Supplementary Materials

Structure-Based Discovery and Bioactivity Evaluation of Novel Aurora-A Kinase Inhibitors as Anti-Cancer Agents via Docking-based Comparative Intermolecular Contacts Analysis (dbCICA)

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**Table S1:** The structures of the (79) seventy-nine Aurora-A Kinase inhibitors collected from (ChEMBL), utilized in modeling.

List for the structures of (79) Aurora-A Kinase inhibitors utilized in modeling and their reported Ki values (expressed in Nm-nanoMolar) collected from the European Bioinformatics Institute database (ChEMBL)

| Compound | R   | Ki (nM) | Reference          |
|----------|-----|---------|--------------------|
| 1        | -H  | 1600    | (Mortlock, et al., 2007) |
| 2        | 2-F | 1400    | (Mortlock, et al., 2007) |
| 3        | 3-F | 450     | (Mortlock, et al., 2007) |
| 4        | 4-F | 2000    | (Mortlock, et al., 2007) |
| 5        | 2,3-di-F | 410  | (Mortlock, et al., 2007) |
| 6        | 3,5-di-F | 230  | (Mortlock, et al., 2007) |
| 7        | 3-Cl | 450     | (Mortlock, et al., 2007) |
| 8        | 3-CN | 2600    | (Mortlock, et al., 2007) |
| 9        | 3-OH | 4000    | (Mortlock, et al., 2007) |
| 10       | 3-OMe| 1900    | (Mortlock, et al., 2007) |
| 11       | 3-CF₃| 510     | (Mortlock, et al., 2007) |

| Compound | R       | X          | Ki (nM) | Reference          |
|----------|---------|------------|---------|--------------------|
| 12       | 2,3-di-F | HO-N        | 55      | (Mortlock, et al., 2007) |
| 13       | 2,3-di-F | HO-N        | 220     | (Mortlock, et al., 2007) |
| 14       | 2,3-di-F | HO-N        | 280     | (Mortlock, et al., 2007) |
| 15       | 3-F     | HO-N        | 690     | (Mortlock, et al., 2007) |
| Compound | R          | X       | Ki (nM) | Reference        |
|----------|------------|---------|---------|------------------|
| 16       | 3-F        | ![Compound 16](image1.png) | 65      | (Mortlock, et al., 2007) |
| 17       | 3-F        | ![Compound 17](image2.png) | 190     | (Mortlock, et al., 2007) |
| 18       | 3-F        | ![Compound 18](image3.png) | 220     | (Mortlock, et al., 2007) |
| 19       | 2,3-di-F   | ![Compound 19](image4.png) | 360     | (Mortlock, et al., 2007) |
| 20       | 2,3-di-F   | ![Compound 20](image5.png) | 87      | (Mortlock, et al., 2007) |
| 21       | 2,3-di-F   | ![Compound 21](image6.png) | 18      | (Mortlock, et al., 2007) |

| Compound | R          | X       | Ki (nM) | Reference        |
|----------|------------|---------|---------|------------------|
| 22       | 2,3-di-F   | ![Compound 22](image7.png) | 160     | (Mortlock, et al., 2007) |
| 23       | 2,3-di-F   | ![Compound 23](image8.png) | 350     | (Mortlock, et al., 2007) |
| 24       | 3-F        | ![Compound 24](image9.png) | 1400    | (Mortlock, et al., 2007) |
| 25       | 3-F        | ![Compound 25](image10.png) | 980     | (Mortlock, et al., 2007) |
| Compound | Structure | Ki (nM) | Reference          |
|----------|-----------|---------|--------------------|
| 26       | ![Structure 26](image) | 0.6     | (Pollard and Mortimore, 2009) |
| 27       | ![Structure 27](image) | 58      | (Pollard and Mortimore, 2009) |
| 28       | ![Structure 28](image) | 4       | (Pollard and Mortimore, 2009) |
| 29       | ![Structure 29](image) | 81      | (Bebbington, et al., 2009) |
| 30       | NH        | 24      | (Bebbington, et al., 2009) |
| 31       | NMe       | 17      | (Bebbington, et al., 2009) |
| 32       | O         | 36      | (Bebbington, et al., 2009) |
| 33       | S         | 20      | (Bebbington, et al., 2009) |
| Compound | Ar             | Ki (nM) | Reference                  |
|----------|----------------|---------|----------------------------|
| 34       | 2-Cl-Ph        | 5       | (Bebbington, et al., 2009) |
| 35       | 3-Cl-Ph        | 4       | (Bebbington, et al., 2009) |
| 36       | 4-Cl-Ph        | 6       | (Bebbington, et al., 2009) |
| 37       | 2,3-Di-Cl-Ph   | 3       | (Bebbington, et al., 2009) |
| 38       | 2,4-Di-Cl-Ph   | 2       | (Bebbington, et al., 2009) |
| 39       | 2,6-Di-Cl-Ph   | 5       | (Bebbington, et al., 2009) |
| 40       | 3,4-Di-Cl-Ph   | 2       | (Bebbington, et al., 2009) |
| 41       | 2-OMe-Ph       | 24      | (Bebbington, et al., 2009) |
| 42       | 4-OMe-Ph       | 9       | (Bebbington, et al., 2009) |
| 43       | 3,4-Di-OMe-Ph  | 17      | (Bebbington, et al., 2009) |
| 44       | 2-Naphthyl     | 1       | (Bebbington, et al., 2009) |

| Compound | R1            | Ar                   | Ki (nM) | Reference                  |
|----------|---------------|----------------------|---------|----------------------------|
| 45       | Me            | 4-(NHSO\textsubscript{2}Me)-Ph | 2       | (Bebbington, et al., 2009) |
| 46       | Me            | 4-(NHC(O)OtBu)-Ph    | 9       | (Bebbington, et al., 2009) |
| 47       | Me            | 4-(NHC(O)Et)-Ph      | 1       | (Bebbington, et al., 2009) |
| 48       | H             | 4-(NHC(O)Me)-Ph      | 24      | (Bebbington, et al., 2009) |
| Compound | R1  | R2  | Ki (nM) | Reference                  |
|----------|-----|-----|---------|----------------------------|
| 49       | H   | Me  | 86      | (Bebbington, et al., 2009) |
| 50       | Me  | Me  | 18      | (Bebbington, et al., 2009) |
| 51       | Ph  | Me  | 2.4     | (Bebbington, et al., 2009) |
| 52       | Me  | Et  | 5.1     | (Bebbington, et al., 2009) |
| 53       | CyPr| Et  | 3.9     | (Bebbington, et al., 2009) |
| 54       | tBu | Et  | 10      | (Bebbington, et al., 2009) |
| 55       | 3-Py| Et  | 3.9     | (Bebbington, et al., 2009) |
| 56       |     | Et  | 2.4     | (Bebbington, et al., 2009) |
| 57       |     | Et  | 1.6     | (Bebbington, et al., 2009) |
| 58       |     | Et  | 1.7     | (Bebbington, et al., 2009) |
| 59       |     | Et  | 3.7     | (Bebbington, et al., 2009) |
| 60       |     | Et  | 1.6     | (Bebbington, et al., 2009) |
| 61       |     | Et  | 1.3     | (Bebbington, et al., 2009) |

| Compound | Structure | Ki (nM) | Reference                  |
|----------|-----------|---------|----------------------------|
| 62       | ![Structure](image) | 490     | (Adams, et al., 2010)      |
| Compound | Structure | Ki (nM) | Reference |
|----------|-----------|---------|-----------|
| 63 | ![Compound 63 Structure](chart) | 2.5 | (Coumar, et al., 2008) |

| Compound | R1      | R2 | R3 | R4 | Ki (nM) | Reference |
|----------|---------|----|----|----|---------|-----------|
| 64 | NH₂     | H  | NO₂| H  | 73.0    | Wang, et al., 2010 |
| 65 | Me      | NMe₂| H  | H  | 6.9     | Wang, et al., 2010 |
| 66 | Me      | NHMe| H  | H  | 18.0    | Wang, et al., 2010 |
| 67 | Me      | NH₂ | H  | H  | 31.0    | Wang, et al., 2010 |
| 68 | Me      | OMe | OMe| OMe| 0.4     | Wang, et al., 2010 |
| 69 | NHMe    | OMe| OMe| OMe| 1.0     | Wang, et al., 2010 |
| 70 | NHEt    | OMe| OMe| OMe| 3.0     | Wang, et al., 2010 |
| 71 | NHEt    | CH₂NHAc| H  | H  | 5.0     | Wang, et al., 2010 |
| 72 | Me      | morpholin-1-yl| H  | H  | 4.0     | Wang, et al., 2010 |
| 73 | NH₂     | morpholin-1-yl| H  | H  | 8.0     | Wang, et al., 2010 |
| 74 | NHMe    | morpholin-1-yl| H  | H  | 19.0    | Wang, et al., 2010 |
| 75 | NHEt    | morpholin-1-yl| H  | H  | 14.0    | Wang, et al., 2010 |
| 76 | NH₂     | 4-acetyl piperazin-1-yl| H  | H  | 7.6     | Wang, et al., 2010 |
| 77 | NHMe    | 4-acetyl piperazin-1-yl| H  | H  | 12.0    | Wang, et al., 2010 |
| 78 | Me      | 4-acetyl piperazin-1-yl| H  | H  | 8.2     | Wang, et al., 2010 |
| 79 | Me      | 4-(methylsulfonyl) piperazin-1-yl| H  | H  | 9.2     | Wang, et al., 2010 |
LibDock enables rapid screening of combinatorial libraries where conformations of the ligands are aligned to polar and apolar receptor interactions sites (i.e., hotspots). Conformations can be either pre-calculated or generated on the fly. Since some of the output poses may have hydrogen atoms in close proximity to the receptor, a CHARMm minimization step can be optionally enabled to further optimize the docked poses.

LibDock docking follows the following steps: (1) Remove hydrogen atoms, (2) Rank ligand conformations and prune by solvent accessible surface area (SASA), (3) find hotspots using a grid that is placed into the binding site and using polar and non-polar probes. The numbers of hotspots are pruned by clustering to a user defined value, (4) Dock ligand poses by aligning to binding site hotspots. This is performed by using triplets (i.e., three ligand atoms are aligned to three receptor hotspots). (5) Poses which result in protein clashes are removed. (6) A final BFGS pose optimization stage is performed using a simple pair-wise score (similar to Piecewise Linear Potential). The top scoring ligand poses are retained (7) Hydrogen atoms are added back to the docked ligands. (8) Optionally, CHARMm minimization can be carried out to reduce steric clashes caused by added hydrogen atoms.

The following LibDock parameters were implemented in the presented project: (1) Prior to docking, the DiscoveryStudio 2.5.5 module CAT-CONFIRM was used to generate a maximum of 255 conformers (not exceeding an energy threshold of 20 kcal/mol from the most stable conformer) for each ligand employing "CAESAR" conformation generation option. (2) A binding site sphere of 12.2 Å radius surrounding the centre of the co-crystallized ligand was used to define the binding site. (3) The maximum number of binding site hotspots (polar and apolar) was set to 100. (4) The ligand-to-hotspots matching RMSD tolerance value was set to 0.25Å. (5) The maximum number of poses saved for each ligand during hotspots matching before final pose
minimization = 100. (6) Maximum number of poses to be saved for each ligand in the binding pocket = 100. (7) Minimum LibDock score (poses below this score are not reported) = 100. (8) Maximum number of rigid body minimization steps during the final pose optimization (using BFGS method) = 50. (9) Maximum number of steric clashes allowed before the pose-hotspot alignment is terminated (specified as a fraction of the heavy atom count) = 0.1.

(10) Maximum value for nonpolar solvent accessible surface area for a particular pose to be reported as successful = 15.0Å². (11) Maximum value for polar solvent accessible solvent area for a particular pose to be reported as successful = 5.0Å². (12) No final ligand minimization was implemented (i.e., in the binding pocket).

- **Section S 2: Scoring of Docked Ligand Poses.**

Highest ranking docked conformers/poses generated by LibDock were scored using 7 scoring functions: Jain (Jain, 1996), LigScore1, LigScore2 (Venkatachalam, et al., 2003), PLP1, PLP2 (Gehlhaar, et al., 1999), PMF and PMF04 (Muegge and Martin 1999; Muegge, 2002).

LigScore1 and LigScore2 scores were calculated employing CFF force field (version 1.02) and using grid-based energies with a grid extension of 7.5 Å across the binding site. PMF scores were calculated employing cutoff distances of 12.0 Å for carbon-carbon interactions and other atomic interactions, while PMF04 scores were calculated employing cutoff values of 6.0 and 9.0Å for carbon-carbon interactions and other atomic interactions, respectively.

- **Section S 3: Genetic Algorithm Implementation in dbCICA Modeling**

The GA toolbox within MATLAB (Version R2007a) was adapted by implementing the following four basic components: the creation function, cross-over function, mutation function, and fitness function. The creation function randomly generates a population of chromosomes of a
predefined size (number of summed contacts columns, as mentioned in steps 5 and 6 in the section of Docking-Based Comparative Molecular Contacts Analysis (dbCICA) under Materials and Methods) in which every chromosome encodes for certain possible column summation model. Chromosomes differ from one another by the set of summed columns and their weights. Crossover children are the offspring created by selecting vector entries (i.e., genes) from a pair of individual chromosomes in the first generation and combining them to form two complementary children, while mutation children are those created via applying random changes to corresponding parents, i.e., each single parent chromosome is mutated to give a single child by randomly replacing selected gene in the parent chromosome with another from the chromosome population. Each chromosome is associated with a fitness value that reflects how good the summation of its encoded genes compares to other chromosomes. The fitness functions in dbCICA can be the correlation coefficient ($r^2$), leave-one-out $r^2$, or K-fold $r^2$.

In this project (dbCICA of Aurora-A Kinase) we implemented a 5-fold $r^2$ as fitness criterion. In this procedure, each chromosome is ranked as follows: The training set is divided into two subsets: fit and test subsets. The test subset is randomly selected to represent ca. 20% of the training compounds. This procedure is repeated over 5 cycles; accordingly, 5 test subsets with their complementary fit subsets are selected for each chromosome (i.e., column summation model).

The 5 test subsets should cover ca. 100% of the training compounds by avoiding selecting the same compound in more than one test subset. The fit sets are then utilized to generate 5 sub-models employing the same chromosome. The resulting sub-models are then utilized to predict the bioactivities of the corresponding testing subsets. Finally, the predicted values of all 5 test subsets are correlated with their experimental counterparts to determine corresponding 5-fold $r^2$.
The best column-summation model is selected as representative db-CICA model. The fitness function in the current db-CICA modelling project was 5-fold $r^2$.

The following parameters were implemented for GA search of best models: (1) Size of chromosome population = 100, (2) Rate of mating (crossover fraction): 80% (3) Elite count = 1 (4) Maximum number of generations which is needed to exit from GA iteration cycles and completion of the algorithm = 1000.

Based on these settings, the numbers of each type of children in the offspring generation is as follows: There is 1 elite child (corresponding to the individual in the parents' generation with the best fitness value), and there are 199 individual children other than the elite child. The algorithm rounds 0.8 (crossover fraction) x 199 = 159.2 to 159 to get the number of crossover children and the remaining 40 (i.e., 199-159) are the mutation population. The elite child is passed to the offspring population without alteration.

• **Section S 4: Receiver-operating characteristic (ROC) curve analysis**

The Testing Set: The classification power of the resulting pharmacophores was validated using receiver-operating characteristic (ROC) curve analysis by testing the ability of a particular pharmacophore to selectively capture diverse Aurora-A kinase inhibitors from large list of inactive compounds. The testing set implemented in this project was entirely composed of experimentally validated active and inactive Aurora-A kinase inhibitors extracted from the European Bioinformatics Institute database (ChEMBL, https://www.ebi.ac.uk/chembl). It included 86 experimentally-validated active compounds (anti-Aurora-A Kinase with Ki values ≤10 nM) & 248 less-active compounds (anti-Aurora-A Kinase with Ki values > 500 nM considered as decoy list). To insure that active testing compounds closely resemble the diversity
of less-active members we computed top three principal components based on 12 physicochemical descriptors (i.e., LogP, molecular weight, hydrogen bond donors and acceptors, rotatable bonds, rings, aromatic rings, fractional polar surface area surface area, polar surface area and number of fragments) for active testing compounds and compared them with corresponding principal components calculated for the inactive testing inhibitors in each case. Below figure shows three-dimensional plot of the principal components representing active and inactive testing compounds testing set.

![Figure S 1: Three-dimensional plot showing three main principal components calculated for the Testing Set (based on 12 physicochemical descriptors, see text). Amber spheres (●) represent active compounds (Ki ≤ 10) while blue spheres (●) represent inactive compounds (Ki ≥ 500) as enlisted in ChEMBL database.](image)

Conformational ensembles were generated for the testing set using "CESEAR" conformation generation option implemented in DiscoveryStudio 2.5.5. The results are presented in the form of ROC curves. A ROC curve is plotted by considering the highest score (fit value against the
tested pharmacophore) of an active molecule as the first threshold then counting the number of
decky compounds within this cut-off value.

The corresponding sensitivity (SE, also known as True Positive Rate) and specificity (SP, also
known as True Negative Rate) are calculated using equation 1 and equation 2, respectively, and
plotted. This process is repeated using the active molecule possessing the second highest score
and so on, until the scores of all active compounds are considered as selection cut-off values (Triballeau, et al., 2006 and Kirchmair, et al., 2008).

\[
Se = \frac{\text{Number of Selected Actives}}{\text{Total Number of Actives}} = \frac{TP}{TP + FN} \quad \text{............... (1)}
\]

\[
Sp = \frac{\text{Number of Discarded Inactives}}{\text{Total Number of Inactives}} = \frac{TN}{TN + FP} \quad \text{............... (2)}
\]

Where, TP (true positive) is the number of active compounds that are captured by the
pharmacophore under concern, FN (false negative) is the number of active compounds discarded
from the hits list by the virtual screening method, TN (true negative) is the number of discarded
decoys, while FP (false positive) is the number of captured decoys (presumably inactive) (Irwin
and Shoichet, 2005; Triballeau et al., 2006; Kirchmair et al., 2008).

If all molecules scored by a virtual screening (VS) protocol with sufficient discriminatory power
are ranked according to their score (i.e., fit values), starting with the best-scored molecule and
ending with the molecule that got the lowest score, most of the actives will have a higher score
than the decoys. Since some of the actives will be scored lower than decoys, an overlap between
the distribution of active molecules and decoys will occur, which will lead to the prediction of
false positives and false negatives. (Irwin and Shoichet, 2005; Triballeau et al., 2006; Kirchmair et al., 2008). The selection of one score value as a threshold strongly influences the ratio of actives to decoys and therefore the validation of a VS method. The ROC curve method avoids the selection of a threshold by considering all SE and SP pairs for each score threshold (Irwin and Shoichet, 2005; Triballeau et al., 2006; Kirchmair et al., 2008). A ROC curve is plotted by setting the score of the active molecule as the first threshold. Afterwards, the number of decoys within this cutoff is counted and the corresponding SE and SP pair is calculated. This calculation is repeated for the active molecule with the second highest score and so forth, until the scores of all actives are considered as selection thresholds.

In practice, the ROC curve for a set of actives and inactive decoys with randomly distributed scores tends towards the SE = 1-SP line asymptotically with increasing number of actives and decoys (Triballeau, et al., 2005). The success of particular virtual screening workflow depending on ROC analysis evaluation can be provided as follow:

1) Area under the ROC curve (AUC): optimal ROC curve has a value of 1 and random distribution with 0.5. Any virtual screening that performs better than a random discrimination of actives and inactives get an AUC value between 0.5 and 1, whereas an AUC value lower than 0.5 represents the unfavourable case of a virtual screening method that has a higher probability to assign the best scores to decoys than to actives (Irwin and Shoichet, 2005; Triballeau, et al., 2006; Taha, 2012).

2) Overall accuracy (ACC): describes the percentage of compounds that were correctly classified by the screening protocol (equation 3). Testing compounds are assigned a binary score value of zero (compound not captured) or one (compound captured) (Triballeau, et al., 2006).
\[ ACC = \frac{TP + TN}{N} = \frac{A}{N}.Se + \left(1 - \frac{A}{N}\right).Sp \]  \hspace{1cm} (3)

Where, \( N \) is the number of all compounds in the testing database, \( A \) is the number of true actives in the testing database.

3) Overall true negative rate (TNR) or overall specificity (SP): that describes the fraction percentage of discarded inactive by the virtual screening tool. Discarded inactive test compounds are assigned a binary score value of zero (compound not captured) or one (compound captured) regardless to their individual fit values (Jacobsson et al., 2003; Irwin and Shoichet, 2005; Triballeau et al., 2006; Kirchmair et al., 2008, Taha, 2012).

4) Overall true positive rate (TPR) or overall sensitivity (SE): describes the fraction percentage of captured actives from the total number of actives. Active test compounds are assigned a binary score value of zero (compound not captured) or one (compound captured) regardless to their individual fit values (Jacobsson et al., 2003; Irwin and Shoichet, 2005; Triballeau et al., 2006; Kirchmair et al., 2008, Taha, 2012).

**Section S5: Steric Refinement of Pharmacophores**

Based on ROC results **Hypo(SB-1)** model had better behavior over **Hypo(SB-2)**, as detailed in results section. In order to improve the classification properties of **Hypo(SB-1)** model, it was complemented with exclusion spheres by employing HIPHOP-REFINE module of DiscoveryStudio 2.5.5 (Khanfar and Taha, 2013). HIPHOP-REFINE identifies spaces occupied by the conformations of inactive compounds and free from conformations of active ones. These areas are filled with exclusion volumes to represent the steric constrains of the binding pocket (Hahn, 1997; Taha, et al., 2011; Khanfar and Taha, 2013). A subset of 32 training compounds
was carefully selected from the molecules in shown below in Table S 2 for HIPHOP-REFINE modelling or construction of appropriate exclusion regions around Hypo(SB-1).

The Principal and Maximum Omitted Features (MaxOmitFeat) parameters are used to define how many molecules fit the selected pharmacophore hypothesis (partially or completely) for steric refinement purposes. Active compounds are assigned MaxOmitFeat parameter of zero and Principal value of 2 to direct the software to fit all their chemical moieties against all the pharmacophoric features of the particular hypothesis. However, inactive compounds are allowed to miss one or two features by assigning them a MaxOmitFeat of 1 or 2, respectively. Moreover, inactives were assigned Principal value of zero to indicate their inferior bioactivities. However, intermediate active compounds are normally assigned a principal value of 1 and a MaxOmitFeat of zero or 1 in accordance with the number of features the compound loses, to indicate their intermediate status (Taha, et al., 2011).

In this project it was decided to consider the Ki value of 510 nM as an arbitrary activity/inactivity threshold, such that compounds with values equal to or more than 510 nM considered “inactives” with Principal value of zero, and were carefully evaluated to assess whether their lower potencies are attributable to missing one or more pharmacophoric features (MaxOmitFeat = 1 or 2), or only related to steric clashes within the binding pocket (MaxOmitFeat = 0).

However, compounds of Ki values ranging from 5 nM to less than 510 nM were considered moderately active and were assigned a principal value of 1 and MaxOmitFeat of 1 or zero (according to their number of missed feature). Compounds of Ki values less than 5.0 nM were considered active, and were assigned Principal value of 2, and MaxOmitFeat of zero. The conformational spaces of training lists were generated using "BEST" conformation generation option in DiscoveryStudio 2.5.5. The training compounds employed for steric refinement of the
generated pharmacophore Hypo(SB-1), and their corresponding Principal and MaxOmitFeat parameters are sown below in Table S 2.

HIPHOP-REFINE was configured to permit a maximum of 100 exclusion spheres to be added to pharmacophoric hypothesis of Hypo(SB-1). The HIPHOP-REFINE process resulted in adding 93 exclusion volumes to Hypo(SB-1), and the sterically refined pharmacophore was named Refined-Hypo (SB-1).
Table S 2: Refinement list for steric refinement of Hypo(SB-1)

| Compound<sup>a</sup> | Ki (nM) | Principal value | MaxOmitFeat<sup>b</sup> |
|----------------------|---------|-----------------|------------------------|
| 1                    | 1,600   | 0               | 2                      |
| 2                    | 1,400   | 0               | 2                      |
| 4                    | 2,000   | 0               | 2                      |
| 8                    | 2,600   | 0               | 2                      |
| 9                    | 4,000   | 0               | 0                      |
| 10                   | 1,900   | 0               | 2                      |
| 11                   | 510     | 0               | 2                      |
| 15                   | 690     | 0               | 2                      |
| 20                   | 87      | 1               | 1                      |
| 24                   | 1,400   | 0               | 2                      |
| 25                   | 980     | 0               | 2                      |
| 26                   | 0.6     | 2               | 0                      |
| 28                   | 4       | 2               | 0                      |
| 34                   | 5       | 1               | 1                      |
| 39                   | 5       | 1               | 1                      |
| 42                   | 9       | 1               | 0                      |
| 43                   | 17      | 1               | 0                      |
| 45                   | 2       | 2               | 0                      |
| 46                   | 9       | 1               | 0                      |
| 47                   | 1       | 2               | 0                      |
| 49                   | 86      | 1               | 0                      |
| 50                   | 18      | 1               | 0                      |
| 52                   | 5.1     | 1               | 0                      |
| 54                   | 10      | 1               | 0                      |
| 57                   | 1.6     | 2               | 0                      |
| 58                   | 1.7     | 2               | 0                      |
| 60                   | 1.6     | 2               | 0                      |
| 61                   | 1.3     | 2               | 0                      |
| 66                   | 18      | 1               | 1                      |
| 71                   | 5       | 1               | 1                      |
| 78                   | 8.2     | 1               | 1                      |
| 79                   | 9.2     | 1               | 1                      |

<sup>a</sup>Compounds’ numbers are as in Table S3
<sup>b</sup>MaxOmitFeat: Maximum omitted features.
Table S3: The 75 high-ranking hits and their anti-Aurora-A kinase inhibition% at 10 µM using Z'-LYTE kinase assay, sum of their critical contacts and their predicted activity. These high-ranking hits captured by Refined-Hypo(SB-1) -3D search query- derived from Hypo(SB-1) pharmacophore were docked into (3w2c) using the docking-scoring settings of (SB-1) and their docked poses were analyzed to identify their critical binding contacts (marked by dbCICA model Table 2.) were used to predict their Ki values by substituting the sum of binding contacts in the respective dbCICA-regression equations (Table 1.). Steps of activity prediction was also employed using docking/scoring settings of (SB-2) dbCICA model to assess the similarity extent in “predicted activity” of both (SB-2) model and the better performing (SB-1) model.

| Hit | NCI Code | SB-1 | SB-2 | % Inhibition at 10 µM |
|-----|----------|------|------|-----------------------|
|     |          | Contact atoms Summationb | Predicted Ki (nM)c | Contact atoms Summationb | Predicted Ki (nM)c |                      |
| 80  | 19024    | 15   | 0.27 | 14                    | 6.96               | 20                    |
| 81  | 34607    | 15   | 0.27 | 14                    | 6.96               | 3                     |
| 82  | 1987     | 14   | 0.58 | 12                    | 18.72              | 5                     |
| 83  | 22650    | 14   | 0.58 | 13                    | 11.41              | 7                     |
| 84  | 4293     | 14   | 0.58 | 13                    | 11.41              | 17                    |
| 85* | 14040*   | 13   | 1.20 | 13                    | 11.41              | 56                    |
| 86  | 22651    | 13   | 1.20 | 13                    | 11.41              | 12                    |
| 87  | 24666    | 13   | 1.20 | 11                    | 30.71              | -4                    |
| 88  | 1576     | 12   | 2.51 | 14                    | 6.96               | 75                    |
| 89  | 18100    | 12   | 2.51 | 13                    | 11.41              | 2                     |
| 90  | 23953    | 12   | 2.51 | 13                    | 11.41              | -2                    |
| 91  | 33654    | 12   | 2.51 | 13                    | 11.41              | -2                    |
| 92  | 34311    | 12   | 2.51 | 12                    | 18.72              | 3                     |
| 93  | 34595    | 12   | 2.51 | 13                    | 11.41              | 14                    |
| 94  | 35036    | 12   | 2.51 | 10                    | 50.37              | -2                    |
| 95  | 4356     | 12   | 2.51 | 12                    | 18.72              | 30                    |
| 96  | 4721     | 12   | 2.51 | 11                    | 30.71              | 0                     |
| 97  | 7506     | 12   | 2.51 | 12                    | 18.72              | -4                    |
| 98  | 10637    | 11   | 5.22 | 9                     | 82.61              | -5                    |
| 99  | 11196    | 11   | 5.22 | 12                    | 18.72              | 5                     |

*a* Hits are as in Figure S3. *b* Contacts summations according to corresponding dbCICA model (Tables 1 and 2). *c* Predicted Ki (nM) by substituting the number of contacts of each docked compound in the regression equation of the corresponding dbCICA model. *Underlined hits with highest Inhibition%
Table S3: The 75 high-ranking hits and their anti-Aurora-A kinase inhibition% at 10 μM using Z’-LYTE kinase assay, sum of their critical contacts and their predicted activity. These high-ranking hits captured by Refined-Hypo(SB-1) -3D search query derived from Hypo(SB-1) pharmacophore were docked into (3w2c) using the docking-scoring settings of (SB-1) and their docked poses were analyzed to identify their critical binding contacts (marked by dbCICA model Table 2.) were used to predict their Kᵢ values by substituting the sum of binding contacts in the respective dbCICA-regression equations (Table 1). Steps of activity prediction was also employed using docking/scoring settings of (SB-2) dbCICA model to assess the similarity extent in “predicted activity” of both (SB-2) model and the better performing (SB-1) model.

| Hit | NCI Code | SB-1 | SB-2 | % Inhibition at 10 μM |
|-----|----------|------|------|----------------------|
|     |          | Contact atoms Summationᵇ | Predicted Kᵢ (nM)ᶜ | Contact atoms Summationᵇ | Predicted Kᵢ (nM)ᶜ |
| 100 | 12847    | 11   | 5.22 | 11                   | 30.71               |
| 101 | 17288    | 11   | 5.22 | 13                   | 11.41               |
| 102 | 18099    | 11   | 5.22 | 12                   | 18.72               |
| 103 | 22645    | 11   | 5.22 | 12                   | 18.72               |
| 104 | 23413    | 11   | 5.22 | 12                   | 18.72               |
| 105 | 33564    | 11   | 5.22 | 13                   | 11.41               |
| 106 | 34873    | 11   | 5.22 | 12                   | 18.72               |
| 107 | 4354     | 11   | 5.22 | 12                   | 18.72               |
| 108 | 6919     | 11   | 5.22 | 11                   | 30.71               |
| 109 | 7501     | 11   | 5.22 | 12                   | 18.72               |
| 110 | 9293     | 11   | 5.22 | 10                   | 50.37               |
| 111 | 10515    | 10   | 10.87| 13                   | 11.41               |
| 112 | 12415    | 10   | 10.87| 14                   | 6.96                |
| 113 | 14341    | 10   | 10.87| 12                   | 18.72               |
| 114 | 22676    | 10   | 10.87| 10                   | 50.37               |
| 115 | 22677    | 10   | 10.87| 11                   | 30.71               |
| 116 | 23825    | 10   | 10.87| 13                   | 11.41               |
| 117 | 26690    | 10   | 10.87| 15                   | 4.24                |

ᵃHits are as in Figure S 3.ᵇContacts summations according to corresponding dbCICA model (Tables 1 and 2).ᶜPredicted Kᵢ (nM) by substituting the number of contacts of each docked compound in the regression equation of the corresponding dbCICA model. *Underlined hits with highest Inhibition%
Table S3: The 75 high-ranking hits and their anti-Aurora-A kinase inhibition% at 10 µM using Z'-LYTE kinase assay, sum of their critical contacts and their predicted activity. These high-ranking hits captured by Refined-Hypo(SB-1) - 3D search query- derived from Hypo(SB-1) pharmacophore were docked into (3w2c) using the docking-scoring settings of (SB-1) and their docked poses were analyzed to identify their critical binding contacts (marked by dbCICA model Table 2.) were used to predict their Ki values by substituting the sum of binding contacts in the respective dbCICA-regression equations (Table 1). Steps of activity prediction was also employed using docking/scoring settings of (SB-2) dbCICA model to assess the similarity extent in “predicted activity” of both (SB-2) model and the better performing (SB-1) model.

| Hit # | NCI Code | SB-1 | SB-2 |
|-------|----------|------|------|
|       |          | Contact atoms Summation | Predicted Ki (nM) | Contact atoms Summation | Predicted Ki (nM) | % Inhibition at 10 µM |
| 118   | 29057    | 10   | 10.87 | 14   | 6.96  | 7 |
| 119   | 31475    | 10   | 10.87 | 13   | 11.41 | -3 |
| 120   | 31937    | 10   | 10.87 | 10   | 50.37 | -2 |
| 121   | 3343     | 10   | 10.87 | 11   | 30.71 | -2 |
| 122   | 33550    | 10   | 10.87 | 13   | 11.41 | -1 |
| 123   | 34304    | 10   | 10.87 | 13   | 11.41 | 4  |
| 124   | 34692    | 10   | 10.87 | 14   | 6.96  | -2 |
| 125   | 6807     | 10   | 10.87 | 14   | 6.96  | -1 |
| 126   | 6848     | 10   | 10.87 | 12   | 18.72 | -2 |
| 127   | 10868    | 9    | 22.62 | 13   | 11.41 | 0  |
| 128   | 11191    | 9    | 22.62 | 13   | 11.41 | -5 |
| 129   | 12840    | 9    | 22.62 | 13   | 11.41 | 3  |
| 130   | 12849    | 9    | 22.62 | 13   | 11.41 | 86 |
| 131   | 23575    | 9    | 22.62 | 12   | 18.72 | 3  |
| 132   | 26084    | 9    | 22.62 | 13   | 11.41 | 22 |
| 133   | 28316    | 9    | 22.62 | 12   | 18.72 | 3  |
| 134   | 31011    | 9    | 22.62 | 13   | 11.41 | 8  |
| 135   | 3289     | 9    | 22.62 | 13   | 11.41 | 7  |
| 136   | 5769     | 9    | 22.62 | 13   | 11.41 | 5  |
| 137   | 6888     | 9    | 22.62 | 12   | 18.72 | -30|

*Hits are as in Figure S 3. Contacts summations according to corresponding dbCICA model (Tables 1 and 2). Predicted Ki (nM) by substituting the number of contacts of each docked compound in the regression equation of the corresponding dbCICA model. Underlined hits with highest Inhibition%
Table S3: The 75 high-ranking hits and their anti-Aurora-A kinase inhibition\% at 10 \( \mu \)M using Z’-LYTE kinase assay, sum of their critical contacts and their predicted activity. These high-ranking hits captured by Refine-Hypo(SB-1) -3D search query- derived from Hypo(SB-1) pharmacophore were docked into (3w2c) using the docking-scoring settings of (SB-1) and their docked poses were analyzed to identify their critical binding contacts (marked by dbCICA model Table 2.) were used to predict their \( K_i \) values by substituting the sum of binding contacts in the respective dbCICA-regression equations (Table 1.). Steps of activity prediction was also employed using docking/scoring settings of (SB-2) dbCICA model to assess the similarity extent in “predicted activity” of both (SB-2) model and the better performing (SB-1) model.

| Hit\(^a\) | NCI Code | SB-1 | SB-2 | % Inhibition at 10 \( \mu \)M |
|---|---|---|---|---|
| | | Contact atoms Summation\(^b\) | Predicted \( K_i \) (nM)\(^c\) | Contact atoms Summation\(^b\) | Predicted \( K_i \) (nM)\(^c\) |
| 138 | 6924 | 8 | 47.07 | 13 | 11.41 | -1 |
| 139 | 10188 | 8 | 47.07 | 13 | 11.41 | 6 |
| 140 | 11193 | 8 | 47.07 | 12 | 18.72 | -7 |
| 141 | 12492 | 8 | 47.07 | 11 | 30.71 | 51 |
| 142 | 12990 | 8 | 47.07 | 13 | 11.41 | -3 |
| 143 | 26037 | 8 | 47.07 | 11 | 30.71 | -72 |
| 144 | 32263 | 8 | 47.07 | 13 | 11.41 | 0 |
| 145 | 33974 | 8 | 47.07 | 13 | 11.41 | 4 |
| 146 | 34870 | 8 | 47.07 | 12 | 18.72 | 0 |
| 147 | 4355 | 8 | 47.07 | 13 | 11.41 | -3 |
| 148 | 7959 | 8 | 47.07 | 13 | 11.41 | 14 |
| 149 | 7960 | 8 | 47.07 | 13 | 11.41 | -1 |
| 150 | 8793 | 8 | 47.07 | 13 | 11.41 | -3 |
| 151 | 11155 | 7 | 97.94 | 13 | 11.41 | -7 |
| 152 | 21194 | 7 | 97.94 | 10 | 50.37 | 1 |
| 153 | 3021 | 7 | 97.94 | 13 | 11.41 | -6 |
| 154 | 34688 | 7 | 97.94 | 13 | 11.41 | -2 |

\(^a\)Hits are as in Figure S3. \(^b\)Contacts summations according to corresponding dbCICA model (Tables 1 and 2). \(^c\)Predicted \( K_i \) (nM) by substituting the number of contacts of each docked compound in the regression equation of the corresponding dbCICA model. *Underlined hits with highest Inhibition\%
Figure S 2. The chemical structures of the tested highest-ranking hits.

| Compound | Structure |
|----------|-----------|
| 80 (NCI 19024) | ![Image of compound 80](image) |
| 81 (NCI 34607) | ![Image of compound 81](image) |
| 82 (NCI 1987) | ![Image of compound 82](image) |
| 83 (NCI 22650) | ![Image of compound 83](image) |
| 84 (NCI 4293) | ![Image of compound 84](image) |
| 85 (NCI 14040) | ![Image of compound 85](image) |
| 86 (NCI 22651) | ![Image of compound 86](image) |
| 87 (NCI 24666) | ![Image of compound 87](image) |
| 88 (NCI 1576) | ![Image of compound 88](image) |
Figure S 2. (Continued) - The chemical structures of the tested highest-ranking hits.

| 89 (NCI 18100) | 90 (NCI 23953) | 91 (NCI 33654) |
|----------------|---------------|---------------|
| ![Chemical Structure](image1) | ![Chemical Structure](image2) | ![Chemical Structure](image3) |

| 92 (NCI 34311) | 93 (NCI 34595) | 94 (NCI 35036) |
|----------------|---------------|---------------|
| ![Chemical Structure](image4) | ![Chemical Structure](image5) | ![Chemical Structure](image6) |

| 95 (NCI 4356) | 96 (NCI 4721) | 97 (NCI 7506) |
|----------------|---------------|---------------|
| ![Chemical Structure](image7) | ![Chemical Structure](image8) | ![Chemical Structure](image9) |
Figure S 2. (Continued)- The chemical structures of the tested highest-ranking hits.

98 (NCI 10637)

99 (NCI 11196)

100 (NCI 12847)

101 (NCI 17288)

102 (NCI 18099)

103 (NCI 22645)

104 (NCI 23413)

105 (NCI 33564)
Figure S 2. (Continued)- The chemical structures of the tested highest-ranking hits.
Figure S 2. (Continued) - The chemical structures of the tested highest-ranking hits.

118 (NCI 29057)

119 (NCI 31475)

120 (NCI 31937)

121 (NCI 3343)

122 (NCI 33550)

123 (NCI 34304)

124 (NCI 34692)

125 (NCI 6807)

126 (NCI 6848)

127 (NCI 10868)

128 (NCI 11191)

129 (NCI 12840)
Figure S 2. (Continued)- The chemical structures of the tested highest-ranking hits.

130 (NCI 12849)

131 (NCI 23575)

132 (NCI 26084)

133 (NCI 28316)

134 (NCI 31011)

135 (NCI 3289)

136 (NCI 5769)

137 (NCI 6888)

138 (NCI 6924)

139 (NCI 10188)

140 (NCI 11193)

141 (NCI 12492)
Figure S 2. (Continued)- The chemical structures of the tested highest-ranking hits.

142 (NCI 12990)

143 (NCI 26037)

144 (NCI 32263)

145 (NCI 33974)

146 (NCI 34870)

147 (NCI 4355)

148 (NCI 7959)

149 (NCI 7960)
Figure S 2. (Continued)- The chemical structures of the tested highest-ranking hits.

150 (NCI 8793)

151 (NCI 11155)

152 (NCI 21194)

153 (NCI 3021)

154 (NCI 34688)
"NMR" Charts & Mass Spectrum
"NMR" Charts & Mass Spectrum For
Hit 88 (NCI 1576)
Figure S 3: $^1$H-NMR Charts for hit 88 (NCI 1576)
Figure S 4: $^1$H-NMR Charts for hit 88 (NCI 1576)
Figure S 5: $^1$H-NMR Charts for Hit 88 (NCI 1576)

Instrument Model:
Bruker 500 MHz - Avance III

Operator: Rola Hassoun
nmr500@ju.edu.jo

Current Data Parameters
NAME: 16octt5jalal
EXPNO: 1561
PROCNO: 1

P1 - Acquisition Parameters
Date: 20161026
Time: 12:49
INSTRUM: spect
PROBMD: 5 mm PA850 BB/
FUPROG: E2
TD: 65536
SOLVENT: DMSO
NS: 16
DC: 0
GWH: 10136.135 Hz
FIDRES: 0.05466 Hz
AQ: 3.2351092 sec
RG: 64.29
DM: 45.333 usec
DE: 6.50 usec
TR: 300.5 K
D1: 2.00000000 sec
TDO: 1

====== CHANNEL f1 ======
SF01: 500.134410 MHz
NUCL: 1H
P1: 10.60 usec
PLW1: 17.39999962 W

P2 - Processing parameters
SI: 131072
SP: 500.130000 MHz
WDN: IM
SSB: 0
LB: 1.00 Hz
GB: 0
PC: 2.00
Figure S 6: $^{13}$C-NMR Charts for Hit 88 (NCI 1576)

The University of Jordan Faculty of Science
Department of Chemistry

Instrument Model:
Bruker 500 MHz—Avance III

Operator: Rola Hassounah
mmr500@ju.edu.jo

Current Data Parameters
THF-D8 300.1 MHz 15.82

PD – Acquisition Parameters
Data 201429
Time 12.67
NSPONK apsack
PFOFS 5 mm FABBO RF
PPOFRO 0.00000
TD 65.56
DQW3147 1000
HE 562
GS 1
SNR 3200-730 Hz
PFR 0.90000 Hz
AQ 0.926472 sec
DS 102.66
DM 15.260 usec
DE 6.60 usec
DEC 366.0 K
DI 2.0000000 sec
DS 0.0000000 sec
TD 4

------- CHARSCL, Z1 -------
CH21 122.7708562 MHz
CH22 135
CH2 14.40 usec
CLH1 83.32496655 MHz

------- CHARSCL, Z2 -------
CH22 599.1327465 MHz
CH22 13
CH21 86.60 usec
CH22 37.39999892 MHz
CHL1 9.31127649 MHz
CHL1 9.15937638 MHz

FD – Processing parameters
SH 32740
SF 327.7577960 MHz
MDH 10
DS 0
LG 1.00 Hz
DB 0
PC 1.00
Figure S 7: $^{13}$C-NMR Charts for Hit 88 (NCI 1576)
Figure S 8: Mass Spectrum for Hit 88 (NCI 1576)
Figure S 9: Mass Spectrum for Hit 88 (NCI 1576)
Figure S 10: Mass Spectrum for Hit 88 (NCI 1576)
"NMR" Charts & Mass Spectrum For Hit 130 (NCI 12849)
Figure S 11: $^1$H-NMR Charts for hit 130 (NCI 12849)

The University of Jordan
Faculty of Science
Department of Chemistry

Instrument Model:
Bruker 500 MHz–Avance III

Operator: Rola Hassouneh
nmr500@ju.edu.jo

Current Data Parameters
NAME  16oct15jalal
EXPNO  2031
PROCNO  1

F2 - Acquisition Parameters
Date_  20161027
Time  7.59
INSTRUM  spect
PROBMD  5 mm PABBO BB/
FULLPROG  EQ
TD  65536
SOLVENT  DMSO
NS  16
DG  0
SNR  10135.135 Hz
FIDRES  0.154650 Hz
AQ  3.2331092 sec
RG  64.29
DW  49.333 ussec
DE  6.50 ussec
TE  300.4 K
DI  2.00000000 sec
TD0  1

====== CHANNEL f1 ======
SP01  500.1344100 MHz
NUCI  1H
F1  10.60 ussec
FLW1  17.39999962 W

F2 - Processing parameters
SI  131072
SP  500.1300000 MHz
WDW  BM
SSB  0  1.00 Hz
GB  0
PC  2.00
Figure S 12: $^1$H-NMR Charts for hit 130 (NCI 12849)

The University of Jordan
Faculty of Science
Department of Chemistry

Instrument Model: Bruker 500 MHz−Avance III
Operator: Rola Hassounah
nrm506@ju.edu.jo

Current Data Parameters
NAME 16oct15jalal
EXPER 2031
PROCNO 1

P2 - Acquisition Parameters
Date_ 20161002
Time 7.59
INSTRUM spect
PROBMHD 5 mm PABBO BR/
FULLPROG zg
TD 65s36
SOLVENT DMSO
R2 16
SS 0
SWH 1013.135 Hz
FIDRES 0.154650 Hz
A2 3.2531092 usec
RG 64.29
DW 49.333 usec
DS 6.50 usec
T9 300.4 K
T1 2.00000000 usec
TDO 1

------- CHANNEL f1 -------
SP01 500.1344108 MHz
S0C1 1H
F1 10.60 usec
PLW1 17.39999962 W

P2 - Processing parameters
SI 131072
SP 500.1300000 MHz
HW 83
SB 0
LB 0
GB 0
PC 2.00
Figure S 13: $^1$H-NMR Charts for hit 130 (NCI 12849)
Figure S 14: $^{13}$C-NMR Charts for hit 130 (NCI 12849)
Figure S 15: $^{13}$C-NMR Charts for hit 130 (NCI 12849)
Figure S 16: $^{13}$C-NMR Charts for hit 130 (NCI 12849)
Figure S 17: Mass Spectrum for hit 130 (NCI 12849)
Figure S 18: Mass Spectrum for hit 130 (NCI 12849)
"NMR" Charts & Mass Spectrum For Hit 85 (NCI 14040)
Figure S 19: $^1$H-NMR Charts for 85 (NCI 14040)
Figure S 20: $^1$H-NMR Charts for hit 85 (NCI 14040)
Figure S 21: \(^1\)H-NMR Charts for Hit 85 (NCI 14040)

The University of Jordan
Faculty of Science
Department of Chemistry

Instrument Model:
Bruker 500 MHz–Avance III

Operator: Rola Hassouneh
nmr500@ju.edu.jo

Current Data Parameters
NAME 16novi5jala
EXPNO 1411
PROCH 1

F2 - Acquisition Parameters
Date_ 20161122
Time 10.25
INSTROM spect
PROBD 5 mm PABBO BB/
PULPROG 2g
TD 655.36
SOLVENT DMSO
NS 4
DG 0
SNR 10135.135 Hz
FIDRES 0.154650 Hz
AQ 3.2331092 sec
KG 3.15
RM 49.333 ussec
DE 6.50 ussec
TB 100.5 K
D1 2.00080008 sec
TDs 1

----------- CHANNEL f1 -----------
SP01 500.1344100 MHz
MIX1 1M
F1 10.60 ussec
PLW1 17.39999962 W

F2 - Processing parameters
c1 131072
SF 500.1300000 MHz
MDR EM
SGS 0
LB 1.00 Hz
GB 0
FC 6.00
Figure S 22: $^{13}$C-NMR Charts for Hit 85 (NCI 14040)

The University of Jordan
Faculty of Science
Department of Chemistry

Instrument Model:
Bruker 500 MHz—Avance III

Operator: Rola Hassouneh
nmr500@ju.edu.jo

Current Data Parameters

Date: 20161222
Time: 10:25

Measurement parameters:

- **F2 - Acquisition Parameters**
  - Data: 512
  - Time: 10.25
  - Z-REDUCTION: 8 ppm
  - FIDPATH: 512
  - DEC: 1940
  - T1: 32004.73 Hz
  - SF0: 0.591838 Hz
  - SF1: 0.096472 sec
  - TN: 15.2 sec
  - TE: 6.5 sec
  - T1: 300.6 sec
  - T2: 2.000000 sec
  - TD: 0.000000 sec
  - T0: 1

- **CHANNEL F2**
  - NPO1: 125.755645 MHz
  - NPO2: 500.132206 MHz

- **CHANNEL F1**
  - NPO1: 15.0 sec
  - NPO2: 9.32245695 W

- **Z-REDUCTION**
  - SF0: 8 ppm
  - SF1: 15.2 sec
  - SF2: 300.6 sec
  - T0: 1 sec

- **Processing parameters**
  - S1: 512
  - S2: 125.755645 MHz
  - SBH: 0
  - LB: 0
  - GB: 1.99 Hz
  - DC: 1.00
Figure S 23: $^{13}$C-NMR Charts for Hit 85 (NCI 14040)
Figure S 24: Mass Spectrum for Hit 85 (NCI 14040)
Figure S 25: Mass Spectrum for Hit 85 (NCI 14040)
"NMR" Charts & Mass Spectrum For Hit 112 (NCI 12415)
Figure S 26: $^1$H-NMR Charts For Hit 112 (NCI 12415)
Figure S 27: $^1$H-NMR Charts For Hit 112 (NCI 12415)
Figure S 28: $^1$H-NMR Charts For Hit 112 (NCI 12415)
Figure S 29: $^{13}$C-NMR Charts for Hit 112 (NCI 12415)
Figure S 30: $^{13}$C-NMR Charts for Hit 112 (NCI 12415)
Figure S 31: Mass Spectrum for Hit 112 (NCI 12415)
Figure S 32: Mass Spectrum for Hit 112 (NCI 12415)
"NMR" Charts & Mass Spectrum For Hit 141 (NCI 12492)
Figure S 33: $^1$H-NMR Charts For Hit 141 (NCI 12492)

The University of Jordan
Faculty of Science
Department of Chemistry

Instrument Model:
Bruker 500 MHz–Avance III

Operator: Rola Hassounah
mmr500@ju.edu.jo

Current Data Parameters
NAME 16nov15jalal
EXPNO 1421
PROCNO 1

F2 - Acquisition Parameters
Date_ 20161122
Time 16.37
INSTRM spect
PROBE 5 mm PABBO BB/
PULPROG 29
TD 66636
SOLVENT DMSO
NS 104
DS 0
SNR 10135.135 Hz
PDRBS 0.154650 Hz
AQ 3.2331092 sec
PG 3.15
DW 49.333 usec
DE 6.50 usec
TE 300.4 K
DI 0
TD0 1

====== CHANNEL f1 ======
SFO1 500.1344108 MHz
WX1 1H
F1 10.60 usec
FLW1 17.39999962 W

F2 - Processing parameters
SI 131072
SF 500.1300000 MHz
WCM RM
SB 0
LB 1.00 Hz
CB 1.00
PC 1.00
Figure S 34: ¹H-NMR Charts For Hit 141 (NCI 12492)
Figure S 35: $^{13}$C-NMR Charts for Hit 141 (NCI 12492)

![13C-NMR Chart](image)

**Instrument Model:**
Bruker 500 MHz—Avance III

**Operator:** Rola Hassounah

**Email:** nm5500@ju.edu.jo

**Current Data Parameters**
- **Date:** 04/05/2013
- **ExpID:** 1442
- **PROCNO:** 3

**F2 - Acquisition Parameters**
- **Sample**: spec
- **PROBNMR**: 5 mm PABBO BB
- **PULNEQ**: 20pGp2
- **TD**: 651.3s
- **SOLVENT**: DMOE
- **H1**: 33.96s
- **DD**: 4
- **SNR**: 328.047 Hz
- **FIDSS**: 2.519136 Hz
- **AQ**: 0.0061472 sec
- **HL**: 202.06
- **DK**: 3.222 usec
- **BF**: 6.50 usec
- **TR**: 300.1 K
- **DI**: 2.0000000 sec
- **EI**: 0.0300000 sec
- **TD0**: 3

**F2 - Processing parameters**
- **SI**: 30560
- **SP**: 125.757780 Hz
- **IH**: 0
- **SB**: 0.106 Hz
- **NR**: 1.00 Hz
- **FC**: 1.20
Figure S 36: $^{13}$C-NMR Charts for Hit 141 (NCI 12492)
Figure S37: Mass Spectrum for Hit 141 (NCI 12492)
Figure S38: Mass Spectrum for Hit 141 (NCI 12492)