Tandem Rearrangement Involving a β-Hydroxysulfoxide and Cyclization Processes Toward the 1-Benzenesulfonyl-5-benzenethio-1,2,2a,3,4,5-hexahydrobenz[*c*,*d*]indole Oxygenated at the 4-Position

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Treatment of compound **4** with trifluoroacetic anhydride under reflux in chlorobenzene underwent a tandem rearrangement to produce compound **5**. When the acetylated derivative of **4**, was treated with trifluoroacetic anhydride in the presence of Lewis acids produced two *cis* cyclized conformers **7a** and **7b**, presumably through the intermediate **B**.

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As a part of a general study directed towards the development of dopaminergic agents, we wished to synthesize derivatives of the tricyclic ketone **7** (OAc, H = O) carrying various substituents at **4** and **5** positions in order to pursue their conformational analysis and pharmacophore identification. Logical choices would include sulfur-, oxygen-, or nitrogen-containing functional groups as substituents.

The most obvious reaction sequence to these structurally simplified analogues of ergot alkaloids in light of such considerations would require the synthesis of the above mentioned ketone from the sulfinyl ketone **3** *via* our recently reported methodology of intrahomoacylation [1].

Of the above plan upon which our intended synthesis of such compounds was based, none was more vital than the intramolecular cyclization step. The experimental viability of this prerequisite had been tested, but only on a substrate in which its electron density was increased at the point of attack thus making it suited for trapping the ensuing thionium ion generated under Pummerer reaction conditions. Indeed as is described below, this step proved to be highly capricious.

Ethyl 3-indolylacetate [2] was reduced with sodium cyanoborohydride in acetic acid to an indoline which was subsequently protected with benzenesulfonyl chloride to produce compound **2** in 88% yield (Scheme 1).

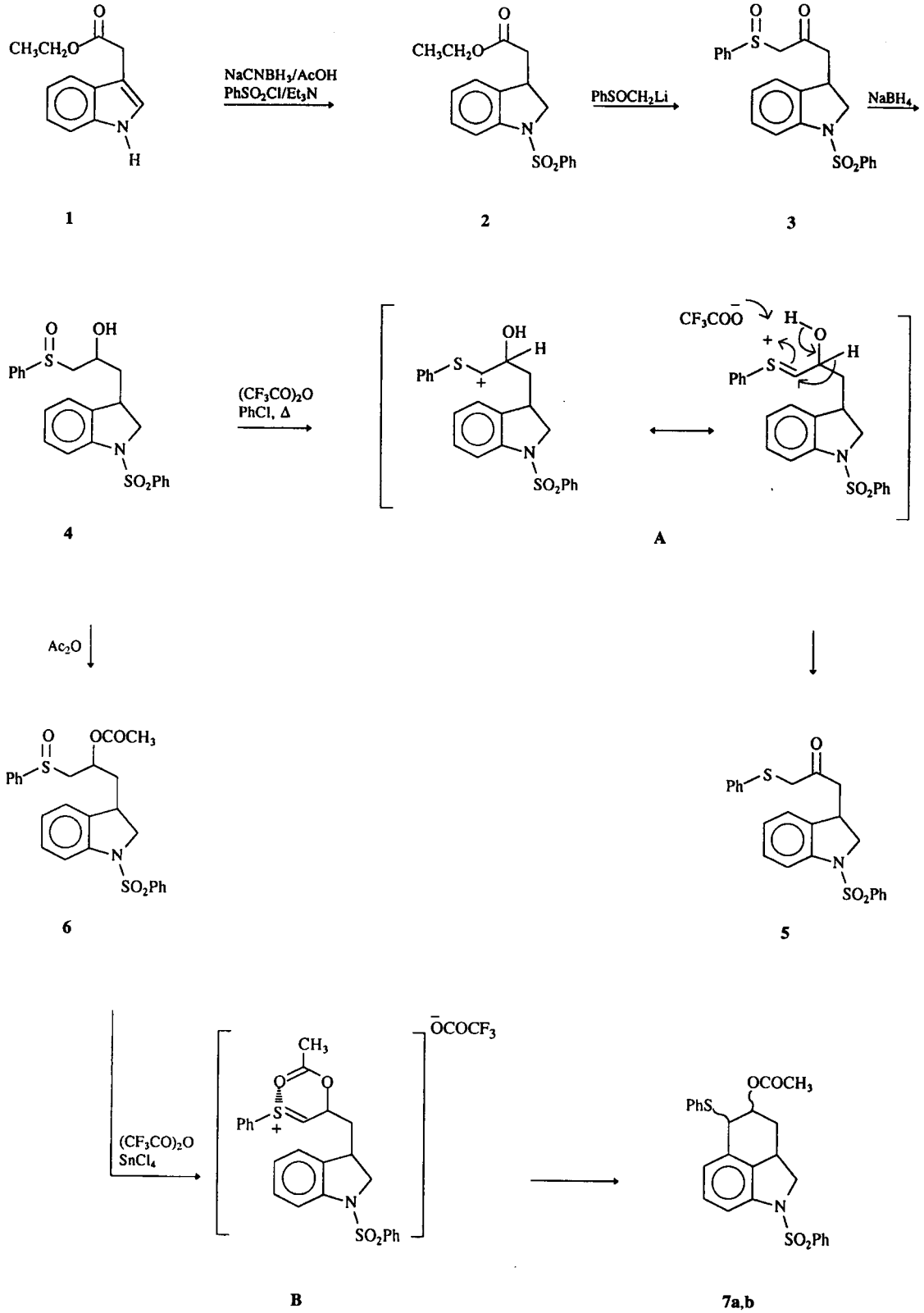
Introduction of the benzenesulfinyl moiety was readily achieved by the addition of the prepared benzenesulfinylmethyl lithium [3] to a tetrahydrofuran solution of ester **2** at 0° to provide the required ketone **3** in 78% yield. With compound **3** in hand we were able to pursue the cycloaddition process. Treatment of **3** with trifluoroacetic anhydride followed by tin tetrachloride under various reaction conditions formed in all cases an intractable mixture of products [4]. However, a methylsulfinyl analogue of **3**, with a methoxy group on the benzenoid moiety *para* to the reaction center, successfully gave a cyclization product in excellent yield [1].

Since a phenyl group is somewhat bulky and hence its stereochemical requirements more demanding in comparison with the methyl group, we turned our attention to the methyl analogue of **3** (C_6H_5 = CH_3) which was prepared in a similar manner [5]. Treatment of this methyl derivative as above, that is with trifluoroacetic anhydride and then with tin tetrachloride under various reaction conditions formed in all cases a heavy white precipitate with a supernatant red solution containing at least five major products according to tlc. The use of other Lewis acid promoters such as titanium tetrachloride and boron trifluoride diethyl etherate provided no better results. Therefore from these results it is suggested that steric interactions caused by the bulkiness of the phenyl group could not account for the failure of the cycloaddition step.

Next, we proceeded to assess the electronic factors which might be inherent to such molecules as **3** and **3** (C_6H_5 = CH_3). For this, we recalled the intermolecular reactions of analogous Pummerer intermediates in which excellent yields of the products were obtained [6]. Accordingly, we subjected the Pummerer intermediate generated as above from compound **3** (C_6H_5 = CH_3) to the same reaction conditions in the presence of toluene as the substrate. As expected, the reaction provided the interhomoacylation product in 76% yield, a viscous material consisting of the *para* and *ortho* isomers in a ratio 2.5:1 after separation by chromatography. Moreover we tried a similar reaction of a Pummerer intermediate generated from the ketosulfoxide ω-(methylsulfinyl)acetophenone with the *N*-benzene-*N*-methylbenzenesulfonamide [7], a substrate which we had not examined before [6]. Again this reaction yielded a crystalline *para*-substituted interhomoacylation product in 75% yield, mp 147-148°.

Evidently, the above results indicated that electronic factors in the benzenoid moiety of compound **3** which could be responsible for the failure of the cycloaddition step do not impose any restrictions since they are comparable to those of toluene and *N*-benzene-*N*-methylbenzenesulfonamide. For that matter even benzene itself is reactive under the same reaction conditions [6]. Finally, methyl and phenyl groups aside, attention was focused on the common and uncommon structural features of sulfox-

Scheme 1


NaCNBH3/AcOH
PhSO2Cl/Et3N
PhSOCH2Li
NaBH4
(CF3CO)2O
PhCl, Δ
Ac2O
(CF3CO)2O
SnCl4
1
2
3
4
A
5
6
B
7a,b

ides **3** and their reported 8-methoxy analogue [1]. The obvious common feature in the side chain is an sp^2 hybridized carbon atom (carbonyl carbon atom). Hence cyclization on the aromatic ring would involve the formation of a strained six-membered ring. In the case of the 8-methoxy analogue, it seems that this strain impeding effect to cyclization is overshadowed by the driving force which is generated by the higher nucleophilicity (a result of relatively higher electron density) of the *para*-position which is involved in the formation of 5-5a bond.

In view of this rationale, it appeared that a way to circumvent the cyclization problem could be found in changing the hybridization of the carbonyl carbon atom from sp^2 to Sp^3. This would possibly, on the one hand, alleviate the unfavorable effect of strain involved, and on the other would reduce somewhat the distance between the carbon atoms involved in the formation of 5-5a bond. The sp^2 hybridization of the carbonyl carbon atom was then changed to sp^3 by reduction with sodium borohydride, obtaining in this way the corresponding alcohol **4**. Exposure of this alcohol to the aforementioned reaction conditions proved equally unsuccessful. We then subjected it to the reaction conditions similar to those which were successful in the synthesis of *Aspidoderma* indole alkaloids [8].

Treatment of the hydroxysulfoxide with six equivalents of trifluoroacetic anhydride followed by heating the reaction solution, now in chlorobenzene, at 135-140° for 2-3 hours produced only one product (tlc). It was not the desired cycloaddition product. Instead, a rearrangement followed the Pummerer rearrangement involving a hydrogen shift, shown in structure **A**, to give the β-ketosulfide **5**. This unexpected sequence of events can be described as an internal double redox process where at first the sulfoxide group is reduced and the α-carbon atom is oxidized (Pummerer rearrangement). Subsequently the α-carbon atom is back reduced to its original state with concomitant oxidation of the β-carbon atom [9]. Thus the net result of the sequence is the transfer of the oxidation state of sulfur atom along the chain to its appositely functionalized β-carbon atom. In this particular case, the β-carbon atom was functionalized with a hydroxy group.

The β-ketosulfide **5** was characterized by its spectroscopic properties which were identical with those of a sample prepared by an alternative route (see Experimental). Therefore, it was decided to replace the labile hydrogen atom of the hydroxy group by an acetyl group, by treating compound **4** with acetic anhydride in the presence of pyridine. Subsequently acetylated compound **6** was treated with trifluoroacetic anhydride in the presence of collidine, followed by a Lewis acid promoter such as tin tetrachloride or boron trifluoride etherate.

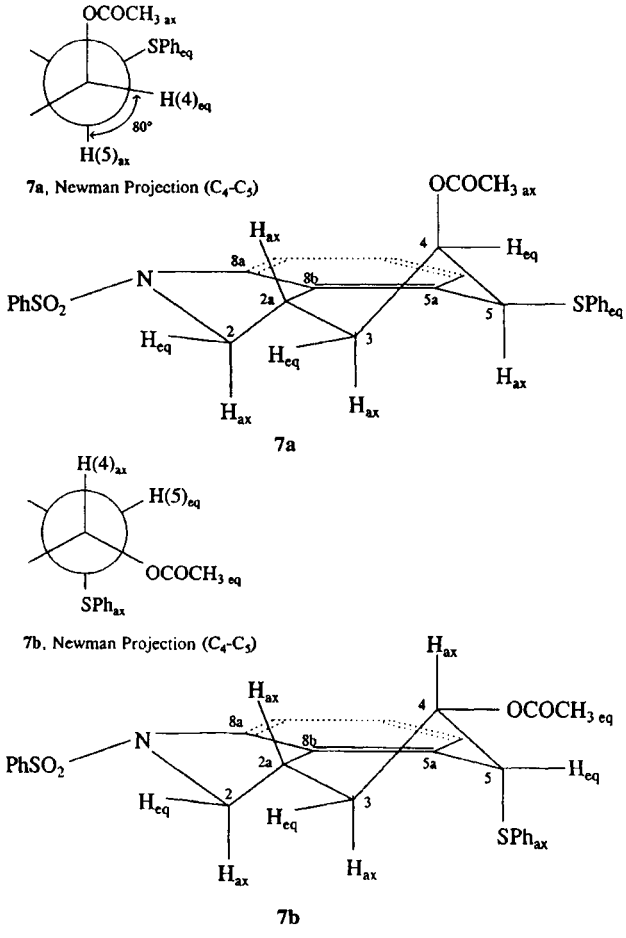
An analysis (tlc, silica gel, toluene:ethyl acetate, 95:5) indicated that the reaction mixture consisted mainly of two major products with $R_f = 0.50$ and $R_f = 0.33$, besides the by-product phenyl disulfide. Column chromatography on silica gel eluting with toluene to remove impurities (diphenyl disulfide) and toluene spiked with small amounts of ethyl acetate (grating) separated the two major products. The product with $R_f = 0.50$, after further purification by column chromatography on silica eluting with dichloromethane, was obtained as a colorless viscous material (yield 25%), homogeneous by tlc. Analysis (^1H nmr) indicated no desired cyclization had occurred, therefore no further characterization was pursued on this by-product.

Evaporation *in vacuo* of the fraction containing the product with $R_f = 0.33$ deposited a white solid which had a surprisingly wide range melting point (134-158°), albeit in low yield (23%). More careful tlc on silica gel eluting with dichloromethane revealed that this solid material consisted of two components. Separation was painstakingly achieved by mplc on silica gel eluting with dichloromethane to yield two distinct, apparently cyclized, products in a ratio 3:1 with mp 160-161° (**7b**), and 147-148° (**7a**) respectively.

Mass spectrometry and elemental analysis indicated that these two compounds had identical masses, indicating that they are stereoisomers which could probably differ in configuration at C-4 and C-5. The stereochemistry of **7b** and **7a** was based on a comparison of the ^1H nmr spectra of these compounds with those of closely related structures [10]. The signal of the axial H-3 proton of compound **7b** appeared at 1.71 ppm as a sharp quartet, J = 11.8 Hz. It has been established that this splitting pattern is a general diagnostic feature in this series [10]. This quartet resulted from equivalent coupling of the axial H-3 proton to the two adjacent methine protons H-2a and H-4 and to the geminal equatorial proton. Thus the relative stereochemistry between the tertiary hydrogens H-2a and H-4 was that involving a *cis* 1,3 diaxial relationship. In turn, the signal of the H-5 proton appeared at 4.87 ppm as a doublet with a coupling constant J = 4.9 Hz. This value of the coupling constant suggests a *cis* 1,2 relationship between the protons H-4 and H-5 according to the Karplus correlation. Hence the H-5 proton must have adopted the equatorial configuration. Therefore, conversely, the vicinal bulky groups located at C-4 and C-5 should be placed in the less favorable *cis* relationship ($-OCOCH_3$)-equatorial and (-SPh)-axial, in this most stable half chair conformation of the C-ring (Structure **7b**, Scheme 2).

In the case of the isomer **7a**, the key signal of the axial H-3 proton lost its quartet pattern and appeared instead as a triplet, J = 13.2 Hz, with additional splitting, J = 1.4 Hz. The loss of the quartet pattern suggests that the H-4 proton has no longer the axial configuration, therefore should

Scheme 2



be equatorially positioned. On the other hand, the signal of the proton H-5 appeared at 4.38 ppm as a singlet which implies a value of the coupling constant between H-4 and H-5 protons to be approximately zero. A zero value ($J \approx 0$) will indicate a dihedral angle between the C_4-H and C_5-H equal to about 80°. This suggests either that the H-4 and H-5 have a *trans* diequatorial configuration, according to theoretical calculations of closely related systems [10], or a *cis* configuration, specifically H-4 equatorial and H-5 axial in a deformed half chair conformation. However, examining the models of these configurations, the equatorial H-5 (case **7b**) lies approximately in the plane of the aromatic ring, while the axial H-5 lies below the plane of the ring. One would expect the H-5 to be deshielded when it is in the same plane as the aromatic ring and, conversely, to be shielded when it is below the plane of the ring under the influence of the π-cloud. This deshielding-shielding difference is evident from the values of the chemical shifts. The value of the chemical shift of equatorial H-5 of the isomer **7b** is 4.87 ppm whereas of the corresponding H-5 of the isomer **7a** is 4.38 ppm, showing an upfield shift of 0.5 ppm for this proton. The observed magnitude of the chemical shift difference cannot be justified by considering an equatorial/equatorial relationship, so much if taken into account only an equatorial/axial identity. Therefore the H-5 of isomer **7a** should have an axial configuration. A dihedral angle of approximately 80° between C_4-H and C_5-H in this **7a** isomer could then be formed from severe interaction between the aromatic C-6 hydrogen and the bulky (PhS-) group, which could make it tilt away from the aromatic ring plane, deforming in this way the half chair conformation of the C-ring. Thus the two compounds **7b** and **7a** are two conformers where the bulky substituents at C-4 and C-5 have anchored them in the 1,2-*cis* conformations depicted in Scheme 2. The formation of these two conformers in the unfavorable *cis* C4-C5 arrangement may be rationalized by considering an SN_1 type of mechanism in the formation of the C-ring.

It is known that sulfoxides can be activated with trifluoroacetic anhydride to give a sulfur stabilized cation involving a thionium ion **A** (Scheme 1) and the latter has been known to react with π-electron systems in the presence of Lewis acids [1,5]. It has been shown also that the chiral thionium ions undergo a high diastereoselective addition of silyl enol ethers to give predominantly the corresponding *syn* product [11].

The stereochemical outcome in the cyclization step can be explained by a nucleophilic attack of the benzenoid π-electron system on the chiral thionium ion *via* the cyclic conformation **B** (Scheme 1). Therefore the electrostatic attraction between the carbonyl of the ester and the positive charge on the sulfur atom to form a six-membered cyclic intermediate as shown in Scheme 1 will be responsible for the formation of the *cis* conformation in the cyclization process.

EXPERIMENTAL

Ethyl (1-Benzenesulfonyl-3-indolinyl)acetate **2**.

To a solution of ethyl (3-indolyl)acetate [2] (10.15 g, 50 mmoles) in glacial acetic acid (100 ml) at 15° under an argon atmosphere was added sodium cyanoborohydride in small portions every 5-10 minutes until almost no starting material remained by tlc (Van Urk's reagent). The crude product was poured into about 500 ml ice-water and 300 ml toluene-ethyl acetate (1:1) and basified cautiously with solid sodium carbonate with stirring maintaining the temperature of the mixture below 5° with an ice-water bath. The organic layer was separated and the aqueous layer was extracted with toluene-ethyl acetate (1:1, 2 x 150 ml). The combined organic phase was dried (sodium sulfate) and concentrated to about 300 ml.

Into this solution of crude indoline, cooled in an ice-water

bath, was added triethylamine (10.1 g, 100 mmoles) and then benzenesulfonyl chloride (12.36 g, 70 mmoles) with stirring in an argon atmosphere. The red solution was allowed to stir overnight, diluted with 200 ml toluene-ethyl acetate (1:1), washed with dilute hydrochloric acid, dried (sodium sulfate), evaporated *in vacuo* to afford a syrup which was chromatographed on silica using toluene and then toluene containing 15-20% ethyl acetate, to yield a colorless syrup which was crystallized from ethyl ether-hexane as white crystals, mp 63-65°, 15.20 g (88%); ir (chloroform): 1720, 1600 cm^{-1}; ^1H nmr (80 MHz, deuteriochloroform, tetramethylsilane): δ 1.24 (3H, t, J = 7.2 Hz, CH_3), 2.16 (1H, dd, J = 16.3, 9.7 Hz, one of the hydrogens of the CH_2CO), 2.51 (1H, dd, J = 16.4, 5.0 Hz, the other hydrogen of the CH_2CO), 3.53 (1H, a singlet split into seven peaks, H-3), 3.65-3.71 (1H, dd, J = 11.1, 5.8 Hz, H-2), 4.09-4.17 (3H, m, the other H-2 overlapped by the quartet of OCH_2), 6.96-7.81 (9H, m, aromatic hydrogens).

Anal. Calcd. for $C_{18}H_{19}NO_4S$: C, 62.59, H, 5.54, N, 4.06. Found: C, 62.30, H, 5.44, N, 4.17.

(1-Benzenesulfonyl-3-indolinyl)methyl Benzenesulfinylmethyl Ketone **3**.

To a solution of benzenemethyl sulfoxide (3.1 g, 22 mmoles) in 20 ml of dry tetrahydrofuran (freshly distilled from lithium aluminum hydride) at 0° was added dropwise with stirring 15 ml of *n*-butyllithium (1.47 *M* in benzene) under an argon atmosphere. After 15 minutes stirring, this solution of benzenesulfinylmethyl lithium was added dropwise *via* a syringe, over a period of about half an hour into a vigorously stirring solution of **2** (3.45 g, 10 mmoles) in 20 ml of dry tetrahydrofuran cooled to 0° with an ice-water bath, under an argon atmosphere. After 5-10 minutes stirring, the reaction mixture was poured into ice-water-dichloromethane and neutralized to *p*H 6-7 with dilute hydrochloric acid. It was extracted with dichloromethane, dried (sodium sulfate) evaporated *in vacuo*, and the residue was chromatographed on silica gel using toluene-ethyl acetate 1:1, to give 3.43 g (78%) of **3** as an amorphous white solid (mixture of the two diastereoisomers), mp 121-126° from toluene; ^1H nmr (300 MHz, deuteriochloroform, tetramethylsilane): δ 2.41 (0.5H, dd, J = 8.8, 7.0 Hz, CCH_2CO), 2.50 (0.5H, dd, J = 7.7, 7.0 Hz, which coalesce to an apparent triplet, CCH_2CO), 2.73 (0.5H, dd, J = 19, 4.4 Hz, CCH_2CO), 2.78 (0.5H, dd, J = 16, 3.9 Hz, CCH_2CO), 3.47 (2H, m, H-2 and H-3), 3.74 (2H, s, $SOCH_2CO$), 4.05 (1H, dd, J = 8.3 Hz for the first doublet, and J = 18.6 Hz for the arising two doublets with additional side splitting, of the two inner peaks with J = 2 Hz, H-2), 6.95-7.79 (14H, m, aromatic hydrogens).

Anal. Calcd. for $C_{23}H_{21}NO_4S_2$: C, 62.85, H, 4.82. Found: C, 63.08, H, 4.63.

1-(1'-Benzenesulfonyl-3'-indolinyl)-3-benzenesulfinylmethyl-2-propanol **4**.

To a stirred solution of β-ketosulfoxide **3** (4.39 g, 10 mmoles) in 100 ml of methanol and 50 ml of tetrahydrofuran cooled in an ice-water bath was added in small portions sodium borohydride (0.5 g, 13.22 mmoles). The reduction was monitored by tlc (silica gel, toluene-ethyl acetate 1:1). The reaction mixture was concentrated *in vacuo*. The residue was partitioned between dichloromethane and water, saturated with sodium-chloride and the aqueous layer extracted exhaustively with dichloromethane, dried (sodium sulfate) and concentrated. The residual solution was filtered through a short column of silica gel using toluene-ethyl acetate 1:1. Concentration of the fraction containing the product gave the alcohol as a white solid inseparable mixture of diastereoisomers which had a wide melting point range (126-155°) 4.28 g (97%). Fractional crystallization from toluene gave fractions with the following melting points: 161-163°, 172-178° and 176-183°.

The proton magnetic resonance spectrum appears as a very complex pattern.

Anal. Calcd. for $C_{23}H_{23}NO_4S_2$: C, 62.56, H, 5.25. Found: C, 62.95, H, 5.17.

(1-Benzenesulfonyl-3-indolinyl)methyl Benzenethiomethyl Ketone **5** from Rearrangement of **4**.

To a stirred solution of hydroxy compound **4** (0.882 g, 2 mmoles) in dry dichloromethane (70 ml) cooled with an ice-water bath, under an argon atmosphere was added dropwise trifluoroacetic anhydride (1.7 ml, 2.52 g, 12 mmoles). After the addition the ice-water bath was removed and stirring continued for an additional 4 hours at room temperature. Chlorobenzene (50 ml) was added to the reaction solution and heated in an oil bath raising the temperature slowly to distill the dichloromethane over a period of more than an hour. Then the solution was refluxed for 2-3 hours, monitoring the reaction by tlc. The solution was cooled to room temperature, then chromatographed on a column of silica gel removing the chlorobenzene down the column with toluene. Then the product was eluted with addition of a little ethyl acetate (2-3%) to toluene. The product was recrystallized from ethyl ether-hexane as white crystals, mp 89-90°, 651 mg, 77%. The mother liquor was chromatographed again to remove traces of an impurity which appears on the column as a yellow band with an R_f slightly faster than the product; ir (potassium bromide): 1710, 1600 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform, tetramethylsilanle): δ 2.52 (1H, dd, J = 13.8, 8.4 Hz, one of the hydrogens of the CCH_2CO), 2.85 (1H, dd, J = 13.8, 4.7 Hz, the other hydrogen of the CCH_2CO), 3.49 (2H, m, H-2 and H-3), 3.56 (2H, s, SCH_2), 4.04 (1H, dd, J = 12.4, 10.5 Hz with additional two small peaks between the middle and outer peaks, the other H-2), 6.93-7.77 (14H, m, aromatic hydrogens).

Anal. Calcd. for $C_{23}H_{21}NO_3S_2$: C, 65.22, H, 5.00, N, 3.31. Found: C, 65.38, H, 4.91, N, 3.25.

(1-Benzenesulfonyl-3-indolinyl)methyl Benzenethiomethyl Ketone **5** from Ester **2**.

To a solution of benzenemethyl sulfide (2.73 g, 20 mmoles) in 20 ml of dry tetrahydrofuran at 0° was added dropwise with stirring 15 ml of *n*-butyllithium (1.47 *M* in benzene) under an argon atmosphere. After 15 minutes stirring, this solution of benzenethiomethyl lithium was added dropwise *via* a syringe into a vigorously stirring solution of ester **2** (3.45 g, 10 mmoles) in 20 ml of dry tetrahydrofuran cooled to 0° in an ice-water bath, under an argon atmosphere. After 5-10 minutes stirring, the reaction mixture was poured into ice-water-dichloromethane and extracted with dichloromethane. The organic layer was dried (sodium sulfate), concentrated *in vacuo*, and the residue was chromatographed on silica gel using initially petroleum ether, to remove impurities, followed by toluene with a small amount of ethyl acetate, to give the title compound **5** (1.9 g, 45%), identical in all respects to the previously prepared sample by the alternative route.

1-(1'-Benzenesulfonyl-3'-indolinyl)-3-benzenesulfinyl-2-propyl Acetate **6**.

Into a dry flask containing hydroxy compound **4** (4.41 g, 10 mmoles) was added dichloromethane (15 ml), dry pyridine (10 ml) and acetic anhydride (5 ml). The flask was stoppered with a rubber septum and the solution stirred gently for 24 hours at room temperature. The reaction mixture was diluted with ice-water-dichloromethane, the organic layer was washed with ice-water, then dilute hydrochloric acid in ice-water, dried (sodium sulfate) and evaporated *in vacuo*. The residue was chromatographed on silica gel using dichloromethane with a small amount of methanol. Evaporation of the solvent left the product as a colorless gum which changes to a white foam under high vacuum, (4.59 g, 95%).

It consisted of a mixture of diastereomers, shown by the ^{1}H nmr spectrum which appears as a complex clusters of multiplets (300 MHz, deuteriochloroform, tetramethylsilane): δ 1.41 (m, 1H), 1.71-1.81 (m, 3H), 1.94-2.12 (m, 12H), 2.87-2.93 (m, 3.5H), 3.03-3.10 (m, 4.5H), 3.55-3.66 (m, 3H), 3.83-3.97 (m, 3H), 5.14-5.19 (m, 2H), 5.35 (m, 1H), 6.92-7.07 (m, 6H), 7.15-7.25 (m, 4H), 7.33-7.70 (m, 26H), 7.72-7.77 (m, 6H).

It was directly used in the next stage to give **7**.

1-Benzenesulfonyl-4-acetoxy-5-benzenethio-1,2,2a,3,4,5-hexahydrobenz[*c*,*d*]indole **7a**,**b**.

To a stirred solution of compound **6** (0.985 g, 2.04 mmoles) in 60 ml of dry dichloromethane cooled to 0° under an argon atmosphere was added dry collidine (0.27 ml, 0.247 g, 2.04 mmoles) and trifluoroacetic anhydride (0.86 ml, 1.28 g, 6.12 mmoles) and the solution was stirred at room temperature for 2.5 hours. Then the solution was cooled to 0° again with an ice-water bath, added dropwise tin tetrachloride (0.24 ml, 0.531 g, 2.04 mmoles) and stirring continued for 2 hours at 0° and for one hour at room temperature. The reaction was quenched with ice-water-dichloromethane, the organic phase was separated and the aqueous layer was extracted once with dichloromethane. The combined extracts were dried (sodium sulfate) and concentrated *in vacuo*. Analysis (tlc) of the residue (toluene-ethyl acetate, 95:5, silica gel) indicated two major products, with R_f = 0.33 and R_f = 0.50. Column chromatography on silica gel, using toluene and then toluene with a small amount of with ethyl acetate, separated the products in two final fractions.

Fraction one containing the product with R_f = 0.50 was evaporated *in vacuo* to provide a syrup, which was subsequently purified further on silica gel column eluting with dichloromethane. Evaporation of the solvent *in vacuo* gave a colorless viscous material which resisted crystallization, but appears as a colorless foam under high vacuum, 0.237 g (25%); ^{1}H nmr analysis indicated that this is uncyclized compound.

Fraction two containing the product with R_f = 0.33 was evaporated *in vacuo* to yield a white solid which had a wide melting point range (134-158°), 0.218 (23%). A careful tlc on silica gel eluting with dichloromethane revealed that this solid material consisted of two products. Separation was achieved by mplc on silica gel eluting with dichloromethane.

Compound **7a** was obtained as a white solid, mp 147-148° from ether-hexane, 56 mg; ^{1}H nmr (300 MHz, deuteriochloroform, tetramethylsilanle): δ 1.61 (1H, t, J = 13.2 Hz with additional splitting J = 1.4 Hz, H-3 axial), 1.93 (3H, s, CH_3), 2.11 (1H, dt, J = 13.4, 4.4 Hz, H-3 equatorial), 3.10 (1H, dd, J = 12.7, 8.2 Hz, H-2 axial), 3.20 (1H, m, H-2α), 4.24 (1H, t, J = 7.5, 8 Hz, H-2 equatorial), 4.38 (1H, s, H-5 axial), 5.34 (1H, t, an apparent singlet splitted to a triplet or coalesced dd, J = 1.92, 1.95 Hz, H-4 equatorial), 7.13 (1H, d, J = 7.8 Hz), 7.19 (3H, m, the aromatic hydrogens of indoline moiety), 7.24 (1H, d, J = 7.9 Hz), 7.32 (2H, m), 7.47 (3H, m), 7.60 (1H, t, J = 7.4, 7.3 Hz), 7.85 (2H, d, J = 7.4 Hz); ms: (EI) m/z = 465 (M^+).

Anal. Calcd. for $C_{25}H_{23}NO_4S_2$: C, 64.52, H, 4.95. Found: C, 64.71, H, 5.15.

Compound **7b** was obtained as a white solid, mp 160-161° from ether-hexane, 162 mg; ^{1}H nmr (300 MHz, deuteriochloroform, tetramethylsilane): δ 1.65 (3H, s, CH_3), 1.71 (1H, q, J = 11.8 Hz, H-3 axial), 1.96 (1H, ddd, J = 11.5, 4.4, 3.6 Hz, degenerated to apparent dt, H-3 equatorial), 3.04 (1H, m, H-2α axial), 3.17 (1H, dd, J = 12.5, 9.2 Hz, H-2 axial), 4.21 (1H, dd, J = 8.5, 8.2 Hz, degenerated to an apparent triplet, H-2 equatorial), 4.87 (1H, d, J = 4.9, H-5 equatorial), 5.19 (1H, ddd, J = 11.8, 4.7, 3.4 Hz, degenerated to an apparent dt, H-4 axial), 7.10 (1H, d, J = 7.8 Hz), 7.15 (3H, m, the aromatic hydrogens of indoline moiety), 7.22 (1H, d, J = 7.9 Hz), 7.28 (2H, m), 7.46 (3H, m), 7.60 (1H, t, J = 7.4 Hz), 7.83 (2H, d, J = 7.5 Hz); ms: (EI) m/z = 465 (M^+).

Anal. Calcd. for $C_{25}H_{23}NO_4S_2$: C, 64.52, H, 4.95. Found: C, 64.67, H, 5.03.

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[2] R. C. Elderfield, B. Fischer and J. M. Lagowski, *J. Org. Chem.*, **22**, 1376 (1957).

[3] When for the preparation of benzenesulfinylmethyl lithium was used lithium dialkylamines as bases, generated *in situ* from *n*-butyllithium and a secondary amine such as diethylamine, the yield of compound **3** was higher most of the times.

[4] Compounds of type **7** (AcO, H = O; PhS = H) are characterized with some degree of inherent instability; see ref 1 and D. E. Nichols, J. M. Robinson, G. S. Li, J. M. Cassady and H. G. Floss, *Org. Prep. Proced. Int.*, **9**, 277 (1977).

[5] The procedure which was followed is that described in ref 1 for the methoxy analogue. The product was a white solid consisting of two diastereomers, in 81% yield having a melting range of mp 137-147°. One of the diastereomers, isolated accidentally during the purification procedure by chromatography on silica gel (ethyl acetate with a small amount of ethanol) and then recrystallization from ethyl acetate-dichloromethane, had mp 149-151°.

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[9] In the transformation of **4** to **5**, although loss of a proton in intermediate **A**, followed by enol to ketone tautomerism is also an alternative pathway likely to occur, we favor at the present time that illus-

trated in the Scheme 1 based on the indication in analogous systems where a carbon-group migrates, when there is not a proton available (unpublished results).

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