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Effect of Salts on the Reaction Direction of (2*R**,3*R**)-2-[(1*R**)-1-Iodoethyl)]-3-methyl(3,5-dimethyl)-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indoles with Dimethylformamide

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Abstract—Transformations of (2*R**,3*R**)-2-[(1*R**)-1-iodoethyl)-3,5-dimethyl-1-(4-methylphenylsulfonyl-2,3-dihydro-1*H*-indole on heating in boiling dimethylformamide in the presence of various salts were studied.

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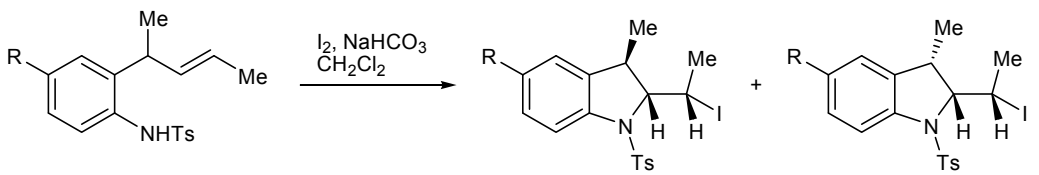
Potent selective androgen receptor modulators have been found among 2-hydroxyalkyldihydroindoles [1, 2]. These compounds were also used as intermediate products in the synthesis of optically active α-amino acids [3] and cycloalkane-fused indole derivatives [4]. 2-Hydroxyalkyldihydroindoles are usually prepared by reduction of 2-(indol-3-yl)alkanoic acid esters [3], epoxidation of *ortho*-crotylanilides [5], thermal intramolecular aminohydroxylation of *N*-aryl- or *N*-methylsulfonyl-2-allylanilines in the presence of copper trifluoromethanesulfonate and TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl) [6, 7], and hydroxylation of *N*-acyl-2-allylanilines with [bis(trifluoroacetoxy)-λ^3-iodanyl]benzene [8].

In the present work we studied reactions of dihydroindoles **IIa** [9] and **IIb** with dimethylformamide under different conditions, and obtained a number of products, including 1-(2,3-dihydro-1*H*-indol-2-yl)ethyl formates (Schemes 1, 2).

We previously found that heating of compound **IIa** in DMF over a period of 2 h yields a mixture of formate **IV** and iodo derivative **V** [9] with the inversed configuration of $C^{1'}$ with respect to **IIa**. In this work, the reaction was prolonged to 4 h; as a result, isomer **V** disappeared almost completely, and the products were (1*R**)-ester **IV** and its (1′*S**)-isomer **VI** at a ratio of ~9 : 1. Presumably, compound **VI** is formed via S_N2 replacement of the halogen atom in **V** by formyloxy group (Scheme 2).

Assuming that the initially high concentration of iodide ion could favor formation of compound **V**, 4 equiv of potassium iodide was added to a solution of **IIa** in DMF with a view to increase the yield of (1′*S**)-stereoisomer **VI**. However, under these condi-

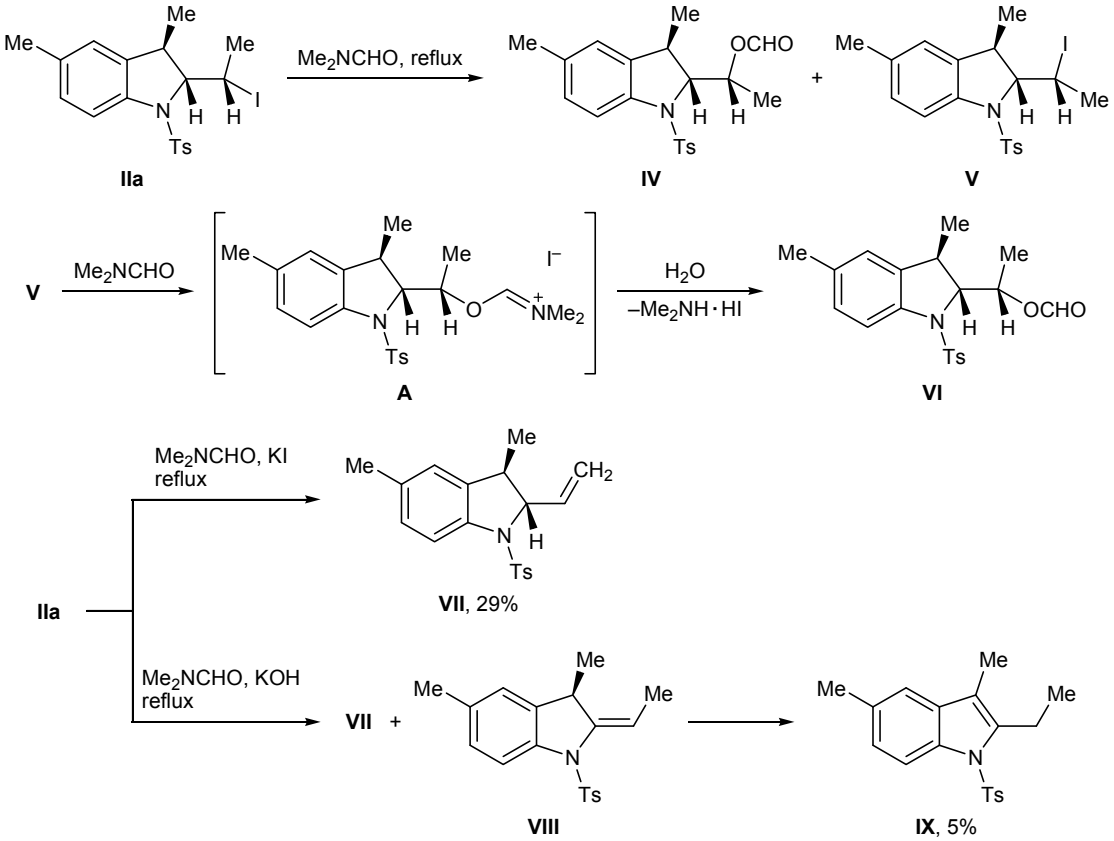
Scheme 1.



Ia, **Ib** **IIa**, **IIb** **IIIa**, **IIIb**

R = Me (**a**), H (**b**).

Scheme 2.

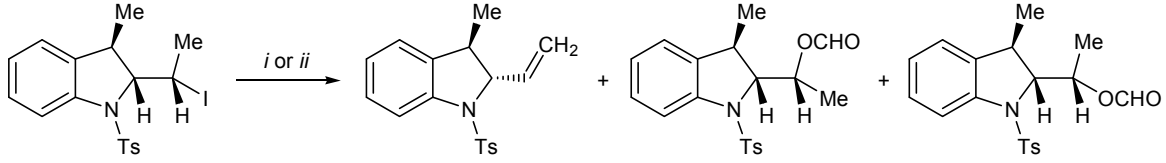


tions, the products were esters **IV** and **VI** and 2-vinyl-substituted dihydroindole **VII** [8]; the latter was isolated in 29% yield by column chromatography on silica gel. Further elution afforded a mixture of stereoisomers **IV** and **VI** at a ratio of 77:23 (overall yield 13%). Presumably, a small amount of ethylidene derivative **VIII** is also formed since its isomerization product, indole **IX** (5%), was also isolated from the reaction mixture.

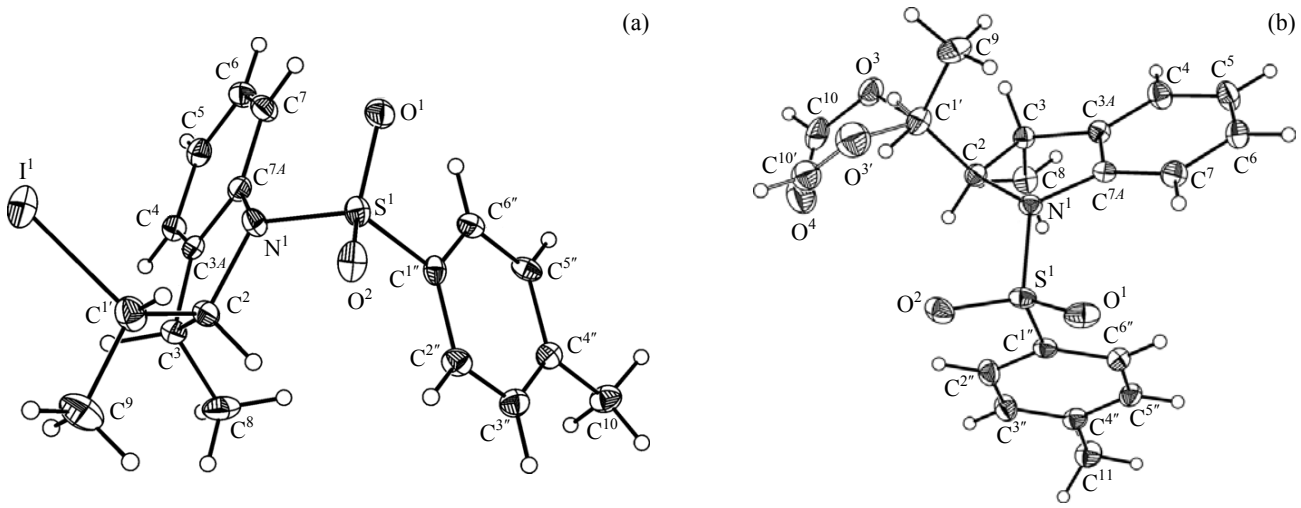
Our attempt to obtain 1-(2,3-dihydro-1*H*-indol-2-yl)ethanol by direct nucleophilic substitution of the iodine atom in **IIa** by hydroxy group on heating with potassium hydroxide in DMF gave ethylidene and vinyl derivatives **VIII** and **VII** at a ratio of ~100:35. According to the ^{1}H NMR data, the fraction of alcohol **XV** did not exceed 10%. *trans* Configuration of the exocyclic double bond in **VIII** was determined by NOE experiments; saturation of protons in the 3-Me group increased the intensity of the signal from protons of the methyl group at the double bond by 1.85%, while saturation of protons of the latter methyl group resulted in increase in intensities of the 3-CH_3 and 3-H signals by 1.62 and 1.90%, respectively.

Heating of compound **IIb** in dimethylformamide for 4 h (Scheme 3, *i*) gave a mixture of compounds **X**–**XII**. As followed from the signal intensities in the ^{1}H NMR spectrum of that mixture, isomeric esters **XI** and **XII** were the major products, the ratio (**XI**+**XII**):**X** being ~6:1. Esters **XI** and **XII** were separated by column chromatography; their ratio was 93:7.

Scheme 3.



i: Me_2NCHO, reflux; *ii*: KI, Me_2NCHO, reflux.



Structure of (a) the molecule of (2*R**,3*R**)-2-[(1*S**)-1-iodoethyl]-3-methyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indole (**IIb**) and (b) superposition of diastereoisomeric 3-methyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indol-2-yl}ethyl formates **XI** and **XII** according to the X-ray diffraction data; the formyl group in molecule **XII** is shown with hollow lines.

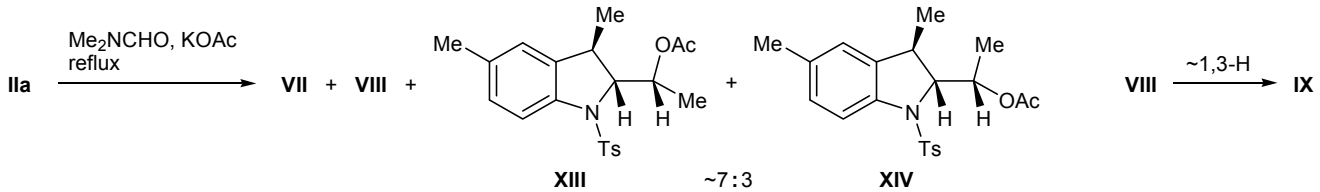
Addition of 4 equiv of potassium iodide to a solution of **IIb** in DMF (Scheme 3, *ii*) increased the fraction of vinyl derivative **X**, and the ratio **X**:(**XI**+**XII**) attained 1:1.

Mutual orientation of the methyl and iodoethyl substituents in the indole fragment of **IIb** was determined by X-ray analysis (see figure). The dihydroindole fragment is planar, the N^1 atom has a pyramidal configuration [the sum of the bond angles is 347.0(5)°], and the exocyclic N–C bond deviates from the dihydroindole ring plane, which may be due to formation of quite weak hydrogen bonds C^7–$H^{7A}\cdots O^1$ [C···O 3.012(3), H···O 2.45 Å, ∠CHO 118°] and C^2–$H^{2A}\cdots O^2$ [C···O 2.868(3), H···O 2.57 Å, ∠CHO 97°]. The methyl and iodoethyl substituents are oriented toward different sides of the ring, so that the 2-H and 3-H protons are arranged *trans*. This is consistent with the known data, according to which vicinal spin–spin coupling constants for *trans*-oriented protons are generally small or equal to zero [10]. In the ^{1}H NMR spectrum of **IIb**, the coupling constant for 2-H and 3-H does not exceed 2.7 Hz (the coupling constant for 2-H and 3-H in compound **IIa** reported previously [9] is 3.5 Hz), while the $^3J_{2,3}$ value for *cis* isomer **IIIb** attains 7.6 Hz.

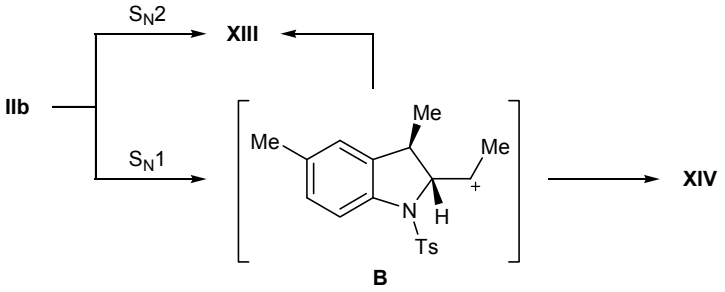
Compound **IIb** crystallized as racemate (noncentrosymmetric but not chiral space symmetry group $Pna2_1$) with a relative configuration of chiral centers given as (1′*R**,2*S**,3*S**). The structure of formic acid ester **XI** was also determined by X-ray analysis (see figure, b), and it appeared to be similar to compound **IIb** [sum of the bond angles at N^1 347.1(2)°; C^7–$H^{7A}\cdots O^1$: C···O 2.972(2), H···O 2.44 Å, ∠CHO 115°; C^2–$H^{2A}\cdots O^2$: C···O 2.944(2), H···O 2.65 Å, ∠CHO 97°). Compound **XI** crystallized as racemate (centrosymmetric space group $P2_1/n$). However, the formyl group is disordered by two positions so that a co-crystal consisting of two diastereoisomers (1′*S**,2*R**,3*R**)-**XI** and (1′*R**,2*R**,3*R**)-**XII** at a ratio of 92(2):8(2) is formed; the same ratio of **XI** and **XII** (within the experimental error) was found by chromatography.

Heating of compound **IIa** in boiling DMF in the presence of 4 equiv of potassium acetate gave compounds **IX** and **VII** and a mixture of esters **XIII** and **XIV**. Ethyl derivative **IX** underwent isomerization during chromatographic separation on silica gel, and the first fractions contained a mixture of compounds **VII**–**IX**. The initial ratio of isomers **VII** and **VIII**

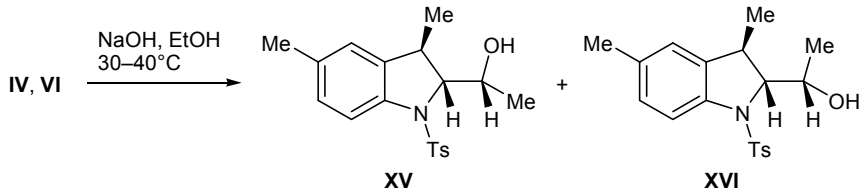
Scheme 4.



Scheme 5.



Scheme 6.



(before applying to a chromatographic column) was 4:5; after chromatographic separation, it changed to 4:1 due to formation of compound **IX**; the ratio of **VII**, **VIII**, and **IX** after chromatography was 4:1:4 (overall yield 59%; Scheme 4).

A mixture of esters **XIII** and **XIV** at a ratio of 7:3 was isolated in an overall yield of ~11%. The formation of (1′*S**)-isomer **XIV** is possible via S_N1 reaction (Scheme 5). GC/MS analysis of mixture **XIII**/**XIV** revealed molecular ions $[M]^+$ with *m*/*z* 387. When a mixture of **IV** and **VI** was kept in a solution of sodium hydroxide in ethanol, a mixture of hydroxyethyl derivatives **XV** and **XVI** was obtained in 53% yield (Scheme 6).

Thus heating of 1-tosyl-2-(1-iodoethyl)-3,5-di- and -3-methyl-2,3-dihydro-1*H*-indoles in DMF leads to replacement of the iodine atom by formyloxy group. When the reaction is carried out in the presence of potassium hydroxide, iodide, or acetate, both dehydrohalogenation and nucleophilic substitution products are formed at different ratios.

EXPERIMENTAL

The X-ray diffraction data for compounds **IIb** and **XI**/**XII** were acquired at 100 K on a Smart Apex2 CCD diffractometer (λ(MoK_α irradiation, λ 0.71073 Å; graphite monochromator; ω-scanning). The initial arrays of reflection intensities were processed using SAINT and SADABS programs built in APEX2 software package [11]. The structures were solved by the direct method and were refined against F^2_{hkl} by the full-matrix least-squares procedure in anisotropic approximation for non-hydrogen atoms using SHELXTL software package [12]. The principal crystallographic data and parameters of X-ray diffraction experiments are given in table. The coordinates of atoms and their temperature factors were deposited to the Cambridge Crystallographic Data Centre (entry nos. CCDC 931026 and CCDC 931027 for **IIb** and **XI**/**XII**, respectively) and are available at *http://www.ccdc.cam.ac.uk/products/csd/request/*.

The IR spectra were recorded on a UR-20 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker Avance III 500 spectrometer at 500.13 and 125.73 MHz, respectively, using tetramethylsilane as internal reference. The mass spectra of **XIII**/**XIV** were obtained on a Thermo Finnigan MAT 95 XP instrument (direct sample admission under standard conditions). The elemental compositions were determined on a EURO EA-3000 CHNS Elemental Analyzer. Column chromatography was performed on silica gel Lankaster LS (40–100 μm). Sorbfil plates (*Sorbpolimer* closed corporation, Krasnodar) were used for analytical thin-layer chromatography; spots were detected by treatment with iodine vapor.

(2*R,3*R**)-2-[(1*S**)-1-Iodoethyl]-3-methyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indole (IIb)** was synthesized according to the procedure described in [9] for **IIa** from 2.84 g (9 mmol) of sulfonamide **Ib**. After appropriate treatment of the reaction mixture, compound **IIb** was isolated by crystallization from ethanol. Yield 0.77 g (21%). Colorless crystals, mp 147°C (from EtOH). ^{1}H NMR spectrum ($CDCl_3$),

Crystallographic data and parameters of X-ray diffraction experiments for compound **IIb** and co-crystal of diastereoisomers **XI** and **XII**

Parameter	**IIb**	**XI/XII**
Formula	$C_{18}H_{20}NO_2IS$	$C_{19}H_{21}NO_4S$
Molecular weight	441.31	359.43
Crystal color	Colorless	Colorless
Crystal shape	Prisms	Prisms
Crystal dimensions, mm	0.24×0.20×0.13	0.32×0.28×0.22
Crystal system	Rhombic	Monoclinic
Space group	$Pna2_1$	$P2_1/n$
Unit cell parameters		
a, Å	14.3184(4)	8.2780(2)
b, Å	13.7659(4)	15.2402(4)
c, Å	9.2503(3)	14.3737(4)
α, deg	90.0	90.00
β, deg	90.0	94.4490(10)
γ, deg	90.0	90.00
V, Å^3	1823.29(9)	1807.90(8)
Z	4	4
d_{calc}, g/cm^3	1.608	1.321
Absorption coefficient μ, mm^{-1}	1.879	0.202
F(000)	880	760
Scan range, θ, deg	2.05–31.00	1.95–30.00
Total number of reflections	24170	23485
Number of independent reflections	5792	5273
R_{int}	0.0444	0.0218
Number of variables	211	237
Number of reflections with $I \geq 2\sigma(I)$	4755	4655
Completeness, %	99.9	99.8
Goodness of fit	0.991	1.022
Divergence factor $R_1(F)$[a] for reflections with $I \geq 2\sigma(I)$	0.0281	0.0369
Divergence factor $wR_2(F^2)$[b] for all reflections	0.0560	0.1010
Van Vleck parameter	–0.010(14)	–
Residual electron density, min/max, e/Å^3	0.733/–0.688	0.463/–0.328

[a] $R_1 = \Sigma||F_o| - |F_c||/\Sigma(F_o)$.
[b] $wR_2 = (\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]^{1/2}$.

δ, ppm: 0.66 d (3H, CH_3, J = 7.3 Hz), 2.02 d (3H, CH_3, J = 7.3 Hz), 2.35 s (3H, CH_3), 3.09 d.q (1H, 3-H, J = 2.7, 7.3 Hz), 3.38 d.d (1H, 2-H, J = 2.7, 6.0 Hz), 4.48 d.q (1H, 1′-H, J = 6.0, 7.3 Hz), 7.02–7.27 m (5H, H_{arom}), 7.55 d (2H, H_{arom}, J = 8.3 Hz), 7.69 d (1H, H_{arom}, J = 8.3 Hz). Found, %: C 48.88; H 4.49; I 28.65; N 3.08; S 7.14. $C_{18}H_{20}INO_2S$. Calculated, %: C 48.99; H 4.57; I 28.76; N 3.17; S 7.26.

(2*R,3*S**)-2-[(1*S**)-1-Iodoethyl]-3-methyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indole (IIIb).** The filtrate obtained after separation of compound **IIb** was evaporated under reduced pressure, the residue was dissolved in 10 ml of ethanol, the solution was cooled, and the precipitate was filtered off. Yield 0.14 g (5%), colorless crystals, mp 153°C (from EtOH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.35 d

(3H, CH_3, J = 7.6 Hz), 1.77 d (3H, CH_3, J = 7.1 Hz), 2.76 quint (1H, 3-H, J = 7.6 Hz), 4.36 d.q (1H, 1′-H, J = 4.6, 7.1 Hz), 4.60 d.d (1H, 2-H, J = 4.6, 7.6 Hz), 6.92 d (1H, H_{arom}, J = 7.6 Hz), 7.10 t (1H, H_{arom}, J = 7.6 Hz), 7.13 d (2H, H_{arom}, J = 8.0 Hz), 7.25 t (1H, H_{arom}, J = 7.9 Hz), 7.47 d (2H, H_{arom}, J = 8.3 Hz), 7.64 d (1H, H_{arom}, J = 7.9 Hz). Found, %: C 48.88; H 4.49; I 28.65; N 3.08; S 7.14. $C_{18}H_{20}INO_2S$. Calculated, %: C 48.99; H 4.57; I 28.76; N 3.17; S 7.26. After 24 h, crystals of a 1:2 mixture of **IIb** and **IIIb**, 0.88 g (23%), separated from the mother liquor.

Reaction of compound IIa with dimethylformamide in the presence of potassium iodide. A solution of 0.444 g (0.975 mmol) of compound **IIa** and 0.648 g (3.9 mmol) of potassium iodide in 4 ml of DMF was heated for 4 h under reflux. The solvent was removed under reduced pressure, the residue was treated with 40 ml of chloroform and 20 ml of water, and the organic phase was separated, washed with water (10 ml), and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel using benzene–petroleum ether (3:7) as eluent. The first fraction contained 0.088 g (29%) of compound **VII** as amorphous powder whose spectral parameters coincided with those given in [9]. From the second fraction we isolated 0.047 g (13%) of a mixture of stereoisomeric esters **IV** and **VI** at a ratio of 77:23, R_f 0.43 (C_6H_6). The spectral parameters of **IV** were identical to those reported in [9].

(1*S)-1-{(2*R**,3*R**)-3,5-Dimethyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indol-2-yl}ethyl formate (VI).** R_f 0.26 (C_6H_6). ^{1}H NMR spectrum ($CDCl_3$), δ,* ppm: 0.54 d (3H, CH_3, J = 7.0 Hz), 1.32 d (3H, CH_3, J = 6.7 Hz), 2.27 s (3H, CH_3), 2.34 s (3H, CH_3), 2.94 d.q (1H, 3-H, J = 2.4, 7.0 Hz), 3.79 d.d (1H, 2-H, J = 2.4, 4.0 Hz), 5.35 d.d (1H, 1′-H, J = 4.0, 6.5 Hz), 6.80 s (1H, 4-H), 7.13 d (1H, H_{arom}), 7.16 d (2H, H_{arom}), 7.45 d (1H, H_{arom}), 7.52 d (2H, H_{arom}), 8.01 s (1H, CHO).

(2*E*)-2-Ethylidene-3,5-dimethyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indole (VIII). A solution of 0.3 g (0.659 mmol) of compound **IIa** and 0.074 g (1.318 mmol) of potassium hydroxide in a mixture of 4 ml of DMF and 1 ml of water was heated for 4 h under reflux. The solvent was evaporated under reduced pressure, the residue was diluted with water (10 ml) and extracted with chloroform (40 ml), the organic phase was dried over Na_2SO_4 and evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel (5 g) using benzene–petroleum ether (1:3) as eluent. A fraction containing compounds **VI** and **VIII** was concentrated and left to stand for 12 h, and colorless crystals of **VIII** were filtered off. Yield 0.062 g (29%), mp 136–138°C (from benzene–petroleum ether). According to the ^{1}H NMR data, the filtrate contained 0.072 g of a mixture of **VI** and **VIII** at a ratio of 1:3. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.52 d (3H, CH_3, J = 7.0 Hz), 1.76 d (3H, CH_3, J = 7.3 Hz), 2.30 s (3H, CH_3), 2.35 s (3H, CH_3), 2.60 q (1H, 3-H, J = 7.0 Hz), 6.13 d.q (1H, 1′-H, J = 1.8, 7.3 Hz), 6.80 s (1H, H_{arom}), 7.20 d (1H, H_{arom}, J = 8.2 Hz), 7.12 d (2H, H_{arom}, J = 8.2 Hz), 7.47 d (2H, H_{arom}, J = 8.2 Hz), 7.67 d (1H, H_{arom}, J = 8.2 Hz). Found, %: C 69.62; H 6.40; N 4.25; S 9.76. $C_{19}H_{21}NO_2S$. Calculated, %: C 69.69; H 6.46; N 4.28; S 9.79.

(2*S,3*R**)-3-Methyl-1-(4-methylphenylsulfonyl)-2-vinyl-2,3-dihydro-1*H*-indole (X)** was synthesized by heating 0.25 g (0.57 mmol) of compound **IIb** in boiling DMF and was isolated by column chromatography of the reaction mixture on silica gel. Yield 0.011 g (5%). When 0.185 g (0.42 mmol) of **IIb** was heated in boiling DMF in the presence of 4 equiv (0.28 g) of KI, the yield of **X** was 0.039 g (29%). Amorphous powder, R_f 0.81 (C_6H_6). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.78 d (3H, CH_3, J = 7.3 Hz), 2.35 s (3H, CH_3), 2.90 d.q (1H, 3-H, J = 4.0, 7.3 Hz), 4.07 m (1H, 2-H), 5.16 d (1H, 2′-H_A, J = 10.3 Hz), 5.86 d (1H, 2′-H_B, J = 16.9 Hz), 5.95 d.d.d (1H, 1′-H, J = 6.6, 10.3, 16.9 Hz), 7.01–7.04 m (2H, H_{arom}), 7.18–7.25 m (3H, H_{arom}), 7.65 d (2H, H_{arom}, J = 8.3 Hz), 7.72 d (1H, H_{arom}, J = 8.0 Hz). Found, %: C 68.94; H 6.08; N 4.42; S 10.17. $C_{18}H_{19}NO_2S$. Calculated, %: C 68.98; H 6.11; N 4.47; S 10.23.

(1*R)-1-{(2*R**,3*R**)-3-Methyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indol-2-yl}ethyl formate (XI).** Heating of 0.25 g (0.57 mmol) of compound **IIb** in boiling DMF, followed by chromatographic separation on silica gel gave 0.068 g (34%) of **XI** containing 7% of stereoisomer **XII**. When 0.185 g (0.42 mmol) of **IIb** was heated in boiling DMF in the presence of 4 equiv of KI, the yield of **XI** was 0.042 g (32%). Colorless crystals, R_f 0.54 (C_6H_6). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.55 d (3H, CH_3, J = 7.0 Hz), 1.19 d (3H, CH_3, J = 6.5 Hz), 2.34 s (3H, CH_3), 3.07 d.q (1H, 3-H, J = 2.3, 7.0 Hz), 3.86 d.d (1H, 2-H, J = 2.3, 6.5 Hz), 5.35 quint (1H, 1′-H, J = 6.5 Hz), 7.00–7.08 m (2H, H_{arom}), 7.15–7.27 m (3H, H_{arom}), 7.57 d

* The positions of signals were derived from the ^{1}H NMR spectrum of a mixture of stereoisomers **IV** and **VI**.

(2H, H_{arom}, J = 8.0 Hz), 7.73 d (1H, H_{arom}, J = 8.0 Hz), 8.03 s (1H, CHO). Found, %: C 63.60; H 5.75; N 3.84; S 8.84. $C_{19}H_{21}NO_4S$. Calculated, %: C 63.49; H 5.89; N 3.90; S 8.92.

Reaction of compound IIa with potassium acetate. A solution of 0.455 g (1 mmol) of compound **IIa** and 0.392 g (4 mmol) of potassium acetate in 5 ml of DMF was heated for 4 h under reflux. The solvent was removed under reduced pressure, the residue was treated with 50 ml of methylene chloride and 30 ml of water, and the organic phase was separated, washed with water (20 ml), and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on silica gel using benzene as eluent to isolate 0.193 g (59%) of a mixture of compouds **IV** [9], **V** [9], and **IX**. Further elution gave 0.041 g (11%) of a mixture of acetates **XIII** and **XIV** at a ratio of 2:1.

(1*R)-1-{(2*R**,3*R**)-3,5-Dimethyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indol-2-yl}ethyl acetate (XIII).** R_f 0.43 (C_6H_6). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.52 d (3H, CH_3, J = 7.3 Hz), 1.15 d (3H, CH_3, J = 6.3 Hz), 2.00 s (3H, CH_3), 2.25 s (3H, CH_3), 2.34 s (3H, CH_3), 3.00 d.q (1H, 3-H, J = 2.0, 6.3 Hz), 3.80 d.d (1H, 2-H, J = 2.7, 5.0 Hz), 5.20 quint (1H, 1′-H, J = 5.0, 7.3 Hz), 6.80 s (1H, 4-H), 7.05–7.63 m (6H, H_{arom}). Mass spectrum: m/z 387.15 $[M]^+$. $C_{21}H_{25}NO_4S$. Calculated: M 387.1499.

(1*S)-1-{(2*R**,3*R**)-3,5-Dimethyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indol-2-yl}ethyl acetate (XIV).** R_f 0.43 (C_6H_6). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.50 d (3H, CH_3, J = 7.1 Hz), 1.20 d (3H, CH_3, J = 6.5 Hz), 2.00 s (3H, CH_3), 2.34 s (3H, CH_3), 2.80 d.q (1H, 3-H, J = 2.0, 6.5 Hz), 3.90 d.d (1H, 2-H, J = 2.0, 4.3 Hz), 4.59 d.q (1H, 1′-H, J = 6.7, 4.3 Hz), 6.80 s (1H, 4-H), 7.05–7.63 m (6H, H_{arom}). Mass spectrum: m/z 387.15 $[M]^+$. $C_{21}H_{25}NO_4S$. Calculated: M 387.1499.

(1*R)-1-{(2*R**,3*R**)-3,5-Dimethyl-1-(4-methylphenylsulfonyl)-2,3-dihydro-1*H*-indol-2-yl}ethanol (XV) with an impurity of isomer XVI.** Compound **IV**, 0.271 g (0.726 mmol), was added to a solution of 0.116 g (2.9 mmol) of sodium hydroxide in 6 ml of ethanol. The progress of the reaction was monitored by TLC. When the reaction was complete, the solvent was evaporated, the residue was treated with 20 ml of water, and the product was extracted into 50 ml of chloroform. The extract was dried over $MgSO_4$ and evaporated under reduced pressure, and the residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (9:1) as eluent. Yield 0.127 g (53%), amorphous powder, R_f 0.2 (petroleum ether–EtOAc, 9:1). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.45 d (3H, CH_3, J = 7.0 Hz), 1.19 d (3H, CH_3, J = 6.3 Hz), 2.28 s (3H, CH_3), 2.35 s (3H, CH_3), 2.61 br.s (1H, OH), 2.84 d.q (1H, 3-H, J = 2.0, 7.3 Hz), 3.54 d.d (1H, 2-H, J = 2.0, 7.3 Hz), 3.82 quint (1H, 1′-H, J = 7.0 Hz), 6.82 s (1H, 4-H), 7.05 d (1H, H_{arom}, J = 8.0 Hz), 7.18 d (2H, H_{arom}, J = 8.3 Hz), 7.55 d (2H, H_{arom}, J = 8.3 Hz), 7.62 d (1H, H_{arom}, J = 8.0 Hz). Found, %: C 65.98; H 6.65; N 3.99; S 9.20. $C_{19}H_{23}NO_3S$. Calculated, %: C 66.06; H 6.71; N 4.05; S 9.28.

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