Tetrahedron 69 (2013) 8785–8789

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Formation of the same pyrimido[1,2-*a*]indoles from 1-(oxiran-2-ylmethyl)-1*H*-indole or [1,3]oxazolo[3,2-*a*]indole derivatives in its reactions with aromatic amines

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ARTICLE INFO

Article history:
Received 19 May 2013
Received in revised form 6 July 2013
Accepted 22 July 2013
Available online 31 July 2013

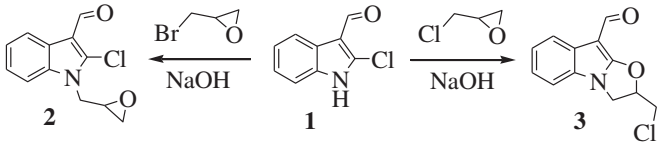
Keywords:
Indole
Oxiran
[1,3]Oxazolo[3,2-*a*]indole
Recyclization
Pyrimido[1,2-*a*]indoles

ABSTRACT

Reactions of two isomers—2-chloro-1-(oxiran-2-ylmethyl)-1*H*-indole-3-carbaldehyde or 2-(chloromethyl)-2,3-dihydro[1,3]oxazolo[3,2-*a*]indole-9-carbaldehyde with aromatic amines lead to the same products in both cases—hydrochlorides of pyrimido[1,2-*a*]indole derivatives containing two fragments of an amine per one part of the indole nucleus. Its structure was confirmed by X-ray analysis of the crystals base, obtained by alkali treatment of the reaction product (when aryl is 4-$MeOC_6H_4$).

1. Introduction

In a previous paper, we found that the direction of the reaction of 2-chloroindole-3-carbaldehyde **1** with epihalogenohydrines depends on the type of the initial halogenohydrin. The use of epibromohydrin leads to aldehyde **2**, whereas the analogous reaction with epichlorohydrin produces a derivative of tricyclic [1,3]oxazolo[3,2-*a*]indole ring system **3** (Scheme 1)[1]



Scheme 1. Interaction of compound **1** with epihalogenohydrines.

In the present paper the reactions of both aldehydes **2** and **3** with amines are discussed. It is known that reactions of 1-(Oxiran-2-ylmethyl)-1*H*-indole-3-carboxaldehyde (the analog of compound **2** without a chlorine atom) with amines initially give 1,2-aminoalcohols.[2] On the other hand, there are a number examples of chlorine substitution in 2-chloroindole-3-carbaldehydes.[3] This allows to suggest the pyrimidine cycle formation in reactions of compound **2** with primary amines. As to the compound **3**, we earlier showed its reactions with secondary amines run as oxazole ring-opening process with the formation of 2-aminoindoles, having 2-hydroxy-3-chloropropyl chain at the indole nitrogen.[1] In the case of primary amines such open chain products can undergo further cyclization. Thus the compound **3** may a priori react with primary amines to give either open chain products, either compounds having five- or six-membered ring, condensed with the indole moiety.

The aim of this work is to investigate recyclizations of poly functional systems **2** and **3** under the action of primary aromatic amines.

2. Results and discussion

We have surprisingly found that reactions of isomers **2** or **3** with aromatic amines lead to the same products in both cases. Elemental analysis, IR and NMR ^{1}H data showed these products to be hydrochlorides, containing two fragments of an amine per one part of the indole core. Treating these hydrochlorides with 40% aqueous NaOH gave bases. But their structure seemed to be ambiguous. We suggested two formulas 4 and 5 (or 4′ and 5′ for bases), which

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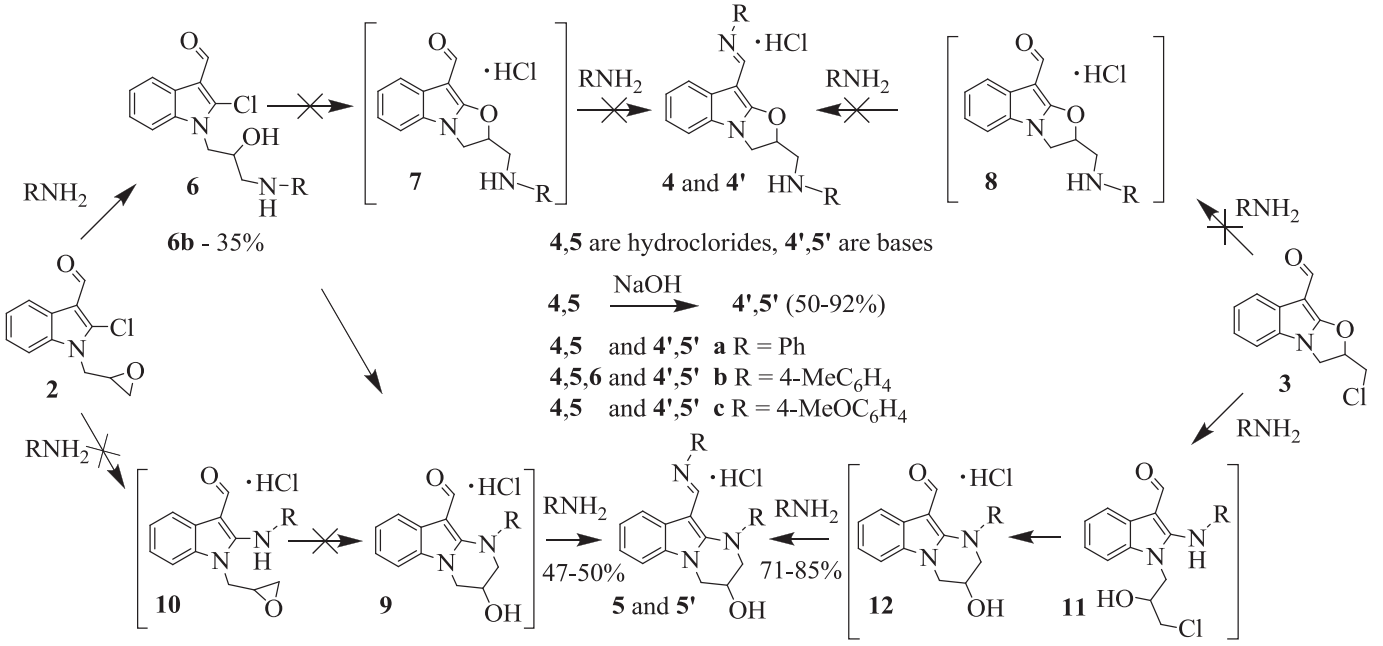
0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.07.074

correspond to spectral data and two pathways to each of them from compound **2** or **3** (Scheme 2). The structure **4** may be formed by the usual oxirane ring opening through intermediates **6** and **7**. The same product **4** may be obtained from tricyclic aldehyde **3** by chlorine substitution and further reaction of amine at the carbonyl group of aldehyde **8**. The alternative structure **5** may be produced from oxirane **2** through the key intermediate **9**, which may arise both from the open-chain compound **6** and from the product of chorine substitution **10**. The appearance of structure **5** from compound **3** is also possible because the formation of intermediates like **11** and **12** is a quite plausible route: our data concerning the reactions of compound **3** with secondary amines show the formation of compounds of type **11**.[1]

the right—its atom C(34) lies in the plane of indole core (only 0.02 Å output), and the atoms C(32) and C(33) leave it in the opposite directions at 0.40 and −0.34 Å [as well as C (32′) and C (33′) at −0.16 and 0.51 Å]. The position of the oxygen atom O(32) for both enantiomers is the same, and is fundamentally different from the location of the atom O(2) of the left molecule. This can be seen from Fig. 2, which demonstrates how the relative positions of fragments of two molecules differ when they overlap in the plane of indole core (the left structure is drawn by shaded, right—by dashed lines).

Note that the positions of the upper benzene rings differ slightly, while the location of lower methoxyphenyl substituents differs more significantly.



Scheme 2. Reactions of compounds **2** and **3** with aromatic amines.

In order to determine which structure (**4** or **5**) is formed, we performed X-ray analysis of the crystals base, obtained by treating the reaction product (R=4-MeOC$_6$H$_4$) with 40% aqueous NaOH. It was shown that the product structure corresponded to formula of **5** (Fig. 1). It should be noted that the mass spectra of all hydrochlorides **5**(**a**–**c**) show peaks with a maximum molecular mass M^+−HCl and are identical to spectra of corresponding bases **5′**(**a**–**c**). It indicates a permanence of the organic skeleton during reactions with alkali.

The X-ray crystal structure of molecule **5′c** (Fig. 1) displays several interesting features.

Compound **5′c** includes an asymmetric carbon atom in the 3 position. Both enantiomers are contained in a single crystal in unequal proportions. The independent part of the unit cell contains two molecules. The left one in Fig. 1 is the *S*-enantiomer. The right structure is either an *S*- or *R*-enantiomer, which is distributed statistically in the ratio of 0.69/0.31. It is noteworthy that the OH group is common in both molecules (The less populated bonds between atoms are drawn by unshaded lines). For convenience of description, atomic numbers of the right molecule are increased at the 30 with respect to the left one. Note that in the left molecule indole atoms and N(5) are in the mean-square plane with a maximum deviation from it 0.02 Å. The atoms C(2), C(4) and C(3) deviate from this plan in one side by 0.06, 0.19 and 0.83 Å. A fundamentally different pattern is observed for the molecule on

In conclusion, it must be said that the left and right molecules shown in Fig. 1, drawn by the shaded lines represent two different conformations of the same enantiomer. Thus, in the investigated single crystal contains two enantiomers in three different conformations.

In order to understand, which way of forming structure **5** is preferred, we conducted the reaction of compound **2** with *p*-toluidine with a limited time. In these conditions, we were able to isolate and identify the product of the initial oxirane ring disclosure **6b**. In its ^{1}H NMR spectra we observed changes in the character of signals of the aliphatic protons in comparison with initial compound **2**, as well as observing the CHO-group intact. From this we can conclude that the product **5** is formed by the sequence **2**→**6**→**9**→**5**. For the synthesis of **5** from the tricyclic compound **3** the sequence **3**→**11**→**12**→**5** is favorable.

The formation of some 1,2,3,4-tetrahydropyrimido[1,2-*a*]indole derivatives has been earlier observed when 2-chloroindole-3-carbaldehyde was alkylated with 3-chloro-*N*,*N*-diethyl- and 3-chloro-*N*,*N*-dimethyl-propylamine in 17 and 29% yield, respectively together with other products.[4] Similar tricyclic-2-aminoindoles were obtained by intramolecular 1,3-dipolar cycloaddition of 1-ω-azidoalkylindoles.[5] An accidental obtaining of a pyrimido[1,2-*a*]indole with aromatic pyrimidine ring from 1-methoxy-6-nitroindole-3-carboxaldehyde has been described by Japanese authors.[6] Most similar to structure of **5** compounds having

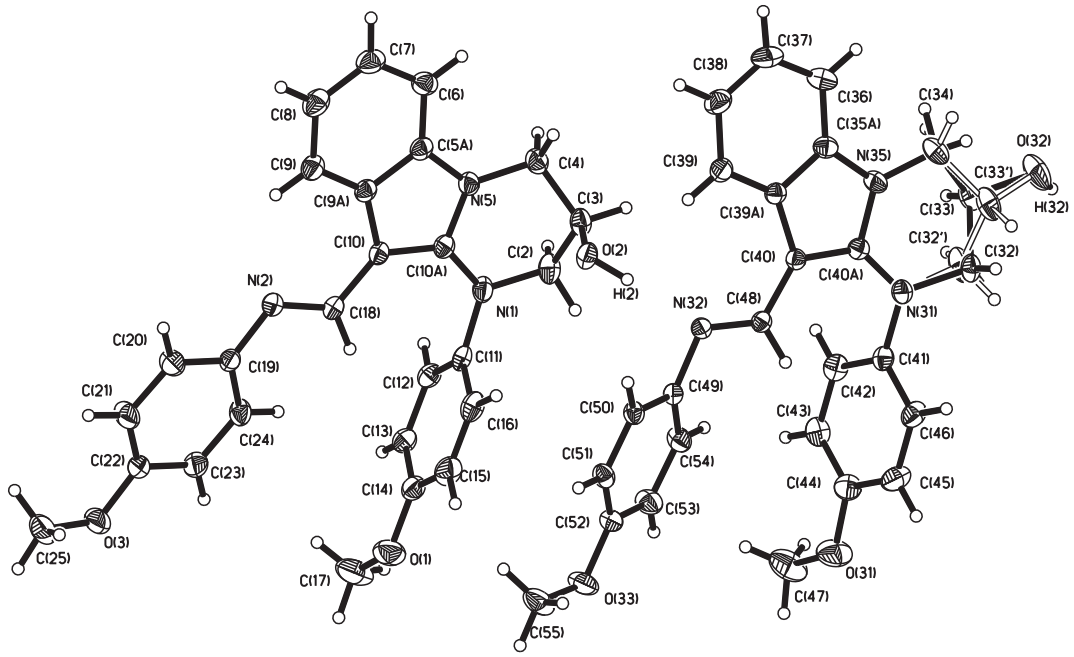


Fig. 1. Molecular structure of compound **5′c** (thermal ellipsoids are drawn at the 30% probability level).

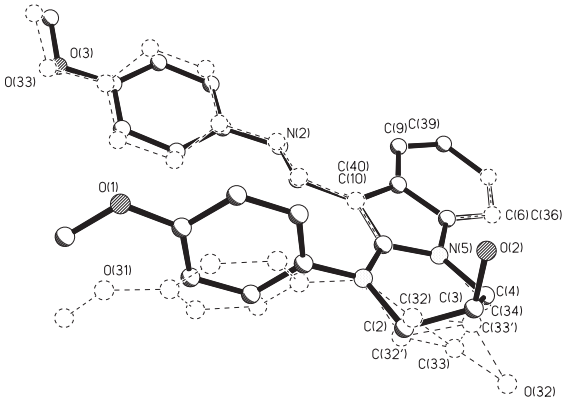


Fig. 2. Superposition of left and right molecules from Fig. 1 (hydrogen atoms are removed).

the same heterocyclic ring skeleton without OH-group in position 3 were synthesized by the reaction of 1-acyl-2-phenylpyrazolidines with Vilsmeier reagent.[7]

Unlike these studies, the synthesized compounds **5**(**a**–**c**), **5′**(**a**–**c**), and **6b** contain a pharmacophore fragment, a 1,2-aminoalcohol in a saturated pyrimidine ring. In recent years there has been an increased interest of derivatives having a 3-amino-2-hydroxypropyl group on indole nitrogen, which promotes water solubility [our hydrochlorides **5**(**a**–**c**) are water soluble]. Thus, aminoalcohols in 5-methoxyindole series have a cytotoxic effect, which may be used in the treatment of cancer.[8] It was found that the aminoalcohols derived from indolocarbazole alkaloid analogues display cytotoxicity against the cell lines representative of solid tumors and leukemia.[9] During study of a new class of non-peptide inhibitors of HIV-1 protease, 1,2-aminoalcohols, containing fragments of anthranilic acid and indole were synthesized.[10] We have earlier shown that the 1,2-unsaturated ketones in indole series having an aminoalcohol moiety at the nitrogen atom exhibit local anesthetic and antiarrhythmic activity, higher than that of well-known, widely used drugs—novocaine, lidocaine, and marcaine.[11] This allows us to hope that the method of synthesis of pyrimido[1,2-*a*]indoles containing aminoalcohol fragment, developed in this paper, will be useful to search for biologically active compounds.

3. Experimental section

3.1. General

All commercially available compounds were used without further purification. The starting compounds **2** and **3** were obtained by described protocols.[1] IR spectra were taken on Varian 3100 FT-IR, Excalibur Series instrument by means of Attenuated Total Reflectance (ATR) method. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DPX-250 instrument. Mass-spectra were obtained on Varian MAT-44 spectrometer.

The X-ray datasets for **5′c** were collected on a Xcalibur (Agilent Technologies) diffractometer with CCD camera Eos (Mo K_{α}, λ=0.71073 Å). The structure was solved by direct methods and using Fourier techniques and was refined by the full-matrix least squares against F^2 with anisotropic thermal parameters for all non-hydrogen atoms. The hydrogen atoms were positioned geometrically and refined using the riding model. All calculations were carried out with the use of the SHELXTL program package.[12]

3.2. *N*-[(1*E*)-(3-Hydroxy-1-phenyl-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-10-yl)methylene]benzenaminium chloride (5a)

*3.2.1. Method A (from compound **2**).* To compound **2** (943 mg, 4 mmol) in propan-2-ol (5 mL) was added aniline (0.73 mL, 8 mmol). The reaction mixture was refluxed for 5 h. After cooling to room temperature, the precipitate was filtered off, washed with propan-2-ol, diethyl ether and dried to give the crude product (820 mg, 50%) as yellow powder. To obtain spectroscopically pure sample it was recrystallized from ethanol [Found: C, 71.59; H, 5.47; Cl, 8.82; N, 10.44. $C_{24}H_{22}ClN_3O$ requires C, 71.37; H, 5.49; Cl, 8.78; N, 10.40%]; mp 226–228 °C; ν_{max} 3236, 1638, 1593, 1560, 1491 cm^{-1}; δ_H (250 MHz, DMSO-d_6) 3.62–3.73 (1H, m, NCH_2), 4.02–4.21 (3H, m, NCH_2, $N_{ind}CH_2$), 4.49–4.59 (1H, m, CH), 5.96 (1H, d, *J* 2.3, OH), 6.74–7.78 (14H, m, H_{Ar}, CH=N), 8.19 (1H, d, *J* 7.2, H_{Ind}-9),

10.33–10.60 (1H, bp, N^+H); δ_C (60 MHz, CF_3COOD): 45.8, 56.5, 61.4, 97.9, 109.7, 117.4 (2C), 117.6, 119.9, 122.4, 125.4, 126.9 (2C), 127.0 (2C), 130.0 (2C), 131.0, 132.6 (2C), 137.7, 138.3, 142.6, 145.3, 155.1; *m*/*z* 367 (20, M^+–HCl), 77 (100%).

3.2.2. Method B (from compound ***3****).* To compound **3** (943 mg, 4 mmol) in propan-2-ol (5 mL) was added aniline (0.73 mL, 8 mmol). The reaction mixture was refluxed and a product began to precipitate through 45 min. The resulting mixture was additionally refluxed for 1 h. After cooling the formed precipitate was filtered off, washed with propan-2-ol, diethyl ether and dried to give the crude product **5a** (1.17 g, 73%) as yellow powder. For obtaining spectroscopically pure substance it was recrystallized from ethanol. Mp and IR data are the same as in *method A*.

3.3. *N*-{(1*E*)-[3-Hydroxy-1-(4-methylphenyl)-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-10-yl]methylene}-4-methylbenzenaminium chloride (5b)

3.3.1. Method A (from compound ***2****).* To compound **2** (943 mg, 4 mmol) in propan-2-ol (5 mL) was added 4-methylaniline (856 mg, 8 mmol). The reaction mixture was refluxed for 3 h and retained at room temperature overnight. The formed precipitate was filtered off, washed with propan-2-ol, diethyl ether and dried to give the crude product (820 mg, 48%) as yellow powder. For obtaining spectroscopically pure substance it was recrystallized from ethanol [Found: C, 71.91; H, 5.98; Cl, 8.16; N, 9.67. $C_{26}H_{26}ClN_3O$ requires C, 72.29; H, 6.07; Cl, 8.21; N, 9.73%]; mp 256–258 °C; ν_{max} 3223, 1638, 1593, 1567, 1492, 1466 cm^{-1}; δ_H (250 MHz, DMSO-d_6) 2.28 (3H, s, CH_3), 2.43 (3H, s, CH_3), 3.58–3.77 (1H, m, NCH_2), 4.03–4.26 (3H, m, NCH_2, $N_{ind}CH_2$), 4.51–4.62 (1H, m, CH), 5.93 (1H, d, *J* 2.84, OH), 6.68–7.62 (12H, m, H_{Ar}, CH=N), 8.21 (1H, d, *J*=7.3, H_{ind}-9), 10.28–10.50 (1H, bp, N^+H); δ_C (60 MHz, CF_3COOD): 19.4, 19.9, 45.7, 56.4, 61.4, 97.4, 109.5, 117.3 (2C), 117.8, 119.8, 122.5, 125.2, 126.8 (2C), 130.5 (2C), 133.0 (2C), 135.9, 137.5, 138.0, 139.7, 142.5, 145.5, 155.0; *m*/*z* 395 (41, M^+–HCl), 91 (100), 65 (51%).

3.3.2. Method B (from compound ***3****).* To compound **3** (943 mg, 4 mmol) in propan-2-ol (5 mL) was added 4-methylaniline (856 mg, 8 mmol). The reaction mixture was refluxed and a product began to precipitate through 20 min. The resulting mixture was additionally refluxed for 1 h. Formed precipitate was filtered off, washed with propan-2-ol, diethyl ether and dried to give the crude product (1.22 g, 71%) as yellow powder. For obtaining spectroscopically pure substance it was recrystallized from ethanol. Mp and IR data are the same as in *method A*.

3.4. *N*-{(1*E*)-[3-Hydroxy-1-(4-methoxyphenyl)-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-10-yl]methylene}-4-methoxybenzenaminium chloride (5c)

3.4.1. Method A (from compound ***2****).* To compound **2** (943 mg, 4 mmol) in propan-2-ol (5 mL) was added 4-methoxylaniline (984 mg, 8 mmol). The reaction was refluxed and a product began to precipitate through 2 h. The resulting mixture was additionally refluxed for 1 h. Formed precipitate was filtered off, washed propan-2-ol, diethyl ether and dried to give the crude product (870 mg, 47%) as yellow powder. For obtaining spectroscopically pure substance it was recrystallized from ethanol [Found: C, 67.51; H, 5.78; Cl, 7.44; N, 9.17. $C_{26}H_{26}ClN_3O_3$ requires C, 67.31; H, 5.65; Cl, 7.64; N, 9.06%]; mp 235–238 °C; ν_{max} 3216, 1629, 1594, 1566, 1491 cm^{-1}; δ_H (250 MHz, DMSO-d_6): 3.53–3.63 (1H, m, NCH_2), 3.69 (3H, s, OCH_3), 3.80 (3H, s, OCH_3), 3.82–3.90 (1H, m, NCH_2), 3.96–4.23 (2H, m, $N_{ind}CH_2$), 4.36–4.46 (1H, m, CH), 5.61 (1H, d, *J* 3.6, OH), 6.58 (2H, d, *J* 9.0, C_6H_4); 6.72 (2H, d, *J* 9.0, C_6H_4); 6.98–7.12 (4H, m, H-7, H-8, C_6H_4), 7.18–7.44 (3H, m, CH=N, C_6H_4), 8.22–8.33 (1H, m, H-9), δ_C (60 MHz, CF_3COOD): 45.9, 55.9, 56.2, 56.8, 61.6, 98.0, 109.8, 116.1 (2C), 117.9 (2C), 119.7 (2C), 120.1, 122.6, 125.42, 127.0, 129.0 (2C), 133.7, 135.9, 137.8, 145.9, 155.4, 157.5, 161.1; *m*/*z* 427 (94, M^+–HCl), 123 (40), 108 (100), 77 (48%).

3.4.2. Method B (from compound ***3****).* To compound **3** (943 mg, 4 mmol) in propan-2-ol (5 mL) was added 4-methoxylaniline (984 mg, 8 mmol). The reaction mixture was refluxed and a product began to precipitate through 30 min. The resulting mixture was additionally refluxed for 1 h. Formed precipitate was filtered off, washed propan-2-ol, diethyl ether and dried to give the crude product (1.57 g, 85%) as yellow powder. For obtaining spectroscopically pure substance it was recrystallized from ethanol. Mp and IR data are the same as in *method A*.

3.5. 1-Phenyl-10-[(phenylimino)methyl]-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-3-ol (5′a)

To compound **5a** (808 mg, 2 mmol) in mixture of water (20 mL) and ethanol (5 mL) was added dropwise 40% aqueous solution of sodium hydroxide (2 mL). The reaction mixture was stirred at room temperature for 20 min. Precipitate was filtered off, washed with water and dried to give the crude product (370 mg, 50%), which was recrystallized from propan-2-ol to give the *title compound* (**5′a**) (260 mg, 35%) as pale yellow powder [Found: C, 78.76; H, 5.78; N, 11.49. $C_{24}H_{21}N_3O$ requires C, 78.45; H, 5.76; N, 11.44%]; mp 165–168 °C; ν_{max} 3324, 1604, 1584, 1561, 1531, 1501, 1485 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 2.14–2.94 (1H, bp, OH), 3.75 (1H, dd, *J* 12.6, 4.1, NCH_2), 3.87 (1H, dd, *J* 12.6, 2.2, NCH_2), 4.05–4.25 (2H, m, $N_{ind}CH_2$), 4.45–4.54 (1H, m, CH), 6.58–7.30 (11H, m, H_{Ar}), 7.75 (1H, s, CH=N), 8.42–8.50 (1H, m, H_{Ind}-9); δ_C (60 MHz, $CDCl_3$) 47.6, 56.3, 62.4, 97.1, 107.8, 121.2 (2C), 121.5, 121.8, 122.7, 124.2, 125.2 (2C), 126.3, 126.7, 129.2 (2C), 130.7 (2C), 134.8, 146.3, 148.1, 154.0, 154.5; *m*/*z* 367 (70, M^+), 77 (100%).

3.6. 1-(4-Methylphenyl)-10-{(*E*)-[(4-methylphenyl)imino]methyl}-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-3-ol (5′b)

To compound **5b** (600 mg, 1.4 mmol) in mixture of water (20 mL) and ethanol (5 mL) was added dropwise 40% aqueous solution of sodium hydroxide (2 mL). The reaction mixture was stirred at room temperature for 20 min. Precipitate was filtered off, washed with water and dried to give the crude product **5′b** (510 mg, 92%). It was recrystallized from propan-2-ol to give the *title compound* (**5′b**) (400 mg, 72%) as pale yellow powder [Found: C, 78.76; H, 6.48; N, 10.49. $C_{26}H_{25}N_3O$ requires C, 78.96; H, 6.37; N, 10.62%]; mp 175–178 °C; ν_{max} 3497, 1612, 1569, 1539, 1508, 1475 cm^{-1}; δ_H (250 MHz, $CDCl_3$): 2.26 (3H, s, CH_3), 2.37 (3H, s, CH_3), 3.72 (1H, dd, *J* 12.6, 4.1, NCH_2), 3.87 (1H, dd, *J* 12.6, 2.2, NCH_2), 4.05–4.25 (2H, m, $N_{ind}CH_2$), 4.45–4.54 (1H, m, CH), 6.58–7.30 (11H, m, H_{Ar}), 7.66 (1H, s, CH=N), 8.42–8.50 (1H, m, H_{ind}-9); δ_C (60 MHz, $CDCl_3$) 21.3, 21.4, 47.5, 56.5, 62.5, 96.7, 107.5, 121.1 (2C), 121.3, 121.9, 122.5, 125.7 (2C), 126.9, 129.7 (2C), 131.3 (2C), 133.6, 134.7, 136.7, 145.4, 146.4, 151.8, 154.3; *m*/*z* 395 (80, M^+), 91 (100), 65 (41%).

3.7. 1-(4-Methoxyphenyl)-10-{(*E*)-[(4-methoxyphenyl)imino]methyl}-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-3-ol (5′c)

To compound **5c** (630 mg, 1.4 mmol) in mixture of water (20 mL) and ethanol (5 mL) was added dropwise 40% aqueous solution of sodium hydroxide (2 mL). The reaction mixture was stirred at room temperature for 20 min. Precipitate was filtered off, washed with water and dried to give the crude product **5′c** (460 mg, 77%). It was recrystallized from propan-2-ol to give the *title compound* (**5′c**) (150 mg, 25%) as pale yellow powder [Found: C, 72.75; H, 5.87; N, 9.79. $C_{26}H_{25}N_3O_3$ requires C, 73.05; H, 5.89; N, 9.83%]; mp

200–202 °C; ν_{max} 3484, 3328, 1605, 1582, 1560, 1542, 1508, 1459, 1444 cm^{-1}; δ_H (250 MHz, $CDCl_3$): 2.33–3.05 (1H, bp, OH), 3.67 (1H, dd *J* 12.1, 4.9 NCH_2), 3.79 (3H, s, OCH_3), 3.84 (3H, s, OCH_3), 3.79–3.90 (1H, m, NCH_2), 4.03–4.19 (2H, m, $N_{ind}CH_2$), 4.43–4.55 (1H, m, CH), 6.67–7.35 (11H, m, H_{Ar}), 7.59 (1H, s, CH=N), 8.46–8.54 (1H, m, 9-H); δ_C (60 MHz, $CDCl_3$): 47.5, 55.9, 56.1, 56.9, 62.4, 96.4, 107.5, 114.4 (2C), 116.1 (2C), 121.2, 121.8, 122.0 (2C), 122.5, 127.0, 127.8 (2C), 134.6, 140.5, 146.6, 147.6, 153.6, 156.9, 158.7; *m*/*z* 427 (90, M^+), 123 (34), 108 (100), 77 (37%).

The crystallographic parameters for **5′c** at *T*=200.01(10) K are as follows: $C_{26}H_{25}N_3O_3$, *fw*=427.49, monoclinic system, space group *P* (1 21/n 1), *a*=14.5789(3) Å, *b*=11.0663(3) Å, *C*=27.8596(6) Å, *b*=97.148(2)°, *V*=4459.80(19) $Å^3$, *Z*=8, R_{calcd}=1.273 g cm^{-3}, μ=0.84 cm^{-1}, 9196 measured reflections, 6782 reflections with $I>2.0\sigma(I)$, R_{int}=0.0212, GooF.1.041, *R*1 ($I>2\sigma(I)$)=0.0476, *wR*2 ($I>2\sigma(I)$)=0.100. CCDC 932060.

3.8. 2-Chloro-1-{2-hydroxy-3-[(4-methylphenyl)amino]propyl}-1*H*-indole-3-carbaldehyde (6b)

To compound **2** (471 mg, 2 mmol) in propan-2-ol (5 mL) was added 4-methylaniline (428 mg, 4 mmol). The reaction mixture was refluxed for 1.5 h and cooled. The product was precipitated after rubbing with a glass rod against the wall of the flask. It was filtered off, washed with propan-2-ol and recrystallized from a mixture of benzene and light petroleum (1:1) to give the *title compound* (**6b**) (240 mg, 35%) as pale yellow powder [Found: C, 66.84; H, 5.61; Cl, 10.38; N, 8.20. $C_{19}H_{19}ClN_2O_2$ requires C, 66.57; H, 5.59; Cl, 10.34; N, 8.17%]; mp 168–170 °C; ν_{max}; δ_H (250 MHz, DMSO-d_6) 2.15 (3H, s, CH_3), 3.04–3.27 (2H, m, NCH_2), 3.98–4.15 (1H, m, CH), 4.23–4.54 (2H, m, $N_{ind}CH_2$), 5.28 (1H, d *J* 5.4, OH), 5.45 (1H, t *J* 6.0, NH), 6.56 (2H, d, *J* 8.2, $H_{4\text{-tolyl}}$), 6.91 (2H, d, *J* 8.2, $H_{4\text{-tolyl}}$), 7.22–7.37 (2H, m, H_{ind}-5 and H_{ind}-6), 7.54–7.67 (1H, m, H_{ind}-7), 8.04–8.17 (1H, m, H_{ind}-4), 10.01 (1H, s, CH=O); δ_C (60 MHz, $CDCl_3$) 20.8, 48.3, 51.4, 69.3, 110.5, 114.1 (2C), 118.5, 122.6, 123.5, 124.6, 128.3, 128.7, 130.3 (2C), 137.9, 140.6, 145.8, 185.2; *m*/*z* 342 (3, M^+), 120 (100), 91 (26), 77 (15%).

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