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Synthesis, Characterization and Fluorescence Study of Newly Synthesized Flavonoid Derivatives From Resorcinol

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ABSTRACT

In this work, substituted coumarin based flavonoids have been synthesized from resorcinol and ethylbenzoylacetate. The main purpose of that synthesis was to study fluorescence activity of synthesized compounds. The entire synthesized compounds were characterized by ^{1}H-NMR, IR, mass spectroscopic techniques. Melting points (M.P) and yields (%) of all the compounds are recorded

The reactions are easy to conduct, under mild conditions, from coumarine substituted chalcone in moderate to excellent yields.

Keywords: Coumarin**,** Chalcone, flavonoid, fluorescence activity.

Introduction

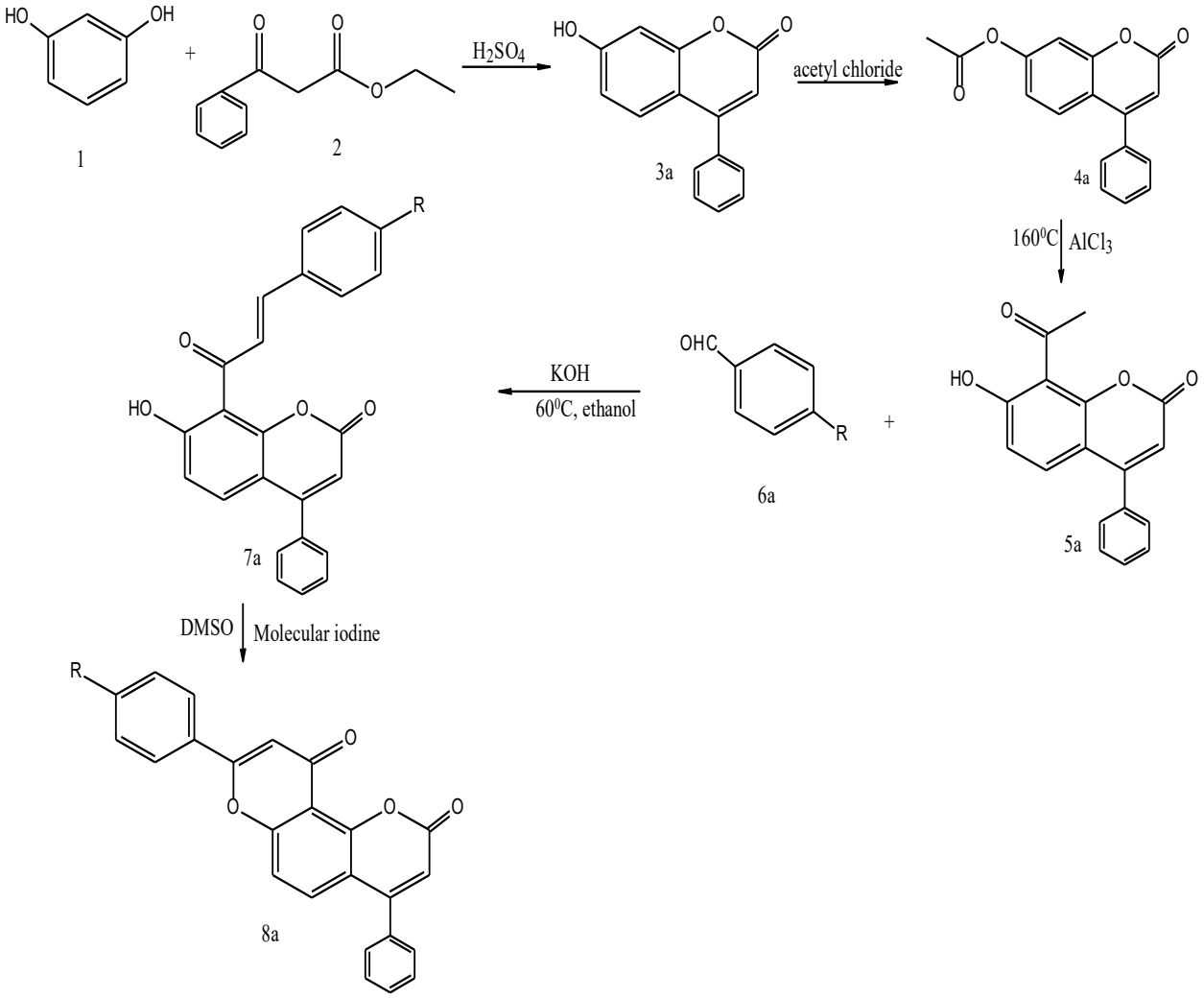
Chalcones, considered being the precursor or starting material of flavonoids and isomers of flavonoids. Generally coumarins are called as open-chain flavonoids, as they are present as in which the two aromatic rings are joined by a bridge of three-carbon α, β-unsaturated carbonyl system. Literature survey revealed that compounds with a chalcone-based structure have wide range of medicinal activities such as anti-inflammatory,[1] anti-bacterial,[2] anti-fungal,[3-5] antitumor[6-9] antitubercular[10] antimicrobial,[11-12] anti-leishmanial[13,14], anti-oxidant[15,16], antiparasitic[17] antiproliferative[18,19] anticancer,[20,21] antimalarial[22,23] activities. These activities are largely attributed due to the α, β- unsaturated ketone moiety. Chalcone derivatives have promising cytotoxic effects in both cell lines than dihydroartemisinin.[24,25] Most of the chalcone compounds posses promising anti-nociceptive[26] activity in acetic acid, formalin, and glutamate-induced pain in mice. [27] Some of the chalcone derivatives have inhibitory action of nitric oxide (NO) production in marine macrophages[28]. Most of the compounds showed good tyrosinase inhibitor activity. [29] Introduction of various substituents into the two aryl rings is also a subject of interest. Beside that both chalcone and flavones shows good to excellent Fluorescence activity.

2. MATERIAL AND METHOD

Study of Fluorescence Behavior of coumarin–flavonoids conjugates (**8a-d**) carried out in four solvent (chloroform, Acetonitrile, methanol and DMSO) to study the effect of solvent on absorption and emission intensities. It was observed that the coumarin–flavonoids conjugates (**8a-d**) showed a good fluorescence.

Representative method for the preparation of final compounds:

The preparation method include following steps. A representative Scheme for synthesis is as shown bellow.



R= -Cl, -OH, $-NO_2$,$-OCH_3$

Synthesis of 7-Hydroxy-4-phenyl-2H-chromen-2-one (Pechmann condensation)

A 100 ml beaker was filled with resorcinol (2g/mol) and Benzylacetoacetate 2.36 (g/mol), concentrated H_2SO_4 (7ml) was added below 10°C with constant stirring. Afterward, the reaction was continuing over the period of 05-06 hour in anhydrous condition. The progress of reaction was monitored by TLC. On completion of reaction, the reaction mass was poured over crushed ice. The formed solid was filtered, washed with water, dried and crystallized from ethanol.

It is yellow amorphous solid; Yield 94%; mp. 215°C ; IR spectrum (KBr),υ (cm^{-1}): 1580 cm^{-1} (C=C str.); 1690cm^{-1} (C=O str.); 3650 cm^{-1} (O-H str.); 1280 cm^{-1} (C-O str.); ^{1}HNMR spectrum (δ ppm): 7.21 (2H, d, AR-CH); 9.62 (1H, s, OH); 6.24 (1H, s, CH); 7.14-7.31 (Ar-H)

(II) Synthesis of 2-oxo-4-phenyl-2H-chromen-7-yl acetate (Acetylation)

A 100 ml beaker was filled with 7-hydroxy-4-phenyl-2-H-chromen-2-one (1g/mol), NaOH (1g/mol) and acetyl chloride (1.5 g/mol). The reaction mass stirred gently over the time of 3 hour, the progress of reaction was monitored by TLC. On completion of reaction, the reaction mass was poured over crushed

ice resulted in the formation of amorphous solid. The formed solid was filtered, washed with water, dried and crystallized from ethanol.

It is brown amorphous solid; Yield 88%; mp. 235°C ; IR spectrum (KBr),υ (cm^{-1}): 1590 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3070 cm^{-1} (C-H str.); 2900 cm^{-1} (C-H str.alk); 1180 cm^{-1} (C-O str.); ^{1}HNMR spectrum (δ ppm): 2.2 (3H, s, CH3); 6.1 (1H, s, C-H); 7.28 (1H, s, CH); 7.3-7.5 (Ar-H)

(III) Synthesis of 8-acetyl-7-hydroxy-4-phenyl-2H-chromen-2-one (Fries rearrangement)

100 ml round bottom flask equipped with reflux condenser with 4-methyl-2-oxo-2H-chromon-7-yl acetate (1g), in solvent (1g) $AlCl_3$, reflux for 2 hour in oil bath and maintained the temperature 145 to 160°C then add 1% HCl for 12 hour. The progress of reaction was monitored by TLC at room temperature. On completion of reaction, the reaction mass was poured over crushed ice.

It is black crystalline solid; Yield 86%; mp. 210°C. IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm): 2.5 (3H, s, CH3); 9.4 (1H, s, OH); 6.2 (1H, d, CH); 7.3-7.5 (Ar-H)

Preparation of 8-((E)-3-(4-chlorophenyl) acryloyl)-7-hydroxy-4-phenyl-2H-chromen-2-one (7a):

Compound (**5a**) and P-Chlorobenzaldehyde (**6a**) was taken in 1:1 proportion, to this add 50 ml of ethanol as a solvent, and 9 ml of 40 % KOH , the reaction mixture was refluxed for 2 hours to get the compound (**7a**). The progress of reaction was monitored by TLC. The product obtained was washed with water and crystallized from ethanol.

It is brownish amorphous solid; Yield 80%; mp. 185°C. IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} ; ^{1}HNMR spectrum (δ ppm): 9.64 (1H, s, OH); 7.53 (2H, d, CH); 7.45 (2H, d, CH); 6.4 (1H, d, CH); 6.6 (1H, d, CH); 7.33 (1H, d, CH); 7.3 (1H, s, CH); 7.28 (1H, d, CH);6.99-7.1 (Ar-H- benzene)

Preparation of 8-((E)-3-(4-hydroxyphenyl) acryloyl)-7-hydroxy-4-phenyl-2H-chromen-2-one (7b):

It is brownish amorphous solid; Yield 75%; mp. 188°C. IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm): 9.61 (1H, s, OH); 9.73 (1H, s, OH); 7.5 (2H, d, CH); 7.42 (2H, d, CH); 6.5 (1H, d, CH); 6.69 (1H, d, CH); 7.3 (1H, d, CH); 7.38 (1H, s, CH); 7.35 (1H, d, CH);7-7.1 (Ar-H- benzene)

Preparation of 8-((E)-3-(4-nitrophenyl) acryloyl)-7-hydroxy-4-phenyl-2H-chromen-2-one (7c):

It is brownish amorphous solid; Yield 76%; mp. 170°C. IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm): 9.7 (1H, s, OH); 7.55 (2H, d, CH); 7.48 (2H, d, CH); 6.43 (1H, d, CH); 6.68 (1H, d, CH); 7.36 (1H, d, CH); 7.4 (1H, s, CH); 7.33 (1H, d, CH);6.99-7.2 (Ar-H-benzene)

Preparation of 8-((E)-3-(4-methoxyphenyl) acryloyl)-7-hydroxy-4-phenyl-2H-chromen-2-one (7d):

It is brownish amorphous solid; Yield 71%; mp. 189°C. IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm): 9.6 (1H, s, OH); 7.5 (2H, d, CH); 7.4 (2H, d, CH); 6.4 (1H, d, CH); 6.66 (1H, d, CH); 7.33 (1H, d, CH); 7.29 (1H, s, CH); 7.25 (1H, d, CH);6.99-7.1 (Ar-H- benzene); 2.4(3H,s,CH_3)

Preparation of 8-(4-chlorophenyl)-4-phenyl-2H,10H-pyrano[2,3-f]chromene-2,10-dione (8a):
Few iodine crystals were added in the mixture of compound (**7a**) and DMSO in round bottom flask. The reaction mixture was refluxed for 1 hour to get the final product 8-(4-chlorophenyl)-4-methyl-2H,10H-pyrano[2,3-f]chromene-2,10-dione (8a).

It is brownish crystalline solid; Yield 73%; mp. 178°C.IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm): ^{1}HNMR spectrum (δ ppm):7.55 (2H, d, CH); 7.48 (2H, d, CH); 6.85 (1H, s, CH); 7.36 (1H, d, CH); 7.32 (1H, d, CH); 7.28 (1H, s, CH); 7.0 (2H, d, CH);6.99(3H, t, CH, AR-CH).

Preparation of 8-(4-hydroxyphenyl)-4-phenyl-2H,10H-pyrano[2,3-f]chromene-2,10-dione (8b):
It is brownish crystalline solid; Yield 72%; mp. 179°C.IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm): 9.75 (1H, s, OH); 7.5 (2H, d, CH); 7.42 (2H, d, CH); 6.8 (1H, s, CH); 7.31 (1H, d, CH); 7.33 (1H, d, CH); 7.28 (1H, s, CH); 7.1 (2H, d, CH);6.99(3H, t, CH, AR-CH).

Preparation of 8-(4-nitrophenyl)-4-phenyl-2H,10H-pyrano[2,3-f]chromene-2,10-dione (8c):
It is brown crystalline solid; Yield 65%; mp. 168°C. IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm):7.5 (2H, d, CH); 7.48 (2H, d, CH); 6.98 (1H, s, CH); 7.36 (1H, d, CH); 7.32 (1H, d, CH); 7.28 (1H, s, CH); 7.0 (2H, d, CH);7.2(3H, t, CH, AR-CH).

Preparation of 8-(4-methoxyphenyl)-4-phenyl-2H,10H-pyrano[2,3-f]chromene-2,10-dione (8d):
It is brown amorphous solid; Yield 75%; mp. 181°C. IR spectrum (KBr),υ (cm^{-1}): 1575 cm^{-1} (C=C str.); 1750cm^{-1} (C=O str.); 3664 cm^{-1} (O-H str.); 1276 cm^{-1} (C-O str.); 3070 cm^{-1} (C-H str.); 2910 cm^{-1} (C-H str.alk); ^{1}HNMR spectrum (δ ppm): 2.35 (3H, s, CH_3); 7.52 (2H, d, CH); 7.48 (2H, d, CH); 6.98 (1H, s, CH); 7.35 (1H, d, CH); 7.3 (1H, d, CH); 7.28 (1H, s, CH); 7.0 (2H, d, CH);7.2(3H, t, CH, AR-CH).

3. RESULT AND DISCUSSION:

3.1 FLUROSCENCE PROPERTIES:

The fluorescence properties of novel flavonoids 8**a-d** were investigated. The effect of different substituent's on flavonoid moiety and different solvents with respect to polarity has been studied. The molecules were designed with unique combination of electron donor at the 7th position like benzene substituted with chloro, hydroxy, nitro, methoxy etc coumarin moiety leading to the formation of push pull system.

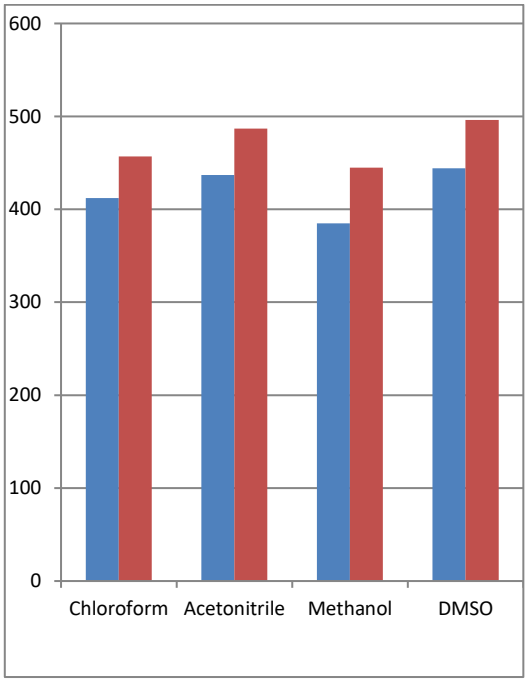
The fluorescence spectral data of all the compounds 2a-d are summarized in Table 1. These compounds exhibited varying trend of fluorescent property with 20 to 48 nanometer strokes shift in chloroform, Acetonitrile, methanol and DMSO respectively when compared with Rhodamine B.

Table 1. Fluorescent property of compound 8a-d in four solvent viz. MeOH, Acetonitrile ,Chloroform dimethylsulphoxide.

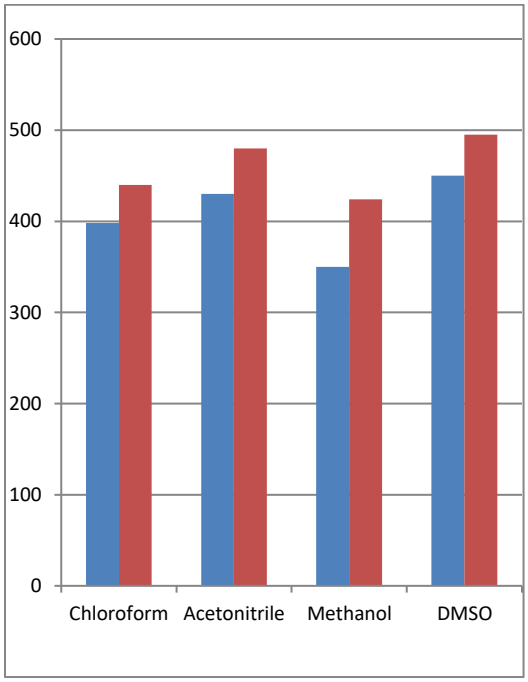
Compounds	Solvent	λabs (nm)	λem (nm)	Strokes shift
8a	Chloroform	412	457	45
	Acetonitrile	437	487	50

	Methanol	385	445	58
	DMSO	444	496	52
8b	Chloroform	398	440	42
	Acetonitrile	430	480	50
	Methanol	350	424	74
	DMSO	450	495	45
8c	Chloroform	408	444	36
	Acetonitrile	413	462	49
	Methanol	415	466	51
	DMSO	442	478	36
8d	Chloroform	444	485	41
	Acetonitrile	425	477	52
	Methanol	421	466	45
	DMSO	441	486	45

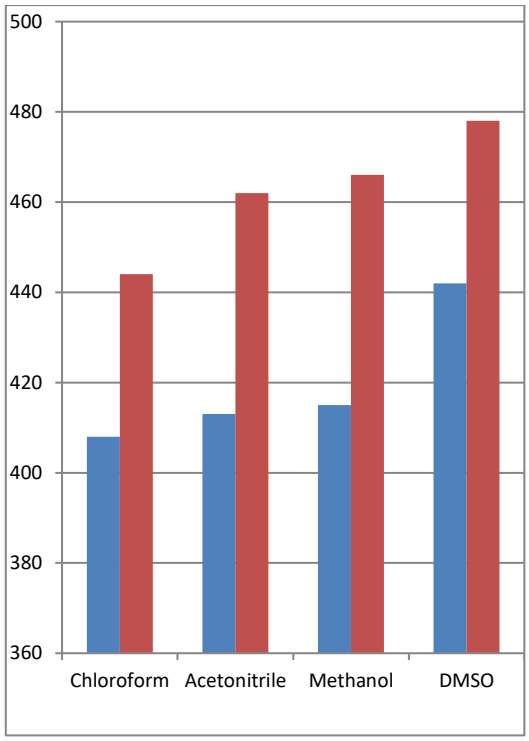
The absorption, emission and strokes shift are given in Table 1 and also plotted in graph.



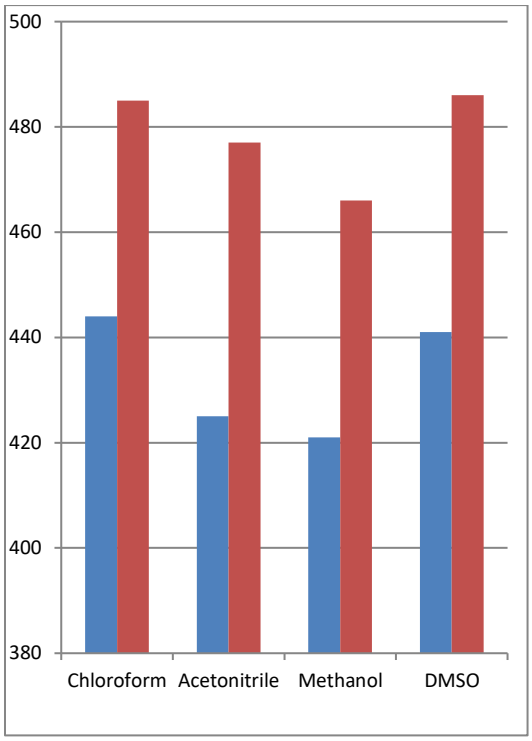
Absorption and emission wavelength of 8a



Absorption and emission wavelength of 8b



Absorption and emission wavelength of 8c



Absorption and emission wavelength of 8d

CONCLUSION

The successful synthesis of flavonoid compounds follows a mild, efficient route with a good to moderate yield. In present work we synthesized flavonoids from early prepared chalcone. The synthesized compounds exhibited good fluorescence activity.

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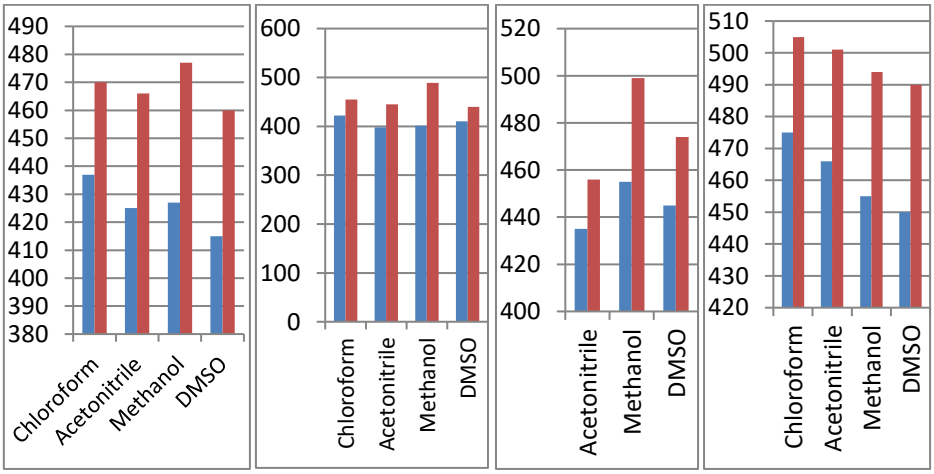
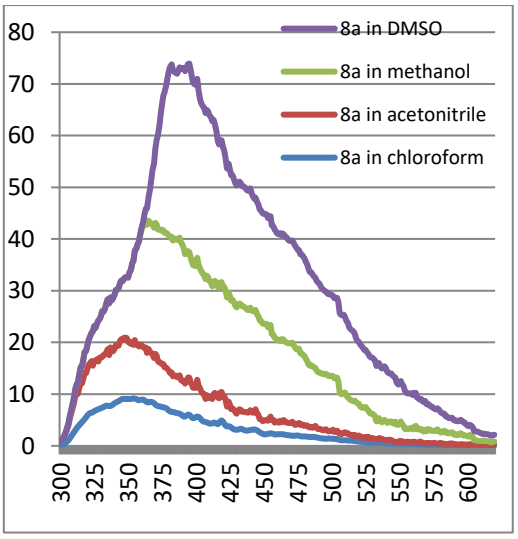
Solvent	**λabs (nm)**	**λem (nm)**	**Strokes shift**
Chloroform	437	470	33
Acetonitrile	425	466	41
Methanol	427	477	50
DMSO	415	460	45
Chloroform	422	455	33
Acetonitrile	398	445	47
Methanol	401	489	88

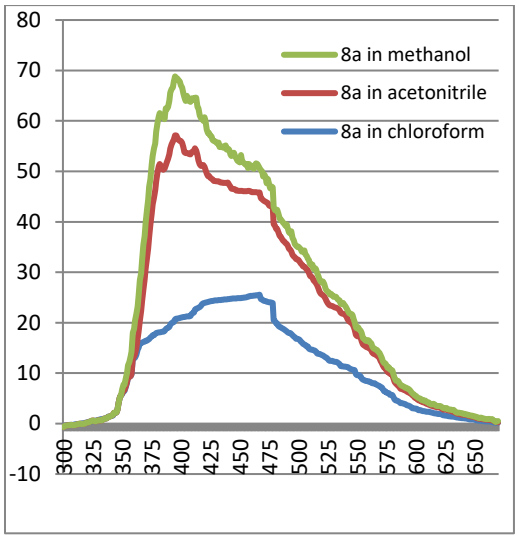
DMSO	410	440	30
Chloroform	--	--	--
Acetonitrile	435	456	21
Methanol	455	499	44
DMSO	445	474	29
Chloroform	475	505	30
Acetonitrile	466	501	35
Methanol	455	494	39
DMSO	450	490	40

Solvent	**λabs (nm)**	**λem (nm)**	**Strokes shift**
Chloroform	402	437	35
Acetonitrile	427	467	40
Methanol	379	427	48
DMSO	434	476	42
Chloroform	388	422	34
Acetonitrile	424	469	45
Methanol	340	404	64
DMSO	448	487	39
Chloroform	401	435	34
Acetonitrile	410	451	41
Methanol	411	455	44
DMSO	440	469	29
Chloroform	444	475	31
Acetonitrile	425	466	41
Methanol	416	455	39
DMSO	438	478	40

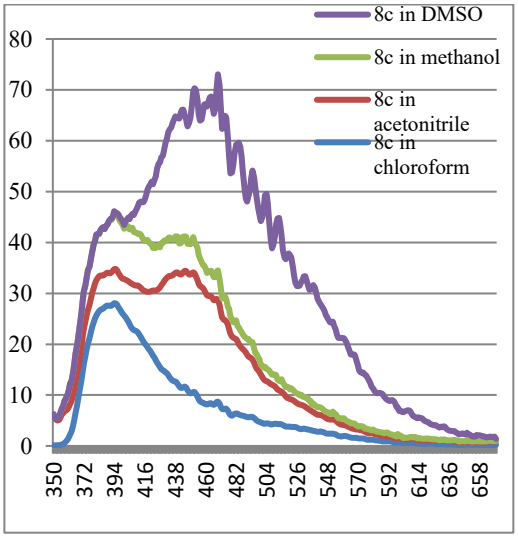




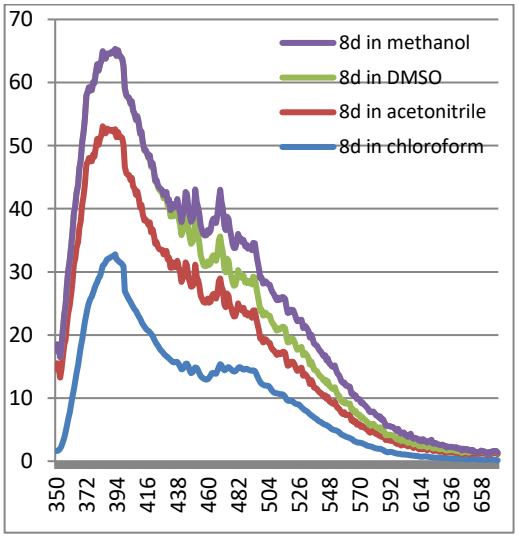
Absorption spectra of 8a



Emission spectra of 8a



Emission spectra of 8c



Emission spectra of 8d

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