SYNTHESIS, ANTI-PROLIFERATIVE ACTIVITY AND 2D-QSAR STUDY OF SOME 8-ALKYL-2,4-BISBENZYLIDENE-3-NORTROPINONES

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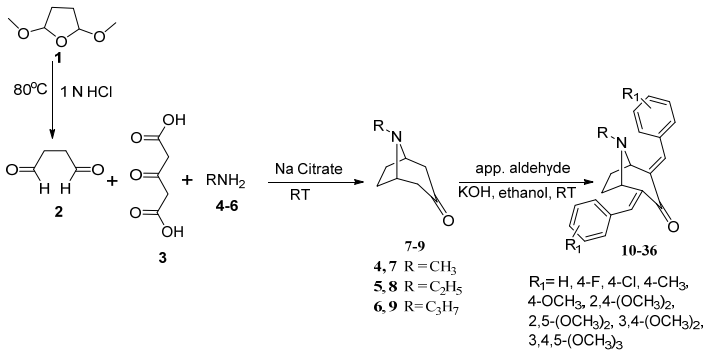
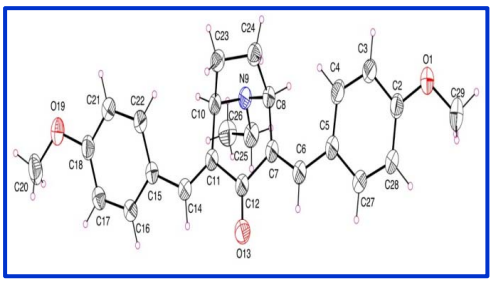
Colon cancer is the third leading cause of death worldwide; therefore, there is a need for an effective therapy with lower side effects. A series of 8-alkyl-2,4-bisbenzylidene-3-nortropinones **10-36** was prepared via Claisen-Schmidt condensation of 8-alkyl-3-nortropinones **7-9** with different aromatic aldehydes. The target compounds were screened for their anti-proliferative activity. Most of the prepared compounds showed promising anti-proliferative activity against many of 60 NCI cell lines at 10 µM. Furthermore, 8-ethyl-2,4-bis(3,4-dimethoxybenzylidene)-8-nortropin-3-one **26** and its 3,4,5-trimethoxy analog **27** were the most active compounds against HCT116 cell line with IC_{50} values 0.01 and 0.46 µM, respectively. Using CODESSA-Pro software, a significant 2D-QSAR model was obtained. Therefore, 8-alkyl-2,4-bisbenzylidene-8-azabicyclo[3.2.1]octan-3-one represents an interesting core for further structural optimization to obtain more promising hits.



Schematic pathway for preparation of 8-alkyl-2,4-bisbenzylidene-3-nortropinones **10-36**



ORTEP projection of single crystal X-ray diffraction of compound **23**