#### Journal of Molecular Structure 1068 (2014) 1-7



Contents lists available at ScienceDirect

### Journal of Molecular Structure

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

# Spectral and structural characterization of 2-(fluorophenylamino)- and 2-(nitrophenylamino)-1,4-naphthoquinone derivatives





Elisa Leyva<sup>b</sup>, Sarah J. Schmidtke Sobeck<sup>a,\*</sup>, Silvia E. Loredo-Carrillo<sup>b</sup>, Diego A. Magaldi-Lara<sup>b</sup>

<sup>a</sup> College of Wooster, Department of Chemistry, 943 College Mall, Wooster, OH, USA <sup>b</sup> Facultad de Ciencias Químicas, Universidad Autónoma de San Luis Potosí, Nava 6, San Luis Potosí, SLP 78290, Mexico

#### HIGHLIGHTS

#### G R A P H I C A L A B S T R A C T

• Novel 2-(nitrophenylamino)-1,4naphthoquinones derivatives were synthesized and characterized.

• Solvent impact on absorbance and emission napthoquinone derivatives is assessed.

- The charge transfer transition is most sensitive to solvent and substituents.
- Quantum calculations confirm the spectral assignments and substituent effects.

#### ARTICLE INFO

Article history: Received 28 September 2013 Received in revised form 20 March 2014 Accepted 21 March 2014 Available online 28 March 2014

Keywords: Solvatochromism Electronic spectroscopy Quantum structure calculations Naphthoquinones



#### ABSTRACT

Naphthoquinone amino derivatives exhibit interesting physicochemical properties and are of interest for potential medicinal purposes. The preparation of novel 2-(nitrophenylamino)-1,4-naphthoquinones derivatives was achieved by reaction of nitroanilines with 1,4-naphthoquinone with a catalytic amount of FeCl<sub>3</sub> or by direct nitration of 2-(phenylamino)-1,4-naphthoquinone (PAN). Structural and photophysical properties of a series of NO<sub>2</sub>PANs and FPANs derivatives are examined using computational and spectroscopic methods. Absorbance and emission spectra are measured in a range of solvent environments to examine the impact of solvent-solute interactions. Additionally quantum calculations are used to evaluate the electronic nature of the spectral transitions and compare structures of the different PAN derivatives. The lowest energy electronic transitions have charge transfer character, and show the most sensitivity to solvent and substituents. Higher energy  $\pi - \pi^*$  transitions are relatively insensitive to both factors. Computational predictions are in good agreement with the experimental spectra, and provide molecular-level insight variations amongst the different aniline-substituents.

A series of novel 2-(nitrophenylamino)-1,4-naphthoquinones derivatives was synthesized, and their

photophysical properties examined using computational and spectroscopic methods.

© 2014 Elsevier B.V. All rights reserved.

#### Introduction

\* Corresponding author. Tel.: +1 330 263 2359; fax: +1 330 263 2386. *E-mail address:* ssobeck@wooster.edu (SJ. Schmidtke Sobeck). Naphthoquinones are a class of molecules that are naturally occurring chromatic pigments in plants, fungi and some animals, and exhibit potentially useful medicinal properties [1]. They have a wide range of biological properties such as significant antimicrobial activity [2]; for example, several plant-derived derivatives have antibacterial effects on some species of aerobic and anaerobic organisms [1]. Antiparasitic [3] and antifungal properties, particularly against species of *Candida*, of naphthoquinones have also been reported [4–7]. Of great potential interest for this type of compounds is their use as anticancer agents with applications in chemotherapy [8].

The biological activity of quinones has been related to their redox properties [9–11] and their capacity to accept one or two electrons to form the corresponding radical-anion (Q<sup>•</sup>) and hydroquinone radical dianion ( $Q^{2-}$ ). This capacity and several physicochemical properties of a given quinone can be modified by the addition of a substituted aniline to the quinone system [12]. The electron donating or withdrawing properties, there-by modifying the ability of the system to exhibit a charge transfer from the substituent to the quinone upon photo-excitation [13].

Several studies of these molecular systems have been reported, and the nature of the electronic spectrum of 1,4-naphthoquinone has been widely investigated [14]. UV–Vis electronic absorption spectra of PAN derivatives show the  $\pi$ – $\pi$ \* electron transitions bands associated with benzene and naphthoquinone in the regions around 203–211 nm and 265–273 nm. A weak n– $\pi$ \* transition band is observed at 310–330 nm. A broad, low energy band can be observed in the visible region centered between 438 and 480 nm for some naphthoquinone derivatives [15]. This latter absorption is quite common for amino-substituted quinones and has been previously assigned to have character corresponding to a charge-transfer (CT) transition and weak n– $\pi$ \* electron transitions of the carbonyl group in the quinone [16].

The impact of solvent environment upon spectral transitions can be used to gain a better understanding about the nature of the electronic states, and types of interactions between solvent and solute. Furthermore, it is interesting to examine the effect of a wide range of solvents varying in properties such as solvent polarity and hydrogen-bonding ability, where the solvent can be proton donor or acceptor [17–19]. Comparison of the solvatochromic behavior of a series of naphthoquinone derivatives provides insight into the specific interactions of different substituents with the solvent and the impact the substituent has upon photo-physical properties of the system. Along with absorbance spectroscopy, fluorescence has proven to be a versatile tool for studying molecular interactions, and can be used to provide a greater understanding about the excited state properties [20].

Theoretical studies are very useful for spectral interpretation and to gain a molecular level understanding about the nature of electronic and structural properties [14]. Interactions between solute and solvent like hydrogen bonding, solvent–solute complexation, changes in the electronic charge distribution and excited-state reactions are important to understand when interpreting spectral events [19,21].

We synthesized several novel NO<sub>2</sub>PAN derivatives and were interested in comparing their physicochemical properties with the FPAN derivatives previously synthesized [15]. We present a combination of spectroscopic and computational analysis of a series shown in Fig. 1 and Table 1. Spectral properties in a wide range of solvents were examined to understand the nature of molecular excited states and the effect of different solvents on solute–solvent interactions. Both absorbance and emission spectroscopy are presented, in combination with computational studies, to gain a greater understanding of the nature of the spectral transitions. A fundamental understanding about the molecular nature of some physicochemical properties of the naphthoquinone derivatives as a function of solvent and substituent provide a basic knowledge



**Fig. 1.** Structure of PAN derivatives, where  $R_n$  are substituents, where the number indicates the position and n = H, F, NO<sub>2</sub>, or OCH<sub>3</sub>. The dihedral angles and bond distances of interest are labeled.

Tabl	e 1		
PAN	derivatives	under	investigation.

Compound	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	m.p. (°C)
PAN <sup>a</sup>	Н	Н	Н	Н	188–189 <sup>20</sup>
2FPAN	F	Н	Н	Н	155-156 <sup>13</sup>
3FPAN	Н	F	Н	Н	200-201 <sup>13</sup>
4FPAN	Н	Н	F	Н	244-245 <sup>13</sup>
23FPAN	F	F	Н	Н	154-155 <sup>13</sup>
24FPAN	F	Н	F	Н	205-206 <sup>13</sup>
25FPAN	F	Н	Н	F	190–191 <sup>13</sup>
34FPAN	Н	F	F	Н	260-261 <sup>13</sup>
35FPAN	Н	F	F	Н	261-262 <sup>13</sup>
245FPAN	Н	Н	F	F	202-203 <sup>13</sup>
2NO <sub>2</sub> PAN <sup>b</sup>	$NO_2$	Н	Н	Н	205-207
4NO <sub>2</sub> PAN	Н	Н	$NO_2$	Н	337-339 <sup>21</sup>
2,4NO <sub>2</sub> PAN <sup>b</sup>	$NO_2$	Н	$NO_2$	Н	264-266
4F2NO <sub>2</sub> PAN <sup>b</sup>	$NO_2$	Н	F	Н	246-248
20MePAN <sup>a</sup>	Ome	Н	Н	Н	147-148 <sup>20</sup>
40MePAN <sup>a</sup>	Н	Н	OMe	Н	154–155 <sup>20</sup>

<sup>a</sup> These compounds were prepared for comparison.

<sup>b</sup> These compounds have not been previously described.

to exploit potentially useful applications of this family of compounds.

#### Experimental

#### Spectral studies

#### Sample preparation

Solutions  $(2 \times 10^{-4} \text{ M})$  were made in five solvents: acetonitrile (Pharmco-AAPer, 99.9% pure), dichloromethane (Pharmco-AAPer, 99.5%), hexane (Pharmco-AAPer, 99% pure), methanol (Pharmco-AAper, 100% pure) and 1-propanol (Sigma–Aldrich, 99.9%). Stock solutions were diluted to ensure the maximum absorbance in the UV region was between 0.1 and 1. For fluorescence measurements solutions were diluted such that the absorbance maximum at the lowest energy absorbance band was between 0.1 and 0.2.

#### UV-Vis absorbance measurements

UV–Vis spectra were obtained at room temperature on a Varian Cary 50 Bio Spectrophotometer. Spectra were corrected for solvent background by calibrating the instrument to the blank solvent. Spectra were taken in the range of 200–600 nm at a scan rate of 600 nm/min using the dual beam mode.

#### Fluorescence measurements

The emission spectra were obtained using a Varian Cary Eclipse fluorescence spectrophotometer. Samples were excited at the lowest energy absorbance, as determined by the UV–Vis measurement. The PMT setting was adjusted to achieve sufficient signal to noise ratio, typically at 1000 V. The scans were run at 600 nm/min. For all scans a sample of just the solvent was measured at the same excitation wavelength, PMT setting and scan speed. The background signal from the neat solvent was sub-tracted from the sample prior to analysis.

#### Computational detail

The PAN derivatives were optimized using Gaussian 09 [22]. The optimizations were performed using DFT calculations at the B3LYP level of theory [23–25] with the Midi! basis set [26]. Frequency calculations were performed to verify the nature of the stationary points.

Excitation energy calculations were conducted for each molecule in the gas and solution phase, smd solvent model for acetonitrile, using their respective optimized structures. The first ten singlet excitations were also calculated using the TD-B3LYP/6-31+G(d) method. For comparison excitation energy calculations were also conducted using semiempirical ZINDO methods in the gas phase. The excitations for the first ten singlet transitions were calculated. For comparison, all excitation energy calculations were carried out using Gaussian 09 [22] and spectra visualized using the Gaussview 5 interface [27].

#### Characterization methods

Melting points were measured with a Fisher Johns apparatus. UV–Vis spectra were obtained on a Shimadzu UV-2401 PC spectrophotometer. IR spectra were recorded on a Nicolet IS10 Thermo Scientific FTIR spectrophotometer. NMR spectra were obtained on a Varian Mercury 400 MHz spectrometer. Mass spectra were recorded on a Finnigan MAT 8200.

#### Synthetic procedures

Preparation of 2-(*R*-phenylamino)-1,4-naphthoquinones by method A PAN derivatives were prepared by the method previously reported with some modifications [15]. 1,4-Naphthoquinone (1 mmol) was dissolved in ethanol (30 mL). A solution of a given aniline (1 mmol) in ethanol (30 mL) was slowly added and the reaction mixture was refluxed for 7 days. The reaction vessel was equipped with a condenser to minimize ethanol losses during the experiment. The solution turned deep red or orange-yellow when the corresponding 2-(R-phenylamino)-1,4-naphthoquinone was formed. The resulting solid was filtered, washed with cold etanol and recrystallized in ethanol.

Preparation of 2-(R-phenylamino)-1,4-naphthoquinones by method B

PAN derivatives were also prepared by the method previously reported with some minor modifications [15,28]. 1,4-Naphthoquinone (1 mmol) was dissolved in ethanol (10 mL) and an amount (0.1 mmol) of the Lewis acid catalyst (FeCl<sub>3</sub> or CeCl<sub>3</sub>·7H<sub>2</sub>O) was added. The reaction mixture was stirred for 15 min to allow the reaction between the Lewis base (1,4-naphthoquinone) and the Lewis acid catalyst. A solution of a given aniline (1 mmol) in ethanol (10 mL) was slowly added and the mixture was refluxed for four hours. The reaction vessel was equipped with a condenser to minimize ethanol losses during the experiment. The solution turned deep red or orange-yellow when the corresponding 2-(R-phenylamino)-1,4-naphthoquinone was formed. The resulting solid was filtered, washed with cold ethanol and recrystallized from ethanol.

#### Preparation of 2-(2,4-dinitrophenylamino)-1,4-naphthoquinone

This derivative was prepared by the method previously reported with some modifications [29]. A mixture of concentrated acids  $HNO_3$  (7 mL) and  $H_2SO_4$  (1.5 mL) was prepared and PAN (0.9 mmol) was added. The reaction mixture was stirred for four hours at room temperature. A volume (100 mL) of cold water (100 mL) was added to induce precipitation. The resulting solid was filtered and washed with NaHCO<sub>3</sub> (5%), distilled water and cold ethanol. The product was purified by chromatography.

#### Purification and elemental analysis

To obtain analytical samples some products were recrystallized several times in ethanol or CHCl<sub>3</sub>. Other products were passed through a small silica column using CHCl<sub>3</sub> as the eluent solvent. Elemental analyses (Table 2) were performed in the laboratories of the Universidad Nacional Autonoma de Mexico or Universidad Autonoma Metropolitana.

#### Characterization of 2-(2-nitrophenylamino)-1,4-naphthoquinone

It was obtained as an orange solid with m.p.  $205-207 \,^{\circ}$ C; IR (KBr, cm<sup>-1</sup>) 3304 (NH), 1671, 1641 (C=O), 1500, 1337 (NO<sub>2</sub>), 1576 (N-H aromatic), 1278 (C-N aromatic); UV-Vis (CH<sub>3</sub>OH, nm) 275, 343, 450; <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  (ppm): 9.74 (1H, bs, N-H), 8.21 (1H, dd, *J* = 8.2, 1.17 Hz, aromatic H), 8.1 (1H, dd, *J* = 8.1, 1.17 Hz, aromatic H), 7.99 (1H, dd, *J* = 7.8, 1.17 Hz, aromatic H), 7.91 (1H, td, *J* = 7.42, 1.17 Hz, aromatic H), 7.84 (1H, td, *J* = 7.42, 1.17 Hz, aromatic H), 7.83 (1H, dd, *J* = 7.42, 1.17 Hz, aromatic H) 7.81 (1H, td, *J* = 8.2, 1.17 Hz), 7.45 (1H, td, *J* = 8.2, 1.17 Hz), 6.26 (1H, s, vinyl H); HRMS calcd for C<sub>16</sub>H<sub>10</sub>N<sub>2</sub>O<sub>4</sub> was 294.0641, found 294.0635.

#### Characterization of 2-(4-nitrophenylamino)-1,4-naphthoquinone

It was obtained as a red solid with m.p. 337-339 °C; IR (KBr, cm<sup>-1</sup>) 3185 (NH), 1671, 1641 (C=O), 1497, 1330 (NO<sub>2</sub>), 1570 (N-H aromatic), 1290 (C-N aromatic); UV-Vis (CH<sub>3</sub>OH, nm) 265, 338, 450; <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  (ppm): 9.56 (1H, bs, NH), 8.33 (1H, dd, *J* = 8.20, 1.37 Hz, aromatic H), 8.17 (1H, dd, *J* = 8.5, 1.47 Hz, aromatic H), 7.89 (1H, td, *J* = 7.03, 1.17 Hz, aromatic H), 7.83 (1H, td, *J* = 7.03, 1.17 Hz, aromatic H), 7.83 (1H, td, *J* = 7.03, 1.17 Hz, aromatic H), 7.89 Hz, aromatic H), 7.22 (2H, d, *J* = 8.59 Hz, aromatic), 6.53 (1H, s, vinyl H); HRMS calcd for C<sub>16</sub>H<sub>10</sub>N<sub>2</sub>O<sub>4</sub> was 294.0641, found 294.0631.

Table 2	
Elemental analyses of PAN derivatives.	

Compound	C(% T) <sup>a</sup>	C(% E) <sup>b</sup>	N(%T) <sup>a</sup>	N(%E) <sup>b</sup>	H(%T) <sup>a</sup>	H (%E) <sup>b</sup>
PAN	77.10	76.96	5.43	5.62	4.45	4.34
2FPAN	71.91	71.88	5.24	5.20	3.77	3.72
3FPAN	71.91	72.09	5.24	5.18	3.77	3.78
4FPAN	71.91	71.85	5.24	5.15	3.77	3.69
23FPAN	67.37	67.12	4.91	4.83	3.18	3.10
24FPAN	67.37	67.15	4.91	4.89	3.18	3.16
25FPAN	67.37	67.22	4.91	4.85	3.18	3.11
34FPAN	67.37	67.13	4.91	4.78	3.18	3.03
35FPAN	67.37	67.19	4.91	4.91	3.18	3.15
245FPAN	63.37	63.13	4.62	4.53	2.66	2.63
2NO <sub>2</sub> PAN	65.31	65.17	9.52	9.40	3.43	3.43
4NO <sub>2</sub> PAN	65.31	64.96	9.52	9.40	3.43	3.49
2,4NO <sub>2</sub> PAN	56.65	56.34	12.39	12.31	2.67	2.47
4F2NO <sub>2</sub> PAN	61.54	61.25	8.97	8.80	2.91	3.14
20MePAN	73.11	72.91	5.02	4.85	4.69	4.75
40MePAN	73.11	73.17	5.02	4.91	4.69	4.91

<sup>a</sup> Calculated value.

<sup>b</sup> Observed value.

#### Characterization of 2-(2, 4-dinitrophenylamino)-1,4-naphthoquinone

It was obtained as an orange solid with m.p. 264–266 °C; IR (KBr, cm<sup>-1</sup>) 3276 (NH), 1689, 1672 (C=O), 1500, 1339 (NO<sub>2</sub>), 1583 (N–H aromatic), 1278 (C–N aromatic); UV–Vis (CH<sub>3</sub>OH, nm) 265, 315, 448; NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  (ppm): 9.04 (1H, bs, NH), 8.56 (1H, d, J = 2.7 Hz, aromatic H), 8.23 (1H, dd, J = 9.1, 2.7 Hz, aromatic H) 8.22 (1H, dd, J = 8.8, 2.7 Hz, aromatic H), 8.15 (1H, td, J = 7.52, 1.17 Hz, aromatic H), 7.92 (1H, td, J = 8.78, 2.7 Hz, aromatic H), 7.88 (1H, dd, J = 8.78, 2.5 Hz, aromatic H), 7.82 (1H, td, J = 7.52, 1.27 Hz), 6.88 (1H, s, vinyl H); HRMS calcd for C<sub>16</sub>H<sub>9</sub>N<sub>3</sub>O<sub>6</sub> was 339.0491, found 339.0485.

## Characterization of 2-(4-fluoro-2-nitrophenylamino)-1, 4-naphthoquinone

It was obtained as an orange solid with m.p. 246–248 °C; IR (KBr, cm<sup>-1</sup>) 3207 (NH), 1677, 1650 (C=O), 1523, 1336 (NO<sub>2</sub>), 1584 (N–H aromatic), 1250 (C–N aromatic), 1112 (C–F); UV–Vis (CH<sub>3</sub>OH, nm) 265, 310, 450; NMR (400 MHz, DMSO-d<sub>6</sub>)  $\delta$  (ppm): 9.81 (1H, bs, NH), 8.23 (1H, d, *J*<sub>ortho</sub> <sub>H-F</sub> = 10.44 Hz, aromatic H), 8.02 (1H, dd, *J* = 9.4, 2.7 Hz, aromatic H), 8.00 (1H, dd, *J* = 9.4, 2.7 Hz, aromatic H), 8.00 (1H, dd, *J* = 9.4, 2.7 Hz, aromatic H), 7.80 (1H, d, *J*<sub>orthoHF</sub> = 9.68 Hz, aromatic H), 7.79 (1H, td, *J* = 7.53, 1.56 Hz), 7.72 (1H, d, *J*<sub>metaHF</sub> = 6.76), 6.36 (1H, s, vinyl H); HRMS calcd for C<sub>16</sub>H<sub>9</sub>N<sub>2</sub>O<sub>4</sub> was 312.0546, found 312.0540.

#### **Results and discussion**

#### Synthesis and reaction pathway

The reaction of anilines with 1,4-naphthoquinone to give 2-(phenylamino)-1,4-naphthoquinones has been known for several years [15]. It is an example of a  $C(sp^2)$ —H bond transformation to  $C(sp^2)$ —N bond via an addition-oxidation reaction sequence [30]. The mechanism for this coupling reaction (Scheme 1) involves a Michael 1,4-addition to give an intermediate which easily tautomerizes and gets oxidized to give the corresponding derivative [15]. However, due to the physicochemical properties of 1,4-naphthoquinone, several compounds are actually produced. In addition, substitution with deactivating groups, such as a nitro-group, yield decreased or no reactivity [31]. In some cases, performing this reaction without an adequate catalyst results in the formation of complex mixtures or no reaction at all.

Recently, some of us have demonstrated that the use of an oxidation agent and a Lewis acid such as CeCl<sub>3</sub> or FeCl<sub>3</sub> results in a cleaner reaction between a fluoroaniline and 1,4-naphthoquinone with better yields [15,28]. However, since o-nitroaniline derivatives have



Scheme 1. Mechanism for oxidative coupling of anilines with 1,4-naphthoquinone.

#### Table 3

Reaction conditions and yields of NO<sub>2</sub>PANs by oxidative-addition reaction.

Compound	Yield (%) <sup>a</sup>	Yield (%) <sup>b</sup>	Yield (%) <sup>c</sup>
PAN <sup>d</sup>	60	85	78
2NO <sub>2</sub> PAN	-	-	35
4NO <sub>2</sub> PAN	traces	55	55
2,4NO <sub>2</sub> PAN <sup>e</sup>	-	-	-
4F2NO <sub>2</sub> PAN	-	-	35
20MePAN <sup>d</sup>	60	70	75
40MePAN <sup>d</sup>	60	85	82

<sup>a</sup> Without catalyst and 7 days.

<sup>b</sup> With catalyst CeCl<sub>3</sub> 7H<sub>2</sub>O and 4 h.

<sup>c</sup> With catalyst FeCl<sub>3</sub> and 4 h.

<sup>d</sup> These compounds were prepared for comparison.

<sup>e</sup> This compound was prepared by nitration with HNO<sub>3</sub>/H<sub>2</sub>SO<sub>4</sub>.

not been previously reported we decided to investigate their preparation. Reacting 1,4-naphthoquinone with an *o*-nitroaniline with a catalytic amount of FeCl<sub>3</sub> resulted in the formation of moderate amounts of adducts (Table 3). Comparing the results, it is clear that nitro-substituted anilines are generally very weak bases and do not react very easily with naphthoquinone. In the case of *o*-nitroanilines, they are sterically hindered due to the presence of a large substituent next to the aniline. Therefore, in this particular reaction the size of the catalyst is very important, a smaller size catalyst [32] like FeCl<sub>3</sub> works better than CeCl<sub>3</sub>. The effect of the catalyst on this addition-oxidation reaction has been previously explained [15,28]. First, it induces the exclusive 1,4-Michael addition and then it favors oxidation to obtain naphthoquinone derivatives (Scheme 1).

#### Electronic spectroscopy

The absorbance spectra for the FPAN derivatives have been previously reported in methanol and assignments were made on the character of the transitions observed [15]. For consistency, the transitions are labeled using the same notation. Table 4 summarizes the lowest energy absorbance bands observed, characterized as the CT +  $n-\pi^*$  ( $\lambda_4$ ) and  $\pi-\pi^*$  ( $\lambda_2$ ) transitions. The absorbance energies are reported in methanol and hexanes, the two most divergent solvents studied.

The high energy  $\pi$ - $\pi^*$  absorbance band shows minimal solvatochromic shifts and solvent-solute interactions would not be anticipated to have a great impact upon the relative stability of these states. The lowest energy band, centered about 435–480 nm, does show sensitivity to the solvent environment. This band was

Table 4					
Summary	of absorbance	maxima	for the	PAN	derivatives.

Compound	$\lambda_2 \max (nm) \pi - \pi^*$		$\lambda_4 \max (nm)$ CT + n- $\pi^*$	
	MeOH	Hexanes	MeOH	Hexanes
PAN	273	269	466	450
2FPAN	269	270	448	442
3FPAN	273	269	459	440
4FPAN	270	269	461	445
2,3FPAN	268	270	439	428
2,4FPAN	267	262	443	439
2,5FPAN	269	269	450	430
3,4FPAN	270	_a	454	-
3,5FPAN	273	-	448	-
2NO <sub>2</sub> PAN	266	-	450	-
4NO <sub>2</sub> PAN	266	-	451	-
2,4NO <sub>2</sub> PAN	259	-	437	-
4F2NO <sub>2</sub> PAN	262	-	448	-
20MePAN	278	280	476	468
40MePAN	273	268	479	458

<sup>a</sup> Where no value is given, the compound is insoluble in hexanes.



**Fig. 2.** Normalized absorbance spectra in a range of solvents for 4FPAN, 4NO<sub>2</sub>PAN, and 4OMePAN. The solvents are acetonitrile (black), methanol (blue), propanol (green), dichloromethane (orange), and hexanes (red). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)



**Fig. 3.** Normalized and solvent subtracted emission spectra in a range of solvents for 2FPAN. The solvents are acetonitrile (black), methanol (blue), propanol (green), dichloromethane (orange), and hexanes (red). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

previously assigned to a combination of a charge transfer (CT) to the carbonyl and weak  $n-\pi^*$  of the quinone system [15]. The PAN derivatives, which are soluble in hexanes, exhibit a blue shift in hexanes relative to polar solvents. This is most likely due to the lower stability and higher energy of the CT state in a nonpolar environment, since a nonpolar solvent provides only weak induced dipole interactions to stabilize the polarized solute. In contrast, polar solvents have stronger permanent dipole–dipole interactions and are better able to stabilize a charge-separated excited state. There are no significant differences in the absorbance energies of this band amongst the polar solvents studied indicating that

Table 5

Summary of optimized geometries of the PAN derivatives. Bond angles and distances are defined in Fig. 1.

PAN         33.0         23.6         1.98         2.34           2FPAN         0.0         0.0         1.96         2.12           3FPAN         30.6         22.1         1.97         2.36           4FPAN         37.6         26.4         1.98         2.38           2,3FPAN         0.0         0.0         1.95         2.13           2,4FPAN         0.0         0.0         1.95         2.13           2,5FPAN         0.0         0.0         1.96         2.12           3,4FPAN         34.9         24.7         1.97         2.39           3,5FPAN         27.0         19.6         1.96         2.34           2,4,5FPAN         0.0         0.0         1.95         2.14           2,5FPAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 3,4FPAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 4NO <sub>2</sub> PAN         35.8         23.8         2.05         2.49 (1.80)           4HO <sub>2</sub> PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO <sub>2</sub> PAN         37.1         25.4         2.06         2.52 (1.83)	Compound	Φ1 (°)	Φ2 (°)	R1 (Å)	R2 (Å)
2FPAN         0.0         0.0         1.96         2.12           3FPAN         30.6         22.1         1.97         2.36           4FPAN         37.6         26.4         1.98         2.38           2,3FPAN         0.0         0.0         1.95         2.13           2,4FPAN         0.0         0.0         1.95         2.13           2,5FPAN         0.0         0.0         1.96         2.12           3,4FPAN         34.9         24.7         1.97         2.39           3,5FPAN         27.0         19.6         1.96         2.34           2,4,5FPAN         0.0         0.0         1.95         2.14           2,02,PAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 3,4FPAN         33.8         23.8         2.05         2.49 (1.80)           4HO <sub>2</sub> PAN         35.8         24.6         2.06         2.52 (1.83)           4HO <sub>2</sub> PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO <sub>2</sub> PAN         37.1         25.4         2.06         2.52 (1.83)	PAN	33.0	23.6	1.98	2.34
3FPAN         30.6         22.1         1.97         2.36           4FPAN         37.6         26.4         1.98         2.38           2,3FPAN         0.0         0.0         1.95         2.13           2,4FPAN         0.0         0.0         1.95         2.13           2,4FPAN         0.0         0.0         1.95         2.13           2,4FPAN         0.0         0.0         1.96         2.12           3,4FPAN         34.9         24.7         1.97         2.39           3,5FPAN         27.0         19.6         1.96         2.34           2,4,5FPAN         0.0         0.0         1.95         2.14           2No_2PAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 4NO_2PAN         24.8         18.3         1.95         2.29           2,4NO_2PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO_2PAN         37.1         25.4         2.06         2.52 (1.83)	2FPAN	0.0	0.0	1.96	2.12
4FPAN37.626.41.982.382,3FPAN0.00.01.952.132,4FPAN0.00.01.952.132,4FPAN0.00.01.952.132,5FPAN0.00.01.962.123,4FPAN34.924.71.972.393,5FPAN27.019.61.962.342,4,5FPAN0.00.01.952.142NO_PAN35.824.62.062.51 (1.82) <sup>a</sup> 4NO_PAN24.818.31.952.292,4NO_PAN33.823.82.052.49 (1.80)4F2NO_PAN37.125.42.062.52 (1.83)	3FPAN	30.6	22.1	1.97	2.36
2,3FPAN         0.0         0.0         1.95         2.13           2,4FPAN         0.0         0.0         1.95         2.13           2,5FPAN         0.0         0.0         1.95         2.13           3,5FPAN         34.9         24.7         1.97         2.39           3,5FPAN         27.0         19.6         1.96         2.34           2,4,5FPAN         0.0         0.0         1.95         2.14           2NO <sub>2</sub> PAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 4NO <sub>2</sub> PAN         24.8         18.3         1.95         2.29           2,4NO <sub>2</sub> PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO <sub>2</sub> PAN         37.1         25.4         2.06         2.52 (1.83)	4FPAN	37.6	26.4	1.98	2.38
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	2,3FPAN	0.0	0.0	1.95	2.13
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	2,4FPAN	0.0	0.0	1.95	2.13
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	2,5FPAN	0.0	0.0	1.96	2.12
3,5FPAN         27.0         19.6         1.96         2.34           2,4,5FPAN         0.0         0.0         1.95         2.14           2NO <sub>2</sub> PAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 4NO <sub>2</sub> PAN         24.8         18.3         1.95         2.29           2,4NO <sub>2</sub> PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO <sub>2</sub> PAN         37.1         25.4         2.06         2.52 (1.83)	3,4FPAN	34.9	24.7	1.97	2.39
2,4,5FPAN         0.0         0.0         1.95         2.14           2NO2PAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 4NO2PAN         24.8         18.3         1.95         2.29           2,4NO2PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO2PAN         37.1         25.4         2.06         2.52 (1.83)	3,5FPAN	27.0	19.6	1.96	2.34
2NO <sub>2</sub> PAN         35.8         24.6         2.06         2.51 (1.82) <sup>a</sup> 4NO <sub>2</sub> PAN         24.8         18.3         1.95         2.29           2,4NO <sub>2</sub> PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO <sub>2</sub> PAN         37.1         25.4         2.06         2.52 (1.83)	2,4,5FPAN	0.0	0.0	1.95	2.14
4NO <sub>2</sub> PAN         24.8         18.3         1.95         2.29           2,4NO <sub>2</sub> PAN         33.8         23.8         2.05         2.49 (1.80)           4F2NO <sub>2</sub> PAN         37.1         25.4         2.06         2.52 (1.83)	2NO <sub>2</sub> PAN	35.8	24.6	2.06	2.51 (1.82) <sup>a</sup>
2,4NO2PAN33.823.82.052.49 (1.80)4F2NO2PAN37.125.42.062.52 (1.83)	4NO <sub>2</sub> PAN	24.8	18.3	1.95	2.29
4F2NO <sub>2</sub> PAN 37.1 25.4 2.06 2.52 (1.83)	2,4NO <sub>2</sub> PAN	33.8	23.8	2.05	2.49 (1.80)
	4F2NO <sub>2</sub> PAN	37.1	25.4	2.06	2.52 (1.83)
20MePAN -14.3 -10.9 1.98 2.06	20MePAN	-14.3	-10.9	1.98	2.06
40MePAN 37.4 26.2 1.99 2.38	40MePAN	37.4	26.2	1.99	2.38

 $^{\rm a}\,$  For the  $2NO_2$  compounds the length in parentheses is from the amine H to the nitro O.



Fig. 4. Representative calculated absorbance spectra for 4FPAN, 4OMePAN, and  $4NO_2PAN$ . The results are shown for the TD-DFT calculations with acetonitrile solvation.

specific interactions with the solvent, such as hydrogen bonding, do not affect the relative energies of the electronic states.

Sample spectra illustrating the solvatochromism of representative derivatives are presented in Fig. 2. An interesting feature of the spectra is the effect of aniline substituent. It is clearly observed that the FPANs and OMePANs have similar absorbance profiles. In comparison, there is a shift in the relative intensities of the absorbance bands for the NO<sub>2</sub>PANs. The absorbance around 340 nm ( $\lambda_3$ ) has a much greater intensity in the nitro-derivative,



Fig. 5. Selected molecular orbitals for 4FPAN: HOMO (a), LUMO (b), and LUMO + 2(c). For comparison the LUMO + 2 of 4NO<sub>2</sub>PAN is shown (d).

comparable to the  $\lambda_2$  and  $\lambda_4$  bands. Computational analysis of the excitation energies and visualization of the molecular orbitals is used to further examine this phenomenon, in the subsequent section.

In solution PAN derivatives have very weak emission, even following degassing and slight cooling of samples (to a minimum of 10 °C). Representative emission spectra in the series of solvents are presented in Fig. 3. These spectra were collected following excitation of the low energy CT band and were verified by excitation scans for the observed emission band. Collectively the variation in substituent group and position did not have a significant impact upon the emission energies nor intensities. A broad, weak emission was observed in the range of 550-600 nm for the polar solvents. In hexanes the band is blue shifted by approximately 50 nm. The lower energy emission in polar solvents indicates a greater stabilization of the CT excited state by dipole-dipole interactions with the surrounding solvent molecules. As in the case of the absorbance spectra no significant differences are observed between the polar solvents studied. Further supporting the conclusion that specific interactions with the solvent, such as hydrogen bonding, do not appear to influence the photophysical properties of the system.

#### Computational studies

The structures were analyzed with respect to relevant hydrogen bonding structure between the two rings relative to the central amine group, as labeled in Fig. 1. Bond lengths and angles are in Table 5. The 2FPANs have a planar geometry for the two rings to maximize the hydrogen bonds between the fluorine substituent and the amine hydrogen [15,33]. In contrast, other PAN compounds with substituents that do not induce hydrogen bonding to the central amine have dihedral angles in the range of 20–40°, quite similar to the parent compound PAN. In the compounds with a nitro-substituent in the two position, it is expected that a hydrogen bond would be formed between an oxygen of the nitro and the central amine hydrogen [15]. However, due to the size of the nitro group this arrangement does not take place and the dihedral angles between the rings do not change significantly from the ones obtained with unsubstituted PAN.

Representative calculated UV–Vis spectra for 4FPAN, 4OMePAN, and 4NO<sub>2</sub>PAN are shown in Fig. 4. Several PAN derivatives studied exhibit similar spectral bands like that of 4FPAN and 4OMePAN, with the exception of the NO<sub>2</sub>PANs. This difference is similar to the experimental spectra, showing more closely spaced absorbance

bands in the nitro-substituted PAN species (Fig. 2). Overall the experimentally predicted spectra capture the key features of the experimental spectra. The complete table of the first ten excitation energies and oscillatory strengths calculated using TD-DFT and ZINDO methods are reported in the supplementary materials.

The lowest energy spectral transition with significant oscillatory strength for all compounds is a HOMO to LUMO transition with CT character. Representative MOs are shown in Fig. 5. The energy of lowest energy transition is in the visible region of the spectrum by ZINDO and TD-DFT methods, with higher wavelengths predicted by the latter. The other dominant spectral band between 250 and 300 nm is made up of excitations exhibiting significant  $\pi$ to  $\pi^*$  character. Some of the weaker transitions in this spectral region have changes in the electron density about the carbonyl groups of the naphthoquinone. The notable spectral change predicted by ZINDO and TD-DFT methods for 4NO<sub>2</sub>PAN, relative to 4FPAN and 4OMePAN, is due to a change in the energy of the HOMO to LUMO + 2 transition. In the nitro-derivative there is CT character accompanying the transition, in contrast to the dominant  $\pi^*$  character centered on the quinone system LUMO + 2 state of 4FPAN and 4OMePAN (Fig. 5). The result is a red shift for the second (lowest) energy absorbance band in the nitro-derivatives.

In general, the calculations agree with the experimental spectra showing minimal differences in the electronic transitions between derivatives with the same substituents, regardless of the position. The main variation that is observed is based upon the derivative itself, with the nitro-substituent being the most divergent. Substitution of a nitro group at either an ortho or para position of aniline results in a guite defined series of absorbance bands, with spectral changes attributed to the nature of the second excited electronic state. Indeed, a nitro group has a strong electron-withdrawing capacity in comparison to the electron-donating ability of methoxy substituents and weak electron-withdrawing ability of a fluorosubstituent [34]. The electronic states with electron density on the aniline moiety of the NO<sub>2</sub>PANs are shifted higher in energy than the other derivatives that are better able to support electron density on the aniline moiety. It follows that higher energy CT states, such as 4NO<sub>2</sub>PAN's LUMO + 2 state (Fig. 5), are lower in energy for the NO<sub>2</sub>PANs than  $\pi^*$  states of the aniline system.

#### Conclusions

Novel NO<sub>2</sub>PAN derivatives were prepared by direct nitration of PAN or oxidative-addition of nitroanilines to 1,4-naphthoquinone

in the presence of FeCl<sub>3</sub>. PANs structures were analyzed with respect to hydrogen bonding between the substituents present in the two rings connected to the amino group. While the 2FPANs have a planar geometry due to a three-center hydrogen bonding, the 2NO<sub>2</sub>PANs have a geometry quite similar to PAN indicating the absence of a hydrogen bonding between neighboring NH and nitro groups.

The impact of substituent and solvent upon the photophysical properties of a series of PAN derivatives are examined using a combination of computational and spectroscopic methods. The dominant electronic transitions are assigned to a low energy CT transition corresponding to a shift in electron density to the naphthoquinone and its carbonyl groups, and a higher energy  $\pi - \pi^*$  transition of the phenyl moiety. Solvent and substituent have a minimal impact upon the latter, high-energy, absorbance band. In contrast polar solvents better stabilize the CT transfer, due to favorable dipole interactions, resulting in a blue shift for the CT band in nonpolar solvents (hexanes). Specific solvent–solute interactions do not have a significant impact upon the photophysical properties of the PAN derivatives.

Although substituent position on the phenyl moiety does not alter its photophysical properties, the type of substituent does.  $NO_2$ -PANs show significant differences in absorbance profiles relative to FPANs and OMePANs. This is rationalized by the strong electronwithdrawing nature of the nitro-group relative to the other substituents. The presence of a nitro-substituent shifts the relative energies of a higher energy CT state making it a stronger transition and subsequently a lower energy relative to the other substituents.

The combination of spectral and computational analysis provides a greater understanding about the origin of the observed photophysical properties of the PAN system. Through understanding of how environment and molecular structure can impact the nature of spectral transitions, modifications can be made to the PAN structure to modulate redox and other physicochemical properties. Minimal tuning is achieved through solvent, but the electronic nature of substituents on the aniline does show potential for tuning photophysical properties.

#### Acknowledgements

We would like to acknowledge financial support by Mexican CONACyT (Grant CB-2010-155678), scholarship for Silvia E. Loredo-Carrillo (No. 165111) and Diego A. Magaldi-Lara (No. 268070).

#### Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molstruc.20 14.0 3.044.

#### References

 A. Riffel, L.F. Medina, V. Stefani, R.C. Santos, D. Bizani, A. Brandelli, Braz. J. Med. Biol. Res. 35 (2002) 811–818.

- [2] M.D. Ball, M.S. Bartlett, M. Shaw, J.W. Smith, M. Nasr, S.R. Meshnik, Antimicrob. Agents Chemother. 45 (2001) 1473–1479.
- [3] A. Ventura-Pinto, S. Lisboa de Castro, Molecules 14 (2009) 4570–4590.
- [4] S. Gafner, J.L. Wolfender, M. Nianga, H. Stoceckli-Evans, K. Hostettmann, Phytochemistry 42 (1996) 1315–1320.
- [5] V.K. Tandon, H.K. Maurya, N.N. Mishra, P.K. Shukla, Bioorg. Med. Chem. Lett. 21 (2011) 6398–6403.
- [6] V.K. Tandon, H.K. Maurya, M.J. Verma, R. Kumar, P.K. Shukla, Eur. J. Med. Chem. 45 (2010) 2418–2426.
- [7] V.K. Tandon, D.B. Yadav, R.V. Singh, A.K. Chaturvedi, P.K. Shukla, Bioorg. Med. Chem. Lett. 21 (2005) 5324–5328.
- [8] S. Bittner, S. Gorohovsky, E. Lozinsky, A.I. Shames, Amino Acids 19 (2000) 439– 449.
- [9] G.E.W. Wolstenholm, C.M. O'Conner (Eds.), Quinones in Electron Transport, Churchill Press, London, 1961.
- [10] M. Aguilar-Martínez, N.A. Macías-Ruvalcaba, J.A. Bautista-Martínez, M. Gómez, F.J. González, I. González, Curr. Org. Chem. (2004) 1721–1738.
- [11] P.S. Guin, S. Das, P.C. Mandal, Int. J. Electrochem. (2011) 816202.
- [12] C.-Y. Li, M.L. Caspar, D.W. Dixon, Electrochim. Acta 25 (1980) 1135-1142.
- [13] M. Aguilar-Martínez, G. Cuevas, M. Jiménez-Estrada, I. González, B. Lotina-Hennsen, N. Macías-Ruvalcaba, J. Org. Chem. 64 (1999) 3684–3694.
- [14] M.S. Khan, Z.H. Khan, Spectrochim. Acta Part A 61 (2005) 777-790.
- [15] E. Leyva, Ll.I. López, S.E. Loredo-Carrillo, M. Rodríguez-Kessler, A. Montes-Rojas, J. Fluorine Chem. 132 (2011) 94–101.
- [16] T. Win, S. Bittner, Tetrahedron Lett. 46 (2005) 3229–3231.
- [17] J. Dong, K.M. Solntsev, L.M. Tolbert, J. Am. Chem. Soc. 128 (2006) 12038– 12039.
- [18] S.Y. Fung, J. Duhamel, P. Chen, J. Phys. Chem. A 110 (2006) 11446-11454.
- [19] B.M. Baughman, E. Stennett, R.E. Lipner, A.C. Rudawsky, S.J. Schmidtke, J. Phys.
- Chem. A 113 (2009) 8011–8019. [20] M. Umadevi, P. Vanelle, T. Terme, V. Ramakrishnan, J. Raman Spectrosc. 34
- (2003) 172–179. [21] S.J. Schmidtke, D.F. Underwood, D.A. Blank, J. Phys. Chem. A 109 (2005) 7033– 7045.
- [22] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, T. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, Gaussian 09, Revision B.01, Gaussian Inc., Wallingford CT, 2010.
- [23] C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 37 (1988) 785–789.
- [24] B. Miehlich, A. Savin, H. Stoll, H. Preuss, Chem. Phys. Lett. 157 (1989) 200–206.
- [25] A.D. Becke, J. Chem. Phys. 98 (1993) 5648–5652.
   [26] R. Easton, D. Giesen, A. Wlech, C. Cramer, D. Truhlar, Theor. Chim. Acta 93
- (1996) 281–301.
- [27] GaussView, Version 5, R. Dennington, T. Keith, J. Millam, Semichem Inc., Shawnee Mission KS, 2009.
- [28] E. Leyva, Ll.I. López, E. Moctezuma, H. De Lasa, Top. Catal. 49 (2008) 281-287.
- [29] T. Win, S. Yerushalmi, S. Bittner, Synthesis 10 (2005) 1631–1634.
- [30] C. da, S. Lisboa, V.G. Santos, B.G. Vaz, N.C. de Lucas, M.N. Eberlin, S.J. Garden, J. Org. Chem. 76 (2011) 5264–5273.
- [31] A.I. Francisco, M.D. Vargas, J.W. Carneiro, M. Lanznaster, J.C. Torres, C.A. Camara, A.C. Pinto, J. Mol. Struct. 891 (2008) 228–232.
- [32] W.M. Haynes, T.J. Bruno, D.R. Lide, CRC Handbook of Chemistry and Physics, International Edition, 94th ed., CRC Press, Taylor & Francis, Boca Raton, FL, 2014.
- [33] S. Vega-Rodríguez, R. Jiménez-Cataño, E. Leyva, S.E. Loredo-Carrillo, J. Fluorine Chem. 145 (2013) 58–62.
- [34] F.A. Carey, Organic Chemistry, third ed., McGraw-Hill Inc., New York, 1996. p. 488.