, 130.0, 129.9, 128.6, 128.2, 127.7, 127.4, 126.8, 121.6, 120.2, 119.1, 116.9, 115.5, 110.2, 65.6, 62.0, 61.8, 47.9, 14.8. HRMS (ESI): calcd for $\text{C}_{32}\text{H}_{31}\text{N}_3\text{O}_4\text{Na}$: 544.22123; found: 544.22151.

Diethyl 1-(2-(diphenylmethylene)-5-(1-methyl-1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3hb). Yield: 68%; yellow viscous liquid; R_f 0.29 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3340, 3068, 2981, 2932, 2857, 1688, 1621, 1602, 1583, 1555, 1514, 1462, 1380, 1315, 1238, 1108, 1042, 931, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.79 (brs, 1H), 7.34–7.19 (m, 14H), 7.09–6.97 (m, 2H), 6.61–6.55 (m, 1H), 6.32 (brs, 1H), 5.82–5.56 (m, 2H), 4.70–4.65 (m, 1H), 4.25–4.15 (m, 4H), 3.76 (brs, 3H), 1.32–1.29 (m, 4H), 1.03 (brs, 1H), 0.69 (brs, 1H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 156.9, 154.9, 142.6, 142.3, 141.3, 140.7, 137.4, 130.0, 129.9, 128.5, 128.1, 127.4, 127.3, 127.1, 126.6, 121.4, 120.2, 118.8, 116.0, 115.3, 108.9, 65.5, 62.0, 61.8, 47.6, 32.6, 14.5, 13.8. HRMS (ESI): calcd for $\text{C}_{33}\text{H}_{33}\text{N}_3\text{O}_4\text{Na}$: 558.23688; found: 558.23721.

3,3'-(5-Cyclohexylidene)cyclopent-3-ene-1,2-diylbis(1H-indole) (4aa). Yield: 64%; pale yellow coloured solid, M. p. 152–156 °C; R_f 0.43 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3405, 2922, 2851, 2362, 2349, 1590, 1459, 1421, 1364, 1120, 1033 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.93 (s, 1H), 7.85 (s, 1H), 7.61–7.57 (m, 2H), 7.38–7.34 (m, 2H), 7.22–7.17 (m, 2H), 7.09–6.94 (m, 4H), 6.78 (d, J = 5.5 Hz, 1H), 6.04 (dd, J_1 = 5.5 Hz, J_2 = 2.5 Hz, 1H), 4.32 (brs, 1H), 4.19 (brs, 1H), 2.46 (t, J = 6 Hz, 2H), 2.04–1.97 (m, 2H), 1.67–1.29 (m, 6H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 139.1, 136.9, 135.9, 133.0, 129.9, 129.1, 128.3, 126.7, 126.6, 125.4, 121.9, 121.8, 121.0, 120.9, 120.2, 120.1, 119.6, 118.9, 111.2, 111.0, 52.3, 45.8, 32.1, 31.8, 28.6, 27.7, 26.9. HRMS (ESI): calcd for $\text{C}_{27}\text{H}_{26}\text{N}_2\text{Na}$: 401.19937; found: 401.19968.

3,3'-(5-Cyclohexylidene)cyclopent-3-ene-1,2-diylbis(1-methyl-1H-indole) (4ab). Yield: 58%; pale yellow viscous liquid; R_f 0.48 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 2935, 2855, 2358, 2353, 1680, 1595, 1449, 1431, 1358, 1156, 1120, 1033 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.56–7.52 (m, 2H), 7.28–7.16 (m, 4H), 7.14–6.99 (m, 2H), 6.83 (s, 1H), 6.75 (s, 1H), 6.71 (dd, J_1 = 5.5 Hz, J_2 = 1 Hz, 1H), 5.97 (dd, J_1 = 5.5 Hz, J_2 = 2.5 Hz, 1H), 4.26 (s, 1H), 4.11 (s, 1H), 3.77 (s, 3H), 3.74 (s, 3H), 2.45–2.41 (m, 2H), 2.02–2.00 (m, 1H), 1.94–1.92 (m, 1H), 1.63–1.45 (m, 4H), 1.34–1.31 (m, 1H), 1.18–1.17 (m, 1H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 139.2, 137.5, 137.4, 136.1, 132.8, 129.6, 129.0, 128.2,

127.1, 126.9, 125.6, 125.3, 121.5, 121.3, 120.4, 120.3, 120.2, 118.8, 118.6, 118.3, 109.1, 108.9, 52.3, 45.7, 32.6, 32.5, 32.0, 31.9, 28.6, 27.7, 26.9. HRMS (ESI): calcd for $C_{29}H_{30}N_2Na$: 429.23067; found: 429.23102.

3,3'-(5-Cyclohexylidenecyclopent-3-ene-1,2-diyl)bis(2-phenyl-1H-indole) (4ac). Yield: 54%; pale yellow solid, M. p. 160–164 °C; R_f : 0.52 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3342, 3075, 2953, 2912, 2857, 1695, 1611, 1514, 1462, 1380, 1238, 1100, 1030, 931, 740 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.98 (s, 1H), 7.88 (s, 1H), 7.68 (d, J = 8 Hz, 1H), 7.59 (d, J = 8 Hz, 1H), 7.42–7.37 (m, 4H), 7.28–6.80 (m, 13H), 6.14 (m, 1H), 4.76 (brs, 1H), 4.71 (brs, 1H), 2.51–2.49 (m, 1H), 2.38–2.18 (m, 1H), 1.83–1.07 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 138.4, 136.5, 136.4, 136.3, 135.1, 134.5, 133.4, 132.6, 132.5, 130.5, 128.4, 128.3, 128.2, 127.9, 127.8, 127.4, 127.3, 122.3, 122.2, 121.3, 120.9, 119.6, 119.2, 117.3, 114.7, 110.5, 110.3, 50.6, 44.8, 32.5, 30.8, 28.6, 27.1, 26.8. HRMS (ESI): calcd for $C_{39}H_{34}N_2Na$: 553.26197; found: 553.26233.

3,3'-(5-Cyclohexylidenecyclopent-3-ene-1,2-diyl)bis(5-fluoro-1H-indole) (4ad). Yield: 52%; pale yellow viscous liquid; R_f : 0.40 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3356, 3052, 2978, 2939, 2849, 1689, 1619, 1583, 1514, 1462, 1415, 1402, 1380, 1304, 1238, 1111, 1047, 942, 740 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.03 (s, 1H), 7.94 (s, 1H), 7.31–7.20 (m, 4H), 7.07 (s, 1H), 7.00–6.77 (m, 4H), 6.00 (t, 1H, J = 3 Hz), 4.22 (s, 1H), 4.09 (s, 1H), 2.46–2.42 (m, 2H), 2.06–2.04 (m, 1H), 1.96–1.94 (m, 1H), 1.67–1.44 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 158.5, 156.7, 138.5, 135.3, 133.8, 133.5, 130.3, 126.9, 122.9, 122.7, 121.9, 120.3, 111.7, 111.6, 110.5, 110.3, 110.2, 105.2, 105.0, 45.6, 32.0, 31.8, 28.5, 27.6, 26.8. HRMS (ESI): calcd for $C_{27}H_{24}F_2N_2Na$: 437.18052; found: 437.18088.

3,3'-(5-Cyclohexylidenecyclopent-3-ene-1,2-diyl)bis(5-nitro-1H-indole) (4ae). Yield: 48%; orange red viscous liquid; R_f : 0.40 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3326, 3056, 2955, 2932, 2850, 1675, 1629, 1583, 1457, 1385, 1300, 1238, 1100, 1040, 931, 7445 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 8.91 (s, 1H), 8.74 (s, 1H), 8.53–8.52 (m, 2H), 8.12–8.09 (m, 2H), 7.45–7.41 (m, 2H), 7.26 (d, J = 10.5 Hz, 1H), 7.14 (s, 1H), 6.86 (d, J = 5.5 Hz, 1H), 5.99 (d, J = 4.5 Hz, 1H), 4.33 (s, 1H), 4.22 (brs, 1H), 2.61–2.58 (m, 1H), 2.44–2.42 (m, 1H), 2.07–2.04 (m, 1H), 1.93–1.90 (m, 1H), 1.89–1.37 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 141.4, 141.2, 140.1, 140.0, 137.6, 135.1, 134.6, 130.9, 125.9, 125.7, 124.1, 124.0, 123.8, 122.2, 117.7, 117.6, 117.5, 112.9, 111.3, 52.3, 45.7, 32.1, 32.0, 28.2, 27.7, 26.7. HRMS (ESI): calcd for $C_{27}H_{24}N_2O_4Na$: 491.16952; found: 491.16993.

3,3'-(5-Cyclohexylidenecyclopent-3-ene-1,2-diyl)bis(1H-indol-5-ol) (4af). Yield: 39%; pale yellow viscous liquid; R_f : 0.19 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3339, 3061, 2990, 2940, 2842, 1680, 1623, 1580, 1514, 1380, 1302, 1240, 1110, 1042, 931, 740 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.87 (brs, 1H), 7.78 (brs, 1H), 7.27–7.22 (m, 2H), 7.03–6.98 (m, 3H), 6.92 (d, J = 2 Hz, 1H), 6.81–6.74 (m, 3H), 6.01–6.00 (dd, J_1 = 6 Hz, J_2 = 3 Hz, 1H), 4.82 (d, J = 6.5 Hz, 2H), 4.16 (s, 1H), 4.07 (s, 1H), 2.45–2.39 (m, 2H), 1.99–1.94 (m, 2H), 1.50–1.44 (m, 3H), 1.33–0.87 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 149.1, 148.9, 138.8, 135.6, 133.1, 132.1, 130.0, 127.3, 122.2, 121.3, 119.8, 111.8, 111.7, 111.6, 111.6, 104.8, 104.7, 51.7, 45.8, 32.0, 31.8,

28.6, 27.6, 26.8. HRMS (ESI): calcd for $C_{27}H_{26}N_2O_2Na$: 433.18920; found: 433.18954.

3,3'-(5-(Propan-2-ylidene)cyclopent-3-ene-1,2-diyl)bis(1H-indole) (4ea). Yield: 64%; colourless viscous liquid; R_f : 0.45 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3315, 2920, 2857, 2377, 1648, 1590, 1520, 1468, 1367, 1160, 1119, 1037 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.99 (s, 1H), 7.92 (s, 1H), 7.60–7.56 (m, 2H), 7.40–7.37 (m, 2H), 7.23–7.18 (m, 3H), 7.09–7.05 (m, 3H), 7.00 (s, 1H), 6.94 (s, 1H), 6.74 (dd, 1H, J_1 = 5.5 Hz, J_2 = 2 Hz), 6.05 (dd, 1H, J_1 = 5.5 Hz, J_2 = 2.5 Hz), 4.28 (s, 1H), 4.22 (s, 1H), 1.93 (s, 3H), 1.61 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 141.9, 137.1, 136.9, 135.8, 130.4, 127.3, 126.8, 125.8, 125.7, 124.4, 121.5, 121.3, 120.5, 120.3, 120.0, 118.4, 118.2, 117.9, 110.8, 110.7, 52.4, 46.4, 21.3. HRMS (ESI): calcd for $C_{24}H_{22}N_2Na$: 361.16807; found: 361.16848.

3,3'-(5-(Propan-2-ylidene)cyclopent-3-ene-1,2-diyl)bis(1-methyl-1H-indole) (4eb). Yield: 56%; pale yellow solid, M. p. 162–164 °C; R_f : 0.50 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 2925, 2852, 2371, 1649, 1586, 1523, 1465, 1364, 1254, 1167, 1122, 1042 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.66–7.61 (m, 2H), 7.38–7.31 (m, 2H), 7.29–7.27 (m, 2H), 7.14–7.09 (m, 2H), 6.90 (s, 1H), 6.83 (s, 1H), 6.78 (dd, 1H, J_1 = 5.5 Hz, J_2 = 2 Hz), 6.09 (dd, 1H, J_1 = 5.5 Hz, J_2 = 2.5 Hz), 4.32 (s, 1H), 4.25 (s, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 1.99 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 142.2, 137.6, 137.5, 135.9, 130.5, 127.1, 127.0, 125.9, 125.7, 124.4, 121.5, 121.3, 120.3, 120.2, 119.9, 118.8, 118.7, 118.4, 109.2, 109.1, 52.6, 46.6, 31.7, 21.4. HRMS (ESI): calcd for $C_{26}H_{26}N_2Na$: 389.19937; found: 389.19969.

3,3'-(5-Cycloheptylidenecyclopent-3-ene-1,2-diyl)bis(1H-indole) (4fa). Yield: 53%; colourless viscous liquid; R_f : 0.43 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3408, 3056, 2923, 2853, 1703, 1619, 1583, 1517, 1485, 1455, 1338, 1227, 1095, 1012, 741 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.97 (s, 1H), 7.89 (s, 1H), 7.59–7.57 (d, J = 8 Hz, 2H), 7.37–7.34 (m, 2H), 7.21–7.16 (m, 2H), 7.07–7.05 (m, 2H), 6.98–6.93 (m, 2H), 6.76 (dd, J_1 = 5.5 Hz, J_2 = 2.5 Hz, 1H), 6.04 (dd, J_1 = 5.5 Hz, J_2 = 3 Hz, 1H), 4.27 (s, 1H), 4.18 (brs, 1H), 2.57–2.51 (m, 2H), 2.25–2.19 (m, 1H), 2.07–2.06 (m, 1H), 1.72–1.29 (m, 8H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 142.1, 136.9, 136.7, 135.9, 134.3, 130.4, 129.0, 128.2, 126.7, 126.6, 121.9, 121.5, 120.8, 120.7, 120.2, 120.1, 119.2, 119.0, 111.0, 110.9, 52.5, 46.1, 32.8, 32.5, 29.8, 28.8, 27.2, 26.9. HRMS (ESI): calcd for $C_{28}H_{28}N_2Na$: 415.21502; found: 415.21538.

Compound 4ga. Yield: 58%; colourless viscous liquid; R_f : 0.43 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{max} : 3289, 3066, 2931, 2857, 1668, 1620, 1582, 1520, 1455, 1304, 1238, 933, 744 cm^{-1} . 1H NMR (500 MHz, $CDCl_3$, TMS): δ 7.88 (s, 1H), 7.79 (s, 1H), 7.62 (d, J = 8 Hz, 1H), 7.55 (d, J = 8 Hz, 1H), 7.54–7.21 (m, 2H), 7.19–7.13 (m, 2H), 7.05–6.93 (m, 4H), 6.72–6.71 (m, 1H), 5.94 (dd, J_1 = 5.5 Hz, J_2 = 3 Hz, 1H), 4.30 (s, 1H), 4.11 (brs, 1H), 3.12 (brs, 1H), 2.49 (brs, 1H), 2.04–1.68 (m, 9H), 1.53–1.43 (m, 2H), 0.88–0.84 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, TMS): δ 140.8, 137.8, 137.0, 136.9, 135.4, 135.2, 129.5, 129.1, 128.3, 126.8, 126.5, 125.4, 122.0, 121.8, 120.9, 120.4, 119.2, 118.9, 111.2, 111.1, 52.4, 45.2, 39.8, 39.4, 38.2, 37.3, 35.1, 34.8, 28.4, 21.6. HRMS (ESI): calcd for $C_{31}H_{30}N_2Na$: 453.23067; found: 453.23101.

Compound 4gb. Yield: 55%; colourless viscous liquid; R_f : 0.48 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3090, 2950, 2932, 2857, 1688, 1621, 1583, 1514, 1462, 1380, 1304, 1238, 1108, 1042, 957, 931, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.65 (d, J = 8 Hz, 1H), 7.58 (d, J = 8 Hz, 1H), 7.33–7.20 (m, 6H), 7.08–7.02 (m, 2H), 6.89 (s, 1H), 6.83 (s, 1H), 6.73 (d, J = 5.5 Hz, 1H), 5.95 (t, J = 2.5 Hz, 1H), 4.32 (s, 1H), 4.13 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.17 (s, 1H), 2.53 (s, 1H), 2.01–1.58 (m, 12H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 140.6, 137.6, 135.6, 135.2, 129.2, 127.2, 127.0, 125.6, 125.5, 121.5, 120.5, 120.3, 118.8, 118.8, 118.6, 109.1, 108.9, 52.5, 45.2, 39.8, 39.3, 38.2, 37.3, 35.0, 34.4, 32.6, 32.5, 28.4, 28.3. HRMS (ESI): calcd for $\text{C}_{33}\text{H}_{34}\text{N}_2\text{Na}$: 481.26197; found: 481.26141.

Compound 4gc. Yield: 74%; colourless viscous liquid; R_f : 0.55 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 2981, 2915, 2833, 1671, 1621, 1586, 1542, 1380, 1300, 1238, 1042, 957, 931, 743 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.62–7.47 (m, 6H), 7.38–6.96 (m, 12H), 6.66 (dd, J_1 = 5.5 Hz, J_2 = 2.5 Hz, 1H), 6.04 (dd, J_1 = 5.5 Hz, J_2 = 2.5 Hz, 1H), 4.41 (brs, 1H), 4.22 (brs, 1H), 3.61 (s, 3H), 3.57 (s, 3H), 2.98 (brs, 1H), 2.32 (brs, 1H), 1.83–1.50 (m, 12H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 140.2, 137.9, 137.4, 136.2, 135.8, 134.6, 133.9, 133.4, 131.3, 130.5, 129.7, 128.7, 128.2, 127.7, 127.5, 126.6, 125.3, 122.3, 121.4, 120.3, 119.5, 119.1, 119.0, 117.5, 115.2, 108.9, 108.7, 51.0, 45.3, 39.3, 38.9, 37.8, 37.4, 34.9, 33.1, 30.9, 28.1. HRMS (ESI): calcd for $\text{C}_{45}\text{H}_{42}\text{N}_2\text{Na}$: 633.32457; found: 633.32486.

3,3'-(5-(Diphenylmethylene)cyclopent-3-ene-1,2-diyl)bis(1H-indole) (4ha). Yield: 84%; pale yellow solid, M. p. 154–156 °C; R_f : 0.43 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3294, 2857, 2366, 2335, 1647, 1590, 1369, 1120, 1037, 702 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.90 (s, 1H), 7.67–7.51 (m, 3H), 7.37–7.06 (m, 9H), 6.98–6.78 (m, 9H), 6.40 (d, J = 4 Hz, 1H), 6.24 (brs, 1H), 4.51–4.49 (m, 2H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 148.1, 143.2, 142.6, 140.4, 136.8, 136.5, 135.0, 133.1, 129.8, 129.3, 127.9, 127.4, 126.7, 126.5, 126.2, 125.9, 122.0, 121.5, 120.8, 120.1, 119.8, 119.5, 119.3, 119.0, 118.9, 111.1, 110.9, 57.7, 48.5. HRMS (ESI): calcd for $\text{C}_{34}\text{H}_{26}\text{N}_2\text{Na}$: 485.19937; found: 485.19969.

3,3'-(5-(Diphenylmethylene)cyclopent-3-ene-1,2-diyl)bis(1-methyl-1H-indole) (4hb). Yield: 81%; yellow solid, M. p. 160–162 °C; R_f : 0.48 (hexane/ethyl acetate = 3 : 1). IR (Neat) ν_{\max} : 3053, 2927, 1709, 1688, 1613, 1513, 1469, 1427, 1372, 1328, 1242, 1156, 1130, 1013, 740 cm^{-1} . ^1H NMR (500 MHz, CDCl_3 , TMS): δ 7.78–7.76 (m, 2H), 7.72–7.30 (m, 9H), 7.20–6.99 (m, 6H), 6.87 (brs, 3H), 6.52 (t, J = 3 Hz, 1H), 6.09 (dd, J_1 = 4 Hz, J_2 = 2.5 Hz, 1H), 4.66 (brs, 1H), 4.57–4.54 (m, 1H), 3.81 (s, 3H), 3.58 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3 , TMS): δ 148.8, 143.3, 143.0, 140.8, 137.6, 137.3, 134.9, 132.9, 129.9, 129.3, 129.2, 128.4, 128.0, 127.4, 127.2, 127.2, 126.8, 126.5, 125.8, 125.7, 121.7, 121.1, 120.3, 120.0, 118.9, 118.4, 118.1, 117.6, 109.3, 109.1, 51.8, 48.9, 32.6, 32.2. MS (ESI): calcd for $\text{C}_{36}\text{H}_{30}\text{N}_2\text{Na}$: 513.23067; found: 513.23098.

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Notes and references

- (a) M. Bandini and A. Eichholzer, *Angew. Chem., Int. Ed.*, 2009, **48**, 9608–9644; (b) A. J. Kochanowska-Karamyan and M. T. Hamann, *Chem. Rev.*, 2010, **110**, 4489–4497; (c) R. J. Sundberg, *The Chemistry of Indoles*, Academic press, New York, 1996, p. 113.
- M. Berger, J. A. Gray and B. L. Roth, *Annu. Rev. Med.*, 2009, **60**, 355–366.
- (a) S. Cacchi and G. Fabrizi, *Chem. Rev.*, 2005, **105**, 2873–2920; (b) K. Krüger (née Alex), A. Tillack and M. Beller, *Adv. Synth. Catal.*, 2008, **350**, 2153–2167; (c) J. Zhou and Y. Tang, *J. Am. Chem. Soc.*, 2002, **124**, 9030–9031; (d) K. B. Jensen, J. Thorhauge, R. G. Hazell and K. A. Jørgensen, *Angew. Chem., Int. Ed.*, 2001, **40**, 160–163.
- (a) R. J. Phipps, N. P. Grimster and M. J. Gaunt, *J. Am. Chem. Soc.*, 2008, **130**, 8172–8174; (b) S. M. A. H. Siddiki, K. Kon and K.-I. Shimizu, *Chem.-Eur. J.*, 2013, **19**, 14416–14419; (c) G. Bartoli, G. Bencivenni and R. Dalpozzo, *Chem. Soc. Rev.*, 2010, **39**, 4449–4465; (d) G. Yan, C. Kuang, Y. Zhang and J. Wang, *Org. Lett.*, 2010, **12**, 1052–1055; (e) A. Mahadevan, H. Sard, M. Gonzalez and J. C. McKew, *Tetrahedron Lett.*, 2003, **44**, 4589–4591; (f) Y. L. Hu, H. Jiang and M. Lu, *Green Chem.*, 2011, **13**, 3079–3087; (g) D. A. Evans, K. A. Scheidt, K. R. Fandrick, H. W. Lam and J. Wu, *J. Am. Chem. Soc.*, 2003, **125**, 10780–10781; (h) G. Blay, I. Fernandez, J. R. Pedro and C. Vila, *Org. Lett.*, 2007, **9**, 2601–2604; (i) K. Gao and J. Wu, *Org. Lett.*, 2008, **10**, 2251–2254.
- (a) G. A. Olah, R. Krishnamurti and G. K. S. Prakash, *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 3, p. 293; (b) K. Manabe, N. Aoyama and S. Kobayashi, *Adv. Synth. Catal.*, 2001, **343**, 174–176.
- H. D. King, Z. Meng, J. A. Deskus, C. P. Sloan, Q. Gao, B. R. Beno, E. S. Kozłowski, M. A. Lapaglia, G. K. Mattson, T. F. Molski, M. T. Taber, N. J. Lodge, R. J. Mattson and J. E. Macor, *J. Med. Chem.*, 2010, **53**, 7564–7572.
- A. W. Schmidt, K. R. Reddy and H. Knolker, *Chem. Rev.*, 2012, **112**, 3193–3228.
- (a) K. S. Ryan and C. L. Drennan, *Chem. Biol.*, 2009, **16**, 351–364; (b) M. Shiri, M. A. Zolfigol, H. G. Kruger and Z. Tanbakouchian, *Chem. Rev.*, 2010, **110**, 2250–2293; (c) J. S. Oakdale and D. L. Boger, *Org. Lett.*, 2010, **12**, 1132–1134; (d) T. Haahimoto, A. Yasuda, K. Akazawa, S. Takaoka, M. Tori and Y. Asakawa, *Tetrahedron Lett.*, 1994, **35**, 2559–2560.

- 9 (a) D. D. Sternbach and C. L. Ensinger, *J. Org. Chem.*, 1990, **55**, 2725–2736; (b) K. Sakai and T. Kobori, *Tetrahedron Lett.*, 1981, **22**, 115–118; (c) B. Lei and A. G. Fallis, *J. Am. Chem. Soc.*, 1990, **112**, 4609–4610; (d) V. Nair, S. Kumar and P. G. Williard, *Tetrahedron Lett.*, 1995, **35**, 1605–1608; (e) V. Nair, C. N. Jayan, K. V. Radhakrishnan, G. Anilkumar and N. P. Rath, *Tetrahedron*, 2001, **57**, 5807–5813; (f) J. M. Kuthanapillil, S. Thulasi, R. Rajan, K. S. Krishnan, E. Suresh and K. V. Radhakrishnan, *Tetrahedron*, 2011, **67**, 1272–1280; (g) K. S. Krishnan, M. M. Bhadbhade, G. V. Bhosekar and K. V. Radhakrishnan, *Tetrahedron Lett.*, 2005, **46**, 4785–4788; (h) K. S. Krishnan, V. S. Sajisha, S. Anas, C. H. Suresh, M. M. Bhadbhade, G. V. Bhosekar and K. V. Radhakrishnan, *Tetrahedron*, 2006, **62**, 5952–5961.
- 10 (a) A. P. Luna, M. Cesario, M. Bonin and L. Micouin, *Org. Lett.*, 2003, **5**, 4771–4774; (b) S. Crotti, F. Bertolini, F. Macchia and M. Pineschi, *Adv. Synth. Catal.*, 2009, **351**, 869–873; (c) A. Martins, S. Lemouzy and M. Lautens, *Org. Lett.*, 2009, **11**, 181–183; (d) C. Bournaud, F. Chung, A. Luna, M. Pasco, G. Errasti, T. Lecourt and L. Micouin, *Synthesis*, 2009, 869–887.
- 11 (a) V. S. Sajisha and K. V. Radhakrishnan, *Adv. Synth. Catal.*, 2006, **348**, 924–930; (b) J. John, V. S. Sajisha, S. Mohanlal and K. V. Radhakrishnan, *Chem. Commun.*, 2006, 3510–3512; (c) J. John, S. Anas, V. S. Sajisha, S. Viji and K. V. Radhakrishnan, *Tetrahedron Lett.*, 2007, **48**, 7225–7227; (d) J. John, U. Indu, E. Suresh and K. V. Radhakrishnan, *J. Am. Chem. Soc.*, 2009, **131**, 5042–5043; (e) R. Rajan, J. John, S. Thulasi, N. Joseph, K. Radhakrishnan and R. Sawant, *Synthesis*, 2010, 3649–3656; (f) N. Joseph, J. John, R. Rajan, S. Thulasi, A. Mohan, E. Suresh and K. V. Radhakrishnan, *Tetrahedron*, 2011, **67**, 4905–4913; (g) J. John, R. Rajan, S. S. Chand, P. Prakash, N. Joseph, E. Suresh and K. V. Radhakrishnan, *Tetrahedron*, 2013, **69**, 152–159; (h) P. Prakash, P. Aparna, E. Jijy, P. Santhini, S. Varughese and K. Radhakrishnan, *Synlett*, 2013, **25**, 275–279; (i) P. Prakash, E. Jijy, P. Preethanuj, P. M. Pihko, S. S. Chand and K. V. Radhakrishnan, *Chem.–Eur. J.*, 2013, **19**, 10473–10477; (j) E. Jijy, P. Prakash, M. Shimi, P. M. Pihko, N. Joseph and K. V. Radhakrishnan, *Chem. Commun.*, 2013, **49**, 7349–7351; (k) E. Jijy, P. Prakash, S. Saranya, E. Suresh and K. V. Radhakrishnan, *Synthesis*, 2013, 2583–2592.
- 12 (a) S. S. Chand, E. Jijy, P. Prakash, J. Szymoniak, P. Preethanuj, B. P. Dhanya and K. V. Radhakrishnan, *Org. Lett.*, 2013, **15**, 3338–3341; (b) S. S. Chand, S. Saranya, P. Preethanuj, B. P. Dhanya, E. Jijy, P. Prakash, B. S. Sasidhar, J. Szymoniak, P. V. Santhini and K. V. Radhakrishnan, *Org. Biomol. Chem.*, 2014, **12**, 3045–3061.