Electronic Supporting Information (ESI) for Dalton Transactions 2017

New organometallics imines of Rhenium (I) as potential ligands of GSK-3β: Synthesis, characterization and biological studies

Michelle Muñoz-Osses[a,c], Fernando Godoy[a,*], Angélica Fierro[b], Alejandra Gómez[a] and Nils Metzler-Nolte[c,*]

[a] Laboratory of Organometallic Chemistry, Faculty of Chemistry and Biology, Universidad de Santiago de Chile, Avenida Libertador Bernardo O'Higgins 3363. Estación Central. Santiago. Chile. E-mail: michelle.munoz@usach.cl ; fernando.godoy@usach.cl; alejandra.gomezs@usach.cl.

[b] Laboratory of Molecular Simulation, Department of Organic Chemistry, Faculty of Chemistry, Pontificia Universidad Católica de Chile, Avda. Vicuña Mackenna 4860, Macul, Santiago, Chile. E-mail: afierroh@uc.cl

[c] Inorganic Chemistry I – Bioinorganic Chemistry, Faculty of Chemistry and Biochemistry, Ruhr University Bochum, Universitätsstrasse 150, 44797 Bochum, Germany. E-mail: nils.metzler-nolte@rub.de

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Experimental Section:

1. Synthesis and characterization of new piperazine derivatives and rhenium complexes.
2. Cytotoxic studies of the new compounds in two cancer cell lines: HT-29 and PT-45.
3. Docking studies.

1. Here we shown the characterization of one family of compounds (example):

1.1. Synthesis of phenyl piperazine HNC_4H_8N (C_6H_5) (1b)

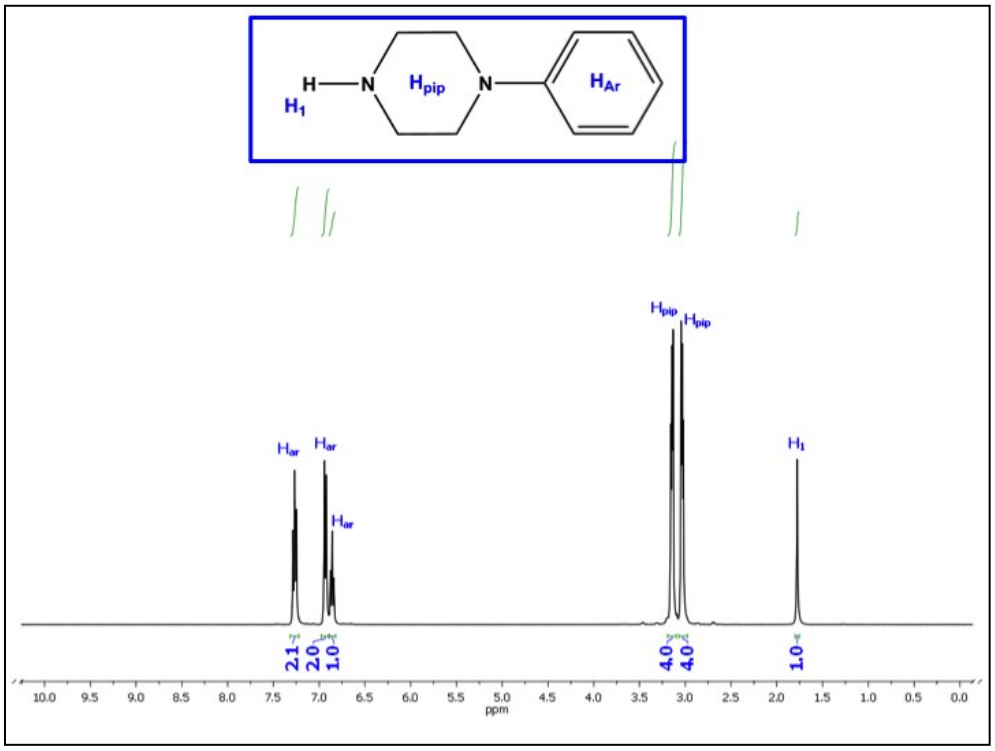


Figure 1. ^1H NMR ($CDCl_3$) cyclophenyl piperazine (**1b**).

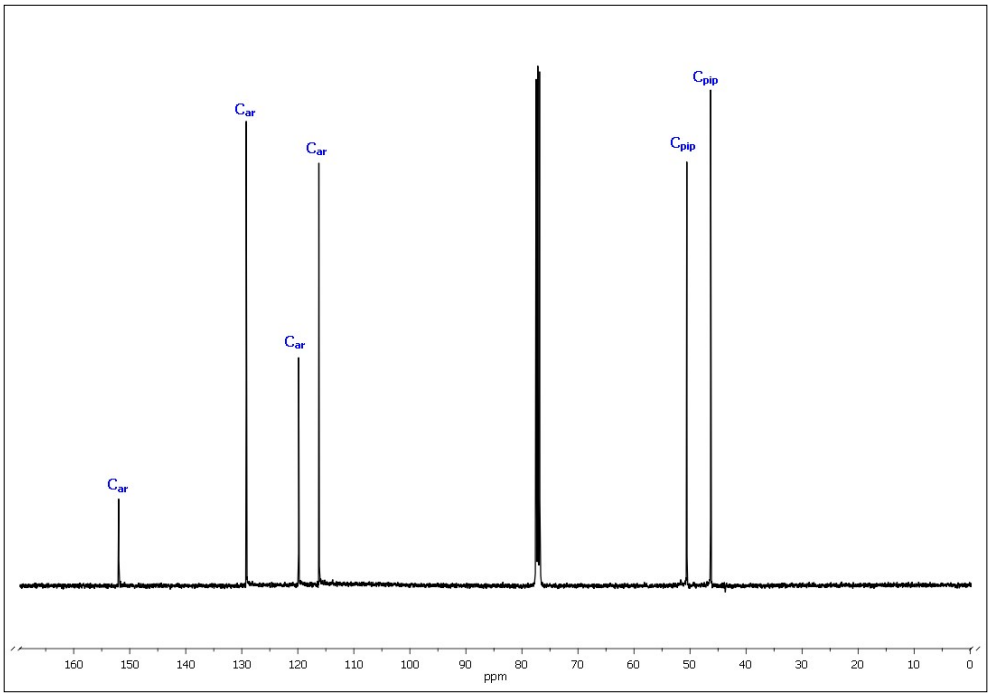


Figure 2. ^{13}C NMR ($CDCl_3$) cyclophenyl piperazine (**1b**).

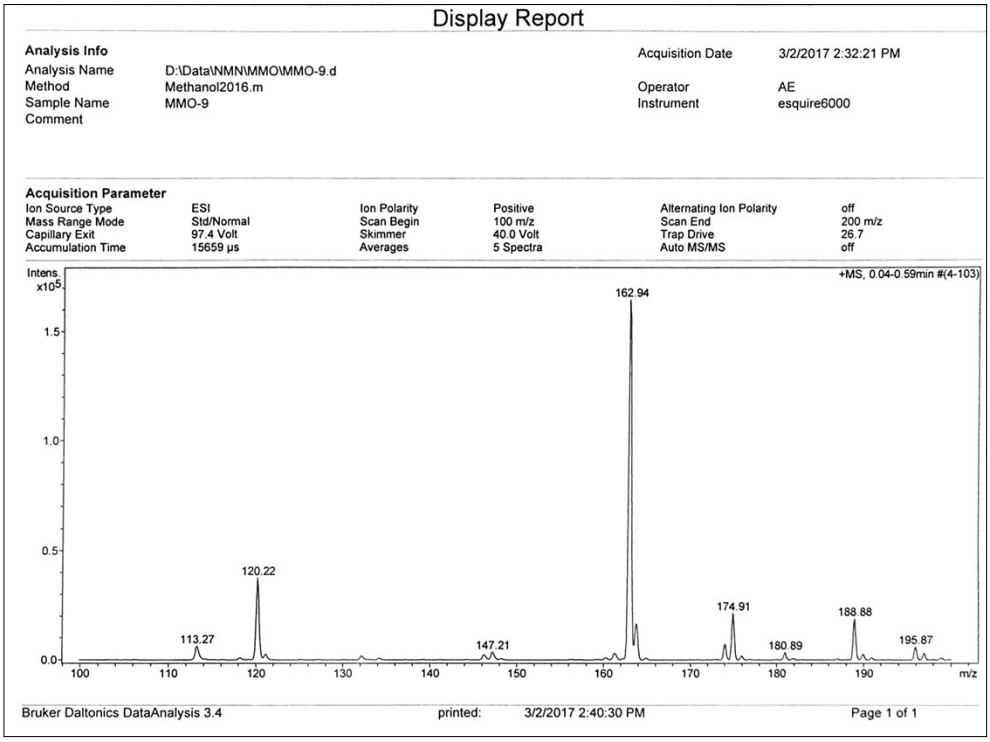
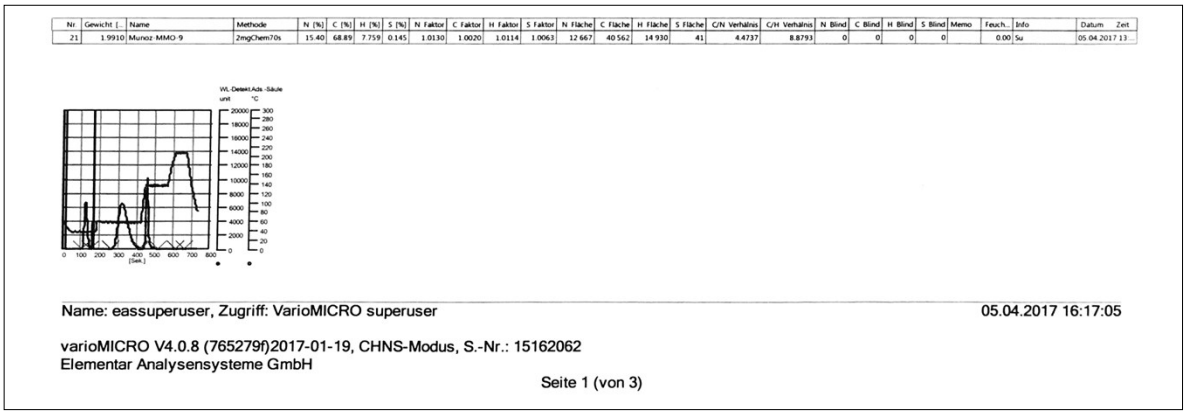


Figure 3. ESI (CH_3OH) of **1b** ligand.



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21	1.9910	Munoz MMO-9	2mgChem70s	15.40	68.89	7.759	0.145	1.0130	1.0020	1.0114	1.0063	12 667	40 562	14 930	41	4.4737	8.8793	0	0	0	0		0.00	Su	05.04.2017 13..

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Elementar Analysensysteme GmbH

Seite 1 (von 3)

Figure 4. Elemental Analysis of **1b** compound.

1.2. Synthesis of $NC(CH_2)_4$-NC_4H_8N-(C_6H_5) (2b)

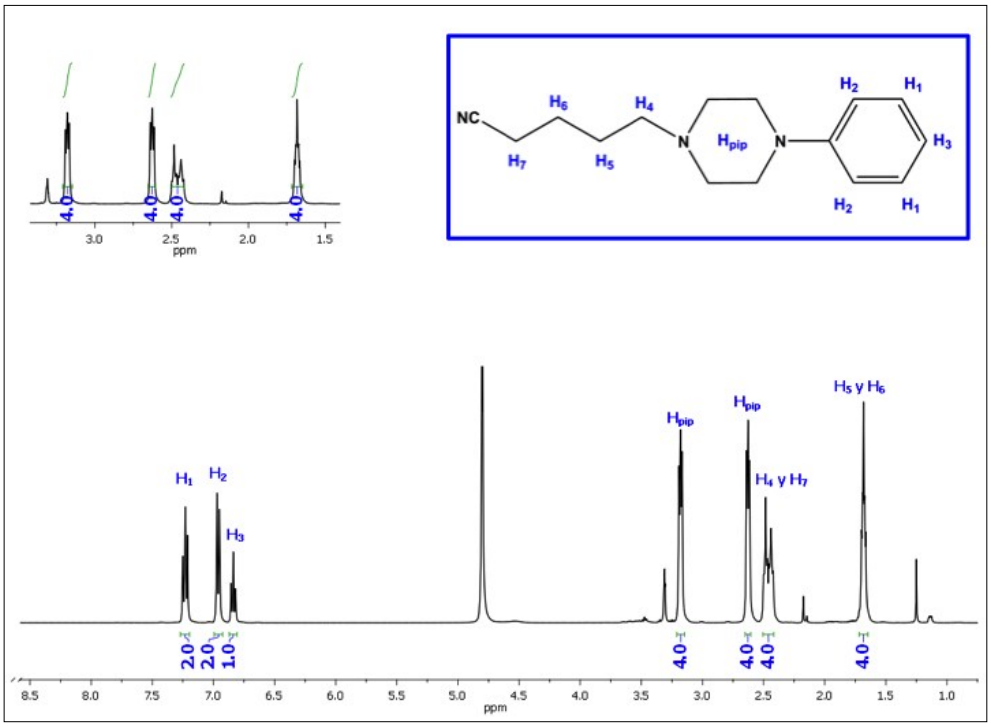

Figure 5. ^1H NMR ($CDCl_3$) phenyl piperazine (**2b**).

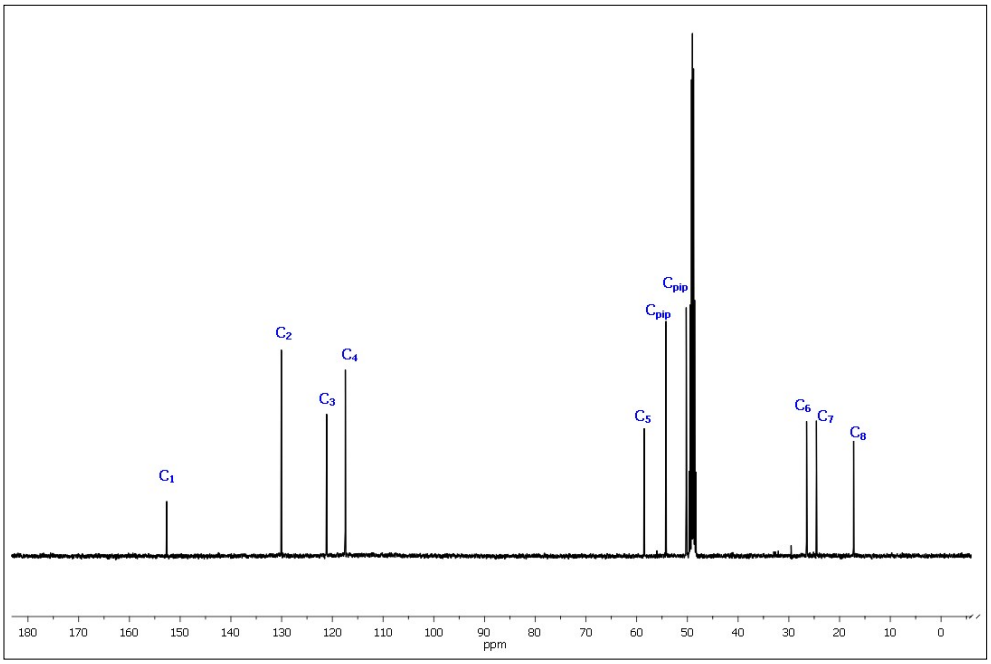

Figure 6. ^{13}C NMR ($CDCl_3$) phenyl piperazine (**2b**).

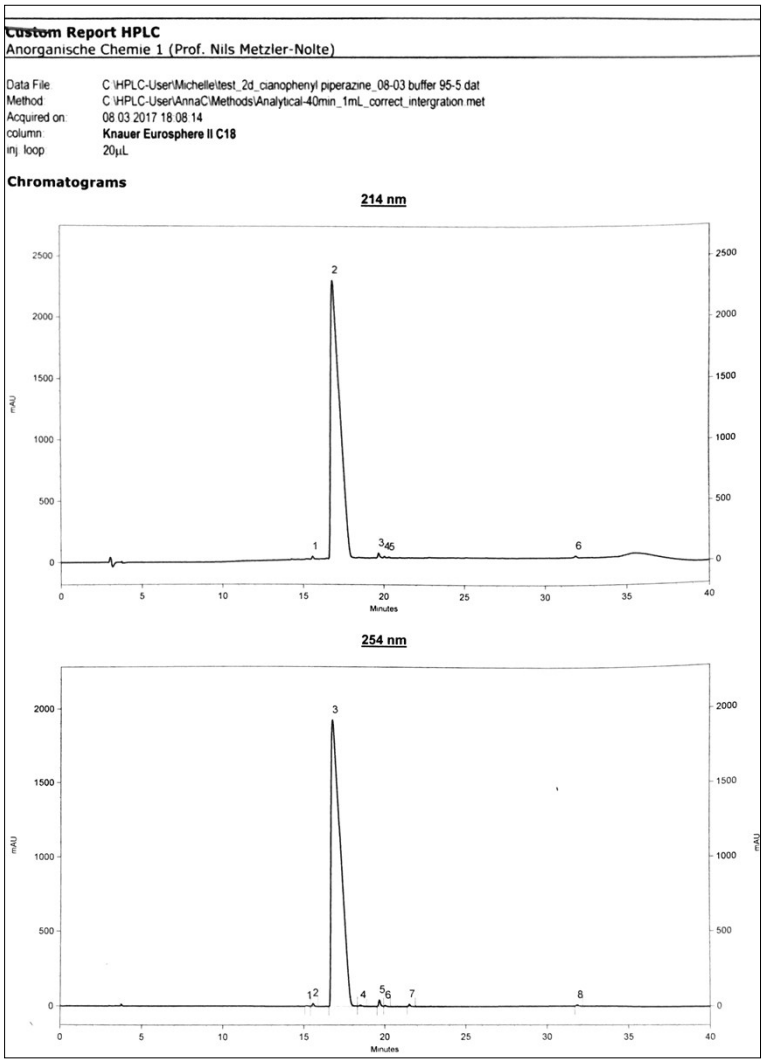

Figure 7. HPLC (CH_3CN:H_2O) of cyano phenyl piperazine ligand (**2b**).

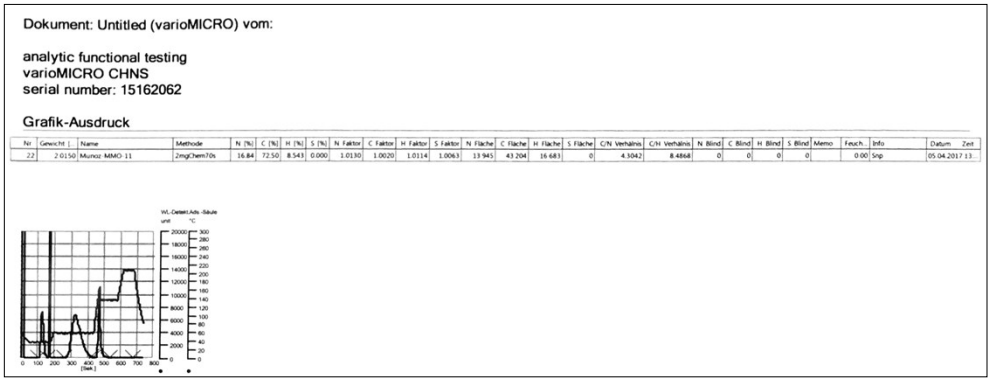

Figure 8. Elemental Analysis of **2b** compound.

1.3. Synthesis of $_2HN\text{-}(CH_2)_5\text{-}NC_4H_8N\text{-}(C_6H_5)$ (3b)

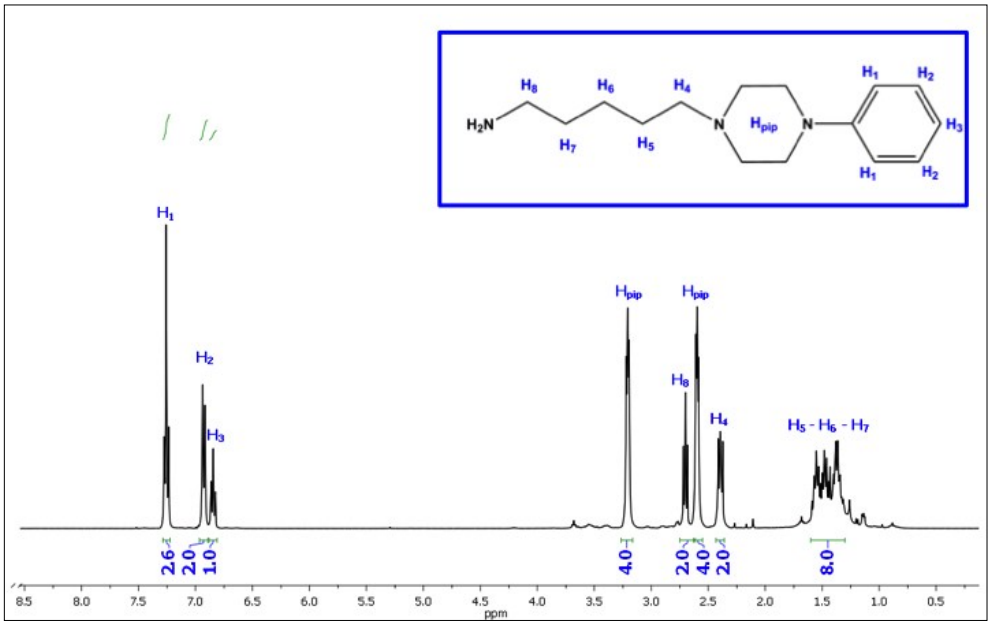

Figure 9. ^1H NMR ($CDCl_3$) phenyl piperazine (**3b**).

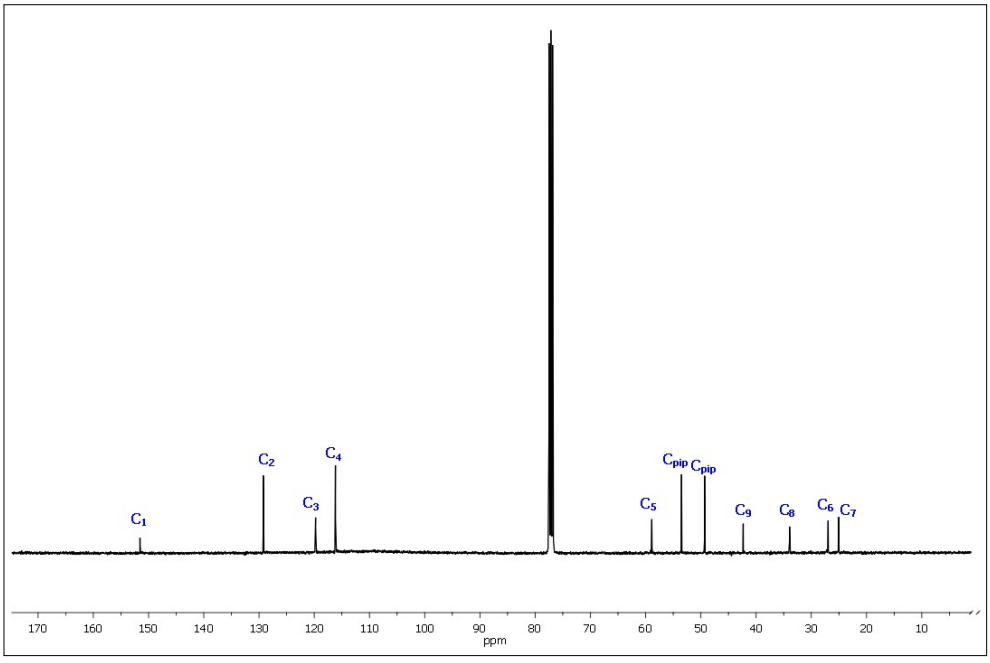

Figure 10. ^{13}C NMR ($CDCl_3$) phenyl piperazine (**3b**).

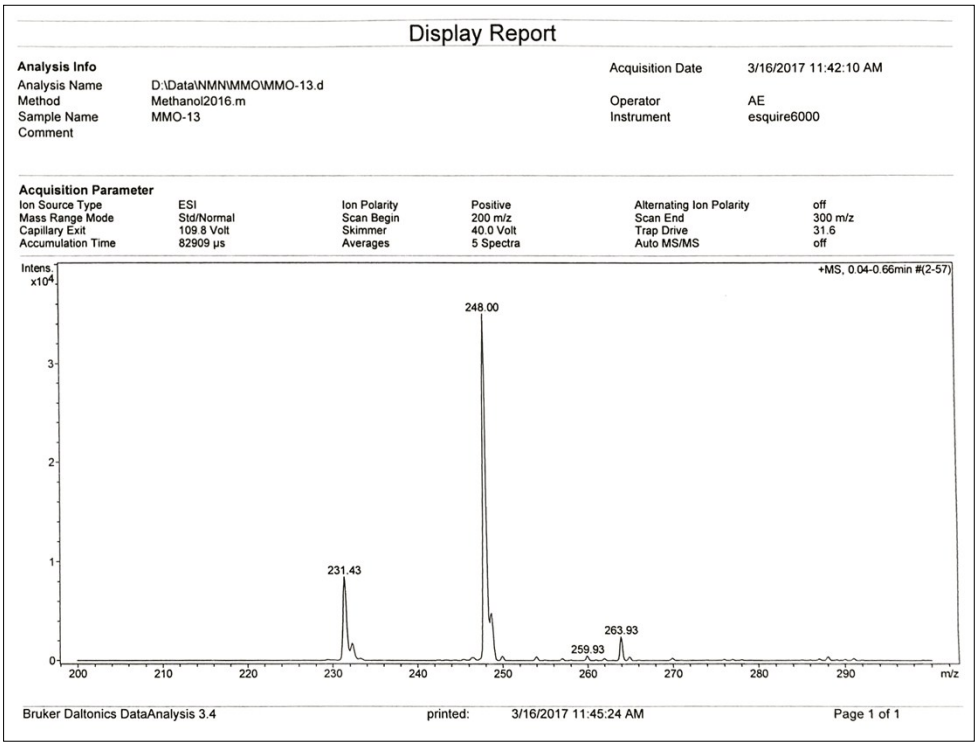

Figure 11. ESI (CH_3OH) of **3b** compound.

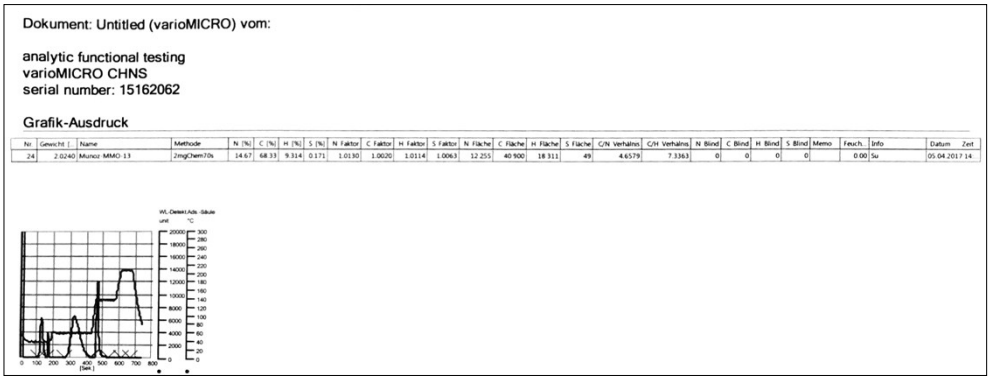

Figure 12. Elemental Analysis of **3b** compound.

1.4. Synthesis of [(η^5-C_5H_4CHNH)-$(CH_2)_5$-NC_4H_8N-1-(C_6H_5))$Re(CO)_3$] (5b)

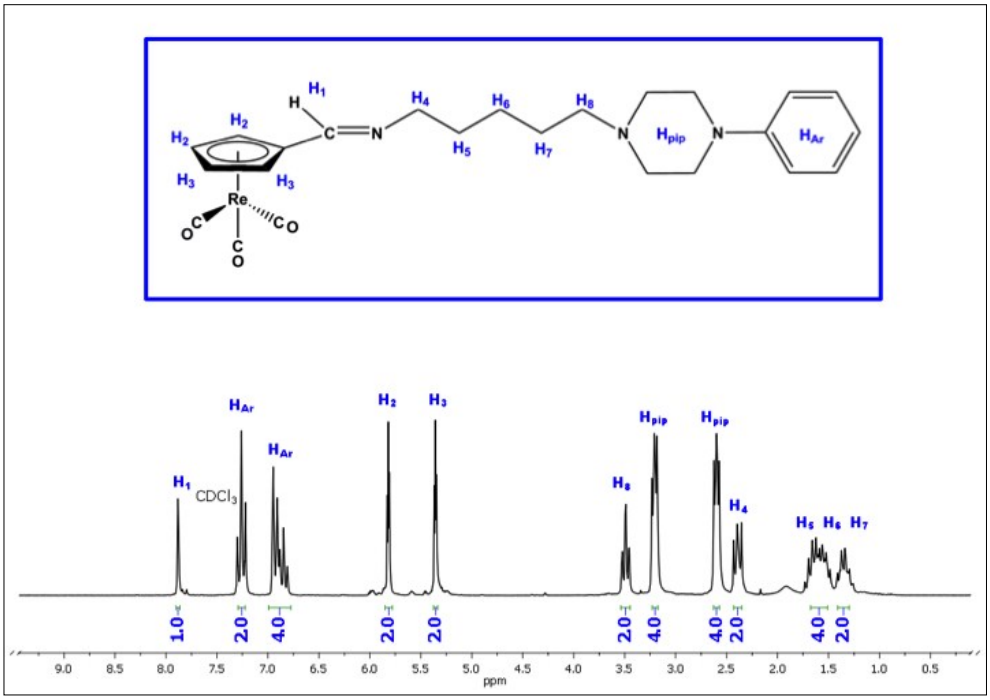

Figure 13. ^1H NMR ($CDCl_3$) **5b.**

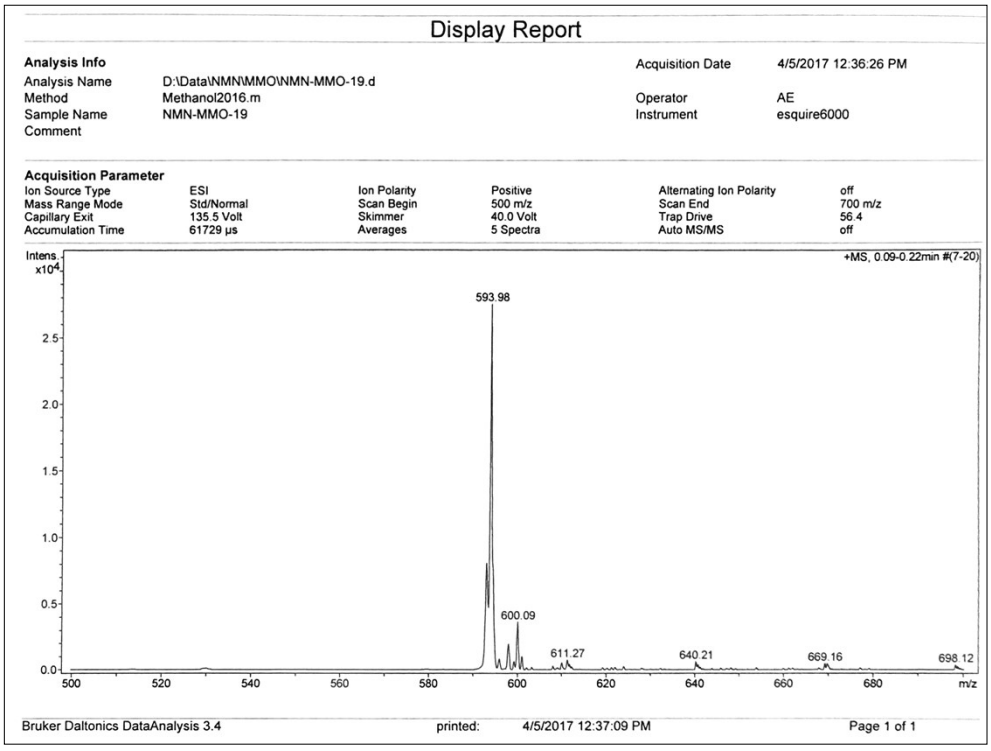

Figure 14. ESI (CH_3OH) of **5b** compound.

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analytic functional testing
varioMICRO CHNS
serial number: 15162062

Grafik-Ausdruck

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16	1.0380	Muñoz MMD 19_1	2mgChem70s	7.05	48.31	4.809	0.638	1.0250	0.9993	1.0156	0.9931	2.909	14.701	4.688	94	6.8558	10.0463	0	0	0	0		0.00	Su	02.08.2017 12...

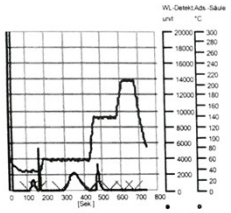


Figure 15. Elemental Analysis of **5b** compound.

2. Cytotoxic studies

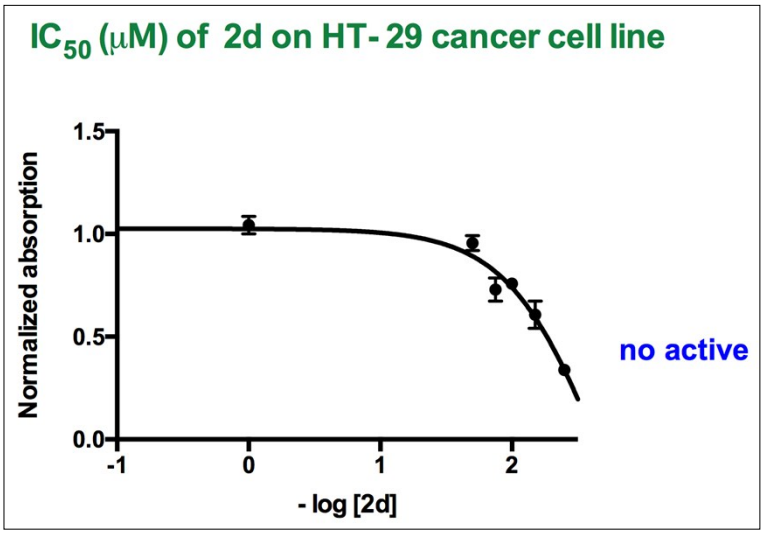


Figure 16. Biological Evaluation of **2d** in **HT-29**.

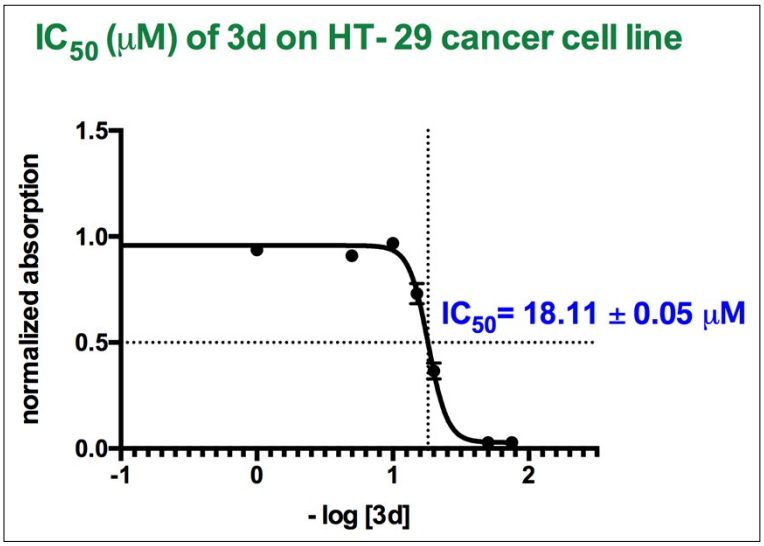


Figure 17. Biological Evaluation of **3d** in **HT-29**.

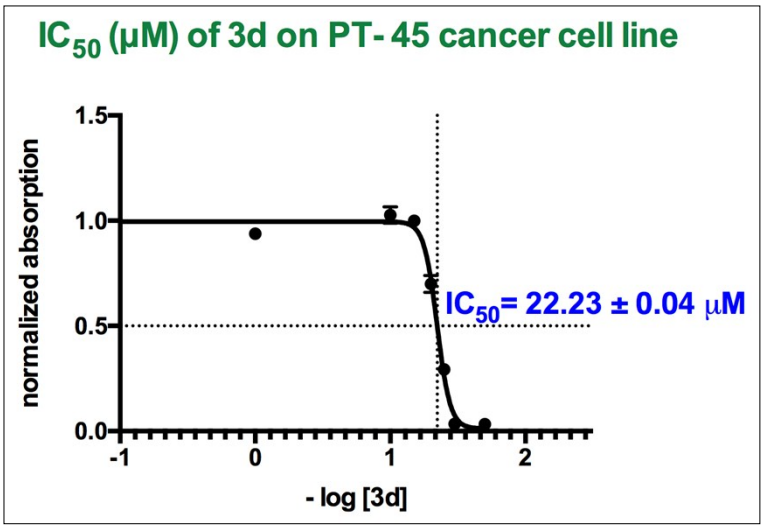


Figure 18. Biological Evaluation of **3d** in **PT-45**.

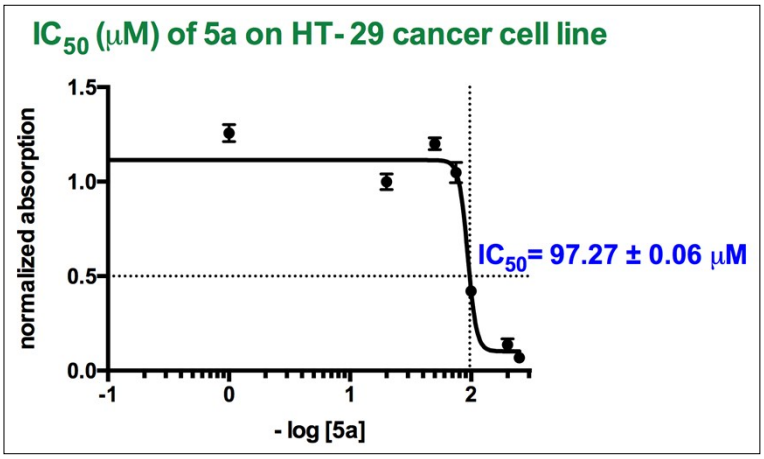


Figure 19. Biological Evaluation of **5a** in **HT-29**.

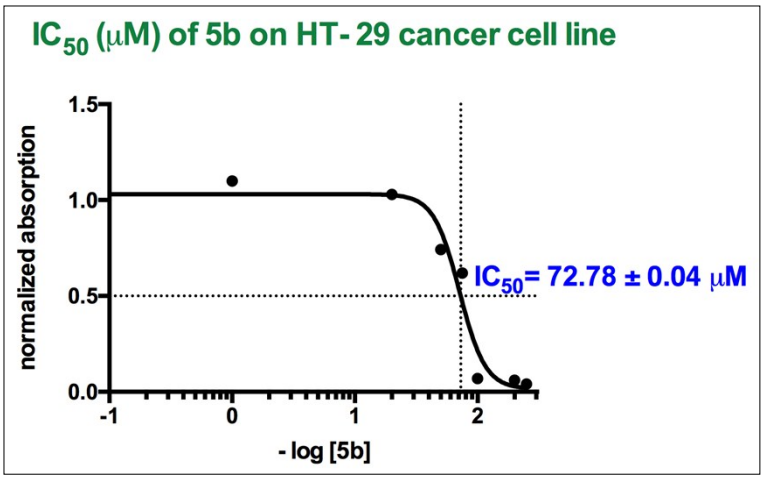


Figure 20. Biological Evaluation of **5b** in **HT-29**.

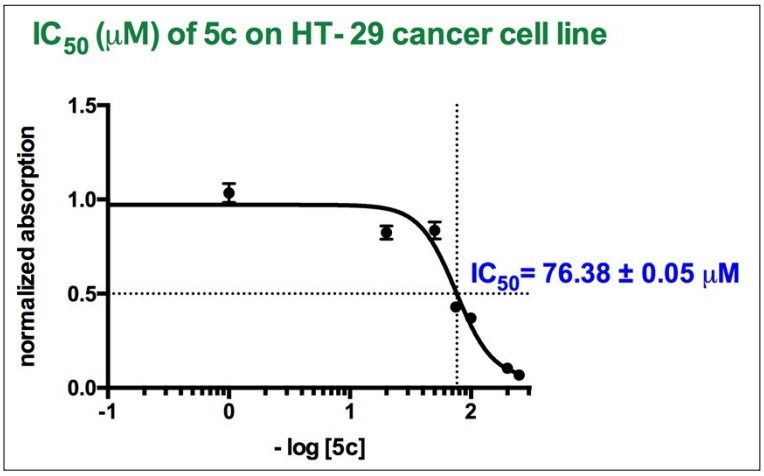


Figure 21. Biological Evaluation of **5c** in **HT-29**.

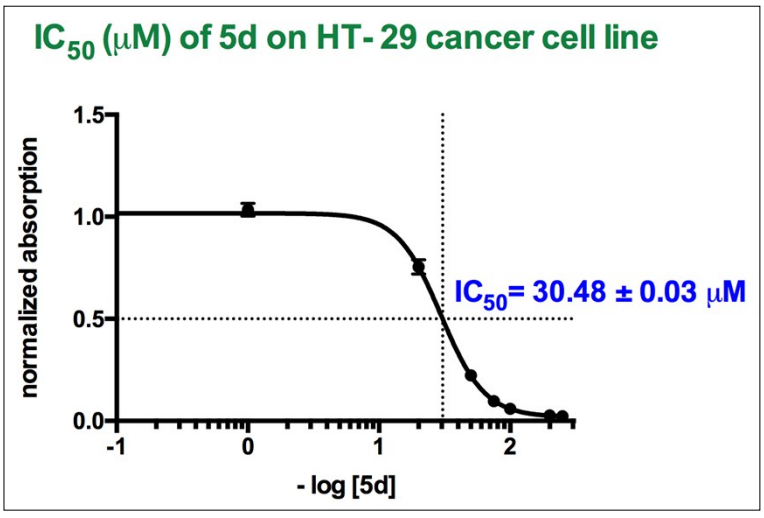


Figure 22. Biological Evaluation of **5d** in **HT-29**.

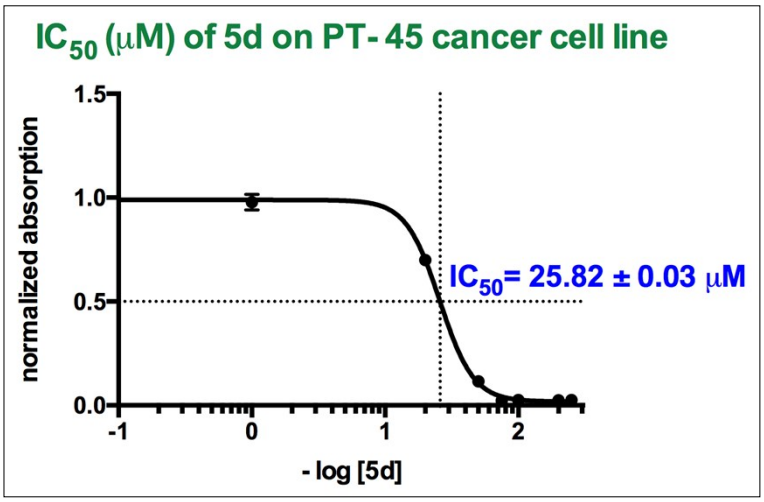
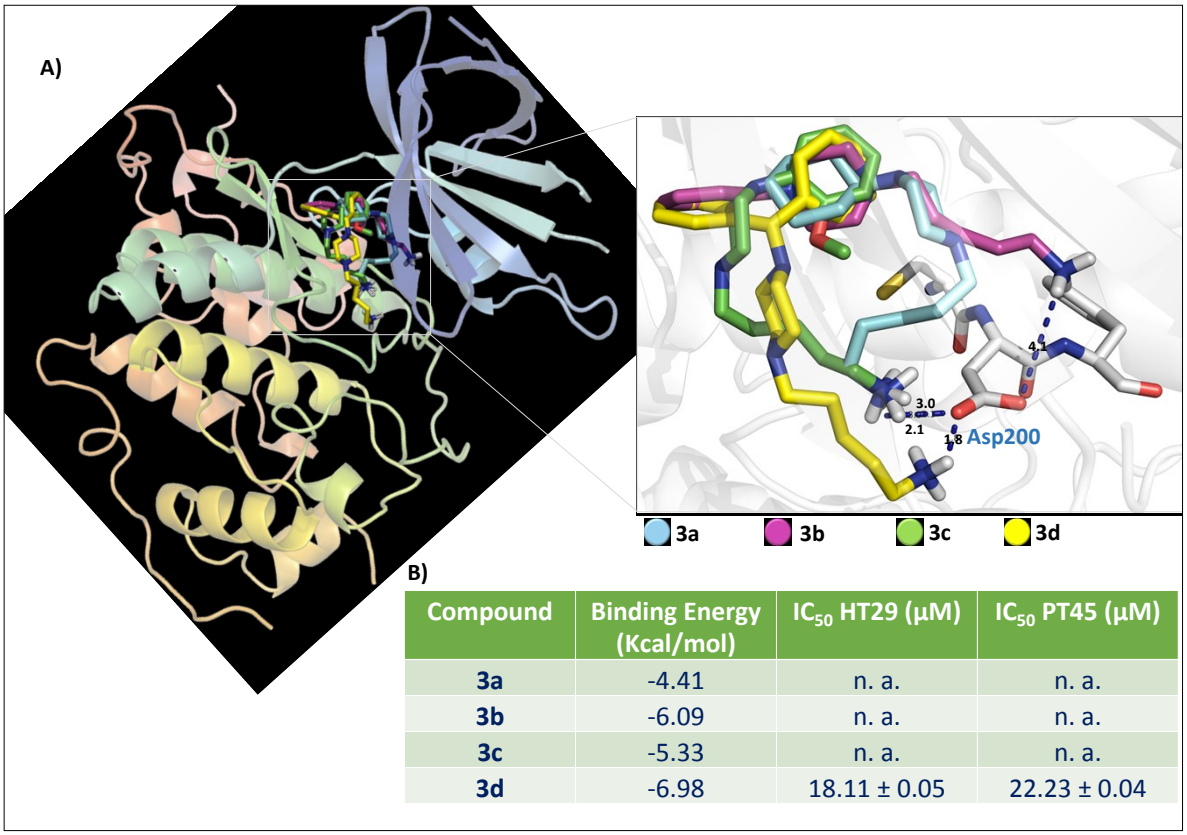


Figure 23. Biological Evaluation of **5d** in **HT-29**.

3. Docking studies



B)

Compound	Binding Energy (Kcal/mol)	IC_{50} HT29 (µM)	IC_{50} PT45 (µM)
3a	-4.41	n. a.	n. a.
3b	-6.09	n. a.	n. a.
3c	-5.33	n. a.	n. a.
3d	-6.98	18.11 ± 0.05	22.23 ± 0.04

Figure 24. Docking studies of amino arilpiperazine ligands **3a**-**3d**. A) Ligands conformation into the binding cavity of GSK-3β. B) Results of binding energy related with cytotoxicity.