Pergamon

Tetrahedron Vol. 50, No. 37, pp. 10971-10982, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4020/94 $7.00+0.00

0040-4020(94)00666-0

Preparation of a 3-Phenyl-4(3H)-isoquinolinone and its Transformation in 12(11H)-Benzo[*c*]phenanthridinone Derivatives. Crystal Structure Determinations.[1]

Ana M. González-Cameno, Dolores Badía,* and Esther Domínguez*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad del País Vasco, P.O.Box 644-48080 Bilbao. Spain.

M. Karmele Urtiaga,[1] M. Isabel Arriortua[1] and Xavier Solans[2]

[1]Departamento de Mineralogía-Petrología, Facultad de Ciencias, Universidad del País Vasco, P.O.Box 644-48080 Bilbao. Spain
[2]Departamento de Cristalografía, Mineralogía y Depósitos Minerales, Universidad de Barcelona, Martí i Franqués s/n, 08028 Barcelona. Spain

Abstract: *Trans*- and *cis*-5-(p-toluenesulfonyl)-5,6,13,14-tetrahydro-12(11H)-benzo[*c*] phenanthridinones have been prepared with excellent yield involving the initial formation of 3-phenyl-2-(p-toluenesulfonyl)-1,2-dihydro-4(3H)-isoquinolinone, as the key intermediate. Spectroscopic studies of the 4(3H)-isoquinolinone and 12(11H)-benzo[*c*]phenanthridinone derivatives have been developed and their relative configurations have been fully established and confirmed unambiguously by X-ray diffraction analyses.

INTRODUCTION

Benzophenanthridine alkaloids[2] occupy an incressingly important position in alkaloid chemistry from the finding of the marked potencies of some of these alkaloids against leukemia.[3] Such interest has been more recently intensified as they were shown to inhibit HIV 1 and 2 reverse transcriptases.[4]

Consequently the past years have seen a tremendous growth in interest in benzophenanthridine alkaloids and their chemistry and syntheses have become one of the most challenging problems. Thus, several total syntheses of different types of benzophenantridines were accomplised. Besides, there has been an increasing reliance on spectral data (mainly ^{1}H- and ^{13}C NMR spectra) and X-ray diffraction analyses[5] as the knowledge of their conformation and chemical reactivity helps in better understanding the mode of action and the biosynthesis of this type of compounds.

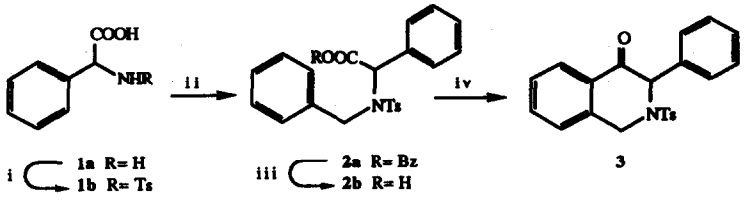
As part of our program of research on the chemistry of heterocyclic systems as potential pharmacological agents, in this paper we report an improved access to 12(11H)-benzophenanthridinone skeleton through formation of isoquinolinones as the key-intermediate, and studies of their conformation by NMR spectroscopic techniques. Moreover, X-ray analyses of both types of heterocycles have been performed, confirming the structure originally predicted by chemical and spectroscopic methods.

Synthesis of benzophenanthridines falls into different categories, which have been reviewed repeatedly.[6] Nevertheless, only few procedures have been previously reported for its regioselective synthesis starting from isoquinolinone derivatives of type 3.[7] These facts, together with our broad experience in the field of 3-arylisoquinolines[8] prompted us to develop a new access to 12(11H)-benzo[*c*]phenanthridinones applying a final intramolecular cyclization reaction to the appropriately functionalized isoquinoline precursor. It is noteworthy to

point out that, to our knowledge, this procedure represents the first known synthesis of the target tetracycles incorporating a carbonyl functionality at C12.

RESULTS AND DISCUSSION

Our first goal was the synthesis of the isoquinolinone intermediate **3**, which was carried out by alkylation with benzyl bromide of tosylated DL-2-phenylglycine **1b**, thus obtaining benzyl 2-[*N*-benzyl-*N*-(*p*-toluenesulfonyl)amino]-2-phenyl acetate **2a**, which upon catalytic hydrogenation/ internal acylation gave rise to formation of the isoquinolinone objective **3**. The overall yield for this preparation was 64%, thus improving the Olugbade's procedure for the synthesis of this type of precursor.[7a]



i) TsCl, NaOH, Et_2O, H_2O, r.t., 16h., 91%; ii) BzBr, K_2CO_3, CH_3CN, r.t., 26h., 89%; iii) 1.4 atm H_2, 10% Pd(C), EtOH, r.t., 1.5h., quantitative; iv) a: $SOCl_2$, benzene, reflux, 2h.; b: $AlCl_3$, CH_2Cl_2, -10°C, 4h., 79%.

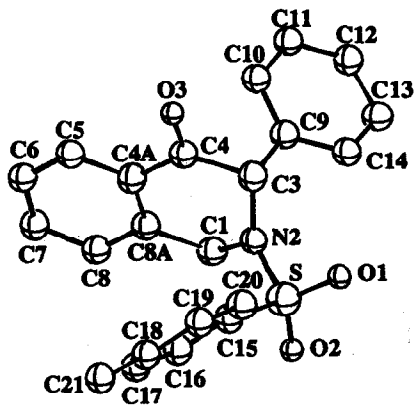


Figure 1. Ball and stick drawing of compound **3**.

The stereochemistry of the latter derivative **3** has been proposed in the basis of NOE experiments. Thus, observation of a NOE between H1a and the phenyl protons indicates a *pseudo-axial* conformation for the substituent at C3. A NOE between H3 and the tosyl aromatic protons determines the *trans* configuration of the substituents in the heterocyclic ring. This assignment was confirmed by the X-ray crystallographic analysis.

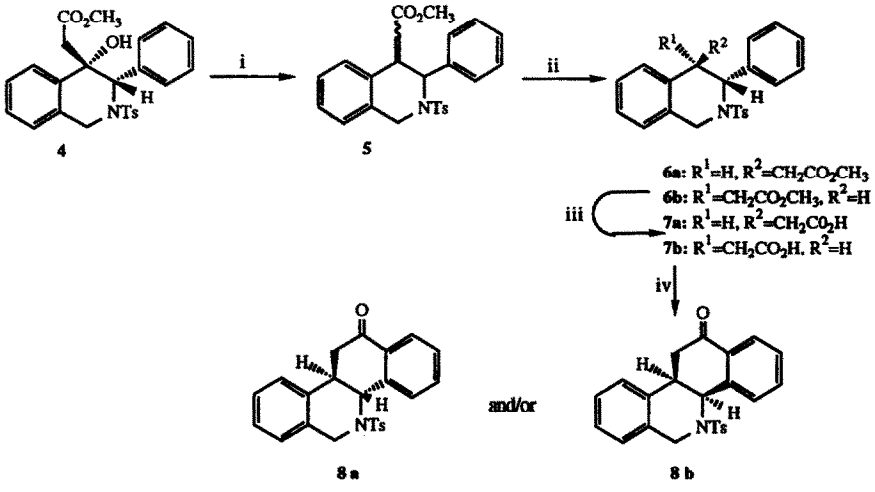
The A and B rings planes of the 4(3H)-isoquinolinone skeleton form an angle of 6.3(1)° and C1, C4 and O3 atoms are *quasi*-planar with the aromatic ring A [C1 deviation: -0.043(4)Å; C4 deviation: 0.002(4)Å and O3 deviation: 0.091(3)Å], however, N2 and C3 deviate from this plane [N2 deviation: 0.436(3)Å and C3 deviation:

-0.129(4)Å]. These deviations determine the *twist-half-chair* conformation of the heterocyclic ring B. On the other hand, the conformation of the phenyl group bonded at C3 is *pseudo-axial* [torsion angle O3-C4-C3-C9: -86.5(5)°] thus differentiating both ring faces towards the subsequent reaction.

Probably, the *p*-toluenesulfonyl group bonded at N2 pushes the phenyl group to the *axial* position in order to avoid steric hindrances [angle between bond lines C3-C9 and S-C15: 156.0(2)°] as in other 3-aryl tetrahydroisoquinolines without substitution at N2 the *axial* conformation has not been observed.[9] Finally, the sum of valence angles around the N2 atom is 358.3°, showing a sp^2 hybridization with a remainer sp^3 character.[10]

Following our synthetic route, compound **3** was submitted to a Reformatsky-type reaction yielding stereoselectively the (3*R**,4*R**)-4-hydroxy-4-methoxycarbonylmethyl-3-phenyl-2-(*p*-toluenesulfonyl)-1,2,3,4-tetrahydroisoquinoline **4**.[11] We presume that attack occurs from the opposite side of the ring from the phenyl substituent, giving the isomer in which the ester and phenyl groups are *trans*. Treatment of **4** with $SOCl_2$/ pyridine afforded derivative **5** (*Z*/*E* ratio, 7:3 as deduced from ^{1}H-NMR spectra), which under catalytic hydrogenation yielded the expected mixture of *cis* and *trans*-4-methoxycarbonylmethyl-3-phenyl-2-(*p*-toluenesulfonyl)-1,2,3,4-tetrahydroisoquinolines **6**. The mixture of isomers was hydrolyzed and then submitted to cyclization conditions yielding a separable mixture of the *cis* and *trans* tetracycle **8**.

The subsequent separation was accomplished by HPLC (hexane/ethyl acetate, 84:16) and then, crystallization was carried out yielding single crystals, which were studied by X-ray diffraction with the following results.



i) $SOCl_2$, pyridine, 60°C, 92%. ii) 1.4 atm H_2, 10% Pd(C), EtOH, r.t., quantitative. iii) KOH, EtOH, reflux, 2h, quantitative. iv) a: $SOCl_2$, benzene, reflux, 2h; b: $AlCl_3$, CH_2Cl_2, -10°C, 4h, 79%.

The molecular conformation of the diastereoisomer **8a** has an *anti-trans* form[12] related to the *trans* fused B/C moiety [torsion angle C16-C14-C13-C17: -165.6(3)°]. The proposed conformation is supported by the dihedral angle between the A and D ring planes [22.0(1)°] and the torsion angles about the C13-C14 bond

(Figure 2). Besides, both rings B and C adopt *sofa* conformations, which are defined by the deviations of their atoms shown in Table 1. The same conformation, *anti-trans*, is observed by means of ^{1}H-NMR experiments carried out in $CDCl_3$ solution ($J_{H13-H14}$: 11.1 Hz, NOE between the *pseudo-axial* H11 and H14 atoms, and no NOE between the *pseudo-axial* H11 and H13 atoms). No diagnostic data were obtained for H13 and H14 when they were adequately irradiated.

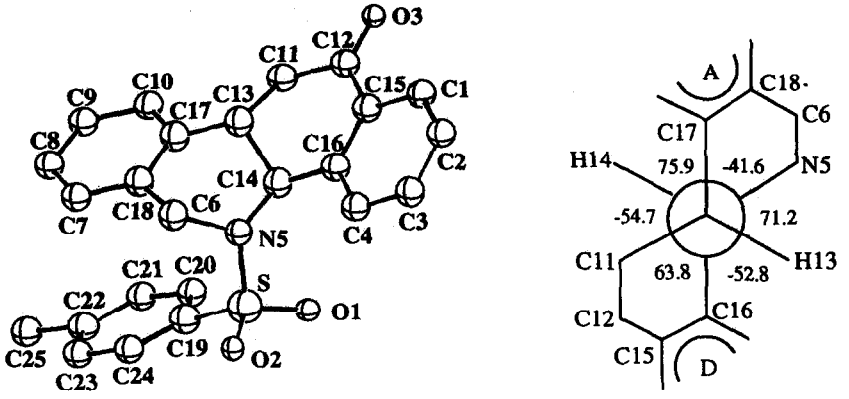


Figure 2. Ball and stick drawing and torsion angles (°) about the C13-C14 bond of diastereoisomer **8a**.

On the other hand, two equivalent molecules, A and B, form the asymmetric unit for diastereoisomer **8b**.

The molecular conformation of both molecules has a *syn-cis* form[13] with respect to the *cis* fused B/C moiety, as deduced from the values of the torsion angles C17-C13-C14-C16: 71.0(4)° in molecule A and 78.0(4)° in molecule B respectively. The proposed conformation is supported by the dihedral angle between the A and D ring planes [101.8(1)°and 90.1(1)° for molecules A and B respectively] and the torsion angles about the C13-C14 bond (Figure 3). Besides, while conformations of rings B and C for molecule A are *twist-half-chair*, the corresponding conformations in the molecule B are *half-chair*. Table 1.

The NOE experiments ($CDCl_3$ solution) carried out on derivative **8b** showed NOE between H13 and H14 atoms with the *pseudo-axial* H11 atom respectively. Moreover, the vicinal coupling constant of 4.7 Hz between H13 and H14 protons indicates a *synclinal* conformation for both atoms.

When the same synthetic strategy was applied to diastereoisomers **6a** and **6b** independently, after being separated by HPLC, similar results were obtained, thus affording diastereoisomers **8a** and **8b** respectively. The observed behaviour indicated that the final cyclization reaction proceeded in the same conditions, and was not influenced by the configurations of the C3 and C4 atoms for both isomers **6a** and **6b**.

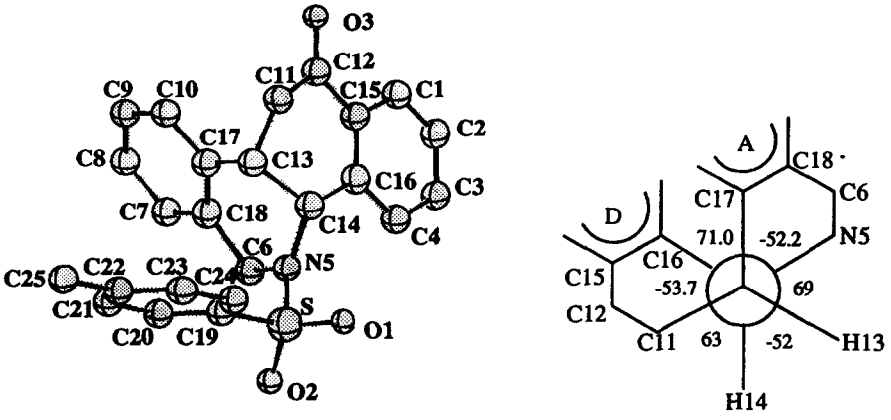


Figure 3. Ball and stick drawing and torsion angles (°) about the C13-C14 bond of the molecule A of diastereoisomer **8b**.

Table 1. Deviations (e.s.d.,Å) of the B and C rings atoms respect to the A and D ring planes of diastereoisomers **8a** and **8b**.

Compound	B ring atoms (A ring plane)				C ring atoms (D ring plane)			
	C6	N5	C14	C13	C14	C13	C11	C12
8a	0.072(4)	1.077(3)	0.965(4)	-0.089(4)	0.016(3)	-0.869(4)	-0.241(4)	-0.037(4)
8b, mol. A	0.015(4)	0.096(3)	-0.596(4)	-0.019(4)	-0.063(4)	-0.611(4)	0.217(5)	0.098(4)
8b, mol. B	0.011(4)	0.269(3)	-0.399(3)	0.039(4)	0.013(3)	-0.486(4)	0.236(4)	0.018(4)

In summary, an efficient approach of new benzo[*c*]phenanthridinones was achieved in 9 steps starting from DL-2-phenylglycine, the key step being the formation of a 3-phenylisoquinolinone derivative, and 40% overall yield.

EXPERIMENTAL

Melting points were determined on a Gallenkamp apparatus and are uncorrected. IR spectra were obtained by using a Perkin-Elmer 1430 spectrophotometer on KBr pellets (solids) or $CHCl_3$ solution (oils) and peaks (υ) are reported in cm^{-1}. NMR spectra were recorded on a Bruker AC-250 spectrometer at 20-25°C, running at 250 MHz for ^1H and 62.8 MHz for ^{13}C in $CDCl_3$ solvent and $CHCl_3$ as an internal reference. Chemical shifts (δ) are given in ppm and coupling constants (J) are reported in hertz (Hz). ^1H-{^1H} NOE experiments were carried out in the difference mode by irradiation of all the lines of a multiplet in $CDCl_3$ solvent.[14] Assignment of individual ^{13}C resonances were supported by DEPT experiments. Elemental analyses were performed on a Perkin-Elmer 2400 CHN apparatus. Mass spectrometer was used at a 70 eV ionization potential to obtain

electron impact spectra. Thin layer chromatography (tlc) was carried out with 0.2 mm thick silica gel plates (Merck Kieselgel GF_{254}) and visualized by UV light or by spraying with Dragendorff's reagent.[15] Flash column chromatography[16] on silica gel was performed with Merck Kieselgel 60 (230-400 mesh). HPLC was accomplished on a Waters 600E apparatus with a Porasil 10M 19 mm x 15 cm column. All solvents used in reactions were anhydrous and purified according to standard procedures.[17] Reactions were carried out under dry and deoxygenated argon atmosphere. Tranfers of solvents and solutions were performed by syringe or *via* canula.[18]

2-Phenyl-2-(*p*-toluenesulfonyl)aminoacetic acid 1b.

To a mechanically stirred solution of DL-2-phenylglycine **1a** (151.1 mg, 1.0 mmol) and NaOH (100.0 mg, 2.5 mmol) in water (2.0 ml) at room temperature, *p*-toluenesulfonyl chloride (228.7 mg, 1.2 mmol) in ethyl ether (2.0 ml) was added. After 16h. of stirring, 12N HCl was added to the mixture until a white precipitate was formed. The so-obtained precipitate was filtered and washed with water. Crystallization was accomplished from ethyl ether affording compound **1b** as a white solid. Yield: 91%. M.p.: 159-160°C. IR (KBr): υ 3300 (NH), 3300-2500 (OH), 1720 (C=O), 1310 and 1180 (SO_2). ^{1}H-NMR ($CDCl_3$, TFA): δ 2.38 (s, 3H, CH_3), 5.09 (s, 1H, CH), 7.19-7.31 (m, 7H, H_{arom}), 7.62 (d, 2H, J_o=8.3, $H_{arom\ Ts}$). ^{13}C-NMR ($CDCl_3$, TFA): δ 21.31 (CH_3), 59.38 (CH), 127.13, 129.26, 129.47, 129.95 (C_{arom}-H), 133.35, 135.06, 145.18 (C_{arom}-C), 176.01 (C=O). MS (m/e, %): no M^+, 260(89), 155(45), 104(22), 91(100), 77(17), 65(18).

DL-Benzyl 2-[*N*-benzyl-*N*-(*p*-toluenesulfonyl)amino]-2-phenylacetate 2a.

A mixture of **1b** (305.3 mg, 1.0 mmol), potassium carbonate (414.6 mg, 3.0 mmol) and benzyl bromide (0.29 ml, 2.5 mmol) in CH_3CN (5.0 ml) was stirred at room temperature for 26h. Then, 5.0 ml of water was added and the mixture was extracted with CH_2Cl_2 and dried over anhydrous sodium sulfate. After evaporation of the solvent under vacuum, the resulting oil was crystallized from methanol to afford derivative **2a** as white crystals. Yield: 89%. M.p.: 79-80°C. IR (KBr): υ 1740 (C=O), 1340 and 1150 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.40 (s, 3H, CH_3), 4.41 (d, 1H, J_{AB}=16.3, CH_2N), 4.64 (d, 1H, J_{AB}=16.3, CH_2N), 5.00 (d, 1H, J_{AB}=12.2, CH_2O), 5.08 (d, 1H, J_{AB}=12.2, CH_2O), 5.85 (s, 1H, CH), 6.83-7.36 (m, 17H, H_{arom}), 7.59 (d, 2H, J_o=8.3, $H_{arom\ Ts}$). ^{13}C-NMR ($CDCl_3$): δ 21.50 (CH_3), 49.28 (CH_2N), 63.11 (CH), 66.99 (CH_2O), 126.64, 127.34, 127.63, 127.88, 128.30, 128.39, 128.49, 128.53, 128.66, 129.30, 129.39 (C_{arom}-H), 133.42, 135.01, 136.80, 137.34, 143.31 (C_{arom}-C), 169.82 (C=O). MS (m/e, %): no M^+, 351(100), 330(96), 260(31), 238(10), 194(92), 167(23), 155(39), 139(16), 117(17), 104(19), 91(98), 77(29), 65(96). Anal. calcd. for $C_{29}H_{27}NO_4S$: C 71.73, H 5.60, N 2.88; found: C 71.72, H 5.67, N 3.00.

DL-2-[*N*-Benzyl-*N*-(*p*-toluenesulfonyl)amino]-2-phenylacetic acid 2b.

A suspension of **2a** (485.6 mg, 1.0 mmol) in absolute ethanol (5.0 ml) was placed in a Parr hydrogen flask and catalytic amounts of 10% Pd(C) catalyst was added. The mixture was hydrogenated for 1.5h. at 1.4 atmospheres and room temperature. The catalyst was removed and the colorless filtrate was concentrated under reduced pressure yielding a solid which was crystallized from ethanol to afford acid **2b** as white crystals. Yield: quantitative. M.p.: 157-158°C. IR (KBr): υ 3300-2500 (OH), 1720 (C=O), 1340 and 1150 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.38 (s, 3H, CH_3), 4.34 (d, 1H, J_{AB}=16.1, CH_2), 4.60 (d, 1H, J_{AB}=16.1, CH_2), 5.76 (s, 1H, CH), 6.83-6.87 (m, 2H, H_{arom}), 7.00-7.08 (m, 3H, H_{arom}), 7.16-7.27 (m, 7H, H_{arom}), 7.62 (d, 2H, J_o=8.3, $H_{arom\ Ts}$). ^{13}C-NMR ($CDCl_3$): δ 21.42 (CH_3), 49.31 (CH_2), 63.31 (CH), 126.88, 127.38, 127.77, 127.96, 128.72, 129.00, 129.47 (C_{arom}-H), 132.83, 136.69, 136.88, 143.69 (C_{arom}-C), 175.78 (C=O). MS (m/e, %): no M^+, 351(100), 260(45), 240(98), 196(96), 165(28), 155(72), 135(29), 117(36), 106(65), 91(98), 77(72), 65(95). Anal. calcd. for $C_{22}H_{21}NO_4S$: C 66.81, H 5.35, N 3.54; found: C 65.70, H 5.48, N 3.49.

3-Phenyl-2-(*p*-toluenesulfonyl)-1,2-dihydro-4(3H)-isoquinolinone 3.

To a stirred suspension of **2b** (395.5 mg, 1.0 mmol) in dry benzene (5.0 ml) cooled with an ice bath, thionyl chloride (0.14 ml, 2.0 mmol) was added dropwise and then, the mixture was refluxed for 2h. The solution was evaporated to dryness in vacuo and the obtained oil was examined by means of IR spectroscopy showing the presence of the acid chloride (band at υ 1820 cm^{-1}). This oil, without further purification, was dissolved in dry dichloromethane (5.0 ml) and the solution cooled to -60°C, anhydrous aluminium chloride (266.7 mg, 2.0 mmol) in one portion with vigorous stirring was added and then the temperature was allowed to reach -10°C. The stirring was continued for 4h. The reaction was quenched by shaking with 12N HCl in crushed ice, extracted with dichloromethane and dried over anhydrous sodium sulfate. After evaporation of the solvent under reduced pressure, the resulting oil was crystallized from ethanol affording isoquinolinone **3** as pale brown crystals. Yield: 79%. M.p.: 83-84°C. IR (KBr): υ 1690 (C=O), 1340 and 1160 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.25 (s, 3H, CH_3), 4.44 (d, 1H, J_{AB}=18.2, H-1 ax), 4.93 (d, 1H, J_{AB}=18.2, H-1 ec), 5.76 (s, 1H, H-3), 6.99 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 7.08-7.11 (m, 1H, H-8), 7.21-7.27 (m, 1H, H_{arom}), 7.31 (s, 5H, $H_{arom\ Ph}$), 7.42-7.45 (m, 1H, H_{arom}), 7.47 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 7.76-7.79 (dd, 1H, J_o=7.9, J_m=1.2, H_{arom}).

^{13}C-NMR ($CDCl_3$): δ 21.26 (CH_3), 43.42 (C-1), 64.53 (C-3), 125.69, 126.97, 127.08, 127.36, 127.46, 128.45, 128.83, 129.41, 134.34 (C_{arom}-H), 129.77, 132.59, 135.87, 137.98, 143.55 (C_{arom}-C), 191.71 (C=O). MS (m/e, %): 377 (M^+, 1), 223(100), 193(15), 155(9), 118(66), 91(98), 77(22), 65(45). Anal. calcd. for $C_{22}H_{19}NO_3S$: C 70.00, H 5.07, N 3.71; found: C 70.54, H 5.15, N 3.70.

(3*R,4*R**)-4-Hydroxy-4-methoxycarbonylmethyl-3-phenyl-2-(*p*-toluene sulfonyl)-1,2,3,4-tetrahydroisoquinoline 4.**

Zinc activation was performed following the Miginiac's procedure.[19] Thus,to a suspension of zinc powder (104.6 mg, 1.6 mmol) in dry diethylic ether (5.0 ml) freshly distilled trimethylchlorosilane (2 μml, 0.16 mmol) was added from a syringe and the mixture was stirred for 15 min. at room temperature.

After the suspension of activated zinc was heated to reflux, the heating was stopped and a mixture of ethyl bromoacetate (0.17 ml, 1.6 mmol) and ketone **3** (377.4 mg, 1.0 mmol) in dry ethylic ether (10.0 ml) was added at such a rate that a gentle reflux was observed. The reflux was continued during 2h. and then, was allowed to reach room temperature. The reaction was quenched by shaking with 20% NH_4OH in crushed ice and extracted with diethylic ether, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The resulting oil, chromatographically pure, was crystallized from methanol to yield **4** as white crystals. Yield: 85%. M.p.: 118-119°C. IR (KBr): υ 3360 (OH), 1700 (C=O), 1350 and 1160 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.31 (s, 3H, CH_3 Ts), 2.76 (d, 1H, J_{AB}=16.4, CH_2C), 3.13 (d, 1H, J_{AB}=16.4, CH_2C), 3.77 (s, 1H, CH_3O), 4.23 (s, 1H, OH), 4.24 (d, 1H, J_{AB}=15.9, H-1), 4.80 (d, 1H, J_{AB}=15.9, H-1), 5.58 (s, 1H, H-3), 6.80-6.83 (m, 2H, H_{arom}), 6.97-7.13 (m, 6H, H-8, H_{arom}), 7.27-7.31 (m, 2H, H_{arom}), 7.46 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 7.58-7.62 (m, 1H, H-5). ^{13}C-NMR ($CDCl_3$): δ 21.32 (CH_3 Ts), 44.00, 45.17 (CH_2C, C-1), 51.98 (CH_3O), 61.91 (C-3), 72.43 (C-4), 125.33, 125.89, 127.27, 127.72, 127.79, 127.85, 127.92, 129.14, 129.23 (C_{arom}-H), 130.16, 135.49, 135.56, 137.92, 143.17 (C_{arom}-C), 172.83 (C=O). MS (m/e, %): no M^+, 433(11), 420(3), 296(100), 260(82), 222(42), 155(32), 149(22), 131(34), 119(33), 91(94), 77(15), 65(22). Anal. calcd. for $C_{25}H_{25}NO_5S$: C 66.50, H 5.58, N 3.10; found: C 66.59, H 5.65, N 3.23.

4-Methoxycarbonylmethin-3-phenyl-2-(*p*-toluenesulfonyl)-1,2,3,4-tetrahydroisoquinoline 5.

To a stirred solution of **4** (451.5 mg, 1.0 mmol) in freshly distilled pyridine (5.0 ml) cooled with an ice bath, thionyl chloride (0.14 ml, 2.0 mmol) was added dropwise and the mixture was heated at 60°C for 2h. After cooling to room temperature, water was added and the mixture was extracted with dichloromethane and dried over anhydrous sodium sulfate. The pyridine was removed under reduced pressure and a brown oil was obtained and crystallized from ethanol to afford a pale brown solid containing a mixture of *(Z)*- and *(E)*-isomers of derivative **5** (*Z/E* ratio: 7:3). Yield: 92%.

The *(Z)*-isomer was extracted from the aqueous mother liquors, concentrated and then recrystallized from methanol. M.p.: 140-141°C. *(Z)*-isomer: IR (KBr): υ 1710 (C=O), 1350 and 1170 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.31 (s, 3H, CH_3 Ts), 3.73 (s, 3H, CH_3O), 4.21 (d, 1H, J_{AB}=18.2, H-1), 4.89 (d, 1H, J_{AB}=18.2, H-1), 6.31 (s, 1H, H-3), 7.14-7.30 (m, 10H, H_{arom}), 7.33 (s, 1H, CH=C), 7.49-7.55 (m, 3H, H_{arom}). ^{13}C-NMR ($CDCl_3$): δ 21.43 (CH_3 Ts), 43.29 (C-1), 51.59 (CH_3O), 54.81 (C-3), 77.19 (CH=C), 114.81, 124.76, 126.25, 127.31, 127.73, 128.51, 129.06, 130.28, (C_{arom}-H), 130.36, 133.33, 136.10, 136.72, 143.20, 146.75 (CH=C, C_{arom}-C). *(E)*-isomer: IR (KBr): υ 1710 (C=O), 1330 and 1160 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.33 (s, 3H, CH_3 Ts), 3.67 (s, 3H, CH_3O), 4.36 (d, 1H, J_{AB}=17.5, H-1), 4.80 (d, 1H, J_{AB}=17.5, H-1), 5.69 (s, 1H, H-3), 5.79 (s, 1H, CH=C), 7.00-7.30 (m, 10H, H_{arom}), 7.59-7.66 (m, 3H, H_{arom}). ^{13}C-NMR ($CDCl_3$): δ 18.38 (CH_3 Ts), 44.85 (C-1), 51.42 (CH_3O), 63.15 (C-3), 118.01, 125.40, 126.77, 129.54, 129.79, 130.00 (CH=C, C_{arom}-H), 129.26, 132.67, 136.29, 143.48, 144.30 (CH=C, C_{arom}-C), 166.05 (C=O). *(Z)*- and *(E)*-isomers: MS (m/e, %): 433(M+, 2), 402(2), 278(100), 246(35), 218(96), 191(15), 155(14), 115(47), 91(81), 77(12), 65(24).

(3*R,4*R**)- and (3*R**,4*S**)-4-Methoxycarbonylmethyl-3-phenyl-2-(*p*-toluene sulfonyl)-1,2,3,4-tetrahydroisoquinoline 6a and 6b.**

A suspension of **5** (433.5 mg, 1.0 mmol) in absolute ethanol (5.0 ml) was hydrogenated at 1.4 atmospheres pressure and room temperature in the presence of catalytic amounts of 10% Pd(C) for 2h. The catalyst was removed and the colorless filtrate was concentrated under reduced pressure to form a colorless oil. This oil showed by tlc (hexane/ ethyl acetate, 8:2) the presence of two spots corresponding to the expected diastereoisomers, which were separated by HPLC (hexane/ ethyl acetate, 86:14) in a ratio **6a / 6b**, 6:4.

(3R,4R*)*-Isomer: the derivative **6a** was crystallized from methanol to afford white crystals. M.p.: 119-120°C. IR (KBr): υ 1740 (C=O), 1340 and 1170 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.37 (s, 3H, CH_3 Ts), 2.48 (dd, 1H, J_{AX}=5.2, J_{AB}=16.7, CH_2C), 2.73 (dd, 1H, J_{BX}=9.3, J_{AB}=16.7, CH_2C), 3.67-3.72 (m, 1H, H-4), 3.73 (s, 3H, CH_3O), 4.28 (d, 1H, J_{AB}=15.8, H-1), 4.69 (d, 1H, J_{AB}=15.8, H-1), 5.45 (d, 1H, J=1.5, H-3), 6.97-7.21 (m, 11H, H_{arom}), 7.65 (d, 2H, J_o=8.3, $H_{arom\ Ts}$). ^{13}C-NMR ($CDCl_3$): δ 21.43 (CH_3 Ts), 40.52, 43.84

(C-1, CH_2C), 41.18 (C-4), 51.76 (CH_3O), 58.63 (C-3), 126.14, 127.05, 127.11, 127.25, 127.30, 127.39, 128.17, 129.10, 129.43 (C_{arom}-H), 131.31, 134.87, 136.56, 139.38, 143.27 (C_{arom}-C), 172.28 (C=O). MS (m/e, %): no M^+, 404(1), 280(100), 220(11), 206(38), 145(12), 115(31), 91(63), 77(8), 65(18). Anal. calcd. for $C_{25}H_{25}NO_4S$: C 68.94, H 5.78, N 3.21; found: C 69.15, H 5.83, N 3.80. (3*R**,4*S**)-isomer: the derivative **6b** was crystallized from ethanol to afford white crystals. M.p.: 114-115°IR (KBr): ν 1740 (C=O), 1350 and 1170 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.31 (dd, 1H, J_{AX}=7.6, J_{AB}=16.6, CH_2C), 2.37 (s, 3H, CH_3 Ts), 2.62 (dd, 1H, J_{BX}=7.0, J_{AB}=16.6, CH_2C), 3.56-3.64 (m, 1H, H-4), 3.72 (s, 3H, CH_3O), 4.44 (d, 1H, J_{AB}=14.4, H-1 ec), 5.06 (d, 1H, J_{AB}=14.4, H-1 ax), 5.34 (d, 1H, J=5.6, H-3), 6.66 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 6.88-6.91 (m, 1H, H-5), 6.92-7.13 (m, 3H, H_{arom}), 7.16-7.24 (m, 5H, H_{arom}), 7.61 (d, 2H, J_o=8.3, $H_{arom\ Ts}$). ^{13}C-NMR ($CDCl_3$): δ 21.45 (CH_3 Ts), 34.11 (CH_2C), 38.30 (C-4), 45.91 (C-1), 51.97 (CH_3O), 59.80 (C-3), 124.99, 126.27,
127.01, 127.42, 127.58, 127.91, 128.14, 129.45 (C_{arom}-H), 133.70, 135.39, 135.83, 138.06, 143.21 (C_{arom}-C), 172.20 (C=O). MS (m/e, %): no M^+, 404(1), 280(100), 260(10), 206(22), 176(30), 144(44), 134(13), 129(6), 116(40), 91(41), 77(5), 65(8). Anal. calcd. for $C_{25}H_{25}NO_4S$: C 68.94, H 5.78, N 3.21; found C 69.05, H 5.79, N 3.57.

4-Carboxymethyl-3-phenyl-2-(*p*-toluenesulfonyl)-1,2,3,4-tetrahydro isoquinoline 7.

General procedure: A suspension of **6** (435.5 mg, 1.0 mmol) in aqueous 6M KOH (10.0 ml) was stirred under reflux for 2h. The mixture was cooled at room temperature and poured onto ice-12N HCl, extracted with dichloromethane and dried over anhydrous sodium sulfate. The solvent was evaporated and the solid was purified as specified for each diastereoisomer of compound **9**. Yield: quantitative.

(3*R,4*R**)-4-Carboxymethyl-3-phenyl-2-(*p*-toluenesulfonyl)-1,2,3,4-tetrahydroisoquinoline 7a.**

Following the general procedure, the isoquinoline derivative **7a** was obtained from **6a** and crystallized from ethylic ether to afford a white solid. M.p.: 200-201°C. IR (KBr): ν 3300-2500 (OH), 1700 (C=O), 1340 and 1160 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.38 (s, 3H, CH_3), 2.54 (dd, 1H, J_{AX}=4.7, J_{AB}=17.3, CH_2C), 2.79 (dd, 1H, J_{BX}=9.5, J_{AB}=17.3, CH_2C), 3.69-3.74 (m, 1H, H-4), 4.29 (d, 1H, J_{AB}=15.9, H-1), 4.70 (d, 1H, J_{AB}=15.9, H-1), 5.51 (d, 1H, J=1.1, H-3), 7.00-7.23 (m, 11H, H_{arom}), 7.69 (d, 2H, J_o=8.3, $H_{arom\ Ts}$). ^{13}C-NMR ($CDCl_3$): δ 21.37 (CH_3), 40.28, 43.78 (C-1, CH_2C), 40.72 (C-4), 58.65 (C-3), 126.24, 127.03, 127.21, 127.41, 127.59, 127.73, 128.32, 129.01, 129.69 (C_{arom}-H), 131.00, 134.08, 135.58, 138.63, 144.06 (C_{arom}-C), 178.69 (C=O). MS (m/e, %): no M^+, 420(1), 266(100), 206(30), 162(7), 155(8), 150(31), 115(21), 91(42), 77(5), 65(9). Anal. calcd. for $C_{24}H_{23}NO_4S$: C 68.38, H 5.50, N 3.32; found: C 68.06, H 5.48, N 3.56.

(3*R,4*S**)-4-Carboxymethyl-3-phenyl-2-(*p*-toluenesulfonyl)-1,2,3,4-tetrahydroisoquinoline 7b.**

Following the general procedure, the derivative **7b** was obtained from **6b** and crystallized from methanol to afford white crystals. M.p.: 169-170°C. IR (KBr): ν 3300-2500 (OH), 1720 (C=O), 1340 and 1160 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 2.39 (dd, 1H, J_{AX}=7.7, J_{AB}=17.2, CH_2C), 2.73 (dd, 1H, J_{BX}=6.5, J_{AB}=17.2, CH_2C), 3.55-3.62 (m, 1H, H-4), 4.45 (d, 1H, J_{AB}=14.5, H-1 ax), 4.59 (d, 1H, J_{AB}=14.5, H-1 ec), 5.39 (d, 1H, J=5.4, H-3), 6.68 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 6.92-6.95 (m, 1H, H-5), 7.03-7.32 (m, 8H, H_{arom}), 7.61 (d, 2H, J_o=8.3, $H_{arom\ Ts}$). ^{13}C-NMR ($CDCl_3$): δ 21.45 (CH_3), 33.82 (CH_2C), 38.07 (C-4), 45.95 (C-1), 59.67 (C-3), 124.91, 126.38, 127.17, 127.40, 127.70, 128.00, 128.12, 129.46 (C_{arom}-H), 133.67, 135.00, 135.53, 137.83, 143.34 (C_{arom}-C), 177.77 (C=O). MS (m/e, %): no M^+, 266(89), 206(26), 155(16), 143(31), 116(50), 91(100), 77(14), 65(33). Anal. calcd. for $C_{24}H_{23}NO_4S$: C 68.38, H 5.50, N 3.32; found: C 68.49, H 5.55, N 3.64.

5-(*p*-Toluenesulfonyl)-5,6,13,14-tetrahydro-12(11H)-benzo[*c*] phenanthridinone 8.

General procedure: To a stirred suspension of diastereoisomers **7** (421.5 mg, 1.0 mmol) in dry benzene (5.0 ml) cooled with an ice bath, thionyl chloride (0.14 ml, 2.0 mmol) was added dropwise and then , the mixture was refluxed for 2h. The solvent was evaporated in vacuo to afford a brown oil, which showed a typical carbonil band at 1810 cm^{-1}. This oil, without further purification, was dissolved in dry dichloromethane (5.0 ml) and the solution cooled to -60°C. Anhydrous aluminium chloride (266.7 mg, 2.0 mmol) was added in one portion with vigorous stirring. The temperature was allowed to reach -10°C and the stirring was continued for 3h. The reaction was quenched by shaking with 12N HCl in crushed ice, extracted with dichoromethane and dried over anhydrous sodium sulfate. The solvent was evaporated under vacuum obtaining a colorless oil in 85% yield. This oil showed by tlc (hexane/ethyl acetate, 8:2) the presence of two diastereoisomers, which were separated by HPLC /hexane/ethyl acetate, 84:16) in a ratio **8a / 8b**, 6:4.

(13*R,14*R**)-5-(*p*-toluenesulfonyl)-5,6,13,14-tetrahydro-12(11H)-benzo[*c*] phenanthridinone 8a.**

Following the general procedure, derivative **8a** was obtained from **7a** and crystallized from methanol to afford pale brown crystals. M.p.: 215-216ºC. IR (KBr): υ 1680 (C=O), 1320 and 1160 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.26 (s, 3H, CH_3), 2.79 (dd, 1H, J_{AX}=13.2, J_{AB}=17.4, H-11 ax), 3.10-3.20 (m, 1H, H-13), 3.42 (dd, 1H, J_{BX}=3.5, J_{AB}=17.4, H-11 ec), 4.22 (d, 1H, J_{AB}= 16.2, H-6 ax), 4.69 (d, 1H, J=11.1, H-14), 4.73 (d, 1H, J_{AB}= 16.2, H-6 ec), 6.76-6.79 (m, 1H, H_{arom}), 6.92 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 6.96-6.99 (m, 1H, H-10), 7.11-7.17 (m, 1H, H_{arom}), 7.31 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 7.45-7.51 (m, 1H, H_{arom}), 7.70-7.76 (m, 1H, H_{arom}), 8.06-8.13 (m, 2H, H_{arom}). ^{13}C-NMR ($CDCl_3$): δ 21.36 (CH_3), 39.83 (C-13), 41.23 (C-11), 46.62 (C-6), 60.51 (C-14), 122.82, 126.18, 126.31, 127.10, 127.54, 127.72, 128.07, 129.13, 134.30 (C_{arom}-H), 131.48, 135.03, 135.19, 135.43, 143.36, 144.66 (C_{arom}-C), 195.52 (C-12). MS (m/e, %): 403 (M^+, 1), 248(81), 231(43), 218(10), 155(7), 130(15), 115(45), 91(100), 77(17), 65(36). Anal. calcd. for $C_{24}H_{21}NO_3S$: C 71.44, H 5.24, N 3.47; found: C 71.52, H 5.20, N 3.51.

(13*R,14*S**)-5-(*p*-toluenesulfonyl)-5,6,13,14-tetrahydro-12(11H)-benzo[*c*] phenanthridinone 8b.**

Following the general procedure, diastereoisomer **8b** was obtained from **7b** and crystallized from ethanol/water, to afford pale brown crystals. M.p.: 115-116ºC. IR (KBr): υ 1690 (C=O), 1340 and 1160 (SO_2). ^{1}H-NMR ($CDCl_3$): δ 2.40 (s, 3H, CH_3), 3.02 (dd, 1H, J_{AX}=5.1, J_{AB}=17.2, H-11 ax), 3.45 (dd, 1H, J_{BX}=3.3, J_{AB}=17.2, H-11 ec), 3.46-3.51 (m, 1H, H-13), 4.26 (d, 1H, J_{AB}= 17.1, H-6 ax), 4.72 (d, 1H, J_{AB}= 17.1, H-6 ec), 5.75 (d, 1H, J=4.7, H-14), 6.86-6.89 (m, 1H, H-7), 7.02-7.13 (m, 2H, H_{arom}), 7.22-7.31 (m, 4H, H_{arom}), 7.52-7.58 (m, 1H, H_{arom}), 7.62-7.65 (m, 1H, H-4), 7.79 (d, 2H, J_o=8.3, $H_{arom\ Ts}$), 7.77-7.84 (m, 1H, H_{arom}). ^{13}C-NMR ($CDCl_3$): δ 21.52 (CH_3), 36.88 (C-13), 41.50, 43.64 (C-6, C-11), 54.90 (C-14), 126.01, 126.51, 126.82, 126.93, 127.07, 127.34, 127.73, 127.96, 129.97, 134.40 (C_{arom}-H), 131.34, 132.47, 132.77, 137.43, 139.46, 143.79 (C_{arom}-C), 194.59 (C-12). MS (m/e, %): 403 (M^+, 2), 248(100), 231(64), 218(10), 115(23), 91(36), 83(80), 65(10). Anal. calcd. for $C_{24}H_{21}NO_3S$: Calc. C 71.44, H 5.24, N 3.47; found C 71.61, H 5.25, N 3.47.

X-RAY CRYSTALLOGRAPHIC ANALYSIS

Prismatic crystals were mounted on an Enraf-Nonius CAD4 or Philips PW-1100 diffractometer. Unit cell parameters were determined from automatic centring of 25 high-angle reflections and refined by least-squares method. Intensities were collected with graphite monochromatized Mo Kα radiation, using ω/2θ scan technique. Reflections were measured in the range $2 \leq \theta \leq 30°$. Data were corrected for Lorentz-polarization effects, but no absorption corrections were performed. All diffractometer data were collected at room temperature. Pertinent crystal, data collection and refinement parameters are summarized in Table 2.

The structures were solved by direct methods, using SHELXS computer program[20] and refined by full-matrix least-squares method, with the SHELX76 computer program.[21] The function minimized was $\sum w \mid |Fo| - |Fc| \mid^2$. f, f' and f" were taken from International Tables of X-ray Crystallography.[22] Hydrogen positions were calculated wherever possible. A final difference Fourier revealed no missing or misplaced electron density. Coordinates, anisotropic temperature factors, distances and angles were submitted to this Journal for deposition to the Cambridge Crystallographic Data Center.

ACKNOWLEDGMENTS

The authors gratefully aknowledge the University of Basque Country and the Basque Government for financial supports (Projects: UPV 170.310-E125/91 and PGV 92-13 respectively). We are particularly grateful to Dr. G. Tojo (University of Santiago de Compostela) and Dr. R. Pérez Afonso (University of La Laguna) for mass spectra. We also thank Petronor, S.A. (Vizcaya, Spain) for kindly supplying hexane during the last years.

Table 2. Crystal data, intensity data collection and structural refinement summary for compounds **3**, **8a** and **8b**.

Compound	3	(13*R**,14*R**)-8a	(13*R**,14*S**)-8b
Chemical formula	$C_{22}H_{19}NO_3S$	$C_{24}H_{21}NO_3S$	$2[C_{24}H_{21}NO_3S].\ 0.5H_2O$
Molecular weight	377.46	403.50	816.0
Crystal System	Triclinic	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a (Å)	12.598(3)	8.540(1)	11.204(3)
b (Å)	10.349(2)	11.057(3)	11.561(3)
c (Å)	8.967(2)	11.755(1)	16.984(5)
α (°)	61.62(2)	71.63(2)	93.58(2)
β (°)	72.79(2)	79.38(2)	90.09(2)
γ (°)	66.29(2)	74.07(2)	107.81(1)
V (Å^3)	933.8(4)	1007.1(3)	2090(2)
Z	2	2	2
D_x (g.cm^{-3})	1.35	1.33	1.31
μ (cm^{-1})	1.86	1.77	1.74
No. measured refl.	3469	5847	12280
No. observed refl.	1970	2995	7559
Criterion observed	$I \geq 2.5\ \sigma(I)$	$I \geq 2.5\ \sigma(I)$	$I \geq 2.5\ \sigma(I)$
No. refining param.	290	263	638
R, Rw	0.056, 0.057	0.053, 0.052	0.070, 0.076
Max. shift / e.s.d.	0.06	0.2	0.2

REFERENCES AND NOTES

1. A preliminary report has been produced for " XVth European Colloquium on Heterocyclic Chemistry", Noordwijkerhout, the Netherlands, **1992**, Com. 85.
2. a) Simeon, S.; Rios, J.L.; Villar, A. *Pharmazie* **1989**, *44*, 593-597; b) Simanek,V. in "The Alkaloids", Brossi,A., Ed.; Academic Press: Orlando, **1985**, *26*, 185-234; b) Ninomiya, I.; Naito, T. *Recent Dev.Chem.Nat.Carbon Comp.* **1984**, *10*, 9-90.
3. a) Cushman, M.; Choong, T.-C.; Valko, J.T.; Koleck, M.P. *J.Org.Chem.* **1980**, *45*, 5067-5073; b) Cordell, G.A.; Farnsworth, N.R. *Heterocycles* **1976**, *4*, 393-427 and *Lloydia* **1977**, *40*, 1; c) Zee-Cheng, R.K.Y.; Cheng, C.C. *J.Med.Chem.* **1975**, *18*, 66-71.

4. Tan, G.T.; Miller, J.F.; Kinghorn, A.D.; Hughes, S.H.; Pezzuto, J.M. ***Biochem.Biophys.Res. Comm.*** **1992**, *185*, 370-378.
5. See for example: Kamigauchi,M.; Miyamoto,Y.; Iwasa,K.; Sugiura,M.; Nishijo,Z.; Takao,N.; Ishida,T.; In,Y.; Inoue,M. *Helv.Chim.Acta* **1990**, *73*, 2171-2178.
6. For a recent review on the synthesis of benzo[*c*]phenanthridines see: Janin, Y.L.; Bisagni, E. *Tetrahedron* **1993**, *49*, 10305-10316 and references therein. Our last research work in the field of the synthesis of these heterocycles is: Sotomayor, N.; Domínguez, E.; Lete, E. *Tetrahedron Lett.* **1994**, *35*, 2973-2976.
7. a) Olugbade, T.A.; Waigh, R.D.; Mackay,S.P. *J.Chem.Soc.,Perkin Trans.*1 **1990**, 2657-2660;b) Olugbade, T.A.; Waigh,R.D. *J.Pharm.Pharmacol.* **1981**, 81.
8 For some selected and new references see: a) Domínguez, E.; Martínez de Marigorta, E.; Carrillo, L.; Fañanás, R. *Tetrahedron* **1991**, *47*, 9253-9258; b) Badía, D.; Domínguez, E.; Tellitu, I. *Tetrahedron* **1992**, *48*, 4419-4430; c) Vicente,T.; Martínez de Marigorta, E.; Domínguez, E.; Carrrillo, L; Badía, D. *Heterocycles* **1993**, *36*, 2067-2072; d) Sotomayor, N.; Domínguez, E.; Lete, E.; *Synlett* **1993**, 431-433; e) Tellitu, I.; Badía, D.; Domínguez, E.; García, F.J. *Tetrahedron Asymmetry*, **1994**, in press (8th issue).
9. a) Arrieta, J.M.; Badía, D.; Domínguez, E.; Lete, E.; Igartua, A.; Germain, G.; Vlassi, M.; Debaerdemaeker, T. *Acta Cryst.* **1988**, *C44*, 1931-33; b) Arrieta, J.M.; Badía, D.; Domínguez, E.; Lete, E.; Martínez de Marigorta, E.; Germain, G.; Vlassi, M.; Debaerdemaeker, T. *J.Chem.Res.(S)* **1988**, 70-71.
10. Urtiaga, M.K.; Arriortua, M.I.; Badía, D.; Domínguez, E.; González-Cameno, A.M.; Solans, X. *Acta Cryst.* **1994**, in press.
11. Any attempt to establish the correct structure of derivative **4** by means of ^{1}H-NMR experiments was unsuccessful. Nevertheless, its relative configuration could be attributed unambiguously by X-ray diffraction analisys, thus showing that the hydroxyl and phenyl substituents at C4 and C3 repectively, adopt a *cis* relative position. See: Urtiaga, M.K.; Badía, D.; Domínguez, E.; González-Cameno, A.M.; Amigó, J.M.; Reventós, M.M.; Debaerdemaeker, T. *Acta Cryst.* **1994**, in press.
12. Takao, N.; Kamigauchi, M.; Iwasa, K.; Tomita, K.; Fujiwara, T.; Wakahara, A. *Tetrahedron* **1979**, *35*, 1099-1107.
13. a) Kamigauchi, M.; Noda, Y.; Takao, N.; Ishida, T.; Inoue, M. *Helv.Chim.Acta* **1986**, *69*, 1418-1423; b) Takao, N.; Morita, N.; Kamigauchi, M.; Iwasa, K. *Acta Cryst.* **1981**, *B37*, 2043-2048; c) Takao, N.; Bessho, N.; Kamigauchi, M.; Iwasa, K.; Tomita, K.; Fujiwara, T.; Fujii, S. *Tetrahedron Lett.* **1979**, 495-496.
14. a) Kinss, M.; Sanders, J.K.M. *J.Magn.Res.* **1984**, *56*, 518-523; b) Hall, D.L.; Sanders, J.K.M. *J.Am.Chem.Soc.* **1980**, *102*, 5703-5711.
15. Krebs, K.G.; Hensser, D.; Wimmer, H. in "Thin-Layer Chromatography", ed.by Stahl, E.; Springer-Verlag: Berlin, **1969**.p. 854
16. Still, W.C.; Kann, H.; Mitra, A. *J.Org.Chem.* **1978**, *43*, 2923-2925.
17. Perrin, D.D.; Armarego, W.L.F. in "Purification of Laboratory Chemicals", 3rd ed., Pergamon Press, Oxford, **1988**.

18. Kramer, G.W.; Levy, A.B.; Midland, M.M. in "Organic Synthesis via Boranes", John Wiley and sons, Inc., New York, **1975**.
19. Picotín, G.; Miginiac, P. *J.Org.Chem.* **1987**, *52*, 4796-4798.
20. Sheldrick, G.M. *Acta Cryst.* **1990**, *A46*, 467-473.
21. Sheldrick, G.M. "SHELX 76. Program for Crystal Structure Determination", University of Cambridge, United Kingdom, **1976**.
22. "International Tables of X-ray Crystallography", Kynoch Press, ed., **1974**, *4*, 99-100 and 149.

(*Received in UK* 7 *June* 1994; *revised* 21 *July* 1994; *accepted* 29 *July* 1994)