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Studies on Tertiary Amine Oxides. LXXII.[1] Some Nucleophilic Reactions of 1-Hydroxy-2-phenylindole[2]

Tsuyoshi Nagayoshi, Seitaro Saeki, and Masatomo Hamana*

Faculty of Pharmaceutical Sciences, Kyushu University, Maidashi, Higashi-ku, Fukuoka 812, Japan

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1-Hydroxy-2-phenylindole (**1**) reacts with tosyl chloride and *p*-nitrobenzenesulfonyl chloride in DMF–pyridine to give the corresponding 2-phenyl-3-sulfonyloxyindole (**2** and **4**). Benzoyl chloride is less reactive, and 1-benzoyloxy-2-phenylindole (**5**) or 3-benzoyloxy-2-phenylindole (**6**) is formed, depending upon the reaction conditions. 3-Acetoxy-2-phenylindole (**7**) is also obtained by refluxing **1** with acetic anhydride or with acetyl chloride in DMF–pyridine.

Treatment of **1** with tosyl chloride and then with 1-morpholinocyclohexene (**9**), ethyl acetoacetate (**17**) and ethyl cyanoacetate (**20**) in DMF–pyridine at room temperature affords 3-(2-oxocyclohexyl)-2-phenylindole (**10**), ethyl α-(2-phenyl-3-indolyl)acetoacetate (**18**) and ethyl α-(2-phenyl-3-indolyl)cyanoacetate (**21**) in 23.2, 41 and 61% yields, respectively.

Keywords——enehydroxylamine system; 1-acyloxy-2-phenylindole; 3-acyloxy-2-phenylindole; 1-morpholinocyclohexene; 3-(2-oxocyclohexyl)-2-phenylindole; ethyl α-(2-phenyl-3-indolyl)acetoacetate; ethyl α-(2-phenyl-3-indolyl)cyanoacetate

The preceding paper of this series described some electrophilic reactions of 1-hydroxy-2-phenylindole (**1**).[1] As a continuation of this work, nucleophilic reactions of **1** were investigated.

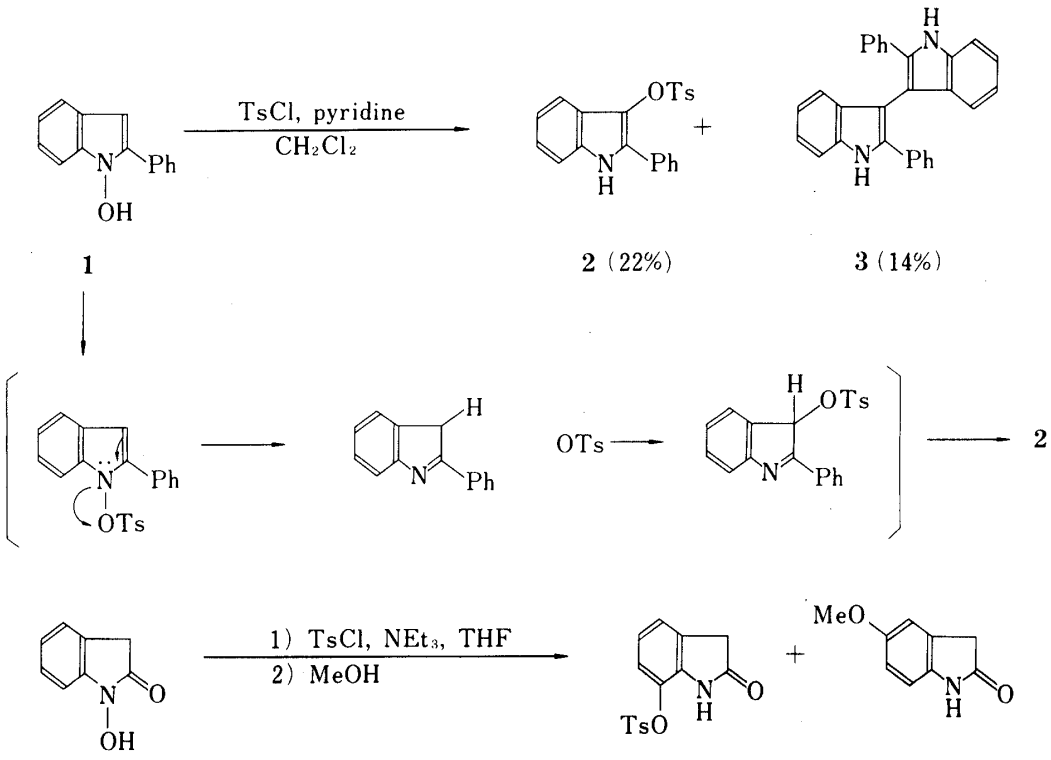


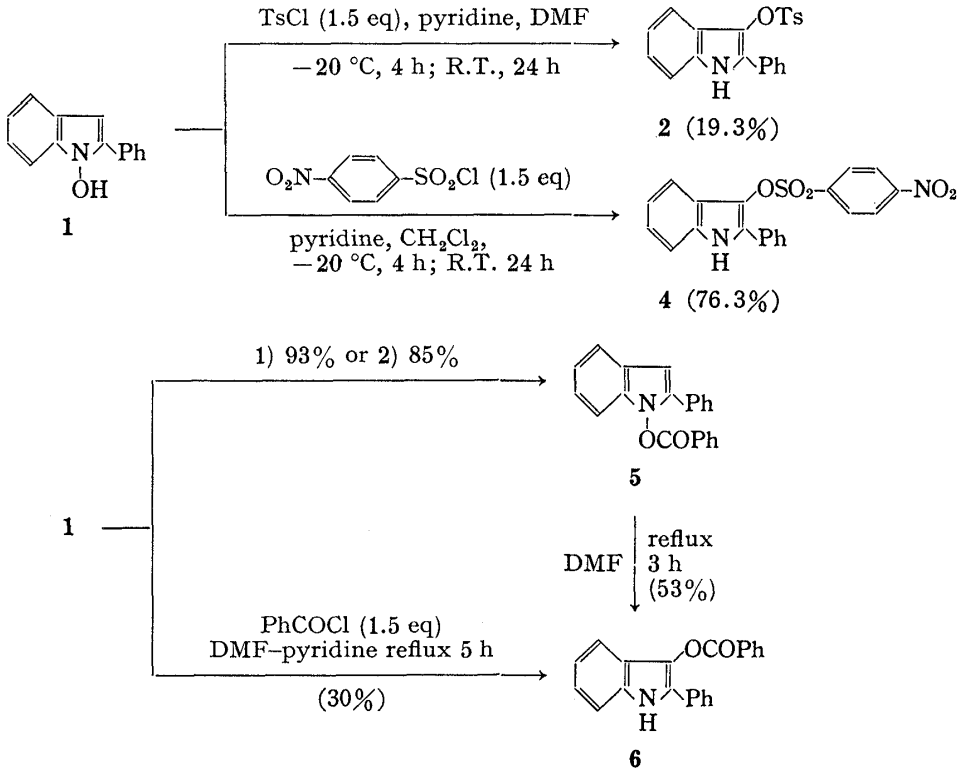
Chart 1

Reaction with Acylating Agents

Sundberg[3] reported that treatment of **1** with tosyl chloride and pyridine in dichloromethane gives 2-phenyl-3-tosyloxyindole (**2**) and 2,2′-diphenyl-3,3′-bisindole (**3**), and he suggested the formation of **2** to involve cleavage of the N–O bond of the initially formed 1-tosyloxy derivative. A somewhat similar reaction was described with 1-hydroxy-2-oxoindoline[4] (Chart 1).

First, the reaction of 1-hydroxy-2-phenylindole **1** with tosyl chloride (1.5 eq) and pyridine was attempted using N,N-dimethylformamide (DMF) as a solvent in place of dichloromethane. When the reaction mixture was stirred at around −20 °C for 4 h and then at room temperature for one day, 2-phenyl-3-tosyloxyindole **2** was obtained in 19.3% yield as the sole product. The reaction with *p*-nitrobenzenesulfonyl chloride and pyridine in dichloromethane gave the corresponding 3-(*p*-nitrobenzenesulfonyloxy)-indole (**4**) 76.3% yield.

Subsequently, the reaction with benzoyl chloride was examined, and it was found that 1-benzoyloxy-2-phenylindole (**5**)[5] is readily obtained in good yields under various conditions, whereas the formation of 3-benzoyloxy-2-phenylindole (**6**) requires rather severe conditions. For example, when a mixture of **1**, benzoyl chloride (1 eq), 10% sodium carbonate solution and dichloromethane was shaken at room temperature for 5 days or when a dichloromethane solution of **1**, benzoyl chloride and pyridine was refluxed for 3 h, **5** was isolated in 93 and 85%



1) PhCOCl (1 eq), 10% Na_2CO_3–CH_2Cl_2, R.T., 5 d
2) PhCOCl (1 eq), CH_2Cl_2–pyridine, R.T., 3 h

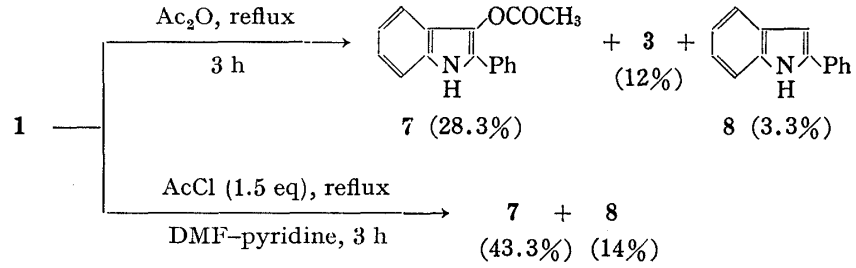


Chart 2

yields, respectively. Similarly, product **5** was obtained from the reaction in benzene or acetonitrile under reflux or by using triethylamine as a base in boiling dichloromethane. However, treatment of **1** with benzoyl chloride (1.5 eq) and pyridine in boiling DMF for 3 h afforded the 3-benzoyloxyindole **6** (colorless needles, mp 88—90 °C) in 30% yield along with a trace of the bisindole **3**. Further, it was found **5** was converted into **6** in 53% yield on refluxing in DMF for 3 h. It should be noted that DMF is the only effective solvent so far examined, and that vigorous refluxing in DMF is required for the reaction to proceed. No reaction occurred if acrylonitrile, benzene, toluene, xylene or pyridine was used as the solvent, and the yield of **6** substantially decreased on only mild refluxing, heating at below 150 °C giving no **6** at all.

The formation of 3-acetoxy-2-phenylindole was also investigated. A solution of **1** in acetic anhydride was vigorously refluxed for 3 h. Chromatographic purification on silica gel afforded the desired product, 3-acetoxy-2-phenylindole (**7**) (colorless needles, mp 79—81 °C) in 28% yield, together with the bisindole **3** (12%) and 2-phenylindole (**8**) (3.3%). When **1** was refluxed with acetyl chloride (1.5 eq) in DMF–pyridine for 3 h, **7** and **8** were obtained in 43.3 and 14% yields, respectively.

These reactions are formulated in Chart 2. The identity of the new compounds, **4**, **6** and **7**, was established by the results of elemental analyses and spectral examinations.

The formation of 3-acyloxy-2-phenylindoles, **2**, **4**, **6** and **7**, from **1** should follow the course proposed by Sundberg,[3] which involves the initial formation of 1-acyloxyindole and subsequent cleavage of the N–O bond followed by nucleophilic attack by acyloxy anions thus extruded at the 3-position of the indole ring (Chart 1). Apparently the crucial step is the cleavage of the N–O bond of 1-acyloxyindoles, but the features of the transformation of 1-acyloxyindoles to 3-acyloxyindoles remain to be elucidated in detail.

Reactions with 1-Morpholinocyclohexene, Ethyl Acetoacetate and Ethyl Cyanoacetate

Although the details of the mechanism have not been established for the above-mentioned reaction, the possibility cannot be excluded that a coexisting nucleophile, instead of an acyloxy anion, attacks the 3-position of the indole nucleus, if the reaction proceeds stepwise by an ionic process. Nucleophilic substitutions of similar pattern are known in a few cases.[4,6]

With the aim of introducing a cyano group at the 3-position of the indole ring, **1** was treated with potassium cyanide in the presence of benzoyl chloride, *p*- nitrobenzoyl chloride or tosyl chloride under various conditions. However all attempts failed, 1-acyloxy- or 3-acyloxy-2-phenylindoles being isolated instead of 3-cyano-2-phenylindole.

The reaction with 1-morpholinocyclohexene (**9**) was next examined. A solution of tosyl chloride (1.1 eq) in pyridine was added to a cooled DMF solution of **1** to form 2-phenyl-1-tosyloxyindole. After 30 min, 2.5 equivalents of **9** was added, and the mixture was stirred at around −20 °C for 4 h and then at room temperature for 1 day. Separation of the products by chromatography on silica gel afforded 3-(2-oxocyclohexyl)-2-phenylindole (**10**) and 2-phenylisatogen (**11**) 23.2 and 7.5% yields, respectively. A similar process using only pyridine as the reaction medium also gave **10** in 14.5% yield as the sole product. The reaction in dichloromethane–pyridine yielded not **10** but the 3-tosyloxyindole **2** (44.0%).

On the other hand, benzoyl chloride was not effective as an acylating agent for the formation of **10**. No participation of the enamine **9** was observed in any of the attempted reactions, and only **5** or **6** was isolated in some cases.

Product **10** was recrystallized from *n*-hexane–benzene as pale yellow scales, mp 202—204 °C, with the empirical formula $C_{20}H_{19}NO$; its infrared (IR) and nuclear magnetic resonance (NMR) spectra were fully consistent with the structure assignment (see the experimental section). Further, in order to confirm the structure chemically the transformation of **10** into the known 2,3-diphenylindole[7] (**13**) was attempted. Treatment of **10** with sodium borohydride in boiling ethanol for 3.5 h afforded the corresponding cyclohexanol derivative (**12**) (colorless

needles, mp 190—191 °C) in 23% yield; the configuration of the hydroxy function was not elucidated. The conversion of **12** to 2,3-diphenylindole **13**[7] (colorless needles, mp 124—126 °C) was successfully performed in 42.6% yield by heating it with selenium at 300—310 °C for 5 h.

The Wolff–Kishner reaction of **10** was also attempted by heating it with hydrazine hydrate and potassium hydroxide at 150—180 °C in diethylene glycol, but satisfactory results were not obtained.

2-Phenylisatogen **11** was identified by direct comparison with an authentic sample prepared by the reaction of 1-hydroxy-2-phenylindole **1** with amyl nitrite.[8] In connection with this experiment, treatment of **1** with N-chloro- or N-bromo-succinimide was found to be superior for the preparation of **11** to the usual methods.[8,9]

Further, it was found that similar treatment of **1** with 1-acetoxycyclohexene (**14**) and tosyl

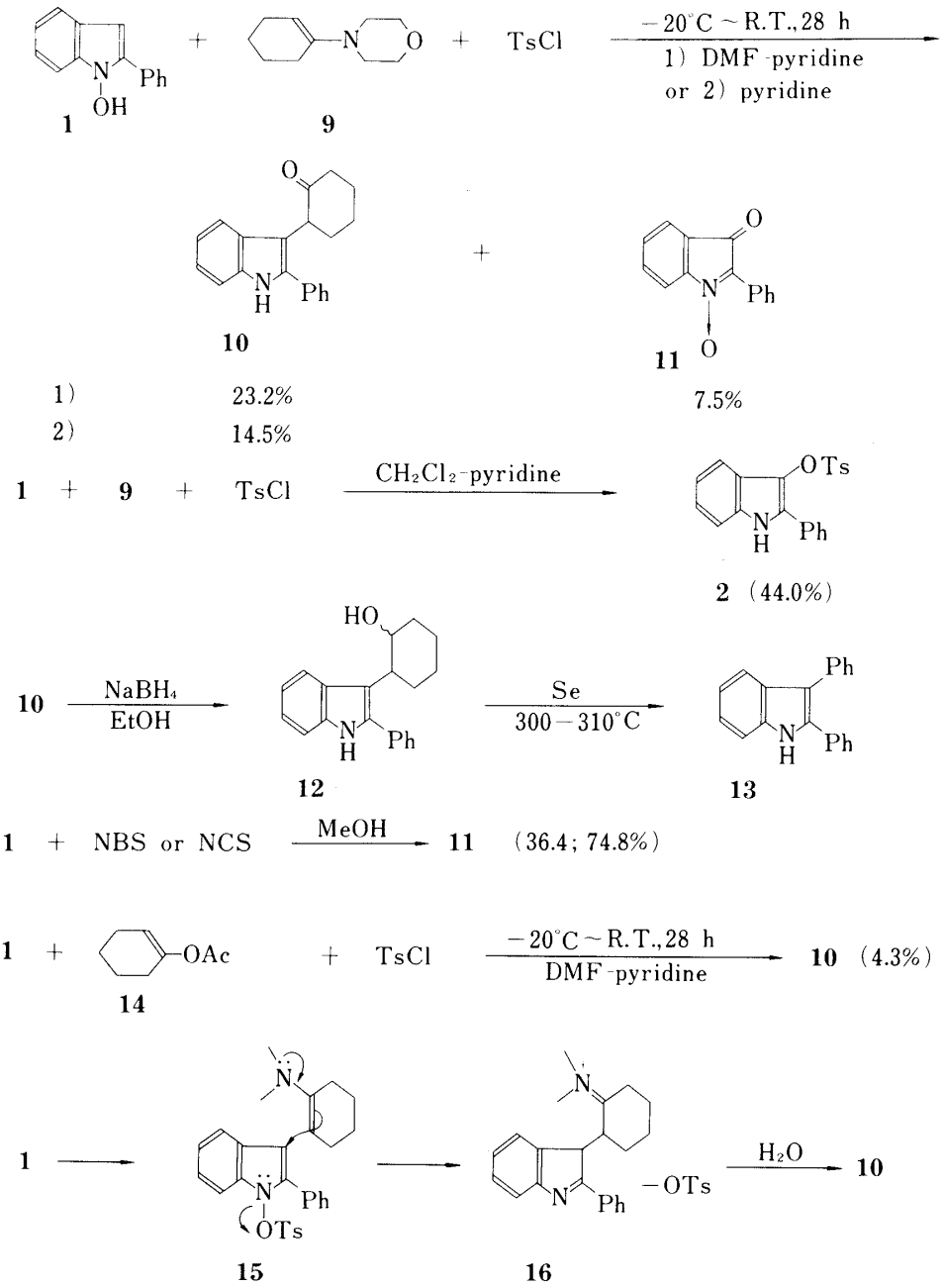


Chart 3

chloride in pyridine and DMF at low temperatures resulted in the formation of **10**, though in a poor yield of 4.3%.

These reactions are illustrated in Chart 3. The formation of **10** may be reasonably rationalized in terms of the course shown in Chart 3. Cleavage of the tosyloxy anion from the intially formed 2-phenyl-1-tosyloxyindole (**15**) and subsequent nucleophilic attack by the enamine **9** at the electron-deficient 3-position of the indole nucleus lead to an indolenine intermediate (**16**), which undergoes a proton shift and hydrolysis to give **10**. 2-Phenylisatogen **11** seems to result from air-oxidation of **1**.

Subsequently, in order to explore the reactivity of **1** towards active methylene compounds, the reaction with ethyl acetoacetate (**17**) was investigated. No reaction occurred at all upon treatment of **1** and **17** with acetic anhydride or benzoyl chloride in DMF at room temperature or under reflux. Nevertheless, it was found that the reaction proceeded smoothly with tosyl chloride under the same conditions as the reaction of **1** with the enamine **9**, An excess (6.5 eq) of **17** was added to a cooled solution of **1** and tosyl chloride (1.5 eq) in DMF–pyridine, and the reactants were stirred at around −20 °C for 4 h and then at room temperature for 3 days. Separation of the products by chromatography on silica gel afforded ethyl α-(2-phenyl-3-indolyl)acetoacetate (**18**) and 2-phenyl-4H-3,1-benzoxazone[10] (**19**) in 41 and 16% yields, respectively.

Product **18** was recrystallized from carbon tetrachloride as pale yellow scales, mp 135—138 °C, with the empirical formula $C_{20}H_{19}NO_3$, and its IR and NMR spectra were fully consistent with the assigned structure (see the experimental section). 2-Phenyl-4H-3,1-benzoxazone **19** was recrystallized from *n*-hexane–dichloromethane as colorless needles of mp 125—127 °C, and its analytical values were consistent with the empirical formula $C_{14}H_9NO_2$. Its IR spectrum exhibited a carbonyl band at 1767 cm^{-1} but no absorption due to NH group, and the NMR spectrum showed signals only in the aromatic region. From these data, a six-membered α,β-unsaturated lactone structure was assigned to **19**. Its formation may involve the rearrangement of **11** formed as a by-product.[10]

Quite similarly, though no reaction was observed when acetic anhydride or benzoyl chloride was used as an acylating agent, **1** reacted smoothly with ethyl cyanoacetate (**20**) in the presence of tosyl chloride under the same conditions, and ethyl α-(2-phenyl-3-indolyl)-cyanoacetate (**21**) (pale yellow needles, mp 158—160 °C) was obtained in 61% yield, together with a trace of **19** (Chart 4).

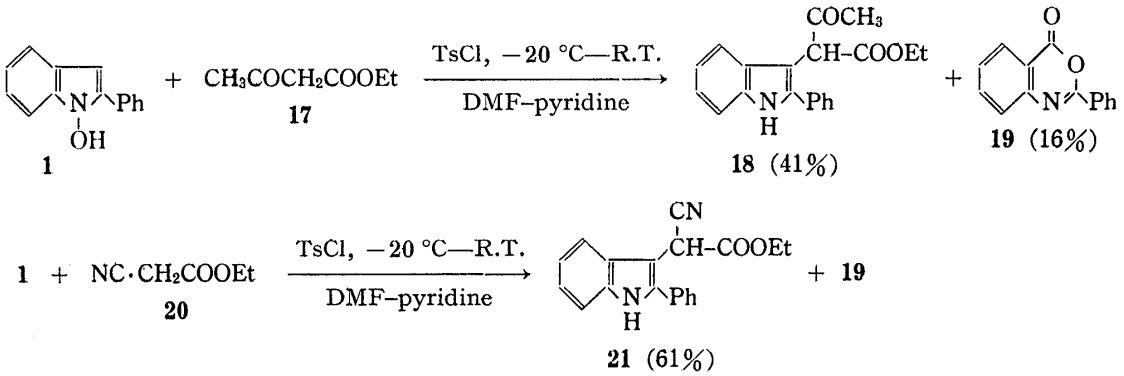


Chart 4

The crucial step in the formation of **18** and **21** is evidently nucleophilic attack of the corresponding carbanions of **17** and **20** at the 3-position of **15**.

Although some reaction apparently occurred upon treatment of **1** with diethyl malonate under the same reaction conditions, no definite product could be isolated. No reactions were observed with rather less acidic compounds such as acetophenone, benzylmethyl ketone, acetone and phenylacetonitrile.

The above-mentioned reactions, particularly the formation of **10**, **18**, and **21**, are very significant nucleophilic reactions of the indole nucleus, and the use of appropriate 1-hydroxyindole derivatives[11] seems promising for the preparation of indole derivatives.

Experimental

All melting points are uncorrected. IR spectra were recorded on a JASCO IR-E spectrophotometer. NMR spectra were measured with a JEOL JNM-C60H at 60 MHz or a JEOL JNM-PS-100 at 100 MHz using TMS as an internal reference.

Reaction of 1-Hydroxy-2-phenylindole (1) with TsCl——TsCl (1.4 g, 1.56 eq) was added dropwise to an ice-salt cooled solution (*ca.* −20°C) of **1** (1 g) in DMF (10 ml)–pyridine (5 ml), and the whole was stirred at around −20°C for 4 h and then at room temperature for 1 d. The reaction mixture was stirred for 1 h with H_2O (10 ml) and extracted with CH_2Cl_2. The residue from the CH_2Cl_2 extract was chromatographed on silica gel with benzene to give 0.31 g (19.3%) of 2-phenyl-3-tosyloxyindole (**2**),[3] mp 152—154°C (*n*-C_6H_{14}–benzene).

Reaction of 1 with *p*-Nitrobenzenesulfonyl Chloride——A solution of **1** (1 g) and *p*-nitrobenzenesulfonyl chloride (1.0 g, 1.5 eq) in CH_2Cl_2 (18 ml)–pyridine (4 ml) was processed in the same way as above to give 1.38 g (76.2%) of 2-phenyl-3-*p*-nitrobenzenesulfonyloxyindole (**4**), orange plates, mp 161—163°C (CH_2Cl_2). *Anal.* Calcd for $C_{20}H_{14}N_2O_5S$: C, 60.91; H, 3.55; N, 7.11. Found: C, 60.60; H, 3.56; N, 6.90. IR ν_{max}^{Nujol} cm^{-1}: 3330 (NH), 1530, 1350, (NO_2), 1370, 1190 (SO_2). NMR (DMF) δ: 7.1—8.2 (13H, m, Ar–H), 11.6 (1H, bs, NH).

Reaction of 1 with Benzoyl Chloride——1) A suspension of **1** (5 g) and PhCOCl (3.5 g, 1.04 eq) in CH_2Cl_2 (50 ml) was stirred with 10% Na_2CO_3 (15 ml) at room temperature for 5 d. The reaction mixture was concentrated and the residue was chromatographed on silica gel with *n*-C_6H_{14} and benzene. The fraction eluted with *n*-C_6H_{14}–benzene (1: 1) gave 7 g (93%) of 1-benzoyloxy-2-phenylindole (**5**),[5] colorless needles, mp 88—91°C (*n*-C_6H_{14}–benzene).

2) A mixture of **1** (1 g), PhCOCl (0.7 g), pyridine (2 ml) and CH_2Cl_2 (10 ml) was refluxed for 3 h to give 1.28 g (85%) of **5**.

Formation of 3-Benzoyloxy-2-phenylindole (6)——1) A solution of **1** (1 g) and PhCOCl (1 g, 1.5 eq) in DMF (20 ml)–pyridine (5 ml) was refluxed for 5 h. The reaction mixture was stirred with saturated $NaHCO_3$ solution (10 ml) at room temperature for 1 h, and extracted with $CHCl_3$. The residue from the $CHCl_3$ extract was chromatographed on silica gel with *n*-C_6H_{14} and benzene. The fraction eluted with *n*-C_6H_{14}–benzene (2: 1) gave a trace amount of 2,2′-diphenyl-3,3′-bisindole (**3**),[3] mp 278°C (*n*-C_6H_{14}–benzene). The eluate with *n*-C_6H_{14}–benzene (1: 1) gave 0.45 g (30%) of **6**,[3] colorless needles, mp 88—90°C (*n*-C_6H_{14}–benzene). *Anal.* Calcd for $C_{21}H_{15}NO_2$: C, 80.51; H, 4.79; N, 4.47. Found: C, 80.62; H, 4.73; N, 4.51. IR ν_{max}^{Nujol} cm^{-1}: 3350 (NH), 1720 (C=O). NMR ($CDCl_3$) δ: 7.0—8.4 (15H, m).

2) A solution of **5** (1 g) in DMF (10 ml) was vigorously refluxed for 3 h. The reaction mixture was worked up in the same way as above to give 0.53 g (53%) of **6**.[3]

Reaction of 1 with Acetic Anhydride——A solution of **1** (1 g) in Ac_2O (20 ml) was refluxed for 3 h. The reaction mixture was concentrated *in vacuo*, and the residue was chromatographed on silica gel with *n*-C_6H_{14} and benzene. The eluate with *n*-C_6H_{14}–benzene (3: 1) gave 0.03 g (33%) of 2-phenylindole (**8**), colorless leaflets, mp 189°C (EtOH). The fraction eluted with *n*-C_6H_{14}–benzene (1: 1) gave 0.22 g (12%) of the bisindole **3**. The fraction eluted with benzene was recrystallized from *n*-C_6H_{14}–benzene to give 0.34 g (28.3%) of 3-acetoxy-2-phenylindole (**7**), colorless needles, mp 79—81°C. *Anal.* Calcd for $C_{16}H_{13}NO_2$: C, 76.49; H, 5.18; N, 5.58. Found: C, 76.61; H, 5.04; N, 5.29. IR ν_{max}^{Nujol} cm^{-1}: 3370 (NH), 1735 (CO), 1215 (C–O–CO). NMR ($CDCl_3$) δ: 2.37 (3H, s, $COCH_3$), 7.07—7.60 (9H, m, Ar–H), 8.10 (1H, bs, NH).

Reaction of 1 with Acetyl Chloride——A solution of **1** (1 g) and AcCl (0.6 g) in DMF (20 ml)–pyridine (5 ml) was refluxed for 3 h. The reaction mixture was stirred with saturated $NaHCO_3$ solution (10 ml) at room temperature for 1 h, and extracted with CH_2Cl_2. The residue from the CH_2Cl_2 extract was chromatographed on silica gel with *n*-C_6H_{14} and benzene. The fraction eluted with *n*-C_6H_{14}–benzene (3: 1) gave 0.13 g (14%) of **8**, and that eluted with benzene afforded 0.53 g (43.3%) of **7**.

Reaction of 1 with 1-Morpholinocyclohexene (9)——-1) TsCl (1 g, 1.1 eq) was added to an ice-salt cooled solution (*ca.* −20°C) of **1** (1 g) in DMF (13 ml)–pyridine (2 ml). After 30 min, **9** (2 g, 2.5 eq) was added, and the whole was stirred at around −20°C for 4 h and then at room temperature for 1 d. The reaction mixture was treated with dil. HCl, and extracted with CH_2Cl_2. The residue from the extract was chromatographed on silica gel with *n*-C_6H_{14} and benzene. The fraction eluted with *n*-C_6H_{14}–benzene (1: 1) gave 0.08 g (7.5%) of 2-phenylisatogen (**11**), orange plates, mp 185—187°C (benzene). It was identified by direct comparison with an authentic sample prepared from **1** and amyl nitrite.[8] The eluate with benzene afforded 0.32 g (23.2%) of 3-(2-oxocyclohexyl)-2-phenylindole (**10**), pale yellow scales, mp 202—204°C (*n*-C_6H_{14}–benzene). *Anal.* Calcd for $C_{20}H_{19}NO$: C, 83.04; H, 6.57; N, 4.84. Found: C, 83.28; H, 6.50; N, 4.84. IR ν_{max}^{Nujol} cm^{-1}: 3360 (NH), 1705, 1690 (C=O). NMR (DMSO-d_6) δ: 1.52—2.4 (9H, m, cyclohexanone-H), 6.55—7.8 (10H, m, NH and Ar–H).

2) A similar reaction using **1** (1 g), **9** (2 g), TsCl (1 g) and pyridine (15 ml) gave 0.2 g (14.5%) of **10**.

3) A solution of **1** (2 g), **9** (2 g, 1.25 eq) and TsCl (2 g, 1.1 eq) in CH_2Cl_2 (25 ml)–pyridine (8 ml), prepared as described above, was stirred at around −20°C for 4 h to give 1.4 g (44%) of **2**.

Transformation of 3-(2-Oxocyclohexyl)-2-phenylindole (10) into 2,3-Diphenylindole (13)——1) A solution of **10** (0.3 g) and $NaBH_4$ (0.3 g) in EtOH (20 ml) was refluxed for 3.5 h. After cooling, the reaction mixture was stirred with 10% NaOH solution (5 ml) and then poured into a large volume of H_2O. The resulting precipitate was filtered off and recrystallized from *n*-C_6H_{14}–benzene to give 0.07 g (23%) of 2-(2-phenyl-3-indolyl)cyclohexanol (**12**), colorless needles, mp 190—191°C. *Anal.* Calcd for $C_{20}H_{21}NO$: C, 82.47; H, 7.22; N, 4.81. Found: C, 82.25; H, 7.39; N, 4.55. MS *m/e*: 291 (M^+). IR ν_{max}^{Nujol} cm^{-1}: 3340 (OH and NH). NMR ($CDCl_3$) δ: 1.1—2.4 (8H, m, methylene-H), 3.2—3.7 (2H, m, methine-H), 5.4 (1H, s, NH), 6.6—7.45 (9H, m, Ar-H).

2) A mixture of **13** (0.05 g) and Se (0.05 g) was heated at 300—310 °C for 5 h. The reaction mixture was extracted with benzene, and the residue from the benzene extract was purified by chromatography with *n*-C_6H_{14} to give 0.02 g (42.6%) of 2,3-diphenylindole[7] (**13**), colorless needles, mp 124—126°C (MeOH).

2-Phenylisatogen (11)——1) A solution of **1** (10 g) and NBS (10 g) in MeOH (200 ml) was stirred at room temperature for 1 d. The deposited orange crystals were filtered and recrystallized from benzene to give 3.9 g (36.4%) of **11**, orange plates, mp 185—187°C.

2) A solution of **1** (2.1 g) and NCS (1.4 g) in MeOH (40 ml) was processed in the same way as above to give 0.8 g (74.8%) of **11**.

Reaction of 1 with 2-Acetoxycyclohexene (14)——TsCl (1 g, 1.1 eq) was added to an ice-salt cooled solution of **1** (1 g) in DMF (16 ml)–pyridine (3 ml). After 30 min, **14** (1 g, 1.5 eq) was added, and the whole was stirred at around −20°C for 4 h and then at room temperature for 1 d. The reaction mixture was stirred with 10% HCl (10 ml), and extracted with CH_2Cl_2. The residue from the CH_2Cl_2 extract was chromatographed on silica gel with *n*-C_6H_{14}–benzene. From the fraction eluted with benzene, 0.06 g (4.3%) of **10** was isolated.

Reaction of 1 with Ethyl Acetoacetate (17)——TsCl (1.4 g, 1.5 eq) was added to an ice-salt cooled solution of **1** (1 g) in DMF (23 ml)–pyridine (5 ml). After 30 min, **17** (4 g, 6.5 eq) was added, and the whole was stirred at around −20°C for 4 h and then at room temperature for 3 d. The reaction mixture was stirred with 10% HCl (10 ml), and extracted with CH_2Cl_2. The residue from the CH_2Cl_2 extract was chromatographed on silica gel with *n*-C_6H_{14} and benzene. The first fraction, eluted with *n*-C_6H_{14}–benzene (1: 1), gave 0.17 g (16%) of 2-phenyl-4H-3,1-benzoxazone[10] (**19**), colorless needles, mp 125—127°C (*n*-C_6H_{14}–CH_2Cl_2). *Anal.* Calcd for $C_{14}H_9NO_2$: C, 75.34; H, 4.04; N, 6.28. Found: C, 75.28; H, 4.06; N, 6.30. IR ν_{max}^{Nujol} cm^{-1}: 1767 (C=O). The second fraction, eluted with benzene, afforded 0.63 g (41%) of ethyl α-(2-phenyl-3-indolyl)-acetoacetate (**18**), pale yellow sand, mp 135—138°C. *Anal.* Calcd for $C_{20}H_{19}NO_3$: C, 74.77; H, 5.92; N, 4.36. Found: C, 74.68; H, 5.97; N, 4.18. IR ν_{max}^{Nujol} cm^{-1}: 3380 (NH), 1705 (C=O). NMR ($CDCl_3$) δ: 0.9 (3H, t, J=6.6 Hz, $C\underline{H}_3CH_2O$), 2.18 (3H, s, $C\underline{H}_3CO$), 3.95 (2H, q, J=6.6 Hz, $CH_3C\underline{H}_2O$), 4.94 (1H, s, >C–H), 6.2 (1H, bs, NH), 6.6—7.6 (9H, m, Ar-H).

Reaction of 1 with Ethyl Cyanoacetate (20)——TsCl (1.4 g, 1.5 eq) was added to an ice-salt cooled solution of **1** (1 g) in DMF (15 ml)–pyridine (3 ml). After 30 min, **20** (3 g, 5.6 eq) was added, and the whole was stirred at around −20°C for 4 h and then at room temperature for 2 d. The reaction mixture was worked up as in the above experiment to give a trace of **19** and 0.89 g (61%) of ethyl α-(2-phenyl-3-indolyl)cyano-acetate (**21**), pale yellow needles, mp 158—160°C (*n*-C_6H_{14}–CH_2Cl_2). *Anal.* Calcd for $C_{19}H_{16}N_2O_2$: C, 75.00; H, 5.26; N, 9.21. Found: C, 75.21; H, 5.14; N, 9.17. IR ν_{max}^{Nujol} cm^{-1}: 3360 (NH), 2280 (CN), 1740, 1705 (C=O). NMR ($CDCl_3$) δ: 0.95 (3H, t, J=7.8 Hz, $C\underline{H}_3CH_2O$), 4.06 (2H, q, J=7.8 Hz, $CH_3C\underline{H}_2O$), 4.80 (1H, s, >C–H), 5.91 (1H, s, NH), 6.75—7.65 (9H, m, Ar-H).

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