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TRYPTAMINE DERIVED AMIDES FROM *CLAUSENA INDICA*

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Key Word Index—*Clausena indica*; Rutaceae-Aurantioideae; leaves; amides; tryptamine derived amides; cinnamides; isovaleric acid amides; lactams.

Abstract—Leaf extracts from different Sri Lankan provenances of *Clausena indica* were compared by HPLC linked with diode array detection. Remarkable chemical differences towards different types of amides were observed between the collections from the northern dry semi-evergreen forests and the central montane rainforests. Apart from the already known phenethyl cinnamide, four new tryptamine derived amides were detected with different acid moieties: the cinnamic acid amides named balasubramide and prebalamide and the isovaleric acid amides named madugin and methylmadugin. Balasubramide is characterised by an eight-membered lactam ring. All structures were established by spectral analyses.

INTRODUCTION

The genus *Clausena* belongs to the tribe Clauseneae of the Rutaceae-subfamily Aurantioideae and, according to a recent generic revision, comprises 15 species and six varieties [1]. They are shrubs or small trees mainly distributed in south and southeast Asia, but also occur in south China and north Australia and one species in Africa. Since *Clausena lansium* (Lour.) Skeels from China and *Clausena anisata* (Willd.) Hook. f. ex. Benth. from Africa represent well known medicinal plants, this genus has been the subject of many phytochemical investigations. Up to now many different coumarins, carbazole alkaloids, amides [2–4] and limonoids [5] have been isolated. Of special pharmacological interest, however, are the amides isolated from *C. lansium* which were shown to be efficacious liver protecting agents against chemical toxins and are useful in treating hypoxia and amnesia [6, 7].

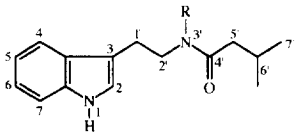
In more recent phytochemical analyses within different provenances of *C. indica* (Dalz.) Oliver (Sinhala: Migon-Karapincha; Tamil: Pannai, Purankainari) collected in Sri Lanka, four novel amides and the already known phenethyl cinnamide (**5**) [8] have been detected together with simple coumarins, furocoumarins and carbazole alkaloids [9]. In the present paper, we report on the isolation and structure elucidation of four new tryptamine derived amides (**1**–**4**) which were found as major components in leaf extracts from collections of the central montane rainforests, whereas a collection of the northern dry semi-evergreen forests was shown to contain the phenethylamine derived amide **5**.

Regarding the pharmacological properties of lactam ring-containing amides, e.g. clausenamide [7], the detection of amide **4** with an eight-membered lactam ring is of special interest. We named it balasubramide in memory of the late Prof. S. Balasubramaniam of the University of Peradeniya and in appreciation of his valuable help in collecting and identifying the plant material. Cinnamide (**3**), a possible biogenetic precursor of **4**, was consequently designated as prebalamide. The remaining isovaleric acid derived amides were designated as madugin (**1**) and methylmadugin (**2**) with reference to the place of collection near Madugoda in Sri Lanka.

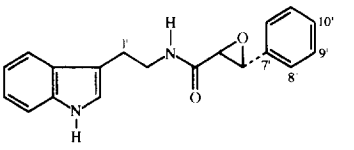
RESULTS AND DISCUSSION

From the $CHCl_3$ fractions of the methanolic leaf extracts of *Clausena indica* five compounds (**1**–**5**) were detected by HPLC linked with diode array detection. Compound **5** was shown to be the already described phenethylamide [8]. Compounds **1**–**4** had identical UV spectra with λ_{max}(MeOH) at 290sh, 282, 272sh, 221 nm, typical for an indole chromophore [10]. This was further confirmed by strong IR absorptions at 3493 cm^{-1} (**1**–**3**) and 3476 cm^{-1} (**4**), respectively, indicating the N-H vibration in the indole moiety. Characteristic signals at 3456 cm^{-1} (**1**) and 3423 cm^{-1} (**3**) are indicative for >N-H stretching of secondary amides and the strong bands at 1641–1690 cm^{-1} in all four compounds are typical for the N-C=O stretching region of amides.

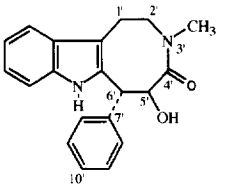
The ^1H NMR spectrum of compound **1**, named



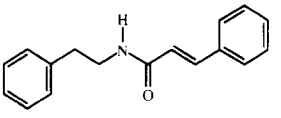
1 R = H Madugin
2 R = CH_3 Methylmadugin



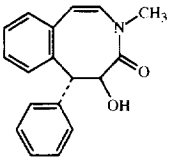
3 Prebalamide



4 Balasubramide



5 Phenethyl cinnamide



6 ζ-Clausenamide [11]

madugin, shows the typical aromatic resonance pattern for 3-substituted indole derivatives. The ABCD-system of the benzene ring can be analyzed by a simple first order interpretation and the signal for H-2 shows the typical small coupling constant of 2.2 Hz to N1-H (Table 1). The side chain attached at C-3 of the indole unit consists of two methylene groups H_2-1′ and H_2-2′ appearing as a *t* and a *dt* (pseudo *q*, due to coupling with the amide proton 3′-H), respectively. The 2-(3-indolyl)-ethylamine (or tryptamine) unit is connected to isovaleric acid via an amide bond. Corresponding resonances for the acid component are a *t* of 2H for -CO-CH_2 (H_2-5′), a *m* (broadened pseudo-nonaplet) of 1 H for H-6′ and a *d* of 6H for the two terminal methyl groups H_3-7′ (compare Table 1). The EI-mass spectrum for $C_{15}H_{20}N_2O$ is fully compatible

Table 1. ^{1}H NMR data of indole amides **1**–**4** (400 MHz, $CDCl_3$, TMS, δ values)

H	1	2*	2*	3	4†
1	8.12 *br s*	8.17 *br s*	8.09 *br s*	8.07 *br s*	7.78 *br s*
2	7.04 *d*	7.05 *s*	6.99 *s*	7.07 *d*	—
4	7.62 *dd*	7.68 *d*	7.58 *d*	7.62 *dd*	7.53
5	7.13 *ddd*	7.15 *dd*	7.12 *dd*	7.15 *ddd*	7.12
6	7.21 *ddd*	7.22 *dd*	7.19 *dd*	7.23 *ddd*	7.17
7	7.38 *dd*	7.39 *d*	7.36 *d*	7.39 *dd*	7.23
1′	3.05 *t*	3.01 *t*	3.01 *t*	3.05, 3.00 *dt*‡	3.04, 3.50 *ddd*‡
2′	3.69 *q*	3.70 *t*	3.60 *t*	3.65 *q*	3.99, 3.42 *ddd*‡
3′	5.53 *br t*	2.98 *s*	2.93 *s*	6.30 *br t*	2.86 *s*
5′	2.03 *d*	2.19 *dd*	1.97 *d*	3.48 *d*	4.96 *dd*, (4.34 *br d*)§
6′	2.14 *m*	2.06 *m*	2.03 *m*	3.66 *d*	4.35 *d*
7′	1.00 *d*	0.97 *br d*	0.80 *d*	—	—
8′–10′	—	—	—	7.20 *d* (2H), 7.32 *m* (3H)	7.28–7.35 *m* (5H)

Coupling constants: **1**: $J(1,2)$ = 2.2 Hz, $J(4,5)$ = 7.9 Hz, $J(4,6)$ = 1.0 Hz, $J(5,6)$ = 7.2 Hz, $J(5,7)$ = 0.9 Hz, $J(6,7)$ = 8.0 Hz, $J(1',2')$ = $J(2',NH)$ = 6.5 Hz, $J(5',6')$ = 7.1 Hz, $J(6',7')$ = 6.7 Hz; **2** (small couplings are often obscured by line broadening due to dynamic effects*): $J(4,5)$ = 7.4 Hz, $J(5,6)$ ~ 7.5 Hz, $J(6,7)$ = 7.5 Hz, $J(1',2')$ = 7.4 Hz, $J(5',6')$ ~ 6.5 Hz, $J(6',6')$ ~ 10 Hz, $J(6',7')$ ~ 6.4 Hz; **3**: $J(1,2)$ = 2.2 Hz, $J(4,5)$ = 7.8 Hz, $J(4,6)$ ~ 1 Hz, $J(5,6)$ = 7.0 Hz, $J(5,7)$ ~ 1 Hz, $J(6,7)$ = 8.0 Hz, $J(1',1')$ = 14.8 Hz, $J(1',2')$ = $J(2',NH)$ = 6.5 Hz, $J(5',6')$ = 2.0 Hz; **4**: $J(4,5)$ = 7.3 Hz, $J(5,6)$ = 6.6 Hz, $J(6,7)$ = 7.8 Hz, $J(4,6)$ = $J(5,7)$ ~ 1.5 Hz, $J(1',1')$ = 16 Hz, $J(2',2')$ = 15 Hz, $J(1'a,2'a)$ ~ 6 Hz, $J(1'a,2'b)$ ~ 3.5 Hz, $J(1'b,2'a)$ ~ 9 Hz, $J(1'b,2'b)$ ~ 7 Hz, $J(5',OH)$ ~ 7 Hz, $J(5',6')$ = 6.4 Hz.

*Two amide conformers ratio 1 : 1 (±2%); due to the equal amounts no assignment between the two conformers was possible, the values of the two corresponding rows are therefore interchangeable; the small aromatic *meta* couplings of ≤1 Hz are only visible for the pseudo-triplets of 5-H and 6-H; the protons 5′-H_2 of one conformer appear as diastereotopic protons with a geminal coupling of ~10 Hz.

†Assignments supported by reverse C,H-COSY.

‡Diastereotopic methylene protons.

§5′-OH; in less pure samples the resonance at δ 4.34 appears as a broad *s* and the resonance of 5′-H at δ 4.96 changes from a *dd* (pseudo *t*) to a clear *d*.

with the derived structure. The molecular mass of $m/z = 244$ shows a relative intensity of 5% and the very characteristic peak at $m/z = 143$ (95%) is due to vinylindole, which is the expected McLafferty product of the amide structure **1**.

The structure of compound **2** is closely related to **1**. In the ^{1}H NMR spectrum it shows essentially the same resonances, but always duplicated. The amide NH proton is missing, and there is a set of two new signals at δ 2.98 and 2.93. Obviously the amide nitrogen is methylated in compound **2** and due to the hindered rotation about the amide bond one observes two conformers with two corresponding sets of resonances. The conformer ratio is 1 : 1 (±2%). For this reason we could not differentiate between the two isomers. The structure of **2** was confirmed by ^{13}C NMR which also showed two sets of signals for the two conformers. A correlation between the ^{1}H and ^{13}C chemical shifts was achieved by reverse C,H-COSY. All NMR data fully support the proposed structure **2**. The mass spectrum is again dominated by the prominent peak for vinylindole [$m/z = 143$, (100%)], the molecular mass peak at $m/z = 258$ shows a relative intensity of 6%. As a derivative of compound **1**, amide **2** was named methylmadugin.

Compound **3**, named prebalamide, is also a tryptamine derived amide. The ^{1}H NMR spectrum shows similar chemical shifts and coupling constants to that of compound **1**. The only differences are the position and shape of the amide H-3′ proton and a slight diastereotopy of H_2-2′ (Table 1). The acid component, however, is a completely different one: the ^{1}H resonances remaining for interpretation consist of a narrow group of signals in the aromatic region (*d* of 2H at δ 7.20 and a *m* of 3H at δ 7.32) which can be attributed to a phenyl group and an AB-system centered at δ 3.48 and 3.66 ($J = 2.0$ Hz). These chemical shift values and the small coupling constant of 2 Hz are in favour of a *trans*-substituted epoxide ring [11], directly linked to the amide carbonyl and to the phenyl ring. The resulting structure is the tryptamine derived amide of epoxy-cinnamic acid. This structure is compatible with the high resolution molecular mass of $m/z = 306.1371$ (5%) and the base peak for vinylindole at $m/z = 143$ (100%). Final confirmation is furnished by the ^{13}C NMR spectrum showing the three characteristic phenyl resonances and the O-C-H signals at δ 59.0. It should be noted that both epoxide carbon resonances coincide accidentally. A spectrum estimation [12] predicted values of δ 57.4 (C-5′) and 62.6 (C-6′) which compare reasonably well with the experimental values of δ 59.0 and 59.0. The corresponding ^{13}C NMR values in C_6D_6 are found at δ 58.8 and 59.5. A closely related cinnamic acid derived *trans*-oxirane carboxamide of phenylethenylamine was recently isolated from *C. lansium* [13] with epoxide carbon resonances at δ 56.9 and 57.9.

Although the UV spectrum indicated a further indole-amide structure for compound **4**, the ^{1}H NMR spectrum looked rather different to those of compounds **1–3**. A closer analysis revealed that the benzene ring of the indole unit and the NH resonance remain essentially unchanged, and positions C-2 and C-3 of the indole moiety seem to be substituted. A phenyl group (*m* for 5H at δ 7.28–7.35) and a dimethylene unit resemble the corresponding structural elements of compound **1**. However, the four resonances for -CH_2-CH_2- appear as four distinct *ddd* with a spacing of >0.4 ppm for the diastereotopic protons (Table 1). This is very much in favour of a ring structure with restricted flexibility. A sharp *s* at δ 2.86 is easily assigned to a N-CH_3 group. The remaining resonances are a *dd* (pseudo *t*) at δ 4.86 (possibly next to oxygen) and a somewhat puzzling resonance for 2H at δ 4.34–4.35 appearing as a broadened *d*. However, a close inspection of this signal shows that it consists of two very close doublets, a sharp one plus a very broad one. In a second measurement of a less pure sample, the second broad one had changed to a broad *s* and the pseudo-*t* at δ 4.96 had changed to a clear *d*. The broad *s* (or *br d*) dissappears after addition of D_2O. The only reasonable explanation for the signals at δ 4.86 and 4.34/4.35 is a fragment -CH(OH)-CH< with a OH resonance sensitive to impurities promoting proton exchange. The ^{13}C NMR spectrum and a reverse C,H-COSY shift correlation helped to solve the structure unambiguously. The carbon resonances in the aromatic region are fully compatible with a 2,3-disubstituted indole, and a separate phenyl group. The two methylene groups are found at δ 46.4 (typical for N-CH_2) and 22.9 (indolyl-CH_2, compare with the data for **2** and **3**). The result is again the structure of a tryptamine derived amide, however, compound **4** possesses a cyclic amide structure (as indicated by the highly diastereotopic methylene groups). The assignments of the four mutually coupling methylene protons to carbon atoms 1′ or 2′ follow clearly from the reverse C,H-COSY spectrum. Together with the N-methyl group at δ 34.2 and the C=O resonance at δ 173.4, the sequence indolyl-CH_2-CH_2-N(CH_3)-CO- is clear. The amide ring can be closed by the unit -CH(OH)-CH(phenyl)- following from the ^{1}H NMR evidence outlined above and the corresponding ^{13}C resonances at δ 73.7 for C-5′ (next to a carbonyl unit and a hydroxyl group) and 54.6 for C-6′ (next to two aromatic systems—phenyl and indolyl). A ^{13}C NMR spectrum estimation [12] and the molecular mass for $C_{20}H_{20}N_2O_2$ fully support the postulated structure. It is interesting to note that the cyclic amide structure can be easily derived from epoxide **3** by ring closure between the C-6′ position of the epoxide and C-2 of the indole moiety plus amide N methylation. The reaction leading from epoxide **3** to lactam **4** may be interpreted as a nucleophilic opening of the *trans*-substituted epoxide by the electron rich C-2 of the indole system. The result is the eight-membered lactam ring **4** with 5′-hydroxyl and 6′-phenyl in *trans* configuration. A similar lactam ring is already known from the unsaturated phenethylamine derived ζ-clausenamide (**6**) [14] as well as from a cor-

responding diol [15], both of which have been isolated from *C. lansium*. Compound **4** was designated as balasubramide (see Introduction).

Biogenetically the amine part of compounds **1**–**4** most likely arises from the amino acid tryptophan by decarboxylation, whereas the acid moieties are derived from isovaleric (**1**,**2**) or cinnamic acid (**3**,**4**). Comparing the amides already known from Rutaceae, the formation of lactam rings appears to be restricted to the genus *Clausena*. From *C. lansium* a series of amides have already been described with five-, six-, and eight-membered lactam rings [14–16], but all are different from the here described tryptamine derived amides from *C. indica* by the formation of phenethylamine or styrylamine moieties.

Apart from the already mentioned chemical differences between the collections of the northern and the central provinces of Sri Lanka, containing either phenethylamine or tryptamine derived amides, more detailed HPLC-comparisons of different samples collected within that regions showed additional chemical variation: The tryptamine amides madugin (**1**) and methylmadugin (**2**), containing isovaleric acid moieties, were only found in a collection from the montane region near Madugoda, whereas another sample collected near Rattota, was characterized by cinnamic acid moieties (**3**,**4**). In a third collection from Udawattakele (near Kandy) by contrast, no amides could be detected at all. A similar situation was also found in the dry semi-evergreen forests near Anuradhapura (north Sri Lanka), where from two different collections only one contained the phenethyl cinnamide **5**, the HPLC profile of the second sample did not show any detectable amount of amides.

In spite of this chemical variability, preliminary HPLC comparisons of many different *Clausena* species and provenances collected in Thailand and Malaysia [B. Riemer unpubl.], indicate that the accumulation of amides seems to be largely restricted to *C. lansium* and *C. indica*. Regarding the common biogenetic trend towards lactam ring formation, one would therefore expect closer affinities between *C. indica* and *C. lansium*. However, this is not in agreement with a more recent taxonomic treatment of the genus, where the two species are grouped into two different sections [1].

EXPERIMENTAL

General. NMR: 400 and 250 MHz, $CDCl_3$; MS: Varian MAT 311 A; HPLC: Hewlett-Packard HP 1090 II, UV diode array detection at 230 nm, column 290 × 4 mm (Spherisorb ODS, 5 μm), mobile phase MeOH (gradient 60–100%) in aq buffer (0.015 M phosphoric acid, 0.0015 M tetrabutylammonium hydroxide, pH 3), flow rate 1 ml min^{-1}.

Plant material. Leaves of *C. indica* were collected from five different localities in Sri Lanka: (i) Madugoda, Mahiyangana Road, A26, milestone 50/3; (ii) Rattota, Knuckles-Mts. (Midlands), Rattota-Illukumbura Road, B274, milestone 12/28; (iii) Kandy, Udawattakele Sanctuary; (iv) Anuradhapura, arboretum of the forest station on Puttalam Road; (v) Anuradhapura, near the Twin Ponds. Voucher specimens are deposited at the Herbarium of the Institute of Botany, University of Vienna (WU) and in Peradeniya.

Extraction and isolation. Dried leaves (48 g) of collection (i) were extracted with MeOH at room temp for 7 days, filtered and concd. The remaining aq phase was extracted with $CHCl_3$. The resulting extract was concd. and the residue was sepd on a silica gel column eluted with petrol–Et_2O mixts with Et_2O increasing from 0 to 100% and finally with 0–40% MeOH in Et_2O. The frs eluted with 10–25% MeOH in Et_2O were combined for prep. MPLC with 50% EtOAc in petrol to afford 60 mg of a fr. containing the amides **1** and **2**. RP-MPLC gave 32 mg of **2** and prep. TLC using CH_2Cl_2–Et_2O (17 : 3) gave 2.2 mg of **1**. The dried leaves (73 g) of collection (ii) were treated as above. The frs with 10–25% MeOH in Et_2O were further sepd by prep. MPLC with 50% EtOAc in petrol affording 10 mg of crude **3** and 21 mg of crude **4**. Both compounds were purified by prep. TLC. Fresh leaves (230 g) of collection (iv) were treated as described for (i). The fraction eluted with 100% Et_2O was separated by prep. MPLC using 30% EtOAc in petrol yielding 60 mg crystalline **5**.

Madugin [*isovaleric acid* 2-(3-*indolyl*)-*phenethylamide*] (**1**). Oil. UV λ^{Et_2O} nm: 292, 283, 274 (sh), 224; IR ν^{CCl_4} cm^{-1}: 3493 m, 3456 w, 3308 w, 3061 w, 2962 s, 2930 s, 2874 m, 2858 m, 1678 s, 1504 s, 1457 s, 1437 m, 1417 m, 1369 m, 1349 m, 1295 m, 1170 w, 1089 w, 924 w, 670 m; ^{1}H NMR: Table 1; MS (70 eV, 150) *m/z*: 244 (5) $[M]^+$, 143 (95) [vinylindole$^+$, McLafferty product], 130 (42), 115 (14), 97 (14), 85 (22), 83 (18), 77 (14), 73 (28), 71 (37), 69 (26), 61 (33), 57 (81), 55 (38), 45 (59), 43 (100); HR-MS: $C_{15}H_{20}N_2O$, $M_{calc.}$ = 244.1576, $M_{exp.}$ = 244.1580.

Methylmadugin [*isovaleric acid* N-*methyl*-2-(3-*indolyl*)-*phenethylamide*] (**2**). Oil. UV λ^{Et_2O} nm: 292, 283, 274 (sh), 224; IR ν^{CCl_4} cm^{-1}: 3493 m, 3283 w, 3062 w, 2961 s, 2930 s, 2874 m, 1641 s, 1457 s, 1417 m, 1401 m, 1384 w, 1366 w, 1348 w, 1302 w, 1262 w, 1227 w, 1180 w, 1089 m, 924 w; ^{1}H NMR: Table 1; ^{13}C NMR ($CDCl_3$, TMS, two conformers): δ 172.7 and 172.4 (*s*, C = O), 136.4 and 136.3 (*s*, C-7a), 127.5 and 127.1 (*s*, C-3a), 122.2, 122.2, and 121.9 (*d*, C-2 and C-6), 119.6 and 119.3 (*d*, C-5), 118.8 and 118.2 (*d*, C-4), 113.3 and 112.2 (*s*, C-3), 111.4 and 111.1 (*d*, C-7), 50.4 and 48.8 (*t*, C-2′), 42.4 and 41.6 (*t*, C-5′), 36.2 and 33.5 (*q*, C-3′), 25.6 and 25.5 (*d*, C-6′), 24.5 and 23.3 (*t*, C-1′), 22.7 and 22.6 (*q*, C-7′); assignments confirmed by reverse C,H-COSY and spectrum estimation [12]. MS (70 eV, 130) *m/z*: 258 (6) $[M]^+$, 143 (100) [vinylindole$^+$, McLafferty product], 130 (36), 116 (5), 103 (3), 97 (2), 85 (6), 77 (4), 71 (4), 57 (19), 44 (55); HR-MS: $C_{16}H_{22}N_2O$, M_{calc} = 258.1732, $M_{exp.}$ = 258.1735.

Prebalamide [2,3-*epoxy*-3-*phenylpropanoic acid* 2-(3-*indolyl*)-*phenylethylamide*] (**3**). Colourless crystals

(Et_2O), mp 125–127°. $[\alpha]_D = +30°$ ($CHCl_3$, $c = 0.5$). UV λ^{Et_2O} nm: 292, 283, 274 (sh), 224; IR ν^{CCl_4} cm^{-1}: 3493 m, 3423 w, 3065 w, 2931 w, 2857 w, 1690 s, 1623 w, 1518 s, 1457 m, 1439 w, 1417 w, 1350 w, 1335 w, 1269, 1226 w, 1090 w, 891 w, 696 m; ^1H NMR: Table 1; ^{13}C NMR ($CDCl_3$, TMS): δ 167.4 (*s*, C = O), 136.4 (*s*, C-7a), 135.0 (*s*, C-7′), 129.0 (*d*, C-10′), 128.6 and 125.8 (ea. *d*, C-8′ and C-9′), 122.4 (*d*, C-6), 122.0 (*d*, C-2), 119.6 (*d*, C-5), 118.7 (*d*, C-4), 112.7 (*s*, C-3), 111.3 (*d*, C-7), 59.0 (*br d*, C-5′ and C-6′), 39.1 (*t*, C-2′), 25.2 (*t*, C-1′); (C_6D_6, TMS): δ 167.4 (*s*, C = O), 128.9 (*d*, C-10′), 128.8 and 126.1 (ea. *d*, C-8′ and C-9′), 122.5 (*d*, C-6), 122.1 (*d*, C-2), 119.9 (*d*, C-5), 119.2 (*d*, C-4), 111.5 (*d*, C-7), 59.5 and 58.8 (ea. *d*, C-5′ and C-6′), 39.5 (*t*, C-2′), 25.6 (*t*, C-1′); assignments confirmed by spectrum estimation [12]. MS (70 eV, 180°) *m/z*: 306 (5) $[M]^+$, 143 (100) [vinylindole$^+$, McLafferty product], 130 (62), 115 (8), 103 (7), 91 (9), 77 (10), 65 (6), 59 (7), 51 (5); HR-MS: $C_{19}H_{18}N_2O_2$, $M_{calc.} = 306.1368$, $M_{exp.} = 306.1371$.

Balasubramide [*7-hydroxy-9-methyl-8-oxo-6-phenylazocino* [5,4-b] *indole*] (**4**). Colourless oil, $[\alpha]_D = +7°$ ($CHCl_3$, $c = 0.5$). UV λ^{Et_2O} nm: 292, 283, 274 (sh), 224; IR ν^{CCl_4} cm^{-1}: 3476 m, 3321 w, 3065 w, 2931 s, 2859 m, 1659 s, 1492 m, 1461 s, 1388 s, 1360 m, 1340, 1270, 1178, 1122 m, 1066 s, 1053 w, 699 m; ^1H NMR: Table 1; ^{13}C NMR ($CDCl_3$, TMS): δ 173.4 (*s*, C = O), 141.0, 135.3, and 132.1 (ea. *s*, C-2, C-7a, and C-7′), 129.4 (*s*, C-3a), 128.8 and 127.6 (ea. *d*, C-8′ and C-9′), 127.3 (*d*, C-10′), 122.2 (*d*, C-6), 119.5 (*d*, C-5), 117.6 (*d*, C-4), 110.6 (*d*, C-7), 106.9 (*s*, C-3), 73.6 (*d*, C-5′), 54.6 (*d*, C-6′), 46.4 (*t*, C-2′), 34.2 (*q*, 3′), 22.9 (*t*, C-1′); assignments confirmed by reverse C,H-COSY and spectrum estimation [12]. MS (70 eV, 140°) *m/z*: 320 (17) $[M]^+$, 236 (10), 233 (11), 220 (67), 218 (26), 130 (9), 115 (14), 109 (9), 91 (17), 77 (14), 71 (16), 63 (10), 60 (16), 57 (43), 51 (13), 43 (100); HR-MS: $C_{20}H_{20}N_2O_2$, $M_{calc} = 320.1525$, $M_{exp.} = 320.1523$.

Phenethyl cinnamide (**5**). Colourless crystals (Et_2O), mp 126–127° [8]. UV λ^{Et_2O} nm: 300 (sh), 268, 220; IR ν^{CCl_4} cm^{-1}: 3447 m, 3342 w, 2993 w, 2929 m, 2858 w, 1669 s, 1630 s, 1580 m, 1507 s, 1451 m, 1365 w, 1351 m, 1300 w, 1281 w, 1084 w, 976 m, 854 w; ^1H NMR ($CDCl_3$, TMS): δ 7.62 (*d*, 1H, $J = 15.6$ Hz, = CH-CO-), 7.48 (*dd*, 2H, $J = 7.7$ and 1.8 Hz, 2 × *ortho*-H of cinnamic acid), 7.38–7.31 (*m*, 5H, remaining 3H from cinnamic acid + 2H from phenethylamine), 7.27–7.21 (*m*, 3H, amine moiety), 6.31 (*d*, 1H, $J = 15.6$, Ar-CH =), 5.60 (*br t*, $J = 6.6$ Hz, N-H), 3.67 (*q*, 2H, $J = 6.6$ Hz, N-CH_2-), 2.90 (*t*, 2H, $J = 6.6$ Hz, Ar-CH_2-).

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