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Synthesis of a 1,3,4,5-Tetrahydrobenz[*cd*]indole *via* the Vicarious Nucleophilic Substitution of Hydrogen

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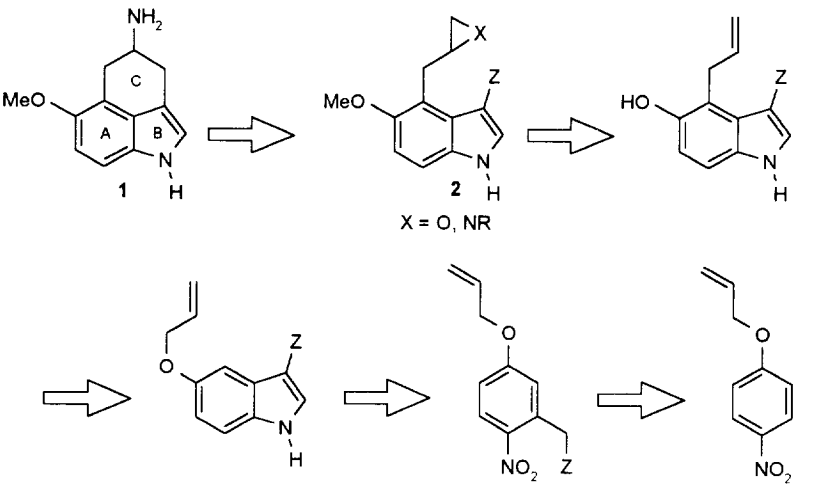
Abstract: Two approaches to synthesis of 6-methoxy-1,3,4,5-tetrahydrobenz[*cd*]indol-4-amine **1** were developed. Indolic precursor **21** of the tricyclic system was prepared *via* the VNS reaction, but attempts to execute the C ring closure failed. The other strategy, based on elaboration of the VNS product **30** to a tetrahydronaphtalene system followed with formation of the fused pyrrole ring, proved successful

Diverse biological activities of ergot alkaloids are well known.[1] More recently also their simplified analogues, such as 1,3,4,5-tetrahydrobenz[*cd*]indoles containing an amino substituent at position 4, have been shown to possess interesting biological properties, especially affinity for serotonin[2, 3] (5-hydroxytryptamine, 5-HT) and also dopamine[4] receptors. These compounds, being conformationally restricted serotonin congeners,[5] bind selectively to different subtypes of 5-HT receptors, which is a very desirable property in the field.[6]

In most of the synthetic work so far described, relating to these products, the tricyclic system has been constructed from an indole *via* electrophilic substitution reactions at positions 3 and/or 4.[2, 3, 7] In other approaches the pyrrole ring has been added to a tetrahydronaphthalene system[8] or the tricyclic system has been formed in a single step from a benzene derivative by tandem radical cyclizations.[9] Most of these strategies have been used in synthesis of ergolines as well.

We have recently shown that the Vicarious Nucleophilic Substitution of Hydrogen reaction (VNS) can be a useful tool in the synthesis of pyrroloquinoline alkaloids.[10] In this paper we present an approach to the synthesis of biologically active compounds containing 1,3,4,5-tetrahydrobenz[*cd*]indole nucleus, such as 6-methoxy-1,3,4,5-tetrahydrobenz[*cd*]indole-4-amine[3] **1** (Scheme 1), based on this reaction.

Our strategy consisted in preparing the suitably substituted indole derivative **2** *via* the VNS reaction followed by formation of the indole system, the Claisen rearrangement, and transformation of the double bond in the side chain into a three-membered heterocycle (Scheme 1). We envisaged that deprotonation of this precursor would result in the

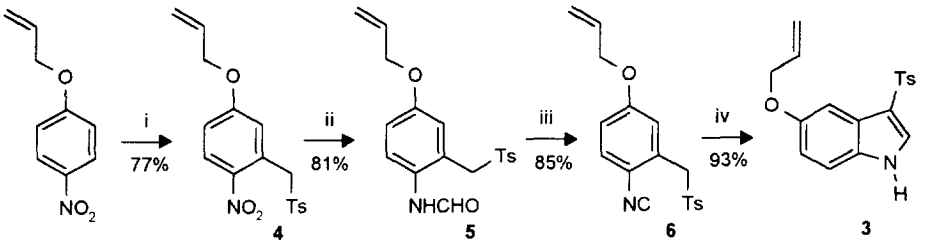


Scheme 1

intramolecular nucleophilic attack of the indole anion on the aziridine or the oxirane ring leading to the formation of the substituted six-membered ring. In view of the Baldwin rules intramolecular opening of oxiranes could proceed either in an 5-*exo* or 6-*endo* fashion.[11a] Although the former is more common, examples of the latter are known.[11b-d] Moreover, to our best knowledge such cyclizations have not been studied for unsaturated systems, in which rotational freedom is limited. In particular, examination of the Dreiding model of **2** suggested that the transition state leading to the five-membered ring would be considerably strained as compared to that resulting in formation of the six-membered ring. It is also noteworthy, that in this case formation of the six-membered ring involved nucleophilic attack on the less substituted carbon atom.

Presence of an electron-withdrawing group Z in indolic products arises from our methodology for construction of the indole system and is advantageous at the step of the double bond functionalization due to protection of the sensitive pyrrole ring against reactions with electrophiles.

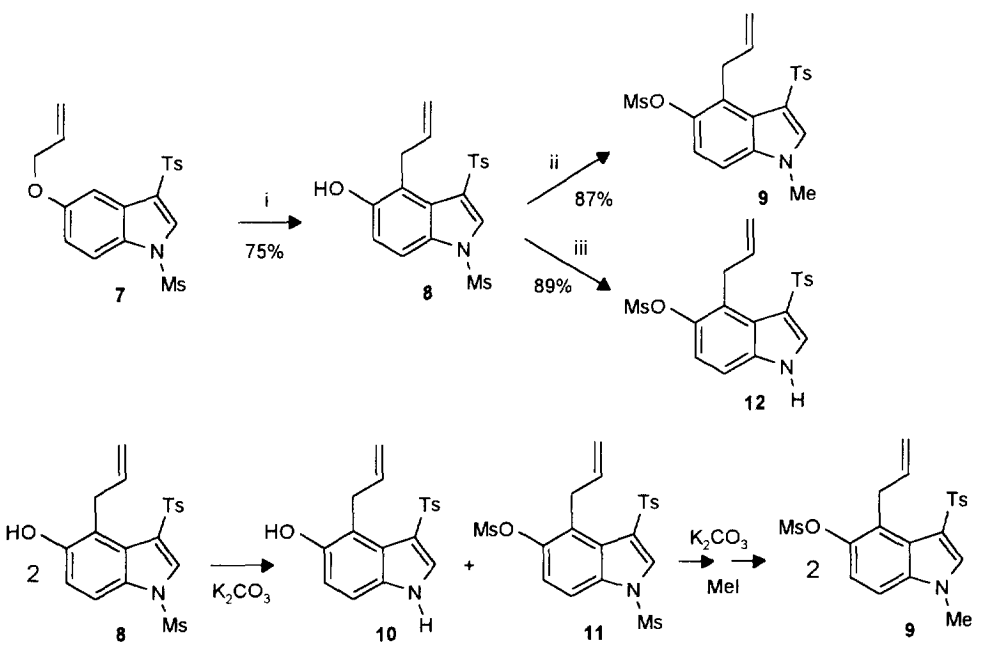
As expected, preparation of indole **3** *via* the VNS reaction according to our modification[12] of the Ito's method[13] was straightforward (Scheme 2). Allyl *p*-nitrophenyl ether was reacted with chloromethyl-*p*-tolyl sulfone in the presence of base giving the VNS product **4**. The nitro group in **4** was converted to the isocyano substituent *via* reduction, formylation of the resulting aniline and dehydration of the obtained formamide **5**. Isonitrile **6** was then treated with base to give **3**.



i: $ClCH_2Ts$, KOH, DMSO; ii: Sn, HCl_{aq}, MeOH, then HCOOH; iii: $POCl_3$, *i*-Pr_2NH, CH_2Cl_2; iv: NaOH, DMSO.

Scheme 2

Initially we performed the Claisen rearrangement in **3**, but attempts to execute selective *O*-alkylation of the product with methyl iodide were unsuccesful due to competitive *N*-alkylation. Therefore we decided to protect the indolic nitrogen atom with the mesyl group prior to the Claisen rearrangement. The protected product **7** was prepared and subjected to reflux in 1,2,4-trichlorobenzene. The 4-allyl- isomer **8** was the sole product of the reaction, as it has been described for other 5-allyloxyindoles.[14] Attempts to alkylate the phenolic oxygen atom in **8** with methyl iodide led however to an unexpected result - product **9** was obtained in which the methyl group resided on the nitrogen atom and the mesyl group - on the oxygen atom.(Scheme 3).



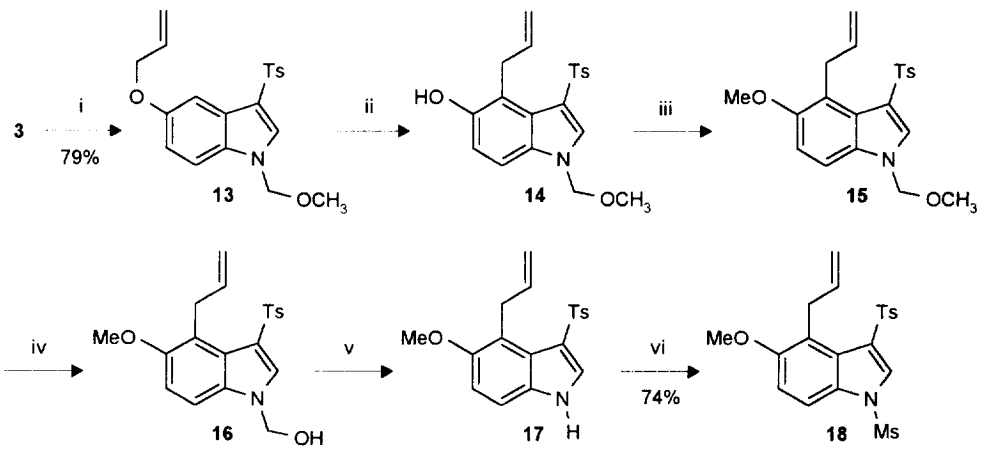
i: –, 1,2,4-trichlorobenzene; ii: MeI, K_2CO_3, Bu_4NBr, DMF; iii: K_2CO_3, Bu_4NBr, DMF.

Scheme 3

Probably the reaction was initiated by the nucleophilic attack of the phenolic anion of **8** on the sulfonamide moiety of another molecule leading to the disproportionation products **10** and **11**. Any species containing free hydroxyl group

could react further with molecules containing *N*-mesyl moiety acoording to the same scheme, and the *N*-demesylated species could undergo *N*-methylation. These two processes combined would eventually lead to the product **9**. This explanation was supported by an experiment in which **8** was subjected to the same basic conditions without addition of an alkylating agent. Indeed, migration of the mesyl group occurred yielding methanesulfonyl ester **12**.

To circumvent the migration problem the *N*-mesyl protecting group was replaced with the methoxymethyl substituent (MOM) (Scheme 4).



overall yield of the steps ii-v: 78%

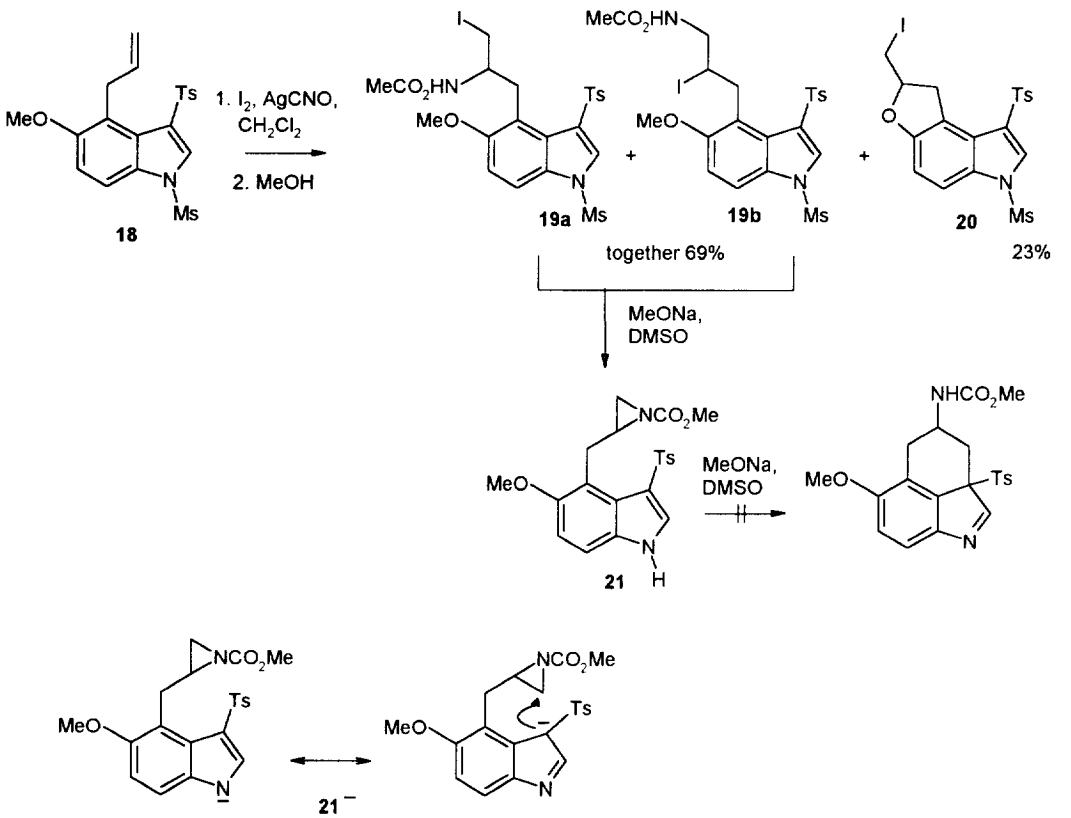
i: $ClCH_2OCH_3$, K_2CO_3, MeCN; ii: 190°C, neat; iii: MeI, K_2CO_3, DMF; iv: HCl, DME, H_2O; v: NaOH, EtOH; vi: MsCl, Et_3N,CH_2Cl_2.

Scheme 4

The protected product **13** smoothly underwent the Claisen rearrangement. The resulting hydroxyindole **14** was *O*-methylated to give compound **15**. In the forthcoming transformations more labile protecting group than the methoxymethyl, such as the mesyl group, was expected to be more appropriate. Removing MOM group from **15** required two-step hydrolysis. Heating compound **15** in an acidic solution resulted in formation of the hydroxymethyl derivative **16** along with a small amount of the fully deprotected product **17**.[15] Subsequent treatment of this mixture with sodium hydroxide gave **17** as the only product. Transformations leading from **13** to **17** were conducted without purification of the intermediate products, except analytical samples. Crude **17** was converted to the *N*-mesyl derivative **18** which crystallized readily.

Further functionalization of **18** required transformation of the double bond into the aziridine moiety. For this purpose we employed the method developed by Hassner, involving addition of iodine isocyanate to olefine and elaboration of the product to the corresponding aziridine.[16] Thus compound **18** was treated with iodine and silver cyanate and subsequently with methanol (Scheme 5). The reaction yielded a mixture of the expected regioisomericiodocarbamates **19a** and **19b** together with a considerable amount of the tricyclic product **20**. The latter was probably formed *via* an electrophilic attack of the intermediate carbocation or iodonium cation on the ether

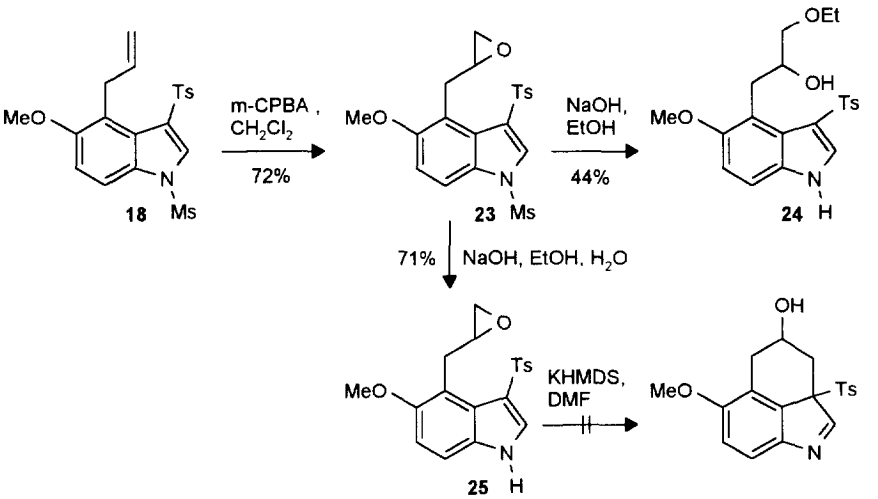
oxygen followed with demethylation of the resulting oxonium cation. Related electrophilic heteroatom cyclizations are widely used for preparation of tetrahydrofurans from unsaturated alcohols.[17]



Scheme 5

The mixture of the carbamates **19** was separated from **20** by column chromatography and treated with sodium methoxide in DMSO, which resulted in the aziridine ring closure and cleavage of the *N*-mesyl group to give the desired product **21**. The stage was set for the crucial step of closing the ring C. A DMSO solution, containing an excess of sodium methoxide and aziridine **21** formed *in situ* from carbamates **19**, was slowly heated up to the boiling point of the solvent. However, even under such drastic conditions no reaction took place and the substrate remained unchanged. Perhaps the presence of the tosyl substituent stabilizes the indole anion **21**$^-$ reducing substantially its nucleophilicity, so it is not sufficiently reactive for opening of the aziridine ring.

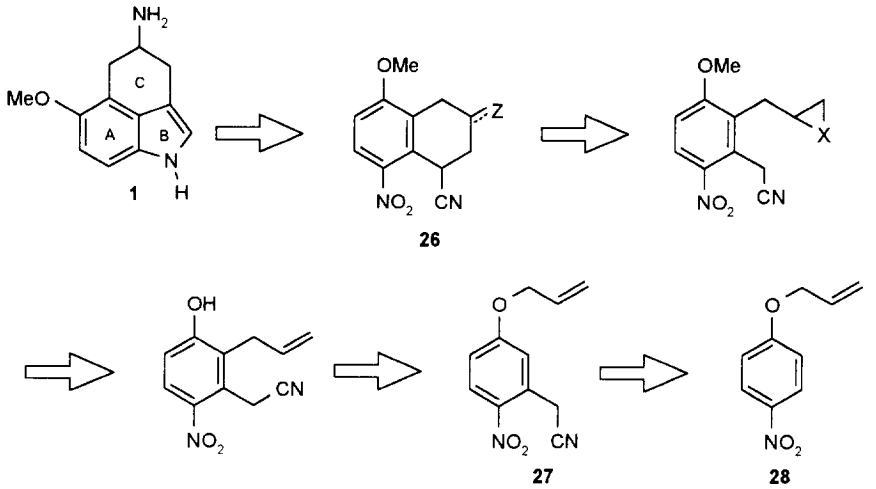
Having failed to close the C ring in aziridine **21** we attempted to carry out analogous transformation in the corresponding oxirane (Scheme 6). Epoxidation of the double bond in **18** with *m*-CPBA gave compound **23**. This product was treated with sodium hydroxide in ethanol, which resulted in opening of the epoxide ring by ethoxide anions accompanied by hydrolysis of the mesyl group, to give **24**. Apparently, EtO^- ions were more nucleophilic than



Scheme 6

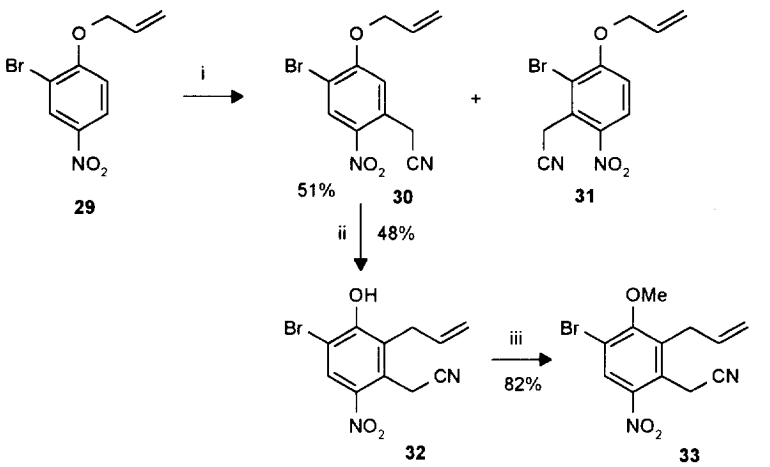
the indole anions (cf. also the transformation **36**→**37**, Scheme 9). Therefore we decided to use a weakly nucleophilic base, such as potassium bis(trimethylsilyl)amide (KHMDS) for the deprotonation of **25**. The reaction was carried out in refluxing DMF, however again the starting material **25** was recovered, perhaps because of insufficient nucleophilicity of its anion.

At this point we abandoned the strategy explored so far. New approach, based on elaboration of a VNS product to a tetrahydronaphthalene derivative followed with construction of the fused pyrrole ring, was developed (Scheme 7). This A-C-B strategy is somewhat similar to that of Haefliger[8] and also to our approach to pyrroloquinoline alkaloids.[10] We planned to obtain the target product **1** *via* catalytic hydrogenation of the key tetrahydronaphthalene derivative **26**. We expected the *o*-nitrobenzyl cyanide moiety in **26** to be converted into the indole ring under these conditions[18] with simultaneous transformation of the amino group precursor Z to NH_2. For the construction of the ring C we planned to use a concept similar to that from the previous approach, i.e. intramolecular nucleophilic attack of a carbanion on the aziridine or the oxirane ring. Two other important steps were the Claisen rearrangement in **27** and the VNS cyanomethylation of the starting nitroarene **28**. As no regioselectivity could be expected in the former reaction, introduction of a substituent into one of the *ortho* positions relative to the allyloxy group was necessary in order to avoid formation of the unwanted 6-allyl isomer. Bromine atom was used as a blocking substituent, because it could be easily removed under catalytic reduction conditions at the final step of the synthesis. Additionally, it exerts activating effect in the VNS reaction. However, the latter process in the brominated starting material **29** (Scheme 8) could result in formation of two regioisomers with cyanomethyl substituent in positions *ortho* and *para* relative to the bromine. We expected the desired isomer **30** to be formed predominantly,[19] however it was a matter of experiment whether this reaction would be preparatively useful in a multigram scale.



Scheme 7

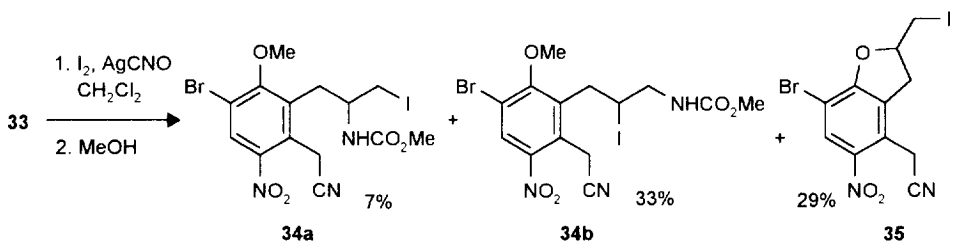
Indeed, two products were formed in the VNS reaction of **29** with *p*-chlorophenoxyacetonitrile (Scheme 8). As expected, **30** was the major one and it was possible to obtain it in a pure form *via* fractional crystallization in a reasonable yield. The second fraction contained a mixture of **30** and another product, structure of which was tentatively assigned as **31**. The next step - the Claisen rearrangment in **30**, appeared extremely difficult to execute. At high temperatures, necessary for the reaction to proceed, decomposition was the main process. We tried to run the reaction in a range of solvents, such as *o*-dichlorobenzene, 1,2,4-trichlorobenzene, acetophenone, aniline, diphenyl ether, as well as neat, but the results were always unsatisfactory. We found however that it was the product, not the substrate, that decomposed: when the reaction was stopped after a short time at partial conversion only minute amounts of tars were observed. Moreover, extraction of the reaction mixture with NaOH solution transferred the decomposition products into the water phase, which indicated that they contained the phenolic hydroxyl groups. Therefore this reaction was carried out "stepwise": after heating a solution of **30** in diphenyl ether for a short time, the reaction mixture was cooled and the product formed was extracted with NaOH solution. The organic phase, containing only substrate, was heated again yielding another portion of the product. After performing this cycle for three times the combined alkaline solutions were acidified to give **32** in a reasonable yield. *O*-Methylation of this product gave anisole **33**.



i: 4-ClPhOCH$_2$CN, *t*-BuOK, DMF; ii: –, PhOPh; iii: Me_2SO_4, K_2CO_3, acetone.

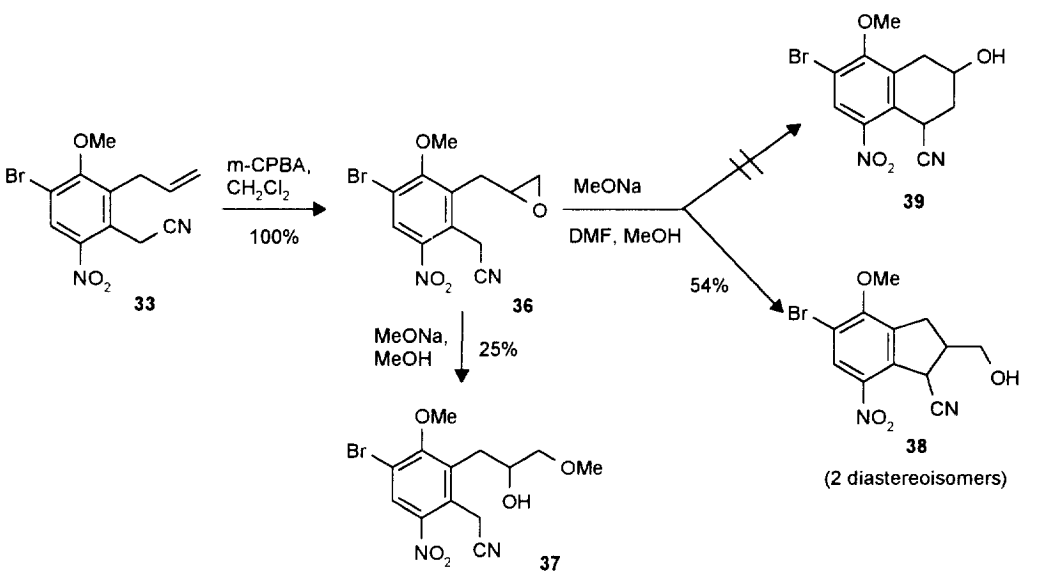
Scheme 8

Our goal now was to convert the double bond in compound **33** into aziridine moiety *via* the procedure used in our first approach. This time we expected the unwanted reaction of electrophilic heteroatom cyclization, observed previously (Scheme 5), to be suppressed, because nucleophilicity of the oxygen atom should be reduced due to conjugation with the nitro group. However this appeared not to be the case - treatment of **33** with iodine and silver cyanate and subsequently with methanol resulted in formation of a mixture of regioisomeric carbamates **34a** and **34b** together with dihydrobenzofuran **35** analogous to **20**:



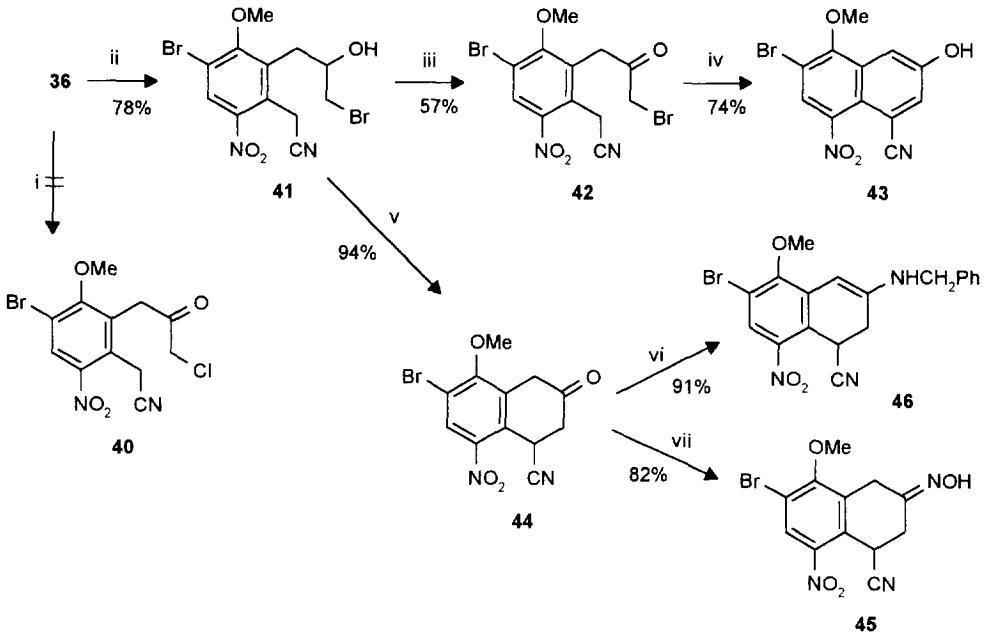
Only one of these products was separated in a pure form and fully characterized. It was one of the isomeric iodocarbamates, probably **34b**. This was deduced on the basis of the mass spectrum in which signals (M-89) and 88 are present. The former might result from the fragmentation M^+- CH_2NHCO_2Me-H and the latter might correspond to the cation $(CH_2{=}NHCO_2Me)^+$. The other iodocarbamate was a minor component of a mixture containing also the "abnormal" product **35**. The ^1H NMR spectra of the mixture was clear enough to make possible assignment of all the signals corresponding to **35**, as well as singlets corresponding to the methyl groups and aromatic proton of **34a**. On the other hand LSIMS spectra of the mixture contained only 512 and 514 peaks coming from protonated molecular ion of **34a**. Anyway, the reaction was not preparatively useful.

Alternative functionalization of the double bond in **33** *via* epoxidation with *m*-CPBA was executed in the quantitative yield, to give **36** (Scheme 9). We expected that upon deprotonation of this product intramolecular epoxide ring opening would take place. After some experimentation suitable conditions for this transformation were found. Applying a mixture of DMF and methanol as a solvent was crucial - in DMF no reaction occurred while in methanol opening of the 3-membered ring by methoxide anions took place, to give hydroxyether **37**. Yet the result of the intramolecular reaction was disappointing - attack on the more substituted carbon atom of the oxirane ring occurred, which led to the closure of the five-membered ring instead of the six-membered one, so two diastereoisomeric products **38**[20] were obtained instead of the desired compound **39**. Apparently, the preference for the 5-*exo* cyclization, predicted by the Baldwin rules for oxiranes, outweighed the factors suggesting that the structural features of the substrate would facilitate the desired 6-*endo* cyclization in this case.



Scheme 9

Thus our plan for construction of the tetrahydronaphthalene system had to be revised (Scheme 10). With epoxide **36** in hand, we attempted to obtain a chloroketone **40** *via* the recently described procedure,[21] related to the Swern oxidation. A complex mixture of products was formed however, therefore an indirect route was used. Epoxide **36** was converted to bromohydrine **41** *via* reaction with tetrabutylammonium bromide in the presence of $Mg(NO_3)_2$ as a catalyst.[22] Jones oxidation of the bromohydrine yielded bromoketone **42**. First attempt to close the six-membered ring *via* the intramolecular alkylation of the nitrobenzyl anion of **42** gave unexpectedly naphthalene **43**. The reaction was run for 2 hours under typical conditions used for alkylation of nitrobenzyl cyanides, i.e. with an excess of K_2CO_3 in DMF at room temperature.[10] Apparently, the aromatic product **43** was produced from the initially formed bicyclic ketone **44**, probably *via* deprotonation and oxidation of the enolate anion with atmospheric oxygen. To stop the reaction at the stage of **44** it was necessary to eliminate oxygen and excess of base and work at lower temperature for

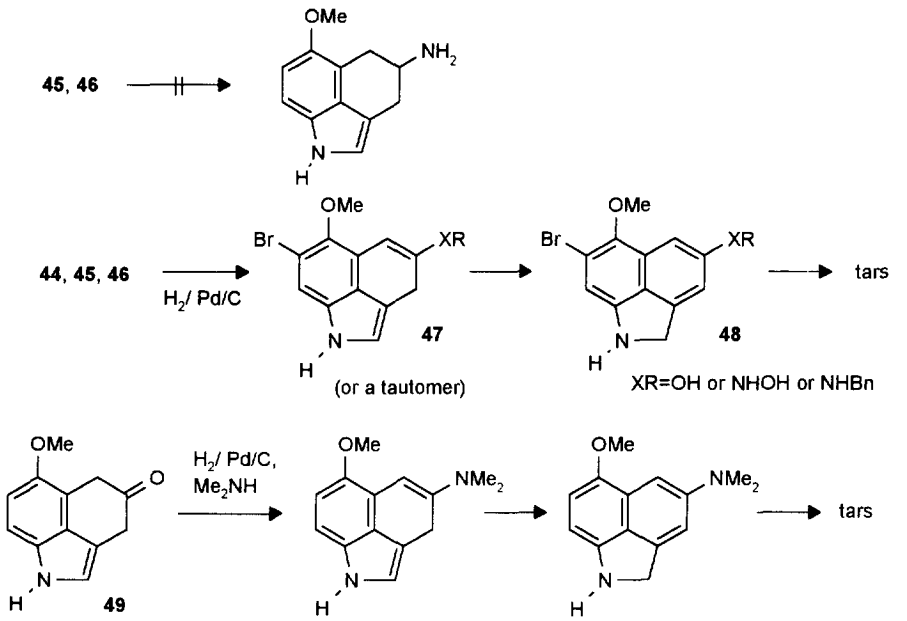


i: 1. DMSO, ClCOCOCl, MeOH, CH_2Cl_2; 2. Et_3N; ii: Bu_4NBr, $Mg(NO_3)_2$ $6H_2O$, $CHCl_3$; iii CrO_3, H_2SO_4, acetone, then *i*-PrOH; iv: K_2CO_3, DMF, (air); v: 1. CrO_3, H_2SO_4, acetone, then *i*-PrOH 2. Et_3N vi: $PhCH_2NH_2$, AcOH, toluene; vii NH_2OH HCl, MeOH, H_2O.

Scheme 10

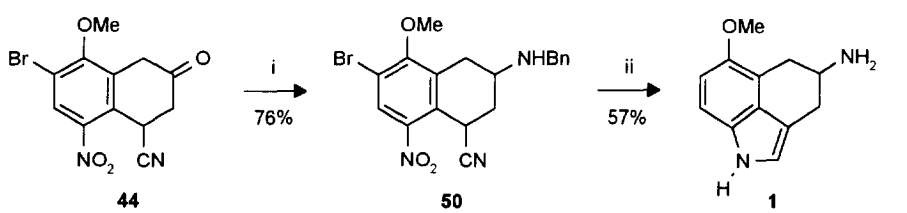
shorter time. Indeed, introducing these changes resulted in formation of **44** as the only product. It was more practical to synthesize **44** directly from **41** without isolation of the bromoketone **42**, which probably decomposed during purification on silica gel. Addition of triethylamine to the reaction mixture, obtained in Jones oxidation of **41**, immediately produced ketone **44** in a high yield. Compound **44** was then converted to two nitrogen derivatives - oxime **45** and enamine **46**.

We hoped, that subjecting one or both of these products to catalytic hydrogenation would directly lead to the target compound **1**. Such a transformation would require indolization of the *o*-nitrobenzyl cyanide system, hydrogenolysis of bromine, and reduction of oxime or *N*-benzyl enamine fragments to C-NH_2 or C-C-NH_2 respectively. Unfortunately, formation of tars was the only result of all attempts to perform these reactions, as well as catalytic reduction of ketone **44** (Scheme 11). We suppose that formation of the indole system took place prior to reduction of the double carbon-carbon or carbon-heteroatom bond and the tricyclic product **47** underwent indole-naphthalene isomerisation to give unstable product **48** which decomposed on air. Such isomerisations are common problem in synthesis of benz[*cd*]indoles and ergolines. [23] Our rationalization is based on that proposed by Kruse,[3] to explain formation of tars in reductive amination of ketone **49**. The logical solution was then to reduce C=C or C=N bond before the hydrogenation step. In an initial experiment enamine **46** was converted to the corresponding amine **50** *via* sodium cyanoborohydride reduction of its hydrochloric salt, formed on addition of ethanolic HCl to a solution of



Scheme 11

the substrate.[24]Attempts to perform reductive amination of ketone **44** by simply reacting the ketone, amine and $NaBH_3CN$ in methanol[24] failed, however transformations **44**→**46**→**50** could be conveniently carried out as a "one-pot" procedure (Scheme 12). Next we focused on converting the amine **50** to the target compound. To our delight, under hydrogenation conditions all the desired processes took place (i.e. indolization, hydrogenolysis of bromine and benzyl group), to give the final product **1** in an acceptable yield.



i: 1.$PhCH_2NH_2$, AcOH, THF, 2. HCl/ EtOH, 3.$NaBH_3CN$ / MeOH; ii: H_2/ Pd/C, EtOH, Me_2NH.

Scheme 12

Thus the VNS reaction proved to be an useful tool in synthesis of 1,3,4,5-tetrahydrobenz[*cd*]indole system. Our approach is very likely to be applicable in synthesis of 4-alkylamino analogues of **1**, serotonergic activity of which is well documented.[2a] Perhaps also dihydrolysergic acid derivatives could be obtained *via* elaboration of ketone **44** according to the Haefliger's procedure.[8c]

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Experimental

Melting points are uncorrected. ^{1}H NMR spectra were recorded on Varian Gemini (200 MHz) or, when indicated, Bruker AMX (500 MHz) instruments; chemical shifts are reported in ppm downfield from TMS as internal standard; coupling constants *J* are given in Hertz; assignments marked with asterisk (*) may be interchanged; protons attached to cyclic systems are indicated by numbers (e.g. H-3) based on the numberation of the cyclic system in a systematic name of given compound; protons of side chains are indicated in a descriptive way (e.g. $OCH_2\underline{C}H{=}CH_2$). Mass spectra were recorded on AMD 604 (AMD Intectra GmbH) spectrometer. IR spectra were taken with Perkin Elmer 1600 FTIR spectrometer and only noteworthy absorptions are listed. Column chromatography was performed on silica gel 230-400 mesh (Merck). Organic extracts were dried with anhydrous $MgSO_4$. 4-Chlorophenoxyacetonitrile was obtained according to the described procedure.[25] 2-Bromo-4-nitro-allyloxybenzene **29** was obtained *via* alkylation of 2-bromo-4-nitrophenol[26] with allyl bromide. Other reagents were commercially available.

1-Allyloxy-4-nitro-3-(4-toluenesulfonylmethyl)benzene (4): To a suspension of powdered KOH (84 g, 1.5 mol) in DMSO a solution of *p*-allyloxynitrobenzene (45 g, 0.25 mol) and chloromethyl-*p*-tolyl sulfone (51.41 g, 0.25 mol) in DMSO (100 ml) was added dropwise at 20-25°C. The mixture was stirred for 90 min and poured into an ice-cold diluted solution of hydrochloric acid. The product was collected by filtration, washed with water, dried and recrystallized from isopropanol to give **4** (67.4 g, 77%) as a colorless crystal. M.p. 129-131°C. δ_H ($CDCl_3$): 2.43 (3H, s, CH_3), 4.62 (2H, dt, *J*=5.3, *J*=1.5, $ArOC\underline{H}_2CH{=}CH_2$), 4.95 (2H, s, $ArCH_2Ts$), 5.32-5.50 (2H, m, $ArOCH_2CH{=}C\underline{H}_2$), 5.93-6.14 (1H, m, $ArOCH_2C\underline{H}{=}CH_2$), 6.92-7.00 (2H, m, H-2 and H-6, AB part of ABX system), 7.23-7.31 (2H, m, Ts), 7.54-7.62 (2H, m, Ts) 7.97-8.04 (1H, m, H-5, X part of ABX system). MS (EI), m/z (%): 347 (M^+, 3), 301 (27), 192 (100), 174 (7), 162 (3), 152 (8), 139 (18), 134 (5), 91 (27). Anal.: calcd. for $C_{17}H_{17}NO_5S$: C 58.78, H 4.93, N 4.03; found: C 58.77, H 4.99, N 3.95.

4-Allyloxy-2-(4-toluenesulfonylmethyl)formanilide (5): To a suspension of **4** (66.4 g, 191 mmol) in a mixture of methanol (400 ml) and conc. hydrochloric acid (260 ml) tin (50.3 g, 424 mmol) was added. The reaction mixture was stirred for 3.5 h at 50-60°C and allowed to cool to r.t. The unreacted tin was filtered off and the filtrate was poured into a mixture of ice (ca. 2 l) and 50% aqueous NaOH (250 ml). The precipitate formed was collected by filtration, washed with water and air-dried. The crude aniline was refluxed in formic acid for 3 h, and the reaction mixture was poured into water. The crude product was collected by filtration, washed with water, dried and recrystallized from isopropanol to give **5** (53.7 g 81%) as a colorless crystal. The NMR spectra of the product showed it to be a mixture of two amide rotamers in ratio ca. 2:1. M.p. 115-117°C. Major rotamer: δ_H ($CDCl_3$): 6.24 (1H, d, *J*=2.8, H-3), 7.65 (1H, d, *J*=8.9, H-6), 8.44 (2H, br s, $\underline{H}C(O)N\underline{H}$). Minor rotamer 4.40 (2H, dm, *J*=5.2, $ArOC\underline{H}_2CH{=}CH_2$), 6.53 (1H, d, *J*=2.8, H-3), 7.15 (1H, d, *J*=8.8, H-6), 8.26 (2H, br s, $\underline{H}C(O)N\underline{H}$). Other signals of the two rotamers overlapped; their chemical shifts were consistent with the structure **5**. MS (EI), m/z (%): 345 (M^+, 21), 276 (7), 190 (100), 162 (57), 139 (13), 93 (24). Anal.: calcd. for $C_{18}H_{19}NO_4S$: C 62.59, H 5.54, N 4.06; found: C 62.56, H 5.68, N 4.05.

4-Allyloxy-2-(4-toluenesulfonylmethyl)phenyl isocyanide (6): To a solution of **5** (53 g, 154 mmol) and diisopropylamine (15.6 g, 154 mmol) in dry CH_2Cl_2 (450 ml) $POCl_3$ (25.8 g, 0.168 mmol) was added dropwise at 0-5°C. The mixture was stirred at this temperature for 3 h, then 20% aqueous K_2CO_3 solution (600 ml) was added and

the resulting mixture was stirred for 1h. The organic layer was separated, dried and evaporated. The residue was recrystallized from isopropanol, to give **6** (42.6 g, 85%) as a colorless crystal. M.p. 143-145°C. δ_H ($CDCl_3$): 2.43 (3H, s, CH_3), 4.54 (2H, s, $ArCH_2Ts$), 4. 56 (2H, dt, *J*=5.2, *J*=1.5, $ArOC\underline{H}_2CH=CH_2$), 5.28-5.50 (2H, m, $ArOCH_2CH=C\underline{H}_2$), 5.94-6.14 (1H, m, $ArOCH_2C\underline{H}=CH_2$), 6.87 (1H, dd, *J*=8.8, *J*=2.7, H-5), 7.06 (1H, d, *J*=2.7, H-3), 7.18 (1H, d, *J*=8.8, H-6), 7.24-7.32 (2H, m, Ts), 7.54-7.62 (2H, m, Ts). MS (EI), m/z (%): 327 (M^+, 28), 222 (23), 188 (32), 172 (100), 139 (41), 127 (15), 117 (28), 91 (38). Anal.: calcd. for $C_{18}H_{17}NO_3S$: C 66.04, H 5.23, N 4.28; found: C 65.85, H 5.15, N 4.33.

5-Allyloxy-3-(4-toluenesulfonyl)-1*H*-indole (3): To a suspension of powdered NaOH (16 g, 400 mmol) in DMSO (120 ml) a solution of **6** (41.6 g, 131 mmol) in DMSO (240 ml) was added dropwise at 17-20°C. The mixture was stirred for 15 min and poured into an ice-cold, diluted solution of hydrochloric acid. The precipitate formed was collected by filtration, washed with water, air-dried and recrystallized from isopropanol, to give **3** (38.6 g, 93 %) as a colorless crystal. M.p. 149-151°C. δ_H ($CDCl_3$): 2.36 (3H, s, CH_3), 4.56 (2H, dm, *J*=2.4, $ArOC\underline{H}_2CH=CH_2$), [5.29 (1H, dm, *J*=10.4), 5.43 (1H, dm, *J*=17.3) $ArOCH_2CH=C\underline{H}_2$], 5.96-6.18 (1H, m, $ArOCH_2C\underline{H}=CH_2$), 6.91 (1H, dd, *J*=8.8, *J*=2.4, H-6), 7.20-7.28 (2H, m, Ts), 7.27 (1H, d, *J*=8.8, H-7), 7.33 (1H, d, *J*=2.4, H-4), 7.78 (1H, d, *J*=2.8, H-2), 7.84-7.92 (2H, m, Ts), 9.11 (1H, br s, H-1). MS (EI), m/z (%): 327 (M^+ 100), 286 (33), 268 (9), 240 (13), 221 (67), 207 (37), 195 (29), 172 (30), 152 (10), 91 (12). Anal.: calcd. for $C_{18}H_{17}NO_3S$: C 66.04, H 5.23, N 4.28; found: C 65.54, H 5.26, N 4.19.

5-Allyloxy-1-methanesulfonyl-3-(4-toluenesulfonyl)-1*H*-indole (7): To a solution of **3** (963 mg, 3 mmol) and methanesulfonyl chloride (378 mg, 3.3 mmol) in CH_2Cl_2 (10 ml) a solution of triethylamine (333 mg, 3.3 mmol) in CH_2Cl_2 (1 ml) was added dropwise. The mixture was stirred for 30 min, washed with water and saturated $NaHCO_3$, dried and evaporated. The residue was recrystallized from ethanol to give **7** (907 mg, 75%) as a colorless crystal. M.p. 132-133°C. δ_H ($CDCl_3$): 2.40 (3H, s, $ArCH_3$), 3.22 (3H, s, CH_3SO_2N), 4.61 (2H, dm, *J*=5.3 Hz $ArOC\underline{H}_2CH=CH_2$), [5.34 (1H, dm, *J*=10.4 Hz), 5.46 (1H, dm, *J*=17.3 Hz), $ArOCH_2CH=C\underline{H}_2$], 5.97-6.17 (1H, m, $ArOCH_2C\underline{H}=CH_2$), 7.05 (1H, dd, *J*=9.2 Hz, *J*=2.6 Hz, H-6), 7.28-7.36 (2H, m, Ts), 7.39 (1H, d, *J*=2.6 Hz, H-4), 7.75 (1H, d, *J*=9.2 Hz, H-7), 7.87-7.95 (2H, m, Ts), 8.09, 1H, s, H-2). MS (EI), m/z (%): 405 (M^+, 100), 379 (3), 364 (25), 350 (6), 326 (17), 299 (5), 285 (67), 267 (12), 250 (8), 236 (17), 220 (31), 194 (9), 170 (53), 155 (8), 139 (33). Anal.: calcd. for $C_{19}H_{19}NO_5S_2$: C 56.28, H 4.72, N 3.45, found: C 56.21, H 4.53, N 3.39.

4-Allyl-1-methanesulfonyl-3-(4-toluenesulfonyl)-1*H*-indol-5-ol (8): A solution of **7** (500 mg, 1.23 mmol) in 1,2,4 trichlorobenzene was refluxed for 1.5 h under argon. After cooling to r.t. the resulting solution was introduced on a short silica-gel column. First the solvent was eluted with hexane followed with the product (hexane-ethyl acetate 3:1), to give **8** (440 mg, 88%) as a colorless crystal. M.p. 161-163°C. δ_H ($CDCl_3$): 2.42 (3H, s, $ArCH_3$), 3.27 (3H, s, CH_3SO_2N), 3.83 (2H, dm, *J*=5.8 Hz $ArC\underline{H}_2CH=CH_2$), 4.88-5.01 (2H, m, $ArCH_2CH=C\underline{H}_2$), 5.25 (1H, s, OH), 5.49-5.71 (1H, m, $ArCH_2C\underline{H}=CH_2$), 7.03 (1H, d, *J*=9.0 Hz, H-6), 7.28-7.36 (2H, m, Ts), 7.73 (1H, d, *J*=9.0 Hz, H-7), 7.72-7.80 (2H, m, Ts), 8.21 (1H, s, H-2). MS (EI), m/z (%): 405 (M^+, 38), 326 (5), 250 (7), 170 (100), 139 (23), 115 (15). Anal.: calcd. for $C_{19}H_{19}NO_5S_2$: C 56.28, H 4.72, N 3.45, found: C 56.25, H 4.81, N 3.39.

Methanesulfonic acid 4-allyl-1-methyl-3-(4-toluenesulfonyl)-1*H*-indol-5-yl ester (9): A mixture of **8** (61 mg, 0.15 mmol), methyl iodide (24 mg, 0.17 mmol), anhydrous K_2CO_3 (200 mg, 1.45 mmol), tetrabutylammonium bromide (5 mg) and acetonitrile (2 ml) was stirred overnight and poured into diluted hydrochloric acid. The product was extracted with CH_2Cl_2, the extract was dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **9** (55 mg, 87%) as a colorless crystal. M.p. 161-163°C. δ_H ($CDCl_3$): 2.38 (3H, s, $ArCH_3$), 3.17 (3H, s, CH_3SO_2O), 3.80-3.90 (5H, m, OCH_3 and $ArC\underline{H}_2CH=CH_2$), 4.60-4.75 (2H, m, $ArCH_2CH=C\underline{H}_2$), 5.40-5.62 (1H, m, $ArCH_2C\underline{H}=CH_2$), 7.20-7.27 (2H, m, Ts), 7.26 (1H, d, *J*=9.0 Hz, H-6), 7.42 (1H, d, *J*=9.0 Hz, H-7), 7.68-7.76 (2H,

m, Ts), 8.02 (1H, s, H-2). MS (EI), m/z (%): 419 (M^+, 7), 355 (1), 340 (7), 264 (10), 200 (3), 185 (100), 168 (7), 157 (7), 115 (3). Anal.: calcd. for $C_{20}H_{21}NO_5S_2$: C 57.26, H 5.05, N 3.34, found: C 57.23, H 4.88, N 3.50.

Methanesulfonic acid 4-allyl-3-(4-toluenesulfonyl)-1*H*-indol-5-yl ester (12): A mixture of **8** (61 mg, 0.15 mmol), anhydrous K_2CO_3 (200 mg, 1.45 mmol), tetrabutylammonium bromide (5 mg) and acetonitrile (2 ml) was stirred overnight and poured into diluted hydrochloric acid. The product was extracted with CH_2Cl_2, the extract was dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **12** (54 mg, 89%) as a colorless oil. δ_H ($CDCl_3$): 2.39 (3H, s, $ArCH_3$), 3.18 (3H, s, CH_3SO_2O), 3.85 (2H, dm, *J*=5.9 Hz, $ArC\underline{H}_2CH=CH_2$), 4.60-4.75 (2H, m, $ArCH_2CH=C\underline{H}_2$), 5.40-5.62 (1H, m, $ArCH_2C\underline{H}=CH_2$), 7.21-7.28 (2H, m, Ts), 7.28 (1H, d, *J*=9.0 Hz, H-6), 7.33 (1H, d, *J*=9.0 Hz, H-7), 7.68-7.66 (2H, m, Ts), 8.07 (1H, d, *J*=3.2 Hz, H-2), 9.25 (1H, br s, H-1). MS (EI), m/z (%): 405 (M^+, 12), 326 (15), 284 (1), 266 (1), 250 (4), 234 (1), 218 (2), 186 (4), 171 (100), 154 (3), 115 (6). Anal.: calcd. for $C_{19}H_{19}NO_5S_2$: C 56.28, H 4.72, N 3.45, found: C 56.25, H 4.86, N 3.27.

5-Allyloxy-1-(methoxymethyl)-3-(4-toluenesulfonyl)-1*H*-indole (13): To a solution of **3** (10 g, 30.6 mmol) in acetonitrile (120 ml) anhydrous K_2CO_3 (20 g, 112 mmol) was added. To the resulting suspension a solution of chloromethyl-methyl ether was added dropwise at 0-5°C during 80 min.. The mixture was stirred for 15 min and then was poured into water. The product was extracted with CH_2Cl_2, the extract was dried, and evaporated. The residue was recrystallized from isopropanol, to give **13** (8.88 g, 78%) as a colorless crystal. M.p. 152-154°C. δ_H ($CDCl_3$): 2.37 (3H, s, $ArCH_3$), 3.25 (3H, s, $C\underline{H}_3OCH_2N$), 4.6 (2H, dm, *J*=5.3 $ArOC\underline{H}_2CH=CH_2$), [5.31 (1H, dm, *J*=11.9), 5.44 (1H, dm, *J*=17.2), $ArOCH_2CH=C\underline{H}_2$)], 5.41 (2H, s, $CH_3OC\underline{H}_2N$), 5.98-6.20 (1H, m, $ArOCH_2C\underline{H}=CH_2$), 6.98 (1H, dd, *J*=9.0, *J*=2.6, H-6), 7.22-7.30 (2H, m, Ts), 7.36 (1H, d, *J*=2.6, H-4) 7.38 (1H, d, *J*=9.0, H-7), 7.81 (1H, s, H-2) 7.85-7.93 (2H, m, Ts). MS (EI), m/z (%): 371 (M^+, 13), 340 (2), 330 (5), 298 (8), 265 (1), 234 (1), 216 (5), 201 (2), 149 (2), 91 (3), 45 (100). Anal.: calcd. for $C_{20}H_{21}NO_4S$: C 64.67, H 5.70, N 3.77; found: C 64.48, H 5.50, N 3.57.

4-Allyl-1-(methoxymethyl)-3-(4-toluenesulfonyl)-1*H*-indol-5-ol (14): Compound **13** (8.55 g, 23 mmol) was kept at 190°C for 80 min under argon. After cooling **14** was obtained as a brownish crystal. M.p. 165-167 (ethyl acetate-hexane). δ_H ($CDCl_3$): 2.38 (3H, s, $ArCH_3$), 3.31 (3H, s, $C\underline{H}_3OCH_2N$), 3.81 (2H, br d, *J*=6.0), $ArC\underline{H}_2CH=CH_2$), 4.85-4.98 (2H, m, $ArCH_2CH=C\underline{H}_2$), 5.45 (2H, s, $CH_3OC\underline{H}_2N$), 5.45-5.65 (1H, m, $ArCH_2C\underline{H}=CH_2$), 6.94 (1H, d, *J*=8.8, H-6), 7.20-7.28 (2H, m, Ts), 7.34 (1H, d, *J*=8.8, H-7), 7.67-7.75 (2H, m, Ts), 8.06 (1H, s, H-2). MS (EI), m/z (%): 371 (M^+, 100), 340 (14), 307 (4), 216 (75), 201 (30), 184 (40), 170 (17), 154 (3), 139 (4), 115 (5), 91 (3). Anal.: calcd. for $C_{20}H_{21}NO_4S$: C 64.67, H 5.70, N 3.77; found: C 64.63, H 5.60, N 3.51.

4-Allyl-5-methoxy-1-(methoxymethyl)-3-(4-toluenesulfonyl)-1*H*-indole (15): To a solution of **14** (8.55 g, 23 mmol, crude product from the previous reaction) and methyl iodide (3.75 g, 26.4 mmol) in DMF (60 ml), anhydrous K_2CO_3 (12 g, 67 mmol) was added. The mixture was stirred overnight and poured into water. The precipitate formed was collected by filtration, washed with water and air-dried to give crude **15** (8.5 g) as a brownish crystal. M.p. 124°C. δ_H ($CDCl_3$): 2.37 (3H, s, $ArCH_3$), 3.73 (2H, dm, *J*=5.8, $ArC\underline{H}_2CH=CH_2$), 3.81 (3H, s, $ArOCH_3$), 4.56-4.68 (2H, m, $ArCH_2CH=C\underline{H}_2$), 5.42-5.63 (1H, m, $ArCH_2C\underline{H}=CH_2$), 5.46 (2H, s, $CH_3OC\underline{H}_2N$), 7.01 (1H, d, *J*=9.0, H-6), 7.20-7.28 (2H, m, Ts), 7.37 (1H, d, *J*=9.0, H-7), 7.68-7.76 (2H, m, Ts), 8.08 (1H, s, H-2). MS (EI), m/z (%): 385 (M^+, 100), 354 (10), 321 (8), 290 (3), 267 (3), 230 (88), 215 (19), 198 (40), 184 (14), 169 (12), 154 (5), 115 (4), 91 (3). Anal.: calcd. for $C_{21}H_{23}NO_4S$: C 65.43, H 6.01, N 3.63; found: C 65.32, H 5.97, N 3.50.

4-Allyl-5-methoxy-1-(hydroxymethyl)-3-(4-toluenesulfonyl)-1*H*-indole (16): A mixture of **15** (8.5 g, crude product from the previous reaction) 6*M* hydrochloric acid (100 ml) and 1,2-dimethoxyethane (120 ml) was refluxed with stirring for 1 h. After cooling to r.t. the product was extracted with ethyl acetate. The extract was dried and boiled with charcoal. The charcoal was filtered off and the filtrate was evaporated, to give crude **16** (7.5 g) contaminated with **17** as a yellow oil. Some of the crude product was subjected to column chromatography (hexane - ethyl acetate 3:1) to give analytical sample of **16** as a colorless crystal. M.p. 134-136°C (ethyl acetate - hexane).

δ_H ($CDCl_3$): 2.35 (3H, s, $ArCH_3$), 3.73 (2H, br d, *J*=5.8, $ArC\underline{H}_2CH=CH_2$), 3.78 (3H, s, $ArOCH_3$), 4.33 (1H, t, *J*=8.1, OH), [4.50-4.56 (1H, m), 4.58-4.62 (1H, m), $ArCH_2CH=C\underline{H}_2$), 5.37-5.55 (1H, m, $ArCH_2C\underline{H}=CH_2$), 5.58 (2H, d, *J*=8.1, $HOC\underline{H}_2N$), 6.98 (1H, d, *J*=9.0, H-6), 7.13-7.20 (2H, m, Ts), 7.38 (1H, d, *J*=9.0, H-7), 7.61-7.69 (2H, m, Ts), 8.16 (1H, s, H-2). MS (EI), m/z (%): 371 (2), 341 (100), 327 (5), 314 (3), 276 (6), 262 (7), 223 (9), 186 (92), 171 (49), 155 (51), 119 (13). Anal.: calcd. for $C_{20}H_{21}NO_4S$: C 64.67, H 5.70, N 3.77; found: C 64.64, H 5.66, N 3.47.

4-Allyl-5-methoxy-3-(4-toluenesulfonyl)-1*H*-indole (17): To a solution of **16** (7.5 g, crude product from the previous reaction) in ethanol (100 ml) 50% aqueous solution of NaOH was added. The mixture was stirred for 30 min and poured into 10% aqueous $NaHCO_3$ solution (750 ml). The product was extracted with ethyl acetate. The extract was dried, treated with charcoal and evaporated, to give crude **17** (6.1 g, 78% from **13**) as a yellow oil. Some of the crude product was passed through a short silica-gel column (hexane - ethyl acetate 3:1) to give analytical sample of **13** as a colorless crystal. M.p. 136-138°C (toluene - hexane). δ_H ($CDCl_3$): 2.37 (3H, s, $ArCH_3$), 3.72 (2H, dm, *J*=5.8, $ArC\underline{H}_2CH=CH_2$), 3.78 (3H, s, $ArOCH_3$), 4.54-4.68 (2H, m, $ArCH_2CH=C\underline{H}_2$), 5.42-5.66 (1H, m, $ArCH_2C\underline{H}=CH_2$), 6.94 (1H, d, *J*=8.8, H-6), 7.18-7.30 (3H, m, Ts and H-7), 7.68-7.76 (2H, m, Ts), 7.99 (1H, d, *J*=3.2, H-2), 9.23 (1H, br s, H-1). MS (EI), m/z (%): 341 (M^+, 100), 314 (4), 280 (7), 230 (16), 198 (9), 186 (92), 171 (48), 155 (46). Anal.: calcd. for $C_{19}H_{19}NO_3S$: C 66.84, H 5.61, N 4.10; found: C 66.88, H 5.56 N 3.79.

4-Allyl-5-methoxy-1-methanesulfonyl-3-(4-toluenesulfonyl)-1*H*-indole (18): To a solution of **13** (6.3 g, ca 18.5 mmol, crude product from the previous reaction) and triethylamine (2.8 g, 27.7 mmol) in CH_2Cl_2 (60 ml) a solution of methanesulfonyl chloride (2.54 g, 22.2 mmol) in CH_2Cl_2 (10 ml) was added dropwise. The mixture was stirred overnight and was washed with water The organic layer was separated, dried and evaporated. The residue was recrystallized from isopropanol, to give **18** (5.74 g, 74%) as a colorless crystal. M.p. 161-163°C. δ_H ($CDCl_3$): 2.42 (3H, s, $ArCH_3$), 3.25 (3H, s, CH_3SO_2N), 3.75 (2H, dm, *J*=5.9, $ArC\underline{H}_2CH=CH_2$), 3.83 (3H, s, $ArOCH_3$), 4.58-4.70 (2H, m, $ArCH_2CH=C\underline{H}_2$), 5.46-5.68 (1H, m, $ArCH_2C\underline{H}=CH_2$), 7.07 (1H, d, *J*=9.1, H-6), 7.27-7.34 (2H, m, Ts), 7.74-7.82 (3H, m, Ts and H-7), 8.22 (1H, s, H-2). MS (EI), m/z (%): 419 (M^+, 100), 405 (10), 355 (13), 341 (59), 276 (13), 264 (45), 249 (11), 230 (11), 200 (25), 185 (88), 170 (54), 155 (24), 139 (41), 119 (22). Anal.: calcd. for $C_{20}H_{21}NO_5S_2$: C 57.26, H 5.05, N 3.34; found: C 57.22, H 5.24, N 3.19

*Reaction of **18** with iodine and silver cyanate*: To a solution of **18** (419 mg, 1 mmol) in CH_2Cl_2 (5 ml) iodine (279 mg, 1.1 mmol) was added and the resulting solution was cooled to -20°C. Silver cyanate (181 mg, 1.2 mmol), was added next. The mixture was stirred for 40 min at -20°C and for 30 min at r.t. Inorganic solids were filtered off on Celite® and washed with CH_2Cl_2 (2 ml). To the filtrate methanol (2 ml) was added and the solution was refluxed for 1.5 h. The solvent was evaporated and the residue was subjected to column chromatography (hexane - ethyl acetate 2:1 do 1:1). Two fractions were obtained. The less polar one contained **20** (123 mg, 23%) as a colorless crystal.

2-Iodomethyl-6-methanesulfonyl-8-(4-toluenesulfonyl)-1,2-dihydro-6*H*-furo[3,2-*e*]indole (20): M.p. 163-164°C. δ_H ($CDCl_3$): 2.43 (3H, s, $ArCH_3$), [3.22 (1H, dd, *J*=16.9, *J*=6.8), 3.68 (1H, dd, *J*=16.9, *J*=9.4), H-1], 3.25 (3H, s, CH_3SO_2N), [3.33 (1H, dd, *J*=10.3, *J*=6.7), 3.40 (1H, dd, *J*=10.3, *J*=5.1), CH_2I], 4.89 (1H, dddd, *J*=9.4, *J*=6.8, *J*=6.7, *J*=5.1, H-2), 6.93 (1H, d, *J*=9.0, H-4), 7.31-7.39 (2H, m, Ts), 7.68 (1H, d, *J*=9.0, H-5), 7.80-7.88 (2H, m, Ts), 8.14 (1H, s, H-7). MS (EI), m/z (%): 531 (M^+, 92), 453 (68), 404 (50), 326 (48), 249 (33), 170 (100), 139 (18). Anal.: calcd. for $C_{19}H_{18}INO_5S_2$: C 42.95, H 3.41, N 2.64; found: C 42.48, H 3.18, N 2.36.

The more polar fraction conatained a mixture of **19a** and **19b** as a colorless oil.

4-[3-Iodo-2-(methoxycarbonylamino)propyl]-5-methoxy-1-methanesulfonyl-3-(4-toluenesulfonyl)-1*H*-indole (19a) and 4-[2-Iodo-3-(methoxycarbonylamino)propyl]-5-methoxy-1-methanesulfonyl-3-(4-toluenesulfonyl)-1*H*-indole (19b): Ratio of these isomers was estimated as ca. 4:1 on the NMR basis, however we do not know which is the major isomer. In the spectra described below chemical shifts of some of the signals corresponding to the minor

product are given in italics. δ_H ($CDCl_3$): 2.43, *2.45* (3H, s, $ArCH_3$), 3.14-3.52 (4H, m, side-chain CH_2 protons), 3.28, *3.27* (3H, s, CH_3SO_2N), 3.61, *3.65* (3H, s, CO_2CH_3), 3.87, *3.90* (3H, s, $ArOCH_3$), 4.70-4.86 (1H, m, aliphatic CH), 5.23 (1H, br s, NH), 7.07 (1H, d, *J*=9.2, H-6), 7.31-7.39 (2H, m, Ts), 7.80-7.89 (3H, m, Ts and H-7), 8.17 (1H, s, H-2). MS (EI), m/z (%): 620 (M^+, 0.1), 493 (6), 478 (18), 460 (2), 446 (7), 418 (72), 403 (18), 393 (37), 321 (24), 315 (28), 262 (40), 248 (32), 235 (33), 199 (19), 184 (61), 169 (39), 142 (80), 105 (100). Anal.: calcd. for $C_{22}H_{25}IN_2O_7S_2$: C 42.59, H 4.06, N 4.51; found: C 43.25, H 4.34, N 4.26.

5-Methoxy-4-[(*N*-methoxycarbonylazirydynyl)methyl]-3-(4-toluenesulfonyl)-1*H*-indole (21): To a suspension of sodium methoxide (22 mg, 0.41 mmol) in DMSO (2 ml) a solution of the mixture of carbamates **19a** and **19b** (62 mg, 0.1 mmol) was added dropwise. The mixture was stirred for 15 min and poured into a 10% aqueous solution of NH_4Cl. The product was extracted with ethyl acetate, the extract was washed with water, dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **21** (31 mg, 75%) as a colorless oil. δ_H ($CDCl_3$): [2.11 (1H, d, *J*=6.0), 2.14 (1H, d, *J*=3.9), aziridine CH_2], 2.37 (3H, s, $ArCH_3$), 2.80 (1H, dddd, *J*=7.1, *J*=6.0, *J*=4.5, *J*=3.9, aziridine CH), [2.97 (1H, dd, *J*=13.5, *J*=7.1), 3.43 (1H, dd, *J*=13.5, *J*=4.5), $ArCH_2$-], 3.73 (3H, s, CO_2CH_3), 3.80 (3H, s, OCH_3), 6.93 (1H, d, *J*=9.0, H-6), 7.2-7.3 (3H, m, Ts and H-7), 7.74-7.82 (2H, m, Ts), 7.98 (1H, d, *J*=3.3, H-2), 9.31 (1H, br s, NH). LSIMS, m/z: 415 $(M+H)^+$. Anal.: calcd. for $C_{21}H_{22}N_2O_5S$: C 60.86, H 5.35, N 6.76; found: C 60.68, H 5.26, N 6.22.

5-Methoxy-1-methanesulfonyl-4-(oxiranylmethyl)-3-(4-toluenesulfonyl)-1*H*-indole (23): A solution of **18** (838 mg, 2 mmol) and *m*-CPBA (507 mg of 85% reagent, 2.5 mmol) in CH_2Cl_2 (10 ml) was stirred for 24 h. After that time another portion of *m*-CPBA (250 mg, 1.23 mmol) was added and the mixture was stirred overnight. The reaction mixture was washed with solutions of Na_2SO_3 and K_2CO_3 and finally with water. The organic layer was dried and evaporated. The residue was recrystallized from toluene to give **23** (625 mg, 72%) as a colorless crystal. M.p. 181-184°C. 2.42 (3H, s, $ArCH_3$), 2.46-2.52 (2H, m, $ArCH_2CH^{oxirane}\underline{C}H_2{}^{oxirane}$), 2.86-2.96 (1H, m, $ArCH_2C\underline{H}^{oxirane}CH_2{}^{oxirane}$), [3.16 (1H, dd, *J*=13.9, *J*=6.2), 3.50 (1H, dd, *J*=13.7, *J*=4.2), $ArC\underline{H}_2CH^{oxirane}CH_2{}^{oxirane}$], 3.26 (3H, s, CH_3SO_2N), 3.86 (3H, s, OCH_3), 7.08 (1H, d, *J*=9.1, H-6), 7.30-7.38 (2H, m, Ts), 7.80 (1H, d, *J*=9.1, H-7), 7.80-7.88 (2H, m, Ts), 8.21 (1H, s, H-2). MS (EI), m/z (%): 435 (M^+, 20), 421 (7), 407 (14), 392 (17), 379 (43), 357 (5), 296 (10), 280 (30), 252 (26), 238 (42), 201 (13), 172 (37), 139 (100), 115 (14), 105 (17). Anal.: calcd. for $C_{20}H_{21}NO_6S_2$: C 55.16, H 4.86, N 3.22; found: C 55.53 H 5.04 N 2.72.

1-Ethoxy-3-[5-methoxy-3-(4-toluenesulfonyl)-1*H*-indol-4-yl]-propan-2-ol (24): To a solution of **23** (100 mg, 0.23 mmol) in anhydrous ethanol NaOH (500 mg, 12.5 mmol) was added and the mixture was refluxed for 1h. After cooling the reaction mixture was poured into a diluted solution of hydrochloric acid and the product was extracted with CH_2Cl_2. The extract was dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **24** (41 mg, 44%) as a colorless oil. δ_H ($CDCl_3$): 1.34 (3H, t, *J*=7.0, $OCH_2C\underline{H}_3$), 2.36 (3H, s, $ArCH_3$), 2.94-3.12 (2H, m, $ArCH_2$), 3.60-3.76 (4H, m, $C\underline{H}_2OC\underline{H}_2CH_3$), 3.81 (3H, s, OCH_3), 4.15-4.22 (1H, m, C<u>H</u>OH), 6.90 (1H, d, *J*=8.9, H-6), 7.11 (1H, d, *J*=8.9, H-7), 7.14 (1H, d, *J*=3.5, H-2), 7.18-7.26 (2H, m, Ts), 7.64-7.82 (2H, m, Ts), 10.00 (1H, br s, H-1). MS (EI), m/z (%): 403 (M^+, 3), 344 (10), 315 (100), 282 (2), 234 (4), 204 (2), 189 (25), 160 (25), 130 (9), 105 (10). HRMS (EI), m/z: calcd. for $C_{21}H_{25}NO_5S$ 403.14535; found: 403.14548.

5-Methoxy-4-(oxiranylmethyl)-3-(4-toluenesulfonyl)-1*H*-indole (25): To a solution of NaOH (132 mg, 3.3 mmol) in a mixture of methanol and water (9:1, 10 ml) solid **23** (476 mg, 1.1 mmol) was added and the resulting suspension was stirred until a clear solution was obtained (1 h). The solution was poured to a solution of $NaHCO_3$ (1%, 100 ml) and the product was extracted with ethyl acetate. The extract was dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **25** (275 mg, 71 %) as a colorless oil. δ_H ($CDCl_3$): 2.36 (3H, s, $ArCH_3$), 2.49 (2H, d, *J*=3.3, $ArCH_2CH^{oxirane}\underline{C}H_2{}^{oxirane}$), 2.89-3.00 (1H, m, $ArCH_2C\underline{H}^{oxirane}CH_2{}^{oxirane}$), [3.14 (1H, dd, *J*=13.7, *J*=6.1), 3.49 (1H, dd, *J*=13.7, *J*=4.1), $ArC\underline{H}_2CH^{oxirane}CH_2{}^{oxirane}$], 3.80 (3H, s, OCH_3), 6.94 (1H, d, *J*=9.0, H-6),

7.20-7.31 (3H, m, Ts and H-7), 7.72-7.80 (2H, m, Ts), 7.95 (1H, d, *J*=3.3, H-2), 9.40 (1H, br s, H-1). MS (EI), m/z (%): 357 (M^+, 76), 343 (57), 329 (36), 314 (40), 301 (68), 296 (18), 281 (16), 264 (7), 249 (10), 234 (20), 218 (15), 202 (55), 188 (13), 174 (87), 160 (70), 157 (100), 147 (16), 139 (15), 130 (33), 115 (13), 105 (38). HRMS (EI), m/z: calcd. for $C_{19}H_{19}NO_4S$: 357.1034; found: 357.1030.

(5-Allyloxy-4-bromo-2-nitrophenylo)acetonitrile (30): To a solution of *t*-BuOK (33.66 g, 300 mmol) in a DMF-THF mixture (1:1, 300 ml), a solution of 2-bromo-4-nitro-allyloxybenzene **29** (24.4 g, 94.6 mmol) and *p*-chlorophenoxyacetonitrile (16.63 g, 99.3 mmol) in the same solvent (100 ml) was added dropwise at -50°C. The mixture was stirred at this temperature for 15 min and poured into an ice-cold diluted solution of hydrochloric acid. The resulting precipitate was washed with water, air-dried and recrystallized from EtOH, to give **30** contaminated with the isomeric product. This mixture was once more recrystallized from EtOH. On cooling of the hot ethanolic solution big heavy crystals were formed falling on the bottom of a flask. At the point, when the solution over the crystals turned turbid, it was immediately decanted. To the precipitate small amount of ethanol was added and the solid product was collected by filtration to give **30** (14.2 g, 51%) as a colorless crystal. M.p. 93-96°C. δ_H ($CDCl_3$): 4.25 (2H, s, $ArCH_2CN$), 4.80 (2H, dm, *J*=5.1, $ArOC\underline{H}_2CH=CH_2$), [5.44 (1H, dm, *J*=10.5), 5.56 (1H, dm, *J*=17.3), $ArOCH_2CH=C\underline{H}_2$], 5.96-6.17 (1H, m, $ArOCH_2C\underline{H}=CH_2$), 7.18 (1H, s, H-3), 8.50 (1H, s, H-6). MS (EI), m/z (%): [M^+, 298 (16), 296 (16)], 281 (1), 279 (1), 102 (3), 41 (100). Anal.: calcd. for $C_{11}H_9BrN_2O_3$: C 44.47, H 3.05, N 9.43; found: C 44.79, H 2.86, N 9.65.

(2-Allyl-4-bromo-3-hydroxy-6-nitrophenyl)acetonitrile (32): A solution of **30** (14.02 g, 47.2 mmol) in diphenyl ether (140 ml) was warmed up to 230°C. External heating was removed and the reaction mixture was allowed to cool. At 140°C charcoal was added, at 80°C the mixture was filtered through Celite® and the solid left on the Celite® layer was washed with diethyl ether. The filtrate was extracted with 5% aqueous NaOH. The water solution was left in refrigerator. The organic layer was dried, Et_2O was removed *in vacuo* and the residue was recycled for the reaction. The sequence reaction - work-up was performed for three times. The combined water solutions, obtained on basic work-up, were washed with diethyl ether and acidified with 6*M* hydrochloric acid solution at 0-5°C. The precipitate formed was collected by filtration, air-dried and recrystallized from ethyl acetate, to give **32** (6.70 g, 48%) as a colorless crystal. M.p. 173-175°C. δ_H ($CDCl_3$): 3.50 (2H, dm, *J*=5.8, $ArOC\underline{H}_2CH=CH_2$), 4.10 (2H, s, $ArCH_2CN$), 4.96-5.14 (2H, m, $ArOCH_2CH=C\underline{H}_2$), 5.90-6.12 (1H, m, $ArOCH_2C\underline{H}=CH_2$), 8.30 (1H, s, ArH). MS (EI), m/z (%): [M^+, 299 (100), 297 (99)], 282 (70), 280 (70), 270 (60), 268 (63), 254 (27), 252 (23), 226 (24), 224 (19), 189 (18), 173 (10), 160 (12), 146 (32), 131 (13), 115 (38). Anal.: calcd. for $C_{11}H_9BrN_2O_3$: C 44.47, H 3.05, N 9.43; found: C 44.04, H 3.10, N 9.75.

(2-Allyl-4-bromo-3-methoxy-6-nitrophenyl)acetonitrile (33): To a solution of **32** (6.40 g, 21.5 mmol) and dimethyl sulfate (2.77 g, 22 mmol) in acetone (70 ml) anhydrous K_2CO_3 (5.52 g, 40 mmol) was added. The mixture was refluxed for 3 h with vigorous stirring. Then the solvent was evaporated, and the residue was partitioned between water and ethyl acetate. The organic solution was dried and evaporated. The residue was recrystallized from ethanol, to give **33** (5.49 g, 82%) as a colorless crystal. M.p. 77-78°C. δ_H ($CDCl_3$): 3.69 (2H, dm, *J*=5.3, $ArC\underline{H}_2CH=CH_2$), 3.92 (3H, s, OCH_3), 3.93 (2H, s, $ArCH_2CN$), [4.89 (1H, dm, *J*=17.2), 5.20 (1H, dm, *J*=10.3), $ArCH_2CH=C\underline{H}_2$], 5.90-6.10 (1H, m, $ArCH_2C\underline{H}=CH_2$), 8.27 (1H, s, H-5). MS (EI), m/z (%): [M^+, 312 (79), 310 (82)], 295 (94), 293 (71), 280 (37), 278 (35), 255 (100), 253 (96), 240 (42), 238 (55), 226 (40), 224 (47), 214 (30), 199 (24), 186 (20), 184 (19), 171 (38), 140 (47), 127 (32), 115 (86). Anal.: calcd. for $C_{12}H_{11}BrN_2O_3$: C 46.32, H 3.56, N 9.00; found: C 46.37, H 3.49, N 9.25.

Reaction of 33 with iodine and silver cyanate: To a solution of **33** (93 mg, 0.3 mmol) in CH_2Cl_2 (3 ml) iodine was added (84 mg, 0.33 mmol) and the resulting solution was cooled to -20°C. Silver cyanate (181 mg, 1.2 mmol) was

added and the mixture was stirred for 30 min at -20°C, and then for 30 min at r.t. Inorganic solids were filtered off on Celite® and washed with CH_2Cl_2 (2 ml). Methanol (2 ml) was added to the filtrate and the resulting solution was refluxed for 2 h. The solvent was evaporated, and the residue was subjected to a column chromatography (hexane - ethyl acetate 5:2). Two fractions were obtained. The less polar one contained a mixture (47 mg) of **34a** and **35** as an oil.

[4-Bromo-2-[3-iodo-2-(methoxycarbonylamino)propyl]-3-methoxy-6-nitrophenyl]acetonitrile (34a) and (7-bromo-2-(iodomethyl)-5-nitro-2,3-dihydrobenzofuran-4-yl)acetonitrile (35): The molar ratio of **35** to **34a** was estimated as 4:1 on the ^{1}H NMR basis; so the estimated yields are 36 mg (29%) and 11 mg (7%) respectively. All the signals in the NMR spectra of the mixture, corresponding to the protons of the product **35** were identified and assigned: δ_H ($CDCl_3$): [3.28 (1H, dd, *J*=16.5, *J*=6.6), 3.69 (1H, dd, *J*=16.5, *J*=9.4), H-3], [3.48 (1H, dd, *J*=10.6, *J*=7.2), 3.57 (1H, dd, *J*=10.6, *J*=4.1), CH_2I] [3.94 (1H, d, *J*=17.1), 4.06 (1H, d, *J*=17.1), $ArCH_2CN$], 5.18 (1H, dddd, *J*=9.4, *J*=7.2, *J*=6.6, *J*=4.1, H-2), 8.32 (1H, s, H-6).

Additionally, three signals corresponding to product **34a** were identified: 3.61 (3H, $NHCO_2C\underline{H}_3$), 3.99 (3H, $ArOCH_3$), 8.25 (1H, ArH).

LSIMS, m/z: 512, 514 $(M_{34a}+H)^+$.

The more polar fraction contained **34b** (50 mg, 33%) as a yellowish crystal.

{4-Bromo-2-[2-iodo-3-(methoxycarbonylamino)propyl]-3-methoxy-6-nitrophenyl}acetonitrile (34b): M.p. 124-126°C. δ_H ($CDCl_3$): [3.23 (1H, dd, *J*=15.1, *J*=9.8), 3.47 (1H, dd, *J*=15.1, *J*=4.7), $ArC\underline{H}_2CH(I)CH_2NHCO_2Me$], 3.65 (2H, "t", $ArCH_2CH(I)C\underline{H}_2NHCO_2Me$), 3.72 (3H, s, $ArCH_2CH(I)CH_2NHCO_2\underline{Me}$), 3.99 (3H, s, $ArOCH_3$), 4.11, 4.15 (2H, AB system, *J*=17.5, $ArCH_2CN$), 4.41-4.55 (1H, m, $ArCH_2C\underline{H}(I)CH_2NHCO_2Me$), 5.22 (1H, br s, NH), 8.27 (1H, s, H-5). MS (EI), m/z (%): [$(M - CH_2NHCO_2Me - H)^+$, 437 (1), 435 (1)], 424 (3), 422 (3), 407 (1), 405 (1), 386 (23), 384 (24), 354 (4), 352 (4), 337 (3), 335 (3), 311 (22), 309 (22), 142 (100), 127 (22), 88 (30). LSIMS, m/z: 512, 514 $(M+H)^+$. Anal.: calcd. for $C_{14}H_{15}BrIN_3O_5$: C 32.84, H 2.95, N 8.21; found: C 33.29, H 3.24, N 7.52.

[4-Bromo-3-methoxy-2-(oxiranylmethyl)-6-nitrophenyl]acetonitrile (36): *m*-CPBA (6 mmol, 2.07 g of the 50% reagent) was dissolved in CH_2Cl_2 (25 ml) and the solution was dried with anhydrous $MgSO_4$. The drying agent was filtered off and **33** (933 mg, 3 mmol) was added to the filtrate. The resulting solution was refluxed for 12 h. After cooling the reaction mixture was washed with 10% aqueous solution of Na_2SO_3 and with saturated solution of $NaHCO_3$. The organic layer was dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **36** (980 mg, 100%) as a colorless crystal. M.p. 83-84°C. δ_H ($CDCl_3$): [2.52 (1H, dd, *J*=4.5, *J*=2.6), 2.84 (1H, "t"), $ArCH_2CH^{oxirane}C\underline{H}_2^{oxirane}$], [2.92 (1H, dd, *J*=14.8, *J*=6.4), 3.51 (1H, dd, *J*=14.8, *J*=2.7), $ArC\underline{H}_2CH^{oxirane}CH_2^{oxirane}$], 3.21 (1H, dddd, *J*=6.4, *J*=4.4, *J*=2.7, *J*=2.6, $ArCH_2C\underline{H}^{oxirane}CH_2^{oxirane}$), 3.99 (3H, s, OCH_3), [4.03 (1H, d, *J*=17.2), 4.13 (1H, d, *J*=17.2), $ArCH_2CN$)], 8.25 (1H, s, H-5). MS (EI), m/z (%): [M^+, 328 (9), 326 (9)], 311 (26), 309 (25), 299 (24), 297 (27), 281 (55), 279 (43), 267 (95), 265 (100), 255 (35), 253 (47), 240 (57), 238 (45), 228 (29), 226 (37), 212 (37), 198 (22), 196 (23), 158 (21), 156 (21), 128 (40), 115 (37). Anal.: calcd. for $C_{12}H_{11}BrN_2O_4$: C 44.06, H 3.39, N 8.56; found: C 44.16, H 3.12, N 8.54. HRMS (EI), m/z: calc.: 325.9902; found: 325.9901.

[4-Bromo-3-methoxy-2-(3-methoxy-2-hydroxypropyl)-6-nitrophenyl]acetonitrile (37): To a solution of **36** (65 mg, 0.2 mmol) in methanol (2 ml) a solution of sodium methoxide in methanol (0.27 *M*, 0.74 ml, 0.2 mmol) was added dropwise under argon. The mixture was stirred overnight and quenched with aqueous NH_4Cl. The product was extracted with ethyl acetate. The extract was dried and evaporated. The residue was subjected to a column chromatography (hexane - ethyl acetate 1:1). The substrate (26 mg, 40%) was recovered and **37** (18 mg, 25%) was obtained as a brown oil. δ_H ($CDCl_3$): [2.50 (1H, dd, *J*=4.7, *J*=2.5), 2.78 (1H, dd, *J*=4.7, *J*=2.5), $ArCH_2CH(OH)C\underline{H}_2OCH_3$], [2.92 (1H, dd, *J*=13.9, *J*=4.7), 3.22 (1H, dd, *J*=13.9, *J*=3.9), $ArC\underline{H}_2CH(OH)CH_2OCH_3$],

3.08-3.18 (1H, m, $ArCH_2C\underline{H}(OH)CH_2OCH_3$), 3.74 (3H, s, $ArCH_2CH(OH)CH_2OC\underline{H}_3$], 3.92 (2H, s, $ArCH_2CN$), 3.97 (3H, s, $ArOCH_3$), 6.91 (1H, br s, OH), 8.13 (1H, s, ArH). MS (EI), m/z (%): [$(M+H)^+$, 361 (2), 359 (2)], [M^+, 360 (1), 358 (1)], 343 (2), 341 (2), 329 (13), 327 (13), [$(M-CH_2OMe)^+$, 315 (19), 313 (20)], 303 (54), 301 (55), 286 (25), 284 (42), 282 (17), 255 (20), 253 (19), 240 (33), 238 (27), 203 (32), 189 (71) 174 (18), 160 (10), 145 (12), 115 (17), 102 (21). HRMS (EI), m/z: calcd. for $C_{13}H_{15}BrN_2O_5$: 358.0164; found: 358.0164.

5-Bromo-2-(hydroxymethyl)-4-methoxy-7-nitro-1-indancarbonitrile (38): To a solution of **36** (82 mg, 0.25 mmol) in DMF (4 ml) a solution of sodium methoxide in methanol (0.27*M*, 1 ml, 0.27 mmol) was added dropwise under argon. The mixture was stirred for 2 h at 50°C and after cooling was poured to an aqueous solution of NH_4Cl. The product was extracted with ethyl acetate. The extract was dried and evaporated. The residue was subjected to a column chromatography (hexane - ethyl acetate 2:1). The substrate (10 mg, 12%) was recovered and a mixture of two diastereoisomeric products **38** (44 mg, 54%) was obtained. The products were separated by HPLC, to give diastereoisomer *trans* **38a** (30 mg) and *cis* **38b** (10 mg), each as a yellow oil.

38a: δ_H ($CDCl_3$): 1.80 (1H, br s, OH), [3.03 (1H, dd, *J*=16.9, *J*=3.6), 3.45 (1H, dd, *J*=16.9, *J*=8.3), H-3], 3.14 (1H, ddddd, *J*=8.3, *J*=7.3, *J*=5.6, *J*=3.6, *J*=3.5, H-2), [3.56 (1H, dd, *J*=10.7, *J*=7.3), 3.76 (1H, dd, *J*=10.7, *J*=5.6), CH_2OH], 3.99 (3H, s, OCH_3), 4.72 (1H, d, *J*=3.5, H-1), 8.38 (1H, s, H-6). MS (EI), m/z (%): [M^+, 328 (32), 326 (32)], 311(9), 309 (8), 297 (95), 295 (62), 281 (100), 279 (65), 269 (31), 267 (34), 255 (78), 253 (88), 240 (37), 238 (42), 225 (33), 223 (36), 210 (36), 208 (30), 173 (48), 158 (27), 156 (32), 140 (52), 129 (55), 127 (55), 115 (42). HRMS (EI), m/z: calcd. for $C_{12}H_{11}BrN_2O_4$: 325.9902; found: 325.9901.

38b: δ_H ($CDCl_3$): 1.94 (1H, br s, OH), [2.95-3.02 (2H, m), 3.24 (1H, m,), H-2 and H-3], 3.99 (3H, s, OCH_3), 4.08-4.16 (2H, m, CH_2OH), 4.90 (1H, d, *J*=9.7, H-1), 8.40 (1H, s, H-6). MS (EI), m/z (%): [M^+, 328 (36), 326 (36)], 297 (58), 295 (55), 281 (65), 279 (57), 269 (25), 267 (27), 255 (96), 253 (100), 240 (32), 238 (38), 225 (31), 223 (32), 210 (27), 208 (24), 173 (38), 158 (22), 156 (22), 140 (42), 129 (41), 127 (45), 115 (30). HRMS (EI), m/z: calcd. for $C_{12}H_{11}BrN_2O_4$: 325.9902; found: 325.9901.

[4-Bromo-3-methoxy-2-(3-bromo-2-hydroxypropyl)-6-nitrophenyl]acetonitrile (41): Mixture of **36** (980 mg, 3 mmol), tetrabutylammonium bromide (1.934 g, 6 mmol) and $Mg(NO_3)_2{\cdot}6H_2O$ (513 mg, 2 mmol) in chloroform (30 ml) was refluxed for 2.5 h. The solvent was evaporated and the residue was purified by passing through a short silica-gel column, to give **41** (956 mg, 78%) as a colorless crystal. M.p. 142-143°C (toluene). δ_H ($CDCl_3$): 2.47 (1H, dd, *J*=4.1, *J*=1.1, OH), [3.01 1H, dd, *J*=14.2, *J*=9.1), 3.21 (1H, ddd, *J*=14.2, *J*=3.1, *J*=1.1), $ArC\underline{H}_2CH(OH)CH_2Br$], [3.49 (1H, dd, *J*=10.5, *J*=7.1), 3.63 (1H, dd, *J*=10.5, *J*=4.3), $ArCH_2CH(OH)C\underline{H}_2Br$], 3.97 (3H, s, OCH_3), 4.01-4.16 (1H, m, $ArCH_2C\underline{H}(OH)CH_2Br$), [4.07 (1H, d, *J*=17.3), 4.25 (1H, d, *J*=17.3), $ArCH_2CN$)], 8.23 (1H, s, H-5). UV (KBr, cm^{-1}): 1340, 1524 (NO_2), 2268 (CN), 3421 (OH). MS (EI), m/z (%): [M^+, 410 (0.3), 408 (0.6), 406 (0.3)], 315 (5), 313 (5), 286 (99), 284 (100), 269 (86), 269 (83), 242 (47), 240 (50), 228 (32), 226 (33). Anal.: calcd. for $C_{12}H_{12}Br_2N_2O_4$: C 35.32, H 2.96, N 6.87; found: C 35.31, H 2.95, N 6.86.

[4-Bromo-3-methoxy-2-(3-bromo-2-oksopropyl)-6-nitrophenyl]acetonitrile (42): To a solution of CrO_3 (105 mg, 1.05 mmol) in water (0.2 ml) sulfuric acid (175 mg, 1.79 mmol) was added dropwise. The resulting solution was added to a solution of **41** (46 mg, 0.11 mmol) in acetone (1 ml). The mixture was stirred for 48 h followed with addition of isopropanol (0.3 ml). After 30 min chromium salts were filtered off, the filtrate was poured into water and the product was extracted with ethyl acetate. The extract was washed with water, dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **42** (26 mg, 57%) as a colorless oil. δ_H ($CDCl_3$): 3.87 (2H, s, $ArC\underline{H}_2COCH_2Br$), 3.91 (3H, s, OCH_3), 4.01 (2H, s, $ArCH_2CN$), 4.34 (2H, s, $ArCH_2COC\underline{H}_2Br$), 8.30 (1H, s, H-5). UV ($CHCl_3$, cm^{-1}): 1345, 1531 (NO_2), 1725 (C=O), 2259 (CN). MS (EI), m/z (%): [M^+, 408 (20), 406 (42), 404 (21)], 365 (4), 363 (8), 361 (7), 313 (9), 311 (10), 284 (100), 269 (86), 267 (83), 253 (26), 251 (24), 242 (42),

240 (45), 228 (26), 226 (34), 128 (32), 123 (87), 121 (80). HRMS (EI), m/z: calcd. for $C_{12}H_{10}Br_2N_2O_4$: 403.9007; found: 403.9007.

6-Bromo-3-hydroxy-5-methoxy-8-nitro-1-naphthalenecarbonitrile (43): To a solution of **42** (10 mg, 0.025 mmol) in DMF (1 ml) anhydrous K_2CO_3 (50 mg, 0.36 mmol) was added. The mixture was stirred for 1.5 h and poured into an ice-cold diluted hydrochloric acid. The product was extracted with ethyl acetate, the extract was washed with water, dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **43** (6 mg, 74%) as a yellow crystal. M.p. 199°C (dec.). δ_H (dmso-d_6): 3.97 (3H, s, OCH_3), 7.75 (1H, d, *J*=2.5, H-2), 7.95 (1H, d, *J*=2.5, H-4), 8.36 (1H, s, H-7), 11.24 (1H, s, OH). UV (KBr, cm^{-1}): 1339, 1529 (NO_2), 2238 (CN), 3345 (OH) MS (EI), m/z (%): [M^+, 324 (97), 322 (100)], 294 (19), 292 (19), 263 (9), 261 (9), 235 (15), 233 (12), 220 (8), 218 (8), 198 (68), 170 (18), 154 (32). HRMS (EI), m/z: calcd. for $C_{12}H_7BrN_2O_4$: 321.9589; found: 321.9581.

6-Bromo-5-methoxy-8-nitro-3-okso-1,2,3,4-tetrahydro-1-naphthalenecarbonitrile (44): To a solution of CrO_3 (468 mg, 4.68 mmol) in water (3 ml) H_2SO_4 (706 mg, 7.20 mmol) was added dropwise. The resulting solution was added to a solution of **41** (956 mg, 2.34 mmol) in acetone (25 ml). The mixture was stirred for 2 h followed with addition of isopropanol (1 ml). After 30 min chromium salts were filtered off and a solution of triethylamine (391 mg, 3.87 mmol)[27] in acetone (2ml) was added dropwise at 0-5°C. The mixture was stirred for 2 min and poured into an ice-cold diluted hydrochloric acid. The product was extracted with CH_2Cl_2. The extract was dried and evaporated. The residue was purified by passing through a short silica-gel column, to give **44** (717 mg, 94%) as a colorless crystal. M.p. 117°C. δ_H ($CDCl_3$): [2.62 (1H, dd, *J*=17.6, *J*=6.0), 3.07 (1H, dd, *J*=17.6, *J*=2.1), H-2], [3.72 (1H, dd, *J*=20.5, *J*=1.0), 4.16 (1H, d, *J*=20.5), H-4], 3.95 (3H, s, OCH_3), 5.12 (1H, dd, *J*=6.0, *J*=2.1, H-1), 8.33 (1H, d, *J*=1.0, H-7). MS (EI), m/z (%): [M^+, 326 (61), 324 (63)], 309 (8), 307 (5), 298 (37), 296 (42), 281 (68), 279 (58), 267 (20), 253 (30), 251 (31), 239 (26), 237 (22), 225 (22), 198 (24), 171 (22), 158 (19), 156 (24), 149 (100), 140 (30), 127 (40), 114 (31), 101 (32). HRMS (EI), m/z: calcd. for $C_{12}H_9BrN_2O_4$: 323.9745; found: 323.9760.

6-Bromo-3-(hydroxyimine)-5-methoxy-8-nitro-1,2,3,4-tetrahydro-1-naphthalenecarbonitrile (45): To a solution of **44** (65 mg, 0.2 mmol) in a mixture of methanol (1.2 ml) and water (0.3 ml) hydroxylamine hydrochloride (20 mg, 0.3 mmol) was added. The reaction mixture was warmed up to 50°C, allowed to cool and diluted with water. The product was extracted CH_2Cl_2, the extract was dried and evaporated. The residue was subjected to a column chromatography (hexane - ethyl acetate 3:1), to give fractions containing pure stereoisomeric oximes **45** as well as their mixture in 82% (56 mg) overall yield. Analytical samples were prepared from the fractions containg the pure compounds. The less polar isomer: δ_H ($CDCl_3$): [2.60 (1H, ddm, *J*=15.2, *J*=4.8), 3.11 (1H, dd, *J*=15.2, *J*=2.6), H-2], [3.96 (1H, d, *J*=22.7,), 4.12 (1H, d, *J*=22.7), H-4], 4.00 (3H, s, OCH_3), 4.85 (1H, dd, *J*=4.8, *J*=2.6, H-1), 8.18 (1H, br s, OH), 8.30 (1H, s, H-7). MS (EI), m/z (%): [M^+, 341 (75), 339 (100)], 310 (10), 308 (15), 297 (43), 295 (40), 278 (22), 276 (17), 267 (35), 265 (31), 252 (22), 236 (16), 199 (10), 183 (14), 169 (16), 153 (18), 140 (35), 127 (42), 114 (32). HRMS (EI), m/z: calcd. for $C_{12}H_{10}BrN_3O_4$: 338.9854; found: 338.9826.

The more polar isomer: δ_H ($CDCl_3$): [2.61 (1H, ddd, *J*=18.5, *J*=6.3, *J*=1.9), 3.53 (1H, dm, *J*=18.5), H-2], [3.72 (1H, dm, *J*=18.2,), 4.17 (1H, d, *J*=18.2), H-4], 3.94 (3H, s, OCH_3), 5.07 (1H, dd, *J*=6.3, *J*=1.8, H-1), 7.56 (1H, br s, OH), 8.28 (1H, d, *J*=0.8, H-7). MS (EI), m/z (%): [M^+, 341 (98), 339 (100)], 310 (14), 308 (22), 297 (77), 295 (71), 278 (31), 267 (56), 265 (49), 252 (29), 236 (19), 199 (13), 183 (15), 169 (12), 153 (15), 140 (40), 127 (48), 114 (34). HRMS (EI), m/z: calcd. for $C_{12}H_{10}BrN_3O_4$: 338.9854; found: 338.9849.

3-(Benzylamino)-6-bromo-5-methoxy-8-nitro-1,2-dihydro-1-naphthalenecarbonitrile (46): To a solution of acetic acid (48 mg, 0.8 mmol) in toluene (3 ml) **44** (130 mg, 0.4 mmol) was added followed with a solution of benzylamine (64 mg, 0.6 mmol) in toluene (1 ml). The mixture was warmed up to the boiling point of the solvent and allowed to cool. The residue was purified by passing through a short silica-gel column, to give **46** (150 mg, 91%) as a red oil. δ_H ($CDCl_3$): [2.46 (1H, br dd, *J*=16.0, *J*=2.0), 2.79 (1H, ddd, *J*=16.0, *J*=6.1, *J*=1.8), H-2], 3.66 (3H, s, OCH_3),

4.31-4.47 (2H, m, NHC<u>H</u>$_2$Ph), 4.76 (1H, dd, *J*=6.1, *J*=2.0, H-1), 5.55 (1H, d, *J*=1.5, H-4), 7.36 (5H, s, Ph), 7.86 (1H, s, H-7). MS (EI), m/z (%): [M$^+$, 415 (7), 413 (8)], 383 (2), 381 (2), 368 (3), 366 (3), 91 (100). HRMS (EI), m/z: calcd. for $C_{19}H_{16}BrN_3O_3$: 413.0375; found: 413.0375.

3-(Benzylamino)-6-bromo-5-methoxy-8-nitro-1,2,3,4-tetrahydro-1-naphthalenecarbonitrile (50): To a solution of **44** (442 mg, 1.36 mmol) and acetic acid (120 mg, 2 mmol) in THF (8 ml) a solution of benzylamine (161 mg, 1.5 mmol) in THF (2 ml) was added. The mixture was stirred for 2 h and to the solution of the formed enamine **46** a solution of HCl in ethanol (1.8 *M*, 0.91 ml, 1.63 mmol) was added dropwise, followed with a solution of $NaBH_3CN$ (128 mg, 2 mmol) in methanol (1.5 ml). After 1h excess $NaBH_3CN$ was decomposed with aqueous HCl, the mixture was poured into 20% aqueous solution of K_2CO_3 and the product was extracted with CH_2Cl_2. The extract was dried and evaporated The residue was subjected to a column chromatography (hexane - ethyl acetate 2:3), to give **50** (430 mg, 76%) as a pale violet oil. δ_H ($CDCl_3$): 1.80 (1H, ddd, *J*=13.4, *J*=10.8, *J*=5.2, H-2), 2.41-2.68 (2H, m, H-2 and H-4), 3.23-3.48 (2H, m, H-3 and H-4) 3.89 (3H, s, OCH_3), 3.94 (2H, s, PhC<u>H</u>$_2$N), 4.76 (1H, dd, *J*=5.2, *J*=3.8, H-1), 7.27-7.40 (5H, m, <u>Ph</u>CH$_2$N), 8.28 (1H, s, H-7). MS (EI), m/z (%): [M$^+$, 417 (13), 415 (13)], 416 (40), 414 (39), 398 (5), 400 (5), 372 (5), 370 (7), 326 (3), 324 (3), 267 (4), 265 (4), 149 (5), 133 (16), 115 (7), 106 (10), 91 (100). HRMS (EI), m/z: calcd. for $C_{19}H_{18}BrN_3O_3$: 415.0531; found: 415.0530.

6-Methoxy-1,3,4,5-tetrahydrobenz[*cd*]-1*H*-indol-4-amine (1): A mixture of **50** (86 mg, 0.21 mmol), Pd/C (10%, 70 mg), ethanol (4 ml) and ethanolic solution of dimethylamine (33%, 0.4 ml) was stirred under hydrogen for 48 h. The catalyst was filtered off and evaporated. The residue was purified by passing through a short silica-gel column (ethyl acetate - 2.5% ethanolic ammonia solution 10:1), to give **1** (24 mg, 57%) as a colorless oil. δ_H ($CDCl_3$): 1.64 (2H, br s, NH_2), [2.66 (1H, ddd, *J*=15.0, *J*=8.3, *J*=1.3), 3.05 (1H, dd, *J*=15.0, *J*=4.2), H-5]*, [2.73 (1H, dd, *J*=16.0, *J*=8.1), 3.18 (1H, dd, *J*=16.0, *J*=4.1), H-3]*, 3.41-3.56 (1H, m, H-4), 3.86 (3H, s, OCH_3), 6.86 (1H, d, *J*=8.7, H-7), 6.88 (1H, s, H-2), 7.11 (1H, d, *J*=8.7, H-8), 7.84 (1H, br s, H-1). MS (EI), m/z (%): [M$^+$, 202 (100)], 185 (27), 171 (19), 159 (33), 144 (27), 130 (13), 115 (14). HRMS (EI), m/z: calcd. for $C_{12}H_{14}N_2O$: 202.1106; found: 202.1104.

The product **1** was converted to the corresponding hemioxalate, according to the described procedure.[3] M.p. 245°C; lit.[3] 260-265°C. δ_H (dmso-d_6, 500 MHz): [2.79 (1H, dd, *J*=15.9, *J*=9.8), 3.25 (1H, dd, *J*=15.9, *J*=4.2), H-5]*, [2.81 (1H, dd, *J*=14.8, *J*=10.2), 3.14 (1H, dd, *J*=14.8, *J*=4.2), H-3]*, 3.54 (1H, m, H-4), 3.76 (3H, s, OCH_3), 6.82 (1H, d, *J*=8.7, H-7), 7.04 (1H, s, H-2), 7.12 (1H, d, *J*=8.7, H-8), 10.60 (1H, s, H-1). Anal.: calcd. for $C_{14}H_{16}N_2O_5$: C 57.53, H, 5.52 N, 9.58; found: C 57.95, H 5.76, N 10.02.

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