The Chemistry of Indoles. IV.^{*,1)} Preparation of Pyridazino[2,3-*a*]-indoles and *as*-Triazino[1,6-*a*]indoles

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Pyridazino[2,3-*a*]indole derivatives, such as (3a—c), (5a), (6a), (10), (12a—b), (13), (14), (19), (20), and (21) were prepared from 1-aminoindoles. *as*-Triazino[1,6-*a*]indole derivatives, such as (17) and (18) were also prepared.

We have recently reported a novel method for the synthesis of 1-aminoindoles³⁾ and their reaction with various reagents.¹⁾ Now we wish to report the synthesis of indolo-heterocycles, such as pyridazino[2,3-*a*]indoles and *as*-triazino[1,6-*a*]indoles, and some of their reactions.

Treatment of 1-aminoindoles (1a—c) with acetylacetone in methanolic acetic acid smoothly brought about condensation to afford 1-(2'-acetyl-1'-methylvinyl)aminoindoles (2a—c) in a relatively good yield, in addition to a small amount of pyridazino[2,3-*a*]indoles (3a—c). The compounds 2a—b were converted to 3a—b in a good yield by the action of boron trifluoride etherate in benzene. These results are shown in Table I. In the case of 1-aminoindole (1c),

TABLE I.

1	2	3
a) R=Me	mp 101.5—102.5° y. 89.1%	mp 83.0° y. 9.7%
b) S-Ph	100.5—101.5 86.9	184.0—184.5 7.5
c) H	89.5—90.5 65.8	oil 12.3

2a	$\xrightarrow{\text{BF}_3\text{-etherate}}$	3a y. 100%
2b	$\xrightarrow{\text{BF}_3\text{-etherate}}$	3b 72.3

y.=yield

2c and 3c were obtained by reaction with acetylacetone in methanolic acetic acid in 65.8% yield and 12.3% yield, respectively. The compound (3c) was found to be rather unstable and the structure was assigned only from spectral data, compared with those of 3a—b.

Ethyl acetoacetate condensed with 1-amino-3-methylindole in methanolic acetic acid to give 1-(2'-ethoxycarbonyl-1'-methylvinyl)amino-3-methylindole (4) in 70.0% yield. The compound (4) was converted to 2,5-dimethyl-4-hydroxypyridazino[2,3-*a*]indole (5a) in 61.1%

* Dedicated to the memory of Prof Eiji Ochiai.

1) Part III: M. Somei and M. Natsume, *Tetrahedron Letters*, 1974, 3605.

2) Location: Tamagawa 2-28-10, Setagaya, Tokyo.

3) Part II: M. Somei and M. Natsume, *Tetrahedron Letters*, 1974, 461.

Chart 1

yield by the action of boron trifluoride etherate in refluxing benzene. Treatment of **5a** with acetic anhydride and pyridine afforded the corresponding acetyl derivative (**6a**) in 93.5% yield. These results are shown in Chart 1. Although other structures (**5b** and **6b**) were possible in place of **5a** and **6a**, **5a** and **6a** were tentatively assigned because the carbonyl absorption was observed at 1779 cm^{-1} in the infrared (IR) spectrum of **6**, whereas the carbonyl absorption was not observed in **5**.

Diketene was reacted with 1-ethylamino-3-methylindole (**7**) to give 1-(N-acetoacetyl-N-ethylamino)-3-methylindole (**8**) in 33.3% yield, whose nuclear magnetic resonance (NMR) spectrum showed the presence of a considerable amount of enol form. Ring closure to indole C-2 was not effected by boron trifluoride etherate, forming a complex in a good yield, whose structure was presumed to be **9**. Both this complex (**9**) and **8** were easily converted to 1-ethyl-4,5-dimethyl-2-oxo-1,2-dihydropyridazino[2,3-*a*]indole (**10**) by the action of 20% sulfuric acid in refluxing methanol.

Boron trifluoride etherate in benzene converted 1-(2-butenylideneamino)-3-methylindole (**11a**) and 1-cinnamylideneamino-3-methylindole (**11b**) into the corresponding 4,5-dimethyl-3,4-

dihydro- (**12a**) and 5-methyl-4-phenyl-3,4-dihydropyridazino[2,3-*a*]indole (**12b**), respectively. The compound (**12a**) was readily oxidized with N-bromosuccinimide in refluxing methylene chloride to afford 4,5-dimethylpyridazino[2,3-*a*]indole (**13**) in 75.5% yield.

When crotonaldehyde was reacted with excess 1-amino-3-methylindole in methanolic acetic acid, a compound (**14**, mp 174—175°) was produced in 81.4% yield, in addition to 1-(2-butenylideneamino)-3-methylindole (**15**, 9.5%). The structure of **14** was tentatively considered as 2,5-dimethyl-4-(3'-methyl-1'-indolyl)amino-1,2,3,4-tetrahydropyridazino[2,3-*a*]indole based on its IR, NMR, and mass spectra, and from elemental analysis. In its NMR spectrum in deuteriochloroform, protons ascribed to 2-methyl, 5-methyl, and 3'-methyl appeared as a diffused doublet (δ 1.20, $J=5$ Hz), a sharp singlet (2.35), and a doublet (2.31, $J=1$ Hz), respectively, together with 1H multiplet at δ 0.97—1.55, 1H multiplet at 1.65—2.03, 2H multiplet at 3.25—4.17, 1H multiplet at 4.55—4.70, 1H multiplet at 4.80—4.98, 1H quartet at 6.95 ($J=1$ Hz), and 8H multiplet at 7.03—7.70. On the addition of deuterium oxide, 2-methyl signal changed to a sharp doublet⁴⁾ and two protons at δ 4.55—4.70 and 3.25—4.17 disappeared. An attempt is being made to determine the configuration of 2-methyl and 4-amino group. The formation of **14** may be explained as illustrated in Chart 2, involving enamine formation, subsequent cyclisation to indole C-2, and deprotonation.

Treatment of 1-ethylideneamino-3-methylindole (**16**) with *p*-toluenesulfonic acid in refluxing benzene afforded 2,4,5-trimethyl-1,2-dihydro-*as*-triazino[1,6-*a*]indole (**17**) in 55.7% yield. One explanation of this is an initial formation of a Diels-Alder type adduct as an

Chart 2

intermediate, followed by the liberation of 3-methylindole (Chart 2). Though another double bond isomer is possible, the structure was confirmed as shown mainly by the NMR spectrum

4) Long-range coupling of this type is known; cf. N.F. Chamberlain, "The Practice of NMR Spectroscopy," Plenum Press, New York, 1974, p. 311.

in which the protons attached to nitrogen-1 and carbon-2 appeared as a doublet at δ 3.73 ($J=10$ Hz) and a multiplet at δ 4.46, respectively. On the addition of deuterium oxide the former signal disappeared and the latter changed to a quartet of quartet ($J=1.5, 6.0$ Hz). The compound (17) was readily oxidized either on exposure to air or by the action of chloranil to give 2,4,5-trimethyl-*as*-triazino[1,6-*a*]indole (18).

It has been observed that the C=N bond in 4,5-dimethyl-3,4-dihydropyridazino[2,3-*a*]indole (12a) resisted the catalytic hydrogenation, while sodium borohydride in methanol slowly reduced it to the corresponding 4,5-dimethyl-1,2,3,4-tetrahydropyridazino[2,3-*a*]indole (19). The compound (19) was acetylated with acetic anhydride and pyridine to 1-acetyl-4,5-dimethyl-1,2,3,4-tetrahydropyridazino[2,3-*a*]indole (20) in 73.9% yield.

When the tetrahydro compound (19) and 1-ethylamino-3-methylindole were subjected to alkylation with sodium hydride and alkyl halide, the corresponding N-alkylated compounds (21 and 22, respectively) were produced and interestingly, the oxidized products (12a, 5.3%, and 16, 4.5%, respectively) were obtained as a by-product (Chart 3). The tetrahydro compound (19) was easily oxidized to the dihydro compound (12a) by the action of sodium nitrite in acetic acid in 63.9% yield.⁵⁾

Few reports are found on the preparation of a Schiff base by the oxidation⁶⁾ of secondary amines, while such oxidation forming a C=N double bond was observed generally in a series of 1-alkylaminoindoles.

Chart 3

Experimental

Melting points were obtained on a Yanagimoto micro-melting point apparatus and were uncorrected. Infrared spectra were determined on a Hitachi 215 infrared spectrophotometer. Proton nuclear magnetic resonance spectra were obtained at 60.0 MHz on Varian A-60A spectrometer. Mass spectra were taken on a

5) This reaction may be explained by the formation of an N-nitroso intermediate and subsequent elimination of HNO [D. Seebach and D. Enders, *Angew. Chem.*, **87**, 1 (1975)].

6) S. Patai, "The Chemistry of the Carbon-Nitrogen Double Bond," Interscience Publishers, New York, 1970.

Hitachi RMS-4 spectrometer with a direct inlet system. Kieselgel 60 PF₂₅₄ (E. Merck) and aluminum oxide GF₂₅₄ (Type E, E. Merck) were used for the preparative thin-layer chromatography (TLC).

1-(2'-Acetyl-1'-methylvinyl)amino-3-methylindole (2a)—Glacial AcOH (0.5 ml) was added to a solution of acetylacetone (207 mg, 2.07 mmoles) and 1-aminoskatole (250 mg, 1.71 mmoles) in MeOH (7 ml) and stirring was continued at room temperature for 5 hr. After evaporation of MeOH, the residue was dissolved in H₂O and extracted with CH₂Cl₂. The extract was subsequently washed with aqueous NaHCO₃, H₂O, dried over Na₂SO₄, and evaporated *in vacuo* to leave a yellow oil, which was subjected to preparative TLC (silica gel) using CH₂Cl₂–hexane (1:1). The lower band gave pink crystals which were recrystallized from MeOH, affording **2a** as colorless prisms (348 mg, 89.1%), mp 101.5–102.5°. *Anal.* Calcd. for C₁₄H₁₆ON₂: C, 73.65; H, 7.06; N, 12.27. Found: C, 73.61; H, 7.19; N, 12.08. IR (KBr) cm⁻¹: 1624, 1575. NMR (CCl₄) ppm: 1.63 (3H, s.), 2.03 (3H, s.), 2.28 (3H, s.), 5.08 (1H, s., C=CH–CO), 6.66 (1H, br. s., C₂–H), 6.80–7.53 (aromatic 4H), 12.33 (1H, br. s., NH). Mass Spectrum *m/e*: 228 (M⁺). The upper band gave pure **3a** (35 mg, 9.7%).

1-(2'-Acetyl-1'-methylvinyl)amino-3-phenylthioindole (2b)—This compound was prepared from 1-amino 3-phenylthioindole (100 mg, 0.41 mmole) in the same manner as above for the synthesis of **2a**. After preparative TLC (silica gel) using CH₂Cl₂, **2b** (115.5 mg, 86.9%) was obtained from the lower band. Recrystallization from MeOH gave **2b** as colorless prisms, mp 100.5–101.5°. *Anal.* Calcd. for C₁₉H₁₈ON₂S: C, 70.79; H, 5.63; N, 8.69. Found: C, 70.80; H, 5.63; N, 8.70. IR (KBr) cm⁻¹: 1620, 1580. NMR (CCl₄) ppm: 1.66 (3H, s., CH₃C=), 2.01 (3H, s., CH₃CO), 5.18 (1H, q., *J* = 1 Hz, C=CHCO), 6.91–7.65 (10H, m., aromatic), 12.30 (1H, br. s., NH). Mass Spectrum *m/e*: 322 (M⁺). From the upper band **3b** (9.5 mg, 7.5%) was obtained.

1-(2'-Acetyl-1'-methylvinyl)aminoindole (2c)—This compound was prepared from 1-aminoindole (60 mg, 0.45 mmole) in the same manner as above for the synthesis of **2a**. After preparative TLC (silica gel) using CH₂Cl₂–hexane (1:1), **2c** (63.2 mg, 65.8%) was obtained from the lower band. Recrystallization from MeOH gave colorless prisms, mp 89.5–90.5°. *Anal.* Calcd. for C₁₃H₁₄ON₂: C, 72.87; H, 6.59; N, 13.08. Found: C, 72.72; H, 6.57; N, 13.17. IR (KBr) cm⁻¹: 1624, 1572. NMR (CCl₄) ppm: 1.61 (3H, s., CH₃C=), 2.05 (3H, s., CH₃CO), 5.14 (1H, br. s., C=CHCO), 6.40 (1H, d., *J* = 3 Hz, C₃–H), 7.01 (1H, d., *J* = 3 Hz, C₂–H), 7.08–7.61 (4H, m., aromatic), 12.20 (1H, br. s., NH). Mass Spectrum *m/e*: 214 (M⁺).

From the upper band, pure **3c** was obtained (11 mg, 12.3%). NMR (CCl₄) ppm: 2.38 (3H, d., *J* = 1 Hz, C₄–CH₃), 2.43 (3H, s., C₂–CH₃), 6.28 (1H, q., *J* = 1 Hz, C₃–H), 6.47 (1H, s., C₅–H), 7.08–8.20 (4H, m., aromatic). This compound was unstable and gradually changed during the measurement of NMR spectrum.

2,4,5-Trimethylpyridazino[2,3-*a*]indole (3a)—To a stirred solution of **2a** (150 mg, 0.65 mmole) in benzene (5 ml), 47% BF₃–etherate (3 ml) was added and stirring was continued at room temperature for 18.5 hr. The solution was poured into ice-water, made basic with 2N NaOH, and extracted with benzene. The extract was washed with H₂O, dried over Na₂SO₄, and evaporated *in vacuo* to leave yellow crystals. Recrystallization from MeOH afforded **3a** (138 mg, quantitative) as yellow needles, mp 83°. *Anal.* Calcd. for C₁₄H₁₄N₂: C, 79.96; H, 6.71; N, 13.32. Found: C, 79.91; H, 6.62; N, 13.32. IR (KBr) cm⁻¹: 1618. NMR (CCl₄) ppm: 2.35 (3H, s., C₂–CH₃ or C₅–CH₃), 2.48 (3H, d., *J* = 1 Hz, C₄–CH₃), 2.58 (3H, s., C₂–CH₃ or C₅–CH₃), 6.05 (1H, br. s., C₃–H), 7.12–8.15 (4H, m., aromatic). Mass Spectrum *m/e*: 210 (M⁺).

2,4-Dimethyl-5-phenylthiopyridazino[2,3-*a*]indole (3b)—Under the conditions described above for the preparation of **3a**, **2b** (50 mg) was cyclized to give crude **3b** (53 mg). After preparative TLC (silica gel) using CH₂Cl₂–hexane (1:3), pure **3b** (34 mg, 72.3%) was obtained. Recrystallization from CH₂Cl₂–MeOH afforded yellow prisms, mp 184–184.5°. *Anal.* Calcd. for C₁₉H₁₆N₂S: C, 74.98; H, 5.30; N, 9.21. Found: C, 74.94; H, 5.27; N, 9.44. IR (KBr) cm⁻¹: 1582. NMR (CDCl₃) ppm: 2.50 (3H, s., C₂–CH₃), 2.73 (3H, d., *J* = 1 Hz, C₄–CH₃), 6.50 (1H, q., *J* = 1 Hz, C₃–H), 6.83–7.23 (5H, phenyl), 7.23–8.33 (4H, m., aromatic). Mass Spectrum *m/e*: 304 (M⁺).

1-(2'-Ethoxycarbonyl-1'-methylvinyl)amino-3-methylindole (4)—To a solution of 1-aminoskatole (100 mg) and ethyl acetoacetate (115 mg) in MeOH (4 ml), glacial AcOH (1 ml) was added, with stirring. After stirring at room temperature for 17.25 hr, the solvent was evaporated *in vacuo*. The residue was dissolved in CH₂Cl₂ and washed subsequently with aqueous NaHCO₃, H₂O, dried over Na₂SO₄. The solvent was evaporated *in vacuo* to leave a crystalline product. Recrystallization from MeOH afforded **4** (80 mg), as colorless prisms, mp 94–95°. The mother liquor was subjected to preparative TLC (silica gel) using CH₂Cl₂–hexane (5:7) and further crop (43 mg) of **4** was obtained. Total yield of **4** was 123 mg (70.0%). *Anal.* Calcd. for C₁₅H₁₈O₂N₂: C, 69.74; H, 7.02; N, 10.85. Found: C, 69.73; H, 6.94; N, 10.66. IR (KBr) cm⁻¹: 1652, 1610. NMR (CCl₄) ppm: 1.26 (3H, t., *J* = 7 Hz, OCH₂–CH₃), 1.62 (3H, s.), 2.28 (3H, s.), 4.10 (2H, q., *J* = 7 Hz, OCH₂–CH₃), 4.69 (1H, br. s., C=CH–CO), 6.79 (1H, q., *J* = 1 Hz, C₂–H), 6.90–7.55 (4H, aromatic), 10.41 (1H, br. s., NH). Mass Spectrum *m/e*: 258 (M⁺).

2,5-Dimethyl-4-hydroxypyridazino[2,3-*a*]indole (5a)—To a stirred solution of **4** (33 mg) in benzene (2 ml), 47% BF₃–etherate (1 ml) was added. After refluxing for 3 hr, the reaction mixture was cooled and the usual work-up, described above for **3a**, gave 27 mg of yellow oil, which was then subjected to preparative TLC (silica gel) using CH₂Cl₂. Pure yellow powder (**5a**) (16.5 mg, 61.1%) was obtained. IR (KBr) cm⁻¹: 1623, 1560. NMR (33% CD₃OD–CDCl₃) ppm: 2.40 (3H, s., CH₃), 2.72 (3H, s., CH₃), 5.87 (1H, br. s., C₃–H), 7.11–7.68 (4H, m., aromatic). Mass Spectrum *m/e*: 212 (M⁺).

4-Acetoxy-2,5-dimethylpyridazino[2,3-*a*]indole (6a)—Ac₂O (1 ml) was added to a solution of **5a** (25 mg) in anhyd. pyridine (3 ml) and the mixture was allowed to stand at room temperature for 18 hr. The solvent was removed *in vacuo* and the residue was dissolved in CH₂Cl₂, washed with aqueous NaHCO₃, H₂O, dried over Na₂SO₄. The solvent was evaporated *in vacuo* to leave an oil, which was subjected to preparative TLC (silica gel) using CH₂Cl₂–hexane (3: 5) to afford **6a** (28 mg, 93.5%). Recrystallization from MeOH afforded yellow prisms, mp 95.5–96.0°. *Anal.* Calcd. for C₁₅H₁₄O₂N₂: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.69; H, 5.62; N, 11.00. IR (KBr) cm⁻¹: 1779. NMR (CCl₄) ppm: 2.35, 2.48, 2.56 (each signal 3H, CH₃), 6.45 (1H, br. s., C₃–H), 7.11–8.20 (4H, aromatic). Mass Spectrum *m/e*: 254 (M⁺).

1-(N-Acetoacetyl-N-ethylamino)-3-methylindole (8)—Freshly distilled diketene (80 mg, 0.95 mmole) was added to MeOH (5 ml) solution of 1-ethylamino-3-methylindole (**7**, 148 mg, 0.85 mmole) and the mixture was refluxed for 47 hr. The solvent was removed *in vacuo* to leave an oil, which was dissolved in CH₂Cl₂, washed with aqueous NaHCO₃, H₂O, dried over Na₂SO₄. The solvent was evaporated to afford 246 mg of a yellow oil. This material was subjected to preparative TLC (silica gel) using CH₂Cl₂–hexane (3: 5). The upper band afforded the starting material (**7**) (91.5 mg, 61.2%). The lower band gave **8** (73 mg, 33.3%). *Anal.* Calcd. for C₁₅H₁₈O₂N₂: C, 69.74; H, 7.02; N, 10.85. Found: C, 69.73; H, 7.08; N, 10.74. IR (KBr) cm⁻¹: 1735, 1684. Mass Spectrum *m/e*: 258 (M⁺). NMR (CCl₄) ppm: Enol form of **8**, 1.15 (t., *J* = 7 Hz, NCH₂–CH₃), 1.71 (s., CH₃–C–CH=CO), 2.33 (d., *J* = 1 Hz, C₃–CH₃), 3.90 (q., *J* = 7 Hz, N–CH₂–CH₃), 4.24 (s., O–C=CH–CO), 6.80 (s., C₂–H), 7.05–7.65 (aromatic H), 13.70 (s., OH); Keto form of **8**, 1.95 (s., CH₃CO), 3.01 (s., CO–CH₂–CO), 3.65 (m., N–CH₂–CH₃), other protons overlapped with those of the enol form. The ratio of enol to keto form was 2.0.

1-Ethyl-4,5-dimethyl-2-oxo-1,2-dihydropyridazino[2,3-*a*]indole (10)—a) To a MeOH (5 ml) solution of **8** (47 mg), 0.5 ml of 20% H₂SO₄ was added and the mixture was refluxed for 46.5 hr. When cooled, MeOH was evaporated *in vacuo* and the residue was dissolved in CH₂Cl₂, washed with aqueous NaHCO₃, H₂O, dried over Na₂SO₄. The solvent was evaporated to give crude **10**, which was subjected to preparative TLC (silica gel) using CH₂Cl₂ to afford **10** (27 mg, 61.7%). Recrystallization from hexane gave yellow prisms, mp 105°. *Anal.* Calcd. for C₁₅H₁₆ON₂: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.83; H, 6.70; N, 11.70. IR (KBr) cm⁻¹: 1644. NMR (CCl₄) ppm: 1.20 (3H, t., *J* = 7 Hz, CH₂CH₃), 2.45 (3H, d., *J* = 1 Hz, C₄–CH₃), 2.58 (3H, s., C₅–CH₃), 4.45 (2H, q., *J* = 7 Hz, CH₂CH₃), 5.95 (1H, br. s., C₃–H), 7.00–7.75 (4H, aromatic). Mass Spectrum *m/e*: 240 (M⁺).

b) To a solution of **8** (18 mg) in benzene (1 ml), 47% BF₃–etherate (0.5 ml) was added with stirring and the mixture was allowed to stand at room temperature for 3 hr. After usual work-up described above for **3a**, **9** (22 mg) was obtained. Mol. wt. for C₁₅H₁₇O₂N₂BF₂, 306 and 305 corresponding to isotope ¹¹B and ¹⁰B. Mass Spectrum *m/e*: 306, 305. NMR (CDCl₃) ppm: 1.25 (3H, t., *J* = 7 Hz, CH₂CH₃), 1.96 (3H, s., CH₃–C=O), 2.35 (3H, d., *J* = 1 Hz, C₃–CH₃), 3.66–4.25 (2H, m., NCH₂CH₃), 4.71 (1H, s., C=CH–CO), 6.86 (1H, br. s., C₂–H), 7.03–7.76 (4H, aromatic). Other enol forms were possible, **9** was assigned only from these data.

To a solution of **9** (22 mg) in MeOH (2 ml), 20% H₂SO₄ (0.5 ml) was added and the mixture was refluxed for 18 hr. After the usual work-up and purification over preparative TLC (silica gel), pure **10** (14 mg, 81.8%), was obtained.

4,5-Dimethyl-3,4-dihydropyridazino[2,3-*a*]indole (12a)—To a solution of 1-(2-butenylideneamino)-3-methylindole (**11a**) (50 mg) in benzene (3 ml), 47% BF₃–etherate (1 ml) was added and the mixture was stirred at room temperature for 17 hr. After the usual work-up and purification over preparative TLC (silica gel) using CH₂Cl₂–hexane (3: 7), **12a** (40 mg, 80.0%) was obtained. Recrystallization from hexane gave colorless prisms, mp 84–85°. *Anal.* Calcd. for C₁₃H₁₄N₂: C, 78.15; H, 7.12; N, 14.13. Found: C, 78.08; H, 7.02; N, 14.30. IR (KBr) cm⁻¹: 1622, 1604. NMR (CCl₄) ppm: 1.15 (3H, d., *J* = 7 Hz, C₄–CH₃), 2.04 (1H, d.t., *J* = 17, 4, 4 Hz, C₃–H), 2.18 (3H, s., C₅–CH₃), 2.46 (1H, d.d.d., *J* = 17, 6, 2 Hz, C₃–H), 2.91–3.45 (1H, m., C₄–H), 6.71–7.61 (5H, aromatic). Mass Spectrum *m/e*: 198 (M⁺).

5-Methyl-4-phenyl-3,4-dihydropyridazino[2,3-*a*]indole (12b)—A mixture of 1-(cinnamylideneamino)-3-methylindole (**11b**) (32 mg) and 47% BF₃–etherate (3 ml) in benzene (3 ml) was refluxed. After the same procedure described for **12a**, **12b** (19 mg, 59.4%) was obtained as an oil. *Anal.* Calcd. for C₁₈H₁₆N₂: C, 83.04; H, 6.20; N, 10.76. Found: C, 83.20; H, 6.18; N, 10.71. IR (film) cm⁻¹: 1625, 1604. NMR (CCl₄) ppm: 1.91 (3H, s., C₅–CH₃), 2.19–3.00 (2H, m., C₃–H), 4.29 (1H, m., C₄–H), 6.56–7.75 (10H, aromatic). Mass Spectrum *m/e*: 260 (M⁺).

4,5-Dimethylpyridazino[2,3-*a*]indole (13)—A mixture of **12** (49.5 mg) in CH₂Cl₂ (4 ml) and NBS (45 mg) was refluxed for 16 hr. When cooled, H₂O was added and organic layer was worked up as usual. Purification over preparative TLC (silica gel) using CH₂Cl₂–hexane (1: 1) gave **13** (37 mg, 75.5%). Recrystallization from MeOH gave yellow needles, mp 94.5–95.0°. *Anal.* Calcd. for C₁₃H₁₂N₂: C, 79.56; H, 6.16; N, 14.28. Found: C, 79.47; H, 6.17; N, 14.15. IR (KBr) cm⁻¹: 1618. NMR (CCl₄) ppm: 2.61 (3H, d., *J* = 1 Hz, C₄–CH₃), 2.68 (3H, s., C₅–CH₃), 6.23 (1H, br. d., *J* = 4 Hz, C₃–H), 7.13–8.21 (5H, aromatic). Mass Spectrum *m/e*: 196 (M⁺).

2,5-Dimethyl-4-(3'-methyl-1'-indolyl)amino-1,2,3,4-tetrahydropyridazino[2,3-*a*]indole (14)—Crotonaldehyde (40 mg, 0.57 mmole) was dissolved in MeOH (2.5 ml) and glacial AcOH (0.2 ml). The resulting solution was added dropwise, with stirring, to a solution of 1-amino-3-methylindole (97.5 mg, 0.67 mmole) in

MeOH (0.1 ml) and glacial AcOH (0.2 ml). During the addition (7 hr) white precipitate separated from the reaction mixture. After stirring for 15 hr at room temperature, the precipitate (**14**, 37 mg) was collected by filtration and washed with MeOH. The combined filtrate was evaporated *in vacuo* to leave an oil, which was dissolved in CH_2Cl_2 , washed with aqueous NaHCO_3 , H_2O , dried over Na_2SO_4 . The solvent was evaporated to afford an oil, which was subjected to preparative TLC (silica gel) using CH_2Cl_2 -hexane (1:1). Elution of the lower band gave **14** (56.5 mg). Total yield of **14** was 93.5 mg (81.4%). Recrystallization from CH_2Cl_2 -MeOH afforded colorless needles, mp 174–175°. *Anal.* Calcd. for $\text{C}_{22}\text{H}_{24}\text{N}_4$: C, 76.71; H, 7.02; N, 16.27. Found: C, 76.64; H, 7.19; N, 16.10. IR (KBr) cm^{-1} : 1615, 1458, 731. NMR (CDCl_3) ppm: 1.20 (3H, br. d., $J=5$ Hz, C_2 - CH_3), 2.31 (3H, d, $J=1$ Hz, C_3 '- CH_3), 2.35 (3H, s., C_5 - CH_3), 0.97–1.55 (1H, m., C_3 -H), 1.65–2.03 (1H, m., C_8 -H), 3.25–4.17 (2H, br., NH and C_2 -H), 4.55–4.70 (1H, br. s., NH), 4.80–4.98 (1H, br. m., C_4 -H), 6.95 (1H, q., $J=1$ Hz, C_9 -H), 7.03–7.70 (8H, aromatic). Mass Spectrum m/e : 344 (M^+). Elution of the upper band gave **15** (12.5 mg, 9.5%).

2,4,5-Trimethyl-1,2-dihydro-*as*-triazino[1,6-*a*]indole (17)—To a solution of 1-ethylideneamino-3-methylindole (**16**) (106 mg, 0.61 mmole) in benzene (5 ml), *p*-toluenesulfonic acid (88 mg) was added and the mixture was refluxed for 30 min. When cooled, the mixture was made basic with 2N NaOH and extracted with benzene. The extract was washed with H_2O , dried over Na_2SO_4 , and evaporated *in vacuo* to leave an oil which was subjected to preparative TLC (aluminum oxide) using CH_2Cl_2 -hexane (1:1) to give **17** (36 mg, 55.7%) as colorless prisms. Recrystallization from MeOH gave pale yellow prisms, mp 139–139.5°. *Anal.* Calcd. for $\text{C}_{13}\text{H}_{15}\text{N}_3$: C, 73.21; H, 7.09. Found: C, 73.32; H, 7.09. IR (KBr) cm^{-1} : 3412, 3130, 1596. NMR (CCl_4) ppm: 1.35 (3H, d., $J=6$ Hz, C_2 - CH_3), 2.34 (3H, d., $J=1.5$ Hz, C_4 - CH_3), 2.43 (3H, s., C_5 - CH_3), 4.46 (1H, m., C_2 -H), 3.73 (1H, d., $J=10$ Hz, NH), 6.66–7.58 (4H, aromatic). On the addition of D_2O , signal at 4.46 changed to double quartet ($J=6$, 1.5 Hz), while 3.73 signal disappeared. Mass Spectrum m/e : 213 (M^+).

2,4,5-Trimethyl-*as*-triazino[1,6-*a*]indole (18)—Chloranil (62 mg) was added to a solution of **17** (50 mg) in benzene (11 ml). The mixture was allowed to stand at room temperature with stirring for 18 hr. The mixture was made basic with 2N NaOH and extracted with benzene. The extract was washed with H_2O , dried over Na_2SO_4 , and evaporated to leave an oil. Purification of the oil by preparative TLC (aluminum oxide) using CH_2Cl_2 -hexane (3:2) gave **18** (24 mg, 48.4%). Recrystallization from hexane gave yellow prisms, mp 95.5–96.5°. *Anal.* Calcd. for $\text{C}_{13}\text{H}_{13}\text{N}_3$: C, 73.90; H, 6.20; N, 19.89. Found: C, 73.74; H, 6.23; N, 19.84. IR (KBr) cm^{-1} : 1612, 1579. NMR (CCl_4) ppm: 2.50, 2.64, 2.73 (each signal 3H, s., CH_3), 7.16–8.16 (4H, aromatic). Mass Spectrum m/e : 211 (M^+).

4,5-Dimethyl-1,2,3,4-tetrahydropyridazino[2,3-*a*]indole (19) from 12a—To a MeOH (11 ml) solution of **12a** (100 mg, 0.51 mmole), 1328.5 mg (34.9 mmoles) of NaBH_4 was added at room temperature. After stirring for 2 hr, MeOH was evaporated *in vacuo* and the residue was dissolved in CH_2Cl_2 , washed with H_2O , dried over Na_2SO_4 . The solvent was evaporated to leave an oil, which was subjected to preparative TLC (silica gel) using CH_2Cl_2 -hexane (1:1). Elution of the upper band gave the starting material (63 mg). Elution of the lower band afforded **19** (33 mg, 32.7%). IR (film) cm^{-1} : 3240, 1460. NMR (CCl_4) ppm: 1.29, (3H, d., $J=6$ Hz, C_4 - CH_3), 1.43–1.95 (2H, m., C_8 -H), 2.20 (3H, s., C_5 - CH_3), 2.95–3.43 (3H, m., C_2 -H and C_4 -H), 3.55 (1H, br. s., NH), 6.88–7.51 (4H, m., aromatic). Mol. wt. for $\text{C}_{13}\text{H}_{18}\text{N}_2$: 200.27. Mass Spectrum m/e : 200 (M^+). This compound was found to be unstable.

1-Acetyl-4,5-dimethyl-1,2,3,4-tetrahydropyridazino[2,3-*a*]indole (20)—To a solution of **19** (33 mg, 0.16 mmole) in pyridine (1 ml), Ac_2O (0.5 ml) was added and stirring was continued at room temperature for 18 hr. After the usual work-up, described above for **6a**, crude product was purified by preparative TLC (silica gel) using CH_2Cl_2 -hexane (1:1) to afford **20** (29.5 mg, 73.9%), as an oil. *Anal.* Calcd. for $\text{C}_{15}\text{H}_{15}\text{ON}_2$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.31; H, 7.47; N, 11.39. IR (film) cm^{-1} : 1689. Mass Spectrum m/e : 242 (M^+). NMR (CCl_4) ppm: 1.30, 1.53 (each d., $J=7$ Hz, C_4 - CH_3), 1.83, 2.00 (each s., COCH_3), 2.23, 2.36 (each s., C_5 - CH_3), 1.76–3.60 (broad m. 4H), 4.45–4.95 (1H, br. m., C_4 -H), 6.83–7.66 (4H, aromatic). In $(\text{CD}_3)_2\text{SO}$ at 60° only one isomer existed and showed a 3H doublet ($J=7$ Hz) at δ 1.18 (tetramethylsilane standard), a 3H singlet at 1.92 (NCOCH_3), and a 3H singlet at 2.15 (C_5 - CH_3).

4,5-Dimethyl-3,4-dihydropyridazino[2,3-*a*]indole (12a) from 19—To a chilled solution of **19** (30 mg) in glacial AcOH (1 ml), saturated solution (0.2 ml) of NaNO_2 was added with stirring. Immediately after the addition was completed, the reaction mixture was neutralized with aqueous NaHCO_3 and extracted with CH_2Cl_2 . The solution was washed with H_2O , dried over Na_2SO_4 and evaporated to leave crude **12a**, which was purified by preparative TLC (silica gel) using CH_2Cl_2 -hexane (1:1) to give pure **12a** (19 mg, 63.8%).

1,4,5-Trimethyl-1,2,3,4-tetrahydropyridazino[2,3-*a*]indole (21)—MeI (220 mg, 1.55 mmoles) in anhyd. benzene (4 ml) was added, in nitrogen, to a mixture of 50% NaH (21 mg, washed three times with benzene) and **19** (60 mg, 0.3 mmole) in anhyd. $(\text{CH}_3)_2\text{NCHO}$ (2 ml). The reaction mixture was kept at 65–72° for 5 hr with stirring. When cooled, the mixture was diluted with H_2O and extracted with benzene. The benzene extract was washed with H_2O , dried over Na_2SO_4 , and evaporated *in vacuo* to leave an oil, which was subjected to preparative TLC (silica gel) using CH_2Cl_2 -hexane (3:1). Elution from the lower band gave **21** (49 mg, 77.9%). *Anal.* Calcd. for $\text{C}_{14}\text{H}_{18}\text{N}_2$: C, 78.46; H, 8.47; N, 13.07. Found: C, 78.25; H, 8.60; N, 12.81. IR (film) cm^{-1} : 1470. NMR (CCl_4) ppm: 1.33 (3H, d., $J=7$ Hz, C_4 - CH_3), 1.33–1.83 (1H, br. m., C_3 -H),

1.83—2.50 (1H, br. m., C₃-H), 2.18 (3H, s., C₅-CH₃), 2.68 (3H, s., NCH₃), 2.97—3.55 (3H, m., C₂-H and C₄-H), 6.82—7.42 (4H, m., aromatic). Mass Spectrum *m/e*: 214 (M⁺). Elution from the upper band gave the dihydro compound (12a) (3 mg, 5.3%).

1-(N-Isoprenyl-N-ethylamino)-3-methylindole (22)—Isoprenyl bromide (113 mg) in anhyd. benzene (1.5 ml) was added in nitrogen, to a mixture of 50% NaH (45 mg, washed three times with benzene), and 1-ethylamino-3-methylindole (110 mg) in anhyd. (CH₃)₂NCHO (3 ml). The reaction mixture was allowed to stand at 93—96° with stirring for 20 hr. After the usual procedure described above for 21, preparative TLC (silica gel) was carried out using CH₂Cl₂. Elution from the lower band gave the starting material (57 mg). From the middle band, 16 (5 mg, 4.5%) was obtained. Elution from the upper band gave 22 (63 mg, 41.4%), as an oil. *Anal.* Calcd. for C₁₆H₂₂N₂: C, 79.29; H, 9.15; N, 11.56. Found: C, 79.07; H, 9.35; N, 11.27. IR (film) cm⁻¹: 1452, 736. NMR (CCl₄) ppm: 0.81 (3H, t., *J* = 7 Hz, CH₂CH₃), 1.50—1.61 (6H, br. s., (CH₃)₂-C=), 2.27 (3H, d., *J* = 1 Hz, C₃-CH₃), 3.05 (2H, q., *J* = 7 Hz, NCH₂CH₃), 3.57 (2H, br. d., *J* = 6.5 Hz, NCH₂-CH=), 4.96—5.30 (1H, m., NCH₂CH=C), 6.86—7.51 (5H, m., aromatic). Mass Spectrum *m/e*: 242 (M⁺).

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