Preprint Title	Photophysical, photostability, and *ROS* generation properties of new trifluoromethylated quinoline-phenol Schiff bases
Authors	Inaiá O. Rocha, Yuri G. Kappenberg, Wilian C. Rosa, Clarissa P. Frizzo, Nilo Zanatta, Marcos A. P. Martins, Isadora Tisoco, Bernardo A. Iglesias and Helio G. Bonacorso
Publication Date	23 Aug. 2021
Article Type	Full Research Paper
Supporting Information File 1	V1 - Supporting Information.pdf; 5.9 MB
ORCID® iDs	Nilo Zanatta - https://orcid.org/0000-0002-0959-9043; Bernardo A. Iglesias - https://orcid.org/0000-0002-4039-6316; Helio G. Bonacorso - https://orcid.org/0000-0002-2745-2061

Photophysical, photostability, and *ROS* generation properties of new trifluoromethylated quinoline-phenol Schiff bases

Inaiá O. Rocha[1], Yuri G. Kappenberg[1], Wilian C. Rosa[1], Clarissa P. Frizzo[1], Nilo Zanatta1, Marcos A. P. Martins[1], Isadora Tisoco[2], Bernardo A. Iglesias[2] and Helio G. Bonacorso[1,*]

Address:

[1]Núcleo de Química de Heterociclos (NUQUIMHE), Departamento de Química, Universidade Federal de Santa Maria, Santa Maria, RS, 97105-900, Brazil

[2]Laboratório de Bioinorgânica e Materiais Porfirínicos, Departamento de Química, Universidade Federal de Santa Maria, Santa Maria, RS, 97105-900, Brazil

Author Email:

*helio.bonacorso@ufsm.br (Helio G. Bonacorso).

Abstract

A new series of ten examples of (*E*)-2-(((2-alkyl(aryl/heteroaryl)-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenols (Schiff bases), was easy synthesized at yields up to 91% from the reactions involving a series of 2-(R-substituted) 6-amino-4-(trifluoromethyl)quinolines and 4(5)-R[1]-substituted salicylaldehydes – in which alkyl/aryl/heteroaryl for 2-(R)-substituents are Me, Ph, 4-MeC$_6$H$_4$, 4-FC$_6$H$_4$, 4-NO$_2$C$_6$H$_4$, and 2-furyl, and (R[1])-substituents are 5-NEt$_2$, 5-OCH$_3$,

4-Br, and 4-NO$_2$. Complementarily, the Schiff bases showed low to good quantum fluorescence yield values both in CHCl$_3$ (Φ_f = 0.12-0.80), DMSO (Φ_f = 0.20-0.75) and MeOH (Φ_f = 0.13-0.85). Higher values of Stokes shifts (SS) were observed in more polar solvents (DMSO; 65-150 nm and MeOH; 65-130 nm) than in CHCl$_3$ (59-85 nm). Compounds **3** presented good stability under white-LED irradiation conditions and, as well as, moderate *ROS* generation properties were observed.

Keywords

Schiff base, quinoline, photophysical properties, photostability, *ROS* generation.

Introduction

Schiff bases are an important class of organic compounds first reported by the German chemist Hugo Schiff in 1864 and formed from the reversible condensation between a primary amine and an aldehyde or a ketone. [1] Also known as azomethines, aldimines, and more commonly as imines, Schiff bases have the general organic function -C=N- [2], of which they have a wide range of biological activities, including antioxidant [3], antitubercular [4], antibacterial [5], antimicrobial [6], and antifungal properties [7], in addition to their role as chemo-sensors [8] (Figure 1).

Quinolines are another important class of compounds and have numerous medicinal chemistry applications due to their biological applicability [9] and promising antimycobacterial [10], antimalarial [11,12], and antibacterial [13] activities. On the other hand, 6-aminoquinoline compounds demonstrate interesting luminescent properties [14] that have aroused great interest because of their potential applicability in the composition of organic light-emitting diodes (OLED), organic solar cells (OSC), and biomolecular markers [15,16].
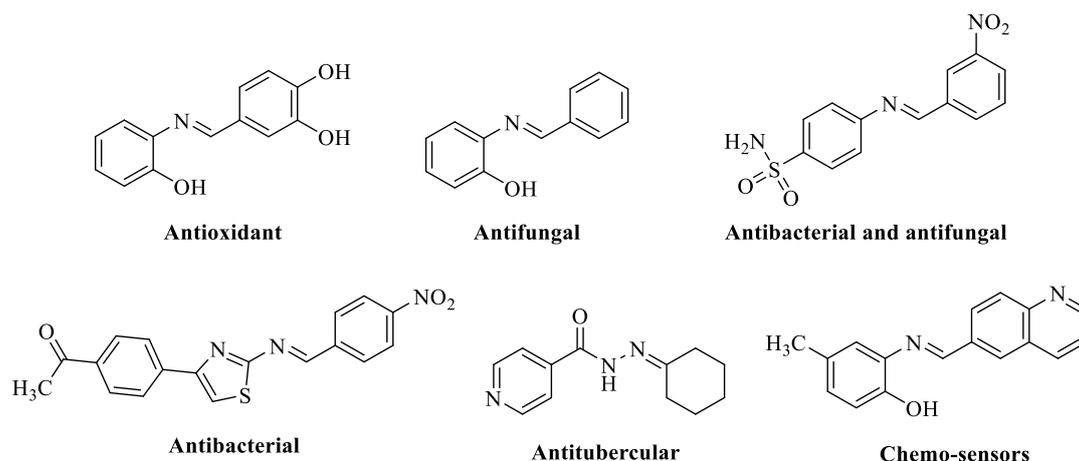
2

Figure 1. Examples of structures and properties of Schiff Bases of interest in the present study.

Moreover, the trifluoromethyl substituent (CF_3) is an interesting electron-withdrawing group that increases the effect of many bioactive molecules due to a significant increase in stability, lipophilicity and high resistance to enzymatic degradation [17,18]. Also, it has been widely applied as a special alkyl substituent for ligands of phosphorescent heavy metal complexes in OLEDs. Due to the ability to increase the electron-transporting and decrease molecule stacking, the trifluoromethyl substituted molecules have been employed to the development of phosphorescent materials [19–21].

On the other hand, antioxidants are known for protecting organisms against cell damage caused by oxidative stress, especially by eliminating reactive oxygen species such as hydroxyl radical (•OH), superoxide anion (O_2^-), and singlet oxygen ($^1O_2$) [3,22,23]. Therefore, research in recent years has focused on new compounds obtained from natural sources or by synthesis methods, which can provide active ingredients to prevent or reduce the effects of oxidative stress on cells.

Recently, our research group previously reported the synthesis of 6-amino-4-(trifluoromethyl)quinolines, which were obtained through an electrophilic aromatic substitution reaction catalyzed by sulfuric acid from 4-substituted 4-methoxy-1,1,1-trifluoroalk-3-en-2-ones in a two-step reaction procedure and with satisfactory yields of up to 87%. These new 6-aminoquinolines presented promising photophysical properties and high thermal stability [14].

In this sense, the present study aimed to synthesize a novel trifluoromethylated hybrid system comprising the Schiff base scaffolds from some 6-aminoquinolines and salicylaldehyde derivatives in order to analyze and evaluate their photophysical, photostability, and antioxidant properties for possible future applications in the pharmacological areas or material sciences (Scheme 1).
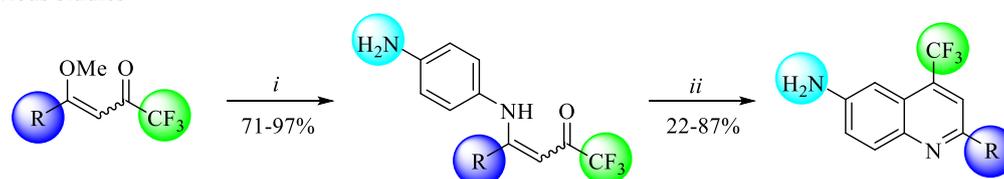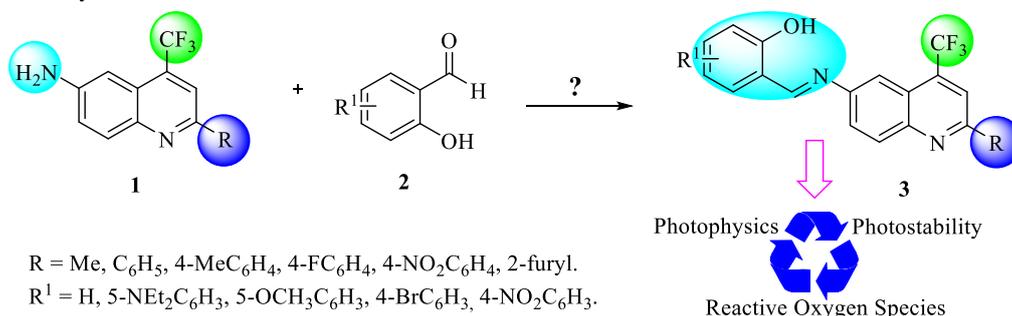
Scheme 1. General view for the present study.

Results and Discussion

Chemistry

The synthetic routes and structures for the synthesis of (*E*)-2-(((2-alkyl(aryl/heteroaryl)-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenols **3** are demonstrated in Schemes 2 and 3.

Firstly, a series of six examples of 6-amino-2-alkyl(aryl/heteroaryl)-4-(trifluoromethyl)quinolines (**1a-f**) were synthesized from the intramolecular cyclization reaction, in which trifluoromethyl substituted enamino ketones reacted with concentrated sulfuric acid at adequate temperature (120 °C) and time (10 hours) to furnish the desired compounds, following the method already described in the literature by our research group [14].

Subsequently, the quinoline **1b** and salicylaldehyde **2a** were initially selected to find the best reaction conditions and obtain a new series of Schiff bases **3**. Hence, the reaction solvent and molar ratio between the precursors were evaluated. The reactions were carried out using an equimolar ratio of both reactants in methanol, ethanol, and acetonitrile of solvent at reflux temperature according to previously reported data [22,24,25]. Thus, we found higher **3ba** yields according to the solvent used, i.e., 70 %, 80 %, and 83 %, respectively.

Acetonitrile was selected as the best solvent and the molar ratio of the reactants was also checked using a 1:2 molar ratio of quinoline **1b** for salicylaldehyde **2a**. This molar ratio increased yield to 90% for **3ba**. The best result was obtained when quinoline **1b** (1 mmol) was added to the salicylaldehyde **2a** (2 mmol) in acetonitrile (10 mL) at a molar ratio of 2:1 and reflux temperature for 48 h. The desired Schiff bases **3aa-fa** (6 examples) were obtained at this optimized condition in 20-90% yields for the isolated products after recrystallization from ethanol (Scheme 2).
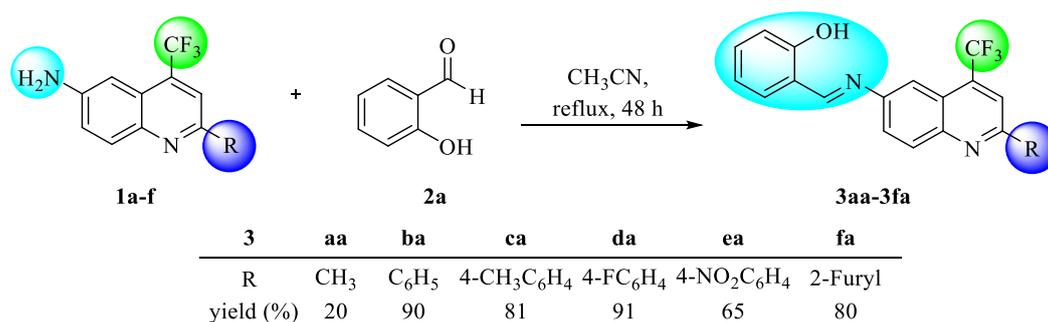
Scheme 2. Synthesis of ((trifluoromethyl)quinolinyl)phenol Schiff bases (**3aa-3fa**).

3	aa	ba	ca	da	ea	fa
R	CH_3	C_6H_5	$4\text{-}CH_3C_6H_4$	$4\text{-}FC_6H_4$	$4\text{-}NO_2C_6H_4$	2-Furyl
yield (%)	20	90	81	91	65	80

In order to evaluate the properties related to the substituents of the portion provided by salicylaldehyde, the same optimized condition was applied by fixing the quinoline **1b** (R = C_6H_5) and varying the salicylaldehydes (**2b-2e**), resulting in four more Schiff bases **3bb-be** at 40-89% yields for the isolated products after recrystallization from ethanol (Scheme 3).

3	bb	bc	bd	be
R^1	$5\text{-}NEt_2$	$5\text{-}OCH_3$	4-Br	$4\text{-}NO_2$
yield (%)	40	75	77	89
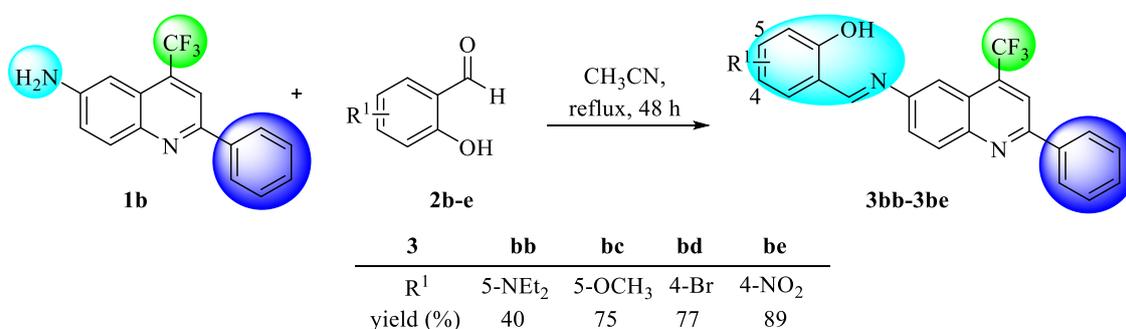
Scheme 3. Synthesis of trifluoromethylated quinolinyl-phenol Schiff bases (**3bb-be**).

With some exceptions, electron-deficient or electron-rich substituted 2-aryl-6-aminoquinolines and aromatic aldehydes worked very well to furnish the Schiff bases **3**. However, a poor yield (20%) was observed when 2-methyl-6-aminoquinoline **1a** was employed to obtain the phenol derivative **3aa**. We initially thought that a competition between the 6-amino group and 2-methyl substituent present in quinoline **1a** might

have occurred, as described by Fu and co-workers [26], which could lead to only the respective 2-alkenylquinoline or to simultaneous reaction products from both moieties (6-amino and 2-methyl substituents). However, at the end of the reaction only compound **3aa** could be isolated and the all the reactants remained intact. In this regard, it is observed that the electron-withdrawing effect of the CF_3 group is decisive in preventing the obtainment of the possible 2-alkenyl derivative.

In contrast to yield obtained for the synthesis of **3bc** (R^1 = 5-OMe, 75 %), the aromatic aldehyde substituted with similar electron-rich group **2c** (R^1 = 5-NEt_2) gave only a regular 40 % yield for **3bb**.

The structures of the new Schiff bases **3** were characterized by ^{1}H-, ^{13}C-, and ^{19}F-NMR spectroscopy and HRMS techniques. The structural assignments for the synthesized quinolines **1a-f** were consistent with the ^{1}H-, ^{13}C-, and ^{19}F-NMR spectra described in the literature [14]. When the ^{1}H-NMR spectral data were registered in $CDCl_3$ as a solvent for the **3aa-be** series and compared with the NMR spectral data of the **1a-f** series, the lack of chemical shift related to the signal for the NH_2 group was clearly noted, which was always present in the series of quinolines **1** at 4.51 ppm, on average. The appearance of a singlet of the azomethine proton (CH=N) with a chemical shift in the 8.53–8.77 ppm range in all ^{1}H-NMR spectra supported the structures of the Schiff bases **3**. Additionally, the hydrogens of the hydroxy group were observed at 13.12 ppm, on average.

The analysis of ^{13}C-NMR spectra in $CDCl_3$ for the new Schiff bases **3** showed chemical shifts in the 162.68-164.71 ppm range for the CH=N moiety, which is in agreement with similar structures described in the literature [7,14,22]. The CF_3 group bonded at C-4 was assigned as a quartet with $^1J_{CF}$ ~274.6 Hz, with chemical shifts of 123.52 ppm, on average. The ^{19}F-NMR spectra in $CDCl_3$ showed a singlet at -61.70 ppm, on average, in relation to the CF_3 group. Furthermore, there were no significant differences in the

chemical shift values between the quinoline precursor and new Schiff bases regarding aromatic ^{1}H-NMR and ^{13}C-NMR data.

Studies in the literature have reported that the imine group may exist as *E/Z* geometrical isomers in the -CH=N double bond [22]. Moreover, the *E* geometrical isomer in the -CH=N- double bond has a higher percentage when in dimethylsulfoxide-d_6 solution. On the other hand, the *Z* isomer can be stabilized in less polar solvents by an intramolecular hydrogen bond. In the present study, the spectral data were registered in CDCl$_3$ solution and no signal belonging to the *Z* isomer was observed in all cases, which can be confirmed by the chemical shift values in the ^{1}H NMR regarding the -CH=N bond.

Finally, in order to determine the real molecular structure of the Schiff bases **3**, Single-Crystal X-Ray Diffraction (SC-XRD) was performed for compound **3ba** in the solid state (Figure 1). The structure was crystallized in the P2$_1$/c space group, and it was possible to verify that the dihedral angles between the substituent (C$_6$H$_5$) and quinoline ring (N1-C2-C21- C26) were 18.1⁰. The dihedral angles between the quinoline ring and the substituent (C$_6$H$_4$) C(621)-C(62)-N(61)-C(6) were 179.0⁰, which shows some degree of planarity over the entire molecule. Additional bond lengths and angles and crystallographic refinement details can be found in the *Supporting information section* (Tables 1and 2).
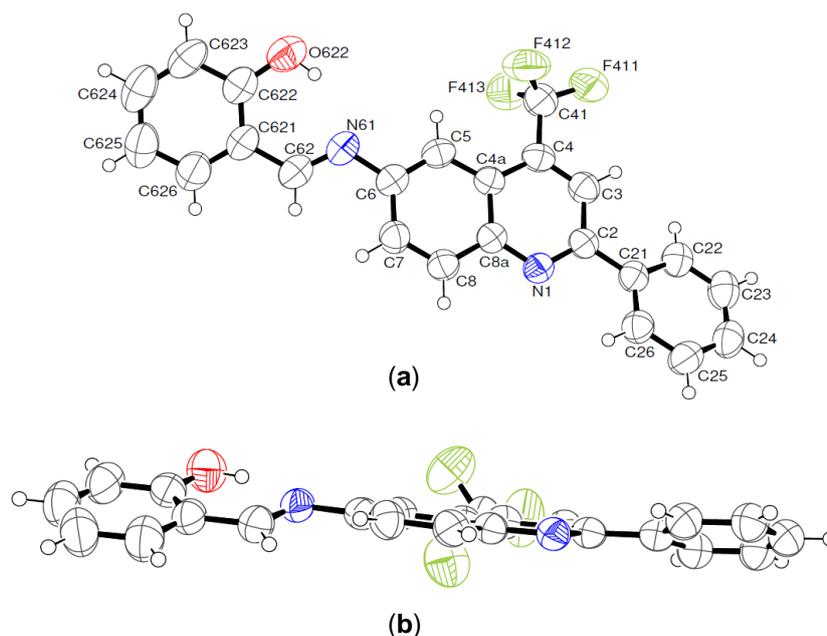
(a)

(b)

Figure 1. ORTEP diagram of the crystal structure of (*E*)-2-(((2-phenyl-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3ba**) (CCDC 2036933). (**a**) Displacement ellipsoids are drawn at the 50% probability level, and circles with arbitrary radio represent the hydrogen atoms; (**b**) Side view showing coplanarity of the same system.

Photophysical behavior

The photophysical study for the series of compounds **3aa-fa** and **3bb-be** was carried out using chloroform (CHCl$_3$), methanol (MeOH) or dimethyl sulfoxide (DMSO) solutions. As example and for comparation, the UV-Vis absorption spectra of compounds **3ea** and **3be** with contain the nitro group in two different ring positions of molecules in all solvents can be seen in Figure 2. The values of maximum molar absorption coefficients (in log ε) and wavelength (nm) of all compounds are listed in Table 1.

The absorption spectra of the studied Schiff base series presented electronic transitions in the 250-500 nm UV-Vis region. In the ultraviolet range, the observed

9

transitions can be attributed to the $\pi \rightarrow \pi^*$ transition and refer to the heterocyclic ring. Transitions above 350 nm can be attributed to the $n \rightarrow \pi^*$ transition referring to the imine moiety, causing an intramolecular charge-transfer type (ICT) transition [27]. Complementary, according already related by Temel and co-workers studying a similar scaffold, namely, 4-bromo-2-((quinoline-8-yl)methyl)phenol [27], no imine-hemiaminal tautomer peak transition was observed in all Schiff bases **3**,.

In general, there were slightly significant changes in the transitions according to the changes in the substituent or polarity of the solvent (behavior in $CHCl_3$, MeOH and DMSO is quite similar). Notably, one can highlight compound **3bb** (R = Ph, R^1 = 5-NEt_2) in which its transitions very significantly with the change in polarity of the medium (4-24 nm), and this may be due to the donor diethylamino group attached to the imine portion of the molecule. In comparison to the absorption spectra of amino-quinolines published by Kappenberg and co-workers [14], Schiff's bases studied here show similarity in the absorption behavior, making it clear that these transitions are originated mostly from the heterocyclic moiety due the presence of the substituent CF_3 and R attached to the quinoline ring at C-2 and C-4, respectively.

Moreover, as shown in Figure 3, the position of the substituent on the molecule (as spectra example - compounds **3ea** and **3be**) in the same solvent and in solvents of different polarities affect the values of the wavelengths and molar absorption coefficients of the derivatives studied here. All absorption spectra are listed in the *Supporting information section* (Figures S2-S4).
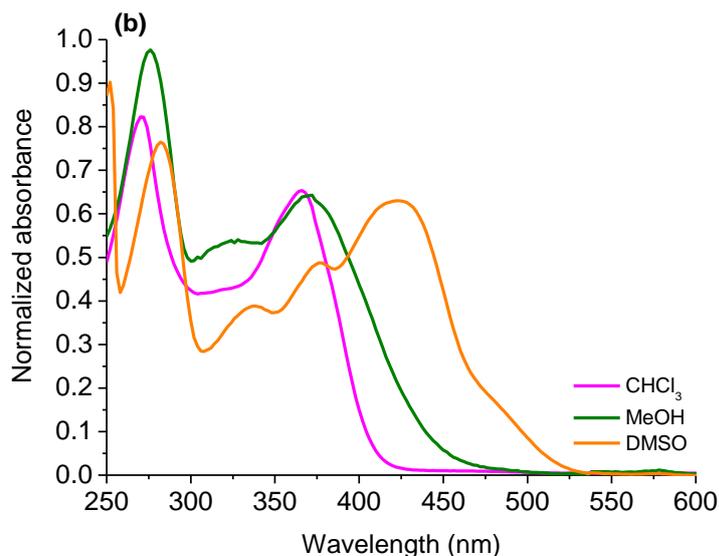
Figure 2. Electronic absorption spectra in the UV-Vis region of compounds **(a) 3ea** and **(b) 3be** in CHCl$_3$, MeOH or DMSO solution, respectively ([ ] = 1.50 x 10^{-5} M).

The steady-state emission fluorescence spectra of the Schiff base compounds from their absorption in the UV-Vis region was carried out. Derivatives **3aa-fa** and **3bb-be** were analyzed in CHCl$_3$, DMSO and MeOH solutions by the emission and excitation spectra and exemplified in the *Supporting information* section (Figures S2-S14). For emission measurements, the maximum wavelength with the lowest absorption energy was used as the excitation parameter for fluorescence measurements. Then, the quantum fluorescence yield (Φ_f) values were calculated in order to prove the quantum efficiency of these derivatives in terms of fluorescence emission and thus discuss the influence of the different substituent groups.

Firstly, by comparing the selected solvents, compound **3ba** (R = Ph, R^1 = H) presented an emission at 450-550 nm region according to the solvent property (CHCl$_3$, DMSO and MeOH). Therefore, it is possible to infer that the polarity difference of the solvent directly influences electronic transitions in the excited state, causing more changes in

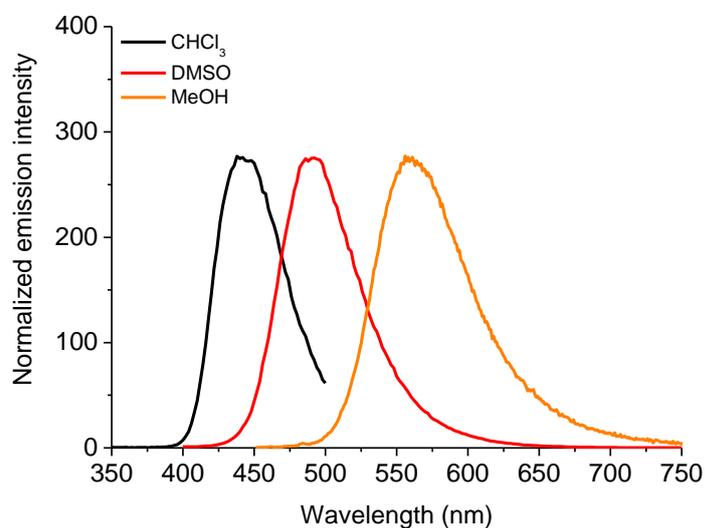the compounds in more polar and protic solvents, take the maximum emission to lower energy values. (Figure 3).

Figure 3. Steady-state emission fluorescence spectra of compound **3ba** (R = Ph, R^1 = H) in CHCl₃ (black solid line), DMSO (red solid line) and MeOH (orange solid line) solutions ([ ] = 1.50 x 10^{-5} M).

Another possible comparison is between substituents with electron-donor and acceptor properties in the same solvent media. Therefore, when the compounds containing a diethylamino group (**3bb**) (R = Ph, R^1 = 5-NMe₂) and a nitro group (**3be**) (R = Ph, R^1 = 4-NO₂) were analyzed, a significant difference was observed compared to the other compounds in series **3**. Thus, we can say that these characteristics exist because there is more stabilization of the excited state in a polar environment (DMSO and MeOH), adding to a possible push-pull effect of the diethylamino group (donor group) [14,28,29]. Moreover, these results should indicate a negative possibility of ESIPT occurring (in protic MeOH solvent), being only a direct influence of the substituents on the excited state (Figure 4) [30,31].
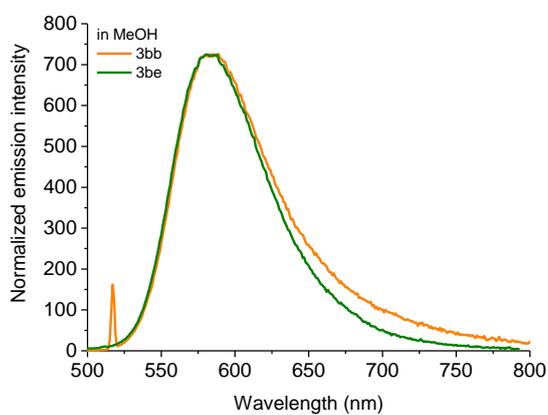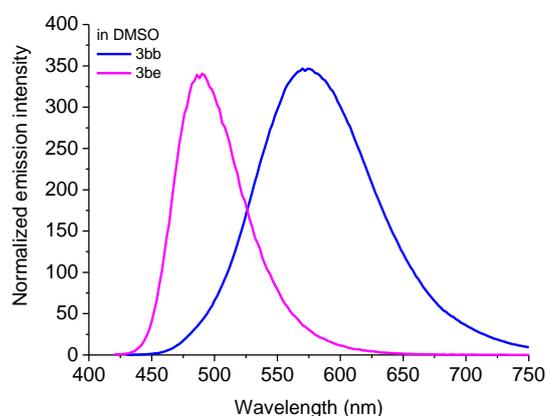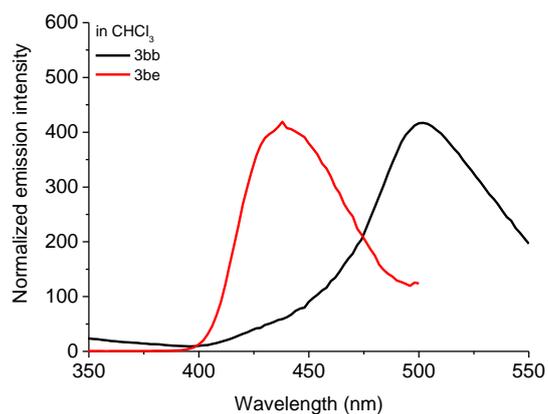
Figure 4. Comparative Steady-state emission fluorescence spectra of compound **3bb** and **3be** in all studied solvents ([ ] = 1.50 x 10^{-5} M).

In general, Schiff bases showed low to good quantum fluorescence yield values both in CHCl$_3$ (Φ_f = 0.12-0.80), DMSO (Φ_f = 0.20-0.75) and MeOH (Φ_f = 0.13-0.85) (see

Table 1) compared to the 9,10-diphenylanthracene (DPA) standard molecule. An analysis of the obtained Φ_f values revealed significant differences, mainly according to the change in solvent polarity, being, for example, the value for compound **3aa** in DMSO and MeOH almost six to seven times higher than in chloroform. Furthermore, the highest values were found in the presence of electron-donor groups (**3ca** (R = 4-tolyl, R^1 = H), **3bb** (R = Ph, R^1 = 5-NEt$_2$), and **3bc** (R = Ph, R^1 = 5-OMe)) (Table 1). These values observed according to the solvent may be related to the stabilization of the excited state in each solution.

Regarding Stokes shifts (SS), higher values were observed for derivatives in a more polar solvent (DMSO; 65-150 nm and MeOH; 65-130 nm) than in CHCl$_3$ (59-85 nm) and also according to the electronic properties of the substituents in the molecules. According to the characteristics and properties described herein, once again, we can attribute these differences to the stabilization of the excited states in more polar solvents combined with the properties of electron-donor groups (push-pull system).

As in the amino-quinolines described in the literature [14], the Schiff base derivatives present emission spectra in a region like the amino-derivatives (purple to blue region), but with higher quantum fluorescence yield values and Stokes shifts, a fact attributed to a greater electronic conjugation provided by the imine function present in the molecules of the series **3**.

Table 1. Photophysical data of derivatives **3aa-3fa** and **3bb-3be** ([ ] = 1.50 x 10^{-5} M).
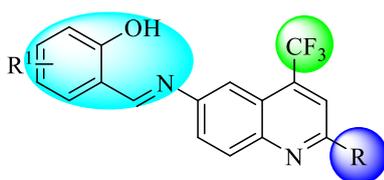
Compd.	3aa	3ba	3ca	3da	3ea	3fa	3bb	3bc	3bd	3be
R	Me	Ph	4-MeC$_6$H$_5$	4-FC$_6$H$_5$	4-NO$_2$C$_6$H$_5$	2-Furyl	Ph	Ph	Ph	Ph
R^1	Ph	Ph	Ph	Ph	Ph	Ph	5-NEt$_2$	5-OMe	4-Br	4-NO$_2$

	CHCl₃			
Compound	**λ, nm (log ε)**	**Emission, nm (Φ_f)[a]**	**SS (nm/cm⁻¹)[b]**	**E_{0-0}(eV)[c]**
3aa	275 (4.76), 354 (4.64)	448 (0.12)	94/5,927	3.10
3ba	274 (4.71), 369 (4.65)	441 (0.47)	72/4,424	2.97
3ca	276 (4.64), 370 (4.59)	429 (0.80)	59/3,717	3.09
3da	274 (4.69), 368 (4.64)	436 (0.43)	68/4,238	3.02
3ea	289 (4.61), 373 (4.67)	444 (0.01)	71/4,287	2.88
3fa	280 (4.72), 383 (4.71)	450 (0.73)	67/3,887	2.92
3bb	322 (4.26), 420 (4.78)	502 (0.58)	82/3,889	2.60
3bc	267 (4.53), 375 (4.70)	440 (0.73)	65/3,939	3.05
3bd	273 (4.71), 371 (4.61)	439 (0.38)	68/4,175	2.95
3be	271 (4.78), 366 (4.68)	438 (0.52)	72/4,491	3.00
	DMSO			
Compound	**λ, nm (log ε)**	**Emission, nm (Φ_f)[a]**	**SS (nm/cm⁻¹)[b]**	**E_{0-0} (eV)[c]**
3aa	277 (4.50), 354 (4.58)	482 (0.61)	128/7,501	2.82
3ba	276 (4.73), 371 (4.66)	491 (0.75)	120/6,587	2.75
3ca	278 (4.52), 374 (4.46)	487 (0.72)	113/6,204	2.77
3da	276 (4.48), 372 (4.42)	491 (0.51)	119/6,515	2.76
3ea	294 (4.22), 380 (4.42)	487 (0.21)	107/5,781	2.74
3fa	281 (4.46), 386 (4.55)	490 (0.74)	104/5,498	2.72
3bb	326 (4.15), 431 (4.64)	573 (0.60)	142/5,749	2.45
3bc	297 (4.41), 381 (4.72)	490 (0.47)	109/5,838	2.78

Compound	λ, nm (log ε)	Emission, nm (Φf)[a]	SS (nm/cm⁻¹)[b]	E₀₋₀ (eV)[c]
3bd	275 (4.32), 374 (4.24)	488 (0.32)	114/6,246	2.75
3be	282 (4.36), 423 (4.27)	488 (0.52)	65/3,148	2.77

		MeOH		

Compound	λ, nm (log ε)	Emission, nm (Φ_f)[a]	SS (nm/cm^{-1})[b]	E_{0-0} (eV)[c]
3aa	273 (4.35), 356 (4.23)	484 (0.72)	128/7,428	2.72
3ba	273 (4.27), 372 (4.37)	488 (0.83)	116/6,390	2.91
3ca	273 (4.65), 367 (4.58)	486 (0.84)	119/6,671	2.82
3da	275 (4.61), 369 (4.39)	490 (0.54)	121/6,692	2.79
3ea	280 (4.30), 371 (4.28)	486 (0.13)	115/6,378	2.91
3fa	276 (4.55), 382 (4.54)	487 (0.24)	105/5,644	2.77
3bb	273 (4.19), 427 (4.06)	492 (0.52)	65/3,094	2.82
3bc	272 (4.25), 371 (4.36)	499 (0.81)	128/6,914	2.81
3bd	274 (4.43), 371 (4.25)	483 (0.28)	112/6,250	2.82
3be	275 (4.51), 370 (4.32)	490 (0.58)	120/6,618	2.75

[a]Using 9,10-diphenylanthracene (DPA) as standard in $CHCl_3$ (Φ_f = 0.65; λ_{exc} = 366 nm); [b]SS = Stokes shifts: $\Delta\lambda = \lambda_{em} - \lambda_{abs}$; [c]$E_{0-0}$ = 1240/λ (eV).

Photostability and singlet oxygen quantum yield (Φ_Δ) assays

Dyes or photosensitizers must be stable under light illumination for long periods to be efficient. Thus, photostability behavior is an important assay considering the application in photo-processes since the photogenerated singlet oxygen species can react with the molecule, promoting its own degradation. From the small changes in the absorbance spectra as a function of the time, the Schiff base derivatives **3aa-3fa** and **3bb-3be** were confirmed to present good stability under white-LED irradiation

conditions (25 mW/cm^2 fluence rate and 90 J/cm^2 light dosage) in the 400-800 nm range for 60 min in DMSO solution (Figure 5).
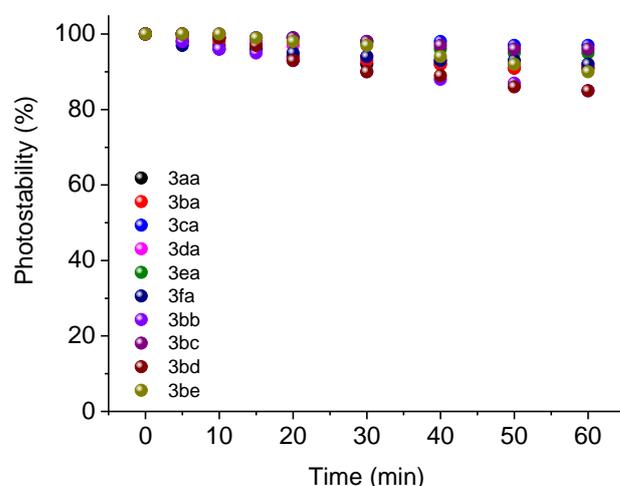

Figure 5. Graph of reduced photostability (%) of derivatives **3aa-3fa** and **3bb-3be** in DMSO solution after irradiation with white-light LED array system (400-800 nm) at a fluence rate of 25 mW/cm^2 for different periods (0 to 60 min; total light dosage = 90 J/cm^2).

The ability of the Schiff bases **3aa-3fa** and **3bb-3be** to produce singlet oxygen species ($^1O_2$) was determined in DMSO solution using a photochemical method based on 1,3-diphenylisobenzofuran (DPBF) photooxidation [32]. In this case, the methylene blue dye (MB) was used as a reference. In this study, the photooxidation rate constants (k) and singlet oxygen quantum yield of derivatives (Φ_Δ) were determined (Table 2). Some typical sets of spectra that monitor the kinetics of DPBF $^1O_2$ quencher photooxidation are shown in the *Supporting Information section* (Figures S15-S23).

In general, all compounds at 0.5 µM showed poor photo-oxidization against DPBF at 50 µM (e.g., **3bb**; Figure 6). Schiff bases were moderate generators of singlet oxygen species (Φ_Δ between 0.07-0.51) after 600 s of irradiation with a red-light diode laser source (λ = 660 nm, 100 mW).

The moderate singlet oxygen production may be attributed to the formation of other reactive oxygen species (e.g., hydroxyl and superoxide radical species) in DMSO solution that are not determined by this type of experiment. The good photostability and ability of Schiff base derivatives under light irradiation to generate $^1O_2$ allowed us to envisage them as potential sensitizers in photodynamic applications.
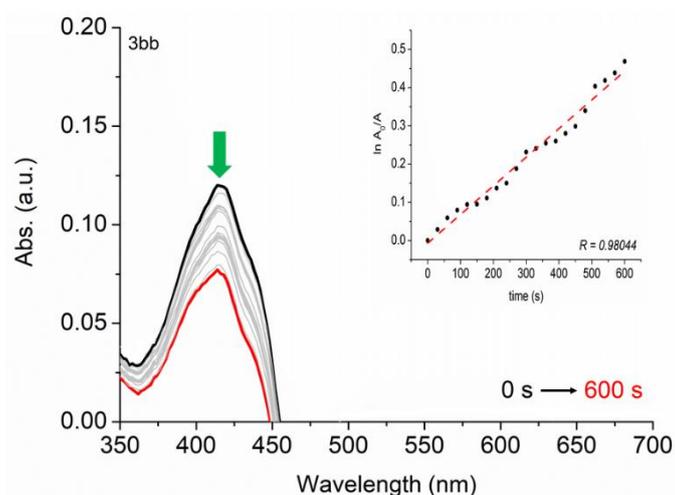

Figure 6. Photooxidation of DPBF by red-light irradiation with diode laser (λ = 660 nm) in the presence of quinoline **3bb** (R = Ph, R^1 = 5-NEt$_2$). The inset shows the first-order kinetic profile.

Table 2. Photooxidation rate constants and singlet oxygen quantum yield of compounds **3aa-3fa** and **3bb-3be** in DMSO solution.

Nr.	R	R^1	k (min^{-1})	Φ_Δ	Nr.	R	R^1	k (min^{-1})	Φ_Δ
3aa	Me	H	2.6×10^{-4}	0.19	**3bb**	Ph	5-NEt$_2$	7.0×10^{-4}	0.51
3ba	Ph	H	2.2×10^{-4}	0.16	**3bc**	Ph	5-OMe	2.5×10^{-4}	0.18
3ca	4-MeC$_6$H$_4$	H	1.0×10^{-4}	0.07	**3bd**	Ph	4-Br	1.6×10^{-4}	0.12
3da	4-FC$_6$H$_4$	H	5.4×10^{-4}	0.40	**3be**	Ph	4-NO$_2$	1.3×10^{-4}	0.09
3ea	4-NO$_2$C$_6$H$_4$	H	1.9×10^{-4}	0.14	**MB**[a]	-	-	7.7×10^{-4}	0.52

| 3fa | 2-Furyl | H | 2.3 x 10^{-4} | 0.17 | **RhB**[b] | - | - | 6.3 x 10^{-4} | 0.78 |

[a]MB = Methylene blue dye standard in ethanol solution (Φ_Δ = 0.52) [33]. [b]RhB = Rhodamine B dye in ethanol solution (Φ_Δ = 0.78) [34].

Conclusion

In conclusion, we reported the accessible synthesis and photophysical and antioxidant properties of a new series of ten novel Schiff Bases **3**. The scaffolds **3** could be synthesized by a simple condensation reaction between 6-aminoquinolines and salicylaldehydes and an easily purified methodology at yields of up to 91%. Photophysical experiments of derivatives exhibited common transitions in these heterocycle units and corroborated the aromatic structures and good fluorescence quantum yield values for all compounds. Additionally, good photostability and moderate *ROS* generation may be interesting features for applying these derivatives in photooxidation and photodamage reactions to biomolecules.

Experimental

General

Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers and without further purification.

^{1}H and ^{13}C NMR spectra were acquired on a Bruker DPX 400 MHz spectrometer for one-dimensional experiments and on a Bruker Avance III 600 MHz for ^{19}F NMR spectra and 2D-experiments (gHMBC). It was used 5 mm sample tubes, at 298 K, digital resolution of ±0.01 ppm, in CDCl$_3$, using TMS as the internal reference. All results are reported as follows: Chemical shift (δ) (multiplicity, integration, coupling constant). The

following abbreviations were used to explain multiplicities: s=singlet, d=doublet, t=triplet, q=quartet, qui=quintet, m=multiplet, dd=doublet of doublets. All NMR chemical shifts are reported in parts per million relatives to the internal reference. All melting points were determined using coverslips on a Microquímica MQAPF-302 apparatus. FT-IR spectra were recorded using the ATR sampling mode on a Bruker VERTEX 70 spectrophotometer with Platinum ATR accessory (diamond crystal) in the 4000–400 cm^{-1} region. High-resolution mass spectra (HRMS) were obtained for all compounds on a hybrid high-resolution and high-accuracy (5µL/L) micrOTOF-Q mass spectrometer (Bruker Scientific®□, Billerica, MA, USA) at (Caxias do Sul University – UCS, Brazil). All NMR and FT-IR spectra can be found in the *Supporting information section* (Figures S24 – S53).

Single crystals of compound **3ba** were obtained by slow evaporation of $CDCl_3$ at 25 °C. Diffraction measurement of compound **3ba** was performed using a Bruker D8 QUEST diffractometer using Cu Kα radiation (λ = 1.54178 Å) with a KAPPA four-circle goniometer equipped with a PHOTON II CPAD area detector, at a temperature of 296K.

For spectroscopic analysis, UV-Vis absorption spectra were recorded using a Shimadzu UV2600 spectrophotometer (2.0 nm data range), using DMSO, MeOH or chloroform as solvent. The steady-state emission fluorescence spectra in DMSO, MeOH or chloroform solutions were measured with a Cary50 Eclipse Fluorescence Spectrophotometer (excitation/emission; slit 2.5 mm). All spectra can be found at the *Supporting information section* (Figures S2 – S14).

Photostability assays were performed using white-light LED array system irradiation (visible range) at 25 mW/cm^2 and total light dosage 90 J/cm^2 at 60 min, according to the current literature. All experiments were performed in duplicate and independently.

In order to measure $^1O_2$ generation, UV-Vis spectra of the solutions (samples and standard) were recorded for different exposure times by using a 660 nm red diode laser positioned 2.0 cm from the sample (TheraLase DMC, São Carlos, SP, Brazil) with an average power of 100 mW, during 10 min (irradiation intervals every 30 s). All spectra can be accessed at *Supporting information section* (Figures S15 – S23).

Synthetic Procedure

General procedure for the preparation of Schiff bases (3aa-3af and 3bb-3be)

A mixture of the respective 6-amino-2-alkyl(aryl/heteroaryl)-4-(trifluoromethyl) quinolines (**1a-f**, 1.0 mmol) and the salicylaldehydes (**2a-e**, 2.0 mmol) in anhydrous acetonitrile (10.0 mL) was heated for 48 h at reflux temperature. After completing the reaction (TLC) and cooling the reactional mixture to room temperature, the solid was filtered under reduced pressure. The crude compounds **3** were purified by recrystallization from ethanol to provide the desired (*E*)-2-(((4-(trifluoromethyl)quinolin-6-yl)imino)methyl) phenols (**3**) in 20 – 91 % yield.

Spectral data

(*E*)-2-(((2-Methyl-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3aa**)

Yellow solid, yield 20 %, mp 129-132 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm): 12.98 (s, 1H, OH), 8.72 (s, 1H, CH=N), 8.15 (d, J = 8.9 Hz, 1H, H-8), 7.85 (p, J = 2.1 Hz, 1H, H-5), 7.74 (dd, J = 9.0, 2.3 Hz, 1H, H-7), 7.61 (s, 1H, H-3), 7.48 – 7.39 (m, 2H, C$_6$H$_4$OH), 7.09 – 7.03 (m, 1H, C$_6$H$_4$OH), 6.98 (td, J = 7.5, 1.1 Hz, 1H, C$_6$H$_4$OH), 2.82 (s, 3H, CH$_3$).

^{13}C NMR (100 MHz, CDCl$_3$) δ (ppm): 164.11 (CH=N), 161.18 (C$_6$H$_4$OH), 158.14 (C-2), 147.63 (C-8a), 147.20 (C-6), 134.40 (q, J = 31.6 Hz, C-4), 133.76 (C$_6$H$_4$OH), 132.67 (C$_6$H$_4$OH), 130.94 (C-8), 124.85 (C-7), 123.36 (q, J = 274.0 Hz, CF$_3$), 121.85 (C-4a),

119.64 (q, *J* = 5.3 Hz, C-3), 119.29 (C$_6$H$_4$OH), 119.01 (C$_6$H$_4$OH), 117.37 (C$_6$H$_4$OH), 114.75 (t, *J* = 2.2 Hz, C-5), 25.34 (CH$_3$).

^{19}F NMR (565 MHz, CDCl$_3$) *δ* (ppm): -61,71 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3061 (υOH), 1627 (υCH=N), 1118 (υC-O).

HRMS (M + H$^+$): Calc. for C$_{18}$H$_{14}$F$_3$N$_2$O: 331.1053. Found: 331.1037.

(*E*)-2-(((2-Phenyl-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3ba**)

Yellow solid, yield 90 %, mp 183-186 °C.

^{1}H NMR (600 MHz, CDCl$_3$) *δ* (ppm): 12.96 (s, 1H, OH), 8.71 (s, 1H, CH=N), 8.27 (d, *J* = 8.9 Hz, 1H, H-8), 8.20 – 8.14 (m, 3H, Ph, H-3), 7.87 (bs, 1H, H-5), 7.74 (dd, *J* = 8.8, 2.3 Hz, 1H, H-7), 7.54 (t, *J* = 7.3 Hz, 2H, Ph), 7.49 (t, *J* = 7.1 Hz, 1H, Ph), 7.45 – 7.38 (m, 2H, C$_6$H$_4$OH), 7.05 (d, *J* = 8.2 Hz, 1H, C$_6$H$_4$OH), 6.96 (t, *J* = 7.4 Hz, 1H, C$_6$H$_4$OH).

^{13}C NMR (151 MHz, CDCl$_3$) *δ* (ppm): 164.09 (CH=N), 161.23 (C$_6$H$_4$OH), 156.13 (C-2), 148.02 (C-8a), 147.58 (C-6), 138.09 (Ph), 134.80 (q, *J* = 31.6 Hz, C-4), 133.81 (C$_6$H$_4$OH), 132.71 (C$_6$H$_4$OH), 131.96 (C-8), 130.11 (Ph), 129.03 (Ph), 127.36 (Ph), 125.08 (C-7), 123.50 (q, *J* = 274.9 Hz, CF$_3$), 122.44 (C-C4a), 119.29 (C$_6$H$_4$OH), 119.01 (C$_6$H$_4$OH), 117.38 (C$_6$H$_4$OH), 116.48 (q, *J* = 5.1 Hz, C-3), 114.71 (C-5).

^{19}F NMR (565 MHz, CDCl$_3$) *δ* (ppm): -61.62 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3057 (υOH), 1625 (υCH=N), 1029 (υC-O).

HRMS (M + Na$^+$): Calc. for C$_{23}$H$_{15}$F$_3$N$_2$NaO: 415.1029. Found: 415.1007.

(*E*)-2-(((2-(p-Tolyl)-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3ca**)

Yellow solid, yield 81 %, mp 210-213 °C.

^{1}H NMR (600 MHz, CDCl$_3$) *δ* (ppm): 12.98 (s, 1H, OH), 8.72 (s, 1H, CH=N), 8.25 (d, *J* = 8.8 Hz, 2H, H-8), 8.15 (s, 1H, H-3), 8.09 (d, *J* = 7.82 Hz, 2H, 4-Tolyl), 7.86 (bs, 2H, H-5), 7.74 (d, *J* = 9.1 Hz, 2H, H-7), 7.46 – 7.40 (m, 2H, 4-Tolyl), 7.34 (d, *J* = 7.8 Hz,

2H, C$_6$H$_4$OH), 7.06 (d, J = 8.3 Hz, 1H, C$_6$H$_4$OH), 6.97 (t, J = 7.4 Hz, 2H, C$_6$H$_4$OH), 2.44 (s, 3H, H-CH$_3$).

^{13}C NMR (151 MHz, CDCl$_3$) δ (ppm): 164.04 (CH=N), 161.29 (C$_6$H$_4$OH), 156.18 (C-2), 148.10 (C-8a), 147.44 (C-6), 140.47 (4-CH$_3$-C$_6$H$_4$), 135.38 (4-Tolyl), 134.75 (q, J = 31.5 Hz, C-4), 133.82 (C$_6$H$_4$OH), 132.74 (C$_6$H$_4$OH), 131.92 (C-8), 129.83 (4-Tolyl), 127.30 (4-Tolyl), 125.04 (C-7), 123.59 (q, J = 274.7 Hz, CF$_3$), 122.37 (C-4a), 119.34 (C$_6$H$_4$OH), 119.10 (C$_6$H$_4$OH), 117.44 (C$_6$H$_4$OH), 116.40 (q, J = 7.3 Hz, C-3), 114.80 (C-5), 21.42 (4-$\underline{C}$H$_3$C$_6$H$_4$).

^{19}F NMR (565 MHz, CDCl$_3$) δ (ppm): -61.65 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3035 (υOH), 1621 (υCH=N), 1112 (υC-O).

HRMS (M + H$^+$): Calc. for C$_{24}$H$_{17}$F$_3$N$_2$O: 407.1366. Found: 407.1365.

(*E*)-2-(((2-(4-Fluorophenyl)-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3da**)

Yellow solid, yield 91%, mp 188-189 °C.

^{1}H NMR (600 MHz, CDCl$_3$) δ (ppm): 12.91 (s, 1H, OH), 8.74 (s, 1H, CH=N), 8.27 (d, J = 9.0 Hz, 1H, H-8), 8.23 – 8.18 (m, 2H, 4-FC$_6$H$_4$), 8.14 (S, 1H, H-3), 7.89 (p, J = 2.0 Hz, 1H, H-5), 7.76 (dd, J = 8.9, 2.3 Hz, 1H, H-7), 7.49 – 7.42 (m, 2H, 4-FC$_6$H$_4$), 7.29 – 7.21 (m, 2H, C$_6$H$_4$OH), 7.09 (dd, J = 8.3, 1.1 Hz, 1H, C$_6$H$_4$OH), 7.00 (td, J = 7.5, 1.1 Hz, 1H, C$_6$H$_4$OH).

^{13}C NMR (151 MHz, CDCl$_3$) δ (ppm): 164.25 (d, J = 250.8 Hz, 4-FC$_6$H$_4$), 164.13 (CH=N), 161.33 (C$_6$H$_4$OH), 154.97 (C-2), 148.03 (C-8a), 147.74 (C-6), 134.99 (q, J = 31.6 Hz, C-4), 134.31 (d, J = 3.6 Hz, 4-FC$_6$H$_4$), 133.86 (C$_6$H$_4$OH), 132.72 (C$_6$H$_4$OH), 131.92 (C-8), 129.32 (d, J = 8.7 Hz, 4-F-C$_6$H$_4$), 125.22 (C-7), 123.51 (q, J = 274.3 Hz, CF$_3$), 122.39 (C-4a), 119.31 (C$_6$H$_4$OH), 119.07 (C$_6$H$_4$OH), 117.44 (C$_6$H$_4$OH), 116.17 – 115.85 (m) (3, 4-FC$_6$H$_4$), 114.67 (d, J = 2.2 Hz, C-5).

^{19}F NMR (565 MHz, CDCl$_3$) δ (ppm): -61.67 (CF$_3$), -110.77 (4-$\underline{F}$C$_6$H$_4$).

FT-IR (ATR, υ (cm^{-1})): 3076 (υOH), 1629 (υCH=N), 1011 (υC-O).

HRMS (M + H$^+$): Calc. for $C_{23}H_{14}F_4N_2O$: 411.1115. Found: 411.1119.

(*E*)-2-(((2-(4-Nitrophenyl)-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3ea**)

Orange solid, yield 65 %, mp 223-226 °C.

^{1}H NMR (600 MHz, CDCl$_3$) *δ* (ppm): 12.85 (s, 1H, OH), 8.77 (s, 1H, CH=N), 8.41 (s, 4H, 4-NO$_2$C$_6$H$_4$), 8.34 (d, *J* = 8.7 Hz, 1H, H-8), 8.24 (s, 1H, H-3), 7.91 (s, 1H, H-5), 7.84 (dd, *J* = 8.9, 2.3 Hz, 1H, H-7), 7.53 – 7.41 (m, 2H, C$_6$H$_4$OH), 7.08 (d, *J* = 8.3 Hz, 1H, C$_6$H$_4$OH), 7.01 (t, *J* = 7.4 Hz, 1H, C$_6$H$_4$OH).

^{13}C NMR (100 MHz, CDCl$_3$) *δ* (ppm): 164.71 (CH=N), 161.29 (C$_6$H$_4$OH), 153.41 (C-2), 148.72 (d, *J* = 3.6 Hz, C-8a e C-6), 148.03 (4-NO$_2$C$_6$H$_4$), 143.81 (4-NO$_2$C$_6$H$_4$), 135.45 (q, *J* = 32.4 Hz, C-4), 134.14 (C$_6$H$_4$OH), 132.87 (C$_6$H$_4$OH), 132.30 (C-8), 128.23 (4-NO$_2$C$_6$H$_4$), 125.92 (C-7), 124.24 (4-NO$_2$C$_6$H$_4$), 123.31 (q, *J* = 275.0 Hz, CF$_3$), 123.08 (C-4a), 119.46 (C$_6$H$_4$OH), 118.96 (C$_6$H$_4$OH), 117.48 (C$_6$H$_4$OH), 116.33 (q, *J* = 5.2 Hz, C-3), 114.64 (C-5).

^{19}F NMR (565 MHz, CDCl$_3$) *δ* (ppm): -61.66 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3085 (υOH), 1625 (υCH=N), 1113 (υC-O).

HRMS (M + H$^+$): Calc. for $C_{23}H_{15}F_3N_3O_3$: 438.1060. Found: 438.1059.

(*E*)-2-(((2-(Furan-2-yl)-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3fa**)

Brown solid, yield 80 %, mp 205-209 °C.

^{1}H NMR (600 MHz, CDCl$_3$) *δ* (ppm): 12.95 (s, 1H, OH), 8.74 (s, 1H, CH=N), 8.23 (dd, *J* = 9.0, 0.5 Hz, 1H, H-8), 8.13 (d, *J* = 0.8 Hz, 1H, H-3), 7.85 (p, *J* = 2.0 Hz, 1H, H-5), 7.75 (dd, *J* = 9.0, 2.3 Hz, 1H, H-7), 7.66 (dd, ^3J = 1.7, ^4J = 0.8 Hz, 1H, H-5"Furyl), 7.49 – 7.39 (m, 2H, C$_6$H$_4$OH), 7.30 (dd, ^3J = 3.5, ^4J = 0.8 Hz, 1H, H-3"Furyl), 7.08 – 7.04

(m, 1H, C$_6$H$_4$OH), 6.98 (td, J = 7.5, 1.1 Hz, 1H, C$_6$H$_4$OH), 6.63 (dd, ^3J = 3.5, ^3J = 1.8 Hz, 1H, H-4"Furyl).

^{13}C NMR (151 MHz, CDCl$_3$) δ (ppm): 164.11 (CH=N), 161.28 (C$_6$H$_4$OH), 152.75 (C-2), 147.97 (d, J = 3.7 Hz, C-6, C-8a), 147.52 (Furyl), 144.82 (Furyl), 134.96 (t, J = 31.9 Hz, C-4), 133.88 (C$_6$H$_4$OH), 132.76 (C$_6$H$_4$OH), 131.58 (C-8), 125.31 (C-7), 123.37 (q, J = 275.0 Hz, CF$_3$), 122.38 (C-4a), 119.37 (C$_6$H$_4$OH), 119.08 (C$_6$H$_4$OH), 117.44 (C$_6$H$_4$OH), 115.40 (q, J = 5.6 Hz, C-3), 114.96 (d, J = 3.1 Hz, C-5), 112.67 (Furyl), 111.28 (Furyl). ^{19}F NMR (565 MHz, CDCl$_3$) δ (ppm): -61.82 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3066 (υOH), 1612 (υCH=N), 1121 (υC-O).

HRMS (M + H$^+$): Calc. for C$_{21}$H$_{13}$F$_3$N$_2$O$_2$: 383.1002. Found: 383.0997.

(*E*)-5-(Diethylamino)-2-(((2-phenyl-4-(trifluoromethyl)quinolin-6-yl)imino)methyl) phenol (**3bb**)

Orange solid, yield 40 %, mp 208-210 °C.

^{1}H NMR (600 MHz, CDCl$_3$) δ (ppm): 13.43 (s, 1H, OH), 8.53 (s, 1H, CH=N), 8.22 (d, J = 9.0 Hz, 1H, H-8), 8.18 (d, J = 7.4 Hz, 2H, Ph), 8.14 (s, 1H, H-3), 7.81 (p, J = 2.2 Hz, 1H, H-5), 7.72 (dd, J = 9.0, 2.3 Hz, 1H, H-7), 7.55 – 7.51 (m, 2H, Ph), 7.49 – 7.45 (m, 1H, Ph), 7.22 – 7.19 (m, 1H, 5-NEt$_2$-C$_6$H$_3$OH), 6.27 (dd, J = 8.8, 2.5 Hz, 1H, 5-NEt$_2$C$_6$H$_3$OH), 6.22 (d, J = 2.4 Hz, 1H, 5-NEt$_2$C$_6$H$_3$OH), 3.41 (q, J = 7.1 Hz, 4H, (N-(C$\underline{H}_2$CH$_3$)$_2$), 1.22 (t, J = 7.1 Hz, 6H, (N-(CH$_2$C$\underline{H}_3$)$_2$).

^{13}C NMR (151 MHz, CDCl$_3$) δ (ppm): 164.11 (CH=N), 161.79 (5-NEt$_2$C$_6$H$_3$OH), 155.33 (C-2), 152.43 (5-NEt$_2$C$_6$H$_3$OH), 148.59 (C-8a), 147.69 (C-6), 138.50 (Ph), 134.48 (q, J = 31.1 Hz, C-4), 134.26 (5-NEt$_2$C$_6$H$_3$OH), 131.74 (C-8), 129.83 (Ph), 128.98 (Ph), 127.33 (Ph), 125.69 (C-7), 123.75 (q, J = 274.7 Hz, CF$_3$), 122.81 (C-4a), 116.24 (q, J = 5.6, 5.2 Hz, C-3), 113.45 (C-5), 109.37 (5-NEt$_2$C$_6$H$_3$OH), 104.26 (5-NEt$_2$C$_6$H$_3$OH), 97.87 (5-NEt$_2$C$_6$H$_3$OH), 44.66 ((N-(C$\underline{H}_2$CH$_3$)$_2$), 12.72 (N-(CH$_2$C$\underline{H}_3$)$_2$).

^{19}F NMR (565 MHz, CDCl$_3$) δ (ppm): -61.73 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 2974 (υOH), 1638 (υCH=N), 1117 (υC-O).

HRMS (M + Na$^+$): Calc. for C$_{27}$H$_{24}$F$_3$N$_3$NaO: 486.1764. Found: 486.1727.

(*E*)-5-Methoxy-2-(((2-phenyl-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3bc**)

Orange solid, yield 75 %, mp 226-230 °C.

^{1}H NMR (600 MHz, CDCl$_3$) δ (ppm): 13.34 (s, 1H, OH), 8.64 (s, 1H, CH=N), 8.26 (d, *J* = 8.9 Hz, 1H, H-8), 8.23 – 8.11 (m, 3H, 2H, Ph, H-3), 7.85 (bs, 1H, H-5), 7.76 – 7.69 (m, 1H, H-7), 7.52 (dt, *J* = 14.2, 7.1 Hz, 3H, Ph), 7.33 (d, *J* = 8.4 Hz, 1H, 5-OCH$_3$C$_6$H$_3$OH), 6.53 (d, *J* = 8.8 Hz, 2H, 5-OCH$_3$C$_6$H$_3$OH), 3.86 (s, 3H, OCH$_3$).

^{13}C NMR (151 MHz, CDCl$_3$) δ (ppm): 164.70 (CH=N), 164.03 (5-OCH$_3$C$_6$H$_3$OH), 162.99 (5-OCH$_3$C$_6$H$_3$OH), 155.99 (C-2), 148.01 (d, *J* = 3.8 Hz, C-6, C-8a), 138.38 (Ph), 134.82 (d, *J* = 31.5 Hz, C-4), 134.05 (5-OCH$_3$C$_6$H$_3$OH), 132.01 (C-8), 130.05 (Ph), 129.05 (Ph), 127.42 (Ph), 125.35 (C-7), 123.69 (q, *J* = 274.7 Hz, CF$_3$), 122.68 (C-4a), 116.46 (q, *J* = 4.9 Hz, C-3), 114.26 (C-5), 113.23 (5-OCH$_3$C$_6$H$_3$OH), 107.60 (5-OCH$_3$C$_6$H$_3$OH), 101.28 (5-OCH$_3$C$_6$H$_3$OH), 55.52 (OCH$_3$).

^{19}F NMR (565 MHz, CDCl$_3$) δ (ppm): -61.74 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3016 (υOH), 1628 (υCH=N), 1000 (υC-O).

HRMS (M + H$^+$): Calc. for C$_{24}$H$_{17}$F$_3$N$_2$O$_2$: 423.1315. Found: 423.1284.

(*E*)-4-Bromo-2-(((2-phenyl-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3bd**)

Orange solid, yield 77 %, mp 194-196 °C.

^{1}H NMR (600 MHz, CDCl$_3$) δ (ppm): 12.86 (s, 1H, OH), 8.63 (s, 1H, CH=N), 8.27 (d, *J* = 9.0 Hz, 1H, H-8), 8.19 (d, *J* = 7.0 Hz, 3H, 2H Ph, H-3), 7.89 – 7.84 (m, 1H, H-5), 7.72

(dd, $J = 9.0, 2.3$ Hz, 1H, H-7), 7.57 – 7.44 (m, 5H, 3H, Ph, 2H, 4-BrC$_6$H$_3$OH), 6.94 (d, $J = 8.8$ Hz, 1H, 4-BrC$_6$H$_3$OH).

^{13}C NMR (151 MHz, CDCl$_3$) δ (ppm): 162.68 (CH=N), 160.34 (4-BrC$_6$H$_3$OH), 156.48 (C-2), 148.32 (C-8a), 147.18 (C-6), 138.15 (Ph), 136.39 (4-BrC$_6$H$_3$OH), 135.02 (q, $J = 31.5$ Hz, C-4), 134.64 (4-BrC$_6$H$_3$OH), 132.22 (C-8), 130.22 (Ph), 129.06 (Ph), 127.44 (Ph), 124.89 (C-7), 123.59 (q, $J = 274.3$ Hz, CF$_3$), 122.49 (C-4a), 120.49 (4-BrC$_6$H$_3$OH), 119.45 (4-BrC$_6$H$_3$OH), 116.60 (q, $J = 5.4$ Hz, C-3), 114.92 (d, $J = 2.4$ Hz, C-5), 110.80 (4-BrC$_6$H$_3$OH).

^{19}F NMR (565 MHz, CDCl$_3$) δ (ppm): -61.63 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3060 (υOH), 1602 (υCH=N), 1112 (υC-O).

HRMS (M + H$^+$): Calc. for C$_{23}$H$_{14}$BrF$_3$N$_2$O: 471.0314. Found: 471.0314.

(E)-4-Nitro-2-(((2-phenyl-4-(trifluoromethyl)quinolin-6-yl)imino)methyl)phenol (**3be**)

Orange solid, yield 89 %, mp 253-256 °C.

^{1}H NMR (600 MHz, CDCl$_3$) δ (ppm): 14.01 (s, 1H, OH), 8.85 (s, 1H, CH=N), 8.48 (d, $J = 2.7$ Hz, 1H, 4-NO$_2$C$_6$H$_3$OH), 8.35 (d, $J = 9.0$ Hz, 1H, H-8), 8.33 – 8.30 (m, 1H, 4-NO$_2$C$_6$H$_3$OH), 8.25 – 8.19 (m, 3H, H-3, Ph), 7.95 (bs, 1H, H-5), 7.81 (dd, $J = 8.9, 2.3$ Hz, 1H, H-7), 7.58 (t, $J = 7.3$ Hz, 2H, Ph), 7.53 (t, $J = 7.2$ Hz, 1H, Ph), 7.16 (d, $J = 9.1$ Hz, 1H, 4-NO$_2$C$_6$H$_3$OH).

^{13}C NMR (151 MHz, CDCl$_3$) δ (ppm): 166.49 (CH=N), 162.31 (4-NO$_2$C$_6$H$_3$OH), 156.92 (C-2), 148.46 (C-8a), 146.05 (C-6), 140.26 (4-NO$_2$C$_6$H$_3$OH), 137.97 (Ph), 135.14 (q, $J = 30.5$ Hz, C-4), 132.44 (C-8), 130.39 (Ph), 129.14 (Ph), 128.86 (4-NO$_2$C$_6$H$_3$OH), 128.74 (4-NO$_2$C$_6$H$_3$OH), 127.47 (Ph), 124.52 (C-7), 123.43 (q, $J = 274.9$ Hz, C-CF$_3$), 122.42 (C-4a), 118.45 (4-NO$_2$C$_6$H$_3$OH), 118.11 (4-NO$_2$C$_6$H$_3$OH), 116.86 (q, $J = 5.4$ Hz, C-3), 115.55 (C-5).

^{19}F NMR (565 MHz, CDCl$_3$) δ (ppm): -61.57 (CF$_3$).

FT-IR (ATR, υ (cm^{-1})): 3072 (υOH), 1602 (υCH=N), 1125 (υC-O).

HRMS (M + H$^+$): Calc. for C$_{23}$H$_{14}$F$_3$N$_3$O$_3$: 438.1060. Found: 438.1063.

Supporting Information

NMR spectra of the compounds, IR spectra, crystallographic data, photophysical and singlet oxygen spectra of new structures reported.

Supporting Information File 1:

File Name: Supporting Information

File Format: .pdf

Title: Photophysical, photostability, and *ROS* generation properties of new trifluoromethylated quinoline-phenol Schiff bases

Acknowledgements

References

(1)   Hameed, A.; al-Rashida, M.; Uroos, M.; Abid Ali, S.; Khan, K. M. *Expert Opin. Ther. Pat.* **2017**, *27* (1), 63–79. doi:10.1080/13543776.2017.1252752

(2)   Al Zoubi, W.; Al-Hamdani, A. A. S.; Kaseem, M. *Appl. Organomet. Chem.* **2016**, *30* (10), 810–817. doi:10.1002/aoc.3506

(3)   Lu, J.; Li, C.; Chai, Y. F.; Yang, D. Y.; Sun, C. R. *Bioorganic Med. Chem. Lett.* **2012**, *22* (17), 5744–5747. doi:10.1016/j.bmcl.2012.06.026

(4)   Hearn, M. J.; Cynamon, M. H.; Chen, M. F.; Coppins, R.; Davis, J.; Joo-On Kang, H.; Noble, A.; Tu-Sekine, B.; Terrot, M. S.; Trombino, D.; Thai, M.; Webster, E. R.; Wilson, R. *Eur. J. Med. Chem.* **2009**, *44* (10), 4169–4178. doi:10.1016/j.ejmech.2009.05.009

(5)   Shakeel, A. S.; Kalyane, N. V; Karjgi, S. R. *Water* **2010**, *1* (5), 246–249

(6)   Kumar, S.; M S, N.; K C, C.; C M, J.; Kadadevar, D. *J. Curr. Pharm. Res.* **2010**, *1*, 39–42

(7)   da Silva, C. M.; da Silva, D. L.; Martins, C. V. B.; de Resende, M. A.; Dias, E. S.; Magalhães, T. F. F.; Rodrigues, L. P.; Sabino, A. A.; Alves, R. B.; de Fátima, Â. *Chem. Biol. Drug Des.* **2011**, *78* (5), 810–815. doi:10.1111/j.1747-0285.2011.01185.x

(8)   Hazra, A.; Roy, A.; Mukherjee, A.; Maiti, G. P.; Roy, P. *Dalt. Trans.* **2018**, *47* (39), 13972–13989. doi:10.1039/c8dt02856g

(9)   Afzal, O.; Kumar, S.; Haider, M. R.; Ali, M. R.; Kumar, R.; Jaggi, M.; Bawa, S. *Eur. J. Med. Chem.* **2015**, *97* (1), 871–910. doi:10.1016/j.ejmech.2014.07.044

(10)   Otevrel, J.; Bobal, P.; Zadrazilova, I.; Govender, R.; Pesko, M.; Keltosova, S.; Koleckarova, P.; Marsalek, P.; Imramovsky, A.; Coffey, A.; O'Mahony, J.; Kollar, P.; Cizek, A.; Kralova, K.; Jampilek, J. *Molecules* **2013**, *18* (9), 10648–10670. doi:10.3390/molecules180910648

(11)   Raynes, K. J.; Stocks, P. A.; O'Neill, P. M.; Park, B. K.; Ward, S. A. *J. Med. Chem.* **1999**, *42* (15), 2747–2751. doi:10.1021/jm9901374

(12)   Nataša Perin, Lidija Uzelac, Ivo Piantanida, Grace Karminski-Zamola, M. K. and M. H. *Bioorg. Med. Chem.* **2011**, *19* (21), 6329–6339

(13)   Prajapati, S. M.; Patel, K. D.; Vekariya, R. H.; Panchal, S. N.; Patel, H. D. *RSC Adv.* **2014**, *4* (47), 24463–24476. doi:10.1039/c4ra01814a

(14)   Kappenberg, Y. G.; Ketzer, A.; Stefanello, F. S.; Salbego, P. R. S.; Acunha, T. V.; Abbadi, B. L.; Bizarro, C. V.; Basso, L. A.; Machado, P.; Martins, M. A. P.; Zanatta, N.; Iglesias, B. A.; Bonacorso, H. G. *New J. Chem.* **2019**, *43* (31), 12375–12384. doi:10.1039/c9nj01681c

(15)   dos Santos, G. C.; Servilha, R. O.; de Oliveira, E. F.; Lavarda, F. C.; Ximenes, V. F.; da Silva-Filho, L. C. *J. Fluoresc.* **2017**, *27* (5), 1709–1720. doi:10.1007/s10895-017-2108-0

(16)   Uchacz, T.; Szlachcic, P.; Wojtasik, K.; Mac, M.; Stadnicka, K. *Dye. Pigment.* **2016**, *124* (October 2017), 277–292. doi:10.1016/j.dyepig.2015.09.016

(17)   Park, B. K.; Kitteringham, N. R.; O'Neill, P. M. *Annu. Rev. Pharmacol. Toxicol.* **2001**, *41*, 443–470

(18)   Smart, B. E. *J. Fluor. Chem.* **2001**, *109* (1), 3–11. doi:10.1016/S0022-1139(01)00375-X

(19)   Liang, X.; Han, H. B.; Yan, Z. P.; Liu, L.; Zheng, Y. X.; Meng, H.; Huang, W. *New J. Chem.* **2018**, *42* (6), 4317–4323. doi:10.1039/c7nj04482h

(20)   Zhu, Y. C.; Zhou, L.; Li, H. Y.; Xu, Q. L.; Teng, M. Y.; Zheng, Y. X.; Zuo, J. L.; Zhang, H. J.; You, X. Z. *Adv. Mater.* **2011**, *23* (35), 4041–4046. doi:10.1002/adma.201101792

(21)   Mei, L.; Hu, J.; Cao, X.; Wang, F.; Zheng, C.; Tao, Y.; Zhang, X.; Huang, W. *Chem. Commun.* **2015**, *51* (65), 13024–13027. doi:10.1039/c5cc04126k

(22)   Mermer, A.; Demirbas, N.; Uslu, H.; Demirbas, A.; Ceylan, S.; Sirin, Y. *J. Mol. Struct.* **2019**, *1181*, 412–422. doi:10.1016/j.molstruc.2018.12.114

(23)   Petrović, Z. D.; Orović, J.; Simijonović, D.; Petrović, V. P.; Marković, Z. *RSC Adv.* **2015**, *5* (31), 24094–24100. doi:10.1039/c5ra02134k

(24)   Corona-López, María M. Pérez, Víctor M. Jiménez Chan-Navarro, Rodrigo Ibarra-Rodríguez, Marisol Dias, H. V. R.; Chávez-Reyes, Arturo Muñoz-Flores, B. M. *J. Organomet. Chem.* **2017**, *1*, 64–73. doi:https://doi.org/10.1016/j.jorganchem.2017.10.003

(25)   Ibrahim, M. N.; Sharif, S. E. A. *E-Journal Chem.* **2007**, *4* (4), 531–535. doi.org/101155/2007/191805

(26)   Fu, S.; Wang, L.; Dong, H.; Yu, J.; Xu, L.; Xiao, J. Tetrahedron Lett. 2016, 57, 4533-4537. doi:10.1016/j.tetlet.2016.08.065

(27)   Temel, B. A.; Kurt, B. Z.; Akar, I.; Keklik, M. *J. Photochem. Photobiol. A Chem.* **2020**, *400*, 112715. doi:10.1016/j.jphotochem.2020.112715

(28)   Bonacorso, H. G.; Calheiro, T. P.; Iglesias, B. A.; Berni, I. R. C.; da Silva Júnior, E. N.; Rocha, J. B. T.; Zanatta, N.; Martins, M. A. P. *Tetrahedron Lett.* **2016**, *57* (46), 5017–5021. doi:10.1016/j.tetlet.2016.09.068

(29)   Bonacorso, H. G.; Calheiro, T. P.; Iglesias, B. A.; Acunha, T. V.; Franceschini, S. Z.; Ketzer, A.; Meyer, A. R.; Rodrigues, L. V.; Nogara, P. A.; Rocha, J. B. T.; Zanatta, N.; Martins, M. A. P. *New J. Chem.* **2018**, *42* (3), 1913–1920. doi:10.1039/c7nj04032f

(30)   Bonacorso, H. G.; Calheiro, T. P.; Acunha, T. V.; Iglesias, B. A.; Franceschini, S. Z.; Ketzer, A.; Meyer, A. R.; Nogara, P. A.; Rocha, J. B. T.; Zanatta, N.; Martins, M. A. P. *Dye. Pigment.* **2019**, *161* (October 2018), 396–402. doi:10.1016/j.dyepig.2018.09.076

(31)   Santos, F. S.; Ramasamy, E.; Ramamurthy, V.; Rodembusch, F. S. *J. Mater. Chem. C* **2016**, *4* (14), 2820–2827. doi:10.1039/c5tc03245h

(32)   Pivetta, R. C.; Auras, B. L.; Souza, B. de; Neves, A.; Nunes, F. S.; Cocca, L. H. Z.; Boni, L. De; Iglesias, B. A. *J. Photochem. Photobiol. A Chem.* **2017**, *332*, 306–315. doi:10.1016/j.jphotochem.2016.09.008

(33)   Tanielian, C.; Golder, L.; Wolff, C. *J. Photochem.* **1984**, *25* (2–4), 117–125. doi:10.1016/0047-2670(84)87016-1

(34)   Gollnick, K.; Franken, T.; Fouda, M. F. R.; Paur, H. R.; Held, S. *J. Photochem. Photobiol. B Biol.* **1992**, *12* (1), 57–81. doi:10.1016/1011-1344(92)85018-P