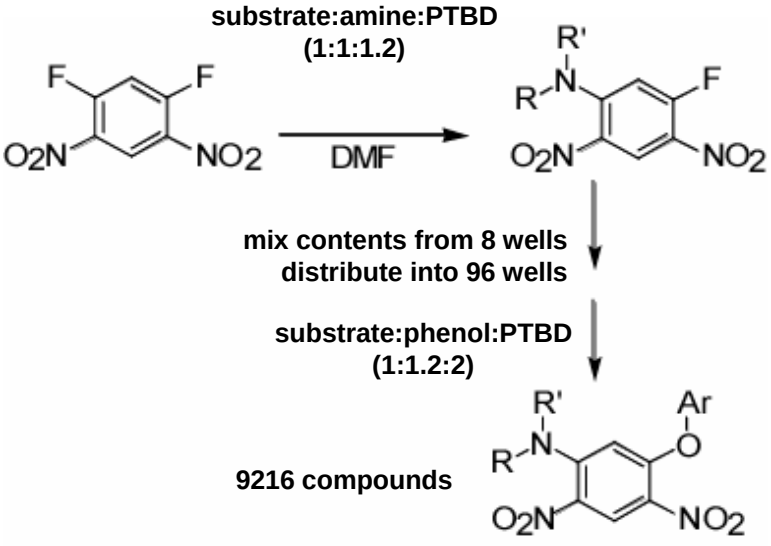
Supplementary Figure 1



Supplementary Fig. 1 - Synthetic route of the 1-alkylamino-5-aryloxyl-2,4-dinitrobenzene library.

Method: In this library 96 alkyl amines and 96 phenol analogs were selected as building blocks. In the first coupling, 96 amines were each reacted with 1,5-difluoro-2,4-dinitrobenzene in 96 separate polypropylene tubes, in the presence of Polystyrene supported 1,5,7-triazabicyclo[4.4.0]dec-5-ene (PTBD) serving as an scavenger, to form 96 different 1-alkylamino-5-fluoro-2,4-dinitrobenzene intermediates. Then the intermediates from 8 tubes (A to H) in the first row of the 96-well microtiter plate foot-print were filtered, mixed and redistributed into 96 wells of a 96-deep well plate. This step was repeated until all the products from the first coupling reaction were pooled (8 tubes each) and redistributed. At this point, there were 12 plates of pooled 1-alkylamino-5-fluroro-2,4-dinitrobenzenes and each well has 8 compounds. In the second coupling, 96 phenols were each added to the corresponding well of each of the 12 plates from the first coupling, then PTBD was distributed to each well to initiate the second coupling reaction. PTBD had dual roles in this step – it functioned as a base to deprotonate the phenols and as scavenger to remove the excess phenols. At the end of the synthesis, there were a total of 1152 wells, and each well contained 8 compounds at a concentration estimated to be 5 mM for each compound. Because the by-product (hydrogen fluoride) and the excess phenols were removed by the polymer-supported reagent (PTBD) and the solvent dimethylformamide is compatible with the bioassay with appropriate dilution, the final products in each well are ready for solution-phase bioassay immediately after simple filtration and without any further purification.