I. D. Kozekov[1], R. I. Koleva and M. D. Palamareva*

University of Sofia, Faculty of Chemistry, 1 James Bouchier Avenue
Sofia 1164, Bulgaria
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The reaction of homophthalic anhydride and *N*-(1-methyl-1*H*-pyrrol-2-yl-methylidene)-benzylamine in boiling benzene afforded as a main product the expected substituted *trans*-1,2,3,4-tetrahydroisoquinoline-4-carboxylic acid **5**. The carboxylic group of **5** was transformed in four steps into cyclic amino-methyl groups yielding numerous new tetrahydroisoquinolinones **11a-j** incorporating a given fragment of pharmacological interest. Reduction of **11a-j** was studied.

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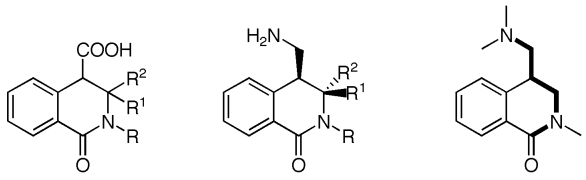
Substituted 1,2,3,4-tetrahydroisoquinolines with asymmetric C^3 and C^4 exist in two racemic diastereoisomeric forms, namely (±)-*trans* and (±)-*cis* that will be denoted simply by *trans* and *cis*. These compounds are important from synthetic and applied point of view. Their structure is incorporated in various alkaloids [1,2] and pharmacologically important compounds (see for instance refs. 3 and 4). The synthesis of *trans* and/or *cis* isomers of such tetrahydroisoquinolines is possible by classical reactions [5,6] but the starting compounds are difficult to obtain. The compounds of type **1** can be prepared by the one step reaction between homophthalic anhydride and an imine, the reaction being reported almost simultaneously from two independent laboratories [7,8]. Since 1977, this reaction has been widely applied [9-21] for preparation of substituted tetrahydroisoquinolinones and polycyclic heterocycles when acyclic and cyclic imines are used, respectively. Bigg and co-workers [22] use the same reaction in combination with other well known reactions to obtain various compounds **2** with a primary amino-methyl group. The authors claim that the fragment given in bold is the reason some of the compounds show sub-micromolar affinity to the NMDA receptor. Another type of cyclization has been used [23] for enantioselective synthesis of tetrahydroisoquinolinones.

The aim of this and future related papers is to further specify the scope and limitation of the reaction of homophthalic anhydrides and imines and subsequent transformations that

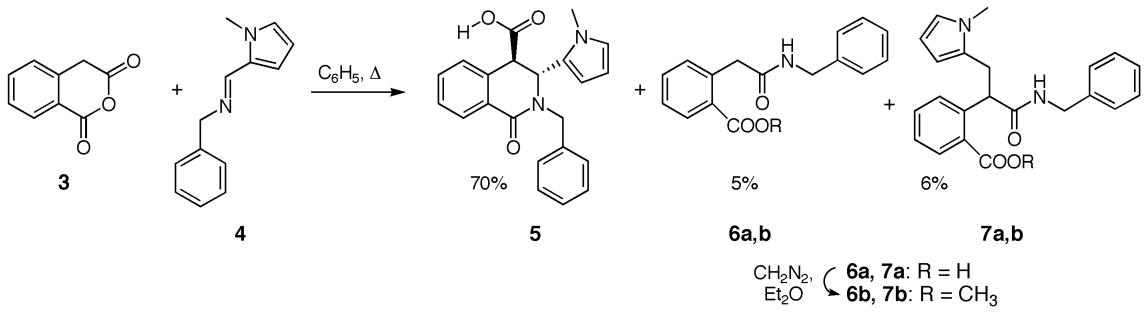


1 **2**

are available in the products functional groups. Attention is paid to the stereochemical course of the reactions.

The reaction between homophtalic anhydride **3** and the imine **4** was carried out in boiling benzene. This enabled us to obtain as a main product, in 70% yield, only the *trans* isomer of tetrahydroisoquinolinone carboxylic acid **5**. The configuration was assigned on the basis of the small [7,8] $J^{3,4}$ of 1.6 Hz. Thus contrary to ref. 22, we succeeded in performing a diastereoselective reaction, thus avoiding the necessity of isomerisation of a mixture of *cis* and *trans* acids. The acyclic compounds **6a** and **7a** were isolated as by-products. In some cases [15,24], Perkin condensation between homophtalic anhydrides and the aldehyde used for the preparation of the imine takes place as a side reaction. The formation of the corresponding products indicates that the imines can decompose to the parent aldehyde and amine in the course of the reaction with **3**. Compound **6a** probably results from the opening of the anhydride ring of **3** by nucleophilic attack of benzyl amine on the C^3 carbonyl group. Perkin type condensation of compound **6a** with the

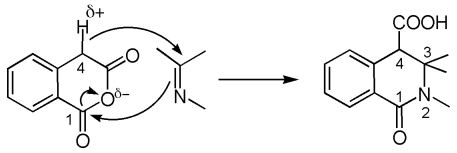
Scheme 1



corresponding aldehyde would lead to *Z* or *E* **7a**. Compounds **6a** and **7a** and the corresponding methyl esters **6b** and **7b** were characterised by ^{1}H and COSY spectra. Compound **6b** was proved by mp and ^{1}H to be identical with the relevant compound described in ref. 16. Its structure was further proved by HMBC spectra. Detailed analysis of these spectra revealed that the protons of the two methylene groups at 3.93 and 4.40 ppm are coupled with same carbonyl carbon at 171.2 ppm, while the methyl protons at 3.88 ppm are coupled with the other carbonyl carbon at 169.0 ppm. This analysis supports the structures of **6a** and **6b**.

Cushman and Madaj [11] consider the reaction between homophtalic anhydride and an imine as a non-concerted addition of the imine to positions 1 and 4 of the anhydride, the formation of C^1 - N bond preceding the formation of C^3 – C^4 bond. These authors base this conclusion on the application of the Hammett equation using three different solvents. The values found (0.206 and 0.088) of the reaction constant, ρ, are close to zero when the solvent is methanol or formamide. Taking into account the use of ρ for mechanism elucidation [25,26], we assume that the synchronous mechanism of the reaction between a homophthalic anhydride and an imine, as shown in Scheme 2, should not be excluded since such a mechanism requires ρ *ca*. 0. It is worth noting that the reaction of homophthalic anhydrides with dienophiles is regarded [27] as [4+2] cycloaddition, *i.e.* as a pericyclic reaction showing ρ *ca*. 0 in general.

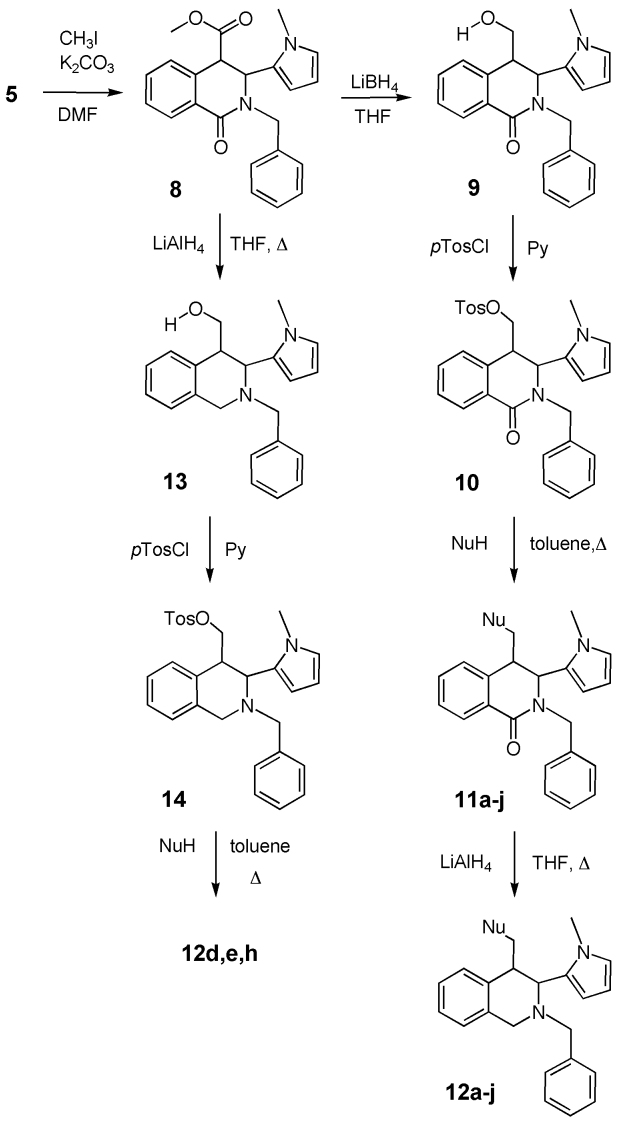
Scheme 2

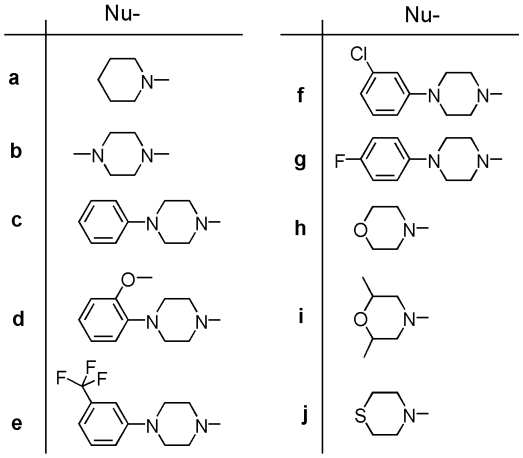


Scheme 3 gives the route of acid **5** to the final compounds **11** and **12**. The pathway to **11a-j** is similar to that used by Bigg and co-workers [22] to prepare a given tetrahydroisoquinolinone having a cyclic amino-methyl group at position 4.

The conversion of acid **5** in methyl ester **8** was accomplished by treatment with iodomethane in the presence of potassium carbonate since the direct esterification of acid **5** lead to a mixture of unidentified products. Ester **8** was reduced with lithium borohydride in tetrahydrofuran to the corresponding hydroxymethyl derivative **9**. The reduction did not affect the amide group. Alcohol **9** was converted to the corresponding tosylate **10**. Reaction of **10** with any of the secondary amines, denoted as NuH, yielded, after a prolonged heating, tetrahydroisoquinolinones **11a-j**. Reduction of the latter with lithium aluminium hydride gave tetrahydroisoquinolines **12a-j** that could be also of pharmacological interest.

Scheme 3

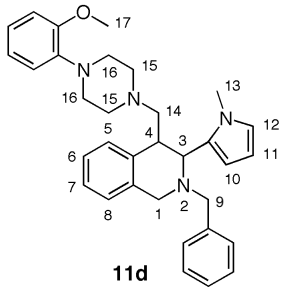




Ester **8** was reduced completely with lithium aluminium hydride to alcohol **13** that was converted to tosylate **14**. Reaction of **14** with three secondary amines gave **12d,e,h** in low yields because of the presence of great number of side products. Thus, this shorter path from **8** to **12** is not convenient.

Starting from *trans* acid **5**, compounds **8-12** obtained have *trans* configuration, *i.e*. all reactions are stereospecific.

The description of the ^{1}H nmr spectra uses the arbitrary numbering given in formula **11d**. The signals in ^{1}H of **11e** and **12g** were attributed by COSY experiments and these data were taken into account in the analysis of the other ^{1}H spectra.



11d

The ir spectra of **11a-j** show CO (amide) of 1640 cm^{-1}. The ir spectra of compounds **12a-j** do not show a band for a carbonyl group.

Majority of the compounds prepared has passed pharmacological screening showing moderate activities [28].

EXPERIMENTAL

Melting points were determined on a Kofler hot stage and are uncorrected. The ir spectra were acquired on a Specord 75 and are reported in reciprocal centimeters. Nujol was used for **5**, **6a** and **7a** and chloroform for all other compounds. The ^{1}H nmr spectra were obtained on a Bruker AM400 NMR spectrometer at 400.13 MHz in deuteriochloroform as solvent, if not stated otherwise. The chemical shift is given in ppm (δ) relative to tetramethylsilane as internal standard. The ^{13}C nmr spectrum of **6b** was obtained on the same spectrometer at 100.6 MHz in deuteriochloroform. Mass spectra were recorded on a Hewlet Packard MS 5973 spectrometer and Hewlet Packard GC-MS 5372 using electron impact of 30 eV and 100 eV, respectively. The mass spectra of **7b**, **11d-g** and **12c-g** were acquired at 30 eV and those of the remaining compounds at 100 eV. Elemental analyses were obtained in the relevant laboratories at the Faculty of Chemisty, University of Sofia and at the Institute of Organic Chemistry, Bulgarian Academy of Sciences. Tlc was done on precoated 0.2 mm Merck silica gel 60F_{254} plates. Mobile phases used are given in ref. 29. Merck silica gel 60 (0.040-0.063 mm) was used for chromatographic filtration and flash-chromatography.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-1-oxo-1,2,3,4-tetrahydro-4-isoquinoline Carboxylic Acid (**5**) and by-products **6a** and **7a**.

To a hot and stirred solution of homophthalic anhydride (23.89 g, 0.147 mole) in 220 mL dry benzene, *N*-(1-methyl-1*H*-pyrrol-2-yl-methylidene)-benzylamine (**4**) (29.20 g, 0.147 mole) in 30 mL dry benzene was added dropwise for 30 min. The reaction mixture was refluxed for 15 min and left overnight. The colorless crystals were filtered and washed with ethyl acetate yielding 33.9 g (64 %) of **5**. The filtrate was extracted twice with 10 % sodium hydroxide and the alkaline solutions were acidified, extracted three times with ethyl acetate. The combined organic layers were dried (sodium sulfate) and evaporated under reduced pressure leaving a dark oil (14.2 g). Fractional recrystallisation of the latter from ethyl acetate gave an additional quantity of acid **5** (3.2 g, 6 %) along with 1.9 g (5 %) **6a** and 3.4 g (6 %) **7a**.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-1-oxo-1,2,3,4-tetrahydro-4-isoquinoline Carboxylic Acid (**5**).

Compound **5** was obtained as white crystals, mp 226-228°; ir (Nujol): 1710 (CO_2H, dimer), 1700 (CO_2H, monomer), 1640 (CON) cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.55 (s, 3H, 13-H), 3.86 (d, 1H, 9-H, J = 15.1 Hz), 4.13 (d, 1H, 4-H, J = 1.6 Hz), 5.20 (d, 1H, 9-H, J = 15.1 Hz), 5.27 (d, 1H, 3-H, J = 1.6 Hz), 5.31-5.33 (m, 1H, 10-H), 5.72-5.75 (m, 1H, 11-H), 6.63-6.65 (m, 1H, 12-H), 7.21-7.48 (m, 8H, phenyl protons), 7.96-8.00 (m, 1H, 8-H), 13.01 (br. s, 1H, CO_2H).

Anal. Calcd. for $C_{22}H_{20}N_2O_3$: C, 73.33; H, 5.59. Found: C, 73.66; H, 5.66.

2-[2-(Benzylamino)-2-oxoethyl]benzenecarboxylic Acid (**6a**).

This by-product was obtained as white crystals, mp 141-143°; ir (Nujol): NH 3300, CO 1710, 1610, cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.92 (s, 2H, -CH_2CO-), 4.27 (d, 2H, -$CH_2C_6H_5$, J = 5.9 Hz), 7.22-7.51 (m, 8H, phenyl protons), 7.82-7.85 (m, 1H, phenyl proton), 8.38 (t, 1H, NH, J = 5.9 Hz), 12.92 (s, 1H, -CO_2H).

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.38; H, 5.62. Found: C, 71.38; H, 5.82.

2-[1-[(Benzylamino)carbonyl]-2-(1-methyl-1*H*-pyrrol-2-yl)ethenyl]benzenecarboxylic Acid (**7a**).

This by-product was obtained as white crystals, mp 194-195°; ir (Nujol): NH 3370, CO 1710, 1640 cm^{-1}; ^{1}H nmr: δ 3.67 (s, 3H, -CH_3), 4.27 (dd, 1H, -$CH_2C_6H_5$, J = 15.4, 5.7 Hz), 4.40 (dd, 1H, -$CH_2C_6H_5$, J = 15.4, 6.4 Hz), 5.05-5.07 (m, 1H, pyrrol), 5.80-5.82 (m, 1H, pyrrol), 6.90-6.92 (m, 1H, pyrrol), 7.06-7.25 (m, 6H, phenyl protons), 7.44-7.50 (m, 2H, phenyl protons), 7.53 (s, 1H, =CH-), 7.70-7.74 (m, 1H, phenyl proton), 8.52 (t, 1H, -NH, J = 5.9 Hz), 12.07 (s, 1H, -CO_2H).

Anal. Calcd. for $C_{22}H_{20}N_2O_3$: C, 73.31; H, 5.59. Found: C, 73.64; H, 5.93.

Methyl 2-[2-(Benzylamino)-2-oxoethyl]benzenecarboxylate (**6b**).

This compound was obtained from the reaction of acid **6a** and diazomethane in diethyl ether at room temperature for 1 hour. It was obtained as white crystals (ethyl acetate) in 90 %, mp 115-118° (lit., [16] 115-118°); ir: NH 3470, 3410, CO 1720, 1675 cm^{-1}; ^{1}H nmr: δ 3.88 (s, 3H, -CH_3), 3.93 (s, 2H, -CH_2CO-), 4.40 (d, 2H, -CH_2NH, J = 5.8 Hz), 6.74 (broad s, 1H, -NH), 7.21-7.56 (m, 8H, phenyl protons), 7.95-8.00 (m, 1H, phenyl proton); ^{13}C nmr: δ 42.9, 44.0, 53.0, 127.8 (2C), 128.0 (2C), 129.2 (2C), 130.2, 131.6, 133.0, 133.3, 137.9, 139.7, 169.0, 171.2.

Methyl 2-[1-[(Benzylamino)carbonyl]-2-(1-methyl-1*H*-pyrrol-2-yl)ethenyl]benzenecarboxylate (**7b**).

This compound was obtained from **7a** as described for **6b** as white crystals (ethyl acetate) in 80%, mp 140-142°; ir: NH 3470, CO 1735, 1670, C=C 1620 cm^{-1}; ^1H nmr: δ 3.76 (s, 6H, $-CH_3$), 4.37 (dd, 1H, $-CH_2C_6H_5$, J = 15.2, 5.6 Hz), 4.61 (dd, 1H, $-CH_2C_6H_5$, J = 15.2, 6.4 Hz), 4.94-4.95 (m, 1H, pyrrol), 5.64 (broad s, 1H, -NH), 5.85 (m, 1H, pyrrol), 6.66 (m, 1H, pyrrol), 7.21-7.40 (m, 6H, phenyl protons), 7.55-7.70 (m, 2H, phenyl protons), 7.79 (s, 1H, =CH-), 8.13-8.15 (m, 1H, phenyl proton); ms: m/z 374 (molecular ion).

Anal. Calcd. for $C_{22}H_{22}N_2O_3$: C, 73.78; H, 5.92. Found: C, 73.60; H, 6.04.

(±)-*trans*-Methyl-2-benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-1-oxo-1,2,3,4-tetrahydro-4-isoquinoline carboxylate (**8**).

To a mixture of potassium carbonate (9.77 g, 0.071 mole) and acid **5** (25.5 g, 0.071 mole) in dimethylformamide (300 mL), iodomethane (20.07 g, 0.142 mole) was added dropwise for 1 hour. The reaction mixture was stirred for 12 hours, added to water and extracted with ethyl acetate. The organic layer was washed with water, dried (sodium sulfate) and evaporated giving an oil. The latter afforded **8** as white crystals (ethyl acetate) in 80%, mp 145-146°; ir: CO 1740, 1640 cm^{-1}; ^1H nmr: δ 3.42 (s, 3H, CO_2CH_3), 3.48 (s, 3H, 13-H), 3.72 (d, 1H, 9-H, J = 14.8 Hz), 3.83 (d, 1H, 4-H, J = 2.2 Hz), 5.08 (d, 1H, 3-H, J = 2.2 Hz), 5.65-5.67 (m, 1H, 10-H), 5.66 (d, 1H, 9-H, J = 14.8 Hz), 5.91-5.92 (m, 1H, 11-H), 6.51-6.52 (m, 1H, 12-H), 7.05-7.07 (m, 1H, phenyl proton), 7.21-7.34 (m, 5H, phenyl protons), 7.43-7.48 (m, 2H, phenyl protons), 8.21-8.28 (m, 1H, 8-H); ms: m/z 374 (molecular ion).

Anal. Calcd. for $C_{23}H_{22}N_2O_3$: C, 73.78; H, 5.92. Found: C, 73.80; H, 6.13.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-hydroxymethyl-1,2,3,4-tetrahydroisoquinolin-1-one (**9**).

To a stirred suspension of potassim borohydride (7.53 g, 0.140 mole) and lithium chloride (5.91 g, 0.140 mole) in tetrahydrofuran (200 mL), ester **8** (20.86 g, 0.056 mole) dissolved in tetrahydrofuran (200 mL) was added dropwise. The reaction mixture was stirred at room temperature for 13 hours, concentrated under reduced pressure, poured into water and extracted with ethyl acetate. The organic layer was washed with water, dried (sodium sulfate) and evaporated affording crystals. The latter gave **9** as white prisms (ethyl acetate) in 97%, mp 157-158°; ir: OH 3610, CO 1640 cm^{-1}; ^1H nmr: δ 0.89 (t, 1H, -OH, J = 5.2 Hz), 2.93 (dd, 1H, 4-H, J = 10.3, 5.2 Hz), 3.27-3.34 (m, 1H, 14-H), 3.46 (s, 4H, 13-, 14- H), 3.53 (d, 1H, 9-H, J = 14.4 Hz), 4.82 (s, 1H, 3-H), 5.57-5.58 (m, 1H, 10-H), 5.76 (d, 1H, 9-H, J = 14.4 Hz), 5.82-5.84 (m, 1H, 11-H), 6.44-6.45 (m, 1H, 12-H), 6.92-6.95 (m, 1H, phenyl proton), 7.27-7.32 (m, 7H, phenyl protons), 8.12-8.16 (m, 1H, 8-H); ms: m/z 346 (molecular ion).

Anal. Calcd. for $C_{22}H_{22}N_2O_2$: C, 76.28; H, 6.40. Found: C, 76.45; H, 6.66.

(±)-*trans*-2-Benzyl-1-oxo-3-(1-methyl-1*H*-pyrrol-2-yl)-4-tosyloxymethyl-1,2,3,4-tetrahydroisoquinoline (**10**).

To a solution of **9** (19.78 g, 0.057 mole) in pyridine (100 mL) kept at -5°, *p*-toluenesulfonyl chloride (21.81 g, 0.114 mole) was added in portions. The reaction mixture was stirred at room temperature for 15 hours, poured into water and extracted with ethyl acetate. The organic layer was thoroughly washed with water, dried (sodium sulfate) and evaporated to dryness. The resulting oil gave **10** as colorless crystals (chloroform) in 66%, mp 103-105 °; ir: CO 1660 cm^{-1}; ^1H nmr: 2.45 (s, 3H, 15-H), 3.30 (m, 1H, 4-H), 3.48 (s, 1H, 13-H), 3.76 (d, 1H, 9-H, J = 14.5 Hz), 3.82 (t, 1H, 14-H, J = 10.4 Hz), 3.97 (dd, 1H, 14-H, J = 10.4, 5.0 Hz), 4.86 (s, 1H, 3-H), 5.56-5.59 (m, 1H, 10-H), 5.57 (d, 1H, 9-H, J = 14.5 Hz), 5.86-5.89 (m, 1H, 11-H), 6.50-6.51 (m, 1H, 12-H), 7.03-7.06 (m, 1H, phenyl proton), 7.22-7.57 (m, 11H, phenyl protons), 8.17-8.23 (m, 1H, 8-H).

Anal. Calcd. for $C_{29}H_{28}N_2O_4S$: C, 69.59; H, 5.64. Found: C, 69.46; H, 5.70.

General Procedure for the Preparation of (±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-(*N*,*N*-disubstituted-aminomethyl)-1,2,3,4-tetrahydroisoquinolin-1-ones (**11**).

A relavent secondary amine NuH (21-28 mmoles) was added to a solution of tosylate **10** (3.5 g, 7 mmoles) in 15 mL toluene. The reaction mixture was refluxed (9-36 hrs) until **10** was consumed, which was followed by tlc. Ethyl acetate (200 mL) was added after cooling. The organic layer was thoroughly washed with water and dried (sodium sulfate). The solvents were removed under reduced pressure. The resulting brown oil was purified by chromatographic filtration or flash chromatography.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(piperidin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11a**).

This compound was obtained as white crystals (ethyl acetate) in 57%, mp 149-151°; ^1H nmr: δ 1.32 (s, 6H, 16-H), 1.64-1.68 (m, 2H, 15-H), 2.02 (dd, 1H, 14-H, J = 12.0, 3.2 Hz), 2.23 (t, 1H, 14-H, J = 12.0 Hz), 2.27-2.46 (m, 2H, 15-H), 2.91 (dd, 1H, 4-H, J = 12.0, 3.0 Hz), 3.53 (d, 1H, 9-H, J = 14.0 Hz), 3.59 (s, 3H, 13-H), 5.18 (s, 1H, 3-H), 5.64-5.65 (m, 1H, 10-H), 5.77 (d, 1H, 9-H, J = 14.0 Hz), 5.91-5.92 (m, 1H, 11-H), 6.52-6.53 (m, 1H, 12-H,), 6.95-6.97 (m, 1H, phenyl proton), 7.26-7.39 (m, 7H, phenyl protons), 8.19-8.23 (m, 1H, 8-H); ms: m/z 413 (molecular ion).

Anal. Calcd. for $C_{27}H_{31}N_3O$: C, 78.42; H, 7.56. Found: C, 78.19; H, 7.45.

(±)-*trans*-2-Benzyl-3-(1-methyl-1H-pyrrol-2-yl)-4-[(4-methylpyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11b**).

This compound was obtained as white prisms (ethyl acetate-hexane) in 88%, mp 147-149°; ^1H nmr: δ 1.63 (broad s, 4H, 15-, 16-H), 2.09 (dd, 1H, 14-H, J = 12.9, 3.2 Hz), 2.23 (s, 7H, 15-, 16-, 17-H), 2.30 (t, 1H, 14-H, J = 12.9 Hz), 2.90 (dd, 1H, 4-H, J = 11.9, 3.0 Hz), 3.50 (d, 1H, 9-H, J = 14.3 Hz), 3.59 (s, 3H, 13-H), 5.14 (s, 1H, 3-H), 5.64-5.65 (m, 1H, 10-H), 5.80 (d, 1H, 9-H, J = 14.3 Hz), 5.92-5.93 (m, 1H, 11-H), 6.53-6.54 (m, 1H, 12-H), 6.95-7.00 (m, 1H, phenyl proton), 7.26-7.42 (m, 7H, phenyl protons), 8.21-8.24 (m, 1H, 8-H); ms: m/z 428 (molecular ion).

Anal. Calcd. for $C_{27}H_{32}N_4O$: C, 75.67; H, 7.53. Found: C, 75.92; H, 7.66.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-phenylpyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11c**).

This compound was obtained as white prisms (ethyl acetate) in 66%, mp 132-134°; ^1H nmr: δ 1.84-1.87 (m, 2H, 15-H), 2.14 (dd,

1H, 14-H, J = 12.8, 3.0 Hz), 2.36 (t, 1H, 14-H, J = 12.8 Hz), 2.56-2.58 (m, 2H, 15-H), 2.94-3.03 (m, 5H, 4-, 16-H), 3.50 (d, 1H, 9-H, J = 14.2 Hz), 3.59 (s, 3H, 13-H), 5.23 (s, 1H, 3-H), 5.65-5.66 (m, 1H, 10-H), 5.83 (d, 1H, 9-H, J = 14.2 Hz), 5.92-5.93 (m, 1H, 11-H), 6.53-6.54 (m, 1H, 12-H), 6.71-6.90 (m, 3H, phenyl protons), 6.99-7.01 (m, 1H, phenyl proton), 7.26-7.41 (m, 9H, phenyl protons), 8.23-8.25 (m, 1H, 8-H); ms: m/z 490 (molecular ion).

Anal. Calcd. for $C_{32}H_{34}N_4O$: C, 78.34; H, 6.98. Found: C, 78.02; H, 7.08.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-(2-methoxyphenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11d**).

This compound was obtained as white prisms (ethyl acetate-Hexane) in 63%, mp 147-148°; ^{1}H nmr: δ 1.72 (broad s, 2H, 15-H), 1.97 (dd, 1H, 14-H, J = 12.8, 3.2 Hz), 2.17 (t, 1H, 14-H, J = 12.8 Hz), 2.43 (broad s, 2H, 15-H), 2.62 (broad s, 4H, 16-H), 2.76 (dd, 1H, 4-H, J = 11.9, 2.6 Hz), 3.32 (d, 1H, 9-H, J = 14.3 Hz), 3.41 (s, 3H, 13-H), 3.66 (s, 3H, 17-H), 5.02 (s, 1H, 3-H), 5.46-5.47 (m, 1H, 10-H), 5.63 (d, 1H, 9-H, J = 14.3 Hz), 5.73-5.75 (m, 1H, 11-H), 6.34-6.36 (m, 1H, 12-H), 6.67-6.83 (m, 4H, phenyl protons), 7.07-7.21 (m, 8H, phenyl protons), 8.03-8.06 (m, 1H, 8-H); ms: m/z 520 (molecular ion).

Anal. Calcd. for $C_{33}H_{36}N_4O_2$: C, 76.12; H, 6.97. Found: C, 76.02; H, 7.05.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-(3-trifluoromethyl-phenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-one (**11e**).

This compound was obtained as colorless prisms (ethyl acetate) in 51%, mp 158-160°; ^{1}H nmr: δ 1.66-1.70 (m, 2H, 15-H), 1.96 (dd, 1H, 14-H, J = 12.8, 3.2 Hz), 2.19 (t, 1H, 14-H, J = 12.8 Hz), 2.38-2.40 (m, 2H, 15-H), 2.75-2.78 (m, 5H, 4-, 16-H), 3.31 (d, 1H, 9-H, J = 14.3 Hz), 3.41 (s, 3H, 13-H), 4.98 (s, 1H, 3-H), 5.47-5.48 (m, 1H, 10-H), 5.64 (d, 1H, 9-H, J = 14.3 Hz), 5.74-5.76 (m, 1H, 11-H), 6.36-6.37 (m, 1H, 12-H), 6.81-6.86 (m, 4H, phenyl protons), 7.15-7.23 (m, 8H, phenyl protons), 8.04-8.07 (m, 1H, 8-H); ms: m/z 558 (molecular ion).

Anal. Calcd. for $C_{33}H_{33}F_3N_4O$: C, 70.95; H, 5.95. Found: C, 70.90; H, 6.19.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-(3-chlorophenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11f**).

This compound was obtained as yellow crystals (ethyl acetate) in 57%, mp 192-194°; ^{1}H nmr: δ 2.00-2.04 (m, 2H, 15-H), 2.32 (dd, 1H, 14-H, J = 12.7, 3.1 Hz), 2.54 (t, 1H, 14-H, J = 12.7 Hz) 2.72-2.75 (m, 2H, 15-H), 3.07-3.13 (m, 5H, 4-, 16-H), 3.67 (d, 1H, 9-H, J = 14.2 Hz), 3.77 (s, 3H, 13-H), 5.35 (s, 1H, 3-H), 5.84-5.85 (m, 1H, 10-H), 6.02 (d, 1H, 9-H, J = 14.2 Hz), 6.11-6.12 (m, 1H, 11-H), 6.72-6.73 (m, 1H, 12-H), 6.93-7.01 (m, 3H, phenyl protons), 7.19-7.59 (m, 9H, phenyl protons), 8.41-8.43 (m, 1H, 8-H); ms: m/z 524 (molecular ion).

Anal. Calcd. for $C_{32}H_{33}ClN_4O$: C, 73.20; H, 6.33. Found: C, 73.09; H, 6.45.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-fluorophenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11g**).

This compound was obtained as white crystals (ethyl acetate) in 63%, mp 232-234°; ^{1}H nmr: δ 1.64-1.68 (m, 2H, 15-H), 1.95 (dd, 1H, 14-H, J = 12.7 Hz), 2.16 (t, 1H, 14-H, J = 12.7 Hz), 2.36-2.38 (m, 2H, 15-H), 2.62-2.66 (m, 4H, 16-H), 2.74 (dd, 1H, 4-H, J = 11.9, 2.6 Hz), 3.30 (d, 1H, 9-H, J = 14.3 Hz), 3.39 (s, 3H, 13-H), 4.97 (s, 1H, 3-H), 5.46-5.47 (m, 1H, 10-H), 5.63 (d, 1H, 9-H, J = 14.3 Hz), 5.72-5.74 (m, 1H, 11-H), 6.34-6.35 (m, 1H, 12-H), 6.62-6.64 (m, 2H, phenyl protons), 6.75-6.79 (m, 3H, phenyl protons), 7.06-7.21 (m, 7H, phenyl protons), 8.03-8.05 (m, 1H, 8-H); ms: m/z 508 (molecular ion).

Anal. Calcd. for $C_{32}H_{33}FN_4O$: C, 75.56; H, 6.54. Found: C, 75.61; H, 6.65.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(morpholin-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11h**).

This compound was obtained as colorless crystals (ethyl acetate) in 82%, mp 178-180°; ^{1}H nmr: δ 1.73 (broad s, 2H, 15-H), 2.11 (dd, 1H, 14-H, J = 12.8, 3.3 Hz), 2.27 (t, 1H, 14-H, J = 12.8 Hz), 2.39 (broad s, 2H, 15-H), 2.91 (dd, 1H, 4-H, J = 11.9, 2.9 Hz), 3.41-3.45 (m, 4H, 16-H), 3.49 (d, 1H, 9-H, J = 14.2 Hz) 3.59 (s, 3H, 13-H), 5.17 (s, 1H, 3-H), 5.64-5.67 (m, 1H, 10-H), 5.82 (d, 1H, 9-H, J = 14.2 Hz), 5.92-5.93 (m, 1H, 11-H), 6.53-6.54 (m, 1H, 12-H), 6.96-6.98 (m, 1H, phenyl proton), 7.24-7.42 (m, 7H, phenyl protons), 8.21-8.24 (m, 1H, 8-H) ; ms: m/z 415 (molecular ion).

Anal. Calcd. for $C_{26}H_{29}N_3O_2$: C, 75.15; H, 7.03. Found: C, 75.20; H, 7.33.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(2,6-dimethyl-morpholin-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11i**).

This compound was obtained as white crystals (ethyl acetate-hexane) in 53%, mp 150-152°; ^{1}H nmr: δ 0.91-1.06 (m, 6H, 17-H), 1.43-1.61 (m, 4H, 15-H), 1.97 (dd, 1H, 14-H, J = 12.7, 3.1 Hz), 2.19 (t, 1H, 14-H, J = 12.7 Hz), 2.85 (dd, 1H, 4-H, J = 11.8, 2.7 Hz), 3.37-3.53 (m, 2H, 16-H), 3.40 (d, 1H, 9-H, J = 14.3 Hz), 3.51 (s, 3H, 13-H), 5.08 (s, 1H, 3-H), 5.56-5.60 (m, 1H, 10-H), 5.76 (d, 1H, 9-H, J = 14.3 Hz), 5.85-5.87 (m, 1H, 11-H), 6.46-6.47 (m, 1H, 12-H), 6.90-6.92 (m, 1H, phenyl proton), 7.22-7.35 (m, 7H, phenyl protons), 8.15-8.17 (m, 1H, 8-H); ms: m/z 443 (molecular ion).

Anal. Calcd. for $C_{28}H_{33}N_3O_2$: C, 75.82, H, 7.50. Found: C, 76.17; H, 7.55.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(thiomorpholin-4-yl)methyl]-1,2,3,4-tetrahydroisoquinolin-1-one (**11j**).

This compound was obtained as white crystals (ethyl acetate) in 77%, mp 195-197°; ^{1}H nmr: δ 1.71-1.75 (m, 2H, 15-H), 1.91-1.99 (m, 2H, 14-H), 2.16-2.23 (m, 4H, 16-H), 2.43 (broad s, 2H, 15-H), 2.67 (dd, 1H, 4-H, J = 11.2, 3.5 Hz), 3.27 (d, 1H, 9-H, J = 14.3 Hz), 3.39 (s, 3H, 13-H), 4.86 (s, 1H, 3-H), 5.43-5.44 (m, 1H, 10-H), 5.62 (d, 1H, 9-H, J = 14.3 Hz), 5.71-5.72 (m, 1H, 11-H), 6.33-6.34 (m, 1H, 12-H), 6.74-6.76 (m, 1H, phenyl proton), 7.07-7.26 (m, 7H, phenyl protons), 8.00-8.03 (m, 1H, 8-H); ms: m/z 431 (molecular ion).

Anal. Calcd. for $C_{26}H_{29}N_3OS$: C, 72.36; H, 6.77. Found: C, 72.38; H, 6.77.

General Procedure for the Preparation of (±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-(*N*,*N*-disubstituted-aminomethyl)-1,2,3,4-tetrahydroisoquinolines (**12**).

Lithium aluminium hydride (1.1 mmoles) was added in portions to a solution of **11** (1 mmole) in 4 mL dry tetrahydrofuran

and the reaction mixture was refluxed 1-2 hours. After cooling, water (4.4 mmoles) was added. The reaction mixture was stirred for 30 minutes and dried (magnesium sulfate). The inorganic precipitate was filtered and washed with dichloromethane. The solvent was removed from the filtrate and the product was purified by chromatographic filtration or recrystallisation.

Compounds **12d,e,h** were prepared also from tosylate **14** and the corresponding secondary amine NuH by the general method for synthesis of **11**.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(piperidin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12a**).

This compound was obtained as white crystals (ethyl acetate) in 72%, mp 113-115°; ^{1}H nmr: δ 1.32-1.45 (m, 6H, 16-H), 2.19 (dd, 1H, 14-H, J = 11.8, 3.1 Hz), 2.24 (broad s, 2H, 15-H), 2.47 (broad s, 2H, 15-H), 2.85 (d, 1H, 4-H, J = 11.0 Hz), 2.96 (t, 1H, 14-H, J = 11.8 Hz), 3.40 (s, 3H, 13-H), 3.45 and 3.52 (d, each 1H, 1-H, J = 13.7 Hz), 3.69 (s, 2H, 9-H), 4.59 (s, 1H, 3-H), 5.42-5.43 (m, 1H, 10-H), 5.87-5.89 (m, 1H, 11-H), 6.43-6.44 (m, 1H, 12-H), 6.91-7.07 (m, 4H, phenyl protons), 7.17-7.28 (m, 5H, phenyl protons); ms: m/z 399 (molecular ion).

Anal. Calcd. for $C_{27}H_{33}N_3$: C, 81.16, H, 8.32. Found: C, 81.20; H, 8.49.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-methylpyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12b**).

This compound was obtained as white crystals (ethyl acetate) in 58%, mp 133-135°; ^{1}H nmr: δ 2.26 (s, 3H, 17-H), 2.33 (dd, 1H, 14-H, J = 12.2, 2.7 Hz), 2.43 (broad s, 4H, 15-, 16-H), 2.65 (broad s, 4H, 15-, 16-H), 2.94 (dd, 1H, 4-H, J = 11.1, 1.7 Hz), 3.10 (t, 1H, 14-H, J = 12.2 Hz), 3.50 (s, 3H, 13-H), 3.53 and 3.60 (d, each 1H, 1-H, J = 13.7 Hz), 3.77 (s, 2H, 9-H), 4.62 (d, 1H, 3-H, J = 1.7 Hz), 5.50-5.52 (m, 1H, 10-H), 5.96-5.97 (m, 1H, 11-H), 6.52-6.54 (m, 1H, 12-H), 6.99-7.04 (m, 1H, phenyl proton), 7.12-7.16 (m, 3H, phenyl protons), 7.26-7.36 (m, 5H, phenyl protons); ms: m/z 414 (molecular ion).

Anal. Calcd. for $C_{27}H_{34}N_4$: C, 78.22, H, 8.26. Found: C, 78.07; H, 8.41.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-phenylpyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12c**).

This compound was obtained as white crystals (ethyl acetate) in 61%, mp 124-126°; ^{1}H nmr: δ 2.41 (dd, 1H, 14-H, J = 12.2, 3.6 Hz), 2.55-2.60 (m, 2H, 15-H), 2.77-2.82 (m, 2H, 15-H), 3.00 (dd, 1H, 4-H, J = 11.0, 1.9 Hz), 3.08-3.21 (m, 5H, 14-, 16-H), 3.48 (s, 3H, 13-H), 3.59 (s, 2H, 1-H), 3.83 (s, 2H, 9-H), 4.67 (d, 1H, 3-H, J = 1.3 Hz), 5.54-5.55 (m, 1H, 10-H), 5.99-6.00 (m, 1H, 11-H), 6.54-6.55 (m, 1H, 12-H), 6.85-6.95 (m, 3H, phenyl protons), 7.08-7.39 (m, 11H, phenyl protons); ms: m/z 476 (molecular ion).

Anal. Calcd. for $C_{32}H_{36}N_4$: C, 80.63, H, 7.61. Found: C, 80.71; H, 7.53.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-(2-methoxyphenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12d**).

This compound was obtained from **11d** in 80% and from **14** in 44% as white crystals (ethyl acetate-hexane), mp 123-125°; ^{1}H nmr: δ 2.41 (dd, 1H, 14-H, J = 12.1, 3.6 Hz), 2.60 (broad s, 2H, 15-H), 2.72 (broad s, 2H, 15-H), 2.91-2.99 (m, 5H, 4-, 16-H), 3.16 (t, 1H, 14-H, J = 12.1 Hz), 3.48 (s, 3H, 13-H), 3.55 and 3.60 (d, each 1H, 1-H, J = 13.7 Hz), 3.80 (s, 2H, 9-H), 3.86 (s, 3H, 17-H), 4.67 (d, 1H, 3-H, J = 1.4 Hz), 5.52-5.53 (m, 1H, 10-H), 5.96-5.98 (m, 1H, 11-H), 6.52-6.53 (m, 1H, 12-H), 6.85-7.32 (m, 13H, phenyl protons); ms: m/z 506 (molecular ion).

Anal. Calcd. for $C_{33}H_{38}N_4O$: C, 78.23, H, 7.56. Found: C, 78.34; H, 7.56.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-(3-trifluoromethyl-phenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12e**).

This compound was obtained from **12e** in 72% and from **14** in 35% as white crystals (ethanol), mp 124-126°; ^{1}H nmr: δ 2.42 (dd, 1H, 14-H, J = 12.3, 3.6 Hz), 2.56-2.61 (m, 2H, 15-H), 2.77-2.82 (m, 2H, 15-H), 3.01 (m, 1H, 4-H), 3.13-3.22 (m, 5H, 14-, 16-H), 3.50 (s, 3H, 13-H), 3.58 and 3.63 (d, each 1H, 1-H, J = 13.7 Hz), 3.84 (s, 2H, 9-H), 4.65 (d, 1H, 3-H, J = 1.6 Hz), 5.55-5.64 (m, 1H, 10-H), 5.99-6.01 (m, 1H, 11-H), 6.55-6.56 (m, 1H, 12-H), 7.02-7.38 (m, 13H, phenyl protons); ms: m/z 544 (molecular ion).

Anal. Calcd. for $C_{33}H_{35}F_3N_4$: C, 72.77, H, 6.48. Found: C, 72.92; H, 6.56.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-(3-chlorophenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12f**).

This compound was obtained as white solvated with ethylacetate crystals in 88%, mp 116-118°; ^{1}H nmr: δ 2.57 (dd, 1H, 14-H, J = 12.3, 3.6 Hz), 2.71-2.75 (m, 2H, 15-H), 2.92-2.97 (m, 2H, 15-H), 3.17 (d, 1H, 4-H, J = 11.3 Hz), 3.27-3.38 (m, 5H, 14-, 16-H), 3.66 (s, 3H, 13-H), 3.76 (s, 2H, 1-H), 4.00 (s, 2H, 9-H), 4.81 (d, 1H, 3-H, J = 1.5 Hz), 5.71-5.73 (m, 1H, 10-H), 6.16-6.17 (m, 1H, 11-H), 6.72-6.73 (m, 1H, 12-H), 6.98-7.05 (m, 3H, phenyl protons), 7.33-7.54 (m, 10H, phenyl protons); ms: m/z 510 (molecular ion). The nmr and ir spectra showed the corresponding signals for ethyl acetate.

Anal. Calcd. for $C_{32}H_{35}ClN_4 \cdot 1/3CH_3CO_2C_2H_5$: C, 74.07, H, 7.03. Found: C, 74.01; H, 7.36.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(4-fluorophenyl)pyperazin-1-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12g**).

This compound was obtained as white crystals (ethanol) in 56%, mp 154-156°; ^{1}H nmr: δ 2.65 (dd, 1H, 14-H, J = 12.1, 3.6 Hz), 2.79-2.83 (m, 2H, 15-H), 3.01-3.05 (m, 2H, 15-H), 3.22-3.33 (m, 5H, 4-, 16-H), 3.42 (t, 1H, 14-H, J = 12.1 Hz), 3.73 (s, 3H, 13-H), 3.80 and 3.84 (d, each 1H, 1-H, J = 13.8 Hz), 4.06 (s, 2H, 9-H), 4.89 (s, 1H, 3-H), 5.77-5.79 (m, 1H, 10-H), 6.22-6.24 (m, 1H, 11-H), 6.78-6.79 (m, 1H, 12-H), 7.09-7.62 (m, 13H, phenyl protons); ms: m/z 494 (molecular ion).

Anal. Calcd. for $C_{32}H_{35}FN_4$: C, 77.70, H, 7.13. Found: C, 77.60; H, 7.25.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(morpholin-4-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12h**).

This compound was obtained from **11h** in 67% and from **14** in 47%, as white crystals (ethyl acetate-Hexane), mp 108-110°; ^{1}H nmr: δ 2.31 (dd, 1H, 14-H, J = 12.2, 3.6 Hz), 2.32-2.37 (m, 2H, 15-H), 2.54-2.57 (m, 2H, 15-H), 2.90 (d, 1H, 4-H, J = 11.2 Hz), 3.04 (t, 1H, 14-H, J = 12.2 Hz), 3.46 (s, 3H, 13-H), 3.50 and 3.55 (d, each 1H, 1-H, J = 13.7 Hz), 3.53-3.63 (m, 4H, 16-H), 3.75 (s, 2H, 9-H), 4.57 (d, 1H, 3-H, J = 1.6 Hz), 5.47-5.48 (m, 1H, 10-H),

5.92-5.94 (m, 1H, 11-H), 6.49-6.50 (m, 1H, 12-H), 7.00-7.13 (m, 4H, phenyl protons), 7.20-7.31 (m, 5H, phenyl protons); ms: m/z 401 (molecular ion).

Anal. Calcd. for $C_{26}H_{31}N_3O$: C, 77.77, H, 7.78. Found: C, 77.98; H, 7.81.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(2,6-dimethylmorpholin-4-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12i**).

This compound was obtained as yellow crystals (ethyl acetate) in 52%, mp 174-176°; ^{1}H nmr: δ 1.03-1.10 (m, 6H, 17-H), 1.63 (t, 1H, 15-H, J = 11.5 Hz), 1.82 (t, 1H, 15-H, J = 11.5 Hz), 2.20 (dd, 1H, 14-H, J = 12.0, 3.4 Hz), 2.52 (d, 1H, 4-H, J = 11.1 Hz), 2.75-2.86 (m, 2H, 15-H), 2.97 (t, 1H, 14-H, J = 12.0 Hz), 3.38 (s, 3H, 13-H), 3.40-3.52 (m, 4H, 1-, 16-H), 3.72 (s, 2H, 9-H), 4.52 (s, 1H, 3-H), 5.42-5.45 (m, 1H, 10-H), 5.87-5.91 (m, 1H, 11-H), 6.44-6.45 (m, 1H, 12-H), 6.96-7.28 (m, 9H, phenyl protons); ms: m/z 429 (molecular ion).

Anal. Calcd. for $C_{28}H_{35}N_3O$: C, 78.28, H, 8.21. Found: C, 78.10; H, 8.27.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-[(thiomorpholin-4-yl)methyl]-1,2,3,4-tetrahydroisoquinoline (**12j**).

This compound was obtained as white crystals (ethyl acetate) in 53%, mp 154-156°; ^{1}H nmr: δ 2.51 (dd, 1H, 14-H, J = 12.2, 3.4 Hz), 2.66-2.79 (m, 6H, 15-, 16-H), 2.98-3.03 (m, 3H, 4-, 15-H), 3.12 (t, 1H, 14-H, J = 12.2 Hz), 3.61 (s, 3H, 13-H), 3.67 (s, 2H, 1-H), 3.92 (s, 2H, 9-H), 4.66 (s, 1H, 3-H), 5.61-5.62 (m, 1H, 10-H), 6.06-6.09 (m, 1H, 11-H), 6.65-6.66 (m, 1H, 12-H), 7.14-7.46 (m, 9H, phenyl protons); ms: m/z 417 (molecular ion).

Anal. Calcd. for $C_{26}H_{31}N_3S$: C, 74.78, H, 7.48. Found: C, 74.76; H, 7.49.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline (**13**).

The completely reduced alcohol **13** was prepared from **8** in analogy to ref. [30] at reaction time 2 hours. It was obtained as white crystals (ethyl acetate) in 53%, mp 108-110°; ir: (OH) 3640 cm^{-1}; ^{1}H nmr: δ 1.57 (broad s, 1H, -OH), 2.98 (d, 1H, 4-H, J = 2.5 Hz), 3.32 (d, 1H, 9-H, J = 12.8 Hz), 3.52 and 3.65 (d, each 1H, 1-H, J = 15.5 Hz), 3.54 (s, 3H, 13-H), 3.71 (d, 1H, 9-H, J = 12.8 Hz), 3.92 and 4.11 (dd, each 1H, 14-H, J = 9.9, 3.5 Hz), 4.36 (d, 1H, 3-H, J = 2.5 Hz), 5.46-5.47 (m, 1H, 10-H), 5.88-5.90 (m, 1H, 11-H), 6.49-6.50 (m, 1H, 12-H), 6.91-6.93 (m, 1H, phenyl proton), 7.08-7.25 (m, 8H, phenyl protons); ms: m/z 322 (molecular ion).

Anal. Calcd. for $C_{22}H_{24}N_2O$: C, 79.48; H, 7.28. Found: C, 79.10; H, 7.27.

(±)-*trans*-2-Benzyl-3-(1-methyl-1*H*-pyrrol-2-yl)-4-tosyloxymethyl-1,2,3,4-tetrahydroisoquinoline (**14**).

The synthesis of the tosylate **14** from the parent alcohol **13** was similar to the preparation of **10**. The product was obtained as colorless crystals (ethyl acetate) in 63%, mp 126-128°; ^{1}H nmr: δ 2.38 (s, 3H, 15-H), 3.25-3.36 (m, 2H, 4-, 9-H), 3.46-3.66 (m, 6H, 1-, 9-, 13-H), 4.17 and 4.64 (t, each 1H, 14-H, J = 9.8 Hz), 4.35 (d, 1H, 3-H, J = 2.0 Hz), 5.43-5.44 (m, 1H, 10-H), 5.92-5.95 (m, 1H, 11-H), 6.55-6.56 (m, 1H, 12-H), 6.93-7.36 (m, 11H, phenyl protons), 7.76-7.80 (m, 2H, phenyl protons).

Anal. Calcd. for $C_{29}H_{30}N_2O_3S$: C, 71.58; H, 6.21. Found: C, 71.42; H, 6.17.

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REFERENCES AND NOTES

[1] Present address: Vanderbilt University, Chemistry Department, P. O. Box 1822-B, Nashville, TN 37235, USA.

* E-mail address: mpalamareva@chem.uni-sofia.bg.

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