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Original article

Synthesis and evaluation of dimeric 1,2,3,4-Tetrahydro-naphthalenylamine and Indan-1-ylamine derivatives with mast cell-stabilising and anti-allergic activity

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ABSTRACT

In a continuation of our studies into 4-Amino-3,4-dihydro-2H-naphthalen-1-ones as novel modulators of allergic and inflammatory phenomena, we have extended our work to include dimeric analogues. Of these derivatives, the most promising activity was seen with tertiary amine **58a**, which exhibited potent mast cell-stabilising activity in vitro against a variety of stimuli and also in vivo against passive cutaneous anaphylaxis.

1. Introduction

The mast cell is an important sentinel of innate and acquired immunity, occupying a frontier of defence at the host-environment interface [1]. Although its classic role in allergic disorders and the immune response to parasites is well established, in recent times more diverse roles in physiological and pathophysiological phenomena are being appreciated, including autoimmune disease processes [2]. Agents that can modify the release of pre-formed mediators from these cells or modulate cytokine responses, or affect other cells intimately associated with the complex immune response have defined roles in medicine. There is a continued interest in, and need for, novel molecular entities with anti-allergic and immunomodulating capabilities [3]. One source for novel lead structures is the natural world, and one secondary metabolite class whose derivatives exhibit interesting pharmacology is the illudoid sesquiterpenes collectively termed the pterosins. These molecules share a 1-indanone skeleton. Early work identified onitin [4] and pterosin Z [5] as smooth muscle relaxants, the latter study also demonstrating that synthetic derivatives of the pterosins share the smooth muscle relaxant effects of the natural products. Additional pharmacological studies revealed hepatoprotective [6] and mast cell stabilising activities, the latter exhibited by both monomeric and dimeric indanes and indanones [7,8]. To investigate the effects of ring expansion within the core structure of these molecules, our earlier work [9] demonstrated that ring expansion from an indanone to a tetralone, yielding a series of 4-Amino-3,4-dihydro-2H-naphthalen-1-ones, was permissible without loss of activity. Within that series, the tertiary benzyl (**1**, Fig. 1) exhibited most promising activity. Given that dimeric indanes such as (**2a** and **2b**, Fig. 1) showed potent mast cell-stabilising activity in rodent models [7,8], we decided to evaluate a series of dimeric tetrahydro-naphthalen-1-ylamine and indan-1-ylamine derivatives, varying the ring size of the two hydroaromatic subunits and oxygenation patterns, to investigate whether this would result in augmentation or annihilation of the requisite activity.

2. Chemistry

From the starting materials 1- and 2-indanone, and 1- and 2-tetralone, many possible dimeric combinations are conceivable. Following a perusal of the results already reported for the nitrogen-linked indan homodimers [7,8], certain structures were identified as more desirable targets than others. The target molecules can be categorised in several ways, depending on the ring position through which the amine link occurs and on whether the molecules are homodimeric or heterodimeric in nature. The first target structural types were tetralin-indan dimers, with the nitrogen link through benzylic positions on both monomers. Analogous indan homodimers inhibit Compound 48/80-induced mast-cell degranulation

Abbreviations: Con A, Concanavalin A; DSCG, Disodium cromoglycate; MCM, Mast cell medium; NBS, *N*-Bromosuccinimide; PCA, Passive cutaneous anaphylaxis; PPA, Polyphosphoric acid; RPMC, Rat peritoneal mast cell.

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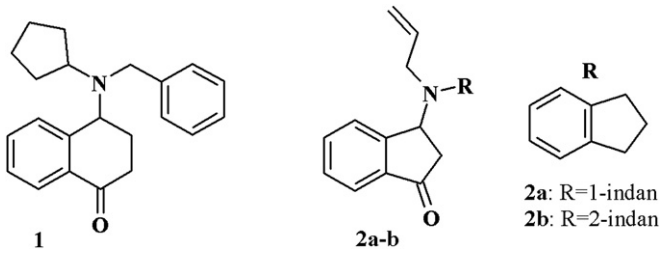


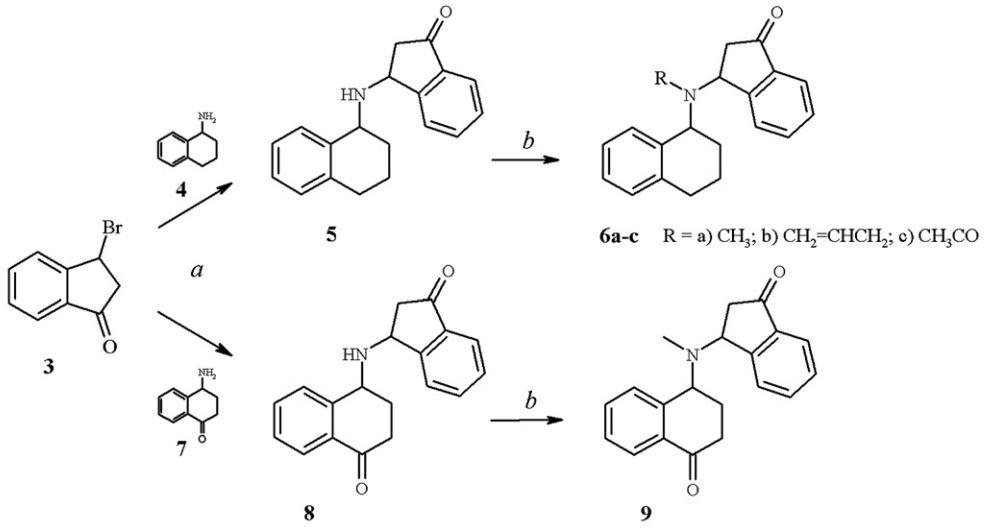
Fig. 1. Aminotetralin and aminoindan lead structures.

by up to 90% [7]. Our synthetic strategy (Scheme 1) towards tetralin-indan dimer **5** involved Wohl–Ziegler bromination [10] of 1-indanone with *N*-bromosuccinimde (NBS) to afford the 3-bromo derivative **3** [11]. Nucleophilic substitution with 1-aminotetralin **4** using triethylamine as tertiary base in CH_2Cl_2 as solvent yielded **5** as a mixture of isomers. Alkylation of **5** with methyl and allyl iodides gave **6a** and **6b**, while N-acetylation gave a low yield of acetamide **6c**. The importance of the ketone substituent and its relative position within these molecules was also the subject of some conjecture, and to examine this question it was decided to synthesise some related indan-tetralin heterodimers possessing alternative patterns of oxygenation. The synthesis of **9**, a tetralone-indanone dimer possessing two benzylic carbonyl groups, involved the reaction of **3** with **7** [12], with ensuing methylation.

Compound **14** (Scheme 2), has an indan component devoid of an oxygen atom, whereas the six-membered ring carries a ketone in the benzylic position. Neither 4-bromotetralone nor acetic acid 4-bromo-1,2,3,4-tetrahydro-naphthalen-1-yl ester [9] reacted successfully with 1-aminoindan. 1-Indanol **10** was converted into halide **12** using PBr_3 in diethyl ether at −15 °C [13]. Halide **12** was immediately reacted with **7** to afford **13**. In a one-pot reaction, **13** was alkylated overnight with methyl iodide, with subsequent isolation of **14**. The effect of expansion of both alicyclic rings of the dimeric indanes by one carbon simultaneously, forming tetralin homodimer compounds, was examined by the preparation of **17** and **19**. Compound **17** was prepared using the reactive benzylic halide 1-bromotetralin **15** (Scheme 2). This halide was prepared via the treatment of 1-tetralol **11** with PBr_3. As with the analogous compound **12**, brominated derivative **15** was not itself isolated, but reacted directly after partial work-up with **7**, to give **16**, methylation of which afforded **17**. The need for at least one carbonyl group for mast cell-stabilising activity in these dimer molecules was investigated by the synthesis of **19**, a tetralin dimer molecule devoid of oxygenation. This compound was prepared by nucleophilic substitution of **4** with **15**, and ensuing methylation.

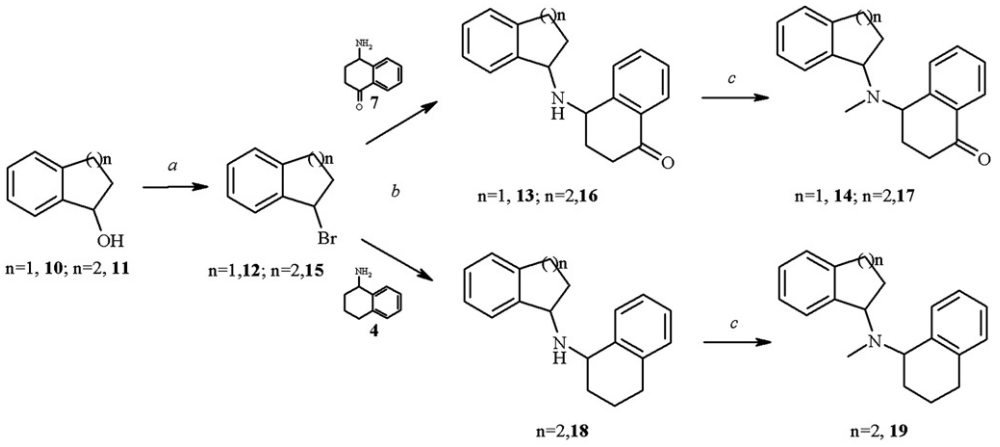
Many natural products exhibit anti-allergic activity, including the methoxylated furanochromone khellin [14] and various flavonoids. All show high degrees of oxygenation within their heterocyclic framework. The patterns of oxygenation have important effects on activity; while khellin is dimethoxylated, increasing methoxylation among the flavonoids reduces activity [15]. The clinically useful compounds sodium cromoglycate and nedocromil, derived from khellin as a natural 'lead', are chromones. To investigate the effect of similar modifications on the activity of **6**, we decided to prepare chroman and methoxylated analogues. The chroman analogue of **6a**, namely **25**, was obtained as shown in Scheme 3. Cyclisation of **20** using polyphosphoric acid (PPA) yielded chromanone. Reduction with $NaBH_4$ gave alcohol **21**, consistent with literature data [16]. Reaction of PBr_3 with **21** gave the halide, which was not isolated but reacted immediately with sodium azide [17] to give azido derivative **22**. Reduction of **22** to *BOC*-protected amine **23** was followed by removal of the protecting group with trifluoroacetic acid (TFA). The free amine was reacted with **3** to yield **24**. Methylation afforded **25**. Substitution on the aromatic portion of the tetralin ring by an electron-donating methoxy group at position 7 was approached through a similar sequence of reactions to those used for **25**. Cyclisation of **26** with PPA (Scheme 3) gave 7-methoxytetralone [18]. Reduction with $NaBH_4$ gave alcohol **27**. Substitution of **27** with PBr_3 gave the bromide, which was reacted directly with sodium azide in DMF. Azide **28** was reduced to afford *BOC*-protected amine **29**. Deprotection with TFA and subsequent reaction with **3** gave **30**. Methylation was performed using methyl iodide in acetone with potassium carbonate as base, to give **31.**

The methoxy group was also chosen as a modifying substituent on the aromatic ring of the indanone fragment of **6**. Cyclisation of the precursor acids is routinely performed using PPA, and there are



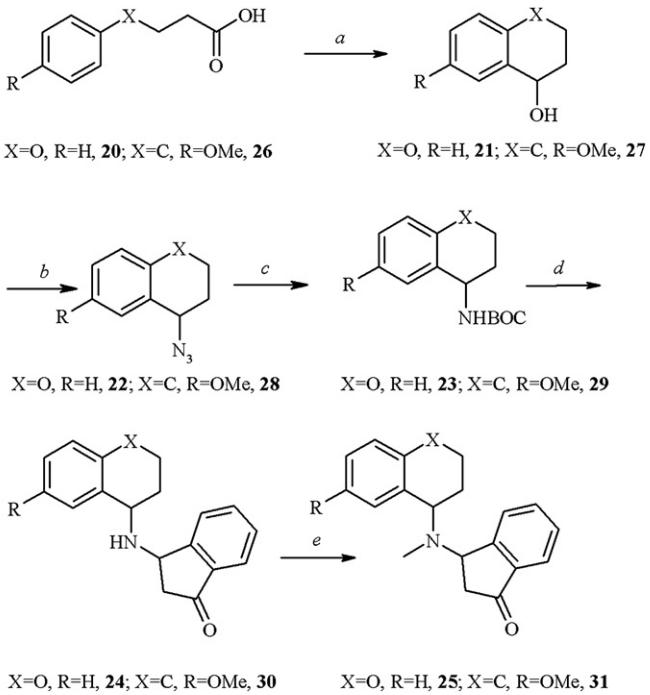
(a) Et_3N, DCM, rt, 24hr; (b) For **6a-b** and **9**: RX, K_2CO_3, CH_3COCH_3, rt, 2days; For **6c**: Ac_2O, DMAP, Et_3N, DCM, rt, 24hr

Scheme 1. Synthetic methods for the preparation of **6a–c** and **9**.

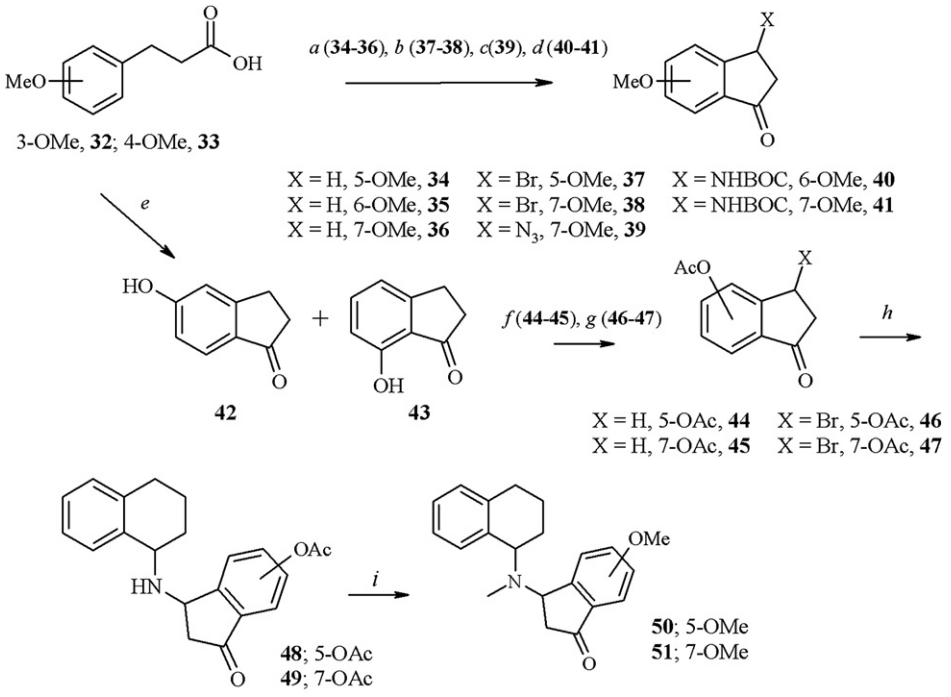


Scheme 2. Synthetic methods for the preparation of **14**, **17** and **19**.

literature procedures for the cyclisation of both **32** [19] and **33** [20]. Attempted cyclisation of 3-(2-methoxyphenyl)propionic acid with polyphosphoric acid results in the formation of a metacyclophane [21]. We also found this to be the case for a pentafluorophenyl ester of this acid. Using **32**, a 4:1 ratio of **34**–**36** was isolated (Scheme 4), while cyclisation of **33** gave **35**. Bromination of **34** and **36** under Wohl–Ziegler conditions afforded **37** and **38**. The former of these has been reported [22], yet only as an intermediate without purification, and characterised by ^{1}H NMR alone. Neither **37** nor **38** reacted with **4**. Substitution of the bromide in **38** by azide to give **39** followed by hydrogenation gave the protected amine derivative **41**. Deprotection followed by attempted coupling with **15** was unsuccessful. Likewise, bromination of **35** followed by reaction with sodium azide, subsequent reduction, and deprotection of carbamate **40**, gave the corresponding amine, which did not react with **15**. As the presence of an electron-donating methoxy substituent may have accelerated the decomposition of **37** and **38**, it was decided to deprotect the methoxy group prior to cyclisation (Scheme 4). Cleavage of methyl ether **32** with HBr in acetic acid followed by cyclisation gave **42** and **43**. As benzylic bromination of these hydroxyindanones was unsuccessful using standard Wohl–Ziegler conditions, they were protected as acetates **44** and **45** prior



Scheme 3. Synthetic methods for the preparation of **25** and **31**.

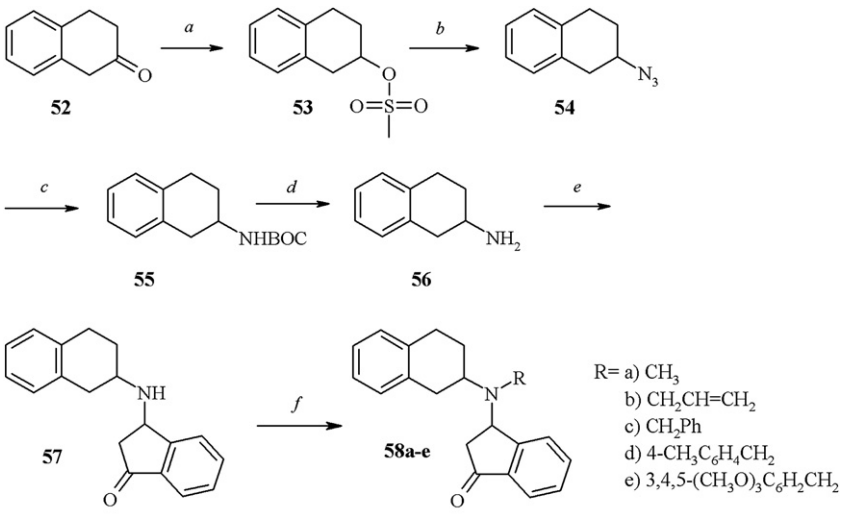


(a) PPA, Δ, 30min; (b) NBS, DBP, CCl_4, Δ, 1hr; (c) NaN_3, DMF, 45°C, 2hr;
(d) Di-*tert*-butyl dicarbonate, Pd/C, EtOH/EtOAc (1:1), H_2, rt, 24hr; (e) 1. HBr, CH_3COOH, Δ, 2days, 2. PPA, Δ, 30min;
(f) Ac_2O, DMAP, Et_3N, DCM, rt, 3hr; (g) NBS, DBP, CCl_4, Δ, 1hr; (h) **4**, Et_3N, DCM, rt, 24hr;
(i) CH_3I, K_2CO_3, MeOH/CH_3COCH_3 (1:1), rt, 24hr.

Scheme 4. Synthetic methods for the preparation of **50** and **51**.

to bromination. Benzylic bromination of the acetates with NBS gave good yields of bromides **46** and **47**. Reaction of the bromides with **4** gave amines **48** and **49**. In a one-pot procedure, both removal of acetate protecting groups and methylation of both phenolic and secondary amine sites were accomplished using methyl iodide in acetone/methanol, utilising sodium carbonate as base, to afford the tertiary *N*-methylated compounds **50** and **51**.

All of the molecules reported to date are dimers linked through the benzylic position of two hydroaromatic rings. Among the objectives in our study of these molecules, however, was the



(a) 1. $NaBH_4$, MeOH, rt, 1hr, 2. *N*,*N*-DIPEA, MsCl, DCM, 0°C, 10min; (b) NaN_3, DMF, 45°C, 2hr;
(c) Di-*tert*-butyl dicarbonate, Pd/C, EtOH/EtOAc (1:1), H_2, rt, 24hr; (d) 1. TFA, DCM, 0°C-rt, 30min;
(e) **3**, Et_3N, DCM, rt, 24hr; (f) For **58a-e**: RX, K_2CO_3, CH_3COCH_3, rt-Δ, 6hr-6days.

Scheme 5. Synthetic methods for the preparation of **58a–e**.

synthesis of compounds with a dimeric link through the benzylic position of one of the monomers to a non-benzylic position of the second. Of primary interest was compound **58a**, where the nitrogen atom contains a tertiary methyl substituent, thus allowing comparison with **6**.

The obvious route to this compound was via the secondary amine, 2-aminotetralin. There has been much interest in the synthesis of 2-aminotetralins, as they possess known pharmacological activity, including dopamine receptor activity [23], and are key precursors in the synthesis of many important structures, including steroids and alkaloids. The two most common approaches to 2-aminotetralin are via reductive amination of 2-tetralone [24] or oxime reduction [25]. Our approach to **58** Scheme 5 used as starting material 2-tetralone **52**. Reduction to the alcohol and mesylation using methane sulphonyl chloride gave methane sulphonate **53**. Substitution with azide in DMF and reduction gave the *BOC*-protected amine. Removal of the protecting group and reaction with **3** gave dimer **57**. As with the earlier compounds, the diastereomers of **57** were unresolvable by TLC. Using our preferred alkylation conditions of alkylating agent, potassium carbonate and acetone, the desired methyl derivative **58a** was obtained after stirring overnight at room temperature. A range of alkylating agents was employed to generate a series of tertiary amine derivatives of **57**, with varying substitution on the amino functionality.

3. Pharmacology

3.1. Animals

Female Wistar rats were used for in vitro mast cell assays and also for in vivo studies. Male Brown Norway rats were used to evaluate the ability of compounds to inhibit anti-IgE induced degranulation of mast cells.

3.2. Mast cell stabilising activity

Test compounds were evaluated for inhibition of compound 48/80-induced degranulation of rat peritoneal mast cells (RPMC), isolated as previously reported [26]. Cell populations were of >90% viability and mast cells comprised 1.4% of the total cell count. The results are shown in Table 1. Compounds **6a**, **17** and **58a** were evaluated in more detail using various elicitors of histamine release in the same cell population; in addition to dose-response studies using compound 48/80, these studies were additionally performed using ionophore A23187, the lectin Concanavalin A (Con A), and for some studies, additionally anti-IgE and Vancomycin. The results obtained using these elicitors are shown in Tables 2 and 3.

Table 1
Mast cell stabilising activity of dimer compounds and the reference compound DSCG in RPMC stimulated by compound 48/80.[a,b,c,d]

Compound	% Inhibition	
6a	93	(5)
6b	92	(6)
6c	NI	–
9	61	(3)
14	14	(7)
17	99	(1)
19	NI	–
25	100	(3)
31	100	(4)
50	55	(15)
51	48	(5)
58a	76	(7)
58b	59	(9)
58c	67	(7)
58d	68	(9)
58e	40	(9)
DSCG	10	(3)

[a] Values are the mean of $n = 5$, standard error in parentheses.
[b] Test compounds and DSCG at 2×10^{-5}.
[c] Challenge with compound 48/80 at 0.2 μg mL^{-1}, 5 min exposure.
[d] NI, no inhibition at concentration tested.

Table 2
Protective activity of **6a** and **17** against degranulation RPMC induced by various stimuli.[a]

Compound	48/80	A23187[b]	Con A[b]	Vancomycin[c]
	IC50 (μM)			
6a	1.5	2.0	0.7	4.7
17	NT	38	2.4	NT

[a] A23187, Con A and Vancomycin at concentrations of 1 μg ml^{-1}, 20 μg ml^{-1} and 2.52 mg mL^{-1}, respectively.
[b] Buffer systems used were mast call medium (MCM).
[c] Buffer systems used were Tyrodes.

3.3. Passive cutaneous anaphylaxis (PCA)

Passive cutaneous anaphylaxis is an immediate type hypersensitivity reaction caused by the interaction of antibodies with mast cells of the skin. The technique was developed in 1958 by Ovary [27]. In our study, an antiserum was raised by means of intraperitoneal inoculation of Wistar rats with 1 mL of heat-killed Bordetella pertussis suspension (10^{10} organisms per mL) and 0.5 mL of chicken egg albumin solution (1 mg per animal) in 0.5 M NaCl. After 14 days, the animals were exsanguinated and the serum isolated. The prepared serum was intradermally injected, and after 48 h, the rats were intravenously challenged via the tail vein with 2.5 mg albumin in 0.25 mL 2% Evans Blue, with simultaneous injection of 0.25 mL of vehicle (positive control) or test compound at a dose of 3 mg kg^{-1}. Thirty minutes after intravenous injection, the animals were sacrificed by cervical dislocation and the skin reflected. The vehicle control and test sites were measured and excised, and the tissue segments added to 1 mL 1 M KOH. Using the method of Katayama [28], the tissue was digested overnight at 37 °C, and to each digest was added 2.5 mL 0.6 M H_3PO_4 and 6.5 mL acetone. The tubes were thoroughly shaken, and centrifuged at 3000 rpm for 15 min. The absorbance of each supernatant was measured using UV spectroscopy at 620 nm. The results, expressed as % inhibition of rat PCA induced by i.v. injection of ovalbumin, are shown in Table 4.

4. Results

From Table 1, it can be seen that several of the dimeric tetrahydro-naphthalenylamine and indan-1-ylamine derivatives exhibited in vitro mast cell-stabilising activity. Both methyl and allyl derivatives **6a** and **6b** almost completely inhibited Compound 48/80-induced histamine release from RPMC at the concentration examined, while acetamide **6c** was inactive. Compound **14**, with a tetralone carbonyl, showed reduced activity compared to regioisomer **6a**, while the presence of the second carbonyl in **9** diminished inhibitory activity to 61%. Compound **17**, a combination of N-linked tetralin and tetralone, retained excellent activity; conversely aminotetralin **19** was devoid of activity. In vitro,

Table 3
Protective activity of **6a** and **58a** against degranulation induced by anti-IgE.[a]

Compound	% Inhibition
6a (10^{-5} M)	68
58a (2×10^{-5} M)	95

[a] PS (physiological saline) buffer used, anti-IgE concentration 5.4 μg mL^{-1}.

Table 4
Protective activity of dimer compounds against PCA in the rat.[a,b]

Compound	% Inhibition
6a	13
6b	72
14	NI
17	29
50	62
58a	98
58b	82
58c	79
58d	73
58e	70
DSCG	99

[a] Rats were passively sensitised with i.d. injections of antiserum (0.1 mL site^{-1}) to ovalbumin and challenged 48 hours late.
[b] Compounds **25** and **31** showed toxicity in vivo.

molecules **25** and **31** completely inhibited degranulation at the dose level tested. Methoxy indanone molecules **50** and **51** showed similar activity. Also, all of the 2-aminotetralin derivatives **58a**–**e** tested exhibited activity; the most active being methylated derivative **58a**.

The dose-response studies (Tables 2 and 3), show the impact of selected compounds **6a**, **17** and **58a** on the effect of non-physiological and physiological degranulatory stimuli. Compounds **6a** and **17** showed dose-dependent inhibition of histamine release caused by a variety of stimuli, notably compound **6a**. Two individual results are of particular note, firstly, compound **6a** inhibited vancomycin-induced degranulation at concentrations of 10^{-6} M or more. Secondly, excellent inhibition (95%) of anti-IgE-induced histamine release was obtained using **58a**.

In the PCA model (Table 4) compound **14** was inactive, correlating with its relative inactivity in vitro. However, the results obtained for compounds **6a** and **17** were disappointing, compared to their activity in vitro. Methoxy indanone dimer **50** was seen to inhibit PCA to some extent, similar to its in vitro activity. Most interesting were the results for compounds **58a**–**e**, as all showed good inhibition of PCA, notably **58a** and **58b**, although substitution of the benzyl group on the tertiary nitrogen atom in **58c** by electron donating groups (methyl or trimethoxy) caused some loss of activity, as seen with **58d** and **58e**.

5. Discussion

Within the indan dimer series exemplified by **2a**–**b**, two important structural themes emerged [7,8]. Firstly, those tertiary derivatives with a small pendant alkyl group (such as *N*-allyl) were most efficacious, the secondary amines, likely metabolites in vivo, having substantially less activity. Secondly, activity was exhibited by both indan-1- and indan-2-ylamines. In the present work, we sought to establish whether ring enlargement of the alicyclic portions of these molecules had a beneficial or a deleterious effect on mast cell-stabilising activity. The in vitro results for **6a**–**c** correlated well with the results reported for **2,** suggesting that ring expansion is possible while retaining activity. In contrast, oxygenation of the hydroaromatic ring system is critical. Addition of a second carbonyl group onto the tetralin ring, as in **9**, did not abolish activity. However, replacement of the carbonyl from the indenyl component to the benzylic position of the tetralin ring as in **14** greatly reduced activity. Although this implies that a benzylic indanyl carbonyl is central to mast cell-stabilising activity, the 6-membered homodimer **17** completely inhibited compound 48/80-induced release of histamine from RPMC. At least one benzylic carbonyl is essential, as **19** offered no protective effect against degranulation. In general, mast cell-stabilising activity was greatest in those molecules with a 1-indanone or 1-tetralone ring linked to a tetralin ring. As in **2b**, activity was retained whether the linkage joined the two ring systems via their benzylic positions or was from one benzylic position to a non-benzylic carbon of the other ring system, as in **58a**. Substitution of the ring or amine positions affected activity to some extent, especially the introduction of electron-donating functional groups. Interestingly, like **2b** [7] and also 4-amino-3,4-dihydro-2H-naphthalen-1-one derivatives [9], dimeric compounds retained activity if either a small alkyl or a planar benzyl group substituted the tertiary nitrogen. Additionally, **58a** inhibited vancomycin-induced degranulation of RPMC. In previous studies, disodium cromoglycate did not inhibit vancomycin-induced degranulation from either RPMC or RBL-1 cells [29]. In the PCA studies, the reference compound DSCG at 3 mg kg^{-1} completely abolished the reaction; this was in good agreement with literature data, where values of 80–100% inhibition have been reported [30]. Compounds **6a** and **17**, despite their in vitro activity, were not protective in the in vivo model of anaphylaxis. In contrast, 2-aminotetralin compounds **58a**–**e** all inhibited the PCA reaction, clearly delineating this series of molecules from all previously synthesised homologs. In particular, **58a** inhibited PCA by 98% while also inhibiting anti-IgE-induced RPMC degranulation by 95%, making it a lead structure worthy of further study.

6. Conclusions

Of the novel dimeric 1,2,3,4-tetrahydro-naphthalenylamine and indan-1-ylamine compounds synthesised and tested, the 2-aminotetralin derivative **58a** showed the best ability to both inhibit in vitro secretagogue-induced degranulation of RPMC and to maintain activity in an in vivo PCA model. Expansion of the indan ring of the known dimeric indanes [7,8] is permissible without loss of mast cell stabilising activity in vitro, and furthermore, a 2-, rather than a 1-amino functionality appears important for activity in vivo within these structural types. Further studies to probe and optimise the anti-allergic activity and mode of action of the novel 2-aminotetralin derivatives described are envisaged, in particular to synthesise and assess the activity of the individual isomers of **58a**.

7. Experimental protocols

7.1. Chemistry

Melting points were obtained using an Electrothermal apparatus, and are uncorrected. Infrared Spectroscopy (IR) of test samples was performed on a Perkin Elmer Paragon 1000 FT-IR. Nuclear Magnetic Resonance (NMR) Spectroscopy was performed using a Bruker DPX-400 instrument, at 400.13 MHz for proton (^{1}H) magnetic resonance and 100.61 MHz for carbon (^{13}C) spectra. All NMR were recorded in $CDCl_3$ unless otherwise specified. Gas chromatographic-Mass Spectral data (GCMS) was obtained using a Saturn GC/MS 2000 [CP-3800 Gas Chromatograph]. High Resolution Mass Spectroscopy (HRMS) was performed using a Micromass LCT instrument, operating in ES$^+$ mode. Flash column chromatography was performed using Silica Gel, Grade 9385, 230–400 mesh, 60 Å (Merck Laboratories). For Thin Layer Chromatographic (TLC) procedures, aluminium foil plates pre-coated with Silica Gel 60 F_{254} were used (Merck Laboratories). TLC plates were visualised under ultraviolet light at 254 nm.

7.1.1. 3-(1,2,3,4-Tetrahydro-1-naphthalenylamino)-1-indanone (5)

To a stirred solution of **3** [11] (4.5 g, 21.3 mmol) in CH_2Cl_2 (30 mL) was added triethylamine (5.58 ml, 42.6 mmol) and **4** (3.14 g, 21.3 mmol). The reaction was stirred overnight at room temperature, the solvent removed in vacuo, and the residue purified by flash

column chromatography on silica gel (eluant: pet ether:ethyl acetate, 5:1) to yield the amine as a mixture of diastereomers (4.3 g, 72%), with the following physical properties: IR (KBr, ν) 2933, 1702, 1602, 1467, 1280, 1132 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.60$ (m, 1H, NH), 1.85–2.20 (m, 4H, $ArCH_2CH_2CH_2$), 2.60 (m, 1H, CH_2), 2.79 (m, 1H, CH_2), 2.91 (m, 1H, CH_2), 3.10 (m, 1H, CH_2), 4.00 and 4.08 (2 × m, 1H, CH), 4.57 and 4.64 (2 × m, 1H, CH), 7.16 (m, 3H, 3 × Ar-H), 7.32–7.45 (m, 2H, 2 × Ar-H), 7.61–7.80 (m, 3H, 3 × Ar-H); ^{13}C NMR $\delta_{ppm} = 18.3$ and 18.5 (CH_2), 27.6 and 28.6 (CH_2), 29.0 and 30.0 (CH_2), 45.8 and 46.7 (CH_2CO), 52.9 and 54.6 (CH), 53.5 and 55.0 (CH), 122.8 × 2 (tert. C), 125.3 and 125.5 (tert. C), 125.5 and 125.6 (tert. C), 126.5 and 126.6 (tert. C), 128.1 × 2 (tert. C), 128.3 and 128.4 (tert. C), 128.7 and 128.8 (tert. C), 134.4 × 2 (tert. C), 136.0 and 136.4 (quat. C), 137.0 and 137.1 (quat. C), 138.4 and 138.6 (quat. C), 156.2 and 156.5 (quat. C), 204.2 × 2 (C=O); MS, m/z, (RI) 278 (M + 1, 4), 277 (M^+, 2), 148 (85), 130 (100), 103 (26).

7.1.2. 3-[Methyl(1,2,3,4-tetrahydro-1-naphthalenyl)amino]-1-indanone (6a)

To a stirred solution of **5** (0.5 g, 1.81 mmol) in acetone (10 mL) was added methyl iodide (0.56 ml, 9.05 mmol) and anhydrous potassium carbonate (0.38 g, 2.75 mmol). The reaction was stirred for 2 days at room temperature, filtered, and the solvent removed in vacuo. The residue was purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield the amine as a yellow solid, with the following physical characteristics (0.34 g, 65%): IR (CCl_4, ν) 2937, 2864, 1718, 1603, 1277, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.56$–2.21 (m, 4H, 2 × CH_2), 1.88 and 2.28 (2 × s, 3H, CH_3), 2.57–2.95 (m, 4H, CH_2 and CH_2CO), 4.01 and 4.09 (2 × dd, $J_1 = 9.5$ Hz, $J_2 = 5$ Hz, 1H, NCHCH$_2$CH$_2$), 4.51 and 4.74 (2 × dd, $J_1 = 7$ Hz, $J_2 = 3.7$ Hz, 1H, NCHCH$_2$CO), 7.10–7.27 (m, 3H, 3 × Ar-H), 7.45 (m, 1H, Ar-H), 7.66–7.79 (m, 2H, 2 × Ar-H), 7.83–7.97 (m, 2H, 2 × Ar-H). ^{13}C NMR $\delta_{ppm} = 18.6$ and 18.8 (CH_2), 27.9 and 29.0 (CH_2), 29.3 and 30.3 (CH_2), 30.8 × 2 (CH_3), 46.1 and 47.1 (CH_2CO), 53.3 and 53.9 (CH), 54.9 and 55.4 (CH), 122.3 and 122.4 (tert. C), 125.38 and 125.42 (tert. C), 126.02 and 126.05 (tert. C), 126.05 and 126.10 (tert. C), 127.6 and 127.8 (tert. C), 127.9 and 128.0 (tert. C), 128.5 and 128.6 (tert. C), 134.4 × 2 (tert. C), 136.0 and 136.3 (quat. C), 137.0 and 137.1 (quat. C), 138.3 and 138.5 (quat. C), 156.1 and 156.4 (quat. C), 204.2 × 2 (C=O); MS, m/z, (RI) 292 (M + 1, 100), 291 (M^+, 27), 221 (16), 198 (15), 162 (79); HRMS $(M + H)^+$ 292.1729, $C_{20}H_{22}NO$ requires 292.1701.

7.1.3. 3-[Allyl(1,2,3,4-tetrahydro-1-naphthalenyl)amino]-1-indanone (6b)

To a stirred solution of **5** (0.5 g, 1.81 mmol) in acetone (10 mL) was added allyl iodide (0.83 ml, 9.05 mmol) and anhydrous potassium carbonate (0.38 g, 2.75 mmol). The reaction was stirred for 2 days at room temperature, filtered, and the solvent removed in vacuo. The residue was purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield the amine as a yellow oil (0.24 g, 42%): IR (KBr disc, HCl salt, ν) 2937, 2523, 1602, 1438, 1278 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.59$–3.23 (m, 10H, 5 × CH_2), 4.16 (m, 1H, CHCH$_2$CH$_2$), 4.51 and 4.66 (2 × m, 1H, CHCH$_2$CO), 4.83 and 5.09 (2 × d, 1H, $J = 10$ Hz, 1H, 1H of CH=CH_2), 4.96 and 5.23 (2 × d, 1H, $J = 17.9$ Hz, 1H, 1H of CH=CH_2), 5.65 and 5.85 (2 × m, 1H, CH=CH_2), 7.09 (m, 1H, Ar-H), 7.15–7.31 (m, 2H, 2 × Ar-H), 7.43 (m, 1H, Ar-H), 7.64–7.82 (m, 3H, 3 × Ar-H), 7.90 and 8.08 (2 × d, $J = 7.5$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 21.5$ and 21.9, 25.1 and 27.6, 29.2 and 29.6 ($CH_2CH_2CH_2$), 40.1 and 41.5 (NCH_2), 47.8 and 49.4 (CH_2CO), 55.0 and 57.0 (CH), 58.1 and 59.7 (CH), 115.4 and 116.4 (CH=CH_2), 122.3 and 122.6 (tert. C), 125.3 and 125.5 (tert. C), 125.9 and 126.0 (tert. C), 126.1 and 126.4 (tert. C), 127.1 and 127.8 (tert. C), 128.0 × 2 (tert. C), 128.5 and 128.6 (tert. C), 133.9 and 134.5 (tert. C), 136.6 and 137.4 (tert. C), 136.6 and 136.8 (quat. C), 138.1 and 138.5 (quat. C), 138.5 × 2 (quat. C), 156.3 and 156.6 (quat. C), 204.3 and 204.4 (C=O); MS, m/z, (RI) 318 (M + 1, 5), 188 (100), 131 (61), 103 (22); HRMS $(M + Na)^+$ 340.1671, $C_{22}H_{23}NONa$ requires 340.1677.

7.1.4. N1-(3-Oxo-2,3-dihydro-1H-1-indenyl)-N1-(1,2,3,4-tetrahydro-1-naphthalenyl)acetamide (6c)

To a stirred solution of **5** (150 mg, 0.54 mmol) in CH_2Cl_2 (10 ml) was added triethylamine (0.15 mL, 1.08 mmol), acetic anhydride (0.10 mL, 1.08 mmol) and a catalytic quantity of DMAP. The reaction was stirred overnight at room temperature, and the solvent removed in vacuo. The residue was purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 3:1) to yield the acetamide as white crystals (85 mg, 49%): Data for 1 pair of isomers: IR (KBr disc, ν); 2946, 1706, 1645, 1449, 1427, 1307 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.94$ (m, 2H, CH_2), 2.08–2.28 (m, 5H, CH_2 and CH_3), 2.47 (m, 2H, CH_2), 2.85 (m, 2H, CH_2), 3.20 (m, 1H, CH), 4.38 and 5.17 (2 × m, 1H, CH), 7.11–7.28 (m, 4H, 4 × Ar-H), 7.38 (dd, $J_1 = 8.5$ Hz, $J_2 = 7.5$ Hz, 1H, Ar-H), 7.48 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.60 (dd, $J_1 = 8.5$ Hz, $J_2 = 7.5$ Hz, 1H, Ar-H), 7.73 (d, $J = 7.5$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 21.7$ (CH_2), 23.7 (CH_3), 29.0, 30.7, 30.7 (3 × CH_2), 42.3, 53.8 (2 × CH), 123.0, 123.0, 123.0, 126.0, 127.3, 129.2, 134.0, 134.0 (8 × tert. C), 154.3 (NC=O), 202.6 (C=O). HRMS $(M + Na)^+$ 342.1441, $C_{21}H_{22}NO_2$ requires 342.1470.

7.1.5. 4-[(3-Oxo-2,3-dihydro-1H-1-indenyl)amino]-1,2,3,4-tetrahydro-1-naphthalenone (8)

The reaction was carried out by reacting compound 3 (0.68 g, 3.23 mmol) with **7** (0.52 g, 3.23 mmol) in a manner similar to the preparation of 5 using Et_3N as base in CH_2Cl_2 to give **8** (0.39 g, 42%). IR (CCl_4, ν); 2955, 1702, 1676, 1600, 1462, 1340, 1285 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.68$ (m, 1H, NH), 2.14 and 2.30–2.41 (2 × m, 2H, CH_2CH_2CO), 2.51–2.63 (m, 2H, CH_2CH_2CO), 3.02–3.21 (m, 2H, $CHCH_2CO$), 4.15 and 4.18 (2 × dd, $J_1 = 5$ Hz, $J_2 = 3.5$ Hz, 1H, CH), 4.40 and 4.64 (2 × dd, $J_1 = 6.7$ Hz, $J_2 = 3.5$ Hz, 1H, CH), 7.33–7.70 (m, 7H, 7 × Ar-H), 7.99 and 8.03 (2 × dd, $J_1 = 7.5$ Hz, $J_2 = 1$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 26.9$ and 29.5 (CH_2CH_2CO), 33.8 × 2 (CH_2CH_2CO), 45.4 and 45.7 ($CHCH_2CO$), 53.3 and 53.5 (CH), 53.9 and 54.1 (CH), 122.7 and 122.8 (tert. C), 125.6 × 2 (tert. C), 126.8 and 127.2 (tert. C), 127.6 and 127.7 (tert. C), 127.7 and 127.9 (tert. C), 128.3 and 128.4 (tert. C), 131.7 and 131.8 (quat. C), 132.9 and 133.4 (tert. C), 134.5 × 2 (tert. C), 136.0 and 136.2 (quat. C), 144.4 and 144.7 (quat. C), 155.4 and 155.7 (quat. C), 197.4 × 2 (C=O), 203.6 × 2 (C=O); MS, m/z, (RI) 292 (M + 1, 23), 291 (M^+, 86), 160 (42), 146 (93), 132 (100), 115 (69), 103 (73), 77 (62), 51 (29).

7.1.6. 4-[Methyl(3-oxo-2,3-dihydro-1H-1-indenyl)amino]-1,2,3,4-tetrahydro-1-naphthalenone (9)

The reaction was carried out using compound 8 (100 mg, 0.34 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base to give 9 (68%): IR (CCl_4, ν); 2949, 2791, 1707, 1678, 1597, 1332, 1284, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.99$ and 2.19 (2 × s, 3H, CH_3), 2.16 and 2.34 (2 × m, 2H, CH_2CH_2CO), 2.51–2.72 (m, 2H, CH_2CO), 2.81 and 2.86 (2 × dd, $J_1 = 12$ Hz, $J_2 \sim 4$ Hz, 1H of CH_2CO), 2.92–3.02 (m, 1H of CH_2CO), 4.05 and 4.10 (2 × dd, $J_1 \sim 9$ Hz, $J_2 = 3.5$ Hz, 1H, CHCH$_2$CH$_2$), 4.52 and 4.64 (2 × dd, $J_1 = 7$ Hz, $J_2 = 4$ Hz, 1H, CHCH$_2$CO), 7.37–7.45 (m, 2H, 2 × Ar-H), 7.57–7.75 (m, 4H, 4 × Ar-H), 7.82 and 7.93 (2 × d, $J = 7.5$ and 8 Hz, 1H, COAr-H), 8.03 (2 × dd, $J_1 = 8$ Hz, $J_2 = 1.5$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 25.6$ and 25.7 (CH_2CH_2CO), 29.3 and 33.2 (CH_3), 35.2 and 36.5 (CH_2), 36.9 and 37.8 (CH_2), 56.6 and 60.3 ($CHCH_2CO$), 60.9 and 61.9 ($CHCH_2CH_2$), 122.6 and 122.7 (tert. C), 125.8 and 125.9 (tert. C), 127.1 and 127.2 (tert. C), 127.1 and 127.2 (tert. C), 127.5 and 127.7 (tert. C), 128.2 and 128.3 (tert. C), 132.5 and 132.6 (quat. C), 132.9 and 133.0 (tert. C), 134.5 × 2

(tert. C), 136.5 and 136.7 (quat. C), 144.4 and 144.6 (quat. C), 155.2 and 155.4 (quat. C), 196.9 and 197.3 (C=O), 203.5 and 203.6 (C=O); MS, m/z, (RI) 306 (M + 1, 15), 305 (M^+, 23), 174 (20), 161 (100), 146 (68), 131 (15); HRMS $(M+H)^+$ 306.1508, $C_{20}H_{20}NO_2$ requires 306.1494.

7.1.7. 4-(2,3-Dihydro-1H-1-indenylamino)-1,2,3,4-tetrahydro-1-naphthalenone (13)

To a solution of 1-indanol **10** (1 g, 7.46 mmol) in ether (5 mL) at −15 °C was slowly added phosphorus tribromide (PBr_3) (0.28 mL, 2.98 mmol). The reaction was stirred for 30 min, and poured into ice/water. The organic layer was separated and the aqueous layer washed twice with ether (2 × 10 mL). The combined organic layers were quickly washed with aqueous sodium bicarbonate (2.5%), dried over sodium sulphate, and concentrated. To the flask, containing bromide **12**, was then added acetone (10 mL), **7** (1.20 g, 7.46 mmol) and triethylamine (2.08 mL, 14.92 mmol). The reaction was stirred overnight at room temperature, the solvent removed in vacuo, and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 2:1) to yield a brown oil (0.52 g, 25%): IR (CCl_4, ν); 2946, 2851, 1687, 1600, 1477, 1452, 1285 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.78$ (m, 1H, NH), 1.93 (2H, m, 2H of CH_2), 2.33 (2H, m, 2H of CH_2), 2.62 (2H, m, 2H of CH_2), 3.09 (2H, m, 2H of CH_2), 4.23 (m, 1H, CH), 4.35 and 4.49 (2 × m, CH), 7.21–7.60 (m, 7H, 7 × Ar-H), 8.08 (m, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 29.4$ and 29.5 (CH_2), 29.9 and 30.0 (CH_2), 34.1 and 34.3 (CH_2), 35.1 and 35.5 (CH_2CO), 53.0 and 53.9 ($CHCH_2CH_2CO$), 60.5 and 61.3 ($ArCH_2CH_2CHAr$), 123.6 and 123.7 (tert. C), 124.2 and 124.4 (tert. C), 125.9 and 126.0 (tert. C), 126.8 and 126.9 (tert. C), 127.1 × 2 (tert. C), 127.3 and 127.4 (tert. C), 127.6 and 127.8 (tert. C), 131.7 and 131.8 (quat. C), 133.0 and 133.3 (tert. C), 142.8 and 142.9 (quat. C), 145.0 and 145.3 (quat. C), 145.7 × 2 (quat. C), 197.8 and 198.0 (C=O); MS, m/z, (RI) 277 (M^+, 80), 160 (44), 145 (21), 132 (100), 117 (72).

7.1.8. 4-[2,3-Dihydro-1H-1-indenyl(methyl)amino]-1,2,3,4-tetrahydro-1-naphthalenone (14)

The reaction was carried out using compound 13 (100 mg, 0.36 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base to give 14 (87%): IR (CCl_4, ν); 2947, 1692, 1284 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 2.14$ and 2.25 (2 × m, 3H, 3H of CH_2), 2.11 and 2.32 (2 × s, 3H, CH_3), 2.40 (m, 1H of CH_2), 2.61 (m, 1H of CH_2), 2.85 (m, 1H of CH_2), 2.96–3.06 (m, 2H, CH_2), 4.15 and 4.22 (2 × dd, $J_1 \sim 9$ Hz, $J_2 \sim 4$ Hz, 1H, CH), 4.55 (m, 1H, CH), 7.25–7.27 (m, 3H, 3 × Ar-H), 7.38–7.52 (m, 2H, 2 × Ar-H), 7.60 (m, 1H, Ar-H), 7.87–7.88 (m, 1H, Ar-H), 8.07 (2 × d, $J = 8$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 25.9$ and 26.0 (CH_2), 26.1 and 26.7 (CH_2), 30.1 and 30.3 (CH_2), 33.9 × 2 (CH_3), 36.1 and 36.7 (CH_2CO), 60.3 and 61.7 (CH), 64.8 and 68.4 (CH), 124.2 × 2 (tert. C), 124.4 and 124.6 (tert. C), 125.9 and 126.0 (tert. C), 127.0–127.2 (3 × tert. C, signal overlap), 127.4 and 127.8 (tert. C), 132.5 × 2 (quat. C), 132.6 (quat. C), 132.9 and 133.0 (tert. C), 142.9 × 2 (quat. C), 197.2 and 197.3 (C=O), 1 quat. C signal obscured; MS, m/z, (RI) 291 (M^+, 31), 174 (23), 146 (100); HRMS $(M+H)^+$ 292.1695, $C_{20}H_{22}NO$ requires 292.1701.

7.1.9. 4-(1,2,3,4-Tetrahydro-1-naphthalenylamino)-1,2,3,4-tetrahydro-1-naphthalenone (16)

The reaction was carried out using 1-tetralol **11** (1 g, 6.76 mmol) in a manner similar to the preparation of 12 using PBr_3 to give bromide 15. To the flask was then added acetone (10 ml), **7** (1.08 g, 6.76 mmol) and, dropwise, triethylamine (1.87 mL, 13.42 mmol). The reaction was stirred overnight at room temperature, the solvent removed in vacuo, the residue extracted with acid, the aqueous acid layer removed and re-extracted with base and CH_2Cl_2, and the re-basified organic extract concentrated and purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 2:1) to yield the amine as a pale golden oil (0.41 g, 21%). IR (CCl_4, ν); 2937, 2863, 1689, 1601, 1451, 1283 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.21$ (m, NH), 1.79–2.27 (m, 5H), 2.41 (m, 1H), 2.64 (m, 1H), 2.74–2.95 (m, 2H), 3.19 (m, 1H), 3.91 and 4.06 (2 × dd, $J_1 \sim 5.5$ Hz, $J_2 \sim 4$ Hz, 1H, CH), 4.21 (m, 1H, CH), 7.13 (m, 1H, Ar-H), 7.20 (m, 2H, 2 × Ar-H), 7.31–7.44 (m, 2H, 2 × Ar-H), 7.56 (m, 2H, 2 × Ar-H), 8.10 (2 × d, $J = 8$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 18.4$ and 18.6 (CH_2), 27.3 and 27.7 (CH_2), 28.9 and 29.1 (CH_2), 29.4 × 2 (CH_2), 34.0 and 34.5 (CH_2CO), 52.0 and 52.1 (CH), 53.3 × 2 (CH), 125.4 and 125.5 (tert. C), 126.4 × 2 (tert. C), 126.7 and 127.0 (tert. C), 127.2 and 127.4 (tert. C), 127.8 and 127.9 (tert. C), 128.4 and 128.7 (tert. C), 128.7 × 2 (tert. C), 131.6 and 131.8 (quat. C), 133.1 and 133.3 (tert. C), 136.8 and 137.0 (quat. C), 138.8 and 139.2 (quat. C), 145.8 and 146.1 (quat. C), 197.8 and 197.9 (C=O); MS, m/z, (RI) 292 (M + 1, 26), 213 (15), 162 (61), 131 (100).

7.1.10. 4-[Methyl(1,2,3,4-tetrahydro-1-naphthalenyl)amino]-1,2,3,4-tetrahydro-1-naphthalenone (17)

The reaction was carried out using compound 16 (100 mg, 0.34 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base to give 17 (88%): IR (CCl_4, ν); 2936, 2361, 2342, 1691, 1550, 1283 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.58$ (m, 1H, NH), 1.63–2.10 (m, 4H, 2 × CH_2), 2.05 and 2.16 (2 × s, 3H, CH_3), 2.27 and 2.41 (2 × m, 2H, CH_2CH_2CO), 2.57 (m, 1H of CH_2CO), 2.66–2.92 (m, 2H, CH_2), 3.03 (m, 1H of CH_2CO), 3.83 and 4.21 (2 × dd, $J_1 \sim 9$ Hz, $J_2 \sim 4.5$ Hz, 1H, $CHCH_2CH_2CH_2$), 4.05 (m, 1H, $CHCH_2CH_2CO$), 7.03–7.17 (m, 3H, 3 × Ar-H), 7.39 (m, 1H, Ar-H), 7.51–7.62 (m, 2H, 2 × Ar-H), 7.67 and 7.70 (2 × d, $J = 7.8$ Hz, 1H, Ar-H), 8.03 (m, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 20.9$ and 21.1 (CH_2), 23.3 × 2 (CH_2), 26.0 and 26.1 (CH_2), 29.0 and 29.2 (CH_2), 31.7 and 33.9 (CH_3), 34.9 and 35.3 (CH_2CO), 57.8 and 58.9 (CH), 59.4 and 59.7 (CH), 125.4 × 2 (tert. C), 125.8 and 126.0 (tert. C), 127.0 × 2 (tert. C), 127.1 and 127.2 (tert. C), 127.5 × 2 (tert. C), 127.7 and 128.0 (tert. C), 128.3 and 128.5 (tert. C), 132.5 × 2 (tert. C), 132.5 × 2 (quat. C), 137.8 × 2 (quat. C), 138.7 × 2 (quat. C), 145.7 × 2 (quat. C), 198.02 and 198.05 (C=O); MS, m/z, (RI) 306 (M + 1, 5), 176 (76), 162 (100), 131 (100); HRMS $(M+H)^+$ 306.1884, $C_{21}H_{24}NO$ requires 306.1858.

7.1.11. N,N-Di(1,2,3,4-tetrahydro-1-naphthalenyl)amine (18)

The reaction was carried out by reacting compound 4 (0.65 g, 3.6 mmol) with **15** (0.76 g, 3.6 mmol) in a manner similar to the preparation of 5 using Et_3N as base in CH_2Cl_2 to give **18** (0.17 g, 17%), with the following physical properties: IR (CCl_4, ν); 2932, 2859, 1489, 1449, 1155, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.37$ (m, 1H, NH), 1.92 (2H, m, CH_2), 2.04–2.36 (m, 6H, 3 × CH_2), 2.83–2.94 (m, 2H, CH_2), 2.97 and 3.01 (2 × dd, $J_1 = 6.5$ Hz, $J_2 = 5.3$ Hz, 2H of CH_2), 4.14 (m, 2H, 2 × NCH), 7.19–7.29 (m, 6H, 6 × Ar-H), 7.47 and 7.48 (2 × d, $J = 3.6$ Hz, 1H, Ar-H), 7.52 (m, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 18.4$ (CH_2), 18.5 (CH_2), 27.8 (CH_2), 28.9 (CH_2), 29.2 (CH_2), 30.0 (CH_2), 51.9 (CH), 54.1 (CH), 125.3, 125.4, 126.1, 126.3, 128.4, 128.5, 128.7, 128.9 (8 × tert. C), 136.9, 137.2, 139.6, 139.9 (4 × quat. C); MS, m/z, (RI) 278 (M + 1, 100), 277 (M^+, 25), 247 (10), 214 (17).

7.1.12. N-Methyl- N,N-di(1,2,3,4-tetrahydro-1-naphthalenyl) amine (19)

The reaction was carried out using compound 18 (0.17 g, 0.61 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base to give 19 (50%): IR (CCl_4, ν); 2933, 2862, 1679, 1550, 1488, 1450 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.75$–1.87 (m, 2H, CH_2), 1.99–2.20 (m, 6H, 3 × CH_2), 2.10 (s, 3H, CH_3), 2.75–2.84 (m, 2H, CH_2), 2.90–3.02 (m, 2H, CH_2), 4.08 (m, 2H, 2 × NCH), 7.12–7.27 (m, 6H, 6 × Ar-H), 7.68 (dd, $J_1 = 6.5$ Hz, $J_2 = 2.0$ Hz, Ar-H), 7.81 (d, $J = 7.5$ Hz, 1H, Ar-H); ^{13}C

NMR δ_{pp} = 20.4, 20.9, 24.9, 25.3, 29.0, 29.0 (6 × $\underline{C}H_2$), 29.8 and 33.8 ($\underline{C}H_3$), 58.7 ($\underline{C}H$), 61.4 ($\underline{C}H$), 125.0, 125.1, 125.8, 125.8, 128.0, 128.3, 128.3, 128.4 (8 × tert. $\underline{C}$), 137.9, 137.9, 138.9, 139.7 (4 × quat. $\underline{C}$); MS, m/z, (RI) 292 (M + 1, 100), 291 (M^+, 46), 278 (45), 223 (18), 160 (33), 132 (82); HRMS $(M+H)^+$ 292.2078, $C_{21}H_{26}N$ requires 292.2065.

7.1.13. 4-Chromanol (21)

To an evaporating dish containing polyphosphoric acid (10 g) was added 3-phenoxypropanoic acid (5 g, 30.1 mmol). The mixture was stirred using a glass rod over a water bath, until the solid material had dissolved. The reaction was heated thus for 30 min, stirring constantly. The coloured raw reaction mixture was quenched using ice water and partitioned between ether and water. The combined ethereal layers (3 × 50 ml) were concentrated in vacuo and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield chromanone (4.1 g, 92%) as a white solid. To a stirred solution of the ketone (4 g, 27 mmol) in methanol (20 mL) was slowly added $NaBH_4$ (1.4 g, 40 mmol). After one hour of stirring, the solvent was removed and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield chromanol (**21**) as a pale colourless oil (3.6 g, 89%). ^{1}H NMR analysis showed homology with literature data [16]: ^{1}H NMR ($CDCl_3$, 400 MHz) δ_{ppm} = 1.93 and 2.04 (2 × m, 2H, $OCH_2\underline{C}H_2$), 3.13 (broad s, 1H, $\underline{O}H$), 4.19 (m, 2H, OCH_2), 4.66 (t, J = 4 Hz, 1H, $\underline{C}H$), 6.84 (d, J = 8.6 Hz, 1H, Ar-$\underline{H}$), 6.91 (dd, J_1 = 8.3 Hz, J_2 = 7 Hz, 1H, Ar-$\underline{H}$), 7.20 (dd, J_1 = 8.5 Hz, J_2 = 7.8 Hz, J_3 = 1 Hz, 1H, Ar-$\underline{H}$), 7.27 (d, J = 7.5 Hz, 1H, Ar-$\underline{H}$); MS, m/z, (RI) 150 (M^+, 57), 134 (100).

7.1.14. 3,4-Dihydro-2H-4-chromenyl azide (22)

Using compound 21 (2 g, 13.3 mmol) in a manner similar to the preparation of **12** using PBr_3 gave the bromide. To the flask was immediately added sodium azide (4 g, 61.5 mmol) and DMF (10 mL), and the reaction stirred at 45 °C on an oil bath for 2 h. To the residue was added water (50 mL) and the aqueous mixture extracted with ether (3 × 25 mL). The combined organic extracts were concentrated in vacuo, and purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield azide **22** as a pale colourless oil (1.86 g, 80%): IR (CCl_4, ν); 2968, 2008, 2105, 1610, 1585, 1490, 1457 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ_{ppm} = 2.05 (m, 1H of $OCH_2\underline{C}H_2$), 2.18 (m, 1H of $OCH_2\underline{C}H_2$), 4.24–4.34 (m, 2H, OCH_2), 4.62 (t, J = 3.8 Hz, 1H, $\underline{C}H$), 7.01 (m, 2H, 2 × Ar-$\underline{H}$), 7.31 (m, 2H,2 × Ar-$\underline{H}$); ^{13}C NMR δ_{ppm} = 27.7 ($\underline{C}H_2$), 54.3 ($\underline{C}H$), 61.7 ($O\underline{C}H_2$), 117.1 (tert. $\underline{C}$), 118.9 (quat. $\underline{C}$), 120.0, 129.5, 129.8 (3 × tert. $\underline{C}$), 154.3 (quat. $\underline{C}$).

7.1.15. tert-Butyl N-(3,4-dihydro-2H-4-chromenyl)carbamate (23)

Di-*tert*-butyl dicarbonate (0.16 g, 0.73 mmol) was added to a solution of **22** (0.12 g, 0.67 mmol) in EtOH:EtOAc (1:1, 4 mL). After addition of 10% Pd/C the reaction was stirred under an atmosphere of hydrogen overnight at room temperature. The reaction was filtered, the solvent removed in vacuo and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield the carbamate as a white crystalline solid (42 mg, 25%) with the following physical properties: mp 106–108 °C; IR (KBr, ν); 2964, 1679, 1523, 1250, 1104, 1066 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ_{ppm} = 1.50 (s, 9H, $((\underline{C}H_3)_3C)$, 2.08 and 2.20 (br. m, 2H, $\underline{C}H_2CH$), 4.17 and 4.25 (br. m, 2H, $C\underline{H}_2CO$), 4.86 (br. m, 2H, $\underline{C}H$ and $N\underline{H}$), 6.82 (d, J = 8.5 Hz, 1H, OAr-$\underline{H}$), 6.91 (dd, J_1 = 8.3 Hz, J_2 = 7 Hz, 1H, Ar-$\underline{H}$), 7.18 (dd, J_1 = 8.8 Hz, J_2 = 7.5 Hz, 1H, Ar-$\underline{H}$), 7.28 (d, J = 7.4 Hz, 1H, COAr-$\underline{H}$); ^{13}C NMR δ_{ppm} = 28.0 ($\underline{C}H_3$), 29.0 ($\underline{C}H_2$), 44.3 ($\underline{C}H$), 62.7 ($O\underline{C}H_2$), 79.2 ($(CH_3)_3\underline{C}$), 116.6, 120.2 (2 × tert. $\underline{C}$), 122.0 (quat. $\underline{C}$), 128.7, 128.9 (2 × tert. $\underline{C}$), 154.5 and 154.7 (quat. $\underline{C}$ and $\underline{C}$=O); MS, m/z, (RI) 194 (95), 148 (100), 133 (55), 131 (44).

7.1.16. 3-(3,4-Dihydro-2H-4-chromenylamino)-1-indanone (24)

A 1:1 mixture of CH_2Cl_2:TFA was added to carbamate **23** (0.5 g, 2.01 mmol) and the reaction mixture stirred at 0 °C for 30 min. The solvent was removed in vacuo, using toluene as azeotrope (3 × 20 mL), to yield the amine trifluoroacetate. Washing with base and extracting the organic layer with CH_2Cl_2 afforded 3,4-dihydro-2*H*-4-chromenylamine, a brown oil. To the flask was added **3** (0.42 g, 2 mmol), triethylamine (0.42 mL, 3 mmol) and acetone (10 mL). The reaction was stirred overnight at room temperature, the solvent removed in vacuo, and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 5:1) to yield the amine as a yellow oil (0.24 g, 44%): IR (CCl_4, ν); 2955, 1721, 1490, 1270, 1226 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ_{ppm} = 1.55 (br. s, 1H, $N\underline{H}$), 1.86 and 2.16 (2 × m, 2H, $OCH_2\underline{C}H_2$), 2.53 and 2.56 (2 × dd, J_1 = 18.5 Hz, J_2 = 3 Hz, 1H, $C\underline{H}_2CO$), 3.06 and 3.10 (2 × dd, J_1 = 18.5 Hz, J_2 = 6.5 Hz, 1H, $C\underline{H}_2CO$), 3.96 and 4.06 (2 × t, J = 3.5 Hz, 1H, $\underline{C}H$), 4.20 and 4.46 (2 × m, 2H, $O\underline{C}H_2$), 4.56 (m, 1H, $\underline{C}H$), 6.81–6.90 (m, 2H, 2 × Ar-$\underline{H}$), 7.11–7.27 (m, 2H, 2 × Ar-$\underline{H}$), 7.41 (m, 1H, Ar-$\underline{H}$), 7.58–7.67 (m, 2H, 2 × Ar-$\underline{H}$), 7.71 (m, 1H, COAr-$\underline{H}$); ^{13}C NMR δ_{ppm} = 26.8 and 29.1 ($CH_2\underline{C}H_2CH$), 45.8 and 46.2 ($\underline{C}H_2CO$), 49.2 and 50.2 ($\underline{C}H$), 52.7 and 54.0 ($\underline{C}H$), 61.8 and 61.9 ($O\underline{C}H_2$), 116.5 and 116.6 (tert. $\underline{C}$), 119.6 and 119.9 (tert. $\underline{C}$), 122.7 and 122.8 (tert. $\underline{C}$), 123.5 and 123.6 (quat. $\underline{C}$), 125.5 and 125.8 (tert. $\underline{C}$), 128.2 and 128.3 (tert. $\underline{C}$), 128.4 and 128.5 (tert. $\underline{C}$), 129.1 and 129.3 (tert. $\underline{C}$), 134.4 × 2 (tert. $\underline{C}$), 136.1 and 136.4 (quat. $\underline{C}$), 154.3 and 154.5 (quat. $\underline{C}$), 155.6 and 156.1 (quat. $\underline{C}$), 203.6 and 203.8 ($\underline{C}$=O); MS, m/z, (RI) 280 (M + 1, 9), 251 (98), 148 (81), 133 (100), 105 (25); HRMS $(M+H)^+$ 280.1348, $C_{18}H_{18}NO_2$ requires 280.1338.

7.1.17. 3-[3,4-Dihydro-2H-4-chromenyl(methyl)amino]-1-indanone (25)

The reaction was carried out using compound 24 (200 mg, 0.72 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base to give 25 (94%): IR (KBr, HCl salt, ν); 2926, 1720, 1609, 1492, 1460, 1228, 1056 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ_{ppm} = 1.89–2.26 (m, 2H, $OCH_2\underline{C}H_2$), 1.91 and 2.24 (2 × s, 3H, $\underline{C}H_3$), 2.57–2.90 (m, 2H, $C\underline{H}_2CO$), 4.06–4.24 (m, 2H, $O\underline{C}H_2$), 4.41 and 4.48 (2 × m, 1H, $\underline{C}H$), 4.57 and 4.72 (2 × m, 1H, $C\underline{H}CH_2CO$), 6.83 (m, 1H, Ar-$\underline{H}$), 6.96 (m, 1H, Ar-$\underline{H}$), 7.16 (m, 1H, Ar-$\underline{H}$), 7.44 (m, 1H, Ar-$\underline{H}$), 7.60–7.77 (m, 3H, 3 × Ar-$\underline{H}$), 7.81 (m, 1H, Ar-$\underline{H}$); ^{13}C NMR δ_{ppm} = 24.2 and 24.5 ($OCH_2\underline{C}H_2$), 28.0 and 33.0 ($N\underline{C}H_3$), 37.8 and 38.1 ($\underline{C}H_2CO$), 55.6 and 57.1 ($\underline{C}H$), 58.4 and 60.9 ($\underline{C}H$), 64.0 and 64.7 ($O\underline{C}H_2$), 116.46 and 116.54 (tert. $\underline{C}$), 119.8 and 120.0 (tert. $\underline{C}$), 122.46 and 122.53 (tert. $\underline{C}$), 123.1 and 123.4 (quat. $\underline{C}$), 125.9 × 2 (tert. $\underline{C}$), 128.01 and 128.08 (tert. $\underline{C}$), 128.1 × 2 (tert. $\underline{C}$), 128.2 and 128.8 (tert. $\underline{C}$), 134.4 and 134.5 (tert. $\underline{C}$), 136.4 and 136.6 (quat. $\underline{C}$), 155.3 and 155.7 (quat. $\underline{C}$), 155.8 × 2 (quat. $\underline{C}$), 203.9 × 2 ($\underline{C}$=O); MS, m/z, (RI) 294 (M + 1, 6), 293 (M^+, 4), 265 (18), 248 (15), 160 (73), 133 (100), 105 (93), 77 (54), 51 (17); HRMS $(M+H)^+$ 294.1470, $C_{19}H_{20}NO_2$ requires 294.1494.

7.1.18. 4-Azido-7-methoxy-1,2,3,4-tetrahydro-1-naphthalenone (28)

Using compound 27 (3 g, 17.0 mmol) in a manner similar to the preparation of 12 using PBr_3 gave the bromide. Reaction with sodium azide was carried out in a manner similar to the preparation of 22, to yield the azide as a pale colourless oil (2.11 g, 62%): IR (CCl_4, ν); 2939, 2097, 1613, 1505 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ_{ppm} = 1.84 (m, 1H, 1H of $C\underline{H}_2$), 1.94–2.06 (m, 3H, 3H of $C\underline{H}_2$), 2.67–2.85 (m, 2H, $C\underline{H}_2$), 3.84 (s, 3H, OCH_3), 4.55 (t, J = 4.6 Hz, 1H, $\underline{C}H$), 6.85 (m, 2H, 2 × Ar-$\underline{H}$), 7.08 (d, J = 8 Hz, 1H, Ar-$\underline{H}$); ^{13}C NMR δ_{ppm} = 18.9 ($\underline{C}H_2$), 27.5 ($\underline{C}H_2$), 28.7 ($\underline{C}H_2$), 54.9 ($\underline{C}H_3$), 59.3 ($\underline{C}H$), 112.9 (tert. $\underline{C}$), 114.4 (tert. $\underline{C}$), 128.8 (quat. $\underline{C}$), 129.9 (tert. $\underline{C}$), 134.3 (quat. $\underline{C}$), 157.4 (quat. $\underline{C}$).

7.1.19. 3-[(7-Methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]-1-indanone (30)

The reduction of compound 28 (1.63 g, 8.03 mmol) and reaction with Di-*tert*-butyl dicarbonate was carried out in a manner similar to the preparation of 23 to give carbamate **29**. Deprotection of **29** was carried out in a manner similar to that during the preparation of 24, and to the flask containing the free amine was added (**3**) (0.36 g, 1.71 mmol), triethylamine (0.47 mL, 3.37 mmol) and CH_2Cl_2 (10 mL). The reaction was stirred overnight at room temperature, the solvent removed in vacuo, and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield the amine as a yellow oil (0.36 g, 69%): IR (CCl_4, ν); 2937, 1719, 1503, 1465, 1271, 1252, 1233 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.50$ (m, 1H, NH), 1.75–2.21 (m, 4H, 2 × CH_2), 2.61 and 3.12 (2 × dd, $J_1 \sim 11$ Hz, $J_2 \sim 7$ Hz 2H, CH_2CO), 2.68–2.87 (m, CH_2), 3.77 and 3.81 (2 × s, 3H, OCH_3), 3.95 and 4.04 (2 × dd, $J_1 = 5.5$ Hz, $J_2 = 4.5$ Hz, 1H, CH), 4.60 and 4.65 (2 × dd, $J_1 = 6.5$ Hz, $J_2 = 3$ Hz, 1H, CH), 6.77 (m, 1H, Ar-H), 6.89–7.07 (m, 2H, 2 × Ar-H), 7.45 (m, 1H, Ar-H), 7.62–7.78 (m, 3H, 3 × Ar-H); ^{13}C NMR $\delta_{ppm} = 18.6$ and 18.9 (CH_2), 27.8 × 2 (CH_2), 28.1 and 30.2 (CH_2), 45.8 and 46.8 (CH_2CO), 52.8 and 53.8 (CH), 54.6 and 55.3 (CH), 54.8 × 2 (OCH_3), 112.3 and 112.8 (tert. C), 113.1 and 113.4 (tert. C), 122.8 × 2 (tert. C), 125.5 × 2 (tert. C), 128.1 × 2 (tert. C), 129.1 and 129.2 (quat. C), 129.6 × 2 (tert. C), 134.4 × 2 (tert. C), 136.1 and 136.4 (quat. C), 139.4 and 139.7 (quat. C), 156.1 and 156.4 (quat. C), 127.2 and 157.4 (quat. C), 204.1 × 2 (C=O); MS, m/z, (RI) 308 (M + 1, 3), 160 (100), 148 (47), 103 (18).

7.1.20. 3-[(7-Methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)(methyl)amino]-1-indanone (31)

The reaction was carried out using compound 30 (0.36 g, 1.17 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base to give **31** (81%): IR (KBr disc, HCl salt, ν); 2939, 1722, 1612, 1508, 1465, 1244, 1034 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.54$–1.92 (m, 2H, CH_2), 1.89 and 2.29 (2 × s, 3H, NCH_3), 2.05–2.16 (m, 2H, CH_2), 2.55–2.94 (m, 4H, CH_2 and CH_2CO), 3.87 and 3.88 (2 × s, 3H, OCH_3), 3.97 and 4.15 (2 × dd, $J_1 \sim 10$ Hz, $J_2 = 5$ and 7.5 Hz, 1H, CH), 4.52 and 4.74 (2 × dd, $J_1 = 7.5$ Hz, 1H, CH), 6.76 (m, 1H, Ar-H), 7.01 and 7.03 (2 × s, 1H, Ar-H), 7.41–7.57 (m, 2H, 2 × Ar-H), 7.66–7.78 (m, 2H, 2 × Ar-H), 7.88 (2 × d, $J = 3.5$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 21.5$ and 21.8 (CH_2), 24.7 and 25.0 (CH_2), 27.3 and 33.2 (NCH_3), 28.2 and 28.7 (CH_2), 38.5 and 38.6 (CH_2CO), 54.8 × 2 (OCH_3), 55.7 and 61.7 (CH), 62.2 and 63.5 (CH), 112.0 × 2 (tert. C), 112.6 and 112.8 (tert. C), 122.4 × 2 (tert. C), 125.8 and 126.0 (tert. C), 127.9 and 128.0 (tert. C), 129.3 and 129.5 (tert. C), 130.1 and 130.3 (quat. C), 134.3 and 134.4 (tert. C), 136.4 and 136.5 (quat. C), 139.2 × 2 (quat. C), 156.2 and 156.4 (quat. C), 157.6 × 2 (quat. C), 204.2 and 204.3 (C=O).

7.1.21. 3-Bromo-5-methoxy-1-indanone (37)

To a solution of **34** (1.51 g, 9.32 mmol) in CCl_4 (30 mL) was added *N*-bromosuccinimide (NBS) (1.66 g, 9.32 mmol) and a catalytic amount of dibenzoyl peroxide (DBP). The reaction mixture was heated under reflux, and on reaching reflux careful monitoring by TLC showed the progress of the reaction. On completion, the reaction was filtered, and the solvent removed in vacuo. The residue was purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield the brominated product as a yellow oil (1.12 g, 50%): ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 3.04$ and 3.35 (2 × dd, $J_1 = 19.7$ Hz, $J_2 = 3.2$ and 7.5 Hz, 2H, CH_2), 3.94 (s, 3H, OCH_3), 5.54 (dd, $J_1 = 7.5$ Hz, $J_2 = 2.5$ Hz, 1H, CHBr), 7.01 (dd, $J_1 = 8.4$ Hz, $J_2 = 2.2$ Hz, 1H, Ar-H), 7.11 (d, $J = 2$ Hz, 1H, Ar-H), 7.69 (d, $J = 8.6$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 40.2$ (CH_2), 47.8 (CH_3), 55.4 (CH), 109.8, 117.5, 124.6 (3 × tert. C), 128.9, 156.7, 165.4 (3 × quat. C), 199.0 (C=O).

7.1.22. 3-Bromo-7-methoxy-1-indanone (38)

The reaction was carried out using compound 36 (0.27 g, 1.67 mmol) in a manner similar to the preparation of 37 using NBS and catalytic DBP in CCl_4 to give **38** (0.16 g, 41%): IR (CCl_4, ν); 2938, 1725, 1597, 1483, 1295, 1277, 1023 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 2.99$ and 3.29 (2 × dd, $J_1 = 19.5$ Hz, $J_2 = 2$ and 7.3 Hz, 2H, CH_2), 3.94 (s, 3H, OCH_3), 5.50 (dd, $J_1 = 7.5$ Hz, $J_2 = 2$ Hz, 1H, CH), 6.86 (d, $J = 8$ Hz, 1H, Ar-H), 7.21 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.61 (dd, $J_1 = 9$ Hz, $J_2 = 8$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 40.0$ (CH), 48.0 (CH_2), 55.5 (OCH_3), 110.7 (tert. C), 118.7 (tert. C), 124.0 (quat. C), 136.9 (tert. C), 156.1 (quat. C), 157.0 (quat. C), 198.6 (C=O).

7.1.23. 3-Azido-7-methoxy-1-indanone (39)

The reaction was carried out using compound 38 (0.12 g, 0.50 mmol) in a manner similar to the preparation of 22 using NaN_3 in DMF to give **39** (55 mg, 54%): IR (CCl_4, ν); 2939, 1718, 1597, 1482, 1293, 1230 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 2.57$ and 2.98 (2 × dd, $J_1 = 18$–19 Hz, $J_2 = 3$ and 7.6 Hz, 2H, CH_2), 3.88 (s, 3H, OCH_3), 4.95 (dd, $J_1 = 7.5$ Hz, $J_2 = 3.3$ Hz, 1H, CH), 6.88 (d, $J = 8$ Hz, 1H, Ar-H), 7.14 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.58 (dd, $J_1 = 8.5$ Hz, $J_2 = 8$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 43.2$ (CH_2), 55.4 (OCH_3), 56.9 (CH), 111.1 (tert. C), 117.1 (tert. C), 124.0 (quat. C), 136.8 (tert. C), 153.1 (quat. C), 157.3 (quat. C), 198.6 (C=O).

7.1.24. tert-Butyl N-(5-methoxy-3-oxo-2,3-dihydro-1H-1-indenyl)carbamate (40)

The reduction of 3-Azido-6-methoxy-indan-1-one, [prepared from 35 via benzylic bromination and azide substitution] (1.67 g, 8.23 mmol) and reaction with Di-*tert*-butyl dicarbonate was carried out in a manner similar to the preparation of 23 to give carbamate **40** (1.64 g, 72%): IR (CCl_4, ν); 2979, 1719, 1492, 1166 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.40$ (s, 9H, $(CH_3)_3C$), 3.07 (dd, $J_1 \sim 19$ Hz, $J_2 = 7$ Hz, 2H, CH_2CO), 3.75 (s, 3H, Ar-OCH_3), 5.22 and 5.17 (2 × br s, 2H, CH and NH), 7.01 (s, 1H, Ar-H), 7.12 (br. d, 1H, Ar-H), 7.44 (dd, $J_1 = 8.5$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 27.9$ ($(CH_3)_3C$), 45.2 (CH_2), 47.7 (CH), 55.1 (Ar-OCH_3), 79.3 ($(CH_3)_3C$), 104.0, 123.8, 126.3 (3 × tert. C), 137.4, 146.5, 155.2 (3 × quat. C), 160.1 (NHC=O), 202.7 (C=O). Upon liberation of the free amine with TFA/DCM (1:1, 10 mL. R.T., 1 h) and reaction with (**15**), only decomposition was observed.

7.1.25. tert-Butyl N-(4-methoxy-3-oxo-2,3-dihydro-1H-1-indenyl)carbamate (41)

The reduction of compound 39 (1.63 g, 8.03 mmol) and reaction with Di-*tert*-butyl dicarbonate was carried out in a manner similar to the preparation of 23 to give carbamate **41** (0.36 g, 71%): IR (CCl_4, ν); 2979, 1714, 1598, 1482, 1289, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.43$ (s, 9H, $(CH_3)_3$), 2.43 and 3.02 (d and irr. dd, J_d and $J_{1dd} = 18.5$ Hz, 2H, CH_2), 3.87 (s, 3H, OCH_3), 5.19 (broad s, 2H, NH and CH), 6.78 (d, $J = 7$ Hz, 1H, Ar-H), 7.11 (d, $J = 7.5$ Hz, 1H, Ar-H), 7.51 (dd, $J_1 = 9.6$ Hz, $J_2 = 7.5$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 27.9$ ($(CH_3)_3$), 44.9 (CH_2), 47.7 ($C(CH_3)_3$), 55.3 (CH), 110.0 (tert. C), 116.8 (quat. C), 116.9 (tert. C), 124.1 (quat. C), 136.5 (tert. C), 157.0 (NC=O), 200.3 (C=O). Upon liberation of the free amine with TFA/DCM and reaction with (**15**), only decomposition was observed.

7.1.26. Acetic acid 3-bromo-1-oxo-indan-4-yl ester (46)

The reaction was carried out using compound 44 (1.46 g, 7.68 mmol) in a manner similar to the preparation of 37 using NBS and catalytic DBP in CCl_4 to give **46** (1.32 g, 64%): IR (CCl_4, ν); 1770, 1722, 1607, 1370, 1194, 1095, 1011 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 2.27$ (s, 3H, CH_3), 2.96 and 3.30 (2 × dd, $J_1 = 19.6$ Hz, $J_2 = 2.8$ and 7 Hz, 2H, CH_2), 5.50 (dd, $J_1 = 7.5$ Hz, $J_2 = 2.5$ Hz, 1H, CHBr), 7.14 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.5$ Hz, 1H, Ar-H), 7.39 (s, 1H, Ar-H), 7.66 (d, $J = 8.5$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 20.6$ (CH_3), 39.6 (CH), 47.7

(CH$_2$), 120.0 (tert. C), 123.3 (tert. C), 124.1 (tert. C), 132.9 (quat. C), 155.5 (quat. C), 155.9 (quat. C), 168.0 (OCOCH$_3$), 199.4 (C=O).

7.1.27. Acetic acid 1-bromo-3-oxo-indan-4-yl ester (47)

The reaction was carried out using compound 45 (0.29 g, 1.53 mmol) in a manner similar to the preparation of 37 using NBS and catalytic DBP in CCl_4 to give **47** (0.25 g, 61%): IR (CCl_4, ν); 1776, 1720, 1608, 1178, 1010 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 2.42$ (s, 3H, CH$_3$), 3.05 and 3.36 (2 × dd, $J_1 \sim 19$–20 Hz, $J_2 = 3$ and ~7 Hz, 2H, CH$_2$), 5.57 (dd, $J_1 = 7.5$ Hz, $J_2 = 2.5$ Hz, 1H, CH), 7.12 (d, $J = 8$ Hz, 1H, Ar-H), 7.60 (d, $J = 8$ Hz, 1H, Ar-H), 7.73 (dd, $J_1 \sim 9$ Hz, $J_2 = 8$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 20.2$ (CH$_3$), 39.4 (CH), 47.9 (CH$_2$), 122.4 (tert. C), 124.7 (tert. C), 127.2 (quat. C), 136.3 (tert. C), 146.4 (quat. C), 155.3 (quat. C), 168.3 (OCOCH$_3$), 197.8 (C=O).

7.1.28. Acetic acid 1-oxo-3-(1,2,3,4-tetrahydro-naphthalen-1-ylamino)-indan-5-yl ester (48)

The reaction was carried out by reacting compound 4 (0.9 g, 4.91 mmol) with **46** (1.32 g, 4.91 mmol) in a manner similar to the preparation of 5 using Et_3N as base in CH_2Cl_2 to give **48** (1.1 g, 67%). IR (CCl_4, ν); 2937, 1772, 1719, 1608, 1370, 1198 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.58$ (m, 1H, NH), 1.75–2.24 (m, 4H, 2 × CH$_2$, CH$_2$CH$_2$CH$_2$CH), 2.29 and 2.32 (2 × s, 3H, CH$_3$), 2.57 (m, 1H of 1H of CH$_2$CO), 2.71–2.89 (2H, CH$_2$), 3.08 (dd, $J_1 \sim 19$ Hz, $J_2 = 6.5$ Hz, 1H, 1H of CH$_2$CO), 3.95 and 4.02 (2 × dd, $J_1 = 5.5$ Hz, $J_2 = 4.5$ Hz, 1H, CHCH$_2$CH$_2$), 4.49 and 4.56 (2 × dd, $J_1 \sim 7$ Hz, $J_2 \sim 3$ Hz, 1H, CHCH$_2$CO), 7.07–7.48 (m, 6H, 6 × Ar-H), 7.72 (m, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 18.1$ and 18.5 (CH$_2$CH$_2$CH$_2$), 20.6 and 20.7 (CH$_3$), 27.4 and 28.6 (CH$_2$), 28.9 and 30.1 (CH$_2$), 45.9 and 46.9 (CH$_2$CO), 52.8 and 53.4 (CH), 54.2 and 54.9 (CH), 118.7 and 118.8 (tert. C), 122.16 and 122.21 (tert. C), 123.99 and 124.01 (tert. C), 125.3 and 125.5 (tert. C), 126.5 × 2 (tert. C), 128.41 and 128.44 (tert. C), 128.7 × 2 (tert. C), 133.6 and 133.9 (quat. C), 137.0 and 137.1 (quat. C), 138.2 and 138.4 (quat. C), 155.5 × 2 (quat. C), 158.1 and 158.5 (quat. C), 168.26 and 168.31 (OCOCH$_3$), 202.55 and 202.61 (C=O).

7.1.29. Acetic acid 3-oxo-1-(1,2,3,4-tetrahydro-naphthalen-1-ylamino)-indan-4-yl ester (49)

The reaction was carried out by reacting compound 4 (0.17 g, 0.93 mmol) with **47** (0.25 g, 0.93 mmol) in a manner similar to the preparation of 5 using Et_3N as base in CH_2Cl_2 to give **49** (0.16 g, 51%): ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.77$–2.26 (m, 4H, CH$_2$CH$_2$CH$_2$CH), 2.42 and 2.43 (2 × s, 3H, CH$_3$), 2.59 (m, 1H of CH$_2$), 2.75–2.94 (m, 2H, CH$_2$), 3.09 (m, 1H of CH$_2$), 3.98 and 4.07 (2 × dd, $J_1 = 5.5$ Hz, $J_2 = 4.5$ Hz, 1H, CHCH$_2$CH$_2$), 4.55 and 4.61 (2 × dd, $J_1 = 7$ Hz, $J_2 = 3.5$ Hz, 1H, CH), 7.04 -7.67 (m, 7H, 7 × Ar-H); ^{13}C NMR $\delta_{ppm} = 18.2$ and 18.5 (CH$_2$CH$_2$CH$_2$), 20.3 × 2 (CH$_3$), 27.5 and 28.6 (CH$_2$), 28.9 and 30.1 (CH$_2$), 46.2 and 47.2 (CH$_2$CO), 52.6 and 53.5 (CH), 54.2 and 55.1 (CH), 121.3 × 2 (tert. C), 123.2 and 123.3 (tert. C), 125.3 and 125.5 (tert. C), 126.6 × 2 (tert. C), 127.6 and 127.9 (quat. C), 128.3 and 128.4 (tert. C), 128.7 and 128.8 (tert. C), 135.5 × 2 (tert. C), 137.0 and 137.1 (quat. C), 138.2 and 138.4 (quat. C), 146.6 × 2 (quat. C), 157.9 and 158.3 (quat. C), 168.6 × 2 (OCOCH$_3$), 200.9 and 201.0 (C=O).

7.1.30. 5-Methoxy-3-[methyl-(1,2,3,4-tetrahydro-naphthalen-1-yl)-amino]-indan-1-one (50)

The reaction was carried out using compound 48 (0.4 g, 1.19 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base in acetone/MeOH to give 50 (76%): IR (KBr, HCl salt, ν); 2923, 1709, 1598, 1266 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.60$–2.30 (m, 4H, CH$_2$CH$_2$CH$_2$CH), 1.89 and 2.30 (2 × s, 3H, NCH$_3$), 2.53–2.94 (m, 4H, ArCH$_2$ and CH$_2$CO), 3.96 and 3.98 (2 × s, 3H, OCH$_3$), 4.02 and 4.17 (2 × dd, $J_1 = 8.8$ Hz, $J_2 = 7.4$ Hz, 1H, CH), 4.43 and 4.66 (2 × dd, $J_1 = 7$–8 Hz, $J_2 \sim 4$ Hz, 1H, CH), 6.96 and 6.99 (m, 1H, Ar-H), 7.11 (m, 1H, Ar-H), 7.18 (m, 1H, Ar-H), 7.22–7.29 (m, 2H, 2 × Ar-H), 7.67 and 7.72 (m, 1H, Ar-H), 7.81 and 7.94 (2 × d, $J = 7.5$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 21.1$ and 21.5 (CH$_2$), 24.8 and 25.1 (CH$_2$), 27.4 and 33.3 (NCH$_3$), 29.0 and 29.5 (CH$_2$), 38.4 and 38.6 (CH$_2$CO), 55.2 and 55.3 (OCH$_3$), 55.6 and 61.4 (CH), 61.7 and 63.3 (CH), 109.1 and 109.3 (tert. C), 115.6 and 115.7 (tert. C), 124.1 and 124.2 (tert. C), 125.3 and 125.4 (tert. C), 126.1 × 2 (tert. C), 127.5 and 127.7 (tert. C), 128.5 and 128.7 (tert. C), 129.9 and 130.0 (quat. C), 137.9 and 138.1 (quat. C), 138.0 and 138.3 (quat. C), 159.4 and 159.6 (quat. C), 165.1 and 165.2 (quat. C), 202.6 × 2 (C=O); MS, m/z, (RI) 322 (M + 1, 58), 192 (100); HRMS (M + H)$^+$ 322.1811, $C_{21}H_{24}NO_2$ requires 322.1807.

7.1.31. 7-Methoxy-3-[methyl-(1,2,3,4-tetrahydro-naphthalen-1-yl)-amino]-indan-1-one (51)

The reaction was carried out using compound 49 (0.21 g, 0.63 mmol) in a manner similar to the preparation of 6a using anhydrous potassium carbonate as a base in acetone/MeOH to give 51 (46%): IR (CCl_4, ν); 2941, 1712, 1595, 1483, 1286 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.55$–1.80 (m, 2H, CH$_2$), 1.85 and 2.25 (2 × s, 3H, CH$_3$), 1.87 and 1.99–2.17 (2 × m, 2H, CH$_2$), 2.51–2.92 (m, 4H, CH$_2$ and CH$_2$CO), 3.94 and 3.96 (2 × s, 3H, OCH$_3$), 3.96 and 4.14 (2 × dd, 1H, CH), 4.39 and 4.63 (2 × dd, $J_1 = 7.3$ Hz, $J_2 = 4$ Hz, 1H, CH), 6.81 and 6.85 (2 × d, $J = 8.1$ Hz, 1H, Ar-H), 7.08 (m, 1H, Ar-H), 7.15 (m, 1H, Ar-H), 7.22 (m, 1H, Ar-H), 7.38 and 7.42 (2 × d, $J = 7.5$ Hz, 1H, Ar-H), 7.60 (m, 1H, Ar-H), 7.80 and 7.91 (2 × d, $J = 7.5$ Hz, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 21.6$ and 21.9 (CH$_2$), 25.2 and 25.5 (CH$_2$), 27.8 and 33.7 (NCH$_3$), 29.5 and 29.9 (CH$_2$), 39.2 and 39.5 (CH$_2$CO), 55.6 and 61.5 (CH), 55.8 × 2 (OCH$_3$), 62.2 and 63.8 (CH), 109.7 × 2 (tert. C), 118.2 × 2 (tert. C), 125.2 × 2 (quat. C), 125.8 × 2 (tert. C), 126.5 × 2 (tert. C), 128.1 and 128.3 (tert. C), 128.9 and 129.0 (tert. C), 136.4 × 2 (tert. C), 138.3 and 138.5 (quat. C), 138.5 and 138.7 (quat. C), 157.5 × 2 (quat. C), 159.6 and 159.7 (quat. C), 202.6 and 202.7 (C=O); HRMS (M + H)$^+$ 322.1823, $C_{21}H_{24}NO_2$ requires 322.1807.

7.1.32. Methanesulphonic acid 1,2,3,4-tetrahydro-naphthalen-2-yl ester (53)

To a stirred solution of 2-tetralone **52** (5 g, 34.2 mmol) in methanol (10 mL), at 0 °C, was added sodium borohydride (1.9 g, 51.4 mmol), over 5 min. The reaction mixture was stirred for one hour, allowing the reaction to reach room temperature. The solvent was then removed in vacuo, and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield the alcohol (4.87 g, 96%) as a colourless oil. To a solution of the alcohol (3.2 g, 21.6 mmol) in dry CH_2Cl_2 under an atmosphere of nitrogen was added methane sulphonyl chloride (3.94 g, 34.6 mmol). To the resultant solution, cooled to 0 °C, was added *N,N*,-diisopropylethanolamine (4.2 g, 32.4 mmol), drop-wise by syringe, over 5 min. After 5 min stirring at this temperature, 5% aqueous $NaHCO_3$ was added and the reaction allowed to return to room temperature. The reaction mixture was partitioned, and the organic layer removed, washed sequentially with water, 2 M HCl and water, then the combined organic layers were dried over anhydrous sodium sulphate and the solvent removed *in vacuo*. The residue was purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 8:1) to yield a pale yellow oil (4.40 g, 90%), with the following physical properties: IR (CCl_4, ν); 2933, 1341, 1175, 1046, 953 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 2.19$ (m, $J = 6.5$ Hz, 2H, CH$_2$CH$_2$CH), 2.87 and 2.92 (2 × dd, $J_1 = 7.5$ Hz, $J_2 = 6.8$ Hz, 1H of ArCH$_2$CH$_2$), 2.99–3.07 (m, 1H of ArCH$_2$CH$_2$), 3.03 (s, 3H, CH$_3$), 3.11 (dd, $J_1 \sim 16$ Hz, $J_2 = 6.5$ Hz, 1H of ArCH$_2$CH), 3.25 (dd, $J_1 \sim 16$ Hz, $J_2 = 5$ Hz, 1H of ArCH$_2$CH), 5.18 (quintet, $J \sim 5.7$ Hz, 1H, CH), 7.10–7.19 (m, 4H, 4 × Ar-H). ^{13}C NMR $\delta_{ppm} = 25.5$, 28.4, 35.0 (3 × CH$_2$), 38.2 (CH$_3$), 77.4 (CH), 125.8, 126.0, 128.2, 128.8 (4 × tert. C), 132.0, 134.5 (2 × quat. C).

7.1.33. 2-Azido-1,2,3,4-tetrahydro-naphthalene (54)

The reaction was carried out using compound 53 (4 g, 17.7 mmol) in a manner similar to the preparation of 22 using NaN_3 in DMF to give **54** (2.73 g, 89%): IR (CCl_4, ν); 2931, 2094, 1496, 1498, 1248, 1112 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.93–2.02$ (m, 1H of CH_2CH_2CH), 2.18–2.25 (m, 1H of CH_2CH_2CH), 2.91–2.98 (m, 2H, CH_2), 3.05 and 3.09 (2 × dd, $J_1 = 6.5$ Hz, $J_2 = 5.5$ Hz, 1H of CH_2), 3.18 (2 × dd, $J_2 \sim 5.5$ Hz, 1H of CH_2), 3.91–3.98 (m, 1H, CH), 7.18–7.28 (m, 4H, 4 × Ar-H); ^{13}C NMR $\delta_{ppm} = 26.7, 27.7, 34.3$ (3 × CH_2), 56.7 (CH), 125.7, 126.0, 128.4, 128.9 (4 × tert. C), 133.0, 134.8 (2 × quat. C).

7.1.34. tert-Butyl N-(1,2,3,4-tetrahydro-2-naphthalenyl)carbamate (55)

The reduction of compound 54 (0.12 g, 0.69 mmol) and reaction with Di-*tert*-butyl dicarbonate was carried out in a manner similar to the preparation of 23 to give carbamate **55** (0.12 g, 79%): IR (KBr, ν); 2982, 2936, 1689, 1522, 1178 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.49$ (s, 3H, CH_3), 1.77 (m, 1H of CH_2CH_2CH), 2.10 (m, 1H of CH_2CH_2CH), 2.64 and 2.68 (dd, $J_1 \sim 16$ Hz, $J_2 = 8.3$ Hz, 1H of $ArCH_2CH_2$), 2.90 (m, 2H, $ArCH_2CH$), 3.12 and 3.16 (dd, $J_1 \sim 16$ Hz, $J_2 = 5$ Hz, 1H of $ArCH_2CH_2$), 4.00 and 4.62 (2 × broad s, 2H, CH and NH), 7.07–7.15 (m, 4H, 4 × Ar-H); ^{13}C NMR $\delta_{ppm} = 26.8$ (CH_2), 28.0 (CH_3 and CH), 28.7, 35.6 (2 × CH_2), 78.8 ($C(CH_3)_3$), 125.4, 125.6, 128.3, 130.0 (4 × tert. C), 133.8, 135.1 (2 × quat. C), 154.9 (C=O); MS, m/z, (RI) 192 (100), 148 (97).

7.1.35. 3-(1,2,3,4-tetrahydro-2-naphthalenylamino)-1-indanone (57)

To a stirred solution of **3** (0.3 g, 1.42 mmol) was added **56** (0.21 g, 1.42 mmol, obtained in quantitative yield from carbamate **55**), and triethylamine (0.40 mL, 2.84 mmol). The reaction was stirred overnight at room temperature, the solvent removed in vacuo, and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 5:1) to yield the amine as a golden brown oil (0.05 g, 13%); IR (CCl_4, ν); 2926, 1718, 1604, 1465, 1279, 1237 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.58$ (m, 1H, NH), 1.76 (m, 1H of $CH_2CH_2CH_2$), 2.07 and 2.22 (2 × m, 1H of $CH_2CH_2CH_2$), 2.50 and 2.56 (2 × dd, $J_1 = 6.5$ Hz, $J_2 \sim 3$ Hz, 1H of CH_2), 2.73 (m, 1H of CH_2), 2.86–3.26 (m, 5H, CH_2, CH_2CO and CH), 4.64 (m, 1H, $CHCH_2CO$), 7.09–7.18 (m, 4H, 4 × Ar-H), 7.45 (m, 1H, Ar-H), 7.65 (m, 1H, Ar-H), 7.70 and 7.72 (2 × d, $J = 2.5$ Hz, 1H, Ar-H), 7.77 (m, 1H, Ar-H); ^{13}C NMR $\delta_{ppm} = 27.3$ and 27.6 (CH_2), 28.8 and 30.4 (CH_2), 36.2 and 37.2 (CH_2), 45.6 and 45.7 (CH_2CO), 51.6 and 51.8 (CH), 53.1 × 2 (CH), 122.8 × 2 (tert. C), 125.4 × 2 (tert. C), 125.5 × 2 (tert. C), 125.7 × 2 (tert. C), 128.2 × 2 (tert. C), 128.3 × 2 (tert. C), 128.9 and 129.0 (tert. C), 134.4 × 2 (tert. C), 134.5 and 134.6 (quat. C), 135.7 × 2 (quat. C), 136.3 × 2 (quat. C), 156.1 × 2 (quat. C), 204.1 × 2 (C=O); MS, m/z, (RI) 277 (M^+, 99), 146 (68), 131 (100), 103 (71), 77 (31); HRMS $(M + H)^+$ 278.1526, $C_{19}H_{20}NO$ requires 278.1545.

7.2. General procedure for the preparation of tertiary amines (58a–e)

Mixtures of 3-(1,2,3,4-tetrahydro-2-naphthalenylamino)-1-indanone (1 mmol), appropriate alkyl halide, namely methyl iodide, allyl iodide, benzyl bromide, 4-methylbenzyl bromide or 3,4,5-trimethoxybenzyl bromide (3 mmol) and anhydrous potassium carbonate (5 mmol) were stirred for 6 h (**58a**) to 6 days at reflux (**58c–e**) in acetone (10 mL). The reaction mixture was filtered, the solvent removed in vacuo, and the residue purified by flash column chromatography on silica gel (eluant: pet ether:ethyl acetate, 10:1) to yield amines **58a–e.**

7.2.1. 3-[Methyl(1,2,3,4-tetrahydro-2-naphthalenyl)amino]-1-indanone (58a)

Yield: 18 mg, 34%; IR (CCl_4, ν); 2930, 1718, 1276, 1044 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.84$ and 2.19 (2 × m, 2H, CH_2CH_2CH), 2.14 and 2.15 (2 × s, 3H, CH_3), 2.67 and 2.71 (2 × dd, $J_1 = 7$ Hz, $J_2 = 4$ Hz, 1H, CH), and 2.81–3.13 (m, 6H, 3 × CH_2), 4.84 (m, 1H, $CHCH_2CO$), 7.14 (m, 4H, 4 × Ar-H), 7.45 (m, 1H, Ar-H), 7.647.79 (m, 3H, 3 × Ar-H); ^{13}C NMR $\delta_{ppm} = 27.2$ and 27.6 (CH_2), 28.7 and 28.9 (CH_2), 31.0 and 31.3 (CH_3), 33.4 and 33.7 (CH_2), 37.2 and 37.5 (CH_2CO), 58.0 and 58.3 (CH), 58.6 and 58.7 (CH), 122.5 × 2 (tert. C), 125.3 × 2 (tert. C), 125.4 × 2 (tert. C), 126.0 × 2 (tert. C), 128.0 × 2 (tert. C), 128.1 × 2 (tert. C), 128.9 and 129.0 (tert. C), 134.4 × 2 (tert. C), 135.2 and 135.3 (quat. C), 135.7 and 135.8 (quat. C), 136.6 and 136.7 (quat. C), 156.0 × 2 (quat. C), 204.3 × 2 (C=O); HRMS $(M + H)^+$ 292.1678, $C_{20}H_{22}NO$ requires 292.1701.

7.2.2. 3-[Allyl(1,2,3,4-tetrahydro-2-naphthalenyl)amino]-1-indanone (58b)

Yield: 32 mg, 56%; IR (CCl_4, ν); 2928, 1717, 1550, 1273 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.63$ and 1.97 (2 × m, 1H of CH_2CH_2CH), 2.11 and 2.19 (2 × m, 1H of CH_2CH_2CH), 2.75–3.25 (m, 7H, CH_2, CH_2CO, CH and NCH_2), 4.78 (m, 1H, $CHCH_2CO$), 5.05 and 5.20 (2 × m, 2H, C=CH_2), 5.77 (m, 1H, CH=CH_2), 7.14–7.17 (m, 4H, 4 × Ar-H), 7.45 (m, 1H, Ar-H), 7.69 (m, 1H, Ar-H), 7.77–7.83 (m, 2H, 2 × Ar-H); ^{13}C NMR $\delta_{ppm} = 26.5$ and 29.3 (CH_2), 29.4 and 29.6 (CH_2), 32.7 and 35.0 (CH_2), 40.2 and 40.3 (CH_2CO), 48.5 and 48.6 (NCH_2), 54.8 and 54.9 (CH), 55.4 and 55.5 (CH), 115.7 × 2 (C=CH_2), 122.4 and 122.5 (tert. C), 125.2 and 125.3 (tert. C), 125.3 and 125.5 (tert. C), 125.9 and 126.0 (tert. C), 128.0 × 2 (tert. C), 128.2 × 2 (tert. C), 128.9 and 129.0 (tert. C), 134.4 × 2 (tert. C), 135.5 and 135.6 (quat. C), 135.8 and 135.9 (quat. C), 136.8 × 2 (quat. C), 137.2 × 2 (tert. C), 156.5 and 156.6 (quat. C), 204.2 × 2 (C=O); MS, m/z, (RI) 317 (M^+, 78), 302 (62), 212 (56), 186 (42), 131 (100), 103 (98); HRMS $(M + H)^+$ 318.1835, $C_{22}H_{24}NO$ requires 318.1858.

7.2.3. 3-[Benzyl(1,2,3,4-tetrahydro-2-naphthalenyl)amino]-1-indanone (58c)

Yield: 0.29 g, 47%; IR (CCl_4, ν); 2928, 1717, 1603, 1495, 1274 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.64$ (m, 1H of CH_2CH_2CH), 2.02 (m, 1H of CH_2CH_2CH), 2.14 (m, 1H of CH_2CH_2CH), 2.31 (m, 1H of CH_2CH_2CH), 2.75–3.19 (m, 7H, 3 × CH_2 and CH), 3.67 (m, 2H, NCH_2), 4.84 (m, 1H, $CHCH_2CO$), 7.10–7.18 (m, 4H, 4 × Ar-H), 7.28 (m, 1H, Ar-H), 7.37 (m, 2H, 2 × Ar-H), 7.42–7.50 (m, 3H, 3 × Ar-H), 7.75 (m, 1H, Ar-H), 7.84 (m, 1H, Ar-H), 7.96 and 7.99 (2 × d, $J \sim 8$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 25.8$ and 29.4 (CH_2), 29.5 and 29.7 (CH_2), 32.2 and 34.9 (CH_2), 39.7 and 39.9 (CH_2CO), 49.5 × 2 (NCH_2), 54.2 and 54.3 (CH), 55.0 and 55.2 (CH), 122.5 and 122.6 (tert. C), 125.3 × 2 (tert. C), 125.4 and 125.6 (tert. C), 126.0 and 126.1 (tert. C), 126.5 and 126.6 (tert. C), 127.7–128.2 (6 × tert. C, signal overlap), 128.9 and 129.1 (tert. C), 134.6 and 134.7 (tert. C), 135.4 and 135.6 (quat. C), 135.8 and 135.9 (quat. C), 136.9 × 2 (quat. C), 139.6 × 2 (quat. C), 156.4 and 156.5 (quat. C), 204.4 × 2 (C=O); MS, m/z, (RI) 368 (M + 1, 60), 367 (M^+, 65), 276 (100), 236 (58), 131 (32), 103 (25); HRMS 368.2007, $C_{26}H_{26}NO$ requires 368.2014.

7.2.4. 3-[(4-Methylbenzyl)(1,2,3,4-tetrahydro-2-naphthalenyl)amino]-1-indanone (58d)

Yield:0.10 g, 15%; IR (CCl_4, ν); 2927, 1718, 1546 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.63$ and 2.00 (2 × m, 1H of CH_2CH_2CH), 2.10 and 2.28 (2 × m, 1H of CH_2CH_2CH), 2.35 (2 × s, 3H, CH_3), 2.73–3.17 (m, 7H, 3 × CH_2 and CH), 3.50 and 3.54 (2 × d, $J = 14$ Hz, 1H, 1H of NCH_2), 3.69 and 3.73 (2 × d, $J = 14.5$ Hz, 1H, 1H of NCH_2), 4.83 (m, 1H, $CHCH_2CO$), 7.07–7.14 (m, 6H, 6 × Ar-H), 7.29 (m, 2H, 2 × Ar-H), 7.46 (m, 1H, Ar-H), 7.72 (m, 1H, Ar-H), 7.79 (m, 1H, Ar-H), 7.92 and 7.96 (2 × d, $J = 8$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 20.6 \times 2$ (CH_3), 25.8 and 29.4 (CH_2), 29.5 and 29.7 (CH_2), 32.1 and 34.9 (CH_2), 39.7 and 40.0 (CH_2CO), 49.1 and 49.2 (NCH_2), 53.9 and 54.0 (CH), 54.9 and 55.2 (CH), 122.5 × 2 (tert. C), 125.2 and 125.3 (tert. C), 125.3 and 125.5 (tert. C), 126.0 and 126.1 (tert. C), 127.6–128.6 (6 × tert. C, signal overlap), 128.9

and 129.0 (tert. C), 134.6 × 2 (tert. C), 135.4 and 135.6 (quat. C), 135.8 and 135.9 (quat. C), 136.0 and 136.1 (quat. C), 136.4 × 2 (quat. C), 136.8 × 2 (quat. C), 156.5 and 156.6 (quat. C), 204.5 × 2 (C=O); MS, m/z, (RI) 251 (66), 129 (39), 120 (38), 105 (100), 103 (32), 91 (21); HRMS $(M+H)^+$ 382.2147, $C_{27}H_{28}NO$ requires 382.2171.

7.2.5. 3-[1,2,3,4-Tetrahydro-2-naphthalenyl(3,4,5-trimethoxybenzyl)amino]-1-indanone (58e)

Yield:0.22 g, 27%; IR (CCl_4, ν); 2936, 2837, 1717, 1592, 1506, 1464, 1420, 1329, 1237, 1132, 1012 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) $\delta_{ppm} = 1.68$ and 2.04 (2 × m, 1H of CH_2CH_2CH), 2.13 and 2.27 (2 × m, 1H of CH_2CH_2CH), 2.76–3.18 (m, 7H, 3 × CH_2 and CH), 3.47 and 3.50 (2 × d, $J = 9$ Hz, 1H, 1H of NCH_2), 3.66 and 3.70 (2 × d, $J = 14.5$ Hz, 1H, 1H of NCH_2), 3.83 and 3.87 (m, 9H, 3 × OCH_3), 4.84 (m, 1H, $CHCH_2CO$), 6.62 and 6.63 (2 × s, 2H, 2 × $(CH_3O)_3$Ar-H), 7.07–7.13 (m, 4H, 4 × Ar-H), 7.45 (m, 1H, Ar-H), 7.69 (m, 1H, Ar-H), 7.77 (m, 1H, Ar-H), 7.86 and 7.89 (2 × d, $J = 8$ Hz, 1H, COAr-H); ^{13}C NMR $\delta_{ppm} = 25.9$ and 29.3 (CH_2), 29.4 and 29.5 (CH_2), 32.3 and 35.0 (CH_2), 39.6 and 39.9 (CH_2CO), 49.8 × 2 (NCH_2), 54.6 and 54.7 (CH), 55.0 and 55.2 (CH), 55.6 and 60.4 (3 × OCH_3, signal overlap), 104.1 and 104.4 (2 × $CH_3O)_3$Ar-CH, signal overlap, 122.6 × 2 (tert. C), 125.3 × 2 (tert. C), 125.4 and 125.6 (tert. C), 125.8 and 125.9 (tert. C), 128.2 × 2 (tert. C), 128.3 × 2 (tert. C), 128.8 and 129.0 (tert. C), 134.5 × 2 (tert. C), 135.3–136.9 (5 × quat. C, signal overlap), 152.7 (2 × quat. C, signal overlap), 156.2 and 156.3 (quat. C), 204.3 × 2 (C=O); MS, m/z, (RI) 328 (8), 181 (100), 147 (13); HRMS $(M+H)^+$ 458.2336, $C_{29}H_{32}NO_4$ requires 458.2331.

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