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## **Electronic Supporting Information**

## Oxidative amidation of benzaldehyde using a quinone/DMSO system as the oxidizing agent

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#### General information

All employed reagents were purchased from commercial sources and used without further purification. Nuclear magnetic resonance spectra were recorded on a Mercury 400 MHz. Chemical shifts were reported as  $\delta$  values (PPM). Couplings constants *j* are reported in Hertz (Hz). Internal reference for NMR to TMS at 0.00 ppm for spectra obtained in CDCl<sub>3</sub>), multiplicities are reports using the standard abbreviations, as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), broad signal (bs), doublet of triplets (dt), triplet of doublets (td), quartet of doublets (qd), multiplet (m), apparent triplet (at). NMR spectral were analyzed using MestReNova software (version 10.01-14719). HRMS spectral were acquired on a Bruker MicroTOF-II spectrometer. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Reactions progress was monitored by thin layer chromatography (TLC) using silica gel 60 F254 from Merck and the spots were visualized under UV light at 245 or 365 nm. Column chromatography was performed using silica gel (230-400 mesh). Chemical names and drawings were obtained using ChemDraw Profesional (version 16.0.1.4 (61)).

#### **Experimental Procedures**

#### Synthesis of pyrrolyl quinones

**2,5-dimethyl-3-(1***H***-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione (4)** The synthesis was carried out using a method described previously.<sup>1</sup> Flash Column chromatography (Hex:EtOAc 99:1) giving purple solid; yield 48 mg 20%, mp. 98-100 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  10.70 (s, 1H), 7.04 (td, *J* = 2.8, 1.3 Hz, 1H), 6.69 (ddd, *J* = 4.0, 2.5, 1.3 Hz, 1H), 6.60 (q, *J* = 1.5 Hz, 1H), 6.36 (dt, *J* = 3.9, 2.6 Hz, 1H), 2.28 (s, 3H), 2.05 (d, J = 1.5 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  190.76, 187.04, 144.68, 134.88, 133.52, 131.71, 125.32, 122.25, 117.25, 109.91, 15.88, 14.75. HRMS (ESI<sup>+</sup>): m/z: Calcd. for C<sub>12</sub>H<sub>11</sub>NO<sub>2</sub>: calc. 201.0790; Found: 201.0783.

**3-(5-chloro-1***H***-pyrrol-2-yl)-2,5-dimethylcyclohexa-2,5-diene-1,4-dione (4a).** The synthesis was carried out using a method described in the literature with some modifications.<sup>2</sup> To a solution of 2,5-dimethyl-3-(1*H*-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione. (100 mg, 0.496 mmol,) dissolved in CH<sub>3</sub>CN (2.5 ml) was added CuCl<sub>2</sub> (33.4mg, 0.248 mmol). The mixture was stirred for 5 min. The solvent was removed under vacuum. The reaction crude was purified by flash column chromatography with Hexane:EtOAc 9:1 (v/v) giving purple solid; yield 78 mg, 66.5%, mp 103-105 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  10.70 (s, 1H), 6.63 (td, *J* = 4.1, 3.6, 2.2 Hz, 2H), 6.21 (dd, *J* = 4.0, 2.7 Hz, 1H), 2.27 (s, 3H), 2.07 (d, *J* = 1.6 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$ 199.65, 186.79, 144.75, 135.12, 133.74, 133.72, 130.85, 130.74, 124.61, 119.87, 118.23, 108.25, 15.91, 14.75. HRMS. (ESI<sup>+</sup>): m/z: Calcd. for C<sub>12</sub>H<sub>11</sub>NClO<sub>2</sub>: calc. 236.0478; Found: 236.0477.

**2,5-dimethyl-3-(5-nitro-1***H***-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione (4b).** To a solution of 2,5-dimethyl-3-(1*H*-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione. (30 mg, 0.149 mmol,) dissolved in  $CH_2Cl_2$  (2.5 ml) was added  $Bi(NO_3)_3$ 5H<sub>2</sub>O (36.15 mg, 0.0745 mmol,). The mixture was stirred for 3 h. The solvent was removed under vacuum. The residue was purified by flash column chromatography (Hex:EtOAc 7:3) giving yellow solid; yield 16 mg, 44%. mp. 116-118 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  11.33 (s, 1H), 7.20 – 7.13 (m, 1H), 6.73 (q, *J* = 1.6 Hz, 1H), 6.64 (dd, *J* = 4.4, 1.7 Hz, 1H), 2.33 (s, 3H), 2.13 (d, *J* = 1.6 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  188.46, 186.23, 145.63, 141.81, 138.89, 13 3.67, 130.22, 128.49, 116.58, 110.37, 15.96, 14.75. HRMS (ESI<sup>+</sup>): m/z: Calcd. for  $C_{12}H_{10}N_2NaO_4$ : calc. 269.0533; Found: 269.0514.

**2,5-dimethyl-3-(5-thiocyanato-1***H***-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione (4c)** To a solution of 2,5-dimethyl-3-(1*H*-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione. (100 mg, 0.496 mmol,) dissolved in CH<sub>3</sub>CN (4 ml) was added KSCN (96.69 mg, 0.995 mmol) and K<sub>2</sub>S<sub>2</sub>O<sub>8</sub> (403 mg, 1.498 mmol). After 24 h was added KSCN (96.69 mg, 0.995 mmol). The solvent was removed under vacuum.<sup>3</sup> The residue was purified by flash column chromatography (Hex:EtOAc 4:1) giving red solid; yield 115mg 90% mp 123-125 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  10.84 (s, 1H), 6.73 (dd, *J* = 4.0, 2.7 Hz, 1H), 6.68 (q, *J* = 1.6 Hz, 1H), 6.65 (dd, *J* = 4.1, 2.6 Hz, 1H), 2.29 (s, 3H), 2.10 (d, *J* = 1.6 Hz, 3H).<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>):  $\delta$  189.56, 186.64, 145.24, 138.68, 133.61, 130.70, 130.39, 119.69, 117.81, 109.43, 107.81 HRMS (ESI<sup>+</sup>): m/z: Calcd. for C<sub>13</sub>H<sub>10</sub>N<sub>2</sub>NaO<sub>2</sub>S: calc. 281.0355; Found: 281.0327.

**3-(5-(2-(1***H***-pyrrol-2-yl)propan-2-yl)-1***H***-pyrrol-2-yl)-2,5-dimethylcyclohexa-2,5-diene-<b>1,4-dione (4d).** The synthesis was carried out using a method described previously.<sup>4</sup>

**2-hydroxy-6-methyl-3-(6-methyl-5-oxoheptan-2-yl)-5-(1***H***-pyrrol-2-yl)cyclohexa-2,5diene-1,4-dione (5). The synthesis was carried out using a method described previously.<sup>1</sup> Flash Column chromatography (Hex:EtOAc 99:1) giving purple solid; yield 79 mg 63%, mp. 53-55 °C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): \overline{0} 7.11 (dt,** *J* **= 4.1, 2.1 Hz, 1H), 6.79 (ddd,** *J* **= 3.9, 2.3, 1.0 Hz, 1H), 6.42 – 6.33 (m, 1H), 3.06 (dp,** *J* **= 8.6, 7.0 Hz, 1H), 2.31 (s, 3H), 1.78 – 1.69 (m, 1H), 1.50 (dq,** *J* **= 13.2, 6.6 Hz, 2H), 1.22 (d,** *J* **= 7.1 Hz, 4H), 1.16 (ddq,** *J* **= 8.4, 4.6, 2.2 Hz, 3H), 0.83 (dd,** *J* **= 6.6, 4.1 Hz, 6H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>): \overline{0}. 190.89, 183.22, 150.99, 133.36, 129.00, 126.40, 123.89, 119.17, 110.49, 29.79, 27.82, 25.93, 22.54, 18.29, 14.44. HRMS (ESI<sup>+</sup>): m/z: Calcd. for C<sub>12</sub>H<sub>11</sub>NO<sub>2</sub>: calc.338.1727; Found: 338.1726.** 

**2-hydroxy-6-methyl-3-(6-methylheptan-2-yl)-5-(1***H***-<b>pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione (6).** The synthesis was carried out using a method described previously.<sup>1</sup>

#### General Procedure for Oxidative Amidation.

A mixture of aldehyde (100 mg, 0.66 mmol), secondary amine (1.2 eq 0.79 mmol), quinone (0.02 mmol), in DMSO (2 mL) was stirred at 70 °C for 19 h. in absence of light. The reaction mixture was concentrated in vacuo. The residue was purified by column chromatography on silica gel using hexane/EtOAc as eluent to obtain tertiary amide products.

## (4-nitrophenyl)(pyrrolidin-1-yl)methanone (7a)

**N-(4-Nitrobenzoyl)pyrrolidine**,<sup>5</sup> Column chromatography (Hexane:EtOAc 80:20) giving yellow solid. Yield 143 mg, 98%. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>);  $\delta$  8.27 (d, *J* = 8.7 Hz, 2H), 7.68 (d, *J* = 8.7 Hz, 2H), 3.67 (t, *J* = 6.9 Hz, 2H), 3.39 (t, *J* = 6.6 Hz, 2H), 2.04 – 1.97 (m, 2H), 1.96 – 1.89 (m, 2H).

#### (4-methoxyphenyl)(pyrrolidin-1-yl)methanone (7b)

Column chromatography (Hexane:EtOAc 80:20) giving a colorless oil 129 mg, 86%. <sup>1</sup>H NMR: 7.52 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 3.82 (s, 3H), 3.63 (t, J = 7.0 Hz, 2H), 3.47 (t, J = 6.5 Hz, 2H), 1.98-1.83 (m, 4H).

#### phenyl(pyrrolidin-1-yl)methanone (7c)

Column chromatography (Hexane:EtOAc 80:20) giving a Yellow oil 117 mg, 64%. <sup>1</sup>H NMR

(400 MHz, CDCl<sub>3</sub>): δ 7.48 – 7.35 (m, 5H), 3.65 (t, *J* = 7.0 Hz, 2H), 3.43 (t, *J* = 6.6 Hz, 2H), 2.01 – 1.84 (m, 9H).

## N-(4-chlorobenzoyl)pyrrolidine (7d)

Column chromatography (CH<sub>2</sub>Cl<sub>2</sub>:EtOAc 25:10) giving colorless oil. Yield 105 mg 71%. <sup>1</sup>H NMR:  $\delta$  7.47 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H), 3.63 (t, *J* = 6.9 Hz, 2H), 3.41 (t, *J* = 6.6Hz, 2H), 1.99 – 1.93 (m, 2H), 1.91 – 1.86 (m, 2H).

## (4-bromophenyl)(pyrrolidin-1-yl)methanone (7e)

Column chromatography (CH<sub>2</sub>Cl<sub>2</sub>:EtOAc 35:10) giving a white crystals. Yield 72 mg, 57 %. <sup>1</sup>H NMR:  $\delta$  7.53 (d, *J* = 8.5 Hz, 2H), 7.40 (d, *J* = 8.5 Hz, 2H), 3.41 (t, J = 6.6 Hz, 2H), 3.62 (t, J = 6.9 Hz, 2H), 2-1.85 (m, 4H).

#### N,N-diethyl-4-nitrobenzamide (8)

Column chromatography (Hexane:EtOAc 80:20) giving a yellow solid. Yield 49 mg, 34%. 1H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.28 (d, *J* = 8.6 Hz, 2H), 7.54 (d, *J* = 8.6 Hz, 2H), 3.58 (q, *J* = 7.2 Hz, 4H), 3.22 (q, *J* = 7.2 Hz, 4H), 1.13 (td, *J* = 7.0, 2.5 Hz, 6H).

## N,N-dibutyl-4-nitrobenzamide (8a)

Column chromatography (Hexane:EtOAc 80:20) giving a yellow oil. Yield 83 mg, 43%. <sup>1</sup>H NMR: δ 8.28 (d, *J* = 8.8 Hz, 2H), 7.93 (d, *J* = 8.8 Hz, 2H), 3.50 – 3.47 (m, 2H), 3.17 (dt, *J* = 24.6, 7.4 Hz, 2H), 1.66 – 1.59 (m, 4H), 1.46 – 1.39 (m, 4H), 0.97 (t, *J* = 7.3 Hz, 6H).

#### N-(4-Nitrobenzoyl)morpholine (8b)

Column chromatography (CH2Cl2:EtOAc 80:10) giving a yellow crystals. <sup>1</sup>H NMR:  $\delta$  8.30 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 3.81 (s, 4H), 3.64 (s, 2H), 3.40 (s, 2H).

#### Piperazine-1,4-diylbis((4-nitrophenyl)methanone) (8c)

Column chromatography (CH2Cl2:EtOAc 80:10) giving a yellow crystals Yield 40.6 mg, 32%. <sup>1</sup>H NMR:  $\delta$  8.28 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 8.7 Hz, 2H), 3.86 – 3.72 (m, 2H), 3.35 (t, *J* = 4.9 Hz, 2H), 2.97 (d, *J* = 5.5 Hz, 2H), 2.83 (t, *J* = 4.9 Hz, 2H).



# NMR Spectra



Cosy NMR (400 MHz, CDCl<sub>3</sub>)

Hetcor NMR (400 MHz, CDCl<sub>3</sub>)



Noesy NMR (400 MHz, CDCl3)



Dept NMR (400 MHz, CDCl<sub>3</sub>)



#### Mass spectrum

File: QDP_PIRROL_LCG	Date Run: 08-19-2014 (Time Run: 12:00:41)
Sample: QUINONA_PIRROL	
Instrument: JEOL GCmate	
Inlet: Direct Probe	Ionization mode: EI+





## 3-(5-chloro-1H-pyrrol-2-yl)-2,5-dimethylcyclohexa-2,5-diene-1,4-dione (4a)

## <sup>1</sup>H NMR (400 MHz, CDC<sub>I3</sub>)



Cosy NMR (400 MHz, CDCl<sub>3</sub>



Hetcor NMR (400 MHz, CDCl<sub>3</sub>)



## Noesy NMR (400 MHz, CDCl<sub>3</sub>)



Dept NMR (400 MHz, CDCl<sub>3</sub>)



Mass spectrum



## 2,5-dimethyl-3-(5-nitro-1*H*-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione (4b)

## <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



## <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)



## Hetcor NMR (400 MHz, CDCl<sub>3</sub>)



Noesy NMR (400 MHz,  $\text{CDCl}_3$ )



## Dept NMR (400 MHz, CDCl<sub>3</sub>)



#### Mass spectrum

Analysis Info		PONO2 d		Acquisition Date	8/24/2018 2:54:00 PM
Method Sample Name Comment	sis Name PQNO2.d d Tune wide Neg.m le Name PQNO2 nent			Operator Carlos Jesús Cort Instrument / Ser# क्रियायीय OF-Q II 10	
Acquisition Para	ameter				
Source Type Focus Scan Begin Scan End	ESI Active 50 m/z 3000 m/z	lon Polarity Set Capillary Set End Plate Offset Set Collision Cell RF	Positive 4500 V -500 V 350.0 Vpp	Set Nebulize Set Dry Hea Set Dry Gas Set Divert V	er 0.3 Bar ter 180 °C 4.0 l/min alve Waste
lon Optics Set Funnel 1 RF ISCID Energy	127.8 Vpp 0.0 eV	Set Funnel 2 RF Set Hexapole RF	347.6 Vpp 400.0 Vpp	Processin Summation Guessed No	g 5000 x ise 200
Quadrupole Collision Energy Set Transfer Time	10.0 eV 80.0 μs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Гіте 5.0 µs	Set Ion Ener Set Isolation	gy (MS only) 5.0 eV Mass (MS only) 300.00 m/z
Intens. x105 4 3 269.	0514				+MS, 0.0-0.6min #(2-34
0	413.2629 413.2629 500	1000	1500	2000	2500 m/
Meas. m/2 269.051	z Formula 4 C 12 H 10 N 2 Na O 4	Score m/z e 100.00 269.0533	rr [ppm] mSigm 7.0 11	na .8	

2,5-dimethyl-3-(5-thiocyanato-1*H*-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione (4c). <sup>1</sup>H NMR (400 MHz,  $CDCl_3$ )



<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)



Cosy NMR (400 MHz, CDCl<sub>3</sub>)



Hetcor NMR (400 MHz, CDCl<sub>3</sub>)



Noesy NMR (400 MHz, CDCl<sub>3</sub>)



Dept NMR (400 MHz, CDCl<sub>3</sub>)



Mass spectrum



2-hydroxy-6-methyl-3-(6-methylheptan-2-yl)-5-(1*H*-pyrrol-2-yl)cyclohexa-2,5-diene-1,4-dione (5)





## Hetcor NMR (400 MHz, CDCl<sub>3</sub>)



## Dept NMR (400 MHz, CDCl<sub>3</sub>)



20 10 0

## Mass spectrum

Analysis Info				Acquisition Date 8/24/2	018 2:28:56 PM
Analysis Name		DHPP.d		in organization batto or 2 m2	010 2.20.00 1 11
Nethod	Tune wide Neg.m			Operator Carlos	Jesús Cortes
Sample Name Comment	DHPP			Instrument / Ser# ARTADE	FOF-Q II 10389
Acquisition Para	meter				
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	4500 V	Set Dry Heater	180 °C
Scan Begin Scan End	3000 m/z	Set Collision Cell RF	350.0 Vpp	Set Dry Gas Set Divert Valve	4.0 l/min Waste
on Optics				Processing	
Set Funnel 1 RF	127.8 Vpp	Set Funnel 2 RF	347.6 Vpp	Summation	5000 x
SCID Energy	0.0 eV	Set Hexapole RF	400.0 Vpp	Guessed Noise	200
Juadrupole					
guadrupoic					
Collision Energy	5.0 eV	Set Collision Cell RF	350.0 Vpp	Set Ion Energy ( MS	only) 5.0 eV
Collision Energy Set Transfer Time	5.0 eV 150.0 µs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Гіте 5.0 µs	Set lon Energy ( MS Set Isolation Mass (	only) 5.0 eV MS only) 300.00 m/z
Collision Energy Set Transfer Time	5.0 eV 150.0 μs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 μs	Set lon Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Intens 2.5 2.0 1.5	5.0 eV 150.0 μs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 μs	Set lon Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Intens. 2.5 2.0 1.5 33	5.0 eV 150.0 µs 38.1726 803.535	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 μs	Set Ion Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Localision Energy Set Transfer Time Intens. x105 2.5 2.0 1.5 30	5.0 eV 150.0 µs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 μs	Set Ion Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Intens. x105 2.5 2.0 1.5 33	5.0 eV 150.0 µs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 µs	Set Ion Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Intens.  30    1.5  30    1.0  0.5	5.0 eV 150.0 µs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Γime 5.0 μs	Set Ion Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Intens x10 <sup>5</sup> 2.5 2.0 1.5 30 1.0 0.5	5.0 eV 150.0 µs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 μs	Set Ion Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Intens.  33    1.5  33    1.0  0.5    0.0	5.0 eV 150.0 µs	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 μs	Set Ion Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32)
Intens.  33    1.5  33    1.0  0.5    0.0	5.0 eV 150.0 µs 38.1726 653.3520 653.3520 500	Set Collision Cell RF Set PrePulseStorage	350.0 Vpp Fime 5.0 μs	Set Ion Energy ( MS Set Isolation Mass (	only ) 5.0 eV MS only ) 300.00 m/z +MS, 0.0-0.5min #(2-32) 

## (4-nitrophenyl)(pyrrolidin-1-yl)methanone (7a) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)







## phenyl(pyrrolidin-1-yl)methanone (7c) <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)



(4-bromophenyl)(pyrrolidin-1-yl)methanone (7e) <sup>1</sup>H NMR (400 MHz, CDCl<sub>2</sub>)







## **N-(4-Nitrobenzoyl)morpholine (8b)** <sup>1</sup>**H NMR** (400 MHz, CDCl<sub>3</sub>)



## Piperazine-1,4-diylbis((4-nitrophenyl)methanone) (8c)



## **Theoretical calculations**

Three definitions of f(r) are obtained from the finite difference scheme,<sup>6</sup> which are helpful descriptors to evaluate a chemical specie for nucleophilic attacks  $(f(r)^+)$ , electrophilic attacks  $(f(r)^-)$  and for free radicals attacks  $(f(r)^0)$  by using the following equations:

 $f(r)^{+} = \rho_{N+1}(r) - \rho_{N}(r) \quad (1)$   $f(r)^{-} = \rho_{N}(r) - \rho_{N-1}(r) \quad (2)$  $f(r)^{0} = 0.5(\rho_{N+1}(r) - \rho_{N-1}(r)) \quad (3)$ 

where  $\rho_{N+1}(r)$ ,  $\rho_N(r)$  and  $\rho_{N-1}(r)$  are the electronic densities at point r for the system with N+1, N and N-1 electrons respectively.

The  $f(r)^0$  form of the Fukui functions was used as a stability descriptor pursuing zones within the pyrrolyl quinones that could stabilize a free radical. The  $f(r)^0$  descriptor indicated regions in the pyrrolyl quinones in which an unpaired electron could potentially be localized after redistribution of the initial electronic density.

The left panel of Scheme 1 presents the isocontours of  $f(r)^0$  in the gas phase. The right side of Scheme 1 plots the isovalues of  $f(r)^0$  in the presence of DMSO as the

solvent. The lowest energy conformers of **4** and its derivatives indicated the formation of a hydrogen bond between  $O_9$  of the quinone and H of the pyrrole ring, with a length of 1.93, 1.92, 1.98, or 1.95 Å for **4**, **4a**, **4b**, and **4c**, respectively, in the gas phase. Although the presence of DMSO promoted hydrogen bonding, the hydrogen bond length increases with respect to the gas phase (being 1.98, 1.95, 2.01, and 1.99 Å for **4**, **4a**, **4b**, and **4c**, respectively).

The highest values of  $f(r)^0$  suggested that the oxygen atoms O<sub>8</sub> and O<sub>9</sub> of the quinones were the most favorable sites for stabilizing a free radical, with a subtle preference for O<sub>8</sub> over O<sub>9</sub>. O<sub>9</sub> participates in non-bonded interactions, whereas O<sub>8</sub> can accept one electron to form a radical. Radical formation raises an interesting question: Do the pyrrolyl quinones accept or donate the electron? To address this question, we calculated the values of  $f(r)^+$  and  $f(r)^-$  of the Fukui functions in the open shell scheme (after radical formation). The value  $f(r)^+$  provides information about sites that stabilize incoming charges on the PQs. The value of  $f(r)^-$  gives information about the electron donor sites from which a charge may "exit" to stabilize the PQs in a subsequent step.

Table 1 indicates that the highest values of the Fukui function occurred at  $O_8$ , particularly for  $f(r)^+$ . Once the radical formed,  $O_8$  preferably accepted the incoming charge. It is important to note that  $f(r)^+$  increased in the presence of DMSO by up to 7.2%, in agreement with our proposed mechanism that the quinones promoted radical formation in the presence of DMSO with synergic effects.

ble 1 Condensed forms of $f(r)^+$ and $f(r)^-$ (in e-), calculated after the radical formed in the PQs								
		Gas	phase			DM	ISO	
Compound	f(r	·) +	$f(r)^{-}$		$f(r)^+$		$f(r)^{-}$	
	$O_8$	O <sub>9</sub>	$O_8$	O <sub>9</sub>	$O_8$	O <sub>9</sub>	$O_8$	O <sub>9</sub>
4	0.184	0.061	0.114	0.075	0.194	0.067	0.122	0.084
4a	0.181	0.069	0.129	0.078	0.194	0.120	0.066	0.083
4b	0.182	0.057	0.125	0.080	0.195	0.063	0.143	0.088
4c	0.184	0.061	0.120	0.078	0.196	0.067	0.138	0.087





Scheme 1 Isocontours of f(r)0 for 4, 4a, 4b, 4c in the gas phase and in the presence of DMSO as a solvent

From the global properties of benzoquinones, we can clearly observe the solvent effect on such properties, e. g., electron affinity (**A**) increases approximately twice in the presence of the solvent with respect to the gas phase. In specific, the superiority of DMSO over CH<sub>3</sub>CN can be observed analyzing the chemical hardness (**η**), which measures the resistance of a chemical specie to change in its electronic configuration<sup>7</sup> it decreases significantly in the presence of both CH<sub>3</sub>CN and DMSO, finding in all cases, the lowest values of **η** in the presence of DMSO. Additionally, we observed that global electrophilicity (**ω**) of all species, increases considerably in the presence of the solvents, finding in the presence of DMSO the highest values of **ω**, which are up to 0.15 eV higher than **ω** calculated in the presence of CH<sub>3</sub>CN. Other proofs of superiority of DMSO over CH<sub>3</sub>CN (and other solvent with dissimilar polarity) we found analyzing the local reactivity descriptors, such as the condensed Fukui functions, which are part of a further publication. Tables 2, 3 and 4 list the results of the discussed global properties:

MOLECULE	A	μ	η	ω	
$NO_2$	2.58	-5.04	4.91	2.58	
SCN	2.36	-4.82	4.92	2.36	
Cl	2.03	-4.46	4.87	2.05	
Н	1.87	-4.36	4.98	1.91	

Table 2. Electron affinity (A), chemical potential ( $\mu$ ), hardness ( $\eta$ ) and electrophilicity ( $\omega$ ) [in eV] of pyrrolyl benzoquinones calculated in the gas phase.

Table 3. Electron affinity (A), chemical potential  $(\mu)$ , hardness  $(\eta)$  and electrophilicity  $(\omega)$  [in eV] of pyrrolil benzoquinones calculated in the presence of CH<sub>3</sub>CN.

MOLECULE	A	μ	η	ω
NO <sub>2</sub>	4.16	-4.96	1.61	7.65
SCN	3.92	-4.74	1.64	6.84
Cl	3.80	-4.57	1.53	6.81
Н	3.73	-4.51	1.55	6.55

Table 4. Electron affinity (A), chemical potential ( $\mu$ ), hardness ( $\eta$ ) and electrophilicity ( $\omega$ ) [in eV] of benzoquinones calculated in the presence of DMSO.

MOLECULE	A	μ	η	ω
NO <sub>2</sub>	4.17	-4.96	1.58	7.78
SCN	3.93	-4.74	1.61	6.95
Cl	3.81	-4.57	1.51	6.92
Н	3.75	-4.51	1.53	6.65

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