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Supporting Information

N-Heterocyclic Carbene (NHC) Silver Complexes as Versatile Chemotherapeutic Agents Targeting Human Topoisomerases and Actin

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Supporting Information

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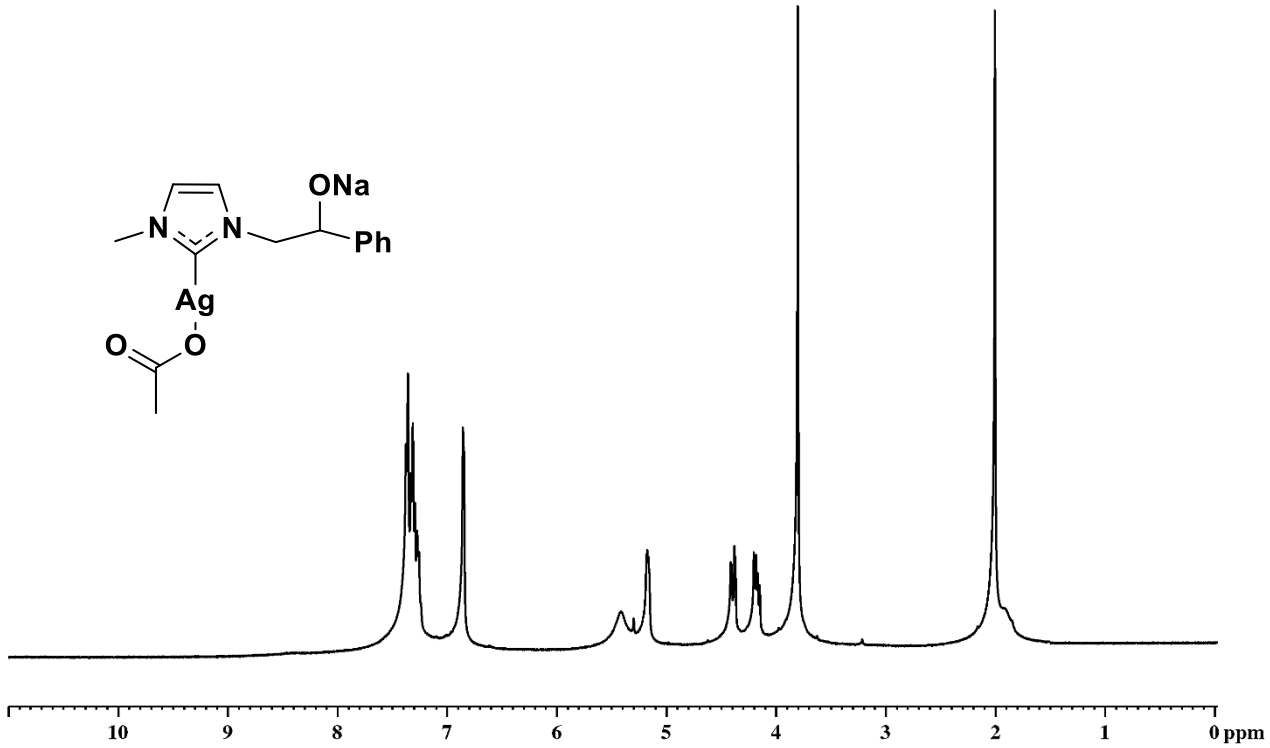
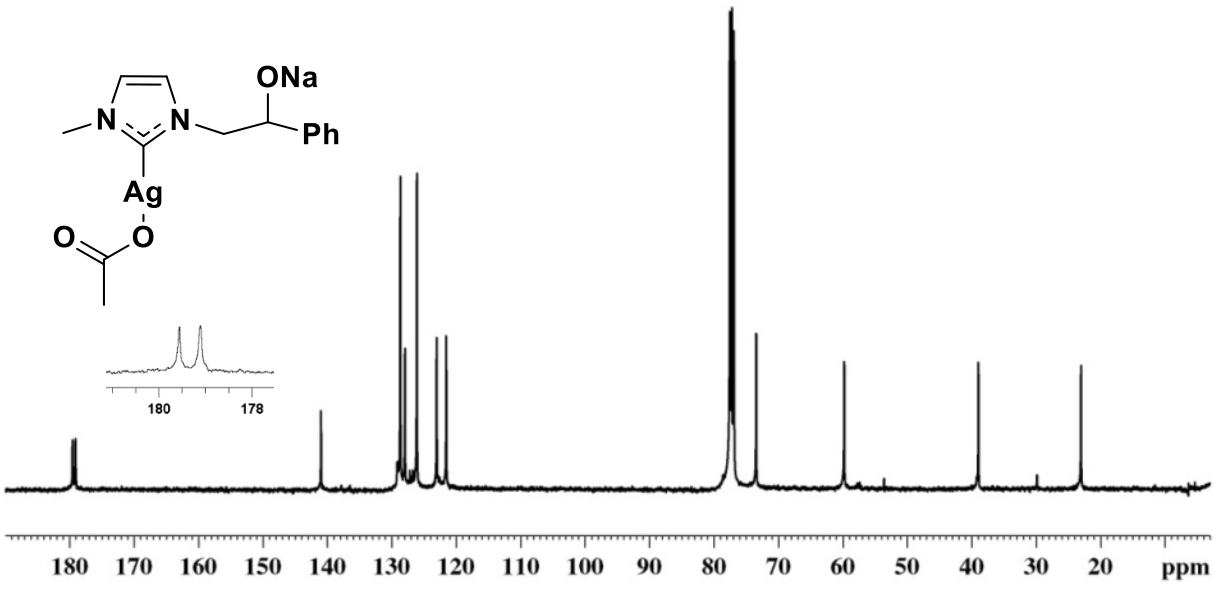
A: Bis[(N-methyl, N'-[(2-sodium alcoholate-2-phenyl-ethyl)imidazole-2-ylidine]silver(I)] acetate (2)

^{1}H-NMR of 2



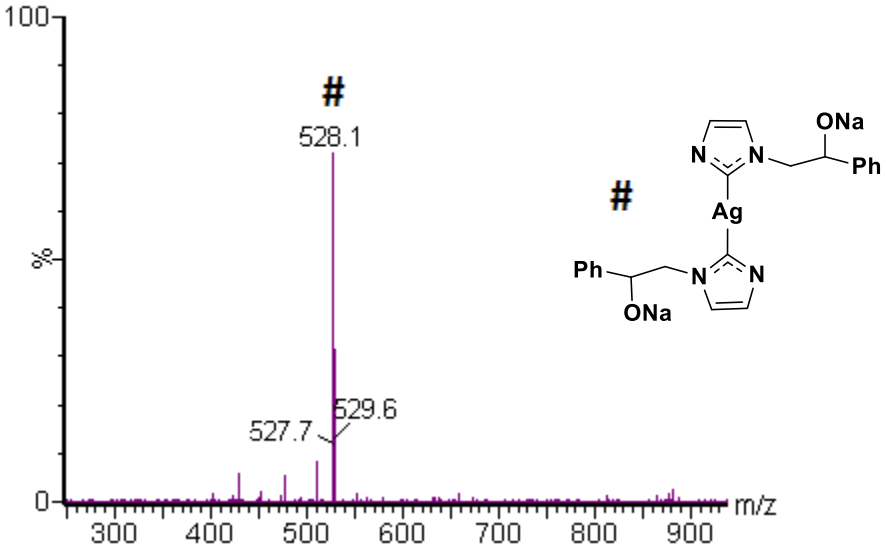
^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.32 (m, 5H, aromatic protons); 6.86 (d, 2H, NC*HCH*N); 5.19 (s, 1H, C*H*O^-); 4.40 (dd, 1H, NCH_2); 4.18 (dd, 1H, NCH_2); 3.80 (s, 3H, NCH_3); 2.01 (s, 3H, OCOCH_3).

^{13}C-NMR of 2



$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 179.5 (N*C*N), 179.0 (*C*=O), 140.9 (*ipso* carbon aromatic ring), 128.6, 127.9, 126.1, (aromatic carbons), 123.0 (N*C*HCHN), 121.5 (NCH*C*HN), 73.4 (*C*HO^-), 59.7 (N*C*H_2), 38.9 (N*C*H_3), 23.0 (CO*C*H_3).

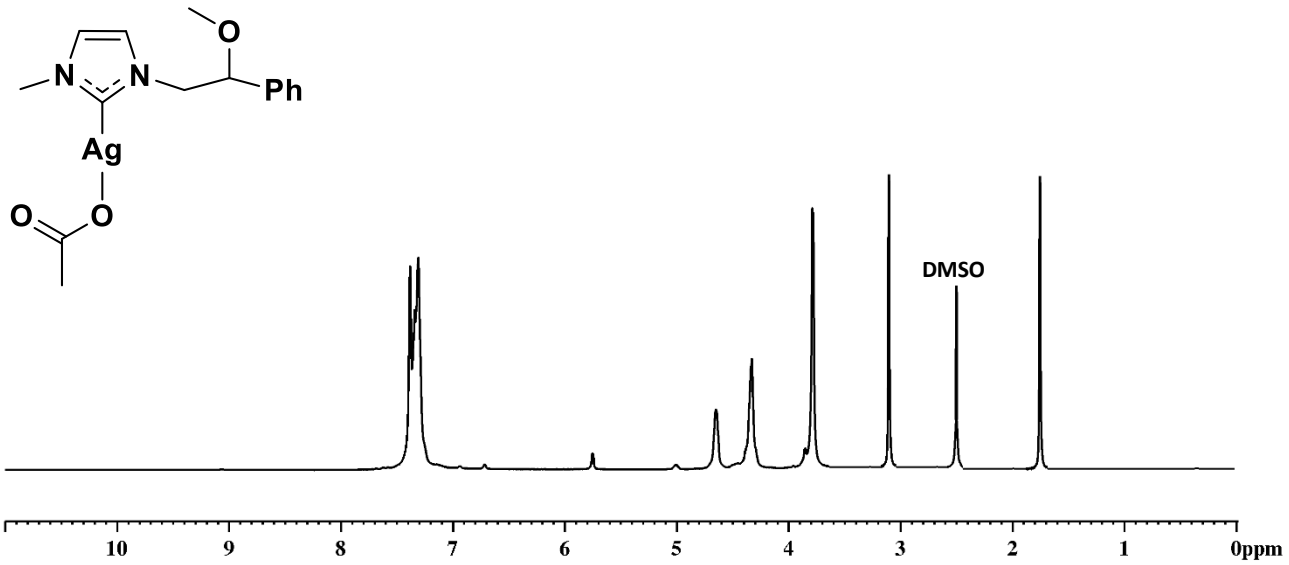
ESI-MS



ESI-MS = 528.1 attributable to $[C_{22}H_{20}AgN_4Na_2O_2]^+$

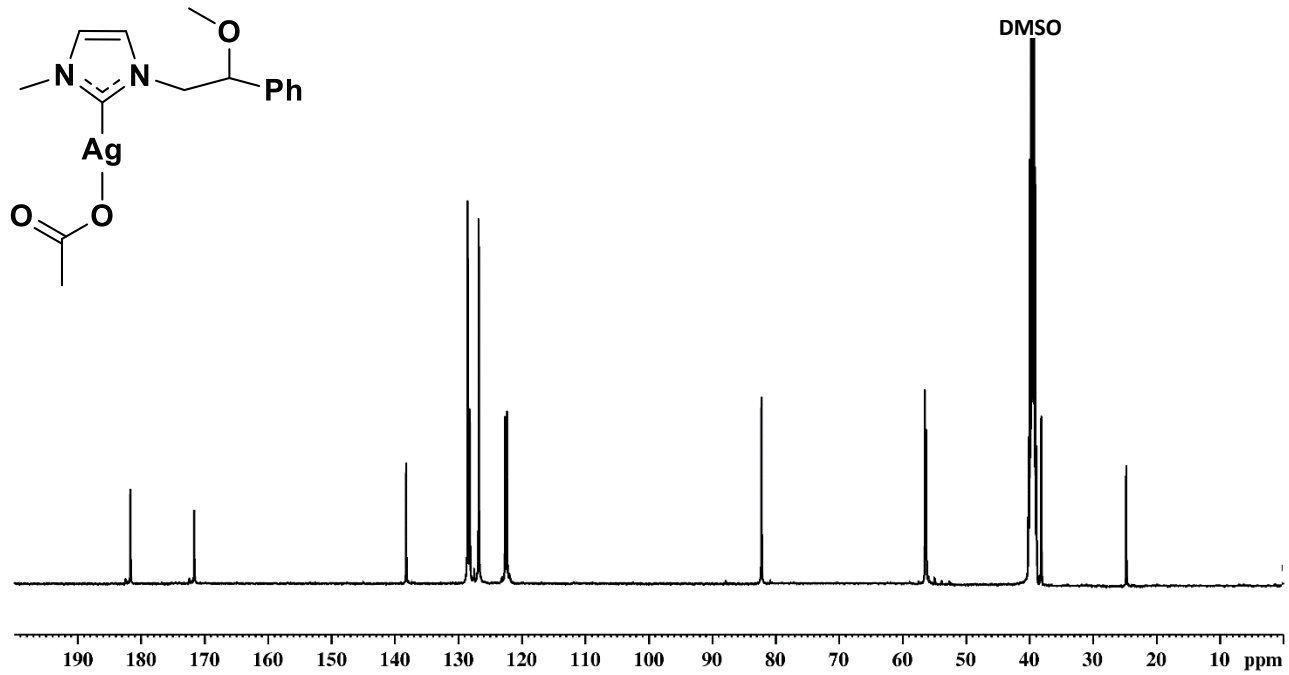
B: Bis[(N-methyl, N'-[(2-methoxy-2-phenyl-ethyl)imidazole-2-ylidine]silver(I)] acetate (4)

^{1}H-NMR of 4



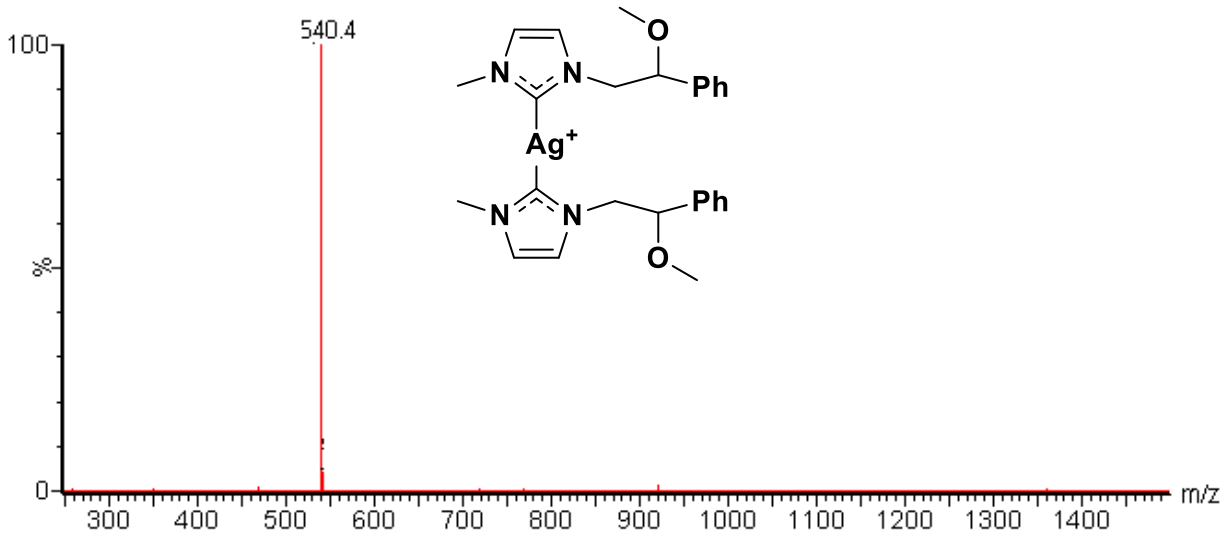
^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.34-7.26 (m, 7H, aromatic protons), 4.60 (m, 1H, OC*H*), 4.30-4.27 (m, 2H, NCH_2), 3.74 (s, 3H, NCH_3), 3.07 (s, 3H, OCH_3), 1.98 (s, 3H, CH_3COO).

^{13}C-NMR of 4



^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6): δ 182.7 (N*C*N), 173.4 (CH_3*C*OO) 137.2 (*ipso* carbon of *Ph ring*), 128.7, 128.3, 126.6 (aromatic carbons, *Ph* ring), 122.6, 122.3 (*backbone carbons C=C*), 83.3 (*C*HO), 56.7 (NCH_2), 54.2 (OCH_3), 38.2 (NCH_3), 24.1 (*C*H_3COO).

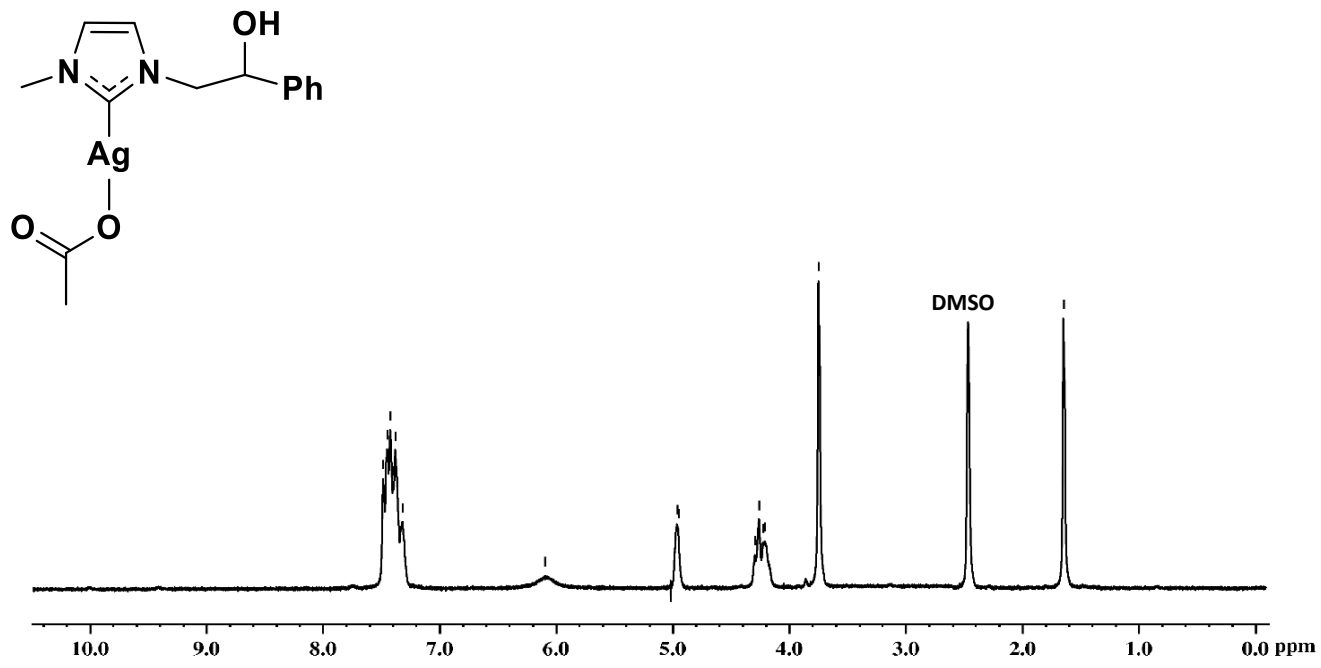
ESI-MS of 4



ESI-MS = 540.4 attributable to $[C_{26}H_{32}AgN_4O_2]^+$

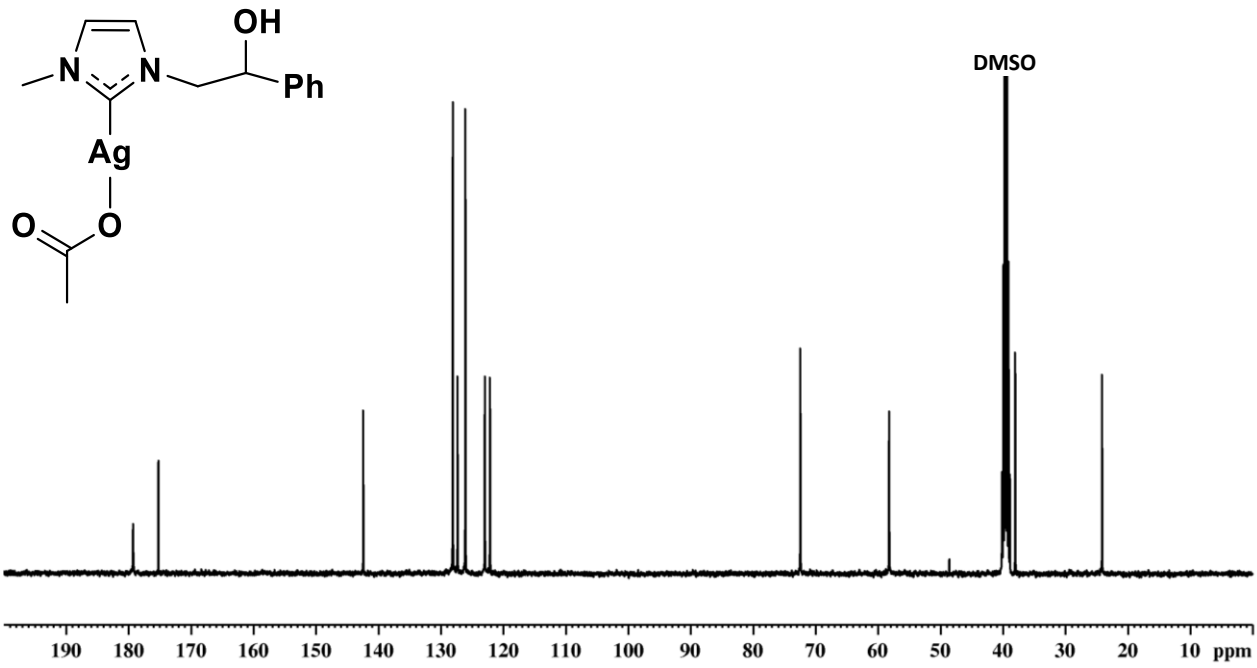
C: Bis [N-methyl, N'-[(2-hydroxy-2-phenyl-ethyl)imidazole-2-ylidine]silver(I)] acetate (5)

^{1}H-NMR of 5



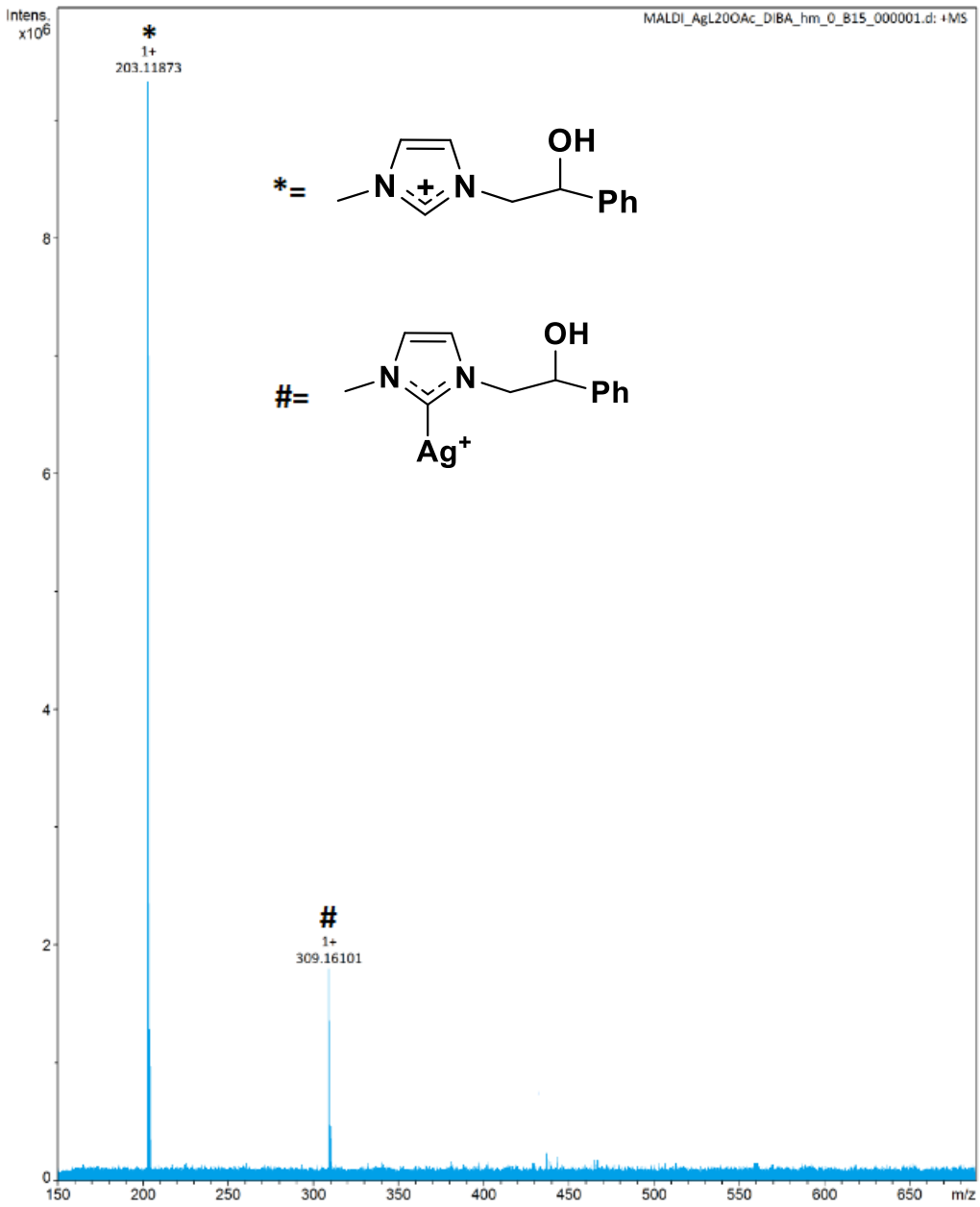
^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.41-7.24 (m, 7H, aromatic protons), 6.05 (b, 1H, O*H*) 4.94 (m, 1H, OC*H*), 4.29 – 4.21 (m, 2H, NCH_2), 3.75 (s, 3H, NCH_3), 1.73 (s, 3H, CH_3COO).

^{13}C-NMR of 5



$^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ 179.3 (N*C*N), 175.2 (CH_3*C*OO) 142.4 *(ipso carbon of Ph ring*), 128.1, 127.3, 126.0 (*aromatic carbons*, *Ph* ring), 122.9, 122.1 (*backbone carbon C=C*), 72.4 (O*C*H), 58.2 (N*C*H_2), 38.0 (N*C*H_3), 24.1 (*C*H_3*C*OO).

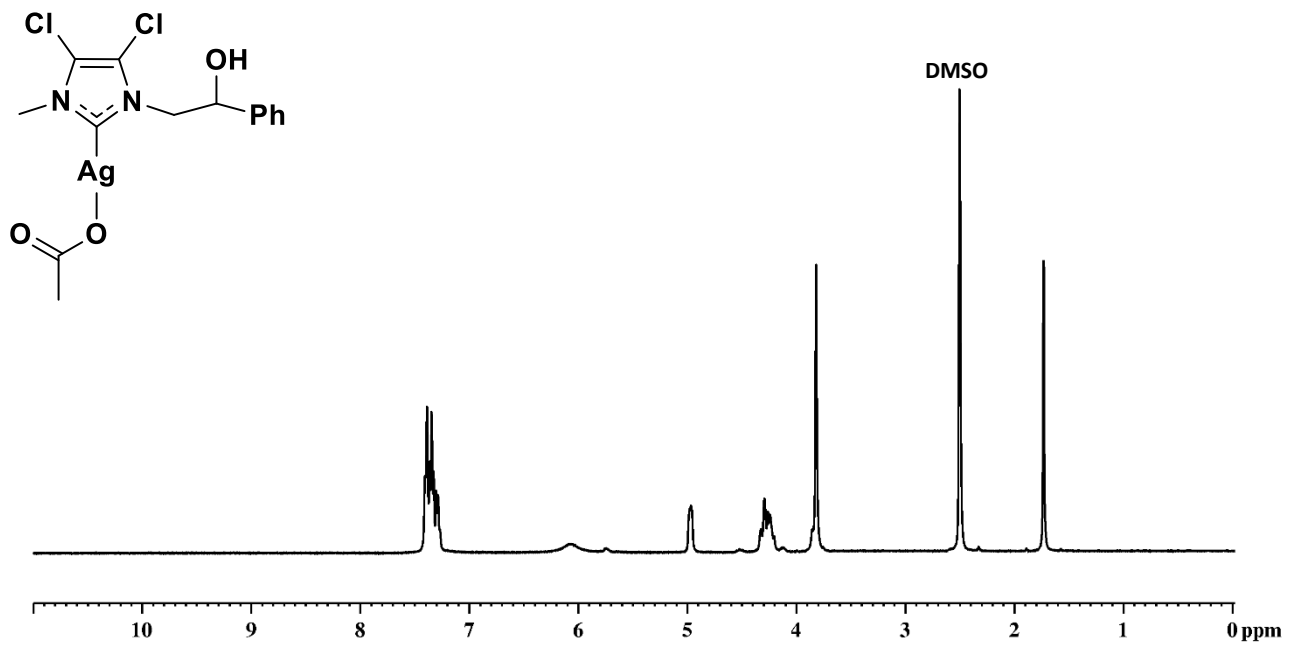
MALDI-MS of 5



MALDI-MS = 309.16101 Dalton attributable to $[C_{12}H_{14}AgN_2O]^+$, 203.11873 Dalton attributable to $[C_{12}H_{15}N_2O]^+$.

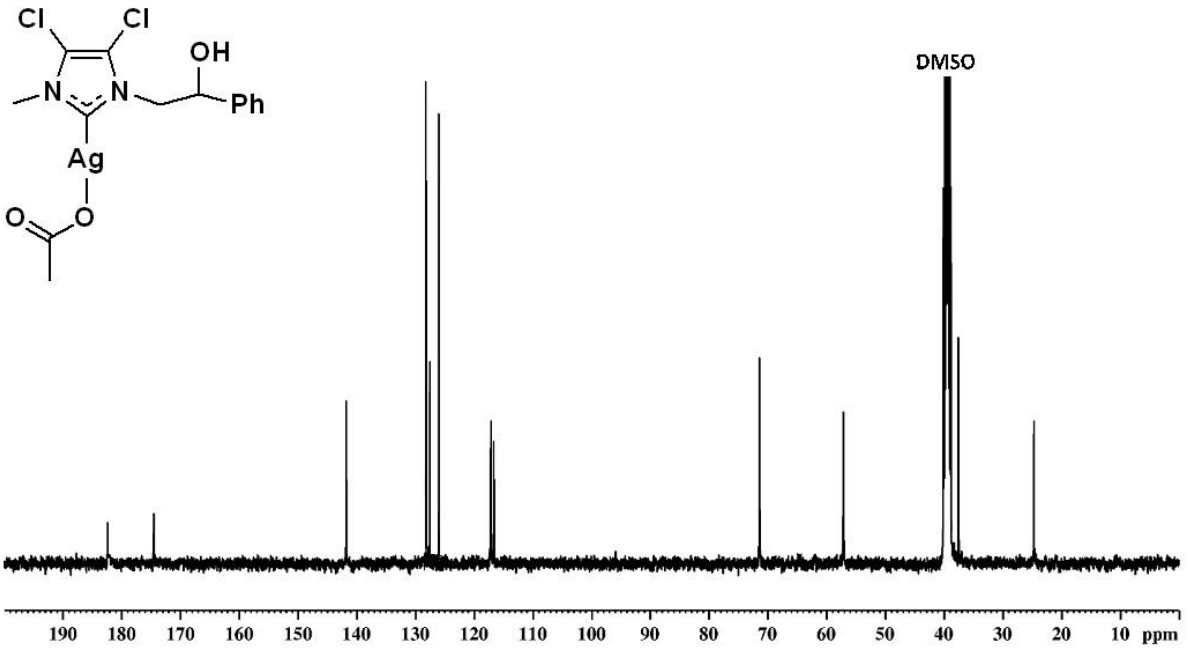
D: Bis[4,5-dichloro-[(N-methyl-N'(2-hydroxy-2-phenyl-ethyl)imidazole-2-ylidene]silver(I)] acetate (6)

^{1}H-NMR of 6



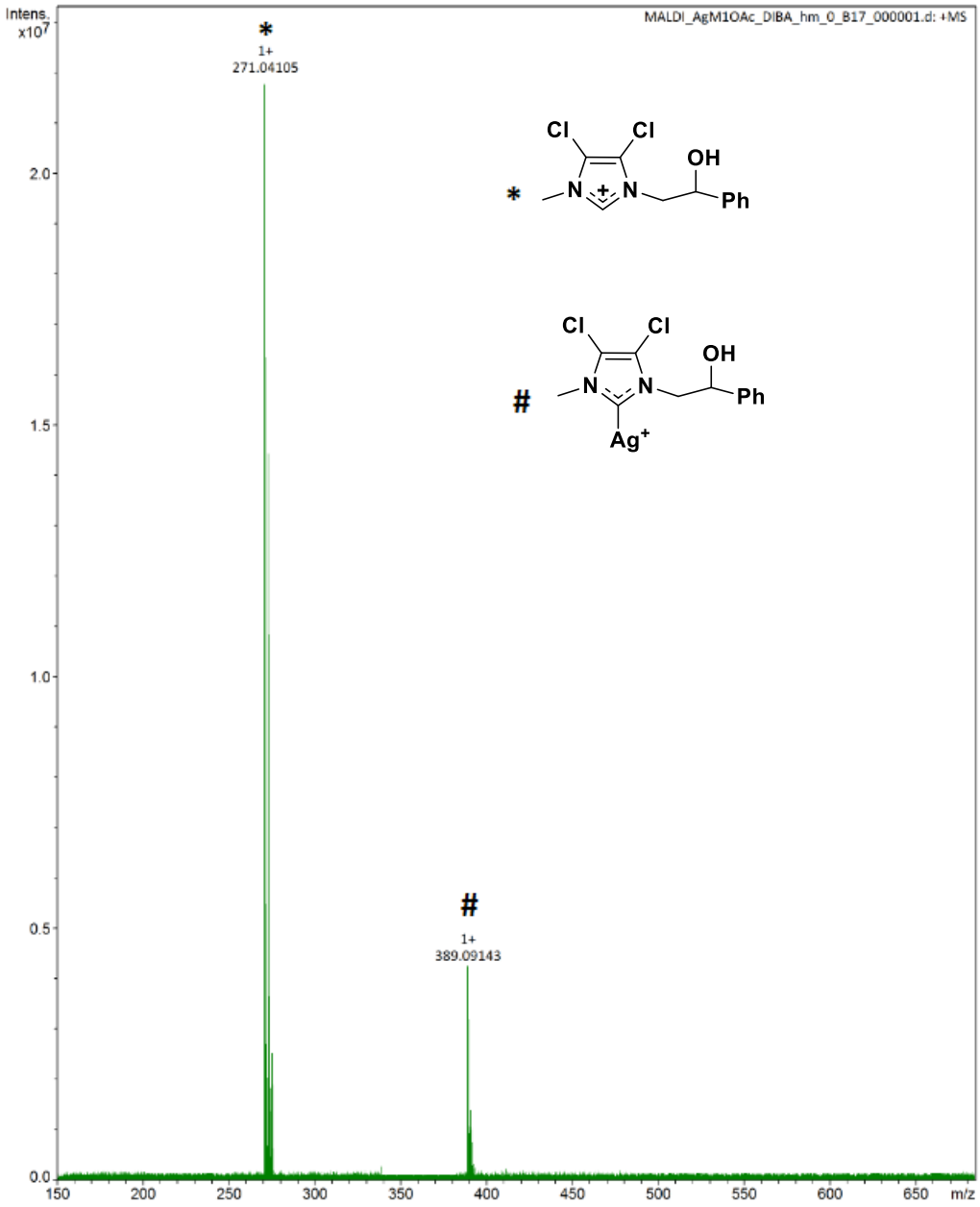
^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.40-7.28 (m, 5H, aromatic protons), 6.05, (b, 1H, O*H*) 4.95 (m, 1H, OC*H*), 4.32 – 4.23 (m, 2H, NCH_2), 3.81 (s, 3H, NCH_3), 1.73 (s, 3H, CH_3COO).

^{13}C-NMR of 6



$^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6): δ 182.2 (N*C*N), 174.5 (CH_3*C*OO), 141.7 *(ipso carbon* of Ph ring), 128.2, 127.5, 126.0, (*aromatic carbons*, *Ph* ring), 117.1, 116.6 (*backbone carbon C*=*C*), 71.4 (O*C*H), 57.1 (N*C*H_2), 37.5 (N*C*H_3), 24.7 (CH_3*C*OO).

MALDI of 6



MALDI-MS = 389.09143 Dalton attributable to $[C_{12}H_{12}AgCl_2N_2O]^+$, 271.04105 Dalton attributable to $[C_{12}H_{13}Cl_2N_2O]^+$.

E: Computational details relative to calculations on Ag and Au complexes and BDE of NHC and halogen ligands.

The DFT calculations were performed with the Gaussian09 set of programs,[1] using the PBE0 model.[2] The electronic configuration of the molecular systems was described with 6-311G(d,p) basis set for H, C, N, O, and Cl.[3] For Ag and I we used the small-core, quasi-relativistic Stuttgart/Dresden effective core potential, with an associated (8s7p6d)/[6s5p3d] valence basis set contracted according to a (311111/22111/411) scheme (standard SDD keywords in gaussian09).[4] The geometry optimizations were performed without symmetry constraints and the characterization of the located stationary points was performed by analytical frequency calculations.

[1] Gaussian 09, Revision A.02, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; N. Kudin, K.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2009**.

[2] C. Adamo and V. Barone, "Toward reliable density functional methods without adjustable parameters: The PBE0 model," *J. Chem. Phys.*, **110** (1999) 6158-69.

[3] (a) A. D. McLean and G. S. Chandler, "Contracted Gaussian-basis sets for molecular calculations. 1. 2nd row atoms, Z=11-18," *J. Chem. Phys.*, **72** (1980) 5639-48. (b) K. Raghavachari, J. S. Binkley, R. Seeger, and J. A. Pople, "Self-Consistent Molecular Orbital Methods. 20. Basis set for correlated wave-functions," *J. Chem. Phys.*, **72** (1980) 650-54.

[4] a) Haeusermann, U., Dolg, M., Stoll, H. and Preuss, H. *Mol. Phys.* **1993**, *78*, 1211– 1224. b) Kuechle, W., Dolg, M., Stoll, H. and Preuss, H. *J. Chem. Phys.* **1994**, *100*, 7535– 7542. c) Leininger, T., Nicklass, A., Stoll, H., Dolg, M. and Schwerdtfeger, P. *J. Chem. Phys.* 1996, 105, 1052– 1059.

Cartesian coordinates and energies of calculated structures.

30
1 E(gas)= -807.708689321 A.U.

Ag	0.993000	-0.093009	-0.064269
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N	0.871514	3.115822	-0.017794
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C	-0.067516	4.100723	0.207457
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H	2.762447	2.312632	-0.085365
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H	-1.772020	0.657833	-1.538882
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C	3.910054	-1.708191	0.128674
O	4.274095	-0.536311	0.285987
C	4.966281	-2.815227	0.162487
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40

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H	4.344077	-2.338607	1.168317

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37
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  N      2.751464    -2.124472     0.022037
  C      0.939334    -3.329429    -0.218651
  C      2.263605    -3.415128     0.041182
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  H     -2.148704     1.409472     0.323030
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  O      1.802936     2.941486    -0.151868
  C      0.633362     3.266108     0.257500
  O     -0.256408     2.451098     0.537780
  C      0.380814     4.753050     0.376863
  H      1.173176     5.216115     0.969098
  H      0.417597     5.204362    -0.618414
  H     -0.590780     4.945752     0.830181
37
6 E(gas)= -1944.02382435 A.U.
  Ag     0.014401    -2.155348    -0.212431
  C     -1.460948    -0.713331    -0.239489
  N     -1.250458     0.610151    -0.425962
  N     -2.780548    -0.831086     0.025863
  C     -2.423328     1.316066    -0.266735
  C     -3.389712     0.405295     0.011569
  C     -3.462433    -2.082713     0.285889
  H     -3.899664    -2.074773     1.286002
  H     -4.248341    -2.246365    -0.453763
  H     -2.720785    -2.877128     0.216188
  C      0.062714     1.196180    -0.674982
  C      0.878711     1.369336     0.603564
  H      0.595928     0.542430    -1.366075
  H     -0.088151     2.165150    -1.153752
  C      2.174772     2.081024     0.285335
  O      0.052411     2.093861     1.495341
  H      1.109647     0.370462     0.998623
  Cl    -5.047023     0.637994     0.288110
  Cl    -2.575456     2.991986    -0.447662
  C      2.205130     3.473645     0.208263
  C      3.385975     4.131703    -0.110507
  C      4.543329     3.401681    -0.358214
  C      4.515499     2.014192    -0.278891
  C      3.337565     1.349398     0.044255
  H      1.300174     4.035994     0.416343
  H      3.403778     5.215583    -0.163685
  H      5.466980     3.914930    -0.605721
  H      5.419440     1.441913    -0.460967
  H      3.316993     0.264338     0.122835
  H      0.542445     2.212230     2.312199
  O      1.528650    -3.625469    -0.162633
  C      2.589205    -2.992218     0.176107
  O      2.622847    -1.776155     0.414242
  C      3.848495    -3.825417     0.250923
  H      3.642619    -4.777575     0.742911
  H      4.183022    -4.049893    -0.766192
  H      4.637147    -3.286006     0.774290
```