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DMAP as a versatile and highly efficient catalyst for N-acylation and N-sulphonation of substituted indole

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ABSTRACT

Indoles undergo smooth N-acylation and N-sulphonation with acetyl, benzoyl and sulfonyl chloride in presence of 10mol% of DMAP (N.N-Dimethylaminopyridine) under mild conditions in excellent yields in very short time. The use of inexpensive and readily available DMAP makes this method quite simple, more convenient and practical.

Key words: DMAP (N.N-Dimethylaminopyridine), N-acylation, N-sulphonation, 4-Thiazolidinone, Indole.

1. INTRODUCTION

The present invention provides highly efficient, catalytic method for N-acylation and N-sulphonation of Indole derivatives using DAMP [1-5]. The indole scaffold is one of the most relevant structures in medicinal chemistry. Substituted indoles have been referred to as privileged structures since they are capable of binding to many receptors with high affinity. Therefore, the synthesis and selective functionalization of indoles have been the focus of active research over the years.

Recently, DMAP has received increasing attention as a water-tolerant catalyst for organic synthesis demonstrating highly pure and selective results. Compared to conventional base, it has advantages of water solubility, operational simplicity, strong tolerance to oxygen and nitrogen-containing substrates and functional groups, and it can often be used in catalytic amounts. DMAP has two distinct advantages as a catalyst - it enhances the yield and rate of reaction and it allows sensitive reactions to be carried out under milder conditions thereby reducing unwanted side effects. Furthermore, there have been no reports on the N-acylation and N-sulphonation of indoles using DMAP as a catalyst. Common approaches to the synthesis of N-acylation and N-sulphonation of indole derivative [6-7], typically require a two-step protocol: (1) formation of an active indole anion by stoichiometric amount of strong base; and (2) reaction of resulting anion with a acetylating and sulphonating agents but by using DMAP as a catalyst for these reactions, it goes spontaneously with short period of time and moreover no strong base is required.

2. MATERIALS AND METHODS

All reagent used were of analytical grade (Thomas Baker). Melting points were determined with Buchi B-545 melting point apparatus in degree celsius and are uncorrected. IR spectra were recorded on Shimadzu using KBr disk technique. ^{1}HNMR spectra were recorded on Bruker Advance spectrometer (400MHz) using tetramethylsilane (TMS) as internal standard. J values are in Hertz. Chemical shifts are reported in ppm (δ) relative to the solvent peak, Mass spectra were recorded on either GCMS (focus GC with TSQ II mass analyzer and thermoelectro) with autosampler/direct injection (EI/CI) or LCMS (APCI/ESI; Buker daltanoics Micro TOFQ). Thin layer chromatography (TLC) was performed in precoated silica gel plates. Visualization was obtained by exposure to iodine vapour and/or under UV light. Ethanol were used for purification of compounds.

2.1. Synthesis

2.1.1. General procedure for Synthesis of 3-Ethyl-2-(3-fluoro-4-morpholin-4-yl-phenylimino)-5-(1H-indol-3-ylmethylene)-thiazolidin-4-one (6)

A well stirred solution of 1.00 mmole of 3-ethyl-2-{[2-fluoro-4-(morpholin-4 l)phenyl]imino}-1,3-thiazolidin-4-one (5) in 16 mL of Ethanol , 0.29 mmole Piperidine, 0.3 mmole Acetic acid and Indole-3-carboxaldehyde (1.00 mmol). The solution was refluxed till the

completion of the reaction, monitored by TLC. The reaction mixture was then cooled to room temperature and solid collected by filtration to give (6) as a yellow solid.

Yield 86%; Melting point-172°C, IR(KBr) cm^{-1}: 3075(NH), 1720(C=O), 1592 (C=N), ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.34-1.37(t,3H), 3.10-3.12(t,4H), 3.89-3.91(t,4H), 4.02-4.07(q,2H), 6.78-6.83(t,2H), 6.93-6.98(t,1H), 7.25-7.32(m,2H), 7.41-7.45 (m,2H),7.84-7.86(d,1H), 8.11(s,1H), 8.61(s,1H) MS (APCI); *m/z* 451.30 [M+1]

2.2. General procedure for synthesis of 7a-g and 8a-k

A well stirred solution of 1.00 mmole of 3-Ethyl-2-(3-fluoro-4-morpholin-4-yl-phenylimino)-5-(1H-indol-3-ylmethylene)-thiazolidin-4-one (6) in 10 mL of dichloromethane, Triethylamine (2.00 mmole) , DMAP (0.10 mmole) and appropriate acetyl/sulfonyl chloride (1.05 mmol). The solution was stirred over different periods till the completion of the reaction, monitored by TLC. The reaction mixture was then distilled out to get oil/solid, which then recrystallized using Ethanol.

2.2.1. Synthesis of 5-((1-acetyl-1H-indol-3-yl) methylene)-3-ethyl-2-(2-fluoro-4-morpholinophenylimino) thiazolidin-4-one (7a)

Yellow Solid. Yield 84%; Melting Point-184°C, IR(KBr) cm^{-1}:1629(C=O), ^{1}HNMR ($CDCl_3$, 400MHz): 1.34-1.38(t,3H), 2.68(s,3H), 3.11-3.12(t,4H), 3.89-3.90(t,4H), 4.03-4.08(q,2H), 6.77-6.82(t,2H), 6.94-6.98(t,1H), 7.37-7.45(m,2H), 7.52(s,1H), 7.76-7.78(d,2H), 7.95(s,1H), 8.38-8.40(d,1H), MS (APCI); *m/z* 493.25 [M+1]

2.2.2. Synthesis of 3-ethyl-2-(2-fluoro-4-morpholinophenylimino)-5-((1-propionyl-1H-indol-3-yl) methylene) thiazolidin-4-one (7b)

Yellow Solid. Yield 84%; Melting Point-186°C, IR(KBr) cm^{-1}:1637(C=O), ^{1}HNMR ($CDCl_3$, 400MHz): 1.07-1.09 (t,3H), 1.33-1.36(t,3H), 2.42-2.44(q,2H), 3.12-3.16(t,4H), 3.88-3.93(t,4H), 4.05-4.08(q,2H), 6.79-6.81(t,2H), 6.97-6.99(t,1H), 7.39-7.44(m,2H), 7.55(s,1H), 7.74-7.78(d,2H), 7.94(s,1H), 8.36-8.39(d,1H), MS (APCI); *m/z* 507.57 [M+1]

2.2.3. Synthesis of 5-((1-benzoyl-1H-indol-3-yl) methylene)-3-ethyl-2-(2-fluoro-4-morpholinophenylimino) thiazolidin-4-one (7c)

Yellow Solid. Yield 86%; Melting Point-178°C, IR(KBr) cm^{-1}:1654 (C=O), ^{1}HNMR ($CDCl_3$, 400MHz): 1.25-1.35(t,3H), 3.08-3.21(t,4H), 3.94-3.95(t,4H), 4.00-4.05(q,2H), 6.73-6.78(t,2H), 6.91-6.95(t,1H), 7.38-7.46(m,5H), 7.59-7.63(m,2H), 7.73-7.75(d,2H), 7.89-7.92(s,1H), 8.25-8.27(d,1H), MS (APCI); *m/z* 555.35 [M+1]

2.2.4. Synthesis of 5-((1-(4-bromobenzoyl)-1H-indol-3-yl)methylene)-3-ethyl-2-(2-fluoro-4-morpholinophenylimino) thiazolidin-4-one (7d)

Yellow Solid. Yield 86%; Melting Point-187°C, IR(KBr) cm^{-1}:1669(C=O), ^{1}HNMR ($CDCl_3$, 400MHz): 1.32-1.35(t,3H), 3.05-3.11(t,4H), 3.90-3.93(t,4H), 4.03-4.07(q,2H), 6.70-6.74(t,2H), 6.51-6.98(t,1H), 7.40-7.46(m,4H), 7.55-7.60(m,2H), 7.74-7.79(d,2H), 7.88-7.92(s,1H), 8.28-8.30(d,1H), MS (APCI); *m/z* 589.15 [M+1]

2.2.5. Synthesis of 5-((1-(4-chlorobenzoyl)-1H-indol-3-yl) methylene)-3-ethyl-2-(2-fluoro-4-morpholinophenylimino) thiazolidin-4-one (7e)

Yellow Solid. Yield 86%; Melting Point-189°C, IR(KBr) cm^{-1}:1645(C=O), ^{1}HNMR ($CDCl_3$, 400MHz): 1.27-1.36(t,3H), 3.10-3.15(t,4H), 3.90-3.94(t,4H), 4.08-4.09(q,2H), 6.77-6.80(t,2H), 6.95-6.98(t,1H), 7.33-7.41(m,4H), 7.50-7.60(m,2H), 7.70-7.74(d,2H), 7.89-7.91(s,1H), 8.23-8.27(d,1H), MS (APCI); *m/z* 681.35 [M+1]

2.2.6. Synthesis of 3-ethyl-2-(2-fluoro-4-morpholinophenylimino)-5-((1-(4-iodobenzoyl)-1H-indol-3-yl) methylene)thiazolidin-4-one (7f)

Yellow Solid. Yield 86%; Melting Point-192°C, IR(KBr) cm^{-1}:1666(C=O), ^{1}HNMR ($CDCl_3$, 400MHz): 1.30-1.35(t,3H), 3.03-3.10(t,4H), 3.91-3.95(t,4H), 4.04-4.06(q,2H), 6.71-6.75(t,2H), 6.94-6.97(t,1H), 7.35-7.43(m,4H), 7.60-7.63(m,2H), 7.78-7.80(d,2H), 7.87-7.92(s,1H), 8.24-8.27(d,1H), MS (APCI); *m/z* 573.55 [M+1]

2.2.7. Synthesis of 3-ethyl-2-(2-fluoro-4-morpholinophenylimino)-5-((1-(4-fluorobenzoyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (7g)

Yellow Solid. Yield 86%; Melting Point-188°C, IR(KBr) cm^{-1}:1650(C=O), ^{1}HNMR ($CDCl_3$, 400MHz): 1.29-1.35(t,3H), 3.01-3.11(t,4H), 3.90-3.95(t,4H), 4.00-4.04(q,2H), 6.71-6.75(t,2H), 6.90-6.95(t,1H), 7.38-7.46(m,4H), 7.55-7.613(m,2H), 7.71-7.75(d,2H), 7.85-7.92(s,1H), 8.29-8.30(d,1H), MS (APCI); *m/z* 534.35 [M+1]

2.2.8. Synthesis of 3-ethyl-2-(3-fluoro-4-morpholinophenylimino)-5-((1-tosyl-1H-indol-3-yl) methylene) thiazolidin-4-one (8a)

Yellow Solid. Yield 91%; Melting Point-182°C, IR(KBr) cm^{-1}: 1707(C=O), 1612 (C=N), 1373 & 1172 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.35-1.38(t,3H), 2.36(s,3H), 3.28(t,4H), 4.00(t,4H), 4.04-4.09(q,2H), 6.83-6.86(d,1H), 7.24-7.27(m,2H), 7.33-7.42(m,2H), 7.69(s,1H), 7.73-

7.75(d,2H), 7.77-7.79(d,2H), 7.91(s,1H), 7.96-7.98(d,2H) MS (APCI); *m/z* 605.15 [M+1]

2.2.9. Synthesis of 3-ethyl-2-(3-fluoro-4-morpholinophenylimino)-5-((1-(4-nitrophenylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (8b)

Yellow Solid. Yield 89%; Melting Point-188°C, IR(KBr) cm^{-1}: 1720(C=O), 1606 (C=N), 1375 & 1174 (SO_2).^{1}HNMR ($CDCl_3$, 400MHz): δ 1.33-1.37(t,3H), 3.23-3.28(t,4H), 4.00(t,4H), 4.05-4.06(q,2H), 6.79-6.82(d,1H), 7.40-7.43(d,2H), 7.61(s,1H), 7.72-7.74(d,2H), 7.96-7.98(d,2H), 8.05-8.07(d,2H), 8.27-8.29(d,2H), 8.94(s,1H), MS (APCI); *m/z* 658.20 [M+23]

2.2.10. Synthesis of 3-ethyl-2-(3-fluoro-4-morpholinophenylimino)-5-((1-(methylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (8c)

Yellow Solid. Yield 88%; Melting Point-220°C, IR(KBr) cm^{-1}: 1716(C=O), 1612(C=N), 1367 & 1176 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.33-1.37(t,3H), 3.12(s,3H), 3.18-3.19(t,4H), 3.88-3.90(t,4H), 4.01-4.06(q,2H), 6.64-6.66(d,1H), 6.75-6.79(m,2H), 6.93-7.00(s,1H), 7.40-7.48(d,2H), 7.82-7.84(d,2H), 8.08-8.10(d,1H), MS (APCI); *m/z* 551.25 [M+23]

2.2.11. Synthesis of (5-((1-(4-ethoxyphenylsulfonyl)-1H-indol-3-yl) methylene)-3-ethyl-2-(3-fluoro-4-morpholinophenylimino) thiazolidin-4-one (8d)

Yellow Solid. Yield 91%; Melting Point-188°C, IR(KBr) cm^{-1}: 1706(C=O), 1597 (C=N), 1360 & 1160 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.33-1.37(t,3H), 1.43-1.47(t,3H), 3.79(q,2H), 3.16(t,4H), 3.90(t,4H), 4.04-4.06(q,2H), 6.79-6.82(d,1H), 6.87-6.89(d,2H), 7.00-7.04(t,1H), 7.10-7.14(m,2H), 7.33-7.42(m,2H), 7.81-7.83 (d,2H), 7.89(s,1H), 7.94-7.96(d,2H), MS (APCI); *m/z* 635.2 [M+1]

2.2.12. Synthesis of -3-ethyl-2-(3-fluoro-4-morpholinophenylimino)-5-((1-(4-fluorophenylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (8e)

Yellow Solid. Yield 90%; Melting Point-183°C, IR(KBr) cm^{-1}: 1716(C=O), 1596 (C=N), 1367 & 1176 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.31-1.35(t,3H), 3.15(t,4H), 3.89(t,4H), 4.01-4.06(q,2H), 6.77-6.79(d,2H), 7.02(s,1H), 7.08-7.13(m,2H), 7.33-7.39(m,2H), 7.62(s,1H), 7.71-7.73(d,1H), 7.88-7.92(m,4H), MS (APCI); *m/z* 609.20 [M+1]

2.2.13. Synthesis of 5-((1-(4-chlorophenylsulfonyl)-1H-indol-3-yl) methylene)-3-ethyl-2-(3-fluoro-4-morpholinophenylimino) thiazolidin-4-one (8f)

Yellow Solid Yield 90%; Melting Point-185°C, IR(KBr) cm^{-1}: 1720(C=O), 1592 (C=N), 1373 & 1172 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.33-1.37(t,3H), 3.13(t,4H), 3.91(t,4H), 4.04-4.08(q,2H), 6.79-6.81(d,2H), 7.05(s,1H), 7.10-7.14(m,2H), 7.35-7.40(m,2H), 7.64(s,1H), 7.73-7.75(d,1H), 7.82-7.86(m,4H), MS (APCI) ; *m/z* 625.11 [M+1]

2.2.14. Synthesis of 3-ethyl-2-(3-fluoro-4-morpholinophenylimino)-5-((1-(4-iodophenylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (8g)

Yellow Solid. Yield 90%; Melting Point-189°C, IR(KBr) cm^{-1}: 1720(C=O), 1598 (C=N), 1373 & 1173 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.30-1.33(t,3H), 3.12(t,4H), 3.84(t,4H), 4.02-4.05(q,2H), 6.74-6.77(d,2H), 7.00(s,1H), 7.06-7.11(m,2H), 7.30-7.35(m,2H), 7.60(s,1H), 7.69-7.71(d,1H), 7.76-7.80(m,4H), MS (APCI); *m/z* 717.1 [M+1]

2.2.15. Synthesis of -5-((1-(4-bromophenylsulfonyl)-1H-indol-3-yl) methylene)-3-ethyl-2-(3-fluoro-4-morpholinophenylimino) thiazolidin-4-one (8h)

Yellow Solid. Yield 89%;Melting Point-187°C, IR(KBr) cm^{-1}: 1710(C=O), 1592 (C=N), 1369 & 1170 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.31-1.34(t,3H), 3.11(t,4H), 3.87(t,4H), 4.00-4.04(q,2H), 6.72-6.76(d,2H), 7.03(s,1H), 7.07-7.10(m,2H), 7.34-7.39(m,2H), 7.63(s,1H), 7.71-7.73(d,1H), 7.68-7.72(m,4H), MS (APCI); *m/z* 669.1 [M+1]

2.2.16. Synthesis of 3-ethyl-2-(3-fluoro-4-morpholinophenylimino)-5-((1-(4-methoxyphenylsulfonyl)-1H-indol-3-yl) methylene)thiazolidin-4-one (8i)

Yellow Solid. Yield 90%; Melting Point-186°C, IR(KBr) cm^{-1}: 1709(C=O), 1590 (C=N), 1365 & 1167 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.33-1.37(t,3H), 3.79(s,3H), 3.16(t,4H), 3.90(t,4H), 4.04-4.06(q,2H), 6.79-6.82(d,1H), 6.87-6.89(d,2H), 7.00-7.04(t,1H), 7.10-7.14(m,2H), 7.33-7.42(m,2H), 7.81-7.83 (d,2H), 7.89(s,1H), 7.94-7.96(d,2H) MS (APCI); *m/z* 621.2 [M+1]

2.2.17 Synthesis of 3-ethyl-2-(3-fluoro-4-morpholinophenylimino)-5-((1-(phenylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (8j)

Yellow Solid. Yield: 88%; Melting Point-179°C, IR(KBr) cm^{-1}: 1706(C=O), 1612 (C=N), 1379 & 1179 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.35-1.38(t,3H), 1.41-1.44(t,3H), 2.56-2.60(q,2H),

3.28(t,4H), 4.00(t,4H), 4.04-4.09(q,2H), 6.83-6.86(d,1H), 7.24-7.27(m,2H), 7.33-7.42(m,2H), 7.69(s,1H), 7.73-7.75(d,2H), 7.77-7.79(d,2H), 7.91(s,1H), 7.96-7.98(d,2H) MS (APCI); *m/z* 591.1 [M+1]

2.2.18. Synthesis of -3-ethyl-5-((1-(4-ethylphenylsulfonyl)-1H-indol-3-yl) methylene)-2-(3-fluoro-4-morpholinophenylimino) thiazolidin-4-one (8k)

Yellow Solid. Yield 86%; Melting Point-185°C, IR(KBr) cm^{-1}: 1709(C=O), 1612 (C=N), 1372 & 1177 (SO_2). ^{1}HNMR ($CDCl_3$, 400MHz): δ 1.33-1.37(t,3H), 1.43-1.47(t,3H), 3.79(q,2H), 3.16(t,4H), 3.90(t,4H), 4.04-4.06(q,2H), 6.79-6.82(d,1H), 6.87-6.89(d,2H), 7.00-7.04(t,1H), 7.10-7.14(m,2H), 7.33-7.42(m,2H), 7.81-7.83 (d,2H), 7.89(s,1H), 7.94-7.96(d,2H), MS (APCI); *m/z* 619.2 [M+1]

3. Results and Discussions

In continuation of our interest on the catalytic use of DMAP, herein we report a novel and efficient N-acylation and N-sulphonation of indole. Initially, we attempted the N-acylation and N-sulphonation of indole with acetyl chloride and sulfonyl chloride in presence of 10mol% of DMAP. The reaction went to completion at room temperature within 30min-60min to give product in excellent yield. (Table-1&2, Scheme-2&3).

Encouraged by this result, we turned our attention to various acetyl, benzoyl and sulfonyl chlorides to react with Indole derivative, 3-Ethyl-2-(3-fluoro-4-morpholin-4-yl-phenylimino)-5-(1H-indol-3-ylmethylene)-thiazolidin-4-one (Prepared as shown in Scheme-1). Interestingly, all above reaction gives N-acylated and N-sulphonated product in excellent yields (Table 1&2). Furthermore all the reaction has been done at room temperature in shortest period of time.

By treating indole derivative with appropriate acetyl/benzoyl/sulfonyl chloride, product formed in range of 80-91% range. In N-Acetylation, acetyl chloride gives maximum yield of 88% while in N-Sulphonation 4-Methyl phenyl (Para toluene), 4-Ethoxy phenyl gives maximum yields. As solvent, dichloromethane (DCM) gave the best results. All the products were characterized by ^{1}HNMR, IR, mass spectroscopy and C, H, N analysis.

Table .1: Physical characterization data:

Compound	Physical state	Mp (°C)	Yield (%)	Molecular formula	Mol. Wt.	Analysis (%) Calcd/Found		
						C	H	N
6	Yellow Solid	176	86	$C_{24}H_{23}FN_4O_2S$	450.52	63.98 63.95	5.15 5.19	12.44 12.34
7a	Yellow Solid	184	88	$C_{26}H_{25}FN_4O_3S$	492.57	63.40 63.55	5.12 5.39	11.37 11.44
7b	Yellow Solid	186	84	$C_{27}H_{27}FN_4O_3S$	506.59	64.01 64.23	5.37 5.23	11.06 11.36
7c	Yellow Solid	178	86	$C_{31}H_{27}FN_4O_3S$	554.63	67.13 67.57	4.91 4.70	10.10 9.96
7d	Yellow Solid	187	82	$C_{31}H_{26}ClFN_4O_3S$	588.14	63.21 63.33	4.45 4.46	9.51 9.70
7e	Yellow Solid	189	84	$C_{31}H_{26}FIN_4O_3S$	680.53	54.71 54.54	3.85 3.94	8.23 8.46
7f	Yellow Solid	192	82	$C_{31}H_{26}F_2N_4O_3S$	572.62	65.02 65.14	4.58 4.26	9.78 9.66
7g	Yellow Solid	188	80	$C_{31}H_{26}FN_4O_3S_2$	633.53	58.11 58.90	4.14 4.36	8.84 8.99
8a	Yellow Solid	182	91	$C_{31}H_{29}FN_4O_3S_2$	604.16	61.57 61.36	4.83 4.60	9.26 9.34
8b	Yellow Solid	188	89	$C_{30}H_{26}FN_5O_6S_2$	635.13	56.68 56.73	4.12 3.99	11.02 10.96
8c	Yellow Solid	220	88	$C_{25}H_{25}FN_4O_4S_2$	528.13	56.80 57.00	4.77 4.66	10.60 10.78
8d	Yellow Solid	188	91	$C_{32}H_{31}FN_4O_5S_2$	634.17	60.55 60.78	4.92 4.84	8.83 8.96
8e	Yellow Solid	183	90	$C_{30}H_{26}F_2N_4O_4S_2$	608.14	59.20 59.32	4.31 4.50	9.20 9.10
8f	Yellow Solid	185	90	$C_{30}H_{26}ClFN_4O_4S_2$	624.11	57.64 57.57	4.19 4.30	8.96 9.16
8g	Yellow Solid	189	90	$C_{30}H_{26}FIN_4O_4S_2$	716.04	50.28 50.23	3.66 3.76	7.82 7.99
8h	Yellow Solid	187	89	$C_{30}H_{26}BrFN_4O_4S_2$	668.06	53.81 53.99	3.91 4.03	8.37 8.20
8i	Yellow Solid	186	90	$C_{31}H_{29}FN_4O_5S_2$	620.16	59.98 60.10	4.71 4.89	9.03 9.39
8j	Yellow Solid	179	88	$C_{30}H_{27}FN_4O_4S_2$	590.15	61.00 60.90	4.61 4.88	9.48 9.59
8k	Yellow Solid	185	86	$C_{32}H_{31}FN_4O_4S_2$	618.18	62.12 62.26	5.05 5.23	9.05 9.23

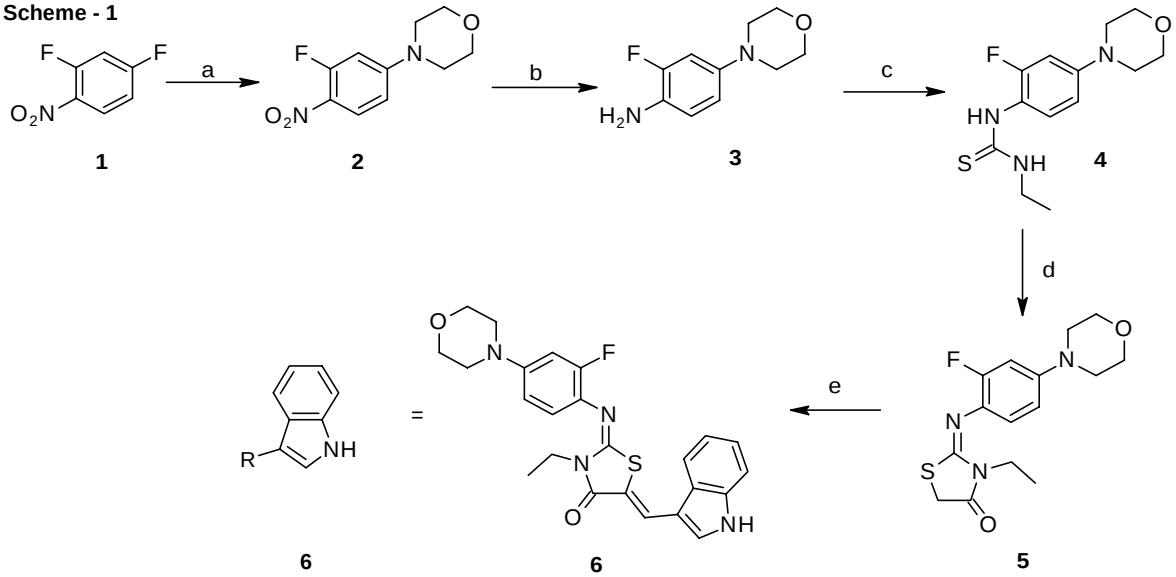
Table .2: DMAP-catalysed acyalation and sulfonation of Indole derivative with acetyl, benzoyl and sulfonyl chlorides

Indole	Acetyl/Benzoyl Chlorides	Product[1]	Time (Min)	Yields[2] (%)
6	Acetyl Chloride	7a	30	86
6	Propanoyl Chloride	7b	35	88
6	Benzoyl Chloride	7c	50	84
6	4-Chlorobenzzoyl Chloride	7d	45	86
6	4-Bromobenzzoyl Chloride	7e	40	82
6	4-Iodobenzzoyl Chloride	7f	45	84
6	4-Fluororobenzzoyl Chloride	7g	50	80

Indole	Sulfonyl Chlorides	Product	Time (Min)	Yields (%)
6	4- methyl benzene sulfonyl Chloride	8a	45	91
6	4-nitrobenzenesulfonyl Chloride	8b	50	89
6	Methane sulfonyl Chloride	8c	35	88
6	4-ethoxybenzenesulfonyl chloride	8d	45	91
6	4-fluorobenzenesulfonyl chloride	8e	50	90
6	4-chlorobenzenesulfonyl chloride	8f	55	90
6	4-iodobenzenesulfonyl chloride	8g	60	90
6	4-bromobenzenesulfonyl chloride	8h	60	89
6	4-methoxybenzenesulfonyl chloride	8i	50	90
6	Benzene sulfonyl chloride	8j	50	88
6	4-ethylbenzenesulfonyl chloride	8k	35	86

All the products were characterised by [1]HNMR, IR, mass spectroscopy.
Yields refer to pure products after crystallisation in ethanol.

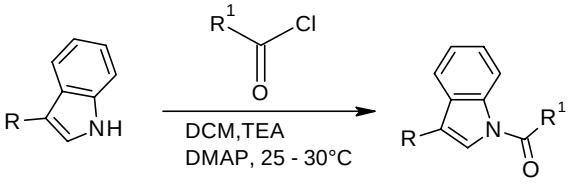
Scheme - 1



1 **2** **3** **4** **5** **6** **6**

Scheme - 1: Reagents and conditions:
a - Morpholine, K_2CO_3 in DMF at 80°C
b - H_2/Pd C, MeOH
c - Ethylisothiocyanate, EtOH at 80°C
d - Ethylbromoacetate,TEA, EtOH at 80°C
e - Indole - 3 - carboxaldehyde, Piperidine,AcOH, EtOH at 80°C

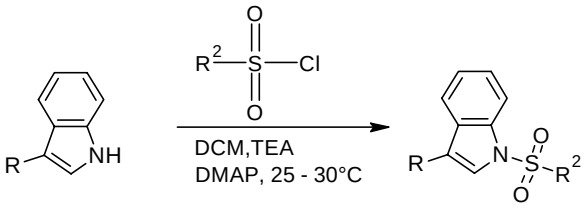
Scheme - 2



6 7a - g

Where R^1= 7a= methyl
7b= ethyl
7c= phenyl
7d= 4 - Chloro phenyl
7e= 4 - Bromo phenyl
7f= 4 - Iodo phenyl
7g= 4 - Flouro phenyl

Scheme - 3



6 **8a - k**

Where R^2= 8a= 4 - methyl phenyl (para toluene)
8b= 4 - Nitro phenyl
8c= methyl
8d= 4 - Ethoxy phenyl
8e= 4 - Flouro phenyl
8f= 4 - Chloro phenyl
8g= 4 - Iodo phenyl
8h= 4 - Bromo phenyl
8i= 4 - Methoxy phenyl
8j= Phenyl
8k= 4 - Ethyl phenyl

4. CONCLUSION

In summary, DMAP has proved to be an effective catalyst for the N-acylation and N-sulphonation of Indole derivatives with acetyl, benzoyl and sulfonyl chlorides in high yields and shortest reaction time with high selectivity, making it a useful and attractive process.

5. ACKNOWLEDGEMENT

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