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SIMPLE SYNTHETIC METHOD FOR 1-HYDROXYINDOLE AND ITS APPLICATION TO 1-HYDROXYTRYPTOPHAN DERIVATIVES[1],#

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Abstract – Simple and general synthetic method for 1-hydroxy- and 1-methoxyindole is reported. Its application to the synthesis of various types of 1-hydroxy- and 1-methoxyindole derivatives is successful, especially for the synthesis of 1-hydroxytryptophan derivatives.

INTRODUCTION

We have 1-hydroxyindole hypotheses[3] in which we imagine the existence of 1-hydroxy- (**A**, Figure 1) and/or 1-hydroperoxytryptophan (**B**) derivatives as a peptide component in living organisms and they could undergo nucleophilic substitution reactions[3] on indole nucleus with 1-hydroxy moiety (or its phosphate ester, etc.) as a leaving group culminating in the formation of various kinds of indole natural products, such as serotonin,[4] melatonin,[4] bufotenin,[4] pyrrolo[2,3-*b*]indole skeleton,[5] leptosin A–C mother

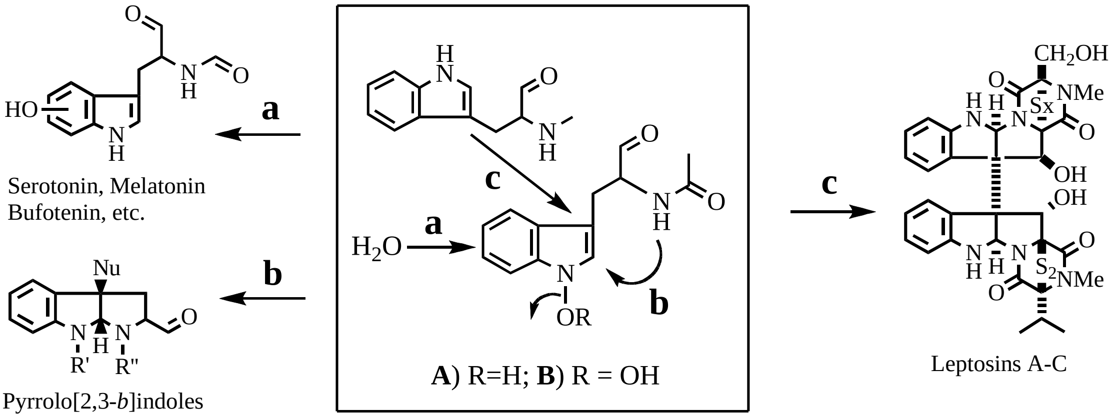
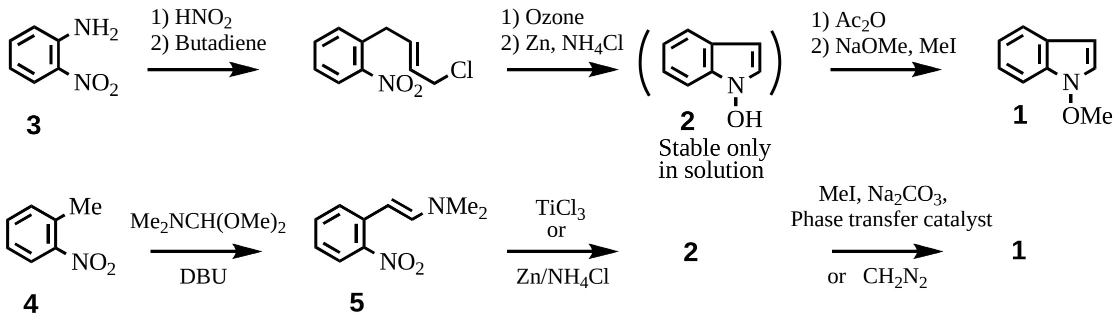


Figure 1 A part of 1-hydroxyindole hypotheses

Dedicated to the 77th birthday of Prof. Isao Kuwajima

skeletons,[6] etc.[3] In order to determine whether our hypotheses is imaginary story or not, we had to create a synthetic method for 1-hydroxyindoles, especially the one suitable for imaginary 1-hydroxytryptophan derivatives.



Scheme 1

When the present study started, two methods were reported for the synthesis of 1-methoxyindole (**1**, Scheme 1). In 1974, Acheson and co-workers[7] succeeded in the first preparation of **1** *via* unstable 1-hydroxyindole (**2**), starting from 2-nitroaniline (**3**). Using this sequence of reactions, they produced some 1-hydroxyindole derivatives,[7] stabilized by electron withdrawing group at the 3-position, but Acheson's method is not applicable for our target, 1-hydroxytryptophan derivatives. In 1981, we discovered the second method[8] reacting 2-nitrotoluene (**4**) with *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA), followed by reduction of the intermediate nitroenamine (**5**) with either titanium chloride or zinc and ammonium chloride. Employing the method, preparation of various 1-hydroxyindoles,[3,8] 1-methoxypimprinine,[9] 1-methoxyindole-3-acetonitrile,[9] (*dl*)-paniculidine B,[10] and (*dl*)-1-methoxy-6,7-secoagroclavine[11] were achieved. However, use of an expensive DMFDMA and anhydrous reaction conditions are cumbersome problems to be improved. Furthermore, it is not applicable for the preparation of 1-hydroxytryptophan derivatives.

As the third one,[12] we have finally discovered an oxidation method of 2,3-dihydroindole (**6**, Table 1) in MeOH–H_2O with 30% aqueous hydrogen peroxide (30% H_2O_2) or urea·H_2O_2 addition compound in the presence of a catalytic amount of metal oxides, such as sodium tungstate,[13] sodium phosphotungstate, and sodium molybdate.

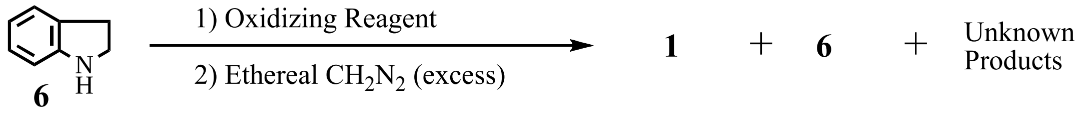
This simple method[12] meets our end and is suitable for the syntheses of various types of 1-hydroxyindoles as well as 1-hydroxytryptophan derivatives. This report is a full paper for the previous communications[12,14] in addition to new results.

RESULTS AND DISCUSSION

I. Simple and mild synthetic method for 1-hydroxyindole (metal oxide–H_2O_2 method)

Since the direct oxidation of indole gave tar or polymer under various reaction conditions, we next extensively examined oxidation conditions of 2,3-dihydroindole (**6**) with 30% H_2O_2 and metal oxides.[12] The formation of 1-hydroxyindole (**2**) in the reaction mixture was clearly deduced by thin layer monitoring. We know that **2** is quite unstable, but once **2** is converted to 1-methoxyindole (**1**), its stability increases to the extent which makes isolation possible,[3] enough to store for six years without any detectable decomposition under protection of light. Therefore, after oxidation of **6** at room temperature for 30 min with 30% H_2O_2 in the presence of metal oxides, we tried to isolate **1** by adding an excess amount of ethereal diazomethane to the reaction mixture. The results obtained under typical reaction conditions are summarized in Table 1.

Table 1. Preparation of 1-methoxyindole (**1**) from 2,3-dihydroindole (**6**)



Entry	Oxidizing Reagent (mol eq.)		Solvent	Reaction Temp. (°C)	Yield (%) of 1	Yield (%) of 6
1	$Na_2WO_4 \cdot 2H_2O$ (0.1)	30% H_2O_2 (1)	$MeOH$-H_2O (10:1, v/v)	13	15	21
2	"	" (3)	"	18	35	5
3	"	" (10)	"	17	50	0
4	$Na_2WO_4 \cdot 2H_2O$ (0.2)	30% H_2O_2 (1)	"	18	24	18
5	"	" (3)	"	16	40	4
6	"	" (10)	"	16	52	0
7	$Na_2WO_4 \cdot 2H_2O$ (1.0)	30% H_2O_2 (1)	"	18	14	28
8	"	" (3)	"	18	5	3
9	"	" (10)	"	16	0	0
10	$2Na_2O \cdot P_2O_5 \cdot 12WO_4 \cdot 18H_2O$ (0.2)	30% H_2O_2 (1)	"	14	26	29
11	"	" (3)	"	15	41	11
12	"	" (10)	"	15	58	0
13	$Na_2WO_4 \cdot 2H_2O$ (0.2)	Urea•H_2O_2 (10)	"	17	54	0
14	*m*-Chloroperbenzoic acid (1.0)		Acetone–CH_2Cl_2 (1:1, v/v)	0	35	0
15	"		CH_2Cl_2	0	40	0

As a result, we have found that sodium tungstate (Entries 1–9) and sodium phosphotungstate (Entries 10–12) are superior oxidizing catalyst to sodium molybdate and oxone. Comparing the results of Entries 1–3, 4–6, and 7–9, the employment of 0.2 mol eq. of sodium tungstate is found to be superior to 0.1 and

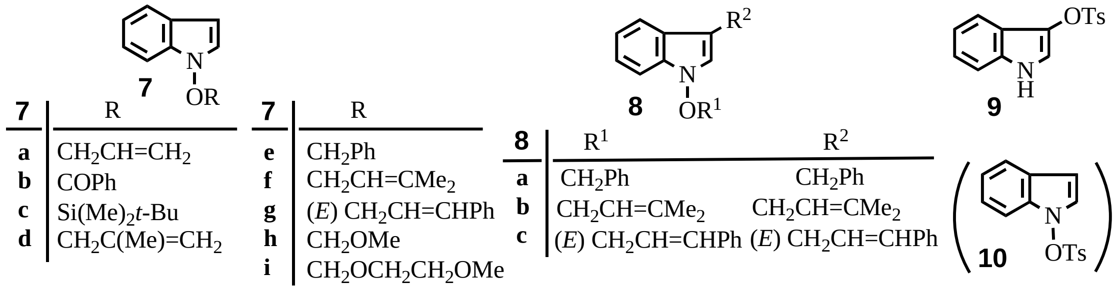
1.0 mol eq. Comparisons of Entries 1–3 and/or 4–6 recommend the use of 10 mol eq. of 30% H_2O_2. Urea·H_2O_2 addition compound can be used instead of 30% H_2O_2 to give **1** in 54% yield (Entry 13).

For the preparation of **1**, *m*-chloroperbenzoic acid was also applicable in acetone or CH_2Cl_2 (Entries 14, 15). Since it is powerful oxidizing agent, reaction was performed at 0 °C for 5 min. So the control of the reaction is more difficult than the metal oxide–H_2O_2 method.

Thus, we could establish a simple and mild synthetic method for 1-methoxyindole which works in the presence of H_2O. Employing the method we can now obtain **1** in the range of 50–58% yield from **6** in one pot operation under the reaction conditions described in the Entries 3, 6, 12, and 13.

II. Trapping of 1-hydroxyindole with alkyl, alkenyl, acyl, silyl halides, etc.

As shown in Table 1,[12] the presence of unstable 1-hydroxyindole (**2**) in the oxidation reaction mixture was confirmed by converting it into 1-methoxyindole (**1**) by methylation with diazomethane. Instead of diazomethane, a mixture of Me_2SO_4 and K_2CO_3 was also found to be successful to obtain **1** in good yield.



7	R
a	$CH_2CH=CH_2$
b	COPh
c	$Si(Me)_2t$-Bu
d	$CH_2C(Me)=CH_2$
e	CH_2Ph
f	$CH_2CH=CMe_2$
g	(*E*) $CH_2CH=CHPh$
h	CH_2OMe
i	$CH_2OCH_2CH_2OMe$

8	R^1	R^2
a	CH_2Ph	CH_2Ph
b	$CH_2CH=CMe_2$	$CH_2CH=CMe_2$
c	(*E*) $CH_2CH=CHPh$	(*E*) $CH_2CH=CHPh$

Figure 2

We next tried to trap **2** as various 1-alkoxyindoles.[14c] Thus, the addition of allyl bromide and K_2CO_3 into the oxidation reaction mixture at room temperature for 1.5 h afforded 1-allyloxyindole (**7a**, Figure 2) in 44% yield. Under similar reaction conditions, when benzoyl chloride, *t*-butyldimethylsilyl chloride, and methallyl chloride were employed, 1-benzoyloxy- (**7b**), 1-*t*-butyldimethylsilyloxyindole (**7c**), and 1-methallyloxyindole (**7d**) were provided in 49, 47, and 6% yields, respectively. In the reaction with benzyl bromide, 1-benzyloxyindole (**7e**) and 3-benzyl-1-benzyloxyindole (**8a**) were isolated in 47 and 5% yields, respectively. Similarly, the reaction with prenyl bromide and cinnamyl bromide provided 1-prenyloxy- (**7f**), 3-prenyl-1-prenyloxyindole (**8b**), 1-cinnamyloxy- (**7g**) and 3-cinnamyl-1-cinnamyloxyindole (**8c**), in 7, 4, 51, and 22% yields, respectively. In the reaction with tosyl chloride, 3-tosyloxyindole (**9**) was obtained in 10% yield, showing that **9** is the [3,3] sigmatropic rearranged product of initially formed 1-tosyloxyindole (**10**).

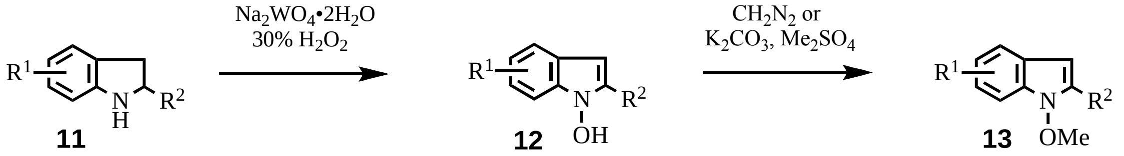
Benzene solution containing unstable **2** was obtained after extraction of the oxidation reaction mixture with benzene. Treating the benzene solution with methoxymethyl chloride (MOMCl), 2-methoxyethoxymethoxy chloride (MEMCl), and prenyl bromide in the presence of K_2CO_3 and phase transfer catalyst ($(n\text{-}Bu)_4NHSO_4$) afforded 1-methoxymethoxy- (**7h**), 1-[2-(methoxy)ethoxy]-

methoxyindole (**7i**), and 1-prenyloxyindole (**7f**) in 39, 11, and 18% yields, respectively.

Generation of pure **2** in THF can be realized by the treatment of 1-*t*-butyldimethylsilyloxyindole (**7c**) with (n-Bu)$_4$NF. Thus, the THF solution was reacted with MEMCl, MOMCl, and prenyl bromide in the presence of [(n-Bu)$_4$NHSO$_4$] and KO*t*-Bu to give **7h**, **7i**, and **7f** in 98, 98, and 100% yields, respectively.

III. Syntheses of various 1-hydroxy- and 1-methoxyindole derivatives

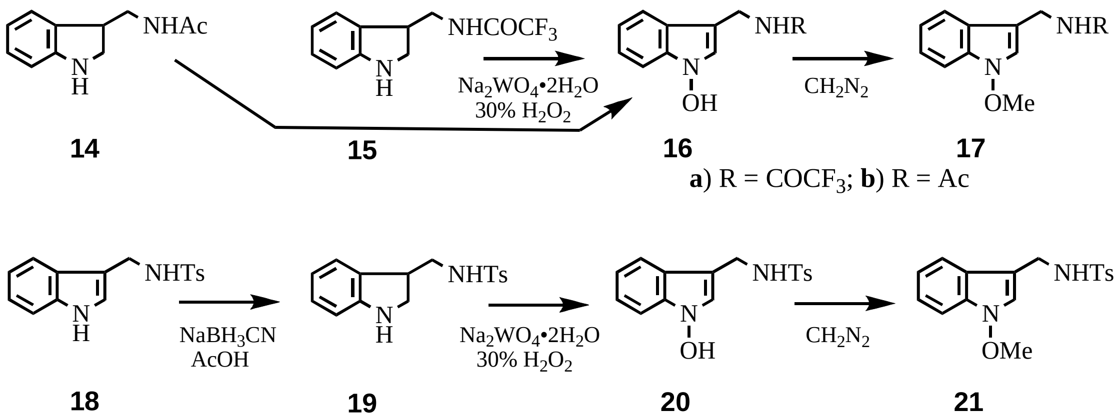
Application of the metal oxide–H$_2$O$_2$ method to various types of 2,3-dihydroindoles was examined. Thus, using sodium tungstate under the reaction conditions described in the Entry 6 (Table 1) without methylation, 1-hydroxy-6-nitro- (**12a**, Scheme 2), 1-hydroxy-5-nitro- (**12b**), and 1-hydroxy-2-phenylindoles (**12d**) were prepared[12] from the corresponding 2,3-dihydroindoles (**11a,b,d**) in 79, 26, and 56% yields, respectively. When CH$_2$N$_2$ is added to the reaction mixture obtained from the corresponding 2,3-dihydroindoles (**11a-d),** 1-methoxy-6-nitro- (**13a**), 1-methoxy-5-nitro- (**13b**), 1-methoxy-7-iodo (**13c**), and 1-methoxy-2-phenylindole[15] (**13d**) were prepared[12] in 60, 49, 26, and 67% yields, respectively. 1-Hydroxy-2-phenylindole (**12d**) was identical with the authentic sample prepared from benzoin oxime.[16] It is interesting to note that considerable oxidative decarboxylation was observed in the case of 2,3-dihydroindole-2-carboxylic acid (**11e**), resulting in the formation of **1** and the desired methyl 1-methoxyindole-2-carboxylate (**13f**) in 22% and 18% yields, respectively.



11–13	R^1	R^2
a	6-NO$_2$	H
b	5-NO$_2$	H
c	7-I	H
d	H	Ph
e	H	CO$_2$H
f	H	CO$_2$Me

Scheme 2

The metal oxide–H$_2$O$_2$ method was successfully applied to indole-3-methanamine derivatives[17] (Scheme 3). Employing Na$_2$WO$_4$·2H$_2$O and 30% H$_2$O$_2$, 3-trifluoroacetylaminomethyl-1-hydroxyindole (**16a**) was prepared in 71% yield from the corresponding 2,3-dihydroindole (**15**).



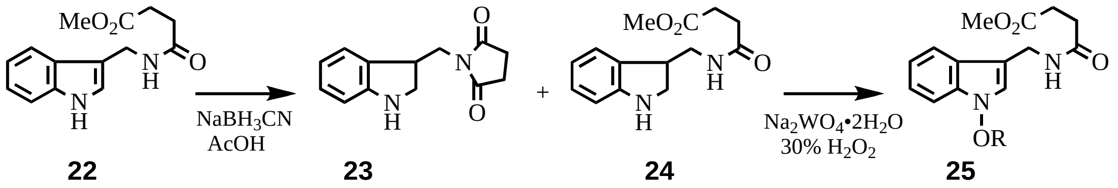
a) R = COCF$_3$; **b**) R = Ac

Scheme 3

When CH_2N_2 was added to the reaction mixture without isolation of **16a**, 77% yield of 1-methoxy-3-trifluoroacetylaminomethylindole (**17a**) was obtained from **15**. Similarly, 3-acetylaminomethyl-1-hydroxyindole (**16b**) was prepared in 66% yield from **14**. Subsequent treatment of **16b** with CH_2N_2 provided 85% yield of 3-acetylaminomethyl-1-methoxyindole (**17b**).

Similarly, 1-hydroxy-3-tosylaminomethylindole (**20**) was obtained in 68% yield from the corresponding 2,3-dihydroindole (**19**), which was derived from 3-tosylaminoindole (**18**) in 71% yield. Methylation of **20** with CH_2N_2 provided 96% yield of 1-methoxy-3-tosylaminomethylindole (**21**).

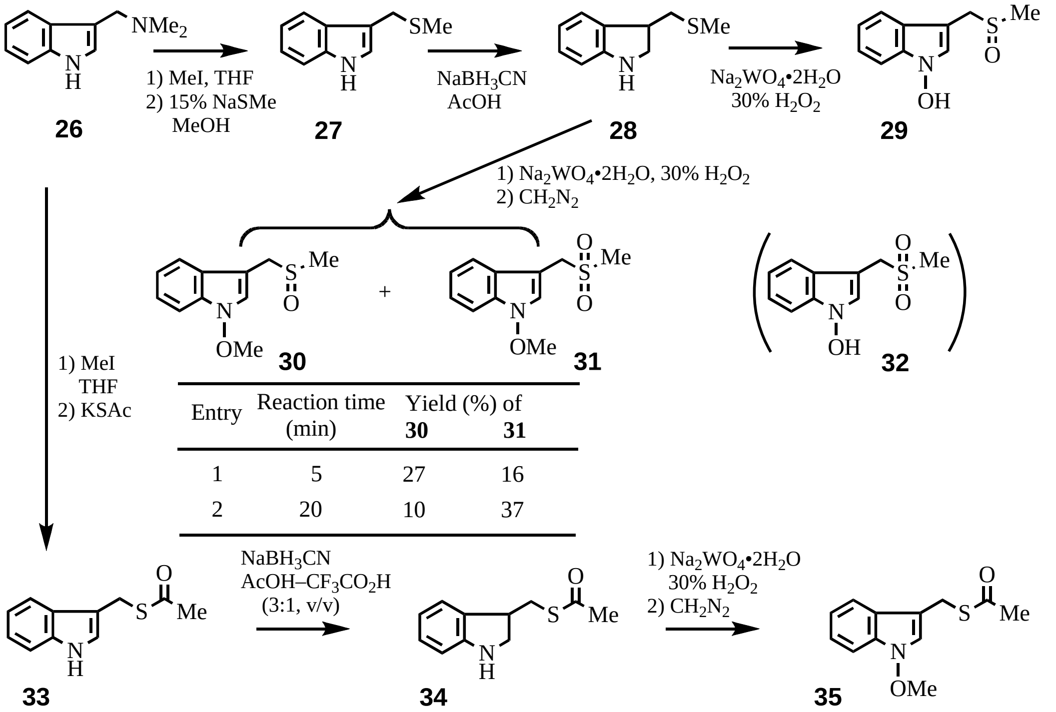
On the other hand, *N*-(2,3-dihydroindol-3-yl)methylsuccinimide (**23**, Scheme 4) and methyl *N*-(2,3-dihydroindol-3-yl)methylsuccinamate (**24**) are prepared by the reduction of methyl *N*-(indol-3-yl)-methylsuccinamate (**22**) with $NaBH_3CN$ in 15 and 82% yields, respectively. The metal oxide–H_2O_2 method worked well in the case of **24** to give the desired 1-hydroxyindole derivative (**25a**) in 63% yield. Subsequent methylation with CH_2N_2 provided the corresponding 1-methoxyindole (**25b**) in 95% yield.



Scheme 4

a) R = H; **b**) R = Me

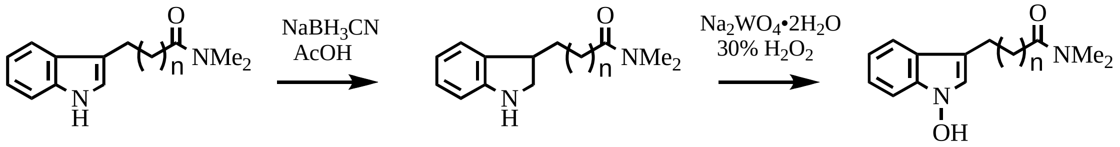
In the cases of indoles having sulfur atom in the molecule, the metal oxide–H_2O_2 method was also successful to give the desired 1-hydroxyindoles (Scheme 5). First, such starting materials as 3-methylthiomethylindole (**27**) and 3-acetylthiomethylindole (**33**) were prepared from gramine (**26**).



Entry	Reaction time (min)	Yield (%) of **30**	Yield (%) of **31**
1	5	27	16
2	20	10	37

Scheme 5

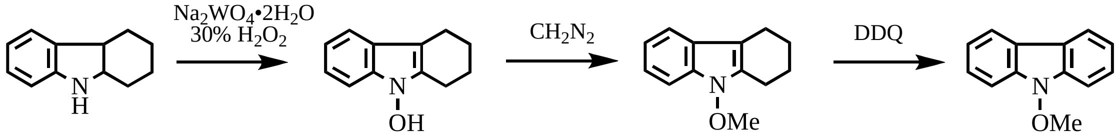
Namely, initial formation of quaternary ammonium salt, followed by the nucleophilic substitution reaction with NaSMe and KSCOMe afforded **27** and **33** in 80 and 79% yields, respectively. Reduction of **27** and **33** with $NaBH_3CN$ afforded 55 and 67% respective yields of the corresponding 2,3-dihydroindoles, **28** and **34**. Subsequent oxidation of **28** with $Na_2WO_4 \cdot 2H_2O$ and 30% H_2O_2 for 20 min, followed by methylation with CH_2N_2 provided 1-methoxy-3-methylsulfinylmethyl- (**30**) and 1-methoxy-3-methylsulfonylmethylindole (**31**) in 10 and 37% yields, respectively. When the reaction time was shortened to 5 min, over oxidation was decreased and the yield of **30** increased to 27% together with 16% yield of **31**. Under similar reaction conditions, omitting methylation, 1-hydroxy-3-methylsulfinylmethylindole (**29**) was isolated in 27% yield, while the formation of 1-hydroxy-3-methylsulfonylmethylindole (**32**) was not detected. Oxidation of **34** with $Na_2WO_4 \cdot 2H_2O$ and 30% H_2O_2, followed by methylation with CH_2N_2 provided 15% yield of 3-acetylthiomethyl-1-methoxyindole (**35**).



36 **a**) n = 0; **b**) n = 1 **37** **a**) n = 0; **b**) n = 1 **38** **a**) n = 0; **b**) n = 1

Scheme 6

The metal oxide–H_2O_2 method worked also well in the cases of 2,3-dihydro-*N,N*-dimethylindole-3-acetamide (**37a**, Scheme 6) and 2,3-dihydro-*N,N*-Dimethylindole-3-propionamide (**37b**). Both compounds were prepared by the corresponding indoles, **36a** and **36b**, in 97 and 98% yields, respectively, by the reduction with $NaBH_3CN$ in AcOH. Employing $Na_2WO_4 \cdot 2H_2O$ and 30% H_2O_2, **37a** and **37b** provided *N,N*-dimethyl-1-hydroxyindole-3-acetamide (**38a**) and *N,N*-Dimethyl-1-hydroxyindole-3-propionamide (**38b**) in 74 and 66% yields, respectively.

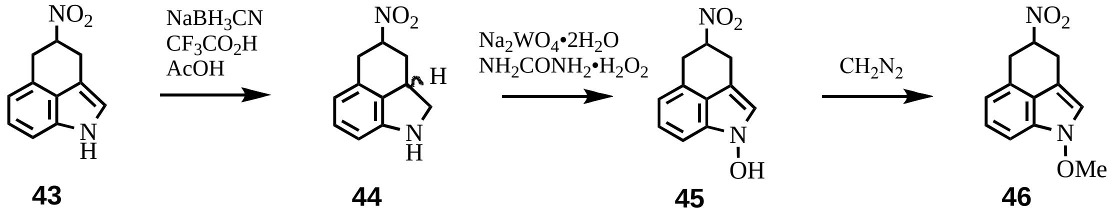


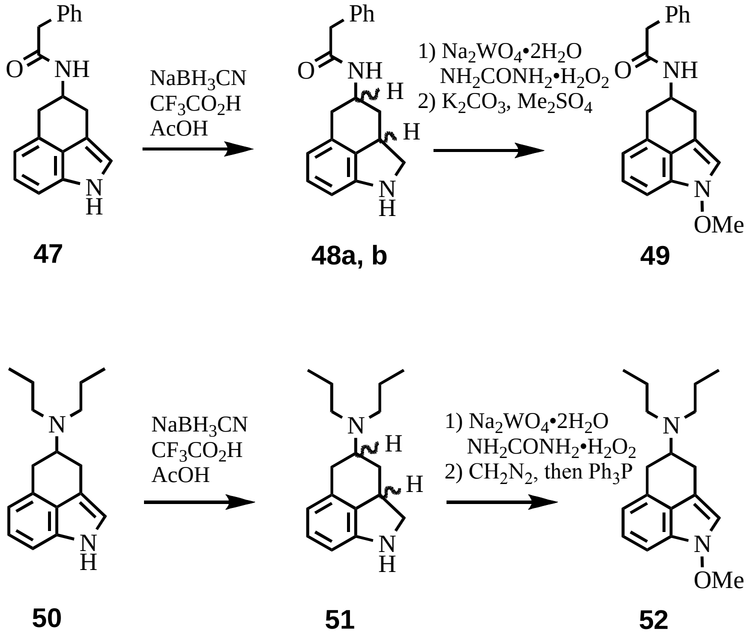
39 **40** **41** **42**

Scheme 7

Similarly, oxidation of 4a,9a-*cis*-1,2,3,4,4a,9a-hexahydrocarbazole (**39**, Scheme 7) afforded 9-hydroxy-1,2,3,4-tetrahydrocarbazole (**40**) in 65% yield. Subsequent methylation with CH_2N_2 provided 70% yield of 9-methoxy-1,2,3,4-tetrahydrocarbazole (**41**), which was also prepared directly from **39** in 55% yield. Oxidation of **41** with dichlorodicyanobenzoquinone in benzene afforded 9-methoxycarbazole (**42**) in 65% yield.

Compounds having benz[*cd*]indole skeletons[2b] were also suitable substrates for the metal oxide–H_2O_2 method (Scheme 8). Thus, reduction of 4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (**43**) with $NaBH_3CN$ in





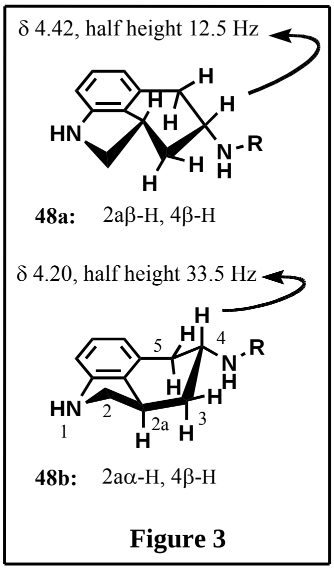


Figure 3

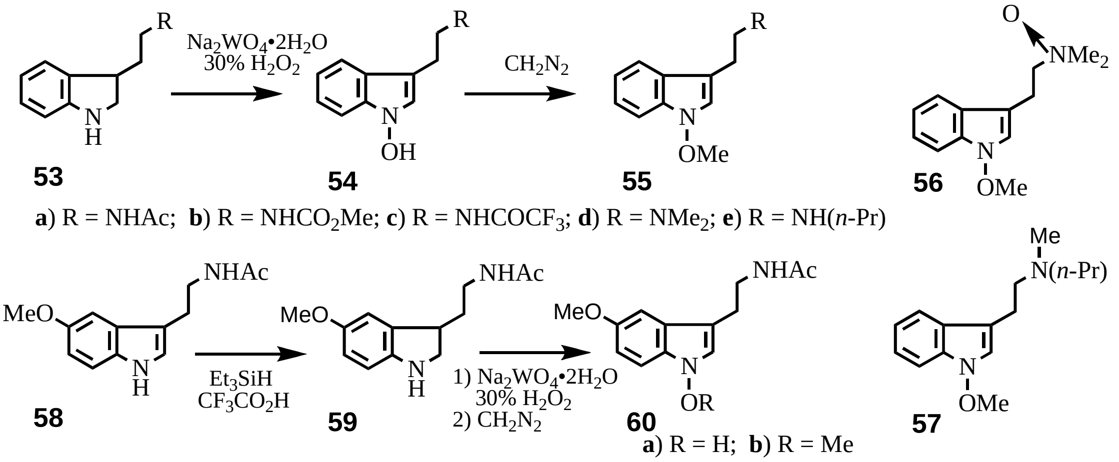
Scheme 8

AcOH–CF_3CO_2H provided 4-nitro-1,2,2a,3,4,5-hexahydrobenz[*cd*]indole (**44**) in 95% yield as a diastereoisomer's mixture. This mixture was subjected to the oxidation with $Na_2WO_4 \cdot 2H_2O$ and urea·H_2O_2 to afford 1-hydroxy-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (**45**) in 52% yield. Subsequent methylation with CH_2N_2 provided 1-methoxy-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (**46**) in 64% yield. Similar reduction of 4-(*N*-phenylacetylamino)-1,3,4,5-tetrahydrobenz[*cd*]indole (**47**) with $NaBH_3CN$ in AcOH–CF_3CO_2H gave a mixture of diastereoisomers, 4-(*N*-phenylacetylamino)-1,2,2aβ,3,4β,5- (**48a**) and 4-(*N*-phenylacetylamino)-1,2,2aα,3,4β,5-hexahydrobenz[*cd*]indole (**48b**) in 47 and 41% yields, respectively. The C(4) proton of the isomer (**48a)** resonates at δ 4.42 with half height coupling constant of 12.5 Hz, while that of **48b** at δ 4.20 with half height coupling constant of 33.5 Hz (Figure 3), suggesting that C3-, C4-, and C5-protons are all quasi-axial conformations. These data suggest both isomers have the assigned stereochemistry. Under the same oxidation conditions as **44** and after methylation with K_2CO_3 and Me_2SO_4, the mixture of **48a** and **48b** produced 1-methoxy-4-(*N*-phenylacetylamino)-1,3,4,5-tetrahydrobenz[*cd*]indole (**49**) in 40% yield.

A mixture of diastereoisomers, 4-*N*,*N*-di(*n*-propylamino)-1,2,2a,3,4,5-hexahydrobenz[*cd*]indole (**51**), prepared in 87% yield from 4-*N*,*N*-di(*n*-propylamino)-1,3,4,5-tetrahydrobenz[*cd*]indole (**50**) by the reduction with $NaBH_3CN$ in $AcOH–CF_3CO_2H$, provided 4-*N*,*N*-di(*n*-propylamino)-1-methoxy-1,3,4,5-tetrahydrobenz[*cd*]indole (**52**) in 46% yield after oxidation with urea·H_2O_2 and $Na_2WO_4·2H_2O$, followed by methylation with CH_2N_2.

IV. Application to tryptamine derivatives

Before application of the metal oxide–H_2O_2 method to tryptophan derivatives, we examined tryptamine derivatives (Scheme 9). Thus *N*b-acetyl-2,3-dihydrotryptamine (**53a**) produced *N*b-acetyl-1-hydroxytryptamine (**54a**) in 55% yield. Similarly, *N*b-methoxycarbonyl- (**53b**) and *N*b-trifluoroacetyl-2,3-dihydrotryptamine (**53c**) afforded 1-hydroxy-*N*b-methoxycarbonyl- (**54b**) and 1-hydroxy-*N*b-trifluoroacetyltryptamine (**54c**) in 67 and 72% yields, respectively. Methylation of **54a**, **54b**, and **54c** with CH_2N_2 afforded **55a**, **55b**, and **55c** in 85, 83, and 78% yields, respectively.



Scheme 9

When the *N*b-substituent has alkyl group, the metal oxide–H_2O_2 method was also effective. Thus, *N*b,*N*b-dimethyl-2,3-dihydrotryptamine (**53d**) afforded 55% yield of **54d**. After oxidation and methylation, the expected **55d** and *N*b,*N*b-dimethyl-1-methoxytryptamine-*N*-oxide (**56**) were formed in 26 and 31% yields, respectively. Compound **55d** is a natural product, lespedamine.[7b,18] In the case of *N*b-*n*-propylamino-2,3-dihydrotryptamine (**53e**), after oxidation and methylation, 1-methoxy-*N*b-*n*-propyltryptamine (**55e**) and 1-methoxy-*N*b-methyl-*N*b-*n*-propyltryptamine (**57**) were obtained in 49 and 9% yields, respectively. It should be mentioned that we have often encountered such type of *N*-methylation in the reaction of 1-hydroxyindolylamines with CH_2N_2.

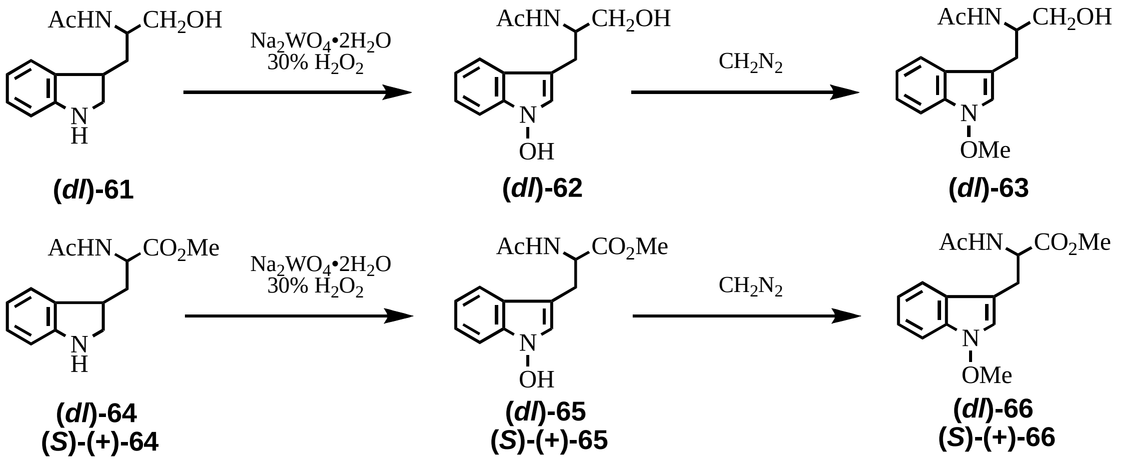
Reduction of melatonin (**58**) with Et_3SiH in CF_3CO_2H gave 2,3-dihydromelatonin (**59**) in 83% yield. The metal oxide–H_2O_2 method worked well on melatonin skeleton (**59**) to give 1-hydroxymelatonin (**60a**) in 58% yield. Further methylation with CH_2N_2 provided 1-methoxymelatonin (**60b**) in 75% yield.

V. Syntheses of methyl *N*b-acetyl-1-hydroxytryptophan methyl ester and related compounds

Based on the success of preparing 1-hydroxyindoles from simple structures to relatively complex molecules, application of the metal oxide–H_2O_2 method to (*dl*)-2-acetoamino-3-(2,3-dihydroindol-3-

yl)propanol ((*dl*)-**61**) was examined,[14b] employing $Na_2WO_4 \cdot 2H_2O$ and 30% H_2O_2, to provide (*dl*)-2-acetoamino-3-(1-hydroxyindol-3-yl)propanol ((*dl*)-**62**) in 30% yield (Scheme 10). After methylation of (*dl*)-**62** with CH_2N_2 77% yield of (*dl*)-2-acetoamino-3-(1-methoxyindol-3-yl)propanol ((*dl*)-**63**) was obtained.

Encouraged with this success, we examined the synthesis of 1-hydroxytryptophan derivative.[14b] The metal oxide–H_2O_2 method can give birth to thus far imagined (*dl*)- ((*dl*)-**65**) and (*S*)-(+)-*N*b-acetyl-1-hydroxytryptophan methyl ester ((*S*)-(+)-**65**) in 73 and 53% yields, respectively, from the corresponding 2,3-dihydroindoles, (*dl*)-**64** and (*S*)-(+)-**64**. Methylation of (*S*)-(+)-**65** and (*dl*)-**65** with CH_2N_2 afforded (*S*)-(+)-*N*b-acetyl-1-methoxytryptophan methyl ester ((*S*)-(+)-**66**) and (*dl*)-**66** in 78 and 83% yields, respectively.



(*dl*)-61 **(*dl*)-62** **(*dl*)-63**

(*dl*)-64
(*S*)-(+)-64

(*dl*)-65
(*S*)-(+)-65

(*dl*)-66
(*S*)-(+)-66

Scheme 10

Contrary to our expectation, (*dl*)-**65** and (*S*)-(+)-**65** are stable crystalline compounds enough to X-ray crystallographic analysis. Figure 4 is an ORTEP drawing of (*dl*)-**65**. It should be stressed that 1-hydroxy group is deviated from the indole plane by 15.2°.[3a-c,19] This is the reason why 1-hydroxytryptophan derivatives undergo nucleophilic substitution.[3a]

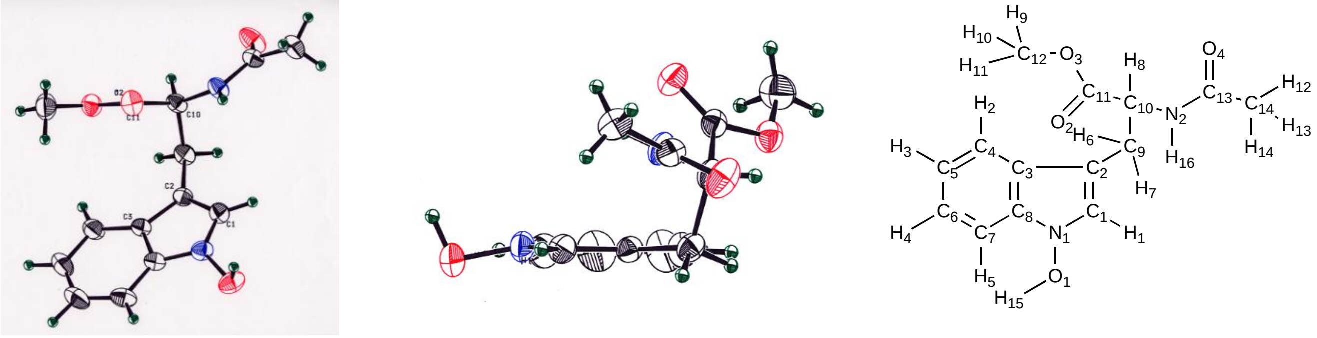


Figure 4. X-Ray Analysis of (dl)-65, R=0.039 and Rw=0.047

We have found that *N*b-acyl-1-hydroxytryptamines are novel and structurally simple α2-blocker[20] for the treatment of erectile dysfunction. Furthermore they have potent inhibitory activities on platelet aggregation.[21] Daikon and wasabi phytoalexins are weak fungicidal alkaloids[22] having stabilized

1-methoxyindole structure. Quite recently, we found that 1-hydroxy-*N*b-nonanoyltryptamine had potent hair growth action.[23] Judging from these facts: we hope that the chemistry of 1-hydroxyindole is a treasure field where a lot of new biologically active compounds are buried under the ground to be dug up.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared (IR) spectra were determined with a Shimadzu IR-420 spectrophotometer, and proton nuclear magnetic resonance (^{1}H-NMR) spectra with a JEOL JNM-GSX 500 or FX100S spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were recorded on a Hitachi M-80 or JEOL SX-102A spectrometer. Preparative thin-layer chromatography (p-TLC) was performed on Merck Kiesel-gel GF_{254} (Type 60) (SiO_2) or Merck Aluminum Oxide GF_{254} (Type 60/E) (Al_2O_3). Column chromatography was performed on silica gel (SiO_2, 100-200 mesh, from Kanto Chemical Co. Inc.) or activated alumina (Al_2O_3, 300 meshes, from Wako Pure Chemical Industries, Ltd.) throughout the present study.

1-Methoxyindole (1) from 2,3-dihydroindole (6) — General method A: A solution of $Na_2WO_4 \cdot 2H_2O$ (2.834 g, 8.42 mmol) in H_2O (40.0 mL) was added to a solution of **6** (5.015 g, 42.1 mmol) in MeOH (375 mL). 30% H_2O_2 (47.657 g, 421 mmol) was added to the resultant solution at 0 °C with stirring. After stirring for 15 min at rt (16 °C), K_2CO_3 (20.456 g, 147 mmol) and a solution of Me_2SO_4 (7.972 g, 631 mmol) in MeOH (25.0 mL) were added to the reaction mixture. After stirring for 90 min at rt (16 °C), brine (330 mL) was added and the whole was extracted with $CHCl_3$ (200 mL x 3). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a black oil, which was column-chromatographed on SiO_2 with $CHCl_3$–hexane (1:4, v/v) to give **1** (3.361 g, 54%).[7,8,12,14]

General method B (Table 1, Entry 3): A solution of $Na_2WO_4 \cdot 2H_2O$ (13.2 mg, 0.04 mmol) in H_2O (0.5 mL) was added to a solution of **6** (47.5 mg, 0.39 mmol) in MeOH (4.0 mL). 30% H_2O_2 (452.5 mg, 4.0 mmol) was added to the resultant solution at 0 °C with stirring. After stirring for 30 min at rt (17 °C), ethereal CH_2N_2 (excess) was added to the reaction mixture with stirring at rt until the starting material was not detected on tlc monitoring. Brine was added and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave oil, which was purified by p-TLC on SiO_2 with CH_2Cl_2–hexane (7:3, v/v) as a developing solvent. Extraction of a band having an *Rf* value of 0.92–0.79 with CH_2Cl_2 afforded **1** (29.6 mg, 50%). **Entry 6**: In the same procedure for Entry 3, $Na_2WO_4 \cdot 2H_2O$ (27.0 mg, 0.08 mmol), **6** (48.8 mg, 0.41 mmol), 30% H_2O_2 (464.9 mg, 4.10 mmol) were used. And the same work-up as Entry 3 afforded **1** (31.1 mg, 52%). **Entry 12**: In the same procedure for Entry 3, $2Na_2O \cdot P_2O_5 \cdot 12WO_4 \cdot 18H_2O$ (23.8 mg, 0.007 mmol), **6** (50.3 mg, 0.42 mmol), 30% H_2O_2 (479.2 mg, 4.22 mmol) were used. And the same work-up as Entry 3 afforded **1** (35.9

mg, 58%).

General method C (Table 1, Entry 13): A solution of $Na_2WO_4·2H_2O$ (591.4 mg, 1.79 mmol) in H_2O (10.0 mL) and urea·H_2O_2 compound (8.437 g, 89.64 mmol) were added to a solution of **6** (1.068 g, 8.96 mmol) in MeOH (100.0 mL) at 0 °C with stirring. After stirring at rt for 15 min, K_2CO_3 (22.300 g, 161.3 mmol) and then a solution of Me_2SO_4 (3.391 g, 26.9 mmol) in MeOH (10.0 mL) were added to the reaction mixture. After the same work-up as Entry 3, **1** (717.5 mg, 54%) was obtained. **Entry 14**: *m*-Chloroperbenzoic acid (231.6 mg, 0.94 mmol), (*n*-Bu)$_4$NHSO$_4$ (7.1 mg, 0.02 mmol) and sat. aq. $NaHCO_3$ (5.0 mL) were added to a solution of **6** (111.4 mg, 0.94 mmol) in acetone–CH_2Cl_2 (1:1, v/v, 5.0 mL) at 0 °C with stirring. After stirring for 5 min, brine was added. The whole was extracted with CH_2Cl_2 and ethereal CH_2N_2 (excess) was added to the extract. After stirring for 3 min, the solvent was evaporated under reduced pressure to leave oil, which was purified by column-chromatography on SiO_2 to afford **1** (47.5 mg, 35%). **Entry 15**: In the same procedure as Entry 14, solvent was changed to CH_2Cl_2 (5.0 mL) only, where *m*-chloroperbenzoic acid (223.2 mg, 0.90 mmol), (*n*-Bu)$_4$NHSO$_4$ (7.2 mg, 0.02 mmol), **6** (107.0 mg, 0.90 mmol), and sat. aq. $NaHCO_3$ (5.0 mL) were used. After usual work-up, **1** (52.9 mg, 40%) was obtained.

1-Allyloxyindole (7a) from 6 — Prepared according to the general method B, where $Na_2WO_4·2H_2O$ (611.6 mg, 1.85 mmol) in H_2O (10.0 mL) was added to a solution of **6** (1.108 g, 9.29 mmol) in MeOH (20.0 mL). 30% H_2O_2 (10.561 g, 101.2 mmol) in MeOH (20.0 mL) was added to the resultant solution at 0 °C with stirring. After stirring for 15 min at rt (20 °C), K_2CO_3 (3.86 g, 27.8 mmol) and allyl bromide (3.313 g, 27.4 mmol) were added and stirred at rt for 1.5 h. Brine was added and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave oil, which was purified by column-chromatography on SiO_2 with CH_2Cl_2–hexane (1:9, v/v) to give **7a** (711.3 mg, 44%). **7a**: colorless oil. IR (film): 3050, 1449, 1220, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.67 (2H, dt, *J*=6.6, 1.2 Hz), 5.21 (1H, m), 5.35 (1H, d, *J*=3.4 Hz), 5.86–6.25 (1H, m), 6.30 (1H, dd, *J*=3.5, 1.0 Hz), 6.94–7.61 (5H, m). High resolution MS *m/z*: Calcd for $C_{11}H_{11}NO$: 173.0782. Found: 173.0811.

Benzoyloxyindole (7b) from 6 — Prepared according to the general method B, where $Na_2WO_4·2H_2O$ (57.1 mg, 0.17 mmol) in H_2O (1.0 mL), **6** (103.0 mg, 0.86 mmol) in MeOH (8.0 mL), and 30% H_2O_2 (981.2 mg, 8.66 mmol) in MeOH (2.0 mL) were used. The reaction mixture was extracted with benzene and benzene layer was dried over Na_2SO_4. After filtering off Na_2SO_4, K_2CO_3 (583.3 mg, 3.89 mmol) and benzoyl chloride (483.2 mg, 2.59 mmol) were added to the benzene solution and stirred at rt for 1.5 h. H_2O was added and the whole was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave oil, which was purified by column-chromatography on SiO_2 with CH_2Cl_2–hexane (3:7, v/v) to give **7b** (100.8 mg, 49%). **7b**: mp

55.5–56.0 °C (lit.[19b] mp 49–50 °C, pale brown needles, recrystallized from MeOH). IR (KBr): 1767, 1600, 1446, 1323, 1236, 1184, 1075, 1039, 1012, 1002, 754, 729, 700 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 217 (4.50), 265 (3.94), 293 (3.60). ^{1}H-NMR ($CDCl_3$) δ: 6.53 (1H, d, *J*=3.7 Hz), 6.96–7.35 (4H, m), 7.35–7.82 (4H, m), 8.21 (2H, dd, *J*=8.2, 1.7 Hz). MS *m/z*: 237 (M^+). *Anal.* Calcd for $C_{15}H_{11}NO_2$: C, 75.94; H, 4.67; N, 5.90. Found: C, 75.85; H, 4.62; N, 5.84.

1-*t*-Butyldimethylsilyloxyindole (7c) from 6 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (75.9 mg, 0.23 mmol) in H_2O (1.3 mL), **6** (136.9 mg, 1.15 mmol) in MeOH (10.0 mL), and 30% H_2O_2 (1.304 g, 11.5 mmol) in MeOH (3.0 mL) were used. Silylation was carried out according to the method for **7b** with K_2CO_3 (715.5 mg, 5.18 mmol) and *t*-butyldimethylsilyl chloride (520.2 mg, 3.45 mmol). After usual work-up and purification, **7c** (133.1 mg, 47%) was obtained. **7c**: colorless oil. IR (film): 1472, 1436, 1266, 1074, 1035, 836, 787, 739 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.23 (6H, s), 1.10 (9H, s), 6.31 (1H, d, *J*=3.4 Hz), 7.01 (1H, t, *J*=6.6 Hz), 7.07 (1H, d, *J*=3.4 Hz), 7.17 (1H, t, *J*=6.6 Hz), 7.31 (1H, d, *J*=6.6 Hz), 7.53 (1H, d, *J*=6.6 Hz). High resolution MS *m/z*: Calcd for $C_{14}H_{21}NOSi$: 247.1390. Found: 247.1376.

1-Methallyloxyindole (7d) from 6 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (26.7 mg, 0.08 mmol) in H_2O (0.5 mL), **6** (48.0 mg, 0.40 mmol) in MeOH (4.0 mL), and 30% H_2O_2 (461.7 mg, 4.0 mmol) in MeOH (1.0 mL) were used. Methallylation was carried out with K_2CO_3 (253.3 mg, 1.80 mmol) and methallyl chloride (110.5 mg, 1.20 mmol). After usual work-up and purification, **7d** (4.2 mg, 6%) was obtained. **7d**: colorless oil. IR (film): 1653, 1450, 1323, 1222, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.97 (3H, t, *J*=1.2 Hz), 4.60 (2H, s), 5.03 (2H, m), 6.32 (1H, dd, *J*=3.4, 0.7 Hz), 7.00–7.63 (5H, m). High resolution MS *m/z*: Calcd for $C_{12}H_{13}NO$: 187.0972. Found: 187.0984.

1-Benzyloxyindole (7e) and 3-benzyl-1-benzyloxyindole (8a) from 6 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (60.3 mg, 0.18 mmol) in H_2O (1.0 mL), **6** (108.7 mg, 0.91 mmol) in MeOH (8.0 mL), and 30% H_2O_2 (1.036 g, 9.13 mmol) in MeOH (2.0 mL) were used. Benzylation was carried out with K_2CO_3 (568.1 mg, 4.11 mmol) and benzyl bromide (483.2 mg, 2.74 mmol). After usual work-up and purification, **7e** (96.0 mg, 47%) and **8a** (14.7 mg, 5%) were obtained. **7e**: colorless oil. IR (film): 1455, 1323, 1221, 1074, 1032, 756, 740, 697 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 5.15 (2H, s), 6.23 (1H, d, *J*=3.4 Hz), 6.98 (1H, d, *J*=3.4 Hz), 6.98–7.22 (2H, m), 7.22–7.44 (6H, m), 7.44–7.60 (1H, m). High resolution MS *m/z*: Calcd for $C_{15}H_{13}NO$: 223.0996. Found: 223.0992. **8a**: colorless oil. IR (KBr, film): 1494, 1450, 734, 695 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.00 (2H, s), 5.12 (2H, s), 6.11 (1H, s), 6.85–7.11 (14H, m). High resolution MS *m/z*: Calcd for $C_{22}H_{15}NO$: 313.1465. Found: 313.1468.

1-Prenyloxyindole (7f) and 3-prenyl-1-prenyloxyindole (8b) from 6 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (61.9 mg, 0.19 mmol) in H_2O (1.0 mL), **6** (111.2 mg, 0.93 mmol) in MeOH (8.0 mL), and 30% H_2O_2 (1.087 g, 10.1 mmol) in MeOH (2.0 mL) were used.

Prenylation was carried out with K_2CO_3 (470.6 mg, 6.84 mmol) and prenyl bromide (380.2 mg, 0.51 mmol). After usual work-up and purification **7f** (13.5 mg, 7%) and **8b** (9.3 mg, 4%) were obtained. **7f**: pale yellow oil. IR (film): 3050, 2980, 2930, 1670, 1450, 1324, 1222, 1075, 1030, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.48 (3H, s), 1.68 (3H, s), 4.54 (2H, d, *J*=7.9 Hz), 5.44 (1H, t, *J*=7.2 Hz), 6.21 (1H, dd, 3.6, 1.0 Hz), 6.88–7.50 (5H, m). High resolution MS *m/z*: Calcd for $C_{13}H_{15}NO$: 201.1153. Found: 201.1155. **8b**: pale red oil. IR (film): 2980, 2920, 1666, 1612, 1447, 1375, 1088, 1008, 735 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.58 (3H, s), 1.74 (3H, s), 1.76 (6H, s), 3.38 (2H, dd, *J*=7.0, 1.0 Hz), 4.60 (2H, d, *J*=7.5 Hz), 5.28–5.61 (2H, m), 6.94–7.56 (5H, m). High resolution MS *m/z*: Calcd for $C_{18}H_{23}NO$: 269.1753. Found: 269.1765.

1-Prenyloxyindole (7f) from 6 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (65.2 mg, 0.19 mmol) in H_2O (1.0 mL), **6** (116.4 mg, 0.98 mmol) in MeOH (9.0 mL), and 30% H_2O_2 (1.143 g, 10.0 mmol) in MeOH (1.0 mL) were used. Prenylation was carried out according to the method for **7b** with NEt_3 (1.4 mL, 9.8 mmol), $(n\text{-Bu})_4NBr$ (32.3 mg, 0.10 mmol), and prenyl bromide (1.339 g, 8.71 mmol). After usual work-up and purification, **7f** (35.7 mg, 18%) was obtained.

1-Prenyloxyindole (7f) from 7c — A solution of prenyl bromide (112.2 mg, 0.72 mmol) in anhydrous THF (1.0 mL), KO*t*-Bu (91.7 mg, 0.82 mmol), and a solution of $(n\text{-Bu})_4NF \cdot 3H_2O$ (120.6 mg, 0.34 mmol) in anhydrous THF (1.0 mL) were added to a solution of **7c** (75.4 mg, 0.37 mmol) in anhydrous THF (1.0 mL) at rt. After usual work-up and purification, **7f** (75.4 mg, 100%) was obtained.

1-Cinnamyloxyindole (7g) and 3-cinnamyl-1-cinnanyloxyindole (8c) from 6 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (57.9 mg, 0.17 mmol) in H_2O (1.0 mL). **6** (104.1 mg, 0.87 mmol) in MeOH (8.0 mL), and 30% H_2O_2 (991.9 mg, 8.7 mmol) in MeOH (2.0 mL) were used. Cinnamylation was carried out with K_2CO_3 (544.6 mg, 3.91 mmol) and cinnamyl bromide (520.8 mg, 2.61 mmol). After usual work-up and purification, **7g** (110.5 mg, 51%) and **8c** (80.2 mg, 22%) were obtained. **7g**: pale brown oil. IR (film): 3050, 3017, 2920, 1495, 1449, 1323, 1221, 1074, 1030, 965, 757, 738, 691 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.81 (2H, d, *J*=6.0 Hz), 6.31 (1H, dd, *J*=3.5, 1.0 Hz), 6.25–6.72 (2H, m), 6.96–7.60 (10H, m). High resolution MS *m/z*: Calcd for $C_{17}H_{15}NO$: 249.1148. Found: 249.1150. **8c**: pale yellow oil. IR (film): 3050, 3017, 2920, 1496, 1449, 964, 738, 692 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.58 (2H, dd, *J*=5.3, 1.0 Hz), 4.77 (2H, d, *J*=5.5 Hz), 6.13–6.72 (4H, m), 6.93–7.61 (15H, m). High resolution MS *m/z*: Calcd for $C_{26}H_{23}NO$: 365.1800. Found: 365.1789.

1-Methoxymethoxyindole (7h) from 6 — Prepared according to the general method C, where $Na_2WO_4 \cdot 2H_2O$ (63.7 mg, 0.19 mmol) in H_2O (1.0 mL), **6** (115.1 mg, 0.96 mmol) in MeOH (10.0 mL), and urea·H_2O_2 compound (927.2 mg, 9.66 mmol) were used. Methoxymethoxylation was carried out according to the method for **7b** with K_2CO_3 (2.403 g, 17.38 mmol), $(n\text{-Bu})_4NBr$ (31.1 mg, 0.09 mmol), and methoxymethyl chloride (233.3 mg, 2.89 mmol) in benzene (1.0 mL). After usual work-up and purification, **7h** (66.0 mg, 39%) was obtained. **7h**: mp 27.0–27.5 °C (colorless prisms, recrystallized from hexane). IR (KBr): 2970, 1445, 1330, 1230, 1182, 1100, 1089, 1030, 920, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.66 (3H, s), 5.17 (2H, s), 6.37 (1H, d, *J*=3.5 Hz), 7.11 (1H, t, *J*=7.4 Hz), 7.20–7.26 (3H, m), 7.42 (1H, d, *J*=8.1 Hz), 7.58 (1H, d, *J*=7.9 Hz). MS *m/z*: 177 (M$^+$). *Anal.* Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.64; H, 6.33; N, 7.86.

1-Methoxymethoxyindole (7h) from 7c — A solution of methoxymethyl chloride (56.2 mg, 0.69 mmol) in anhydrous THF (1.0 mL), KO*t*-Bu (91.2 mg, 0.81 mmol), and a solution of $(n\text{-Bu})_4NF\cdot 3H_2O$ (111.1 mg, 0.35 mmol) in anhydrous THF (1.0 mL) were added to a solution of **7c** (85.4 mg, 0.34 mmol) in anhydrous THF (1.0 mL) at rt. After usual work-up and purification, **7h** (59.7 mg, 98%) was obtained.

1-(2-Methoxyethoxymethoxy)indole (7i) from 6 — Prepared according to the general method B, where $Na_2WO_4\cdot 2H_2O$ (61.4 mg, 0.19 mmol) in H_2O (1.0 mL), **6** (111.1 mg, 0.93 mmol) in MeOH (9.0 mL), and 30% H_2O_2 (1.073 g, 9.46 mmol) in MeOH (1.0 mL) were used. Methoxyethoxymethoxylation was carried out according to the method for **7b** with NEt_3 (2.6 mL, 18.6 mmol), $(n\text{-Bu})_4NBr$ (29.9 mg, 0.09 mmol), and 2-methoxyethoxymethyl chloride (1.038 g, 8.35 mmol). After usual work-up and purification, **7i** (23.2 mg, 11%) and indole (2.2 mg, 2%) were obtained. **7i**: colorless oil. IR (KBr): 2920, 2890, 1450, 1320, 1220, 1105, 1030, 920, 875, 845, 760, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.41 (3H, s), 3.59–3.65 (2H, m), 3.93–3.99 (2H, m), 5.27 (2H, s), 6.36 (1H, dd, *J*=3.5, 1.0 Hz), 7.10 (1H, ddd, *J*=7.9, 6.9, 1.0 Hz), 7.22 (1H, ddd, *J*=8.3, 6.9, 1.0 Hz), 7.33 (1H, d, *J*=3.5 Hz), 7.42 (1H, dd, *J*=8.3, 1.0 Hz), 7.58 (1H, ddd, *J*=7.9, 1.0, 1.01 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{15}NO_3$: 221.1050. Found: 221.1049.

1-(2-Methoxyethoxymethoxy)indole (7i) from 7c — A solution of 2-methoxyethoxymethyl chloride (98.8 mg, 0.79 mmol) in anhydrous THF (1.0 mL), KO*t*-Bu (97.2 mg, 0.86 mmol), and a solution of $(n\text{-Bu})_4NF\cdot 3H_2O$ (125.8 mg, 0.39 mmol) in anhydrous THF (1.0 mL) were added to a solution of **7c** (94.9 mg, 0.38 mmol) in anhydrous THF (1.0 mL) at rt. After usual work-up and purification, **7i** (83.3 mg, 98%) was obtained.

3-Tosyloxyindole (9) from 6 — Prepared according to the general method B, where $Na_2WO_4\cdot 2H_2O$ (559.6 mg, 1.69 mmol) in H_2O (10.0 mL), **6** (1.009 g, 8.48 mmol) in MeOH (80.0 mL), and 30% H_2O_2 (9.610 g, 84.8 mmol) in MeOH (20.0 mL) were used. Tosylation was carried out with K_2CO_3 (5.270 g, 38.2 mmol) and tosyl chloride (4.848 g, 25.5 mmol). After usual work-up and purification, **9** (252.2 mg, 10%) was obtained. **9**: mp 112–114°C (colorless prisms, recrystallized from MeOH). IR (KBr): 3390, 3120, 1595, 1453, 1370, 1190, 1175, 1090, 1063, 843, 812, 742, 723, 657, 555, 545, 503 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.41 (3H, s), 6.95–7.30 (8H, m), 7.75 (2H, d, *J*=8.3 Hz). MS *m/z*: 287 (M$^+$). *Anal.* Calcd for $C_{15}H_{13}NO_3S$: C, 62.70; H, 4.56; N, 4.87. Found: C, 62.70; H, 4.53; N, 4.72.

1-Hydroxy-6-nitroindole (12a) from 11a — Prepared according to the general method B, where $Na_2WO_4\cdot 2H_2O$ (18.8 mg, 0.06 mmol), **11a** (101.3 mg, 0.57 mmol) in MeOH (10.0 mL), and 30% H_2O_2 (0.58 mL, 5.7 mmol) were used. After usual work-up and purification, **12a** (80.1 mg, 79%) was obtained.

12a: mp 153–155 °C (decomp., pale orange needles, recrystallized from $CHCl_3$). IR (KBr): 3240, 1617, 1586, 1514, 1481, 1357, 1332, 1280, 1095, 1056, 863, 811, 751, 731 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 264 (4.01), 321 (3.94), 361 (3.73). ^{1}H-NMR ($CDCl_3$–CD_3OD. 95:5, v/v) δ: 6.43 (1H, d, *J*=3.3 Hz), 7.51 (1H, d, *J*=3.3 Hz), 7.61 (H, d, *J*=8.8 Hz), 7.95 (1H, dd, *J*=8.8, 2.1 Hz), 8.42 (1H, dd, *J*=2.1 Hz). MS *m/z*: 178 (M^+). *Anal*. Calcd for $C_8H_6N_2O_3$: C, 53.94; H, 3.39; N, 15.72. Found: C, 54.03; H, 3.45; N, 15.73.

1-Hydroxy-5-nitroindole (12b) from 11b — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (81.6 mg, 0.25 mmol) in H_2O (2.0 mL), **11b** (202.9 mg, 1.23 mmol) in MeOH (20.0 mL), and 30% H_2O_2 (1.26 mL, 12.3 mmol) were used. After usual work-up and purification, **11b** (52.7 mg, recovery, 26%)**,** 5-nitroindole (9.4 mg, 5%), and **12b** (91.7 mg, 42%) were obtained. The mixture of **11b** and 5-nitroindoe was successfully separated by column chromatography on Al_2O_3 with benzene–EtOAc (10:1, v/v). **12b**: mp 175–176 °C (decomp., brown needles, recrystallized from $CHCl_3$). IR (KBr, film): 1613, 1584, 1508, 1358, 1339, 756, 720 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 254 (4.07), 275 (4.20), 331 (3.81). ^{1}H-NMR ($CDCl_3$–CD_3OD, 95:5, v/v) δ: 6.45 (H, d, *J*=3.4 Hz), 7.52 (1H, d, *J*=3.4 Hz), 7.60 (1H, d, *J*=8.9 Hz), 7.98 (1H, dd, *J*=8.8, 2.2 Hz), 8.38 (1H, br s). MS *m/z*: 178 (M^+). *Anal*. Calcd for $C_8H_6N_2O_3$: C, 53.94; H, 3.39; N, 15.72. Found: C, 53.66; H, 3.37; N, 15.71.

1-Hydroxy-2-phenylindole (12d) from 2,3-dihydro-2-phenylindole (11d) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (17.4 mg, 0.053 mmol), **11d** (51.5 mg, 0.26 mmol) in 4.0 mL of MeOH, and 30% H_2O_2 (299.4 mg, 2.64 mmol) in MeOH (1.0 mL) were used. The crude product was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (98:2, v/v) as a developing solvent to afford **12d** (30.9 mg, 56%). **12d**: mp 174.0–175.0 °C (decomp., pale yellow needles, recrystallized from $CHCl_3$, lit.,[16] mp 175 °C). IR (KBr): 2400, 1625, 1370, 756, 740, 683 cm^{-1}. ^{1}H-NMR (10% CD_3OD in $CDCl_3$) δ: 6.52 (1H, s, C3–H, deuterated during measuring), 6.88–7.62 (7H, m), 7.68–7.92 (2H, m). MS *m/z*: 209 (M^+). Identical with the authentic sample prepared from benzoin oxime.[16]

1-Methoxy-6-nitroindole (13a) from 2,3-dihydro-6-nitroindole (11a) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (9.0 mg, 0.027 mmol), **11a** (44.8 mg, 0.27 mmol) in MeOH (3.0 mL), and 30% H_2O_2 (309.7 mg, 2.73 mmol) were used. After methylation, usual work-up, and purification, **13a** (31.3 mg, 60%) and 6-nitroindole (3.8 mg, 9%) were obtained. **13a**: mp 90.0–91.0 °C (yellow needles, recrystallized from MeOH). IR (KBr): 1613, 1584, 1508, 1358, 1339, 756, 720 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.17 (3H, s), 6.45 (1H, dd, *J*=3.4 and 1.0 Hz), 7.52 (1H, d, *J*=3.4 Hz), 7.60 (1H, d, *J*=8.8 Hz), 7.98 (1H, dd, *J*=8.8, 2.2 Hz), 8.38 (1H, br d, *J*=2.2 Hz). MS *m/z*: 192 (M^+). *Anal*. Calcd for $C_9H_8N_2O_3$: C, 56.25; H, 4.20; N, 14.58. Found: C, 56.21; H, 4.17; N, 14.73.

1-Methoxy-5-nitroindole (13b) from 2,3-dihydro-5-nitroindole (11b) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (16.4 mg, 0.05 mmol), **11b** (40.8 mg, 0.29 mmol) in MeOH (3.0 mL), and 30% H_2O_2 (282.0 mg, 2.48 mmol) in MeOH (2.0 mL) were used. After methylation, usual work-up, and purification, **13b** (23.2 mg, 49%), unreacted starting material (17.1 mg, 42%), and 5-nitroindole (1.1 mg, 3%) were obtained. **13b**: mp 89.5–90.5 °C (yellow plates, recrystallized from MeOH). IR (KBr): 1615, 1580, 1512, 1324, 1066, 737 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.14 (3H, s), 6.54 (1H, dd, *J*=3.6, 0.8 Hz), 7.38 (1H, d, *J*=3.6 Hz), 7.44 (1H, d, *J*=9.0 Hz), 8.12 (1H, dd, *J*=9.0, 2.1 Hz), 8.54 (1H, d, *J*=2.1 Hz). MS *m/z*: 192 (M^+). *Anal.* Calcd for $C_9H_8N_2O_3$: C, 56.25; H, 4.20; N, 14.58. Found: C, 56.25; H, 4.17; N, 14.50.

7-Iodo-1-methoxyindole (13c) from 2,3-dihydro-7-iodoindole (11c) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (14.7 mg, 0.045 mmol), **11c** (218.7 mg, 0.89 mmol) in MeOH (5.0 mL), and 30% H_2O_2 (303.6 mg, 2.68 mmol) in MeOH (4.0 mL) were used. After usual work-up and purification, **13c** (62.6 mg, 26%), 7-iodoindole (9.9 mg, 5%), and unreacted starting material (117.5 mg, 54%) were obtained. **13c**: mp 35.0–35.5 °C (colorless plates, recrystallized from hexane). IR (KBr): 1544, 1333, 1276, 1033, 948, 775 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.08 (3H, s), 6.31 (1H, d, *J*=3.4 Hz), 6.82 (1H, t, *J*=7.6 Hz), 7.29 (1H, d, *J*=3.4 Hz), 7.54 (1H, dd, *J*=7.6, 1.0 Hz), 7.68 (1H, dd, *J*=7.6, 1.0 Hz). MS *m/z*: 273 (M^+). *Anal.* Calcd for C_9H_8INO: C, 39.59; H, 2.95; N, 5.12. Found: C, 39.53; H, 2.99; N, 5.13.

1-Methoxy-2-phenylindole (13d) — a) From 2,3-dihydro-2-phenylindole (11d); prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (17.7 mg, 0.054 mmol), **11d** (52.3 mg, 0.27 mmol) in MeOH (4.0 mL), and 30% H_2O_2 (304.1 mg, 2.68 mmol) in MeOH (1.0 mL) were used. After usual work-up and purification, **13d** (40.0 mg, 67%) and 2-phenylindole (3.9 mg, 8%) were obtained. **13d**: mp 47.0–48.0 °C (lit.,[15] mp 49–51 °C, pale yellow plates, recrystallized from MeOH). IR (KBr): 1597, 956, 760, 741 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.73 (3H, s), 6.56 (1H, s), 7.00–7.66 (7H, m), 7.73–7.91 (2H, m). *Anal.* Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87; N, 6.27. Found: C, 80.77; H, 5.91; N, 6.04. **b) From 1-hydroxy-2-phenylindole (12d)**: ethereal CH_2N_2 (excess) was added to a solution of **12d** (30.9 mg, 0.15 mmol) in MeOH (3.0 mL) with stirring at rt until the starting material was not detected on tlc monitoring. The crude product was purified by p-TLC on SiO_2 with EtOAc–hexane (1:4, v/v) as a developing solvent to afford **13d** (28.3 mg, 86%).

Methyl 1-methoxyindole-2-carboxylate (13f) from 2,3-dihydroindole-2-carboxylic acid (11e) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (20.8 mg, 0.063 mmol), **11e** (51.5 mg, 0.31 mmol) in MeOH (4.0 mL), and 30% H_2O_2 (358.2 mg, 3.16 mmol) in MeOH (1.0 mL) were used. After usual work-up and purification, **1** (10.4 mg, 22%) and **13f** (11.4 mg, 18%) were obtained. **13f**: mp 40.5–41.5 °C (colorless plates, recrystallized from MeOH). IR (KBr): 1723, 1239, 1209, 1085, 738 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.93 (3H, s), 4.19 (3H, s), 7.08 (1H, d, *J*=1.2 Hz), 7.02–7.54 (3H, m), 7.61 (1H, dt, *J*=7.9, 1.0 Hz). MS *m/z*: 205 (M^+). *Anal.* Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.19; H, 5.45; N, 7.00.

1-Hydroxy-*N*b-trifluoroacetylindole-3-methanamine (16a) from 15 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (148.7 mg, 0.45 mmol) in H_2O (4.5 mL), **15** (551.2 mg, 2.26 mmol) in MeOH (50.0 mL), and 30% H_2O_2 (2.575 g, 22.6 mmol) in MeOH (5.0 mL) were used. After usual work-up, the crude product was column-chromatographed on SiO_2 with EtOAc–hexane (3:1, v/v) to give **16a** (414.5 mg, 71%). **16a**: mp 123.5–124.5 °C (colorless needles, recrystallized from CH_2Cl_2). IR (KBr): 3390, 3305, 1694, 1566, 1541, 1353, 1252, 1206, 1178, 1169, 1151, 1103, 755, 747, 682 cm^{-1}. ^1H-NMR (CD_3OD) δ: 4.59 (2H, s), 7.03 (1H, dd, *J*=8.0, 0.9 Hz), 7.17 (1H, dd, *J*=8.0, 0.9 Hz), 7.28 (1H, s), 7.38 (1H, ddd, *J*=8.0, 0.9, 0.7 Hz), 7.57 (1H, ddd, *J*=8.0, 0.9, 0.7 Hz). High resolution MS *m/z*: Calcd for $C_{11}H_9F_3N_2O_2$: 258.0615. Found: 258.0617.

3-Acetylaminomethyl-1-hydroxyindole (16b) from 3-acetylaminomethyl-2,3-dihydroindole (14) — Prepared according to the method for **16a**, where $Na_2WO_4 \cdot 2H_2O$ (149.8 mg, 0.45 mmol) in H_2O (4.5 mL), **14** (688.0 mg, 3.16 mmol) in MeOH (55.0 mL), and 30% H_2O_2 (2.574 g, 22.7 mmol) in MeOH (5.0 mL) were used. After usual work-up and purification, **16b** (302.5 mg, 66%) was obtained. **16b**: mp 132.5–133.0 °C (pale yellow prisms, recrystallized from CH_2Cl_2). IR (KBr): 3330, 2810, 1603, 1538, 1406, 1366, 1320, 1244, 1103, 1028, 1006, 743, 667, 570 cm^{-1}. ^1H-NMR (5% CD_3OD–$CDCl_3$) δ: 1.96 (3H, s), 4.49 (2H, s), 7.08 (1H, dd, *J*=7.7, 7.3 Hz), 7.18 (1H, s), 7.22 (1H, dd, *J*=8.1, 7.3 Hz), 7.45 (1H, d, *J*=8.1 Hz), 7.54 (1H, d, *J*=7.7 Hz). MS *m/z*: 204 (M^+). *Anal.* Calcd for $C_{11}H_{12}N_2O_2 \cdot 1/8H_2O$: C, 63.99; H, 5.98; N, 13.57. Found: C, 64.15; H, 5.79; N, 13.60.

1-Methoxy-*N*b-trifluoroacetylindole-3-methanamine (17a) from 2,3-dihydro-3-trifluoroacetylindole-3-methanamine (15) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (14.8 mg, 0.04 mmol) in H_2O (0.5 mL), **15** (54.1 mg, 0.22 mmol) in MeOH (6.0 mL), and 30% H_2O_2 (266.6 mg, 2.35 mmol) in MeOH (1.0 mL) were used. After methylation and work-up, the product was purified by column-chromatography on SiO_2 with $CHCl_3$–hexane (3:1, v/v) to give **17a** (46.5 mg, 77%). **17a**: mp 70.5–71.0 °C (colorless prisms, recrystallized from benzene–hexane). IR (KBr): 3290, 1715, 1695, 1561, 1208, 1180, 1159, 738, 722 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 219 (4.57), 272 (3.73), 288 (3.72). ^1H-NMR ($CDCl_3$) δ: 4.10 (3H, s), 4.68 (2H, d, *J*=5.3 Hz), 6.43 (1H, br s), 7.18 (1H, t, *J*=7.8 Hz), 7.31 (1H, s), 7.31 (1H, t, *J*=7.8 Hz), 7.46 (1H, d, *J*=7.8 Hz), 7.57 (1H, d, *J*=7.8 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{11}F_3N_2O_2$: 272.0772. Found: 272.0756.

1-Methoxy-*N*b-acetylindole-3-methanamine (17b) from 3-acetylaminomethyl-2,3-dihydroindole (14) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (22.8 mg, 0.07 mmol) in H_2O (0.5 mL), **14** (64.9 mg, 0.34 mmol) in MeOH (6.0 mL), and 30% H_2O_2 (388.0 mg, 3.42 mmol) in MeOH (1.0 mL) were used. After methylation and work-up, the product was purified by column-chromatography on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (100:1:0.1, v/v) to give **17b** (43.6 mg, 59%). **17b**: mp 132.5–133.0 °C (colorless prisms, recrystallized from benzene). IR (KBr): 3200, 3040, 1623, 1533, 1450, 1245, 735 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 222 (4.51), 273 (3.72), 288 (3.72). ^1H-NMR ($CDCl_3$) δ: 1.98

(3H, s), 4.07 (3H, s), 4.56 (2H, d, *J*=5.1 Hz), 5.65 (1H, br s), 7.14 (1H, t, *J*=8.2 Hz), 7.24 (1H, s), 7.28 (1H, t, *J*=8.2 Hz), 7.43 (1H, d, *J*=8.2 Hz), 7.60 (1H, d, *J*=8.2 Hz). MS *m/z*: 218 (M^+). *Anal.* Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 65.91; H, 6.47; N, 12.71.

3-Acetylaminomethyl-1-methoxyindole (17b) from 16b — Ethereal CH_2N_2 (excess) was added to a solution of **16b** (11.8 mg, 0.058 mmol) in MeOH (1.0 mL) and stirring was continued at rt for 30 min. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (97:3, v/v) to give **17b** (10.7 mg, 85%).

2,3-Dihydro-3-tosylaminomethylindole (19) from 3-tosylaminomethylindole (18) — 95% $NaBH_3CN$ (247.7 mg, 3.74 mmol) was added to a solution of **18** (201.8 mg, 0.67 mmol) in AcOH (10.0 mL) at rt and stirring was continued for 5 h. After adding H_2O under ice cooling, the solvent was evaporated under reduced pressure. The residue was made alkaline by adding H_2O and 8% NaOH. The whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a residue, which was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to give **18** (16.5 mg, recovery, 8%) and **19** (144.3 mg, 71%) in the order of elution. **19**: colorless hard oil. IR (KBr): 3320, 3050, 2910, 1592, 1481, 1460, 1423, 1323, 1155, 1041, 755 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.42 (3H, s), 2.92 (1H, dd, *J*=12.8, 5.3 Hz), 3.06 (1H, dd, *J*=12.8, 5.3 Hz), 3.27 (1H, dd, *J*=9.3, 5.7 Hz), 3.30–3.38 (1H, m), 3.51 (1H, dd, *J*=9.3, 8.6 Hz), 6.63 (1H, d, *J*=7.9 Hz), 6.65 (1H, td, *J*=7.3, 0.9 Hz), 6.98 (1H, t, *J*=7.9 Hz), 7.03 (1H, d, *J*=7.3 Hz), 7.37 (2H, m), 7.72 (2H, m). MS *m/z*: 302 (M^+). *Anal.* Calcd for $C_{16}H_{18}N_2O_2S$: C, 63.55; H, 6.00; N, 9.26. Found: C, 63.45; H, 6.04; N, 9.16.

1-Hydroxy-3-tosylaminomethylindole (20) from 19 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (60.6 mg, 0.18 mmol) in H_2O (1.8 mL), **19** (277.4 mg, 0.92 mmol) in MeOH (13.0 mL), and 30% H_2O_2 (1.049 g, 9.26 mmol) in MeOH (5.0 mL) were used. After usual work-up, **20** (197.5 mg, 68%) was obtained. **20**: mp 134.0–135.5 °C (colorless needles, recrystallized from $CHCl_3$). IR (KBr): 3390, 3320, 1396, 1318, 1303, 1230, 1157, 1097, 1020, 817, 732 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.39 (3H, s), 4.18 (2H, s), 6.94 (1H, ddd, *J*=8.0, 7.0, 1.0 Hz), 7.08 (1H, s), 7.11 (1H, ddd, *J*=8.0, 7.0, 1.0 Hz), 7.28 (2H, m), 7.29 (1H, dt, *J*=8.0, 1.0 Hz), 7.39 (1H, dt, *J*=8.0, 1.0 Hz), 7.68 (2H, m). MS *m/z*: 316 (M^+). *Anal.* Calcd for $C_{16}H_{16}N_2O_3S \cdot 1/4H_2O$: C, 59.89; H, 5.18; N, 8.73. Found: C, 59.91; H, 5.00; N, 8.71.

1-Methoxy-3-tosylaminomethylindole (21) from 20 — Ethereal CH_2N_2 (excess) was added to a solution of **20** (32.3 mg, 0.10 mmol) in MeOH (1.0 mL) and stirring was continued at rt for 30 min. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with CH_2Cl_2 to give **21** (32.2 mg, 96%). **21**: mp 176.0–178.5 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3300, 1600, 1423, 1315, 1243, 1145, 1089, 1024, 952, 866, 812, 746, 681, 541 cm^{-1}. ^{1}H-NMR (5% CD_3OD–$CDCl_3$) δ: 2.43 (3H, s), 4.02 (3H, s), 4.25 (2H, s), 7.07 (1H, ddd, *J*=8.0, 7.1, 1.0

Hz), 7.10 (1H, s), 7.23 (1H, ddd, *J*=8.2, 7.1, 1.0 Hz), 7.28 (2H, m), 7.37 (1H, dt, *J*=8.2, 1.0 Hz), 7.41 (1H, dt, *J*=8.0, 1.0 Hz), 7.74 (2H, m). MS *m/z*: 330 (M^+). *Anal.* Calcd for $C_{17}H_{18}N_2O_3S$: C, 61.80; H, 5.49; N, 8.48. Found: C, 61.71; H, 5.50; N, 8.41.

Methyl *N*-(2,3-dihydroindol-3-yl)methylsuccinamate (24) and *N*-(2,3-Dihydroindol-3-yl)methylsuccinimide (23) from methyl *N*-(indol-3-yl)methylsuccinamate (22) — Prepared according to the method for **19**, where 95% $NaBH_3CN$ (66.0 mg, 1.00 mmol) and **22** (49.8 mg, 0.19 mmol) in AcOH (2.0 mL) were used. After usual work-up and purification, **23** (6.5 mg, 15%) and **24** (41.0 mg, 82%) were obtained. **24**: mp 73.0–74.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3290, 1726, 1638, 1609, 1542, 1483, 1433, 1338, 1197, 1174, 745 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.50 (2H, t, *J*=6.8 Hz), 2.61 (2H, t, *J*=6.8 Hz), 3.25 (1H, dd, *J*=9.3, 5.5 Hz), 3.28–3.32 (1H, m), 3.41–3.47 (2H, m), 3.56 (1H, t, *J*=9.3 Hz), 3.66 (3H, s), 6.68 (1H, d, *J*=7.6 Hz), 6.69 (1H, td, *J*=7.6, 1.0 Hz), 7.00 (1H, t, *J*=7.6 Hz), 7.14 (1H, d, *J*=7.6 Hz). MS *m/z*: 262 (M^+). *Anal.* Calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68. Found: C, 64.11; H, 6.90; N, 10.69. **23**: mp 94.5–96.0 °C (colorless prisms, recrystallized from MeOH). IR (KBr): 3370, 2990, 2820, 1778, 1689, 1608, 1405, 1351, 1247, 1124, 1151, 755 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.71 (4H, s), 3.29 (1H, dd, *J*=9.5, 5.1 Hz), 3.48 (1H, dd, *J*=9.5, 8.4 Hz), 3.57 (1H, m), 3.64 (1H, dd, *J*=13.1, 8.7 Hz), 3.71 (1H, dd, *J*=13.1, 5.4 Hz), 6.66 (1H, t, *J*=7.8 Hz), 6.68 (1H, td, *J*=7.3, 1.0 Hz), 7.01 (1H, m), 7.08 (1H, d, *J*=7.3 Hz). MS *m/z*: 230 (M^+). *Anal.* Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.77; H, 6.11; N, 12.08.

Methyl *N*-(1-hydroxyindol-3-yl)methylsuccinamate (25a) from 24 — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (14.6 mg, 0.04 mmol) in H_2O (0.4 mL), **24** (56.8 mg, 0.21 mmol) in MeOH (3.5 mL), and 30% H_2O_2 (249.9 mg, 2.21 mmol) in MeOH (1.0 mL) were used. After usual work-up and purification, **25a** (37.5 mg, 63%) was obtained. **25a**: mp 115.5–116.0 °C (colorless needles, recrystallized from EtOAc). IR (KBr): 3350, 3120, 2930, 1710, 1637, 1535, 1443, 1387, 1358, 1243, 1218, 1174, 735 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.48 (2H, t, *J*=6.7 Hz), 2.62 (2H, t, *J*=6.7 Hz), 3.61 (3H, s), 4.48 (2H, s), 7.01 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.15 (1H, ddd, *J*=8.3, 7.1, 1.0 Hz), 7.24 (1H, s), 7.36 (1H, dt, *J*=8.3, 1.0 Hz), 7.54 (1H, dt, *J*=8.1, 1.0 Hz). MS *m/z*: 276 (M^+). *Anal.* Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.72; H, 5.85; N, 10.12.

Methyl *N*-(1-methoxyindol-3-yl)methylsuccinamate (25b) from 25a — Ethereal CH_2N_2 (excess) was added to a solution of **25a** (25.5 mg, 0.09 mmol) in MeOH (1.0 mL) and stirring was continued at rt for 30 min. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to give **25b** (25.5 mg, 95%). **25b**: mp 75.0–76.5 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3280, 1730, 1634, 1537, 1445, 1349, 1319, 1201, 1136, 736 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.49 (2H, t, *J*=7.1 Hz), 2.62 (2H, t, *J*=7.1 Hz), 3.61 (3H, s), 4.05 (3H, s), 4.48 (2H, s), 7.06 (1H, ddd, *J*=7.8, 7.1, 1.0 Hz), 7.20 (1H, ddd, *J*=8.3, 7.1, 1.0 Hz), 7.36 (1H, s), 7.39 (1H, dt, *J*=8.3, 1.0 Hz), 7.58 (1H, dt, *J*=7.8, 1.0 Hz). MS *m/z*: 290 (M^+). *Anal.* Calcd for $C_{15}H_{18}N_2O_4$: C, 62.05; H, 6.25; N, 9.65. Found: C, 62.05; H, 6.33; N, 9.60.

3-Methylthiomethylindole (27) from gramine (26) — MeI (1.45 mL, 23.3 mmol) was added to a solution of **26** (399.3 mg, 2.30 mmol) in THF (23.0 mL) and stirred at rt for 1 h. The solvent was evaporated under reduced pressure to leave a residue, which was dissolved in MeOH (20.0 mL). To the resultant solution, 15% aqueous NaSMe (10.7 mL, 23.3 mmol) was added and stirred at rt for 15 h. After addition of H_2O, the whole was extracted with CH_2Cl_2–MeOH (95:5, v/v). The extract was washed with brine, dried over Na_2SO_4, and evaporated under reduced pressure to leave a residue, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (100:20:2, v/v) to give **27** (325.7 mg, 80%) and **26** (65.7 mg, recovery, 17%) in the order of elution. **27**: mp 91.0–92.5 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3310, 1645, 1555, 1456, 1421, 1354, 1253, 1097, 745, 639 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.98 (3H, s), 3.89 (2H, s), 7.00 (1H, ddd, *J*=8.1, 7.2, 0.9 Hz), 7.09 (1H, ddd, *J*=8.2, 7.2, 1.1 Hz), 7.14 (1H, s), 7.32 (1H, dd, *J*=8.2, 0.9 Hz), 7.62 (1H, dd, *J*=8.1, 1.1 Hz). *Anal.* Calcd for $C_{10}H_{11}NS$: C, 67.79; H, 6.25; N, 7.88. Found: C, 67.76; H, 6.25; N, 7.90.

2,3-Dihydro-3-methylthiomethylindole (28) from 27 — Prepared according to the method for **19**, where 95% $NaBH_3CN$ (355.5 mg, 5.37 mmol) and **27** (100.2 mg, 0.56 mmol) in AcOH (6.0 mL) were used. After usual work-up and purification, **27** (21.8 mg, recovery, 22%) and **28** (55.5 mg, 55%) were obtained. **28**: colorless oil. IR (film): 3370, 2920, 1607, 1488, 1465, 1249, 747 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.15 (3H, s), 2.68 (1H, dd, *J*=12.8, 9.4 Hz), 2.91 (1H, dd, *J*=12.8, 5.1 Hz), 3.44 (1H, dd, *J*=9.2, 6.2 Hz), 3.49–3.55 (1H, m), 3.75 (1H, t, *J*=9.2 Hz), 6.68 (1H, d, *J*=7.6 Hz), 6.75 (1H, t, *J*=7.6 Hz), 7.06 (1H, t, *J*=7.6 Hz), 7.17 (1H, d, *J*=7.6 Hz). MS *m/z*: 179 (M^+). *Anal.* Calcd for $C_{10}H_{13}NS$: C, 66.99; H, 7.31; N, 7.81. Found: C, 67.10; H, 7.36; N, 7.93.

1-Hydroxy-3-methylsulfinylmethylindole (29) from 28 — Prepared according to general method B, where $Na_2WO_4 \cdot 2H_2O$ (47.5 mg, 0.14 mmol) in H_2O (0.7 mL), **28** (128.9 mg, 0.72 mmol) in MeOH (6.0 mL), and 30% H_2O_2 (803.7 mg, 7.09 mmol) in MeOH (1.0 mL) were used. Then, a solution of Me_2S (0.42 mL, 5.76 mmol) in MeOH (1.0 mL) was added to the reaction mixture. After usual work-up and purification, **29** (41.2 mg, 27%) was obtained. **29**: mp 114.0–115.0 °C (pale orange prisms, recrystallized from EtOAc). IR (KBr): 2580, 1349, 1322, 1240, 1093, 1007, 947, 735 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.53 (3H, s), 4.23 (1H, d, *J*=13.7 Hz), 4.30 (1H, d, *J*=13.7 Hz), 7.08 (1H, ddd, *J*=8.1, 7.0, 1.0 Hz), 7.20 (1H, ddd, *J*=8.1, 7.0, 1.0 Hz), 7.39 (1H, s), 7.42 (1H, d, *J*=8.1 Hz), 7.62 (1H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{10}H_{11}NO_2S$: 209.0510. Found: 209.0508.

1-Methoxy-3-methylsulfinylmethylindole (30) and 1-methoxy-3-methylsulfonylmethylindole (31) from 28 — [Entry 1]: Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (35.5 mg, 0.11 mmol) in H_2O (0.5 mL), **28** (94.7 mg, 0.53 mmol) in MeOH (4.0 mL), and 30% H_2O_2 (600.3 mg, 5.30

mmol) in MeOH (1.0 mL) were used. After stirring at rt for 5 min, a solution of Me_2S (0.31 mL, 4.23 mmol) in MeOH (1.0 mL) was added and stirred for 30 min. Ethereal CH_2N_2 (excess) was then added and stirred for 30 min. After usual work-up and purification by column-chromatography on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v), **31** (20.1 mg, 16%) and **30** (31.8 mg, 27%) were obtained. **30**: mp 67.0–69.0 °C (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3420, 1453, 1435, 1349, 1321, 1093, 1063, 1025, 965, 946, 747 cm^{-1}. ^1H-NMR (CD_3OD) δ: 2.54 (3H, s), 4.11 (3H, s), 4.21 (1H, dd, *J*=13.8, 0.6 Hz), 4.30 (1H, dd, *J*=13.8, 0.6 Hz), 7.13 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.25 (1H, ddd, *J*=8.3, 7.1, 1.0 Hz), 7.45 (1H, dt, *J*=8.3, 1.0 Hz), 7.53 (1H, s), 7.66 (1H, dt, *J*=8.1, 1.0 Hz). MS *m/z*: 223 (M^+). *Anal.* Calcd for $C_{11}H_{13}NO_2S\cdot 1/8H_2O$: C, 58.58; H, 5.81; N, 6.21. Found: C, 58.49; H, 5.84; N, 6.14. **31**: mp 101.5–102.5 °C (colorless plates, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3100, 2930, 1455, 1320, 1263, 1244, 1147, 1120, 968, 945, 747, 736 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.75 (3H, s), 4.13 (3H, s), 4.41 (2H, s), 7.21 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.31 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.48 (1H, dt, *J*=8.1, 1.0 Hz), 7.48 (1H, s), 7.62 (1H, dt, *J*=8.1, 1.0 Hz). MS *m/z*: 239 (M^+). *Anal.* Calcd for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.48; N, 5.85. Found: C, 55.19; H, 5.47; N, 5.81.

3-Acetylthiomethylindole (33) from 26 — MeI (0.12 mL, 1.85 mmol) was added to a solution of **26** (32.2 mg, 0.19 mmol) in THF (2.0 mL) at rt and stirring was continued for 1 h. The solvent was evaporated under reduced pressure to leave a residue, which was dissolved in DMF–H_2O (3:1, v/v, 2.0 mL). To the resultant solution, KSCOMe (31.7 mg, 0.28 mmol) was added and stirred at rt for 2 h. After usual work-up and purification by column-chromatography on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (100:20:2, v/v), **33** (29.8 mg, 79%) and **26** (6.9 mg, recovery, 21%) were obtained. **33**: colorless oil. IR (film): 3350, 1676, 1454, 1419, 1352, 1339, 1136, 1116, 1095, 959, 740 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.34 (3H, s), 4.35 (2H, d, *J*=0.7 Hz), 7.14 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.18 (1H, d, *J*=2.4 Hz), 7.21 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.35 (1H, dt, *J*=8.1, 1.0 Hz), 7.60 (1H, d, *J*=8.1 Hz), 8.03 (1H, br s). High resolution MS *m/z*: Calcd for $C_{11}H_{11}NOS$: 205.0561. Found: 205.0541.

3-Acetylthiomethyl-2,3-dihydroindole (34) from 33 — Prepared according to the method for **19**, where 95% $NaBH_3CN$ (42.6 mg, 0.64 mmol) and **33** (26.2 mg, 0.13 mmol) in AcOH–CF_3CO_2H (3:1, v/v, 1.5 mL) were used. After usual work-up, **34** (17.8 mg, 67%) was obtained. **34**: colorless oil. IR (film): 3370, 1692, 1611, 1487, 1465, 1252, 1138, 957, 748 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 2.36 (3H, s), 3.10 (1H, dd, *J*=13.6, 8.3 Hz), 3.28 (1H, dd, *J*=13.6, 5.4 Hz), 3.30 (1H, dd, *J*=9.1, 6.1 Hz), 3.48–3.53 (1H, m), 3.68 (1H, t, *J*=9.1 Hz), 6.65 (1H, d, *J*=7.5 Hz), 6.73 (1H, td, *J*=7.5, 1.0 Hz), 7.06 (1H, t, *J*=7.5 Hz), 7.19 (1H, d, *J*=7.5 Hz). High resolution MS *m/z*: Calcd for $C_{11}H_{13}NOS$: 207.0718. Found: 207.0763.

3-Acetylthiomethyl-1-methoxyindole (35) from 33 — Crude **34**, prepared with 95% $NaBH_3CN$ (60.6 mg, 0.92 mmol) and **33** (37.9 mg, 0.18 mmol) in AcOH–CF_3CO_2H (3:1, v/v, 2.0 mL), was dissolved in MeOH (1.5 mL). To the resultant solution, a solution of $Na_2WO_4\cdot 2H_2O$ (12.3 mg, 0.04 mmol) in H_2O

(0.2 mL) and then a solution of 30% H_2O_2 (207.8 mg, 1.83 mmol) in MeOH (0.5 mL) were added under ice cooling and stirred at rt for 20 min. Ethereal CH_2N_2 (excess) was added to the mixture and stirring was continued at rt for 1 h. After usual work-up and purification, **35** (6.6 mg, 15%) was obtained. **35**: colorless oil. IR (film): 2940, 1689, 1452, 1354, 1232, 1133, 1097, 1031, 954, 758, 737 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.34 (3H, s), 4.06 (3H, s), 4.29 (2H, d, *J*=0.7 Hz), 7.13 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.24–7.27 (2H, m), 7.43 (1H, dt, *J*=8.1, 1.0 Hz), 7.57 (1H, dt, *J*=8.1, 1.0 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}NO_2S$: 235.0667. Found: 235.0685.

2,3-Dihydro-*N,N*-dimethylindole-3-acetamide (37a) from *N,N*-dimethylindole-3-acetamide (36a) — Prepared according to the method for **19**, where 95% $NaBH_3CN$ (394.5 mg, 5.96 mmol) and **36a** (241.1 mg, 1.20 mmol) in AcOH (10.0 mL) were used. After work-up, **37a** (236.6 mg, 97%) was obtained. **37a**: colorless oil. IR (film): 3310, 2930, 1630, 1488, 1465, 1407, 1322, 1254, 1143, 748 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.58 (1H, dd, *J*=16.0, 8.9 Hz), 2.73 (1H, dd, *J*=16.0, 4.8 Hz), 2.94 (3H, s), 2.97 (3H, s), 3.23–3.26 (1H, m), 3.78–3.86 (2H, m), 6.65 (1H, d, *J*=7,7 Hz), 6.71 (1H, td, *J*=7.3, 1.0 Hz), 7.04 (1H, d, *J*=7.7 Hz), 7.10 (1H, d, *J*=7.3 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{16}N_2O$: 204.1263. Found: 204.1255.

2,3-Dihydro-*N,N*-dimethylindole-3-propionamide (37b) from *N,N*-dimethylindole-3-propionamide (36b) — Prepared according to the method for **19**, where 95% $NaBH_3CN$ (303.5 mg, 4.59 mmol) and **36b** (201.4 mg, 0.93 mmol) in AcOH (10.0 mL) were used. After usual work-up and purification, **37b** (199.8 mg, 98%) was obtained. **37b**: colorless oil. IR (film): 3290, 2920, 1628, 1486, 1459, 1399, 1247, 1143, 747 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.88–1.96 (1H, m), 2.11–2.18 (1H, m), 2.33–2.45 (2H, m), 2.95 (3H, s), 2.99 (3H, s), 3.24 (1H, dd, *J*=8.8, 6.4 Hz), 3.33–3.39 (1H, m), 3.70 (1H, t, *J*=8.8 Hz), 6.64 (1H, d, *J*=7.6 Hz), 6.72 (1H, td, *J*=7.6, 1.0 Hz), 7.03 (1H, d, *J*=7.6 Hz), 7.11 (1H, d, *J*=7.6 Hz). High resolution MS *m/z*: Calcd for $C_{13}H_{18}N_2O$: 218.1419. Found: 218.1427.

***N,N*-Dimethyl-1-hydroxyindole-3-acetamide (38a) from 37a** — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (131.6 mg, 0.40 mmol) in H_2O (4.0 mL), **37a** (407.4 mg, 2.00 mmol) in MeOH (3.0 mL), and 30% H_2O_2 (2.214 g, 19.5 mmol) in MeOH (5.0 mL) were used. After usual work-up, **38a** (321.4 mg, 74%) was obtained. **38a**: mp 146.0–147.0 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 2600, 1590, 1405, 1316, 1216, 1086, 758, 741 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.97 (3H, s), 2.97 (3H, s), 3.61 (2H, s), 6.52 (1H, s), 6.98 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.16 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.23 (1H, d, *J*=8.1 Hz), 7.43 (1H, d, *J*=8.1 Hz), 10.72 (1H, s, D_2O exchange). *Anal.* Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 65.74; H, 6.36; N, 12.69.

***N,N*-Dimethyl-1-hydroxyindole-3-propionamide (38b) from 37b** — Prepared according to general method B, where $Na_2WO_4 \cdot 2H_2O$ (208.4 mg, 0.63 mmol) in H_2O (6.0 mL), **37b** (688.0 mg, 3.16 mmol) in MeOH (55.0 mL), and 30% H_2O_2 (3.543 g, 31.3 mmol) in MeOH (5.0 mL) were used. After usual work-up and purification, **38b** (483.9 mg, 66%) was obtained. **38b**: mp 144.0–145.0 °C (colorless prisms, recrystallized from $CHCl_3$–hexane). IR (KBr): 2760, 1598, 1402, 1310, 1140, 1026, 736 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.63 (2H, dd, *J*=8.2, 7.2 Hz), 2.82 (3H, s), 2.88 (2H, dd, *J*=8.2, 7.2 Hz), 2.93 (3H, s), 6.97 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.12 (1H, ddd, *J*=8.1, 7.1, 1.0 Hz), 7.23 (1H, s), 7.31 (1H, d, *J*=8.1 Hz), 7.51 (1H, d, *J*=8.1 Hz), 10.98 (1H, s, D_2O exchange). *Anal.* Calcd for $C_{13}H_{16}N_2O_2\cdot 1/4H_2O$: C, 65.94; H, 7.02; N, 11.83. Found: C, 66.14; H, 6.85; N, 11.80.

9-Hydroxy-1,2,3,4-tetrahydrocarbazole (40) from 1,2,3,4,4a,9a-hexahydrocarbazole (39) — Prepared according to general method B, where $Na_2WO_4\cdot 2H_2O$ (28.7 mg, 0.087 mmol) in H_2O (1.0 mL), **39** (71.8 mg, 0.41 mmol) in MeOH (10.0 mL), and 30% H_2O_2 (0.45 mL, 3.92 mmol) were used. After usual work-up and purification, **39** (13.3 mg, 18%) and **40** (50.1 mg, 65%) were obtained. **40**: yellow oil. IR (film): 3061, 2931, 2857, 1458, 1238, 1178, 740 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.73–1.84 (4H, m), 2.55–2.57 (2H, m), 2.64–2.66 (2H, m), 6.83 (1H, t, *J*=7.9 Hz), 6.94 (1H, t, *J*=7.9 Hz), 7.18 (1H, d, *J*=7.9 Hz), 7.23 (1H, d, *J*=7.9 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{13}NO$: 187.0997. Found: 187.1001.

9-Methoxy-1,2,3,4-tetrahydrocarbazole (41) from 1,2,3,4,4a,9a-hexahydrocarbazole (39) — Prepared according to the general method B, where $Na_2WO_4\cdot 2H_2O$ (19.3 mg, 0.028 mmol), **39** (50.6 mg, 0.29 mmol) in MeOH (4.0 mL), and 30% H_2O_2 (331.6 mg, 2.92 mmol) in MeOH (1.0 mL) were used. After methylation and work-up, product purification was carried out by p-TLC on SiO_2 with CH_2Cl_2–hexane (7:3, v/v) as a developing solvent to afford **41** (32.2 mg, 55%). **41**: colorless oil. IR (KBr): 2942, 2842, 1459, 1443, 1230, 1046, 735 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.68–2.08 (4H, m), 2.52–2.92 (4H, br m), 3.99 (3H, s), 6.88–7.48 (4H, m). High resolution MS *m/z*: Calcd for $C_{13}H_{15}NO$: 201.1152. Found: 201.1134.

9-Methoxy-1,2,3,4-tetrahydrocarbazole (41) from 40 — K_2CO_3 (173.3 mg, 1.25 mmol) and Me_2SO_4 (0.053 mL, 0.56 mmol) were added to a solution of **40** (67.0 mg, 0.33 mmol) in acetone (10.0 mL) and the mixture was stirred at rt for 2 h. After usual work-up and purification, **41** (54.8 mg, 70%) was obtained.

9-Methoxycarbazole (42) from 41 — Dichlorodicyanoquinone (469.4 mg, 2.38 mmol) was added to a solution of **41** (188. 9 mg, 0.94 mmol) in benzene (30.0 mL) and stirred at rt (14 °C) for 3 h. Precipitates were filtered off through silica gel and washed with CH_2Cl_2. Washings and filtrates were combined and evaporated under reduced pressure to leave a crystalline solid, which was column-chromatographed on SiO_2 with hexane–EtOAc (9:1, v/v) as an eluent to afford **42** (121.1 mg, 65%). **42**: mp 40.0–41.0 °C (colorless needles, recrystallized from MeOH). IR (KBr): 1601, 1450, 1320, 1233, 1052, 946 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.12 (3H, s), 7.19 (1H, dd, *J*=7.3, 2.7 Hz), 7.25 (1H, dd, *J*=7.3, 2.7 Hz), 7.34–7.58 (4H, m), 8.02 (2H, dt, *J*=7.3, 1.0 Hz). MS *m/z*: 197 (M^+). *Anal.* Calcd for $C_{13}H_{11}NO$: C, 79.17; H, 5.62; N, 7.10. Found: C, 79.36; H, 5.55; N, 7.21.

A mixture of diastereoisomers, 4-nitro-1,2,2a,3,4,5-hexahydrobenz[*cd*]indole (44) from 4-nitro-

1,3,4,5-tetrahydrobenz[*cd*]indole (43) — Prepared according to the method for **19**, where 95% $NaBH_3CN$ (60.8 mg, 0.97 mmol) and **43** (35.9 mg, 0.18 mmol) in AcOH–CF_3CO_2H (3:2, v/v, 2.0 mL) were used. After usual work-up, crude **44** was subjected to p-TLC on SiO_2 with CH_2Cl_2–hexane (3:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.39–0.14 with CH_2Cl_2–MeOH (95:5, v/v) afforded pure **44** (34.4 mg, 95%). Although ^{1}H-NMR analysis of **44** showed 2:1 mixture of diastereoisomers, further separation was not examined.

1-Hydroxy-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (45) from a diastereoisomer's mixture (44) — Prepared according to general procedure C, where $Na_2WO_4 \cdot 2H_2O$ (10.5 mg, 0.03 mmol) in H_2O (0.2 mL), urea·H_2O_2 (138.6 mg, 1.47 mmol), and diastereoisomer's mixture, **44** (30.2 mg, 0.15 mmol), in MeOH (2.0 mL) were used. The reaction mixture was adjusted to pH 4 by adding 0.6% HCl and extracted with CH_2Cl_2–MeOH (95:5, v/v). After usual work-up and purification, **45** (16.9 mg, 52%) was obtained. **45**: mp 134–134.5 ℃ (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3427, 3112, 2971, 1604, 1530, 1442, 1419, 1349, 1149, 1001, 848, 769, 751 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.50 (2H, br s), 3.52 (1H, dd, *J*=15.6, 4.4 Hz), 3.61 (1H, dd, *J*=15.6, 9.3 Hz), 4.98 (1H, ddd, *J*=13.7, 9.3, 4.4 Hz), 6.79 (1H, br s, D_2O exchange), 6.89 (1H, br s), 7.01 (1H, br s), 7.21 (1H, dd, *J*=7.8, 7.3 Hz). High resolution MS *m/z*: Calcd for $C_{11}H_{10}N_2O_3$: 218.0690. Found: 218.0692.

1-Methoxy-4-nitro-1,3,4,5-tetrahydrobenz[*cd*]indole (46) from 45 — Ethereal CH_2N_2 solution (excess) was added to a solution of **45** (7.5 mg, 0.04 mmol) in MeOH (1.0 mL) at rt with stirring for 0.5 h. After evaporation of solvent under reduced pressure, the residue was purified by p-TLC on SiO_2 with CH_2Cl_2–hexane (1:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.50–0.31 with CH_2Cl_2–MeOH (95:5, v/v) afforded **46** (5.1 mg, 64%). **46**: pale brown oil. IR (KBr): 3450, 2941, 1605, 1521, 1440, 1561, 1540, 983, 761, 747 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.48 (2H, dd, *J*=17.3, 1.0 Hz), 3.54 (1H, dd, *J*=15.6, 4.6 Hz), 3.61 (1H, dd, *J*=15.6, 9.3 Hz), 4.07 (3H, s), 4.99 (1H, ddt, *J*=9.3, 7.3, 4.6 Hz), 6.90 (1H, d, J *J*=7.3 Hz), 7.02 (1H, s), 7.20 (1H, dd, *J*=7.8, 7.3 Hz), 7.25 (1H, d, *J*=7.8 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{12}N_2O_3$: 232.0847. Found: 232.0893.

A mixture of diastereoisomers, 4-(*N*-phenylacetylamino)-1,2,2aβ,3,4β,5-hexahydrobenz[*cd*]indole (48a) and 4-(*N*-phenylacetylamino)-1,2,2aα,3,4β,5-hexahydrobenz[*cd*]indole (48b) from 4-(*N*-phenylacetylamino)-1,3,4,5-tetrahydrobenz[cd]indole (47) — Prepared according to the method for **19**, where 95%$NaBH_3CN$ (46.0 mg, 0.73 mmol) and **47** (40.1 mg, 0.14 mmol) in AcOH–CF_3CO_2H (4:1, v/v, 2.0 mL) were used. After work-up and purification, **48a** (17.0 mg, 47%) and **48b** (16.7 mg, 41%) were obtained. **48a**: colorless oil. IR (KBr) : 3261, 3037, 2910, 2843, 1637, 1603, 1532, 1491, 1452, 1333, 1247, 1233, 761, 718, 692 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.45 (1H, dt, *J*=12.8, 3.2 Hz), 2.29 (1H, dt, *J*=12.8, 4.6 Hz), 2.70 (1H, d, *J*=18.3 Hz), 2.96 (1H, dd, *J*=18.3, 6.4 Hz), 3.00 (1H, dd, *J*=11.9, 8.3 Hz), 3.10–3.19 (1H, m), 3.46 (1H, d, *J*=14.2 Hz), 3.50 (1H, d, *J*=14.2 Hz), 3.57 (1H, dd, *J*=8.3, 7.3 Hz), 4.39–4.46 (1H, m), 6.51 (2H, t, *J*=7.3 Hz), 6.94 (1H, dd, *J*=8.3, 7.3 Hz), 7.19–7.24 (1H, m), 7.27 (2H, s), 7.28 (2H, s). High resolution MS *m/z*: Calcd for $C_{19}H_{20}N_2O$: 292.1575. Found: 292.1578. **48b**: mp 161–162℃ (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 3233, 3054, 2928, 2883, 1637, 1551, 1452, 1280, 1243, 762, 727, 691 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.39 (1H, q, *J*=11.9 Hz), 2.24 (1H, dt, *J*=11.9, 3.7 Hz), 2.48 (1H, dd, *J*=16.5, 11.9 Hz), 2.99 (1H, dd, *J*=11.9, 8.3 Hz), 3.06 (1H, dd, *J*=16.5, 6.4 Hz), 3.12–3.22 (1H, m), 3.51 (2H, s), 3.58 (1H, t, *J*=8.3 Hz), 4.20 (1H, ddt, *J*=11.9, 6.4, 3.7 Hz), 6.49 (2H, d, *J*=7.3 Hz), 6.91 (1H, dd, *J*=8.3, 7.3 Hz), 7.20–7.26 (1H, m), 7.30 (2H, s), 7.31 (2H,s). MS *m/z*: 292 (M^+). *Anal.* Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.90; N, 9.58. Found: C, 77.91; H, 6.92; N, 9.42.

1-Methoxy-4-(*N*-phenylacetylamino)-1,3,4,5-tetrahydrobenz[*cd*]indole (49) from a mixture of diastereoisomers, 4-(*N*-phenylacetylamino)-1,2,2a,3,4,5-hexahydrobenz[*cd*]indoles (48a, 48b) — Prepared according to general method C, where $Na_2WO_4 \cdot 2H_2O$ (6.6 mg, 0.02 mmol) in H_2O (0.2 mL), urea·H_2O_2 (95.2 mg, 1.01 mmol), and diastereoisomer's mixture, **48a** and **48b** (29.1 mg, 0.10 mmol), in MeOH (2.0 mL) were used. To the reaction mixture, K_2CO_3 (247.1 mg, 1.79 mmol) and Me_2SO_4 (80.0 mg, 0.64 mmol) were added and stirred at rt for 1.5 h. After usual work-up and purification, **49** (12.8 mg, 40%) was obtained. **49**: mp 138–139 ℃ (colorless prisms, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3301, 3053, 2943, 1635, 1543, 1493, 1442, 1342, 985, 752, 731 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.74 (1H, dd, *J*=15.6, 5.9 Hz), 2.90 (1H, dd, *J*=15.6, 5.9 Hz), 3.01 (1H, dd, *J*=15.6, 3.7 Hz), 3.11 (1H, dd, *J*=15.6, 3.7 Hz), 3.43 (2H, s), 4.05 (3H, s), 4.61–4.69 (1H, m), 5.44 (1H, br d, *J*=8.3 Hz), 6.79 (1H, d, *J*=7.3 Hz), 6.89 (1H, s), 7.03 (1H, dd, *J*=7.3, 1.8 Hz), 7.13–7.22 (2H, m). MS *m/z*: 320 (M^+). *Anal.* Calcd for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.70; H, 6.20; N, 8.31.

A mixture of diastereoisomers, 4-*N*,*N*-di(*n*-propylamino)-1,2,2a,3,4,5-hexahydrobenz[*cd*]indole (51), from 4-*N*,*N*-di(*n*-propylamino)-1,3,4,5-tetrahydrobenz[*cd*]indole (50) — Prepared according to the method for **19**, where 95% $NaBH_3CN$ (27.2 mg, 0.43 mmol) and **50** (22.0 mg, 0.09 mmol) in AcOH–CF_3CO_2H (2:1, v/v, 1.5 mL) were used. After usual work-up, the reaction residue was subjected to p-TLC on SiO_2 with $CHCl_3$–MeOH–aq. 30% NH_3–hexane (92:10:1:1, v/v) as a developing solvent. Extraction of the band having an *Rf* value of 0.53–0.24 with $CHCl_3$–MeOH–aq. 30% NH_3 (46:5:0.5, v/v) afforded **51** (19.0 mg, 86%). Although ^{1}H-NMR analysis of **51** showed 6:1 mixture of diastereoisomers, further separation was not examined.

4-*N*,*N*-Di(*n*-propylamino)-1-methoxy-1,3,4,5-tetrahydrobenz[*cd*]indole (52) from a diastereoisomer's mixture (51) — Prepared according to general method C, where $Na_2WO_4 \cdot 2H_2O$ (8.1 mg, 0.02 mmol) in H_2O (0.2 mL), urea·H_2O_2 (116.8 mg, 1.24 mmol), and diastereoisomer's mixture, **51** (30.7 mg, 0.12 mmol), in MeOH (2.0 mL) were used. Then, the reaction mixture was treated with ethereal CH_2N_2 (excess), followed by addition of PPh_3 (319.5 mg, 1.26 mmol) under ice cooling, and the whole was stirred at rt for 20 min. After usual work-up, products were separated by p-TLC on Al_2O_3 with

EtOAc–hexane (1:14, v/v) to give **52** (15.8 mg, 46%) and **51** (4.2 mg, 14%). **52**: pale brown oil. IR (KBr): 2950, 1606, 1460, 1441, 1375, 1152, 1071, 984, 747 cm^{-1}. ^{1}H-NMR (pyridine-*d*$_5$) δ: 0.90 (6H, t, *J*=7.3 Hz), 1.42 (4H, sex, *J*=7.3 Hz), 2.47 (4H, t, J *J*=7.3 Hz), 2.73 (1H, ddd, *J*=15.1, 12.0, 1.5 Hz), 2.92 (1H, dd, *J*=15.1, 4.1 Hz), 2.95 (1H, d, *J*=12.0 Hz), 3.02 (1H, dd, *J*=15.1, 4.1 Hz), 3.20–3.27 (1H, m), 3.97 (3H, s), 6.98 (1H, d, *J*=7.8 Hz), 7.16 (1H, d, *J*=1.5 Hz), 7.29 (1H, dd, *J*=7.8, 6.8 Hz), 7.36 (1H, d, *J*=7.8 Hz). High resolution MS *m/z*: Calcd for $C_{18}H_{26}N_2O$: 286.2043. Found: 286.2044.

1-Hydroxy-*N*b-acetyltryptamine (54a) from *N*b-acetyl-2,3-dihydrotryptamine (53a)— Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (66.4 mg, 0.20 mmol), **53a** (205.2 mg, 1.00 mmol) in MeOH (20.0 mL), and 30% H_2O_2 (1.0 mL, 10.0 mmol) were used. After usual work-up and purification, **54a** (121.5 mg, 55%) was obtained. **54a**: mp 138.0–139.0 °C (colorless prisms, recrystallized from EtOAc). IR (KBr): 3250, 3105, 1619, 1602, 1580, 743 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 225 (4.52), 281 (3.62), 295 (3.66). ^{1}H-NMR (CD_3OD) δ: 1.89 (3H, s), 2.89 (2H, t, *J*=7.3 Hz), 3.43 (2H, t, *J*=7.3 Hz), 6.99 (1H, dd, *J*=8.3, 8.3 Hz), 7.10 (1H, s), 7.12 (1H, dd, *J*=8.3, 8.3 Hz), 7.34 (1H, d, *J*=8.3 Hz), 7.52 (1H, d, *J*=8.3 Hz), 7.46 (1H, d, *J*=8.3 Hz). MS *m/z*: 218 (M$^+$). *Anal.* Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.02; H, 6.53; N, 12.77.

1-Hydroxy-*N*b-methoxycarbonyltryptamine (54b) from *N*b-methoxycarbonyl-2,3-dihydrotryptamine (53b) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (56.1 mg, 0.17 mmol) in H_2O (1.8 mL), **53b** (185.9 mg, 0.85 mmol) in MeOH (18.0 mL), and 30% H_2O_2 (0.86 mL, 8.42 mmol) were used. After usual work-up and purification, **54b** (131.5 mg, 67%) was obtained. **54b**: mp 114.0–115.0 °C (colorless needles, recrystallized from CH_2Cl_2–hexane). IR (KBr): 3380, 3190, 1698, 1533, 1267, 983, 751 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 225 (4.53), 295 (3.66). ^{1}H-NMR (CD_3OD) δ: 2.89 (2H, t, *J*=7.5 Hz), 3.36 (2H, t, *J*=7.9 Hz), 3.61 (3H, s), 6.99 (1H, t, *J*=7.9 Hz), 7.09 (1H, s), 7.13 (1H, t, *J*=7.9 Hz), 7.34 (1H, d, *J*=7.9 Hz), 7.53 (1H, d, *J*=7.9 Hz). MS *m/z*: 234 (M$^+$). *Anal.* Calcd for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.40; H, 6.02; N, 11.90.

1-Hydroxy-*N*b-trifluoroacetyltryptamine (54c) from *N*b-trifluoroacetyl-2,3-dihydrotryptamine (53c) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (57.8 mg, 0.18 mmol) in H_2O (2.2 mL), **53c** (218.6 mg, 0.85 mmol) in MeOH (20.0 mL), and 30% H_2O_2 (984.0 mg, 8.68 mmol) in MeOH (2.0 mL) were used. After usual work-up, the crude product was purified by column-chromatography on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to give **54c** (165.3 mg, 72%). **54c**: colorless oil. IR (film): 3310, 2935, 1721, 1698, 1566, 1553, 1451, 1354, 1205, 1098, 1008, 741 cm^{-1}. ^{1}H-NMR (5% CD_3OD in $CDCl_3$) δ: 2.99 (2H, t, *J*=6.6 Hz), 3.62 (2H, q, *J*=6.6 Hz), 7.07 (1H, s), 7.08 (1H, t, *J*=8.0 Hz), 7.22 (1H, t, *J*=8.0 Hz), 7.38 (1H, br s), 7.44 (1H, d, *J*=8.0 Hz), 7.53 (1H, d, *J*=8.0 Hz). High resolution MS *m/z*: Calcd for $C_{12}H_{11}F_3N_2O_2$: 272.0772. Found: 272.0779.

***N*b,*N*b-Dimethyl-1-hydroxytryptamine (54d) from *N*b,*N*b-dimethyl-2,3-dihydrotryptamine (53d)**—

Prepared according to the general method B, where $Na_2WO_4·2H_2O$ (132.5 mg, 0.40 mmol) in H_2O (4.0 mL), **53d** (378.9 mg, 1.99 mmol) in MeOH (40.0 mL), and 30% H_2O_2 (2.0 mL, 19.6 mmol) in MeOH (40.0 mL) were used. After usual work-up, the crude product was purified by column-chromatography on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (46:5:0.5, v/v) to give **54d** (70.5 mg, 55%). **54d**: mp 179.5–180.0 °C (colorless needles, recrystallized from MeOH–H_2O). IR (KBr): 2415, 1470, 1447, 1320, 1226, 838, 737 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 223 (4.48), 292 (3.62). ^{1}H-NMR (CD_3OD) δ: 2.35 (6H, s), 2.64–2.68 (2H, m), 2.89–2.93 (2H, m), 6.99 (1H, dt, *J*=0.9 and 8.1 Hz), 7.09 (1H, s), 7.13 (1H, dt, *J*=0.9, 8.1 Hz), 7.34 (1H, dt, *J*=8.1, 0.9 Hz), 7.50 (1H, dt, *J*=8.1, 0.9 Hz). MS *m/z*: 204 (M^+). *Anal.* Calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.35; H, 8.04; N, 13.66.

1-Hydroxy-*N*b-*n*-propyltryptamine (54e) from *N*b-*n*-propyl-2,3-dihydrotryptamine (53e) — Prepared according to the general method B, where $Na_2WO_4·2H_2O$ (56.5 mg, 0.17 mmol) in H_2O (1.8 mL), **53e** (173.4 mg, 0.85 mmol) in MeOH (18.0 mL), and 30% H_2O_2 (0.85 mL, 8.42 mmol) were used. After usual work-up, the crude product was purified by column-chromatography on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (46:5:0.5, v/v) to give **54e** (96.3 mg, 52%). **54e**: mp 147.0–148.0 °C (colorless needles, recrystallized from MeOH). IR (KBr): 2960, 2840, 1970, 1515, 1447, 1343, 1322, 1221, 1089, 785, 734 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 0.90 (3H, t, *J*=7.3 Hz), 1.52 (2H, sext, *J*=7.3 Hz), 2.63 (2H, m), 2.94 (4H, m), 6.96 (1H, dd, *J*=8.0, 1.1 Hz), 7.09 (1H, s), 7.11 (1H, dd, *J*=8.0, 1.1 Hz), 7.37 (1H, ddd, *J*=8.0, 1.1, 0.7 Hz), 7.50 (1H, ddd, *J*=8.0, 1.1, 0.7 Hz). MS *m/z*: 218 (M^+). *Anal.* Calcd for $C_{13}H_{18}N_2O·1/8H_2O$: C, 70.80; H, 8.34; N, 12.70. Found: C, 70.91; H, 8.29; N, 12.70.

1-Methoxy-*N*b-acetyltryptamine (55a) from 54a — Ethereal CH_2N_2 (excess) was added to a solution of **54a** (51.6 mg, 0.23 mmol) and stirred at rt for 1 h. After evaporation of the solvent under reduced pressure, the residue was column-chromatographed on SiO_2 with CH_2Cl_2–MeOH (99:1, v/v) to give **55a** (46.7 mg, 85%). **55a**: colorless oil. IR (film): 3280, 3075, 1650, 1551, 1451, 740 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.93 (3H, s), 2.93 (2H, t, *J*=6.6 Hz), 3.56 (2H, dt, *J*=5.9, 6.6 Hz), 4.06 (3H, s), 5.66 (1H, br s, D_2O exchange), 7.11 (1H, s), 7.12 (1H, br d, *J*=8.3 Hz), 7.26 (1H, br d, *J*=8.3 Hz), 7.42 (1H, d, *J*=8.2 Hz), 7.56 (1H, d, *J*=8.3 Hz). High resolution MS *m/z*: Calcd for $C_{13}H_{16}N_2O_2$: 232.1210. Found: 232.1214.

1-Methoxy-*N*b-methoxycarbonyltryptamine (55b) from 54b — Ethereal CH_2N_2 (excess) was added to a solution of **54b** (39.1 mg, 0.18 mmol) and stirred at rt for 1 h. After usual work-up and purification, **55b** (34.3 mg, 83%) was obtained. **55b**: colorless oil. IR (film): 3320, 2930, 1705, 1525, 1452, 1254, 737 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.93 (2H, t, *J*=6.6 Hz), 3.49 (2H, q, *J*=6.6 Hz), 3.66 (3H, s), 4.06 (3H, s), 4.76 (1H, br s), 7.10 (1H, s), 7.12 (1H, dt, *J*=1.1, 8.0 Hz), 7.25 (1H, dt, *J*=1.1, 8.0 Hz), 7.42 (1H, d, *J*=8.0 Hz), 7.57 (1H, d, *J*=8.0 Hz). High resolution MS *m/z*: Calcd for $C_{13}H_{16}N_2O_3$: 248.1160. Found: 248.1163.

1-Methoxy-*N*b-trifluoroacetyltryptamine (55c) from 54c — Ethereal CH_2N_2 (excess) was added to a solution of **54c** (32.7 mg, 0.12 mmol) and stirred at rt for 1 h. After usual work-up, **55c** (26.8 mg, 78%)

was obtained. **55c**: mp 70.5–71.0 °C (colorless prisms, recrystallized from benzene–hexane). IR (KBr): 3270, 1732, 1702, 1567, 1454, 1215, 1186, 1148, 735 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 223 (4.53), 276 (3.68), 290 (3.69). ^{1}H-NMR ($CDCl_3$) δ: 3.02 (2H, t, *J*=6.7 Hz), 3.67 (2H, q, *J*=6.7 Hz), 4.07 (3H, s), 6.35 (1H, br s), 7.12 (1H, s), 7.14 (1H, t, *J*=8.0 Hz), 7.28 (1H, t, *J*=8.0 Hz), 7.44 (1H, d, *J*=8.0 Hz), 7.56 (1H, d, *J*=8.0 Hz). High resolution MS *m/z*: Calcd for $C_{13}H_{13}F_3N_2O_3$: 286.0928. Found: 286.0877.

Lespedamine (*N*b,*N*b-Dimethyl-1-methoxytryptamine, 55d) from 54d — Ethereal CH_2N_2 (excess) was added to a solution of **54d** (13.1 mg, 0.064 mmol) in MeOH (5.0 mL) with stirring at rt until the starting material was not detected on tlc monitoring. After usual work-up and purification, **55d** (8.0 mg, 57%) was obtained. **55d**: colorless oil. IR (film): 2930, 2855, 2820, 2770, 1460, 1093, 1051, 1034, 1007, 953 cm^{-1} (lit.[18] 1459 cm^{-1}). ^{1}H-NMR ($CDCl_3$) δ: 2.37 (6H, s), 2.65 (2H, t, *J*=8.0 Hz), 2.93 (2H, t, *J*=8.0 Hz), 4.05 (3H, s), 7.10 (1H, dt, *J*=0.9, 7.8 Hz), 7.10 (1H, s), 7.23 (1H, dt, *J*=0.9, 7.8 Hz), 7.40 (1H, dd, *J*=7.8, 0.9 Hz), 7.57 (1H, dd, *J*=7.8, 0.9 Hz) (lit.[7b,18] ^{1}H-NMR (CCl_4) δ: 2.19 (6H, s), 2.32–2.96 (4H, m), 3.92 (3H, s), 6.62–7.45 (5H, m)).

Lespedamine (55d) and lespedamine-*N*b-oxide (56) from 2,3-dihydro-*N*b,*N*b-dimethyltryptamine (53d) — Prepared according to the general method B, where $Na_2WO_4\cdot 2H_2O$ (15.1mg, 0.04 mmol) in H_2O (0.5 mL), **53d** (43.9 mg, 0.23 mmol) in MeOH (5 mL), and 30% H_2O_2 (0.24 mL, 2.35 mmol) were used. After methylation and work-up, the product was purified by column-chromatography on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (46:2:0.2, v/v) to give **55d** (13.1 mg, 26%) and **56** (17.0 mg, 31%) in the order of elution. **56**: colorless oil. IR (film): 3420, 1644, 1453, 954, 742 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.31 (6H, s), 3.37–3.40 (2H, m), 3.57–3.60 (2H, m), 4.06 (3H, s), 7.13 (1H, dt, *J*=1.1, 7.9 Hz), 7.18 (1H, s), 7.25 (1H, dt, *J*=1.1, 7.9 Hz), 7.42 (1H, ddd, *J*=7.9, 1.1, 0.9 Hz), 7.59 (1H, ddd, *J*=7.9, 1.1, 0.9 Hz). MS *m/z*: 234 (M$^+$). *Anal.* Calcd for $C_{13}H_{18}N_2O_2\cdot$MeOH: C, 63.13; H, 8.33; N, 10.52. Found: C, 63.24; H, 8.14; N, 10.74. High resolution MS *m/z*: Calcd for $C_{13}H_{18}N_2O_2$: 234.1368. Found: 234.1370.

1-Methoxy-*N*b-*n*-propyltryptamine (55e) and 1-methoxy-*N*b-methyl-*N*b-*n*-propyltryptamine (57) from *N*b-*n*-propyl-2,3-dihydrotryptamine (53e)— Prepared according to the general method B, where $Na_2WO_4\cdot 2H_2O$ (13.9 mg, 0.04 mmol) in H_2O (0.4 mL), **53e** (41.9 mg, 0.21 mmol) in MeOH (4.0 mL), and 30% H_2O_2 (0.21 mL, 2.06 mmol) were used. After work-up, the product was purified by column-chromatography on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (46:2:0.2, v/v) to give **57** (4.6 mg, 9%) and **55e** (23.3 mg, 49%) in the order of elution. **55e**: pale yellow oil. IR (film): 2960, 2930, 2875, 2820, 1451, 1094, 738 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, t, *J*=7.5 Hz), 1.53 (2H, sext, *J*=7.5 Hz), 2.63 (2H, t, *J*=7.5 Hz), 2.97 (4H, m), 4.05 (3H, s), 7.10 (1H, dt, *J*=1.1 and 8.0 Hz), 7.11 (1H, s), 7.24 (1H, dt, *J*=1.1, 8.0 Hz), 7.41 (1H, dt, *J*=8.0, 1.1 Hz), 7.59 (1H, dt, *J*=8.0, 1.1 Hz). High resolution MS *m/z*: Calcd for $C_{14}H_{20}N_2O$: 232.1575. Found: 232.1575. **57**: colorless oil. IR (film): 2955, 2940, 2870, 2780, 1450, 1098, 1010, 956, 736 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, t, *J*=7.3 Hz), 1.58 (2H, br sext, *J*=7.3 Hz), 2.40

(3H, s), 2.47 (2H, br t, *J*=7.3 Hz), 2.75 (2H, br t, *J*=7.5 Hz), 2.95 (2H, br t, *J*=7.5 Hz), 4.05 (3H, s), 7.11 (1H, dt, *J*=0.9, 8.1 Hz), 7.11 (1H, s), 7.24 (1H, dt, *J*=0.9, 8.1 Hz), 7.40 (1H, d, *J*=8.1 Hz), 7.57 (1H, d, *J*=8.1 Hz). High resolution MS *m/z*: Calcd for $C_{15}H_{22}N_2O$: 246.1731. Found: 246.1734.

2,3-Dihydromelatonin (59) from melatonin (58) — A solution of **58** (1.01 g, 4.35 mmol) in CF_3CO_2H (20.0 mL) was added to Et_3SiH (0.85 mL, 5.32 mmol) and stirred at 58 °C for 1 h. After usual work-up and purification, by column-chromatography on SiO_2 with $CHCl_3$–MeOH (97:3, v/v), **59** (847.7 mg, 83%) was obtained. **59**: mp 83–84 °C (colorless prisms, recrystallized from EtOAc–hexane). IR (KBr): 3550, 1645, 1550, 1495, 1360, 1220, 1110, 1025, 890, 795, 740, 690, 585, 535 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.73–1.79 (1H, m), 1.94–2.03 (1H, m), 1.95 (3H, s), 3.22–3.43 (4H, m), 3.70 (1H, br t, *J*=8.8 Hz), 3.75 (3H, s), 5.71 (1H, br s), 6.60 (1H, d, *J*=8.5 Hz), 6.62 (1H, dd, *J*=8.5, 2.20 Hz), 6.73 (1H, d, *J*=2.20 Hz). *Anal.* Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.47; H, 7.80; N, 11.91.

1-Hydroxymelatonin (60a) from 2,3-dihydromelatonin (59) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$, (107.1 mg, 0.325 mmol) in H_2O (3.8 mL), **59** (379.5 mg, 1.62 mmol) in MeOH (38.0 mL), and 30% H_2O_2 (1.8 mL, 15.9 mmol) were used. After usual work-up and purification by column-chromatographed on SiO_2 with EtOAc, **60a** (234.9 mg, 58%) was obtained. **60a**: mp 113–114 °C (colorless prisms recrystallized from $CHCl_3$–hexane. IR (KBr): 3600, 3200, 2900, 2850, 1610, 1560, 1480, 1360, 1280, 1260, 1215, 1170, 1095, 1035, 995, 950, 900, 823, 795, 760, 600 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.91 (3H, s), 2.86 (2H, t, *J*=7.3 Hz), 3.42 (2H, t, *J*=7.3 Hz), 3.82 (3H, s), 6.80 (1H, dd, *J*=8.8, 2.4 Hz), 7.03 (1H, d, *J*=2.4 Hz), 7.07 (1H, s), 7.23 (1H, d, *J*=8.8 Hz). MS *m/z*: 248 (M^+). *Anal.* Calcd for $C_{13}H_{16}N_2O_3 \cdot 1/8H_2O$: C, 62.32; H, 6.54; N, 11.18. Found: C, 62.20; H, 6.40; N, 11.01.

1-Methoxymelatonin (60b) from 1-hydroxymelatonin (60a) — Excess CH_2N_2 in Et_2O was added to a solution of **60a** (40.2 mg, 0.16 mmol) in MeOH (5.0 mL) at rt and stirred for 15 min. Evaporation of the solvent under reduced pressure afforded oil, which was column-chromatographed on SiO_2 with $CHCl_3$–MeOH–28% aq. NH_3 (46:2:0.2, v/v) to give **60b** (39.1 mg, 75%). **60b**: pale yellow oil. IR (film): 3280, 2930, 1643, 1553, 1480, 1440, 1220, 1090 cm^{-1}. ^{1}H-NMR (5%CD_3OD–$CDCl_3$) δ: 1.93 (3H, s), 2.87 (2H, t, *J*=6.8 Hz), 3.53 (2H, t, *J*=6.8 Hz), 3.85 (3H, s), 4.04 (3H, s), 6.91 (1H, dd, *J*=8.9, 2.3 Hz), 7.00 (1H, d, *J*=2.3 Hz), 7.08 (1H, s), 7.30 (1H, dd, *J*=8.9, 2.3 Hz). MS *m/z*: 262 (M^+). High resolution MS *m/z*: Calcd for $C_{14}H_{18}N_2O_3$: 262.1317. Found: 262.1331.

(*dl*)-2-Acetoamino-3-(1-hydroxyindol-3-yl)propanol ((*dl*)-62) from (*dl*)-2-acetoamino-3-(2,3-dihydroindol-3-yl)propanol ((*dl*)-61) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (44.6 mg, 0.14 mmol), (*dl*)-**61** (158.2 mg, 0.68 mmol) in MeOH (16 mL), and 30% H_2O_2 (0.69 mL, 6.76 mmol) were used. After usual work-up and purification, (*dl*)-**62** (40.8 mg, 30%) was obtained. (*dl*)-**62**: colorless unstable oil. IR (film): 3265, 3110, 1629, 1547, 738 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 1.88 (3H, s), 2.80 (1H, dd, *J*=14.5, 7.5 Hz), 3.00 (1H, dd, *J*=14.5, 6.5 Hz), 3.53 (2H, d, *J*=5.1 Hz), 4.14

(1H, m), 6.96 (1H, dd, *J*=7.6, 7.1 Hz), 7.10 (1H, s), 7.12 (1H, dd, *J*=7.6, 6.8 Hz), 7.32 (1H, d, *J*=7.1 Hz), 7.57 (1H, d, *J*=6.8 Hz). High resolution MS *m/z*: Calcd for $C_{13}H_{16}N_2O_3$: 248.1159. Found: 248.1146.

(*dl*)-2-Acetoamino-3-(1-methoxyindol-3-yl)propanol ((*dl*)-63) from (*dl*)-62) — Ethereal CH_2N_2 (excess) was added to a solution of (*dl*)-**62** (32.8 mg, 0.13 mmol) in MeOH (3.0 mL) and stirring was continued at rt for 10 min. After usual work-up and purification by column-chromatography on SiO_2 with CH_2Cl_2–MeOH (95:5, v/v), (*dl*)-**63** (26.7 mg, 77%) was obtained. (*dl*)-**63**: mp 117–118°C (colorless prisms, recrystallized from EtOAc). IR (KBr): 3275, 3180, 3090, 1630, 1584, 1440, 1081, 1052, 757, 737 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 223 (4.43), 278 (3.63), 291 (3.65). ^{1}H-NMR ($CDCl_3$) δ: 1.96 (3H, s), 2.54 (1H, br s, D_2O exchange), 2.97 (2H, d, *J*=6.3 Hz), 3.63 (2H, dd, *J*=5.6, 3.9 Hz), 4.04 (3H, s), 4.08–4.38 (1H, m), 5.88 (1H, d, *J*=7 Hz), 7.08 (1H, dd, *J*=7.1, 6.8 Hz), 7.12 (1H, s), 7.23 (1H, dd, *J*=7.3, 6.8 Hz), 7.40 (1H, d, *J*=7.1 Hz), 7.60 (1H, d, *J*=7.3 Hz). MS *m/z*: 262 (M^+). *Anal.* Calcd for $C_{14}H_{18}N_2O_2$: C, 64.11; H, 6.92; N, 10.68. Found: C, 63.89; H, 7.24; N, 10.54.

(*S*)-(+)-*N*b-Acetyl-1-hydroxytryptophan methyl ester ((*S*)-(+)-65) from (*S*)-(+)-*N*b-acetyl-2,3-dihydrotryptophan methyl ester ((*S*)-(+)-64) — Prepared according to the general method B, where $Na_2WO_4 \cdot 2H_2O$ (40.2 mg, 0.12 mmol), (*S*)-(+)-**64** (159.5 mg, 0.61 mmol) in MeOH (15.0 mL), and 30% H_2O_2 (0.62 mL, 6.09 mmol) were used. After usual work-up, the product was purified by p-TLC on SiO_2 with CH_2Cl_2–MeOH (98:2, v/v) to give (*S*)-(+)-**65** (89.7 mg, 53%). (*S*)-(+)-**65**: mp 116.0–117.0 °C (colorless prisms, recrystallized from MeOH–H_2O). $[\alpha]_D^{24}$ +11.8° (c=0.102, MeOH). IR (KBr): 3370, 3240, 1733, 1655, 1534, 745 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 224 (4.53), 282 (3.64), 293 (3.66). ^{1}H-NMR (5% CD_3OD in $CDCl_3$) δ: 1.90 (3H, s), 3.19 (1H, dd, *J*=15.0, 5.8 Hz), 3.27 (1H, dd, *J*=15.0, 5.2 Hz), 3.71 (3H, s), 4.86 (1H, dd, *J*=5.8, 5.2 Hz), 7.01 (1H, s), 7.06 (1H, t, *J*=8.3 Hz), 7.19 (1H, t, *J*=8.3 Hz), 7.42 (1H, d, *J*=8.3 Hz), 7.45 (1H, d, *J*=8.3 Hz). MS *m/z*: 276 (M^+). *Anal.* Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.85; H, 5.88; N, 10.14.

(*dl*)-*N*b-Acetyl-1-hydroxytryptophan methyl ester ((*dl*)-65) from (*dl*)-64 — Prepared under the same reaction conditions as described in the procedure for (*S*)-(+)-**65**. Yield was 73%. (*dl*)-**65**: mp 153.0–154.0 °C (decomp., colorless prisms, recrystallized from MeOH). IR (KBr): 3259, 3125, 1739, 1640, 1547, 727 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 224 (4.55), 282 (3.65), 294 (3.68). ^{1}H-NMR (CD_3OD) δ: 1.92 (3H, s), 3.06 (1H, dd, *J*=13.9, 7.6 Hz), 3.28 (1H, dd, *J*=13.9, 5.9 Hz), 3.65 (3H, s), 4.66 (1H, dd, *J*=7.6, 5.9 Hz), 6.97 (1H, ddd, *J*=7.1, 6.8, 1.5 Hz), 7.09 (1H, s), 7.12 (1H, ddd, *J*=7.6, 6.8, 1.5 Hz), 7.32 (1H, dm, *J*=7.1 Hz), 7.47 (1H, dm, *J*=7.6 Hz). MS *m/z*: 276 (M^+). *Anal.* Calcd for $C_{14}H_{16}N_2O_4$: C, 60.86; H, 5.84; N, 10.14. Found: C, 60.78; H, 5.92; N, 10.09.

(*S*)-(+)-*N*b-Acetyl-1-methoxytryptophan methyl ester ((*S*)-(+)-66) from (*S*)-(+)-65 — Ethereal CH_2N_2 (excess) was added to a solution of (*S*)-(+)-**65** (46.8 mg, 0.17 mmol) in MeOH (2.0 mL) and stirring was continued at rt for 15 min. After work-up and purification by column-chromatography on SiO_2 with

CH_2Cl_2–MeOH (98:2, v/v), (*S*)-(+)-**66** (38.3 mg, 78%) was obtained. (*S*)-(+)-**66**: colorless oil. $[\alpha]_D^{20}$ +16.8° (c=0.107, MeOH). IR (film): 3270, 1741, 1658, 1540, 736 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 223 (4.47), 276 (3.66), 289 (3.68). ^{1}H-NMR ($CDCl_3$) δ: 1.97 (3H, s), 3.25 (1H, dd, *J*=14.6, 4.9 Hz), 3.31 (1H, dd, *J*=14.6, 5.4 Hz), 3.70 (3H, s), 4.05 (3H, s), 4.93 (1H, ddd, *J*=7.8, 5.4, 4.9 Hz), 6.03 (1H, d, *J*=7.8 Hz), 7.04 (1H, s), 7.11 (1H, dd, *J*=8.3, 7.8 Hz), 7.24 (1H, t, *J*=8.3 Hz), 7.40 (1H, d, *J*=8.3 Hz), 7.49 (1H, d, *J*=7.8 Hz). High resolution MS *m/z*: Calcd for $C_{15}H_{18}N_2O_4$: 290.1266. Found: 290.1296.

(*dl*)-*N*b-Acetyl-1-methoxytryptophan methyl ester ((*dl*)-66) from (*dl*)-65 — Ethereal CH_2N_2 (excess) was added to a solution of (*dl*)-**65** (40.1 mg, 0.15 mmol) in MeOH (2.0 mL) and stirring was continued at rt for 30 min. After usual work-up, (*dl*)-**66** (35.1 mg, 83%) was obtained. (*dl*)-**66**: mp 95–96°C (colorless plates, recrystallized from MeOH-H_2O). IR (KBr): 3235, 1737, 1657, 1545, 1443, 1376, 1313, 1241, 1210, 1173, 747, 741 cm^{-1}. UV λ_{max}^{MeOH} nm (log ε): 224 (4.50), 277 (3.70), 290 (3.17). ^{1}H-NMR ($CDCl_3$) δ: 1.97 (3H, s), 3.26 (1H, dd, *J*=15.1, 4.9 Hz), 3.31 (1H, dd, *J*=15.1, 5.4 Hz), 3.71 (3H, s), 4.05 (3H, s), 4.93 (1H, ddd, *J*=7.8, 5.4, 4.9 Hz), 5.88 (1H, d, *J*=7.8 Hz, D_2O exchange), 7.04 (1H, s), 7.11 (1H, br d, *J*=8.3 Hz), 7.24 (1H, br d, *J*=8.3 Hz), 7.41 (1H, d, *J*=8.3 Hz), 7.49 (1H, d, *J*=8.3 Hz). MS *m/z*: 290 (M^+). *Anal*. Calcd for $C_{15}H_{18}N_2O_4$: C, 62.06; H, 6.25; N, 9.65. Found: C, 62.04; H, 6.37; N, 9.52.

X-Ray analysis (Table 2) – A single crystal (0.10 x 0.20 x 0.30 mm) of (*dl*)-**65** was obtained by recrystallization from MeOH. All measurements were made on a Rigaku AFC5R diffractometer with graphite monochromated Cu-*Kα* radiation (*λ*=1.54178 Å). Crystal data: $C_{14}H_{16}N_2O_4$, *M*=276.29, triclinic,

Table 2. Positional Parameters and *B* (eq) for (*dl*)-**65**

atom	x	y	z	*B* (eq)	atom	x	y	z	*B* (eq)
O (1)	0.7722 (2)	0.3704 (2)	0.0440 (2)	5.63 (8)	C (13)	0.0586 (3)	0.5761 (2)	0.3249 (3)	3.96 (9)
O (2)	0.4835 (2)	0.3861 (1)	0.5934 (2)	4.95 (7)	C (14)	0.0700 (4)	0.7014 (2)	0.3501 (4)	5.0 (1)
O (3)	0.3578 (2)	0.2287 (1)	0.5073 (2)	4.60 (7)	H (1)	0.441 (3)	0.441 (2)	0.071 (3)	4.55 (1)
O (4)	–0.0859 (2)	0.5469 (1)	0.2748 (2)	5.96 (8)	H (2)	0.509 (3)	0.058 (2)	0.232 (3)	5.23 (1)
N (1)	0.6773 (2)	0.3248 (2)	0.1124 (2)	4.29 (8)	H (3)	0.789 (3)	–0.067 (3)	0.274 (4)	7.49 (2)
N (2)	0.2116 (2)	0.4990 (1)	0.3592 (3)	4.15 (8)	H (4)	1.031 (4)	–0.022 (3)	0.232 (4)	7.67 (2)
C (1)	0.4998 (3)	0.3658 (2)	0.1011 (3)	4.1 (1)	H (5)	0.991 (3)	0.158 (2)	0.153 (3)	5.62 (1)
C (2)	0.4390 (2)	0.2864 (2)	0.1411 (2)	3.56 (8)	H (6)	0.235 (3)	0.220 (2)	0.140 (3)	4.61 (1)
C (3)	0.5868 (2)	0.1893 (2)	0.1740 (3)	3.62 (8)	H (7)	0.167 (3)	0.338 (2)	0.063 (3)	4.61 (1)
C (4)	0.6091 (3)	0.0825 (2)	0.2188 (3)	5.0 (1)	H (8)	0.115 (3)	0.363 (2)	0.349 (3)	3.776 (9)
C (5)	0.7725 (4)	0.0071 (2)	0.2374 (4)	6.7 (1)	H (9)	0.475 (5)	0.101 (3)	0.634 (4)	10.58 (3)
C (6)	0.9146 (4)	0.0347 (3)	0.2131 (4)	6.7 (1)	H (10)	0.605 (4)	0.156 (3)	0.612 (4)	8.02 (2)
C (7)	0.8983 (3)	0.1383 (2)	0.1673 (4)	5.4 (1)	H (11)	0.512 (7)	0.232 (3)	0.753 (5)	15.44 (5)
C (8)	0.7338 (3)	0.2156 (2)	0.1512 (3)	3.91 (9)	H (12)	0.159 (5)	0.722 (3)	0.444 (4)	10.75 (4)
C (9)	0.2568 (3)	0.2983 (2)	0.1559 (3)	4.1 (1)	H (13)	0.059 (6)	0.720 (3)	0.246 (4)	13.95 (5)
C (10)	0.2237 (2)	0.3742 (2)	0.3400 (3)	3.79 (8)	H (14)	–0.027 (5)	0.754 (3)	0.376 (4)	9.19 (3)
C (11)	0.3691 (3)	0.3336 (2)	0.4964 (3)	3.78 (8)	H (15)	0.818 (5)	0.428 (3)	0.143 (4)	10.46 (3)
C (12)	0.4935 (5)	0.1790 (3)	0.6500 (5)	6.3 (1)	H (16)	0.304 (3)	0.526 (2)	0.388 (3)	4.73 (1)

space group $P\bar{1}$ (#2), a=8.163 (1)Å, b=12.086 (1)Å, c=8.0126 (9)Å, α=107.940 (8)°, β=109.560 (9)°, γ=73.161 (8)°, V=693.2 (1)Å^3, Z=2, D_{calc}=1.324 g/cm^3, F(000)=292, and μ(Cu$K\alpha$)=7.77 cm^{-1}. The structure was solved by direct methods using MITHRIL[24] The non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 2685 observed reflections (I>3.00σ (I), 2θ<120.1°) and 245 variable parameters. The final refinement converged with R=0.039 and Rw=0.047.

REFERENCES AND NOTES

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