An Unusual and Chemoselective Reduction of Ester Grouping in N-substituted-3-acetylindoles by Sodium Borohydride

Muvvala Venkatanarayana* and Pramod K. Dubey

Department of Chemistry, Jawaharlal Nehru Technological University, Hyderabad College of Engineering, Kukatpally, Hyderabad (A.P), 500 085, India

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Abstract: Treatment of 3-acetylindoles **1(a-e)** with ethyl chloroacetate in the presence of K_2CO_3 and tetrabutylammoniumbromide (TBAB) as phase transfer catalyst in DMF, resulted in the formation of the corresponding *N*-substituted derivatives, ethyl 2-(3-acetyl-1*H*-indol-1-yl)acetate **2(a-e)** which on reaction with $NaBH_4$ yielded, unexpectedly, ethanol derivatives, 1-(1-(2-hydroxyethyl)-1*H*-indol-3-yl)ethanone **3(a-e)** by the unusual and chemoselective reduction of ester grouping in preference to the acetyl group. Alternative synthesis of the latter was achieved by the treatment of **1(a-e)** with 2-chloroethanol under phase transfer catalytic conditions (PTC). **1(a-e)**, on treatment with benzenesulphonyl chloride, under PTC conditions, yielded the corresponding *N*-benzenesulphonyl-3-acetylindoles **7(a-e)**, which on reduction with $NaBH_4$ in methanol afforded the corresponding hydroxy derivatives *N*-benzenesulphonyl-(α-hydroxyethyl)indoles **8(a-e)**. These reactions throw light on the ease of reduction of the 3-acetyl group on indoles with $NaBH_4$.

Keywords: 3-acetylindole, *N*-benzenesulphonyl-3-acetylindole, chemoselective, reduction, $NaBH_4$-MeOH.

INTRODUCTION

Reduction plays a very important role in organic synthesis. One of the most common reagents used for this purpose is sodium borohydride [1]. Usually, the reactions carried out with $NaBH_4$ are safe, inexpensive and can be done under mild conditions [2, 3]. Although this reducing agent has been constantly used for reduction of aldehydes, ketones and other important functional groups, it is not commonly used for the reduction of esters [4-7].

Due to this low reactivity towards esters, the use of additives to enhance the activity of $NaBH_4$ has been reported [8]. For example, the addition of iodine to $NaBH_4$ in THF provides H_3B–THF, which is useful for hydroborations, reduction of esters and various other functional groups [9]. Another example is the addition of zinc chloride along with the presence of tertiary amine that enhances the reducing property of $NaBH_4$ toward ester function [8].

3-Acetylindole derivatives [11] have been the centre of attention of researchers over many years due to the high practical value of these compounds [12], the unusually broad spectrum of biological activities occupying the first place [13]. For example, 4- (1*H*-indol-3-yl)-2-hydroxy-4-oxobut-2-enoic acid was useful as an anti-HIV agent [14]. Other compounds derived from 3-acetylindoles are used in the treatment of gastrointestinal, cardiovascular and CNS disorders, and also used as HIV-1 integrate inhibitors [10].

In this context, the aim of the present article is to describe the reduction of ethyl 2-(3-acetyl-1*H*-indol-1-yl)acetates and 1-benzenesulphonyl-3-acetylindoles giving the alcohols using $NaBH_4$-MeOH system.

RESULTS AND DISCUSSION

Treatment of each of the 3-acetylindoles **1(a-e)** independently, with ethyl chloroacetate in the presence of a mild base i.e. K_2CO_3, tetrabutylammoniumbromide (TBAB) as a phase transfer catalyst, in DMF at r.t. for 1 h, resulted in the formation of ethyl 2-(3-acetyl-1*H*-indol-1-yl)acetate products **2(a-e)** respectively in 89-95% yields which when treated with $NaBH_4$ in methanol at r.t. within 5 min afforded unexpectedly, ethanol derivatives i.e. 1-(1-(2-hydroxyethyl)-1*H*-indol-3-yl)ethanone of **3 (a-e)** respectively in 79-85% yields instead of the expected **4 (a-e)** or **5(a-e)** (Scheme **1**) (Table **1**).

Alternative synthesis of **3(a-e)** was achieved by the treatment of **1(a-e)** with 2-chloroethanol in the presence of K_2CO_3 and TBAB in DMF at r.t. for 1 h, yielding the products in almost equal yields as above. **3a** on treatment with $NaBH_4$ in methanol at r.t. or even under refluxing for 24 h gave, almost quantitatively **3a** on processing the reaction mixture instead of the expected **4a** or **5a**.

Each of the compounds, **1(a-e)** when treated with $NaBH_4$ in methanol at r.t. or even under refluxing conditions for 24 h, gave the starting **1(a-e)** almost quantitatively, on processing the reaction mixture, instead of the expected **6(a-e)**. **1(a-e),** when treated independently with benzenesulphonyl chloride in the presence of K_2CO_3 and TBAB in $CHCl_3$ at r.t. for 1 h, gave **7(a-e)** in 90-98% yields, each of which on independent reduction with $NaBH_4$ in methanol at r.t. for just 3 min led to the formation of the corresponding alcohols **8(a-e)** (Scheme **1**) (Table **2**).

*Address correspondence to this author at the Department of Chemistry, Jawaharlal Nehru Technological University, Hyderabad College of Engineering, Kukatpally, Hyderabad (A.P), 500 085, India; Tel: 040-2315-8661, Ext: 4331; Fax: 040-2305-7787; E-mail: venkatmuvvala@in.com

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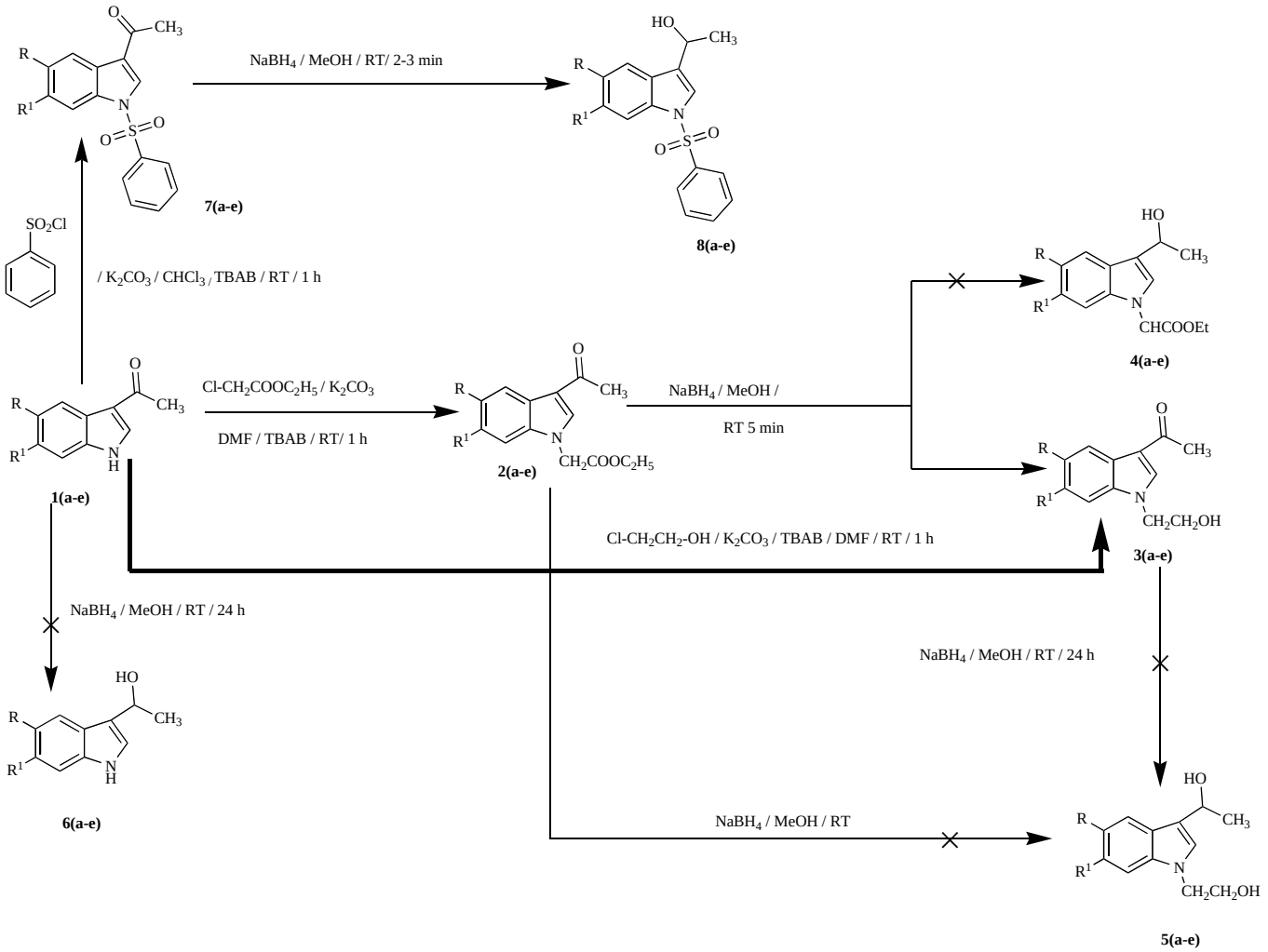


Scheme 1. Reduction of ester grouping on *N*-substitued-3-acetylindoles by using $NaBH_4$.

Table 1. Preparation of *N*-ethylacetate-3-acetylindoles and their Corresponding Alcohols[*,#]

S. No.	Starting material used	Reaction conditions	Product obtained	Yield (%)	M.P (^{O}C)
1.	**1a**(R=H, R^1=H)	RT / 1 h	**2a**(R=H, R^1=H)	91	
2	**1b**(R=OMe, R^1=H)	RT / 1 h	**2b**(R=OMe, R^1=H)	89	120
3.	**1c**(R=H, R^1=OMe)	RT / 1 h	**2c**(R=H, R^1=OMe)	85	115-117
4.	**1d**(R=Br, R^1=H)	RT / 1 h	**2d**(R=Br, R^1=H)	92	178-180
5.	**1e**(R=NO_2, R^1=H)	RT / 1 h	**2e**(R=NO_2, R^1=H)	95	126
6.	**2a**(R=H, R^1=H)	RT/ 5 min	**3a**(R=H, R^1=H)	84	168-170
7.	**2b**(R=OMe, R^1=H)	RT / 5 min	**3b**(R=OMe, R^1=H)	79	122
8.	**2c**(R=H, R^1=OMe)	RT / 5 min	**3c**(R=H, R^1=OMe)	82	90
9.	**2d**(R=Br, R^1=H)	RT / 5 min	**3d**(R=Br, R^1=H)	85	156-157
10	**2e**(R=NO_2, R^1=H)	RT / 5 min	**3e**(R=NO_2, R^1=H)	83	112

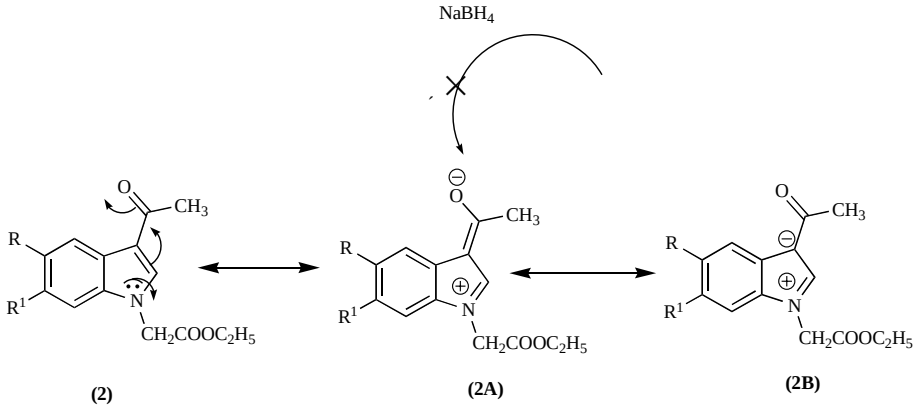
* = Reaction Conditions: 3-acetylindoles, ethyl chloroacetate, TBAB, K_2CO_3 / DMF / RT / 1 h.
# = Reaction Conditions: N-ethylacetae-3acetylindoles, $NaBH_4$ / MeOH / RT / 5 min.

In the above reactions, for example in the conversion of **2→3**, only the ester group gets reduced with $NaBH_4$ instead of the keto carbonyl. This is probably due to the fact that the keto carbonyl group exists predominantly in the form of enolate ion due to conjugation between the double bond and lone pair electrons of indole nitrogen (Sheme **2**). In ester

Table 2. Preparation of 1-benzenesulphonyl-3-acetylindole and their Corresponding Alcohols*,#

S. No.	Starting Material	Reaction Conditions	Product obtained	Yield (%)	M.P (^{O}C)
1.	**1a**(R=H, R^1=H)	RT / 1 h	**7a**(R=H, R^1=H)	98	245
2	**1b**(R=OMe, R^1=H)	RT / 1 h	**7b**(R=OMe, R^1=H)	94	>280
3.	**1c**(R=H, R^1=OMe)	RT / 1 h	**7c**(R=H, R^1=OMe)	92	199-200
4.	**1d**(R=Br, R^1=H)	RT / 1 h	**7d**(R=Br, R^1=H)	94	>280
5.	**1e**(R=NO_2, R^1=H)	RT / 1 h	**7e**(R=NO_2, R^1=H)	90	212
6.	**7a**(R=H, R^1=H)	RT/ 2 min	**8a**(R=H, R^1=H)	88	45
7.	**7b**(R=OMe, R^1=H)	RT / 3 min	**3b**(R=OMe, R^1=H)	82	39
8.	**7c**(R=H, R^1=OMe)	RT / 3 min	**3c**(R=H, R^1=OMe)	80	61
9.	**7d**(R=Br, R^1=H)	RT / 3 min	**3d**(R=Br, R^1=H)	81	74
10	**7e**(R=NO_2, R^1=H)	RT / 2 min	**3e**(R=NO_2, R^1=H)	86	58

* = Reaction Conditions: 3-acetylindoles, benzenesulphonyl chloride, TBAB, K_2CO_3 / DMF / RT / 1 h.
# = Reaction Conditions: 1-benzenesulphonyl-3-acetylindole, $NaBH_4$ / MeOH / RT / 2-3 min.



Scheme 2. The plausible resonance structures of *N*-ethylacetat-3-acetylindole.

carbonyl group, such type of conjugation is absent and it exists in the keto form only. That is why it reacts with $NaBH_4$ resulting in reduction. This is shown below with the help

of resonance structures involving **2** and **2A** (Scheme **2**). This line of explanation further seems to be supported by the fact that the parent compounds, i.e. simple 3-acetylindoles **1(a-e)**, are resistant to the reduction of the keto carbonyl at 3-postion with $NaBH_4$ in methanol either at r.t. or at reflux even after 24 h. Also, simple *N*-methyl or *N*-ethyl-3-acetylindoles were resistant to reduction with $NaBH_4$ in methanol even when kept at r.t. for 24 h.

In the case of **7**, the reduction of the keto group of 3-acetyl moiety seems to be facile because, in **7** the benzenesulphonyl group on indole exerts a strong electron withdrawing field effect on the nitrogen, preventing the facile resonance as observed in **2A** between the indole-2, 3-double bond and the acetyl group, thereby allowing an attack by hydride ion on the electrophilic carbonyl carbon of **7**.

CONCLUSION

We have observed in the above reactions that $NaBH_4$ brings about the chemoselective reduction of ester group in ethyl 2-(3-acetyl-1*H*-indol-1-yl)acetates **2(a-e)** and the keto group in 1-benzenesulphonyl-3-acetylindoles **7(a-e)** in methanol at r.t. only. Moreover, ethyl 2-(3-acetyl-1*H*-indol-1-yl)acetate **2(a-e)** and 1-benzenesuphonyl-3-acetylindole **7(a-e)** could be readily prepared by the reaction of 3-acetylindole with ethyl chloroacetate and benzenesulphonyl chloride respectively, under mild conditions using PTC method.

EXPERIMENTAL SECTION

Melting points were determined using a Buchi melting point B-545 apparatus and were uncorrected. TLC checking was done on glass plates coated with Silica Gel –G and spotting was done using iodine or UV lamp. IR spectra were recorded using Perkin Elmer model-2000 FT-IR instrument in KBr phase. ^{1}H- NMR spectra were recorded on a Bruker DPX 400- instrument operating at 400 MHz.

General Procedure for the Preparation of 2 from 1

To a stirred solution of DMF containing K_2CO_3 (4.14 gms, 30 mmol) and catalytic amount of TBAB (0.5 gms) was added **1** (10 mmol), followed by ethyl chloroacetate (1.3 ml, 12 mmol) and the resulting mixture stirred at r.t. for 1 h. At

the end of this period, the mixture was poured into ice-cold (100 ml) water. The separated solid was filtered, washed with water, dried and recrystallized from hot ethyl acetate to obtain pure **2**.

2a: Colorless solid**;** m.p. 90 ^{o}C ; Yield = 2.22 gms (91%); IR(KBr): 1742 cm^{-1} (sharp, strong, -CO, ester carbonyl) and 1638 cm^{-1} (sharp, strong, -CO, keto carbonyl); ^{1}H- NMR (DMSO-d_6/TMS): δ1.24 (t, *J* = 7.2 Hz, 3H, -C**H$_3$**), 2.44 (s, 3H, -CO-C**H$_3$**), 4.20 (q, *J* = 7.2 Hz 2H, -C**H$_2$**), 5.25 (s, 2H, N-C**H$_2$**), 7.21-8.10 (m, 4H, aryl protons of the indole ring), 8.4 (s, 1H, α-proton of the indole ring); MS m/z: 246 ($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{14}H_{15}NO_3$: C 68.56 %, H 6.16 %, N 5.71%. Found: C 68.61 %, H 6.19 %; N 5.66 %.

2b: Colorless solid; m.p. 120 ^{o}C; Yield = 2.44 gms (89%); IR(KBr): 1742 cm^{-1} (strong, sharp due to ester carbonyl stretching –O-CO) and 1639 cm^{-1}(sharp, strong due to carbonyl stretching -CO); ^{1}H- NMR spectrum (DMSO-d_6/TMS): δ 1.21 (t, *J* = 7.2 Hz, 3H, -C**H$_3$**), 2.48 (s, 3H, -CO-C**H$_3$**), 3.63 (s, 3H, -O-C**H$_3$**) 4.16 (q, *J* = 7.2, 2H, -C**H$_2$**), 5.14 (s, 2H, -N-C**H$_2$**), 7.33-8.29 (m, 3**H**), 8.40 (s, 1**H**, α-proton of the indole ring); MS m/z = 276($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{15}H_{17}NO_4$: C, 65.44 %; H, 6.22 %; N, 5.09 %. Found: C, 65.39 %; H, 6.26 % and N, 5.14 %.

2c: Colorless solid; m.p. 115-117 ^{o}C; Yield = 2.33 gms. (85%); IR (KBr): 1741 cm^{-1} (strong, sharp, -CO, ester carbonyl) and 1641 cm^{-1}(sharp, strong, -CO); ^{1}H- NMR (DMSO-d_6/TMS): δ 1.22 (t, *J* = 7.2 Hz, 3H), 2.50 (s, 3H, -CO-C**H$_3$**), 3.65 (s, 3H, -O-C**H$_3$**) 4.17 (q, *J* = 7.2, 2H), 5.25 (s, 2H, N-C**H$_2$**), 7.39-8.32 (m, 3H), 8.39 (s, 1H, α-proton of the indole ring); MS m/z = 276($M^{+\cdot}$ + 1); Elemental Anal. Calcd. for $C_{15}H_{17}NO_4$: C, 65.44 %; H, 6.22 %, N, 5.09 %. Found: C, 65.39 %; H, 6.26 %; N, 5.14 %.

2d: Colorless solid; m.p. 178-180 ^{o}C; Yield = 3.23 gms (92%); IR(KBr): 1743 cm^{-1} (strong, sharp, -CO, ester carbonyl) and 1636 cm^{-1}(sharp, strong, -CO); ^{1}H- NMR (DMSO-d_6/TMS): δ 1.22 (t, *J* = 7.2 Hz, 3H), 2.50 (s, 3H, -CO-C**H$_3$**), 4.18 (q, *J* = 7.2, 2H), 5.23 (s, 2H, -N-C**H$_2$**), 7.20-8.20 (m, 3H), 8.32 (s, 1H, α-proton of the indole ring); MS m/z = 324($M^{+\cdot}$ +1); Anal. Calcd. for $C_{14}H_{14}BrNO_3$: C 51.87 %, H 4.35 %, N 4.32 %. Found: C 51.96 %, H 4.40 %, and N 4.29 %.

2e Colorless solid; m.p. 126 ^{o}C; Yield = 2.75 gms (95%); IR (KBr): 1735 cm^{-1} (strong, sharp, -CO, ester carbonyl) and 1656 cm^{-1}(sharp, strong, -CO); ^{1}H- NMR spectrum (DMSO-d_6/TMS): δ 1.24 (t, *J* = 7.2 Hz, 3H), 2.51 (s, 3H, -CO-C**H$_3$**), 4.19 (q, *J* = 7.2, 2H), 5.37 (s, 2H, -N-C**H$_2$**), 7.79-8.6 (m, 3H), 9.061 (s, 1H, α-proton of the indole ring); MS m/z = 291($M^{+\cdot}$ +1); Elemental Anal.Calcd. for $C_{14}H_{14}N_2O_5$: C 57.93 %, H 4.86 %, N 9.65 %. Found: C 57.99 %, H 4.84 %, and N 9.70 %.

General Procedure for the Preparation of 3 from 2

A mixture of **2** (10 mmol) and $NaBH_4$ (0.42 gms, 11 mmol) in methanol was stirred at r.t. for 5 min. Progress of the reaction was monitored by TLC. After completion of the reaction (5 min), the mixture was poured into ice-cold water (40 ml), treated with aq. HCl (2%, 5 ml) until neutral. The separated solid was filtered, washed with water and dried to obtain crude **3** which on recrystallization from hot ethyl acetate gave pure **3**.

Alternative Method for the Preparation of 3 from 1

To a stirred solution of DMF containing K_2CO_3 and catalytic amount of TBAB was added **1** (10 mmol) followed by chloroethanol (1.4 ml, 20 mmol). The whole mixture was then stirred at r.t. for 1 hr. At the end of this period, the solution was poured into ice-cold water. The separated solid was washed with water, dried and recrystallized from hot ethyl acetate to obtain pure **3**.

3a: Colorless solid**;** m.p. 168-170 ^{o}C**;** Yield = 1.70 gms (84%); IR(KBr): 3420cm^{-1} (broad, medium, –OH) and 1616 cm^{-1} (strong, sharp, –CO); ^{1}H- NMR (DMSO-d_6/TMS): δ 2.42 (s, 3H, -C**H$_3$**), 3.75 (q, 2H, -C**H$_2$**-OH), 4.29-4.31(t, 2H, -N-C**H$_2$**), 4.99 (t, 1H, -O**H**, D_2O-exchangeble proton), 7.16-7.25 (m, 2H,), 7.55-7.57 (m, 1H), 8.16-8.29 (m, 2H, one is aryl proton of the indole ring and one is α-proton of the indole ring); MS m/z: 204 $M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{12}H_{13}NO_2$: C 70.92 %, H 6.45 %, N 6.89 %. Found: C 71.01 %, H 6.50 %, and N 6.93 %.

3b: Colorless solid; m.p. 120-121 ^{o}C; Yield = 1.84 gms (79%); IR (KBr): 3360 cm^{-1} (broad, medium, -OH) and 1623 cm^{-1} (strong, sharp, -CO); ^{1}H- NMR spectrum (DMSO-d_6/TMS): δ 2.41 (s, 3H, -CO-C**H$_3$**), 3.63 (s, 3H, -OC**H$_3$**), 3.78 (t, 2H, -N-C**H$_2$**), 4.98 (t, 2H, -C**H$_2$**-OH), 5.02 (t, 1H, D_2O-exchangeble, -O**H**), 7.32-8.12 (m, 3H), 8.34 (s, 1H, α-proton of the indole ring); MS m/z = 234($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{13}H_{15}NO_3$: C 66.94 %, H 6.48 %, N 6.00 %. Found: C 67.00 %, H 6.51 %, and N 5.97 %.

3c: Colorless solid; m.p. 89-90 ^{o}C; Yield = 1.91 gms (82%); IR (KBr): 3360 cm^{-1} (broad, medium, -OH), 1630 cm^{-1} (strong, sharp, -CO); ^{1}H- NMR spectrum (DMSO-d_6/TMS): δ 2.43 (s, 3H, -CO-C**H$_3$**), 3.61 (s, 3H, -OC**H$_3$**), 3.79 (t, 2H, -N-C**H$_2$**), 4.98 (t, 2H, -C**H$_2$**-OH), 5.04 (t, 1H, D_2O-exchangeble, -O**H**), 7.36-8.19 (m, 3H), 8.29-8.30 (s, 1H, α -proton of the indole ring); MS m/z = 234($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{13}H_{15}NO_3$: C 66.94 %, H 6.48 %, N 6.00 %. Found: C 67.00 %, H 6.51 %, and N 5.97 %.

3d: Colorless solid; m.p. 156-157 ^{o}C; Yield = 2.38 gms (85%); IR (KBr): 3342 cm^{-1} (broad, medium, -OH) and 1638 cm^{-1} (strong, sharp, -CO); ^{1}H- NMR (DMSO-d_6/TMS): δ 2.42 (s, 3H, -CO-C**H$_3$**), 3.83 (t, 2H, -N-C**H$_2$**), 4.93 (t, 2H, -C**H$_2$**-OH), 5.1 (t, 1H, D_2O-exchangeble, -O**H**), 7.23-8.24 (m, 3H), 8.35 (s, 1H, α -proton of the indole ring); MS m/z = 282($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{12}H_{12}BrNO_2$: C 51.09 %, H 4.29 %, N 4.96 %. Found: C 51.11 %, H 4.26 %, and N 4.90 %.

3e: Colorless solid; m.p. 111-112 ^{o}C; Yield = 2.48 gms (83%); IR (KBr): 3349 (broad, medium, -OH), 1646 (strong, sharp, -CO); ^{1}H- NMR (DMSO-d_6/TMS): δ 2.42 (s, 3H, -CO-C**H$_3$**), 3.99 (t, 2H, -N-C**H$_2$**), 4.96 (t, 2H, -C**H$_2$**-OH), 5.01 (t, 1H, D_2O-exchangeble, -O**H**), 7.65-8.45 (m, 3H), 9.03 (s, 1H, α -proton of the indole ring); MS m/z = 249($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{12}H_{12}N_2O_4$: C 58.06 %, H 4.87 %, N 11.29 %. Found: C 58.03 %, H 4.91 %, and N 11.31 %.

General Procedure for the Preparation of 7 from 1

To a stirred solution of $CHCl_3$ containing K_2CO_3 (4.14 gms, 30 mmol) and catalytic amount of TBAB was added **1** (10 mmol), followed by benzenesulphonoyl chloride (1.42 ml, 11 mmol) and the reaction mixture stirred at r.t. for 1h. At the end of this period, the reaction mixture was poured into ice-cold (50 ml) water and the organic layer was separated. The separated organic layer was evaporated to obtain the crude solid product **7** which on recrystallization from hot methanol gave pure **7**.

7a: Colorless solid; Yield = 2.93 gms (98%); m.p: > 245 ^oC; IR(KBr) 1688 cm^{-1} (sharp, strong, –CO), and a strong unequal doublet at 1170 and 1140 cm^{-1} (due to $–SO_2$); ^1H-NMR (DMSO-d_6/TMS): δ 2.4(s, 3H, -C**H$_3$**), 7.31-8.17(m, 9H, five phenyl + four aryl protons of the indole ring), 8.31 (s, 1H, α -proton of the indole ring); MS m/z: 300 ($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{16}H_{13}NO_3S$: C 64.20 %, H 4.38 %, N 4.68 %. Found: C 64.18 %, H 4.37 %, and N 4.62 %.

7b: Grey colored solid; Yield = 3.09 games (94%); m.p: > 280 ^oC; IR(KBr): 1691 cm^{-1} (sharp, strong, –CO), and a strong unequal doublet at 1169 and 1114 cm^{-1} (due to $–SO_2$); ^1H- NMR (DMSO-d_6/TMS): δ 2.61 (s, 3H, -C**H$_3$**), 3.76 (s, 3H, -OC**H$_3$**), 7.36-8.21 (m, 8H, five phenyl + three aryl protons of the indole ring), 8.63 (s, 1H, α -proton of the indole ring); MS m/z: 330 ($M^{+\cdot}$ +1); Elemental Anal. Calcd. For $C_{17}H_{15}NO_4S$: C 61.99 %, H 4.59 %, and N 4.25 %. Found: C 62.01 %, H 5.00 % and N 4.21 %.

7c: Colorless solid; Yield = 3.02 gms (92%); m.p: 199-200 ^oC; IR (KBr): 1696 cm^{-1} (sharp, strong, –CO), and a strong unequal doublet at 1170 and 1116 cm^{-1} (due to $–SO_2$); ^1H- NMR (DMSO-d_6/TMS): δ 2.62 (s, 3H, -C**H$_3$**), 3.74 (s, 3H, -OC**H$_3$**), 7.30-8.19 (m, 8H, five phenyl + three aryl protons of the indole ring), 8.34 (s, 1H, α -proton of the indole ring); MS m/z: 330 ($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{17}H_{15}NO_4S$: C 61.99 %, H 4.59 %, N 4.25 %. Found: C 62.01 %, H 5.00 %, and N 4.21 %.

7d: Ash Colored solid; Yield = 3.40 gms (94%); m.p. > 280 ^oC; IR (KBr) 1699 cm^{-1} (sharp, strong, –CO), and a strong unequal doublet at 1174 and 1117 cm^{-1} (due to $–SO_2$); ^1H- NMR (DMSO-d_6/TMS): δ 2.59 (s, 3H, -C**H$_3$**), 7.28-8.12 (m, 8H, five phenyl an+ three aryl protons of the indole ring), 8.53 (s, 1H, α -proton of the indole ring); MS m/z: 378 ($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{16}H_{12}BrNO_3S$: C 50.81 %; H 3.20 %, N 3.70 %. Found: C 50.79 %, H 3.22 %, and N 3.72 %.

7e: Light yellow solid; Yield = 3.09 gms (90%); m.p. 212 ^oC; IR (KBr) 1695 cm^{-1} (sharp, strong, –CO), and a strong unequal doublet at 1170 and 1114 cm^{-1} (due to $–SO_2$); ^1H-NMR (DMSO-d_6/TMS): δ 2.63 (s, 3H, -C**H$_3$**), 7.19-8.19 (m, 8H, five phenyl an+ three aryl protons of the indole ring), 8.60 (s, 1H, α -proton of the indole ring); MS m/z: 345 ($M^{+\cdot}$ +1); Elemental Anal. Calcd. for $C_{16}H_{12}N_2O_5S$: C 55.81 %, H 3.51 %, N 8.14 %. Found: C 55.83 %, H 3.53 %, and N 8.16 %.

General Procedure for the Preparation of 8 from 7

A mixture of **7** (10 mmol) and $NaBH_4$ (0.42 gms, 11 mmol) in methanol was stirred at room temperature for 3 min. Progress of the reaction was monitored by TLC. After completion of the reaction (3 min), the mixture was poured into ice-cold water (40 ml), treated with aq. HCl (2%, 5 ml) until neutral. The separated solid was filtered, washed with water and dried to obtain crude **8** which on recrystallization from hot ethyl acetate gave pure **8.**

8a: Colorless solid; m.p. 45 ^oC; Yield = 2.64 gms (88%); IR**(**KBr):3390 cm^{-1} (medium, broad, –OH), 1176 and 1124cm^{-1} (strong, $–SO_2$); H^1- NMR (DMSO-d_6/TMS): δ 1.43 (d, *J* = 6.8, 3H, -C**H$_3$**), 4.94 (q, J = 5.6, 1H, -C**H**), 5.23(d, J = 4.8, 1H, -O**H**, D_2O-exchangeble), 7.21-7.96 (m, 10H, five phenyl protons + four aryl protons + one is α -proton of the indole ring); MS m/z: 300 (M^{+}-1**)**; Elemental Anal. Calcd. for $C_{16}H_{15}NO_3S$: C 63.77 %, H 5.02 %, N 4.65 %. Found: C 63.79 %, H 5.09 %, and N 4.68 %.

8b: Colorless solid; m.p. 36 ^oC; Yield = 2.71 gms (82%); IR**(**KBr): 3384 cm^{-1} (medium, broad, –OH), 1169 and 1131cm^{-1} (strong, $–SO_2$); H^1- NMR (DMSO-d_6/TMS): δ 1.43 (d, *J* = 6.81, 3H, -C**H$_3$**), 3.62 (s, 3H, -OC**H$_3$**0, 4.90 (q, J = 5.6, 1H, -C**H**), 5.22 (d, J = 4.8, 1H, -O**H**, D_2O-exchangeble), 7.21-8.31 (m, 9H, five phenyl protons + three aryl protons + one is α -proton of the indole ring); MS m/z: 333 (M^{+} +1**)**; Elemental Anal Calcd. for $C_{17}H_{17}NO_4S$: C 61.61 %, H 5.17 %, N 4.23 %. Found: C 61.70 %, H 5.10 %, and N 4.20 %.

8c: Colorless solid; m.p. 61 ^oC; Yield = 2.64 gms (80%); IR**(**KBr): 3400 cm^{-1} (medium, broad, –OH), 1171 and 1129cm^{-1} (strong, $–SO_2$); H^1- NMR (DMSO-d_6/TMS): δ 1.41 (d, J = 6.8, 3H, -C**H$_3$**), 3.59 (s, 3H, -OC**H$_3$**), 4.93 (q, J = 5.6, 1H, -C**H**), 5.21 (d, J = 4.8, 1H, -O**H**, D_2O-exchangeble), 7.24-8.21 (m, 9H, five phenyl protons + three aryl protons + one is α -proton of the indole ring); MS m/z: 333 (M^{+} +1**)**; Elemental Anal. Calcd. for $C_{17}H_{17}NO_4S$: C 61.61 %, H 5.17 %, N 4.23 %. Found: C 61.70 %, H 5.10 %, and N 4.20 %.

8d: Colorless solid; m.p. 74 ^oC; Yield = 3.06 gms (80%); IR**(**KBr): 3381 cm^{-1} (medium, broad, –OH), 1176 and 1126cm^{-1} (strong, $–SO_2$); H^1- NMR (DMSO-d_6/TMS): δ 1.48 (d, J = 6.9, 3H, -C**H$_3$**), 4.84 (q, J = 5.5, 1H, -C**H**), 5.29 (d, J = 4.8 1H, -O**H**, D_2O-exchangeble), 7.29-8.39 (m, 9H, five phenyl protons + three aryl protons of the indole ring + one is α -proton of the indole ring); MS m/z: 380 (M^{+} +1**)**; Elemental Anal Calcd. for $C_{16}H_{14}BrNO_3S$: C 50.54 %, H 3.71 %, N 3.68 %. Found: C 50.60%, H 3.82 %, and N 3.66 %.

8e: Colorless solid; m.p. 58 ^oC; Yield = 3.46 gms (86%); IR**(**KBr): 3406 cm^{-1} (medium, broad, –OH), 1170 and 1120cm^{-1} (strong, $–SO_2$); H^1- NMR (DMSO-d_6/TMS): δ 1.49 (d, *J* = 6.9, 3H, -C**H$_3$**), 4.94 (q, *J* = 5.6, 1H, -C**H**), 5.40 (d, J = 4.9, 1H, -O**H**, D_2O-exchangeble), 7.32-8.49 (m, 9H, five phenyl protons + three aryl protons of the indole ring + one is α -proton of the indole ring); MS m/z: 347 (M^{+} +1**)**; Elemental Anal. Calcd. for $C_{16}H_{14}N_2O_5S$: C 55.48 %, H 4.07 %, N 8.09 %. Found: C 55.54 %; H 4.02 % and N 8.12 %.

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CONFLICT OF INTEREST

Declared none.

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