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Synthesis and ring transformations of 1-amino-1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-ones

Joana Dumčiūtė,[a] Vytas Martynaitis,[a] Wolfgang Holzer,[b] Sven Mangelinckx,[c] Norbert De Kimpe[c] and Algirdas Šačkus[a,*]

[a]*Department of Organic Chemistry, Kaunas University of Technology, LT-50270 Kaunas, Lithuania*
[b]*Department of Drug Synthesis, Faculty of Life Sciences, University of Vienna, Pharmaziezentrum, A-1090 Vienna, Austria*
[c]*Department of Organic Chemistry, Faculty of Bioscience Engineering, Ghent University, Coupure links 653, B-9000 Gent, Belgium*

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Abstract—Heating 1-carbamoylmethyl-2,3,3-trimethyl-3*H*-indolinium chloride in the presence of hydrazine bishydrate produces regioselectively the five-membered heterocycle 1-amino-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one. The assignment of the structure is based on extensive ^{1}H, ^{13}C and ^{15}N NMR spectroscopic studies. No ring-chain tautomerism of the 1-amino-1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-one was observed to open-chain hydrazides or the corresponding six-membered 1,2,10,10a-tetrahydro[1,2,4]triazino[4,3-*a*]indol-3(4*H*)-one. Further transformations of 1-amino-1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-one were performed by treatment with aromatic aldehydes, acid chlorides and isocyanates giving access to 40 novel hydrazones, *N*,*N*′-diacylhydrazines, *N*-acyl-*N*′-carbamoylhydrazines and 1,3,4-oxadiazoles.

1. Introduction

1-Carbamoylmethyl-3*H*-indolinium salts **1** are known to cyclize to 1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-ones upon treatment with base.[1] If, however, the 1-carbamoylmethyl-3*H*-indolinium salts **1** are transformed to the corresponding hydrazides **2**, further cyclization could either lead to 1-amino-1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-ones **3**, similar as to ring closure of the amides, or to the corresponding six-membered ring systems, that is, 1,2,10,10a-tetrahydro[1,2,4]triazino[4,3-*a*]indol-3(4*H*)-one **4**, if the terminal NH_2 group enters into reaction (Scheme 1). The objective of this work is to investigate the reaction of such hydrazides and, apart from the structural investigations, to study the reactivity of the novel cyclic products and route to novel heterocyclic compounds. The potential biological activity of the unknown 1-amino-1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-ones is also of interest, as these tricyclic derivatives contain both the 2,3-dihydro-1*H*-indole and imidazolidin-4-one nuclei. Via the reaction of an α-amino amide with a carbonyl compound followed by intramolecular cyclization, the conformationally rigid imidazolidin-4-one scaffold has already been introduced in some compounds to modify their physiological activities such as cognition enhancing activity,[2] nootropic activity,[3] antimalarial activity,[4] and analgesic activity.[5] Metabolic stable N-terminal imidazolidin-4-one prodrugs of Leu-enkephalin have also been prepared.[6] Compounds containing the indole-1-acetamide moiety also exhibit interesting physiological activities such as central muscle relaxation,[7] anticonvulsive activity,[8] and CNS depressant activity.[9]

2. Results and discussion

Heating 1-carbamoylmethyl-2,3,3-trimethyl-3*H*-indolinium chloride **1** in the presence of hydrazine bishydrate, resulted in the isolation of a cyclized compound identified as the racemic five-membered heterocycle 1-amino-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one (**3**) (Scheme 2).

The main evidence for the assignment of structure **3**, containing the 3-aminoimidazolidin-4-one ring, follows from the ^{15}N NMR data. The ^{15}N,^{1}H HMBC spectrum shows three different N-atoms (δ −317.6, −299.1 and −224.6 ppm). In a ^{15}N DEPT experiment (optimized for $^{1}J_{NH}$=70 Hz) only the N-atom with the smallest chemical shift (δ −317.6) emerges, namely as a triplet (^{1}J=68.9 Hz)

Keywords: Hydrazides; Structural identification; 1,2,3,9a-Tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-ones; Hydrazines; Oxadiazoles.
* Corresponding author. Tel./fax: +370 37 451432; e-mail: algirdas.sackus@ktu.lt

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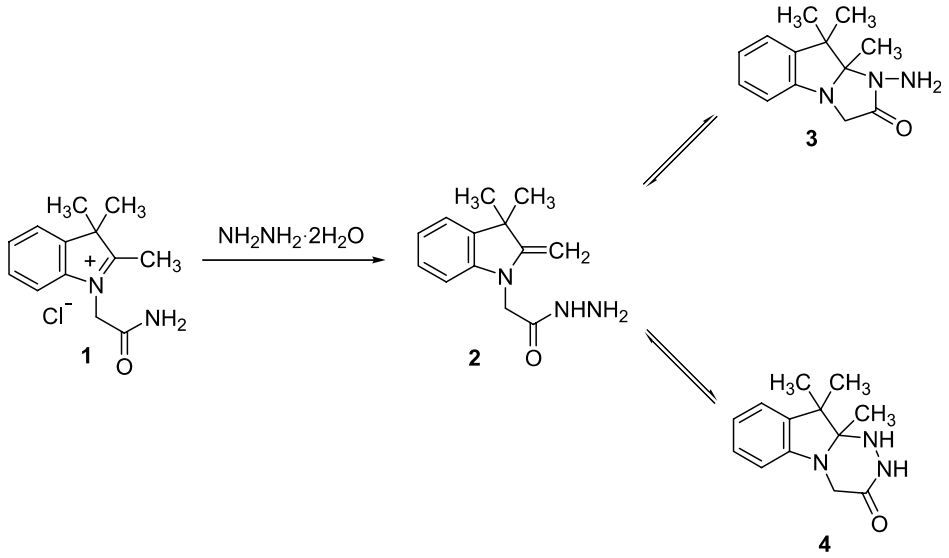
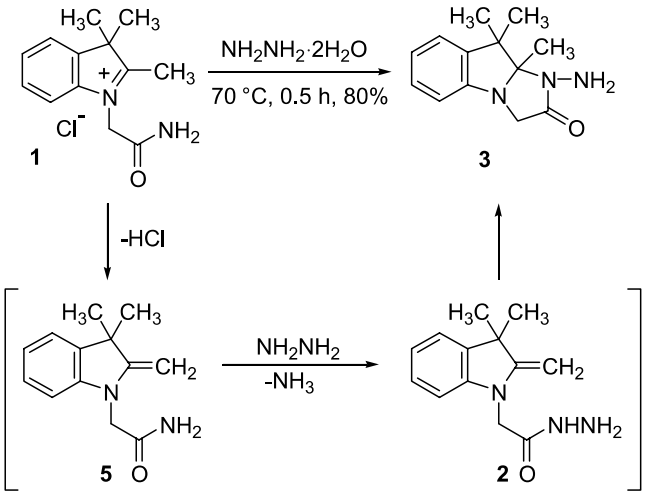


Scheme 1.



Scheme 2.

and thus proving to origin from an NH_2 moiety what definitely rules out structure **4**. Moreover, the ^{15}N, ^{1}H HMBC spectrum exhibits a correlation between the nitrogen atom with the largest chemical shift (N-1, δ −224.6) and the protons of 9a-CH_3 (δ 1.40 ppm), what seems improbable with structure **4** where the involved nuclei would be separated by four bonds and thus no correlation is expected. In addition, in the ^{1}H NMR spectrum there is only one sharp signal of relative intensity two for the NH-protons. For structure **4**, two different type of NH-signals have to be expected (CONH, N–NH). The assignments presented in Figure 1a are based on the combined application of standard NMR techniques such as NOE-difference (Fig. 1b), NOESY, APT, DEPT, HSQC, HMBC and long-range INEPT spectra with selective excitation.[10]

Although the amino nitrogen atom of the hydrazide moiety of **2** is more reactive[11] than the amide one, the condensation reaction involves the latter exclusively to give a five-membered ring. This observed reactivity is similar to addition reactions of phenylhydrazine in which it was proven that the N-1 of phenylhydrazine reacts as the nucleophilic site and not the NH_2-group.[12] The exclusive formation of the five-membered ring can be tentatively rationalized on the basis of the *E*/*Z* rotamerism of hydrazide **2** with respect to the nitrogen–carbon hydrazide bond with partial double bond character (Scheme 3). Studies concerning this hindered rotation of hydrazine derivatives have shown that steric effects of the substituents are driving the equilibrium towards the (*Z*) forms, augmented by intramolecular hydrogen bonding in the (*Z*) form.[13] It can be assumed that the large steric effect of the indolylmethyl carbonyl substituent of hydrazide **2** and the two possible intramolecular hydrogen bonds between the hydrogen atoms attached to the nitrogen and the oxygen atom, make the (*Z*) form much more favored. This (*Z*)-hydrazide is

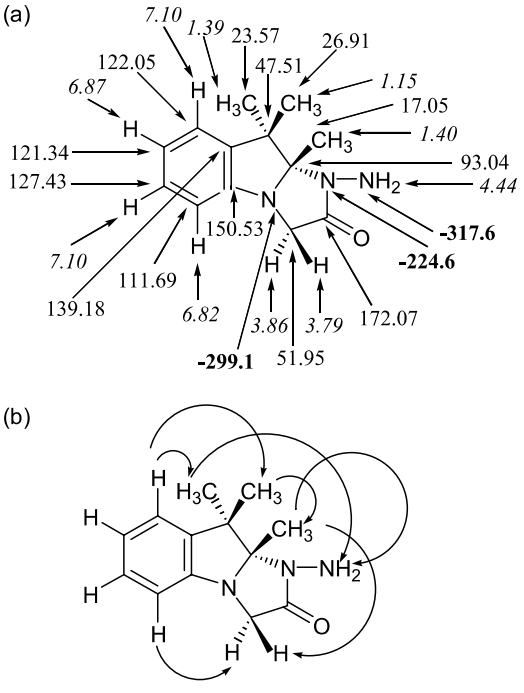
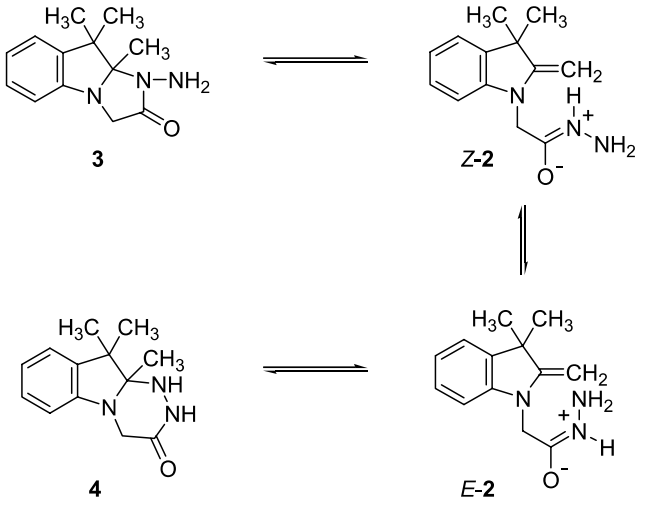


Figure 1. (a) ^{1}H (italics), ^{13}C and ^{15}N NMR (bold) chemical shifts [ppm; ref. TMS (^{1}H and ^{13}C) and CH_3NO_2 (^{15}N)] for **3** in DMSO-d_6. (b) Relevant NOE correlations.

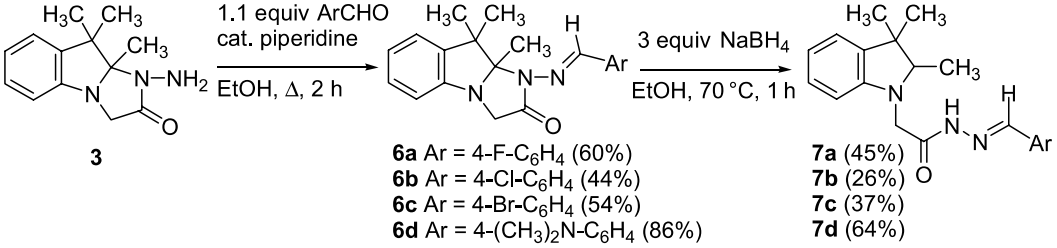


Scheme 3.

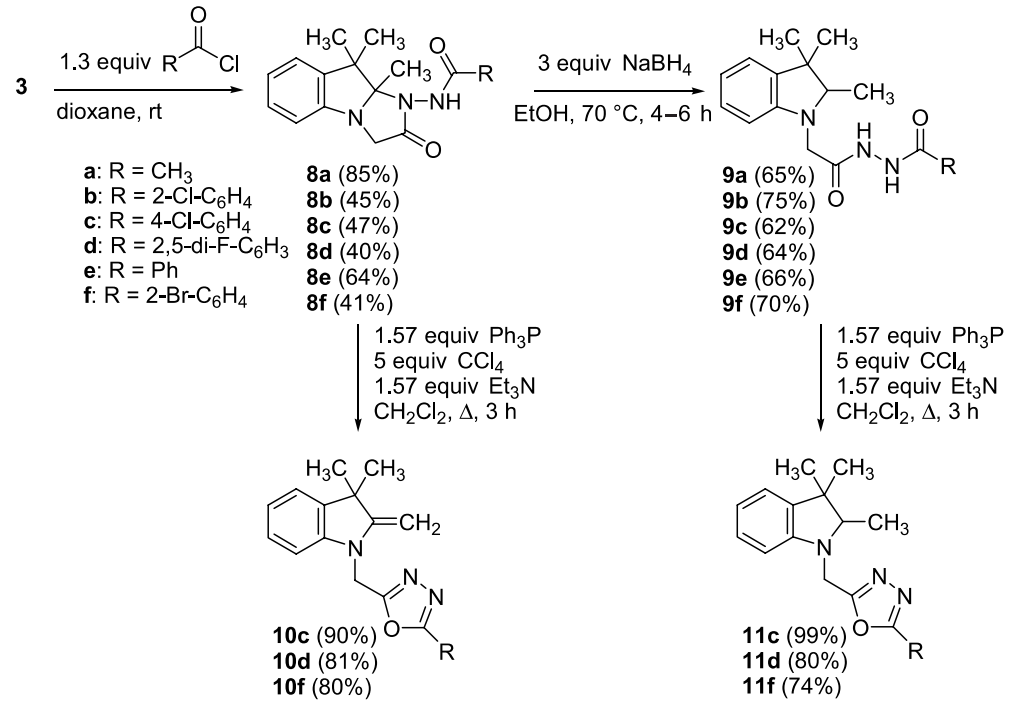
potentially capable of ring-chain tautomerism (*Z*)−**2**⇄**3**, while the unfavorable (*E*)-form would potentially be capable of ring-chain tautomerism (*E*)−**2**⇄**4**. No other ring-chain tautomeric forms of 1-amino-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one (**3**) were, however, visible by ^{1}H and ^{13}C NMR in $CDCl_3$ or DMSO-d_6, which can be explained by the annellation effect, that is, due to higher substitution and thereby higher conjugation the tricyclic compound **3** is expected to be more favored than the open-chain hydrazide **2**. These observations are in agreement with similar ring closures of α-amino acid hydrazides with aldehydes or ketones, which also resulted in 3-aminoimidazolidin-4-ones,[14] or the open-chain hydrazone tautomers in the case of low substituted compounds.[14c] Similarly, glycine hydroxamic acid condenses with benzaldehyde[15] and ketones,[16] leading to the formation of five-membered 3-hydroxyimidazolidin-4-ones. To the best of our knowledge, only few reports have been made on the synthesis of 1,2,4-triazin-6-ones from the reaction of α-amino acid hydrazides with aldehyde or ketone functions. Regarding a first report on the reaction of α-amino acid phenylhydrazides with formaldehyde,[17] it was stated by the same group in a later disclosure,[14a] that the proposed six-membered ring structures might be incorrect. A second report involved the intramolecular reaction of oxamic hydrazides with a ketone function giving 1,2,4-triazin-5,6-diones.[18] Also reported is the synthesis of pyrazolotriazines by reaction of pyrazolecarboxylic acid hydrazides and acetone.[19] Another special case involved reaction of aziridine-2-carboxylic acid hydrazides with acetone or cyclohexanone giving 1,3,4-triazabicyclo[4.1.0]-heptan-5-ones.[20] Moreover, reactions between α-amino acid hydrazides and carbonyl functions like imidoyl chlorides,[21] thioesters,[22] orthocarboxylates,[23] in which both five- and six-membered compounds could be formed, seem to give systematically the six-membered 1,2,4-triazin-6-ones. Therefore, it seems acceptable to assume that 3-amino-imidazolidin-4-ones are the preferred ring-chain tautomers with respect to 1,2,4-triazin-6-ones if imidazolidinone C-2 and C-5 are sp^3-hybridized, otherwise 1,2,4-triazin-6-ones seem to be favored. The only exception observed so far being the 1,3,4-triazabicyclo[4.1.0]heptan-5-ones,[20] in which, however, C-5 also has more double-bond character, being part of a three-membered ring. Interesting to mention also is the fact that acid-catalyzed rearrangement of substituted *N*-aminoimidazolidinones to 3-imino-hexahydro-1,2,4-triazine-6-ones has been reported.[24]

Further proof for the presence of the primary amino group in the cyclized compound was given by reacting the 3-aminoimidazolidin-4-one **3** with different types of electrophiles. Heating compound **3** with aromatic aldehydes in ethanol in the presence of catalytic amounts of piperidine afforded the corresponding hydrazones **6a–d** as single *E*-isomers in good to fair yield after crystallization (Scheme 4).[25] Further reduction of these 1-(arylidenamino)-imidazo[1,2-*a*]indolones **6a–d** with sodium borohydride in ethanol at 70 °C resulted in ring cleavage of the annelated imidazolidin-4-one ring,[26] to give acylated hydrazones **7a–d**. The lower yields can probably be explained by partial reduction of the hydrazone moiety.

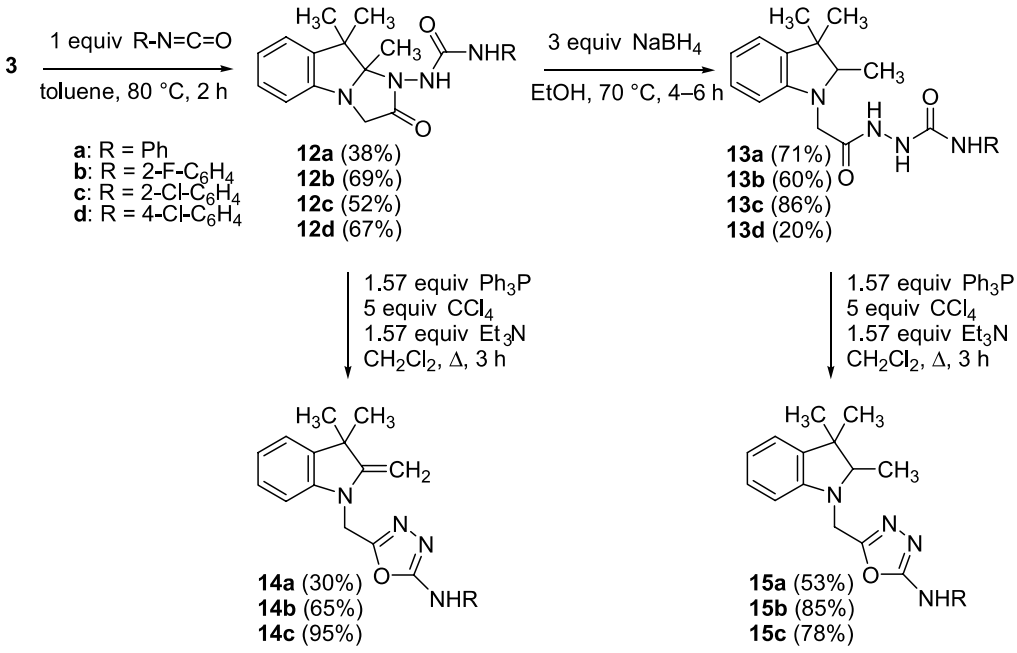
Acylation of 3-aminoimidazolidin-4-one **3** with acetyl chloride or benzoyl chlorides afforded *N*,*N*′-diacylhydrazines **8a–f**, which also could be reduced upon reaction with sodium borohydride to give ring cleaved *N*,*N*′-diacyl-hydrazines **9a–f** (Scheme 5). Both *N*,*N*′-diacylhydrazines **8c**,**d**,**f** and **9c**,**d**,**f** were cyclized to 1,3,4-oxadiazoles **10c**,**d**,**f** and **11c**,**d**,**f** under dehydration condition utilizing triphenyl-phosphine in carbon tetrachloride in the presence of triethylamine.[27] Similarly, *N*-acyl-*N*′-carbamoylhydrazines **12a–d** and **13a–d**, prepared by reaction of imidazolidinone **3** with isocyanates and further reduction, respectively, were cyclized to 2-amino-1,3,4-oxadiazoles **14a–c** and **15a–c** (Scheme 6). Substituted 1,3,4-oxadiazoles exhibit numerous pharmacological properties, including analgesic, antiinflammatory, anticonvulsive, diuretic, antiemetic, hypnotic and sedative activities.[28] More specific, 2-amino-1,3,4-oxadiazoles act as muscle relaxants[29] and possess antimitotic activity.[30]



Scheme 4.



Scheme 5.



Scheme 6.

3. Conclusion

1-Carbamoylmethyl-3*H*-indolinium salt **1** is regioselectively cyclized into a five-membered ring compound, that is, 1-amino-1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-one **3**, via an intermediate hydrazide **2**. No indication of the presence of other ring chain tautomers was observed and 1-amino-1,2,3,9a-tetrahydro-9*H*-imidazo[1,2-*a*]indol-2-one **3** was readily transformed into novel hydrazones **6**, *N*,*N*′-diacylhydrazines **8** and **9** and *N*-acyl-*N*′-carbamoylhydrazines **12** and **13** upon treatment with aromatic aldehydes, acid chlorides and isocyanates, respectively. Further cyclizations to potentially active 1,3,4-oxadiazoles **10**, **11**, **14** and **15** were performed under dehydration conditions.

4. Experimental

4.1. General

The melting points were determined in open capillary tubes on a Büchi B-540 melting point apparatus and are

uncorrected. Infrared spectra were recorded on a Perkin Elmer Spectrum One spectrometer using potassium bromide pellets. ^{1}H NMR spectra were recorded at 270 MHz on a Jeol-270 spectrometer, at 300 MHz on a Varian Unity Inova spectrometer and at 500 MHz on a Bruker Avance 500 spectrometer; ^{13}C NMR spectra were registered at 67.5, 75 and 125 MHz, respectively. Chemical shifts, expressed in parts per million, were relative to tetramethylsilane (TMS). ^{15}N NMR spectra (50.69 MHz) were obtained on a Bruker Avance 500 spectrometer using a 'directly' detecting broadband observe probe and were referenced against neat, external nitromethane (coaxial capillary). Mass spectra were recorded on a Agilent 110 (series MS with VL) instrument. For thin-layer chromatographic (TLC) analyses, Merck precoated TLC plates (silica gel 60 F254) were used.

4.2. Synthetic procedures

4.2.1. Synthesis of 1-amino-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one 3. A mixture of 1-carbamoylmethyl-2,3,3-trimethyl-3*H*-indolinium chloride **1** (2.53 g, 10 mmol) and hydrazine hydrate (55%, 10 mL) was heated at 70 °C for 0.5 h. The reaction mixture was cooled to room temperature, the liquid layer was poured out from the resulting resinous substance, and the latter was crystallized from diethyl ether. The obtained crystalline material was recrystallized from ethanol to yield 1.85 g (80%) of **3**. Mp 100–101 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 1.15 (3H, s, 9-CH_3), 1.39 (3H, s, 9-CH_3), 1.40 (3H, s, 9a-CH_3), 3.75–3.90 (2H, AB-q, ^2J=16.5 Hz, NCH_2), 4.44 (2H, s, NH_2), 6.81–6.89 (2H, m, 5-H, 7-H), 7.01–7.12 (2H, m, 6-H, 8-H). ^{13}C NMR (125 MHz, DMSO-d_6): δ 17.1 (9a-CH_3), 23.6 (9-CH_3), 26.9 (9-CH_3), 47.5 (C-9), 52.0 (C-3), 93.0 (C-9a), 111.7 (C-5), 121.3 (C-7), 122.1 (C-8), 127.4 (C-6), 139.2 (C-8a), 150.5 (C-4a), 172.1 (C=O). ^{15}N NMR (50.69 MHz, DMSO-d_6): δ −224.6 (N-1), −299.1 (N-4), −317.6 (t, ^1J=68.9 Hz, NH_2). IR (KBr, cm^{-1}): ν_{N-H}=3330; ν_{N-H}=3210; $\nu_{C=O}$=1705. MS *m*/*z* (%): 232 (M+H$^+$, 100). Anal. Calcd for $C_{13}H_{17}N_3O$: C 67.51; H 7.41; N 18.17. Found: C 67.33; H 7.31; N 18.39.

4.3. General procedure for the condensation of 1-amino-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one (3) with aromatic aldehydes

To a solution of **3** (0.93 g, 4 mmol) and appropriate benzaldehyde (4.4 mmol) in absolute ethanol (20 mL) three drops of piperidine were added and the mixture was refluxed for 2 h, after which the mixture was cooled to room temperature. The reaction mixture was poured into water (40 mL) and extracted with diethyl ether (3×20 mL). The combined organic extracts were washed with water (20 mL), dried over anhydrous sodium sulfate. Evaporation of the solvent gave a residue, which was crystallized from absolute ethanol to give the corresponding 1-arylidenamino-imidazo[1,2-*a*]indolones (**6a–d**).

4.3.1. 1-{[(1*E*)-(4-Fluorophenyl)methylene]amino}-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one 6a. Yield 60%. Mp 158–159 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (3H, s, 9-CH_3), 1.34 (3H, s, 9-CH_3), 1.76 (3H, s, 9a-CH_3), 3.98 (1H, d, *J*=16.6 Hz, C*H*(H)), 4.04 (1H, d, *J*=16.6 Hz, CH(*H*)), 6.77–7.74 (8H, m, aromatic protons), 8.96 (1H, s, N=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.4 (9a-CH_3), 24.5 (9-CH_3), 27.2 (9-CH_3), 48.7 (9-C), 53.5 (CH_2), 94.6 (9a-C), 111.9, 115.7 (d, *J*=22.0 Hz, 2×CH), 122.2, 122.3, 127.9, 129.3 (d, *J*=8.5 Hz, 2×CH), 130.8 (d, *J*=3.1 Hz, C), 139.2, 149.9 (Ar-C), 154.6 (C=N), 162.5 (d, *J*=251.4 Hz, C–F), 168.9 (C=O). IR (KBr, cm^{-1}): $\nu_{C=O}$=1703; $\nu_{C=N}$=1607. MS *m*/*z* (%): 338 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{20}FN_3O$: C 71.20; H 5.97; N 12.45. Found: C 71.47; H 5.63; N 12.14.

4.3.2. 1-{[(1*E*)-(4-Chlorophenyl)methylene]amino}-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one 6b. Yield 44%. Mp 168–169 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.30 (3H, s, 9-CH_3), 1.31 (3H, s, 9-CH_3), 1.73 (3H, s, 9a-CH_3), 3.98 (1H, d, *J*=16.2 Hz, C*H*(H)), 3.99 (1H, d, *J*=16.2 Hz, CH(*H*)), 6.74–7.65 (8H, m, aromatic protons), 8.99 (1H, s, N=CH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 19.5 (9a-CH_3), 24.6 (9-CH_3), 27.1 (9-CH_3), 48.7 (9-C), 53.5 (CH_2), 94.6 (9a-C), 111.9, 122.19, 122.3, 127.9, 128.6 (2×C), 128.9 (2×C), 133.2, 136.5, 139.3, 149.9 (Ar-C), 154.2 (C=N), 169.6 (C=O). IR (KBr, cm^{-1}): $\nu_{C=O}$=1700; $\nu_{C=N}$=1603. MS *m*/*z* (%): 356/54 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{20}ClN_3O$: C 67.89; H 5.70; N 11.88. Found: C 67.58; H 5.35; N 11.73.

4.3.3. 1-{[(1*E*)-(4-Bromophenyl)methylene]amino}-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one 6c. Yield 54%. Mp 170–171 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.30 (3H, s, 9-CH_3), 1.32 (3H, s, 9-CH_3), 1.74 (3H, s, 9a-CH_3), 3.98 (1H, d, *J*=16.5 Hz, C*H*(H)), 3.98 (1H, d, *J*=16.5 Hz, CH(*H*)), 6.75–7.66 (8H, m, aromatic protons), 8.98 (1H, s, N=CH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 19.5 (9a-CH_3), 24.6 (9-CH_3), 27.1 (9-CH_3), 48.8 (9-C), 53.6 (CH_2), 94.7 (9a-C), 112.0, 122.2, 122.3, 124.9, 127.9, 128.8 (2×C), 131.9 (2×C), 133.7, 139.3, 149.9 (Ar-C), 154.3 (C=N), 169.6 (C=O). IR (KBr, cm^{-1}): $\nu_{C=O}$=1703; $\nu_{C=N}$=1595. MS *m*/*z* (%): 400/398 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{20}BrN_3O$: C 60.31; H 5.06; N 10.55. Found: C 59.98; H 5.35; N 10.78.

4.3.4. 1-{[(1*E*)-(4-[Dimethylamino]phenyl)methylene]-amino}-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one 6d. Yield 86%. Mp 205–206 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.28 (3H, s, 9-CH_3), 1.31 (3H, s, 9-CH_3), 1.73 (3H, s, 9a-CH_3), 2.99 (6H, s, $N(CH_3)_2$), 3.96 (2H, s, CH_2), 6.66–7.60 (8H, m, aromatic protons), 8.78 (1H, s, N=CH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 19.6 (9a-CH_3), 24.9 (9-CH_3), 27.0 (9-CH_3), 40.1 ($N(CH_3)_2$), 48.7 (9-C), 53.7 (CH_2), 94.3 (9a-C), 111.6 (2×C), 111.9, 121.9, 122.2, 122.4, 127.8, 128.9 (2×C), 139.6, 150.1, 152.0 (Ar-C), 157.0 (C=N), 168.4 (C=O). IR (KBr, cm^{-1}): $\nu_{C=O}$=1700; $\nu_{C=N}$=1602. MS *m*/*z* (%): 363 (M+H$^+$, 100). Anal. Calcd for $C_{22}H_{26}N_4O$: C 72.90; H 7.23; N 15.46. Found: C 72.64; H 6.99; N 15.70.

4.4. General procedure for the acylation of 1-amino-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one (3) with acetyl and benzoyl chlorides

To a stirred solution of **3** (1.16 g, 5 mmol) in dioxane (7.5 mL), a solution of acetyl chloride or the appropriate benzoyl chloride (6.5 mmol) in dioxane (10 mL) was added dropwise at room temperature. The formed crystals (**8a** and

8e) were separated by filtration, or the formed resinous substance (**8b–d**, **8f**) was separated by decantation of the solvent, and dissolved in water (25 mL). Solid $NaHCO_3$ was added in portions to basify the mixture to pH 8–9. The mixture was extracted with diethyl ether (3×25 mL), the combined extracts were washed with water (25 mL) and dried over anhydrous sodium sulfate. The solvent was evaporated in vacuo and the residue was crystallized from ethanol to give the corresponding 1-(*N'*-acylamino)-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-ones (**8a–f**).

4.4.1. *N*-(9,9,9a-Trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)acetamide 8a. Yield 85%. Mp 201–202 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.10 (3H, s, 9-CH_3), 1.28 (3H, s, 9-CH_3), 1.41 (3H, s, 9a-CH_3), 1.48 (3H, s, CH_3CO), 3.80 (1H, d, J=16.5 Hz, C*H*(H)), 3.93 (1H, d, J=16.5 Hz, CH(*H*)), 6.67–7.30 (4H, m, aromatic protons), 8.22 (1H, s, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 16.9 (9a-CH_3), 20.0 (9-CH_3), 23.4 (9-CH_3), 27.4 (C=OCH_3), 48.4 (9-C), 52.7 (CH_2), 95.3 (9a-C), 112.0, 122.3, 122.5, 127.9, 138.7, 149.6 (Ar-C), 168.4 (C=O), 172.5 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3250; $\nu_{C=O}$=1730; $\nu_{C=O}$=1680. MS *m/z* (%): 274 (M+H$^+$, 100). Anal. Calcd for $C_{15}H_{19}N_3O_2$: C 65.91; H 7.01; N 15.37. Found: C 65.54; H 7.39; N 15.12.

4.4.2. 2-Chloro-*N*-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)benzamide 8b. Yield 45%. Mp 177–178 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.24 (3H, s, 9-CH_3), 1.48 (3H, s, 9-CH_3), 1.67 (3H, s, 9a-CH_3), 3.85 (1H, d, J=16.7 Hz, C*H*(H)), 4.02 (1H, d, J=16.7 Hz, CH(*H*)), 6.72–7.73 (9H, m, aromatic protons and NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 17.7 (9a-CH_3), 24.0 (9-CH_3), 27.6 (9-CH_3), 48.5 (9-C), 52.4 (CH_2), 95.2 (9a-C), 112.1, 122.2, 122.3, 127.3, 128.0, 130.1, 130.5, 130.8, 132.0, 132.6, 138.5, 149.8 (Ar-C), 164.7 (C=O), 170.8 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3290; $\nu_{C=O}$=1730; $\nu_{C=O}$=1690. MS *m/z* (%): 372/70 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{20}ClN_3O_2$: C 64.95; H 5.45; N 11.36. Found: C 65.20; H 5.11; N 11.17.

4.4.3. 4-Chloro-*N*-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)benzamide 8c. Yield 47%. Mp 202–203 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.17 (3H, s, 9-CH_3), 1.29 (3H, s, 9-CH_3), 1.47 (3H, s, 9a-CH_3), 3.66 (1H, d, J=16.6 Hz, C*H*(H)), 3.91 (1H, d, J=16.6 Hz, CH(*H*)), 6.64–7.26 (8H, m, aromatic protons), 8.93 (1H, s, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 18.0 (9a-CH_3), 23.8 (9-CH_3), 26.9 (9-CH_3), 48.4 (9-C), 52.5 (CH_2), 95.2 (9a-C), 112.2, 121.9, 122.4, 127.9, 128.6, 128.8 (2×C), 128.9 (2×C), 138.6, 138.9, 149.2 (Ar-C), 164.4 (C=O), 172.3 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3250; $\nu_{C=O}$=1730; $\nu_{C=O}$=1695. MS *m/z* (%): 372/70 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{20}ClN_3O_2$: C 64.95; H 5.45; N 11.36. Found: C 65.33; H 5.09; N 11.21.

4.4.4. 2,5-Difluoro-*N*-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)benzamide 8d. Yield 40%. Mp 203–204 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.24 (3H, s, 9-CH_3), 1.52 (3H, s, 9-CH_3), 1.64 (3H, s, 9a-CH_3), 3.92 (1H, d, J=16.3 Hz, C*H*(H)), 4.05 (1H, d, J=16.3 Hz, CH(*H*)), 6.73–7.77 (7H, m, aromatic protons), 8.16 (1H, s, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 17.4 (9a-CH_3), 23.6 (9-CH_3), 27.7 (9-CH_3), 48.6 (9-C), 52.4 (CH_2), 95.4 (9a-C), 112.2, 117.8, 118.8, 121.3, 121.4, 122.2, 125.8, 127.6, 138.4 (2×C), 149.8 (2×C) (Ar-C), 160.3 (C=O), 170.6 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3224; $\nu_{C=O}$=1737; $\nu_{C=O}$=1717. MS *m/z* (%): 372 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{19}F_2N_3O_2$: C 64.68; H 5.16; N 11.31. Found: C 64.33; H 5.37; N 11.52.

4.4.5. *N*-(9,9,9a-Trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)benzamide 8e. Yield 64%. Mp 168–169 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.20 (3H, s, 9-CH_3), 1.36 (3H, s, 9-CH_3), 1.52 (3H, s, 9a-CH_3), 3.70 (1H, d, J=16.5 Hz, C*H*(H)), 3.97 (1H, d, J=16.5 Hz, CH(*H*)), 6.67–7.67 (9H, m, aromatic protons), 8.92 (1H, s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.9 (9a-CH_3), 23.8 (9-CH_3), 26.9 (9-CH_3), 48.4 (9-C), 52.4 (CH_2), 95.0 (9a-C), 112.1, 121.9, 122.3, 127.4 (2×C), 127.8, 128.3 (2×C), 130.8, 131.9, 138.9, 149.3 (Ar-C), 165.6 (C=O), 172.0 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3266; $\nu_{C=O}$=1724; $\nu_{C=O}$=1687. MS *m/z* (%): 336 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{21}N_3O_2$: C 71.62; H 6.31; N 12.53. Found: C 71.25; H 6.43; N 12.72.

4.4.6. 2-Bromo-*N*-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)benzamide 8f. Yield 41%. Mp 173–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (3H, s, 9-CH_3), 1.49 (3H, s, 9-CH_3), 1.70 (3H, s, 9a-CH_3), 3.87 (1H, d, J=16.6 Hz, C*H*(H)), 4.04 (1H, d, J=16.6 Hz, CH(*H*)), 6.73–7.59 (9H, m, aromatic protons and NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.8 (9a-CH_3), 24.1 (9-CH_3), 27.6 (9-CH_3), 48.6 (9-C), 52.3 (CH_2), 95.2 (9a-C), 112.1, 119.3, 122.2, 122.3, 127.6, 128.0, 129.9, 131.9, 133.3, 135.2, 138.5, 149.8 (Ar-C), 165.7 (C=O), 170.8 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3257; $\nu_{C=O}$=1726; $\nu_{C=O}$=1684. MS *m/z* (%): 416/14 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{20}BrN_3O_2$: C 57.98; H 4.87; N 10.14. Found: C 57.58; H 5.12; N 9.98.

4.5. General procedure for the reaction of 1-amino-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-one (3) with isocyanates

To a solution of **3** (1.0 g, 4.32 mmol) in dry toluene (10 mL), the appropriate phenylisocyanate (4.32 mmol) was added and the mixture was heated at 80 °C for 2 h. Then the reaction mixture was cooled to room temperature, the precipitated solid was filtered off and recrystallized from ethanol to give the corresponding 1-(1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-on-1-yl)-3-phenylureas (**12a–d**).

4.5.1. 1-Phenyl-3-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)urea 12a. Yield 38%. Mp 182–183 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 1.15 (3H, s, 9-CH_3), 1.42 (3H, s, 9-CH_3), 1.51 (3H, s, 9a-CH_3), 3.92 (2H, s, NCH_2CO), 6.88–7.41 (9H, m, aromatic protons), 8.26 (1H, br s, NH), 8.79 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 17.3 (9a-CH_3), 23.0 (9-CH_3), 27.3 (9-CH_3), 47.8 (9-C), 51.7 (CH_2), 93.0 (9a-C), 112.0, 118.0 (2×C), 121.7, 121.9, 122.2, 127.6, 128.7 (2×C), 138.9, 139.3, 150.1 (Ar-C), 153.7 (C=O), 171.4 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3312; $\nu_{C=O}$=1711; $\nu_{C=O}$=1687. MS *m/z* (%): 351 (M+H$^+$, 100). Anal.

Calcd for $C_{20}H_{22}N_4O_2$: C 68.55; H 6.33; N 15.99. Found: C 68.32; H 6.65; N 15.97.

4.5.2. 1-(2-Fluorophenyl)-3-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)urea 12b. Yield 69%. Mp 194–196 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 1.15 (3H, s, 9-CH_3), 1.43 (3H, s, 9-CH_3), 1.51 (3H, s, 9a-CH_3), 3.94 (2H, s, NCH_2CO), 6.89–7.43 (8H, m, aromatic protons), 8.24 (1H, br s, NH), 8.79 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 17.8 (9a-CH_3), 25.6 (9-CH_3), 27.8 (9-CH_3), 48.8 (9-C), 52.2 (CH_2), 93.7 (9a-C), 112.7, 115.5, 115.7, 120.8, 122.4, 122.8, 123.2, 125.1, 127.8, 128.3, 139.5, 150.7 (Ar-C), 153.8 (C=O), 171.9 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3325; $\nu_{C=O}$=1712; $\nu_{C=O}$=1690. MS *m*/*z* (%): 369 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{21}FN_4O_2$: C 65.20; H 5.75; N 15.21. Found: C 65.03; H 5.92; N 15.52.

4.5.3. 1-(2-Chlorophenyl)-3-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)urea 12c. Yield 52%. Mp 199–200 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 1.17 (3H, s, 9-CH_3), 1.44 (3H, s, 9-CH_3), 1.55 (3H, s, 9a-CH_3), 3.98 (2H, s, NCH_2CO), 6.90–8.16 (8H, m, aromatic protons), 8.34 (1H, br s, NH), 8.93 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 17.1 (9a-CH_3), 23.7 (9-CH_3), 27.3 (9-CH_3), 47.7 (9-C), 51.5 (CH_2), 93.2 (9a-C), 112.0, 120.4, 121.4, 121.8, 122.2, 123.4, 127.6 (2×C), 129.2, 135.5, 138.8, 150.1 (Ar-C), 153.4 (C=O), 172.1 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3365; $\nu_{C=O}$=1749; $\nu_{C=O}$=1697. MS *m*/*z* (%): 387/85 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{21}ClN_4O_2$: C 62.42; H 5.50; N 14.56. Found: C 62.13; H 5.72; N 14.78.

4.5.4. 1-(4-Chlorophenyl)-3-(9,9,9a-trimethyl-2-oxo-2,3,9,9a-tetrahydro-1*H*-imidazo[1,2-*a*]indol-1-yl)urea 12d. Yield 67%. Mp 211–212 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 1.14 (3H, s, 9-CH_3), 1.41 (3H, s, 9-CH_3), 1.50 (3H, s, 9a-CH_3), 3.92 (2H, s, CH_2), 6.88–7.46 (8H, m, aromatic protons), 8.32 (1H, br s, NH), 8.96 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 17.3 (9a-CH_3), 22.8 (9-CH_3), 27.3 (9-CH_3), 47.8 (9-C), 51.6 (CH_2), 93.0 (9a-C), 112.0, 119.5, 119.6, 121.7, 121.8, 125.5, 127.6, 128.5 (2×C), 138.4, 138.9, 151.1 (Ar-C), 153.6 (C=O), 171.4 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3362; $\nu_{C=O}$=1723; $\nu_{C=O}$=1681. MS *m*/*z* (%): 387/85 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{21}ClN_4O_2$: C 62.42; H 5.50; N 14.56. Found: C 62.11; H 5.89; N 14.34.

4.6. General procedure for the reduction of 1-(*N*-substituted amino)-1,2,3,9a-tetrahydro-9,9,9a-trimethylimidazo[1,2-*a*]indol-2(9*H*)-ones (6a–d, 8a–f, 12a–d) with sodium borohydride

To a solution of an appropriate *N*′-substituted 1-amino-1,2,3,9a-tetrahydroimidazo[1,2-*a*]indol-2(9*H*)-one (**6a–d**, **8a–f**, **12a–d**) (1.35 mmol) in 20 mL of ethanol (**6a–d**, **8a–f**) or 20 mL of tetrahydrofuran (**12a–d**), sodium borohydride (0.153 g, 4.05 mmol) was added. The mixture was heated at 70 °C for the indicated period, then cooled to room temperature, poured into water (30 mL) and extracted with ether (3×20 mL). The combined extracts were washed with water (20 mL), dried over sodium sulfate, the solvent removed under reduced pressure, and the residue crystallized from ethanol to obtain the various *N*′-substituted 2,3-dihydro-2,3,3-trimethyl-1*H*-indole-1-acetic acid *N*′-substituted hydrazides (**7a–d**, **9a–f**, **13a–d**).

4.6.1. *N*′-[(1*E*)-(4-Fluorophenyl)methylene]-2-(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetohydrazide 7a. Yield 45%. Mp 148–150 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13 (3H, s, 3-CH_3), 1.25 (3H, d, J=6.6 Hz, 2-CH_3), 1.34 (3H, s, 3-CH_3), 3.17 (1H, q, J=6.6 Hz, 2-CH), 3.77 (2H, s, CH_2), 6.50–7.75 (8H, m, aromatic protons), 8.06 (1H, s, NH), 9.73 (1H, s, N=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.9 (2-CH_3), 23.6 (3-CH_3), 25.8 (3-CH_3), 43.1 (3-C), 53.1 (CH_2), 72.3 (CH), 108.7, 116.1 (d, J=22.1 Hz, 2×CH), 120.9, 122.5, 128.0, 129.8 (d, J=3.0 Hz, C), 129.9 (d, J=8.6 Hz, 2×CH), 139.5, 148.0 (Ar-C), 150.3 (C=N), 164.4 (d, J=251.4 Hz, C–F), 167.1 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3190; $\nu_{C=O}$=1685; $\nu_{C=N}$=1606. MS *m*/*z* (%): 340 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{22}FN_3O$: C 70.77; H 6.53; N 12.38. Found: C 70.43; H 6.67; N 12.01.

4.6.2. *N*′-[(1*E*)-(4-Chlorophenyl)methylene]-2-(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetohydrazide 7b. Yield 26%. Mp 147–148 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.14 (3H, s, 3-CH_3), 1.25 (3H, d, J=6.6 Hz, 2-CH_3), 1.34 (3H, s, 3-CH_3), 3.18 (1H, q, J=6.6 Hz, 2-CH), 3.77 (2H, s, CH_2), 6.50–7.66 (8H, m, aromatic protons), 8.06 (1H, s, NH), 9.80 (1H, s, N=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.6 (2-CH_3), 23.2 (3-CH_3), 25.4 (3-CH_3), 42.8 (3-C), 52.7 (CH_2), 71.9 (CH), 108.3, 120.6, 122.1, 127.7, 128.8 (2×C), 128.9 (2×C), 131.7, 136.5, 139.2, 147.6 (Ar-C), 149.9 (C=N), 166.9 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3190; $\nu_{C=O}$=1680; $\nu_{C=N}$=1607. MS *m*/*z* (%): 358/56 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{22}ClN_3O$: C 67.50; H 6.23; N 11.81. Found: C 67.32; H 6.65; N 11.41.

4.6.3. *N*′-[(1*E*)-(4-Bromophenyl)methylene]-2-(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetohydrazide 7c. Yield 37%. Mp 143–144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13 (3H, s, 3-CH_3), 1.25 (3H, d, J=6.6 Hz, 2-CH_3), 1.34 (3H, s, 3-CH_3), 3.17 (1H, q, J=6.6 Hz, 2-CH), 3.78 (2H, s, CH_2), 6.51–8.05 (9H, m, aromatic protons and NH), 9.76 (1H, s, N=CH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.6 (2-CH_3), 23.3 (3-CH_3), 25.5 (3-CH_3), 42.8 (3-C), 52.8 (CH_2), 71.9 (CH), 108.3, 120.7, 122.2, 124.9, 127.7, 129.1 (2×C), 131.9 (2×C), 132.2, 139.2, 147.6 (Ar-C), 149.9 (C=N), 166.9 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3204; $\nu_{C=O}$=1677; $\nu_{C=N}$=1605. MS *m*/*z* (%): 402/00 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{22}BrN_3O$: C 60.01; H 5.54; N 10.50. Found: C 60.33; H 5.72; N 10.37.

4.6.4. *N*′-[(1*E*)-(4-[Dimethylamino]phenyl)methylene]-2-(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetohydrazide 7d. Yield 64%. Mp 153–154 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.14 (3H, s, 3-CH_3), 1.25 (3H, d, J=6.6 Hz, 2-CH_3), 1.34 (3H, s, 3-CH_3), 3.00 (6H, s, $N(CH_3)_2$), 3.17 (1H, q, J=6.6 Hz, 2-CH), 3.76 (2H, s, CH_2), 6.52–7.86 (9H, m, aromatic protons and NH), 9.53 (1H, s, N=CH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 12.6 (2-CH_3), 23.3 (3-CH_3), 25.4 (3-CH_3), 40.1 ($N(CH_3)_2$), 42.8 (3-C), 52.7 (CH_2), 71.9 (CH), 106.5, 111.5 (2×C), 120.4, 120.6, 122.0, 127.7, 129.3 (2×C), 139.2, 149.5, 150.0, 151.9, 166.0 (C=O). IR (KBr, cm^{-1}): ν_{N-H}=3195; $\nu_{C=O}$=1690; $\nu_{C=N}$=1609. MS

m/z (%): 365 ($M+H^+$, 100). Anal. Calcd for $C_{22}H_{28}N_4O$: C 72.50; H 7.74; N 15.37. Found: C 72.84; H 7.91; N 15.12.

4.6.5. *N′*-Acetyl-2-(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetohydrazide 9a. Yield 65%. Mp 172–173 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.09 (3H, s, CH_3), 1.24 (3H, d, $J=6.6$ Hz, CH_3), 1.31 (3H, s, CH_3), 2.03 (3H, s, $COCH_3$), 3.16 (1H, q, $J=6.6$ Hz, CH), 3.72 (1H, d, $J=17.8$ Hz, C*H*(H)CO), 3.76 (1H, d, $J=17.8$ Hz, CH(*H*)CO), 6.48–7.25 (4H, m, aromatic protons), 9.35 (1H, s, NH), 9.62 (1H, s, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 12.5 (2-CH_3), 20.4 (3-CH_3), 23.0 (3-CH_3), 25.4 (*C*H_3CO), 42.8 (3-C), 51.7 (CH_2), 71.9 (CH), 107.9, 120.2, 122.0, 127.5, 139.1, 149.8 (Ar-C), 167.2 (C=O), 167.6 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3280$; $\nu_{C=O}=1710$; $\nu_{C=O}=1675$. MS *m/z* (%): 276 ($M+H^+$, 100). Anal. Calcd for $C_{15}H_{21}N_3O_2$: C 65.43; H 7.69; N 15.26. Found: C 65.11; H 7.82; N 15.54.

4.6.6. 2-Chloro-*N′*-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]benzohydrazide 9b. Yield 75%. Mp 169–170 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.14 (3H, s, CH_3), 1.30 (3H, d, $J=6.6$ Hz, CH_3), 1.34 (3H, s, CH_3), 3.18 (1H, q, $J=6.6$ Hz, CH), 3.76 (1H, d, $J=17.0$ Hz, C*H*(H)CO), 3.80 (1H, d, $J=17.0$ Hz, CH(*H*)CO), 6.53–7.78 (8H, m, aromatic protons), 9.23 (1H, d, $J=6.12$ Hz, NH), 9.46 (1H, d, $J=6.12$ Hz, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 12.7 (2-CH_3), 23.2 (3-CH_3), 25.5 (3-CH_3), 42.9 (3-C), 52.1 (CH_2), 72.1 (CH), 108.2, 120.4, 122.1, 127.1, 127.7, 130.5, 130.8, 131.3, 131.5, 132.3, 139.2, 149.9 (Ar-C), 162.4 (C=O), 167.3 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3350$; $\nu_{N-H}=3220$; $\nu_{C=O}=1703$; $\nu_{C=O}=1671$. MS *m/z* (%): 374/72 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{22}ClN_3O_2$: C 64.60; H 5.96; N 11.30. Found: C 64.91; H 6.13; N 11.05.

4.6.7. 4-Chloro-*N′*-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]benzohydrazide 9c. Yield 62%. Mp 174–175 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.13 (3H, s, CH_3), 1.27 (3H, d, $J=6.4$ Hz, CH_3), 1.34 (3H, s, CH_3), 3.19 (1H, q, $J=6.4$ Hz, CH), 3.78 (1H, d, $J=18.0$ Hz, C*H*(H)CO), 3.81 (1H, d, $J=18.0$ Hz, CH(*H*)CO), 6.52–7.75 (8H, m, aromatic protons), 9.35 (1H, d, $J=4.8$ Hz, NH), 9.89 (1H, d, $J=4.8$ Hz, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 12.6 (2-CH_3), 23.2 (3-CH_3), 25.5 (3-CH_3), 42.9 (3-C), 52.2 (CH_2), 72.1 (CH), 108.0, 120.5, 122.5, 127.6, 128.7 (2×C), 128.9 (2×C), 129.5, 138.6, 139.2, 149.8 (Ar-C), 163.6 (C=O), 168.7 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3220$; $\nu_{C=O}=1696$; $\nu_{C=O}=1684$. MS *m/z* (%): 374/72 ($M+H^+$, 73), 160 (100). Anal. Calcd for $C_{20}H_{22}ClN_3O_2$: C 64.60; H 5.96; N 11.30. Found: C 64.93; H 5.79; N 11.12.

4.6.8. 2,5-Difluoro-*N′*-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]benzohydrazide 9d. Yield 64%. Mp 114–115 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.14 (3H, s, CH_3), 1.27 (3H, d, $J=6.8$ Hz, CH_3), 1.34 (3H, s, CH_3), 3.19 (1H, q, $J=6.8$ Hz, CH), 3.80 (1H, d, $J=17.8$ Hz, C*H*(H)), 3.83 (1H, d, $J=17.8$ Hz, CH(*H*)), 6.54–7.79 (7H, m, aromatic protons), 9.28 (1H, d, $J=6.0$ Hz, NH), 9.44 (1H, d, $J=6.0$ Hz, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 12.6 (2-CH_3), 23.2 (3-CH_3), 25.4 (3-CH_3), 42.9 (3-C), 52.0 (CH_2), 72.1 (CH), 108.0, 117.5, 117.8, 118.2, 120.4, 120.9, 122.2, 127.6, 139.2, 149.9, 156.4, 158.4 (Ar-C), 160.8 (C=O), 167.2 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3205$; $\nu_{C=O}=1700$; $\nu_{C=O}=1684$. MS *m/z* (%): 374 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{21}F_2N_3O_2$: C 64.33; H 5.67; N 11.25. Found: C 64.05; H 5.81; N 11.42.

4.6.9. *N′*-[(2,3,3-Trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]benzohydrazide 9e. Yield 66%. Mp 125–126 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 1.11 (3H, s, CH_3), 1.25 (3H, d, $J=6.8$ Hz, CH_3), 1.31 (3H, s, CH_3), 3.16 (1H, q, $J=6.8$ Hz, CH), 3.76 (1H, d, $J=17.8$ Hz, C*H*(H)), 3.83 (1H, d, $J=17.8$ Hz, CH(*H*)), 6.45–7.85 (9H, m, aromatic protons), 9.43 (1H, d, $J=6.0$ Hz, NH), 9.73 (1H, d, $J=6.0$ Hz, NH). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 12.6 (2-CH_3), 23.2 (3-CH_3), 25.5 (3-CH_3), 42.9 (3-C), 52.1 (CH_2), 72.1 (CH), 108.1, 120.4, 122.1, 127.3 (2×C), 127.6, 128.6 (2×C), 131.2, 132.3, 139.2, 149.9 (Ar-C), 164.3 (C=O), 167.9 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3257$; $\nu_{C=O}=1697$; $\nu_{C=O}=1684$. MS *m/z* (%): 338 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{23}N_3O_2$: C 71.19; H 6.87; N 12.45. Found: C 71.01; H 7.19; N 12.17.

4.6.10. 2-Bromo-*N′*-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]benzohydrazide 9f. Yield 70%. Mp 167–168 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.13 (3H, s, CH_3), 1.28 (3H, d, $J=6.6$ Hz, CH_3), 1.33 (3H, s, CH_3), 3.18 (1H, q, $J=6.6$ Hz, CH), 3.71 (1H, d, $J=17.8$ Hz, C*H*(H)), 3.79 (1H, d, $J=17.8$ Hz, CH(*H*)), 6.52–7.62 (8H, m, aromatic protons), 9.14 (1H, br s, NH), 9.43 (1H, br s, NH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 12.6 (2-CH_3), 23.2 (3-CH_3), 25.5 (3-CH_3), 42.8 (3-C), 52.0 (CH_2), 72.1 (CH), 108.2, 119.9, 120.4, 122.1, 127.5, 127.6, 130.2, 132.1, 133.6, 134.2, 139.2, 149.9 (Ar-C), 163.6 (C=O), 167.4 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3355$; $\nu_{N-H}=3213$; $\nu_{C=O}=1711$; $\nu_{C=O}=1671$. MS *m/z* (%): 418/16 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{22}BrN_3O_2$: C 57.70; H 5.33; N 10.09. Found: C 57.42; H 5.70; N 9.98.

4.6.11. *N*-Phenyl-2-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]hydrazinecarboxamide 13a. Yield 71%. Mp 189–190 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 0.98 (3H, s, 3-CH_3), 1.17 (3H, d, $J=6.3$ Hz, 2-CH_3), 1.24 (3H, s, 3-CH_3), 3.32 (1H, q, $J=6.3$ Hz, CH), 3.68 (1H, d, $J=16.8$ Hz, C*H*(H)), 3.88 (1H, d, $J=16.8$ Hz, CH(*H*)), 6.53–7.52 (9H, m, aromatic protons), 8.07 (1H, br s, NH), 8.66 (1H, br s, NH), 9.76 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 12.0 (2-CH_3), 22.9 (3-CH_3), 25.6 (3-CH_3), 42.1 (3-C), 47.8 (CH_2), 69.3 (CH), 107.3, 117.9, 118.3 (2×C), 121.4, 121.8, 126.9, 128.6 (2×C), 138.4, 139.5, 150.3 (Ar-C), 155.2 (C=O), 169.4 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3288$; $\nu_{C=O}=1725$; $\nu_{C=O}=1652$. MS *m/z* (%): 353 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{24}N_4O_2$: C 68.16; H 6.86; N 15.90. Found: C 68.45; H 7.11; N 15.56.

4.6.12. *N*-(2-Fluorophenyl)-2-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]hydrazinecarboxamide 13b. Yield 60%. Mp 178–179 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 0.98 (3H, s, 3-CH_3), 1.17 (3H, d, $J=6.6$ Hz, 2-CH_3), 1.24 (3H, s, 3-CH_3), 3.29 (1H, q, $J=6.6$ Hz, CH), 3.67 (1H, d, $J=16.9$ Hz, C*H*(H)), 3.87 (1H, d, $J=16.9$ Hz, CH(*H*)), 6.36–7.99 (8H, m, aromatic protons), 8.04 (1H, br s, NH), 8.51 (1H, br s, NH), 9.87 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 11.9 (2-CH_3), 22.9 (3-CH_3), 25.6 (3-CH_3), 42.1 (3-C), 47.9 (CH_2), 69.4 (CH), 107.2, 114.8, 115.1, 117.9, 120.9, 121.4, 124.4, 127.6, 129.1, 135.4,

138.7, 150.0 (Ar-C), 154.7 (C=O), 169.3 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3305$; $\nu_{C=O}=1727$; $\nu_{C=O}=1646$. MS *m/z* (%): 371 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{23}FN_4O_2$: C 64.85; H 6.26; N 15.13. Found: C 64.79; H 6.41; N 15.43.

4.6.13. *N*-(2-Chlorophenyl)-2-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]hydrazinecarboxamide 13c. Yield 86%. Mp 180–181 °C. ^1H NMR (270 MHz, DMSO-d_6): δ 0.98 (3H, s, 3-CH_3), 1.17 (3H, d, $J=6.6$ Hz, 2-CH_3), 1.24 (3H, s, 3-CH_3), 3.30 (1H, q, $J=6.6$ Hz, CH), 3.67 (1H, d, $J=16.6$ Hz, C*H*(H)), 3.89 (1H, d, $J=16.6$ Hz, CH(*H*)), 6.51–8.11 (8H, m, aromatic protons), 8.19 (1H, br s, NH), 9.14 (1H, br s, NH), 9.63 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 12.0 (2-CH_3), 23.0 (3-CH_3), 25.6 (3-CH_3), 42.1 (3-C), 48.0 (CH_2), 69.3 (CH), 107.3, 117.9, 120.9, 121.4, 121.8, 123.2, 126.9, 127.6, 129.1, 135.8, 138.4, 150.3 (Ar-C), 154.5 (C=O), 168.9 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3314$; $\nu_{C=O}=1724$; $\nu_{C=O}=1659$. MS *m/z* (%): 389/87 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{23}ClN_4O_2$: C 62.09; H 5.99; N 14.48. Found: C 61.78; H 5.75; N 14.59.

4.6.14. *N*-(4-Chlorophenyl)-2-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)acetyl]hydrazinecarboxamide 13d. Yield 20%. Mp 172–173 °C. ^1H NMR (270 MHz, DMSO-d_6): δ 0.97 (3H, s, 3-CH_3), 1.16 (3H, d, $J=6.6$ Hz, 2-CH_3), 1.23 (3H, s, 3-CH_3), 3.29 (1H, q, $J=6.6$ Hz, CH), 3.68 (1H, d, $J=16.8$ Hz, C*H*(H)), 3.87 (1H, d, $J=16.8$ Hz, CH(*H*)), 6.52–7.54 (8H, m, aromatic protons), 8.15 (1H, br s, NH), 8.84 (1H, br s, NH), 9.75 (1H, br s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 11.9 (2-CH_3), 22.9 (3-CH_3), 25.6 (3-CH_3), 47.8 (3-C), 64.9 (CH_2), 69.3 (CH), 107.3, 117.9, 119.8, 121.4, 125.3, 126.9, 128.2, 128.4 (2×C), 138.3, 138.6, 150.3 (Ar-C), 155.1 (C=O), 169.4 (C=O). IR (KBr, cm^{-1}): $\nu_{N-H}=3293$; $\nu_{C=O}=1700$; $\nu_{C=O}=1655$. MS *m/z* (%): 389/87 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{23}ClN_4O_2$: C 62.09; H 5.99; N 14.48. Found: C 62.13; H 6.18; N 14.72.

4.7. General procedure for the synthesis of 1-(1,3,4-oxadiazol-2-yl)methylindole derivatives (10c,d,f, 11c,d,f, 14a–c, 15a–c)

To a stirred suspension of appropriate hydrazide (**8c**,**d**,**f**, **9c**,**d**,**f**, **12a**–**c**, **13a**–**c**) (1 mmol) in dichloromethane (12 mL) were added triphenylphosphine (1.57 mmol), carbon tetrachloride (5 mmol), triethylamine (1.57 mmol), and the mixture was heated to reflux for 3 h. Then the mixture was cooled to room temperature, poured into water (15 mL) and extracted with dichloromethane (3×15 mL). Combined organic layers were dried over sodium sulfate, the solvent evaporated under reduced pressure. The residue was chromatographed on a silica gel column with hexane/ethyl acetate 2:1 as eluent to yield 1,3,4-oxadiazoles (**10c**,**d**,**f**, **11c**,**d**,**f**, **14a**–**c**, **15a**–**c**).

4.7.1. 1-{[5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl]-methyl}-3,3-dimethyl-2-methyleneindoline 10c. Yield 90%. Mp 125–126 °C. ^1H NMR (270 MHz, DMSO-d_6): δ 1.21 (6H, s, 2×3-CH_3), 4.01 (1H, d, $J=2.2$ Hz, =C*H*(H)), 4.15 (1H, d, $J=2.2$ Hz, =CH(*H*)), 5.18 (2H, s, CH_2), 6.78–7.92 (8H, m, aromatic protons). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 30.4 (2×3-CH_3), 37.8 (CH_2), 44.5 (3-C), 76.8 (=CH_2), 106.8, 120.1, 122.7, 122.8, 128.3, 128.9 (2×C), 129.0, 130.4 (2×C), 137.5, 145.4 (Ar-C), 160.8 (2-C), 163.9, 164.3 (C–O–C). IR (KBr, cm^{-1}): $\nu_{C=N}=1655$. MS *m/z* (%): 354/52 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{18}N_3ClO$: C 68.28; H 5.16; N 11.94. Found: C 68.08; H 5.10; N 11.80.

4.7.2. 1-{[5-(2,5-Difluorophenyl)-1,3,4-oxadiazol-2-yl]-methyl}-3,3-dimethyl-2-methyleneindoline 10d. Yield 81%. Oil. ^1H NMR (270 MHz, DMSO-d_6): δ 1.31 (6H, s, 2×3-CH_3), 4.00 (1H, d, $J=2.2$ Hz, =C*H*(H)), 4.13 (1H, d, $J=2.2$ Hz, =CH(*H*)), 5.21 (2H, s, CH_2), 6.78–7.75 (7H, m, aromatic protons). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 29.7 (2×3-CH_3), 36.9 (CH_2), 43.8 (3-C), 76.1 (=CH_2), 106.1, 112.8, 115.3, 115.7, 119.1, 119.4, 120.9, 122.1, 127.5, 136.8, 142.1, 144.7 (Ar-C), 160.1 (2-C), 163.6, 163.7 (C–O–C). IR (KBr, cm^{-1}): $\nu_{C=N}=1655$. MS *m/z* (%): 354 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{17}N_3F_2O$: C 67.98; H 4.85; N 11.89. Found: C 67.53; H 4.56; N 11.53.

4.7.3. 1-{[5-(2-Bromophenyl)-1,3,4-oxadiazol-2-yl]-methyl}-3,3-dimethyl-2-methyleneindoline 10f. Yield 80%. Oil. ^1H NMR (270 MHz, DMSO-d_6): δ 1.31 (6H, s, 2×3-CH_3), 4.01 (1H, d, $J=2.2$ Hz, =C*H*(H)), 4.15 (1H, d, $J=2.2$ Hz, =CH(*H*)), 5.22 (2H, s, CH_2), 6.77–7.85 (8H, m, aromatic protons). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 29.7 (2×3-CH_3), 36.9 (CH_2), 43.7 (3-C), 76.2 (=CH_2), 106.2, 119.3, 120.7, 122.0, 124.5, 127.5, 128.3, 131.6, 133.4, 134.3, 136.8, 144.7 (Ar-C), 160.0 (2-C), 163.2, 163.4 (C–O–C). IR (KBr, cm^{-1}): $\nu_{C=N}=1652$. MS *m/z* (%): 398/96 ($M+H^+$, 50). Anal. Calcd for $C_{20}H_{18}N_3BrO$: C 60.62; H 4.58; N 10.60. Found: C 60.31; H 4.75; N 10.29.

4.7.4. 1-{[5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl]methyl}-2,3,3-trimethylindoline 11c. Yield 99%. Mp 121–122 °C. ^1H NMR (270 MHz, DMSO-d_6): δ 0.96 (3H, s, 3-CH_3), 1.24 (6H, m, 2-CH_3, 3-CH_3), 3.28 (1H, q, $J=6.5$ Hz, CH), 4.59 (1H, d, $J=16.8$ Hz, C*H*(H)), 4.87 (1H, d, $J=16.8$ Hz, CH(*H*)), 6.67–7.93 (8H, m, aromatic protons). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 11.8 (2-CH_3), 22.9 (3-CH_3), 25.3 (3-CH_3), 42.2 (3-C, CH_2), 68.5 (CH), 107.6, 118.7, 121.8, 122.1, 127.0, 128.2 (2×C), 129.7 (2×C), 136.7, 138.5, 148.9 (Ar-C), 163.4, 163.8 (C–O–C). IR (KBr, cm^{-1}): $\nu_{C=N}=1606$. MS *m/z* (%): 356/54 ($M+H^+$, 50). Anal. Calcd for $C_{20}H_{20}N_3ClO$: C 67.89; H 5.70; N 11.88. Found: C 67.55; H 5.35; N 11.69.

4.7.5. 1-{[5-(2,5-Difluorophenyl)-1,3,4-oxadiazol-2-yl]-methyl}-2,3,3-trimethylindoline 11d. Yield 80%. Mp 104–105 °C. ^1H NMR (270 MHz, DMSO-d_6): δ 0.96 (3H, s, 3-CH_3), 1.25 (6H, m, 2-CH_3, 3-CH_3), 3.29 (1H, q, $J=6.5$ Hz, CH), 4.61 (1H, d, $J=16.8$ Hz, C*H*(H)), 4.90 (1H, d, $J=16.8$ Hz, CH(*H*)), 6.66–7.76 (7H, m, aromatic protons). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 11.7 (3-CH_3), 22.8 (2-CH_3), 25.3 (3-CH_3), 39.3 (3-C), 42.1 (CH_2), 68.4 (CH), 107.5, 112.5, 115.5, 118.6, 119.0, 120.7, 121.7, 126.9, 138.4, 148.7, 156.9, 159.4 (Ar-C), 160.0, 164.1 (C–O–C). IR (KBr, cm^{-1}): $\nu_{C=N}=1604$. MS *m/z* (%): 356 ($M+H^+$, 100). Anal. Calcd for $C_{20}H_{19}N_3F_2O$: C 67.59; H 5.39; N 11.82. Found: C 67.15; H 5.26; N 11.45.

4.7.6. 1-{[5-(2-Bromophenyl)-1,3,4-oxadiazol-2-yl]-methyl}-2,3,3-trimethylindoline 11f. Yield 74%. Mp

124–125 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 0.95 (3H, s, 3-CH_3), 1.23 (6H, m, 2-CH_3, 3-CH_3), 3.34 (1H, q, J=6.5 Hz, CH), 4.61 (1H, d, J=16.8 Hz, C*H*(H)), 4.92 (1H, d, J=16.8 Hz, CH(*H*)), 6.66–7.84 (8H, m, aromatic protons). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 11.8 (2-CH_3), 22.9 (3-CH_3), 25.3 (3-CH_3), 42.2 (CH_2, 3-C), 68.3 (CH), 107.8, 118.7, 120.7, 121.7, 124.7, 127.1, 128.3, 131.7, 133.4, 134.2, 138.5, 148.2 (Ar-C), 163.2, 164.1 (C–O–C). IR (KBr, cm^{-1}): $\nu_{C=N}$=1602. MS *m*/*z* (%): 400/98 (M+H$^+$, 50). Anal. Calcd for $C_{20}H_{20}N_3BrO$: C 60.31; H 5.06; N 10.55. Found: C 60.80; H 5.51; N 10.35.

4.7.7. 5-[(3,3-Dimethyl-2-methylene-2,3-dihydro-1*H*-indol-1-yl)methyl]-*N*-phenyl-1,3,4-oxadiazol-2-amine 14a. Yield 30%. Oil. ^{1}H NMR (270 MHz, DMSO-d_6): δ 1.29 (6H, s, 2×3-CH_3), 3.98 (1H, d, J=2.0 Hz, =C*H*(H)), 4.11 (1H, d, J=2.0 Hz, =CH(*H*)), 4.99 (2H, s, CH_2), 6.77–7.53 (9H, m, aromatic protons), 10.46 (1H, s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 29.7 (2×3-CH_3), 36.9 (CH_2), 43.7 (3-C), 76.0 (=CH_2), 106.0, 116.9 (2×C), 119.2, 121.8, 122.1, 127.6, 129.0 (2×C), 136.8, 138.6, 144.8 (Ar-C), 156.0 (2-C), 160.0, 160.1 (C–O–C). IR (KBr, cm^{-1}): ν_{N-H}=3189; $\nu_{C=N}$=1655. MS *m*/*z* (%): 333 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{20}N_4O$: C 72.27; H 6.06; N 16.86. Found: C 71.93; H 5.87; N 16.59.

4.7.8. 5-[(3,3-Dimethyl-2-methylene-2,3-dihydro-1*H*-indol-1-yl)methyl]-*N*-(2-fluorophenyl)-1,3,4-oxadiazol-2-amine 14b. Yield 65%. Mp 141–142 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 1.30 (6H, s, 2×3-CH_3), 3.98 (1H, d, J=2.1 Hz, =C*H*(H)), 4.11 (1H, d, J=2.1 Hz, =C*H*(H)), 4.98 (2H, s, CH_2), 6.66–7.84 (8H, m, aromatic protons), 10.31 (1H, s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 29.7 (2×3-CH_3), 37.0 (CH_2), 43.7 (3-C), 75.9 (=CH_2), 106.0, 115.4, 115.6, 119.2, 120.6, 122.1, 123.6, 124.6, 126.5, 127.5, 136.8, 144.8 (Ar-C), 156.6 (2-C), 160.0, 160.4 (C–O–C). IR (KBr, cm^{-1}): ν_{N-H}=3160; $\nu_{C=N}$=1654. MS *m*/*z* (%): 351 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{19}N_4FO$: C 68.56; H 5.47; N 15.99. Found: C 68.09; H 5.90; N 15.59.

4.7.9. 5-[(3,3-Dimethyl-2-methylene-2,3-dihydro-1*H*-indol-1-yl)methyl]-*N*-(2-chlorophenyl)-1,3,4-oxadiazol-2-amine 14c. Yield 95%. Mp 125–126 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 1.29 (6H, s, 2×3-CH_3), 3.98 (1H, d, J=2.1 Hz, =C*H*(H)), 4.11 (1H, d, J=2.1 Hz, =CH(*H*)), 4.97 (2H, s, CH_2), 6.77–7.91 (8H, m, aromatic protons), 9.89 (1H, s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 29.7 (2×3-CH_3), 37.1 (CH_2), 43.7 (3-C), 75.9 (=CH_2), 106.0, 119.2, 122.1, 122.2, 124.1, 124.8, 127.5, 127.8, 129.8, 135.3, 136.8, 144.8 (Ar-C), 156.8 (2-C), 160.0, 160.7 (C–O–C). IR (KBr, cm^{-1}): ν_{N-H}=3201; $\nu_{C=N}$=1627. MS *m*/*z* (%): 369/67 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{19}N_4ClO$: C 65.48; H 5.22; N 15.27. Found: C 65.22; H 5.66; N 15.03.

4.7.10. *N*-Phenyl-5-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)methyl]-1,3,4-oxadiazol-2-amine 15a. Yield 53%. Mp 167–168 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 0.94 (3H, s, 3-CH_3), 1.21 (6H, m, 2×CH_3), 3.18 (1H, q, J=6.5 Hz, CH), 4.39 (1H, d, J=16.4 Hz, C*H*(H)), 4.68 (1H, d, J=16.5 Hz, CH(*H*)), 6.66–7.53 (9H, m, aromatic protons), 10.43 (1H, s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 11.8 (2-CH_3), 22.9 (3-CH_3), 25.3 (3-CH_3), 30.2 (CH_2), 42.2 (3-C), 68.5 (CH), 107.7, 116.8 (2×C), 118.6, 121.7, 121.8, 127.1, 128.9 (2×C), 138.5, 138.7, 149.1 (Ar-C), 156.8, 160.0 (C–O–C). IR (KBr, cm^{-1}): ν_{N-H}=3201; $\nu_{C=N}$=1627. MS *m*/*z* (%): 335 (M+H$^+$, 30). Anal. Calcd for $C_{20}H_{22}N_4O$: C 71.83; H 6.63; N 16.75. Found: C 72.16; H 7.03; N 16.25.

4.7.11. *N*-(2-Fluorophenyl)-5-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)methyl]-1,3,4-oxadiazol-2-amine 15b. Yield 85%. Mp 144–145 °C. ^{1}H NMR (270 MHz, DMSO-d_6): δ 0.95 (3H, s, 3-CH_3), 1.21 (3H, d, J=6.5 Hz, 2-CH_3), 1.24 (3H, s, 3-CH_3), 3.23 (1H, q, J=6.5 Hz, CH), 4.39 (1H, d, J=16.5 Hz, C*H*(H)), 4.65 (1H, d, J=16.5 Hz, CH(*H*)), 6.66–7.97 (8H, m, aromatic protons), 10.26 (1H, s, NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 11.8 (2-CH_3), 22.9 (3-CH_3) 25.3 (3-CH_3), 30.2 (CH_2), 42.2 (3-C), 68.5 (CH), 107.7, 115.3, 115.6, 118.6, 120.5, 121.7, 124.6, 126.4, 126.6, 127.0, 138.5, 149.0 (Ar-C), 157.4, 160.3 (C–O–C). IR (KBr, cm^{-1}): ν_{N-H}=3165; $\nu_{C=N}$=1655. MS *m*/*z* (%): 353 (M+H$^+$, 100). Anal. Calcd for $C_{20}H_{21}N_4FO$: C 68.16; H 6.01; N 15.90. Found: C 68.58; H 5.99; N 15.53.

4.7.12. *N*-(2-Chlorophenyl)-5-[(2,3,3-trimethyl-2,3-dihydro-1*H*-indol-1-yl)methyl]-1,3,4-oxadiazol-2-amine 15c. Yield 78%. Mp 94–95 °C. ^{1}H NMR (270 MHz, $CDCl_3$): δ 0.99 (3H, s, 3-CH_3), 1.25 (6H, m, 2-CH_3, 3-CH_3), 3.19 (1H, q, J=6.5 Hz, CH), 4.37 (1H, d, J=16.4 Hz, C*H*(H)), 4.55 (1H, d, J=16.4 Hz, C*H*(H)), 6.69–8.12 (9H, m, aromatic protons and NH). ^{13}C NMR (67.5 MHz, DMSO-d_6): δ 12.1 (2-CH_3), 22.9 (3-CH_3), 25.4 (3-CH_3), 40.1 (CH_2), 42.6 (3-C), 69.1 (CH), 107.6, 118.3, 119.2, 121.0, 121.9, 123.3, 127.3, 128.0, 129.1, 134.0, 138.8, 148.9 (Ar-C), 157.9, 171.0 (C–O–C). IR (KBr, cm^{-1}): ν_{N-H}=3208; $\nu_{C=N}$=1621. MS *m*/*z* (%): 371/69 (M+H$^+$, 50). Anal. Calcd for $C_{20}H_{21}N_4ClO$: C 65.12; H 5.74; N 15.19. Found: C 64.77; H 6.21; N 15.04.

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