



**DISSENY I SÍNTESE DE L·LIGANDS I  
COMPLEXOS DE PLATÍ I ESTUDI  
DE LA SEVA ACTIVITAT  
ANTITUMORAL**

TESI DOCTORAL

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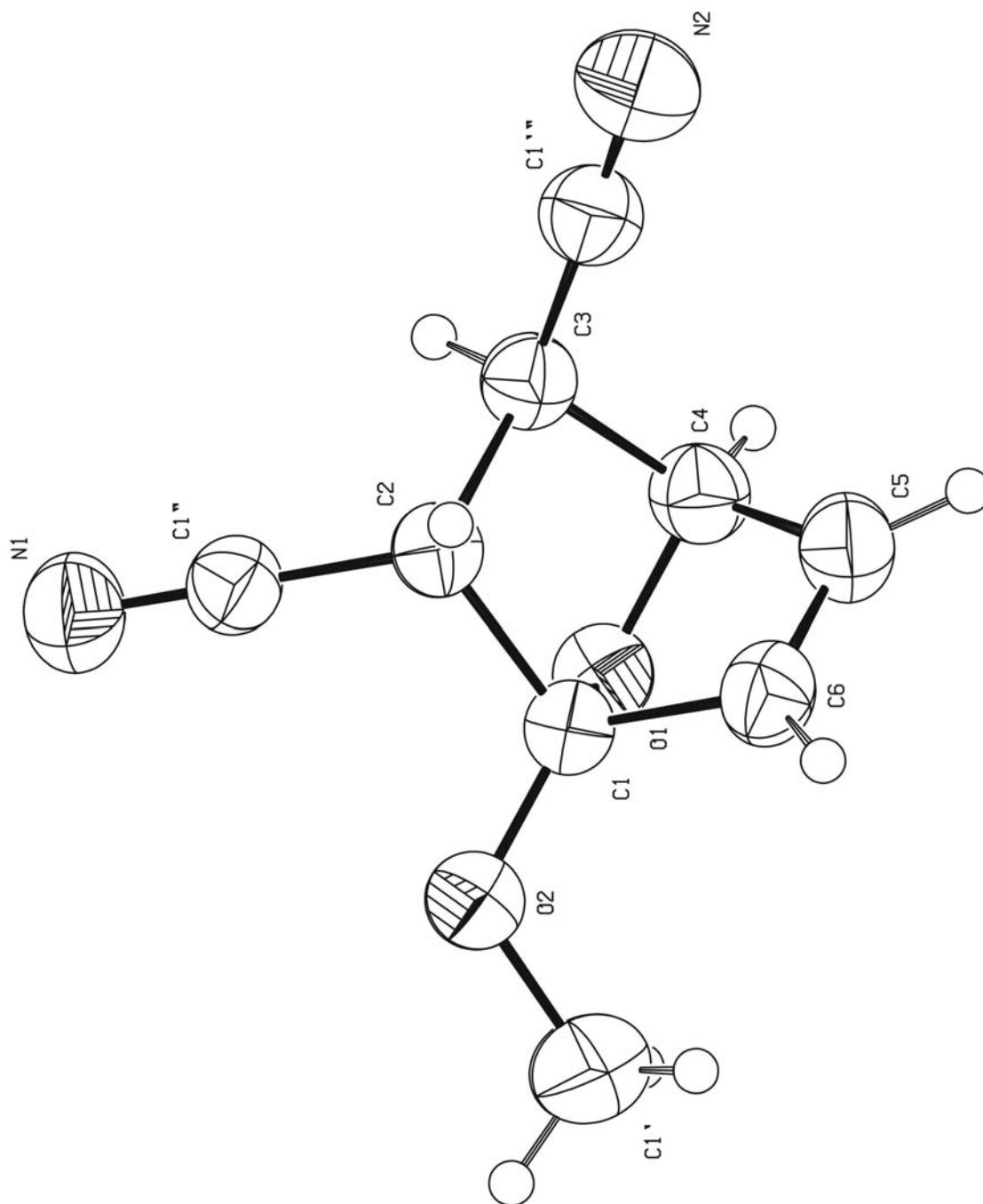
Febrer de 2007

## **APÈNDIXS**



APÈNDIX I.-DADES CRISTAL·LOGRÀFIQUES

A continuació es descriuen les característiques cristal·logràfiques obtingudes per als compostos **83** i **88**.



83

Dades cristal·logràfiques i de refinament del compost **83**:

Empirical formula	C <sub>9</sub> H <sub>8</sub> N <sub>2</sub> O <sub>2</sub>
Formula weight	176.17
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Orthorhombic, Pbca
Unit cell dimensions	a = 8.052(4) Å   α = 90 °. b = 11.593(4) Å   β = 90 °. c = 18.627(7) Å   γ = 90 °.
Volume	1738.8(12) Å <sup>3</sup>
Z, Calculated density	8, 1.346 Mg/m <sup>3</sup>
Absorption coefficient	0.098 mm <sup>-1</sup>
F(000)	736
Crystal size	0.2 x 0.1 x 0.1 mm
Theta range for data collection	3.51 to 29.98 °.
Limiting indices	0 ≤ h ≤ 10, 0 ≤ k ≤ 16, 0 ≤ l ≤ 25
Reflections collected / unique	2354 / 2354 [R(int) = 0.0510]
Completeness to theta = 29.98	92.9 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	2354 / 5 / 118
Goodness-of-fit on F <sup>2</sup>	1.157
Final R indices [I > 2σ(I)]	R1 = 0.0542, wR2 = 0.1499
R indices (all data)	R1 = 0.0581, wR2 = 0.1539
Largest diff. peak and hole	0.238 and -0.337 e.Å <sup>-3</sup>

Taula V.1. Longituds d'enllaç [Å] i angles [°] obtinguts per al compost **83**.

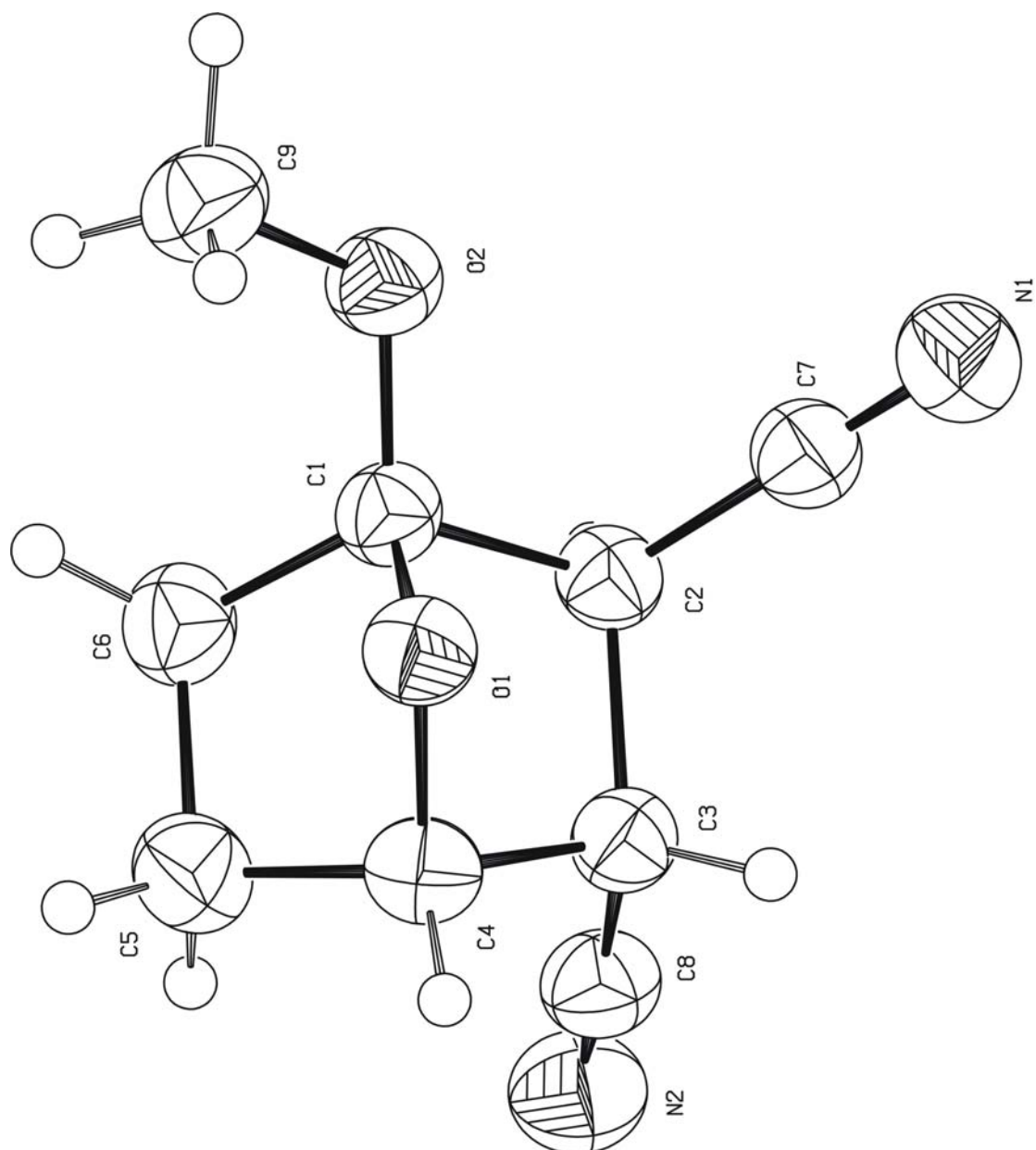
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O(1)-C(4)	1.4298(16)
O(1)-C(1)	1.4499(14)
O(2)-C(1)	1.3597(15)
O(2)-C(1')	1.4166(19)
N(1)-C(1'')	1.1438(19)
N(2)-C(1''')	1.142(2)
C(1)-C(6)	1.5158(18)
C(1)-C(2)	1.5800(16)
C(2)-C(1'')	1.4586(18)
C(2)-C(3)	1.5638(18)
C(3)-C(1''')	1.4616(18)
C(3)-C(4)	1.5812(18)
C(4)-C(5)	1.507(2)
C(5)-C(6)	1.329(2)
C(4)-O(1)-C(1)	96.62(9)
C(1)-O(2)-C(1')	115.50(12)
O(2)-C(1)-O(1)	112.81(10)
O(2)-C(1)-C(6)	121.48(10)
O(1)-C(1)-C(6)	102.12(9)
O(2)-C(1)-C(2)	111.74(9)
O(1)-C(1)-C(2)	99.85(9)
C(6)-C(1)-C(2)	106.34(10)
C(1'')-C(2)-C(3)	111.83(10)
C(1'')-C(2)-C(1)	110.53(10)
C(3)-C(2)-C(1)	100.76(9)
C(1''')-C(3)-C(2)	113.32(10)
C(1''')-C(3)-C(4)	114.88(11)
C(2)-C(3)-C(4)	100.61(9)
O(1)-C(4)-C(5)	103.02(11)
O(1)-C(4)-C(3)	99.50(10)
C(5)-C(4)-C(3)	107.06(11)
C(6)-C(5)-C(4)	105.96(12)
C(5)-C(6)-C(1)	105.58(12)
N(1)-C(1'')-C(2)	178.92(15)
N(2)-C(1''')-C(3)	179.23(16)

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Taula V.2. Longituds [Å] i angles [°] d'enllaç per als enllaços C-H del compost **83**.

C(2)-H(2)	0.9800
C(3)-H(3)	0.9800
C(4)-H(4)	0.9800
C(5)-H(5)	0.9300
C(6)-H(6)	0.9300
C(1')-H(1A)	0.9600
C(1')-H(1B)	0.9600
C(1')-H(1C)	0.9600
C(1'')-C(2)-H(2)	111.1
C(3)-C(2)-H(2)	111.1
C(1)-C(2)-H(2)	111.1
C(1''')-C(3)-H(3)	109.2
C(2)-C(3)-H(3)	109.2
C(4)-C(3)-H(3)	109.2
O(1)-C(4)-H(4)	115.2
C(5)-C(4)-H(4)	115.2
C(3)-C(4)-H(4)	115.2
C(6)-C(5)-H(5)	127.0
C(4)-C(5)-H(5)	127.0
C(5)-C(6)-H(6)	127.2
C(1)-C(6)-H(6)	127.2
O(2)-C(1')-H(1A)	109.5
O(2)-C(1')-H(1B)	109.5
H(1A)-C(1')-H(1B)	109.5
O(2)-C(1')-H(1C)	109.5
H(1A)-C(1')-H(1C)	109.5
H(1B)-C(1')-H(1C)	109.5



88



Dades cristal·logràfiques i de refinament del compost **88**:

Empirical formula	C <sub>9</sub> H <sub>10</sub> N <sub>2</sub> O <sub>2</sub>
Formula weight	178.19
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2 <sub>1</sub> /c
Unit cell dimensions	a = 5.479(4) Å    α = 90 °. b = 7.105(3) Å    β = 94.50(3) °. c = 22.646(13) Å    γ = 90 °.
Volume	878.9(9) Å <sup>3</sup>
Z, Calculated density	4, 1.347 Mg/m <sup>3</sup>
Absorption coefficient	0.097 mm <sup>-1</sup>
F(000)	376
Crystal size	0.2 x 0.1 x 0.1 mm
Theta range for data collection	3.01 to 29.98 °.
Limiting indices	-6<=h<=7, -8<=k<=9, -30<=l<=30
Reflections collected / unique	6544 / 2029 [R(int) = 0.0396]
Completeness to theta = 29.98	79.3 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	2029 / 12 / 118
Goodness-of-fit on F <sup>2</sup>	1.229
Final R indices [I>2σ(I)]	R1 = 0.0490, wR2 = 0.1364
R indices (all data)	R1 = 0.0502, wR2 = 0.1374
Largest diff. peak and hole	0.221 and -0.339 e.Å <sup>-3</sup>

Taula V.3. Longituds d'enllaç [Å] i angles [°] obtinguts per al compost **88**.

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O(1)-C(4)	1.4360(14)
O(1)-C(1)	1.4437(14)
O(2)-C(1)	1.3760(13)
O(2)-C(9)	1.4363(15)
N(1)-C(7)	1.1474(17)
N(2)-C(8)	1.1302(18)
C(1)-C(6)	1.5380(18)
C(1)-C(2)	1.5457(15)
C(2)-C(7)	1.4653(17)
C(2)-C(3)	1.5615(15)
C(3)-C(8)	1.4812(18)
C(3)-C(4)	1.5531(16)
C(4)-C(5)	1.5184(19)
C(5)-C(6)	1.5361(19)
C(4)-O(1)-C(1)	96.71(9)
C(1)-O(2)-C(9)	116.19(10)
O(2)-C(1)-O(1)	112.78(9)
O(2)-C(1)-C(6)	118.61(9)
O(1)-C(1)-C(6)	103.56(10)
O(2)-C(1)-C(2)	110.34(9)
O(1)-C(1)-C(2)	100.35(8)
C(6)-C(1)-C(2)	109.51(9)
C(7)-C(2)-C(1)	109.88(9)
C(7)-C(2)-C(3)	111.23(9)
C(1)-C(2)-C(3)	100.45(9)
C(8)-C(3)-C(4)	113.40(9)
C(8)-C(3)-C(2)	112.55(9)
C(4)-C(3)-C(2)	101.35(9)
O(1)-C(4)-C(5)	102.06(10)
O(1)-C(4)-C(3)	101.78(9)
C(5)-C(4)-C(3)	111.53(10)
C(4)-C(5)-C(6)	100.91(10)
C(5)-C(6)-C(1)	101.94(10)
N(1)-C(7)-C(2)	178.12(13)
N(2)-C(8)-C(3)	178.50(13)

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Taula V.4. Longituds [Å] i angles [°] d'enllaç per als enllaços C-H del compost **88**.

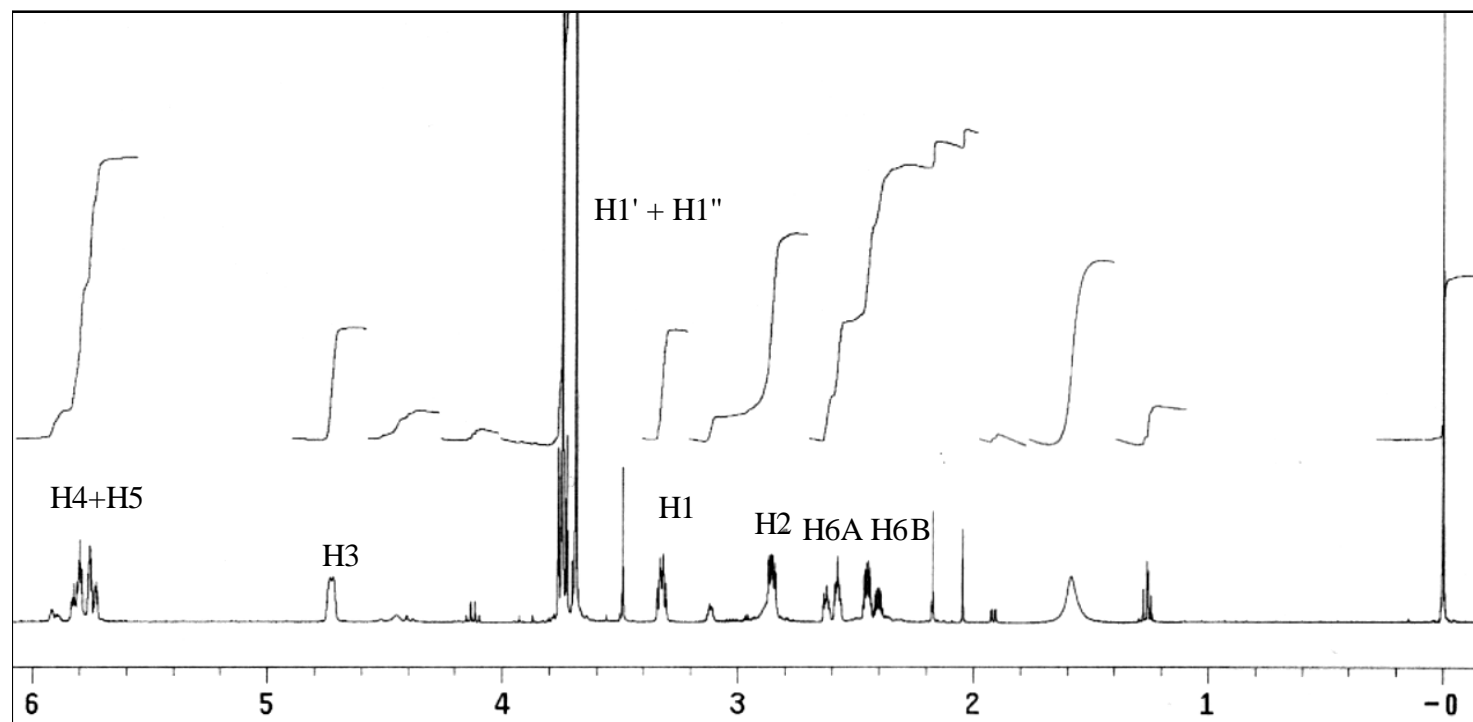
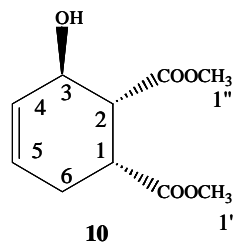
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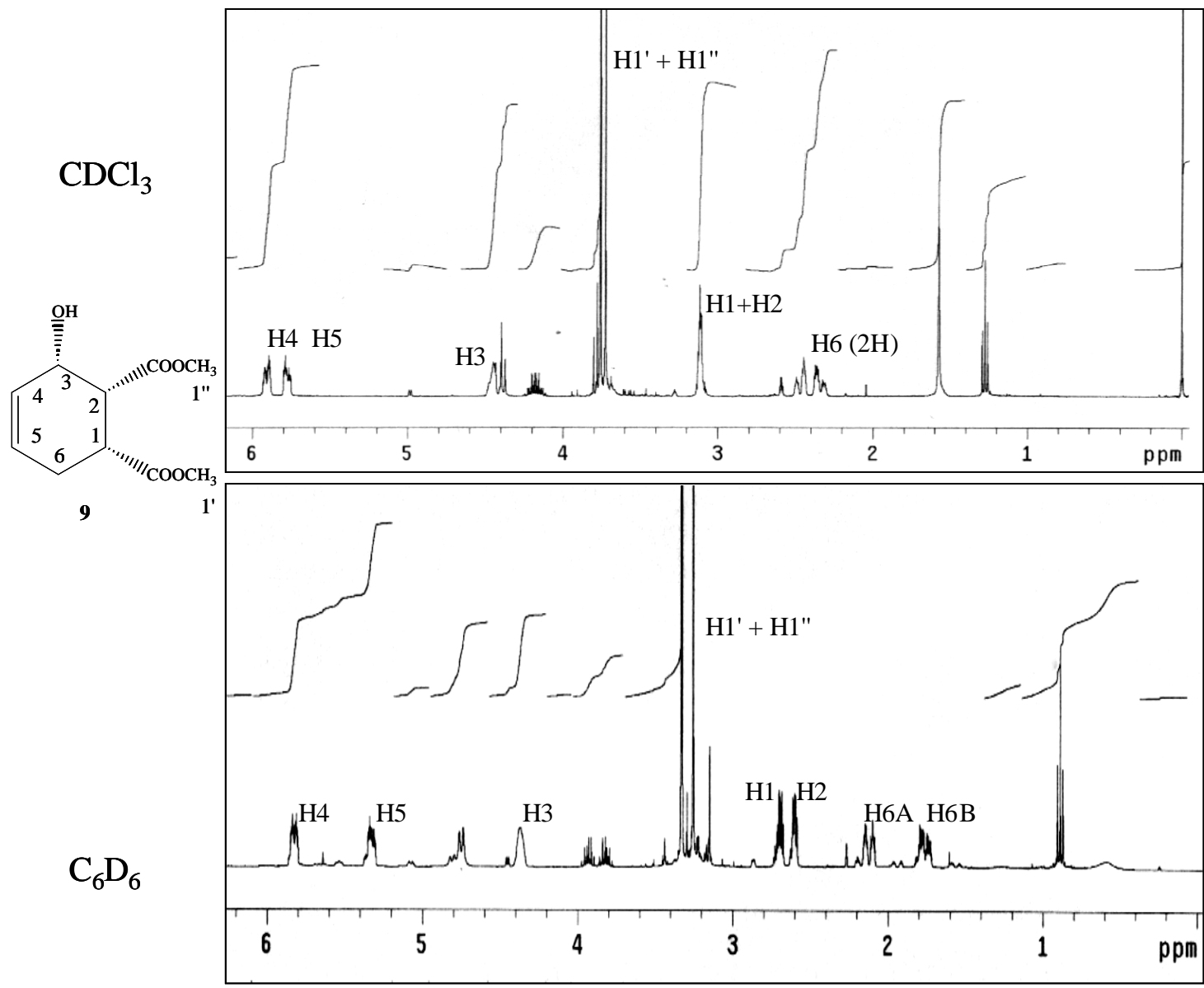
C(3)-H(3)	0.9800
C(4)-H(4)	0.9800
C(2)-H(2)	0.9800
C(5)-H(5A)	0.9700
C(5)-H(5B)	0.9700
C(6)-H(6A)	0.9700
C(6)-H(6B)	0.9700
C(9)-H(9A)	0.9600
C(9)-H(9B)	0.9600
C(9)-H(9C)	0.9600
C(7)-C(2)-H(2)	111.6
C(1)-C(2)-H(2)	111.6
C(3)-C(2)-H(2)	111.6
C(8)-C(3)-H(3)	109.8
C(4)-C(3)-H(3)	109.8
C(2)-C(3)-H(3)	109.8
O(1)-C(4)-H(4)	113.4
C(5)-C(4)-H(4)	113.4
C(3)-C(4)-H(4)	113.4
C(4)-C(5)-H(5A)	111.6
C(6)-C(5)-H(5A)	111.6
C(4)-C(5)-H(5B)	111.6
C(6)-C(5)-H(5B)	111.6
H(5A)-C(5)-H(5B)	109.4
C(5)-C(6)-H(6A)	111.4
C(1)-C(6)-H(6A)	111.4
C(5)-C(6)-H(6B)	111.4
C(1)-C(6)-H(6B)	111.4
H(6A)-C(6)-H(6B)	109.2
O(2)-C(9)-H(9A)	109.5
O(2)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
O(2)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5

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## APÈNDIX II.-COMPARACIÓ DELS ESPECTRES DE RMN DE $^1\text{H}$ DELS PRODUCTES **9** I **10**

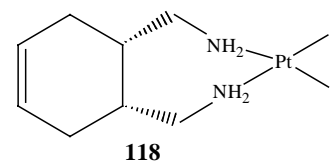
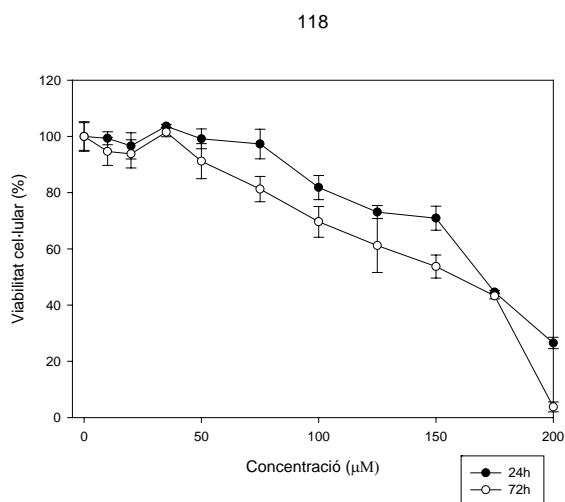
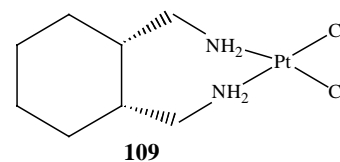
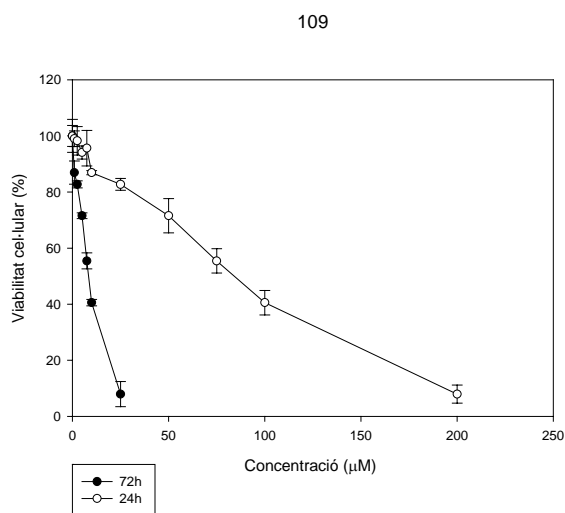
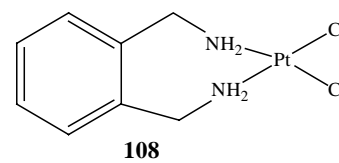
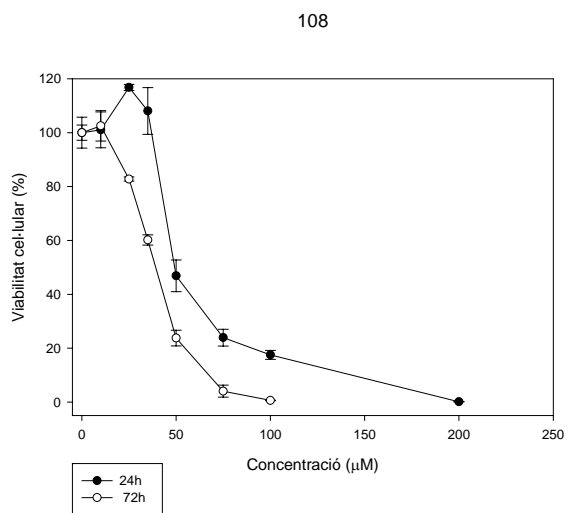
A continuació es mostren els espectres de RMN de  $^1\text{H}$  en  $\text{CDCl}_3$  dels alcohols diastereomèrics **9** i **10**, amb l'assignació de senyals obtinguda a partir de l'espectroscòpia bidimensional. En el cas del producte **9**, també es compara el seu espectre obtingut en  $\text{C}_6\text{D}_6$ , dissolvent en el que s'observa una millor separació dels senyals.

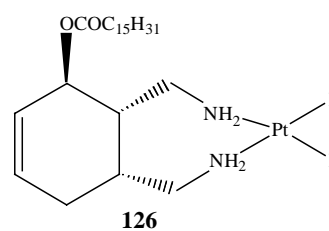
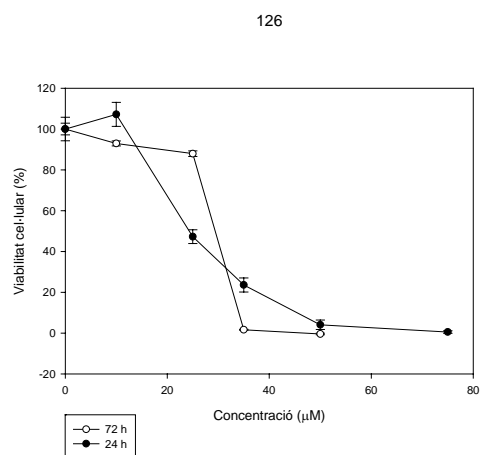
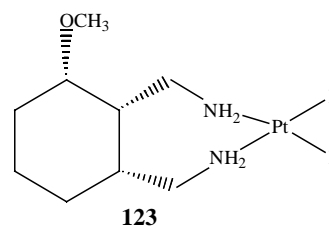
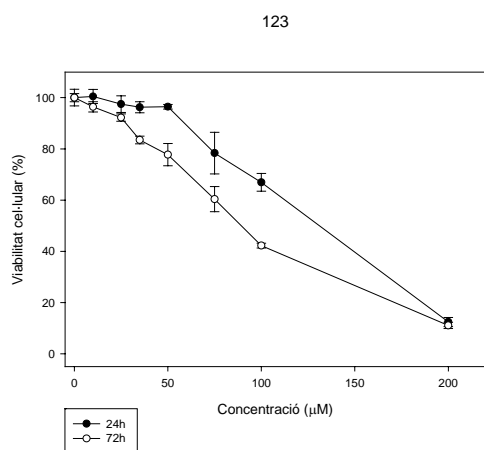
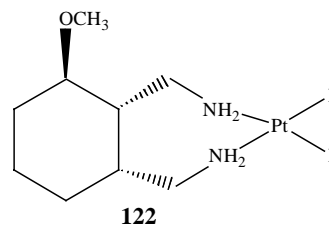
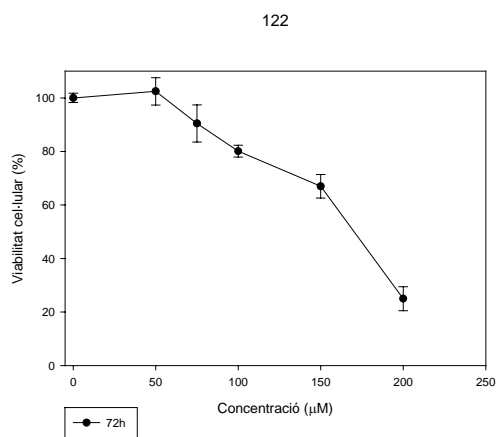
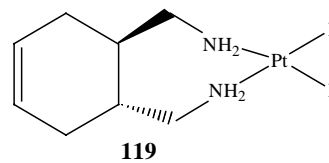
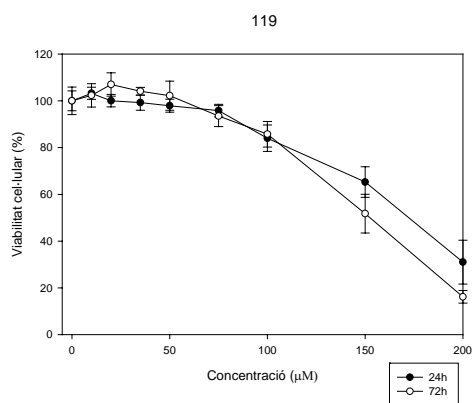




APÈNDIX III.-CORBES DE VIABILITAT CEL·LULAR

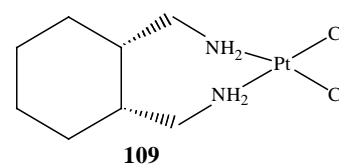
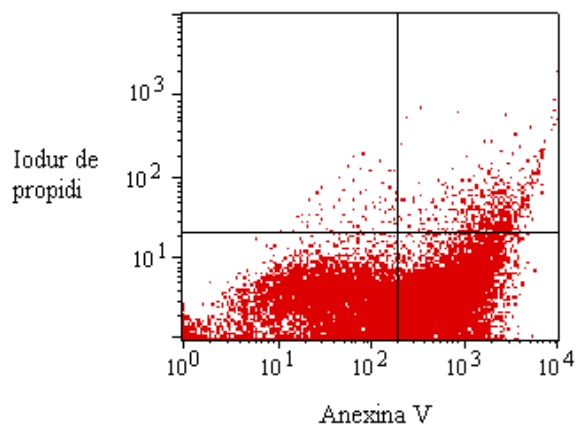
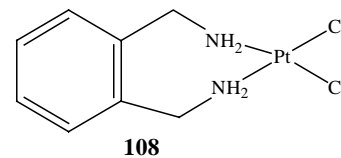
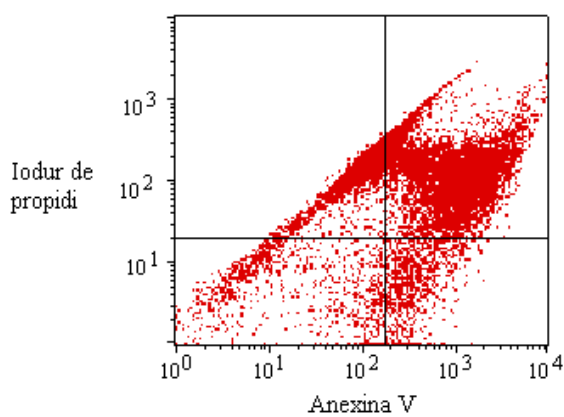
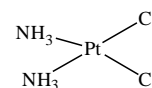
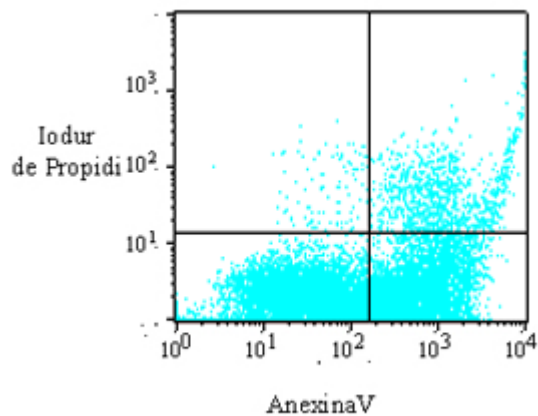
A continuació es mostren les corbes de viabilitat cel·lular per als compostos que han mostrat millors activitats biològiques *in vitro* (108, 109, 118, 119, 122, 123 i 126).



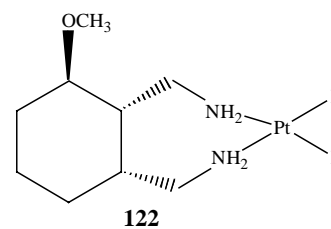
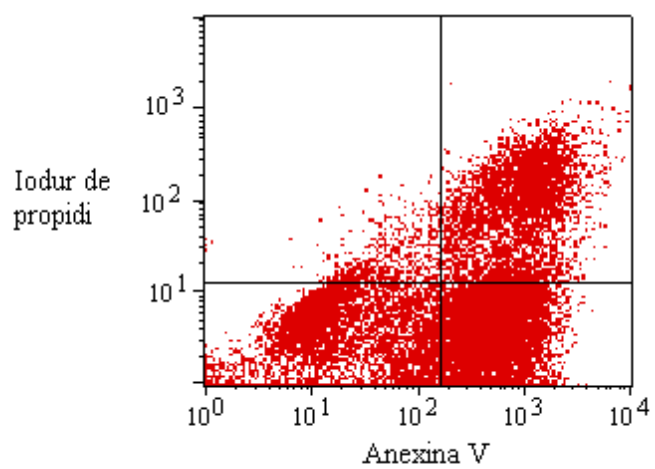
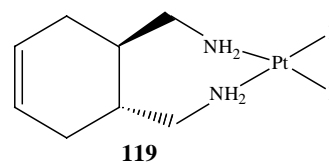
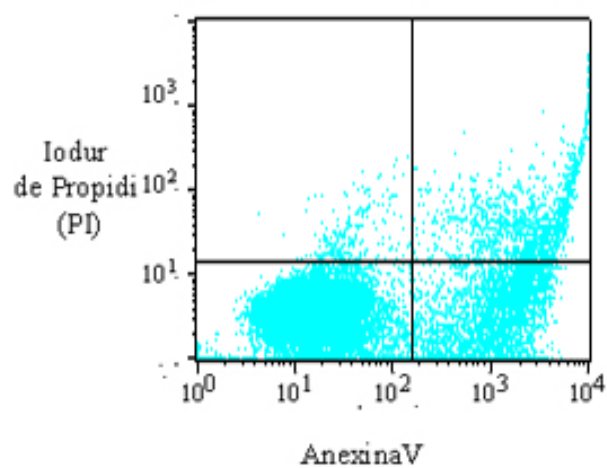
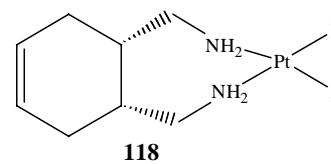
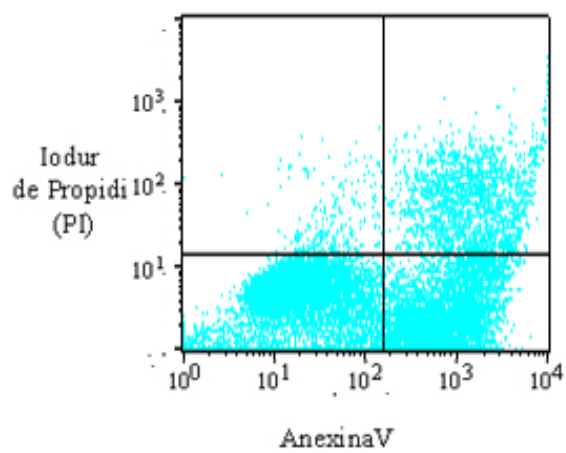


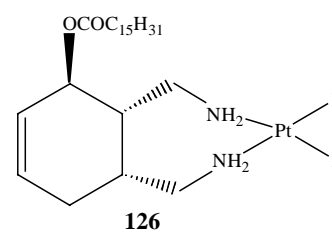
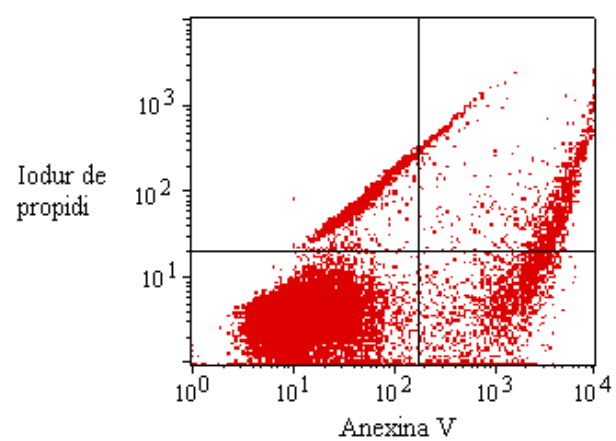
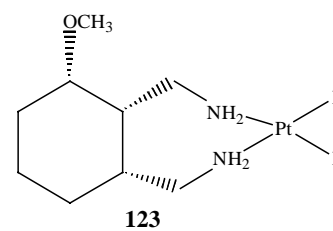
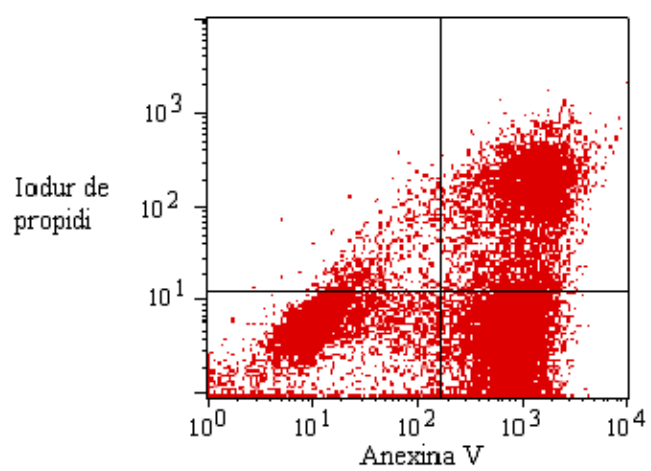
APÈNIDX IV.-CITOGAMES DE FLUX

A continuació es mostren els citogrames de flux obtinguts per al cisplatí i els compostos **108**, **109**, **118**, **119**, **122**, **123** i **126**.













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