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Synthetic routes for Thiazole-chalcone derivatives and their Biological activities : A brief Review

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Abstract : Thiazolecantainingchalcone and their analogues has getting remarkable attention of researchers to develop new potential therapeutic agents cantaining improved activities .In this review we provided the various synthetic routes for preparation of thiazole bearing chalcones,there biological properties like anticancer,antibacterial,antimalarial etc.

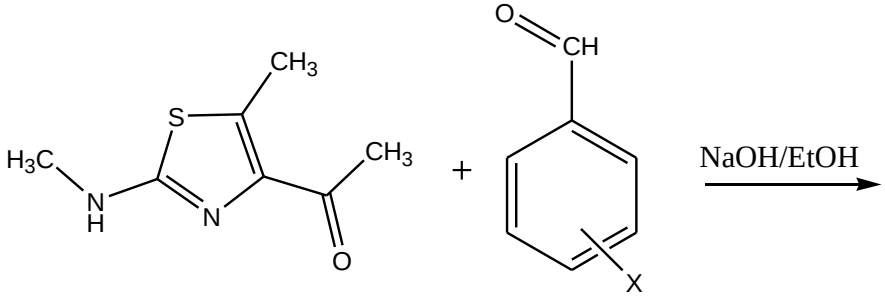
Keywords:Thiazole,Aldolcondensation,ClaisenSchmidthreaction,antibacterial,antimalarial,antiviral.

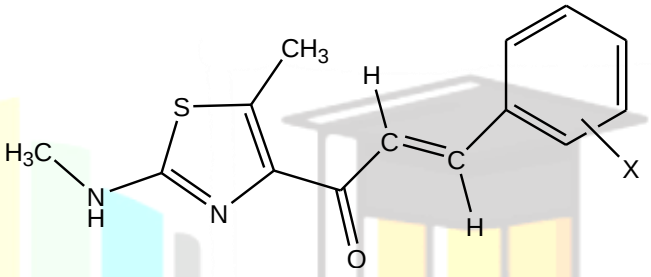
Introduction : Thiazoles were found in several naturally occurring and manufactured drugs with important biological properties. These include Thiamine, Mycothiazole, and homobuteinchalcones. These chalcones were known to have biological properties like antibacterial and inflammation. The imidazo[2,1,b]thiazole composites have become interesting because they have many medicinal properties, like antifungal, antibacterial, anti-inflammatory, and antihypertensive funtions versus a wide range of human cancer cell lines. As a result, chalcones, whether natural or synthetic, were known to have a numurous biological activities, including anti-HIV, tyrosine inhibition, anti-inflammatory, anti-invasion, antibacterial, and antimalarial properties. Their heterocyclics were also known to have a wide range of biological activities.Thiazoles, chromones, and their variants are drawn a lot of interest because they have a wide range of biological functions. The modified chromones that come from both synthetic and natural sources also have a wide range of biological actions, like antifungal, antibacterial, and antiviral properties, as well as other properties. Organic and medicinal chemists spent a lot of time looking into the wide range of biological effects that thiazole derivatives could have. The important changes in the pharmacokinetics and pharmacodynamic features of the drug molecules are significant. Thiazole-chalcone hybrids have been shown to have hopeful antimicrobial, anticancer, and lipoxygenase-inhibiting properties. Chlcones are naturally occurring biarylpropenones that are part of the flavonoid family. They have a lot of different biological functions that make them perfect for a multitude of activities, from malaria and cancer to viruses. In many fruits and vegetables, there are a lot of these things. Cancer is a group of diseases that cause abnormal cells to grow and spread all over the body. Thiazoles were heterocycles that had S and N atoms at positions 1,3 each. Thiazole derivatives were said to have anti-cancer properties versus many types of cancer, and they were found to be JAK2 and EGFR inhibitors. Chalcones were a unique class of ketones that were predecessors to flavonoids and iso-flavanoids that had biological effects. They had a broad range of biological activities, antimitotic, anti-cancer, antimalarial, antifungal, antioxidants, antituberculosis, antigenic, antileishmanial, antiviral, and antibacterial impacts

Synthetic Routes :

1. **Aldol condensation**

ThorayaA.Fraghaly et.al(Farghaly, n.d.)were made by combining the 4-acetyl thiazole derivative with different types of aromatic aldehydes 2a-f derivatives in an aldol reaction.

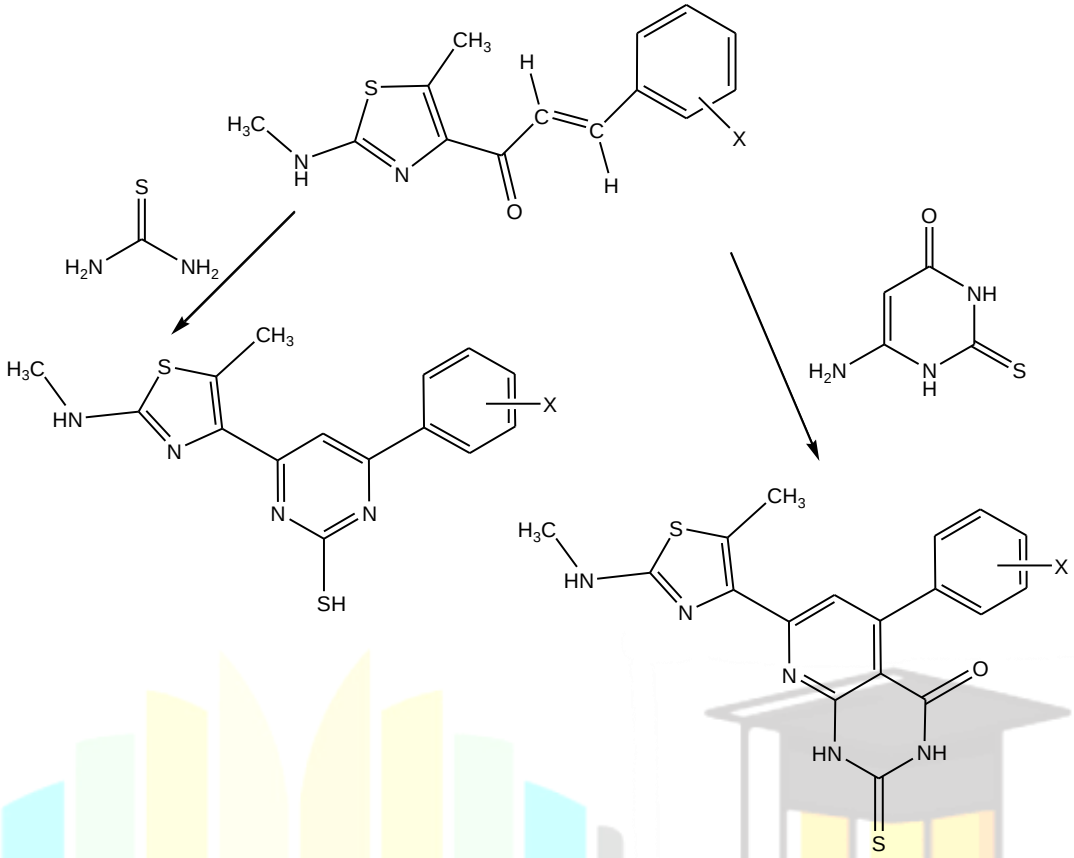




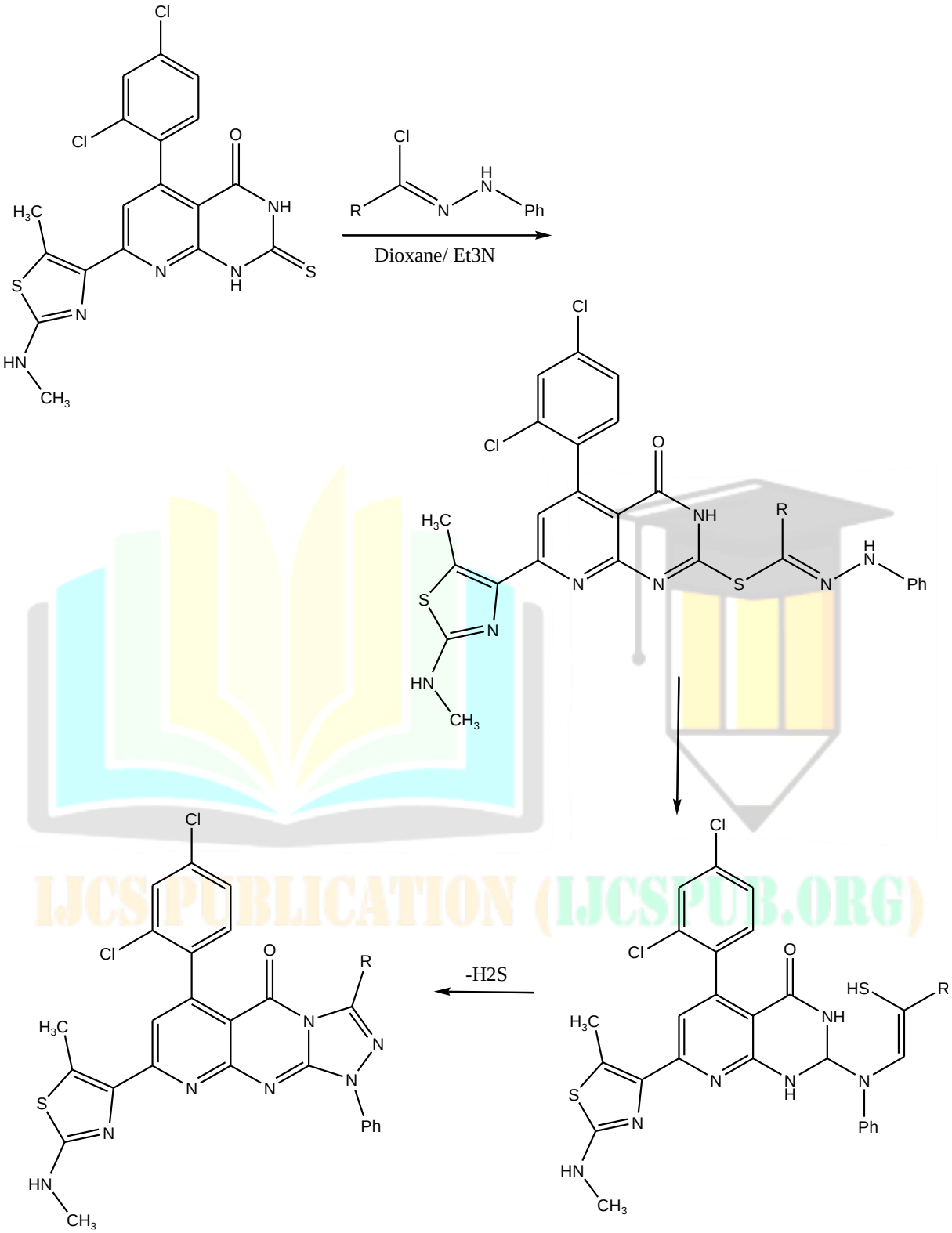
2a-f

a	b	c	d	e	f
X =	OCH_3CH_3	H	F	Cl	2,4- Cl_2

They were made by different pyrimidine thione substituents such as follows.

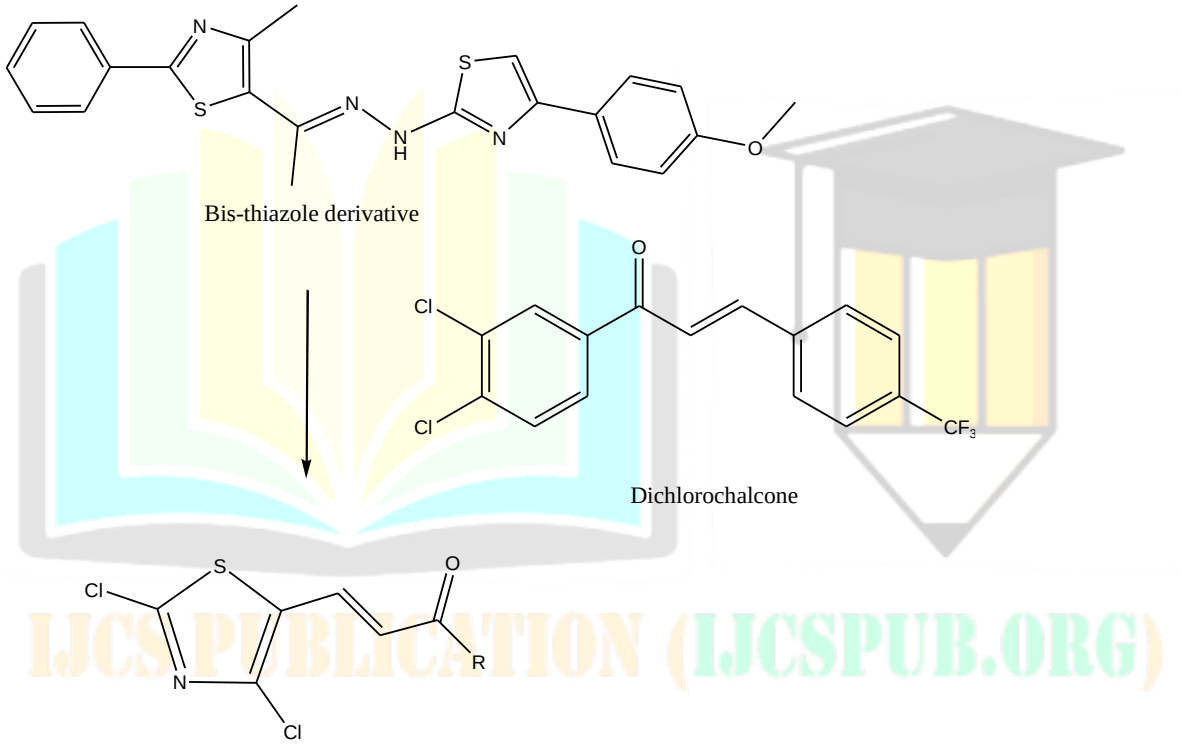


They were made frompyridopyrimidinethione substituentswith hydrazonoyl chlorides.



Biological activity: A group of thiazole derivatives that had been prepared was examined in order to fight three different types of tumours in a lab. The liver cancer cell line (HepG-2), the lung cancer cell line (A549), and the breast cancer cells were all used (MCF-7). The IC50 values of these thiazolyl derivatives were compared to Doxorubicin. All of the derivedchalcones had potent cytotoxicity versus the three cell lines that were investigated, except for 3F, which had a 2,4-dichlorophenyl group. The most active compound, 3a, had a 3-Methoxyphenyl moiety and was twice as efficient as Doxorubicin against Hep-G-2, A549, and MCF-7. Moreover, chalcone had similar antitumor impacts to the drug used as a reference for the pyrimidine series. The chalcones show very similar antitumor effects to the pyrimidines, respectively. The S-alkylated derivatives, on the other hand, constructed the pyrimidine nucleus bigger, which made them less efficient against cancer.

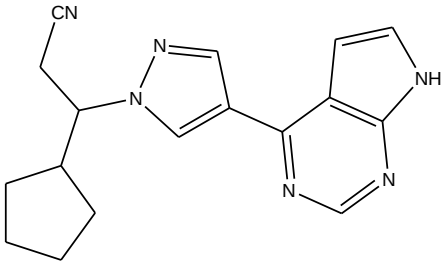
Ashok BabuKasetti et al.(Kasetti et al., 2021)were made various substituted aromatic ketones were blended with 2,4-dichlorothiazole-5-carboxaldehyde in the presence of glacial acetic acid and hydrochloric acid to make thiazolechalcones hybrids. They were isolated in 75% to 91% of the mixture.



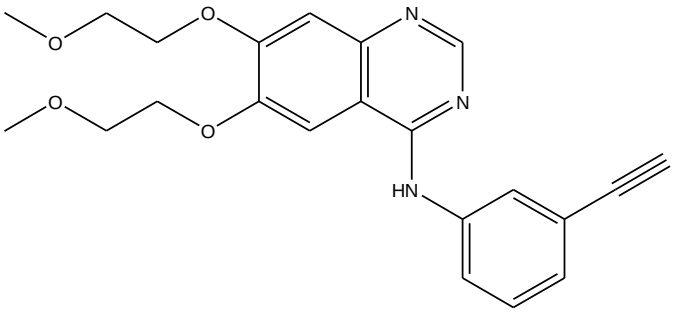
Biological activity : The compounds were screened for their antitubercular, antiproliferative, and cytotoxic strengths by MASA and MTT tests, and there outcomes are shown. The target compounds were divided into three groups: monosubstituted phenyl-based chalcones, disubstituted phenyl-based chalcones, and unsubstitutedheteroaryl variants (bioisosteres of the phenyl ring). In the monosubstituted group, the electron-withdrawing group's Cl and F were at the ortho (1,9), meta (2,10), and para (3,11) positions on the phenyl ring. In the disubstituted group, the electron-withdrawing group's Cl and F were at the 2,3-, 2,6-, 2,5-, 2,4-, 3,4.

KampanSanchai et al.(Sanachai et al., 2021)were placed together are a class of heterocyclic compounds with sulfur and nitrogen atoms at positions 1 and 3. The thiazole derivatives were found to have anticancer action versus number of forms of cancer and were recognized as JAK2 and EGFR inhibitors. Because HMC-1.1 cells are hematopoietic progenitors in the bone marrow, the drug that produced them less plausible to develop had an IC-50 valine value of 138nm. The 4,5-dimethyl thiazole analog, on the other hand, might be able to prevent the JAKZ and JAK2 activities of the EGFR-TK31 cell line. The thiazole analog, 2-

[benzo(4,5)imidazo[2,1b]thiazol-3-yl]-N-[2-hydroxyphenyl]acetamide, was found to be a productive EGFR blocker [IC50 = 55 mM] by making a hydrogen bond with Met 769 at the hinge region of EGFR-TK31A.



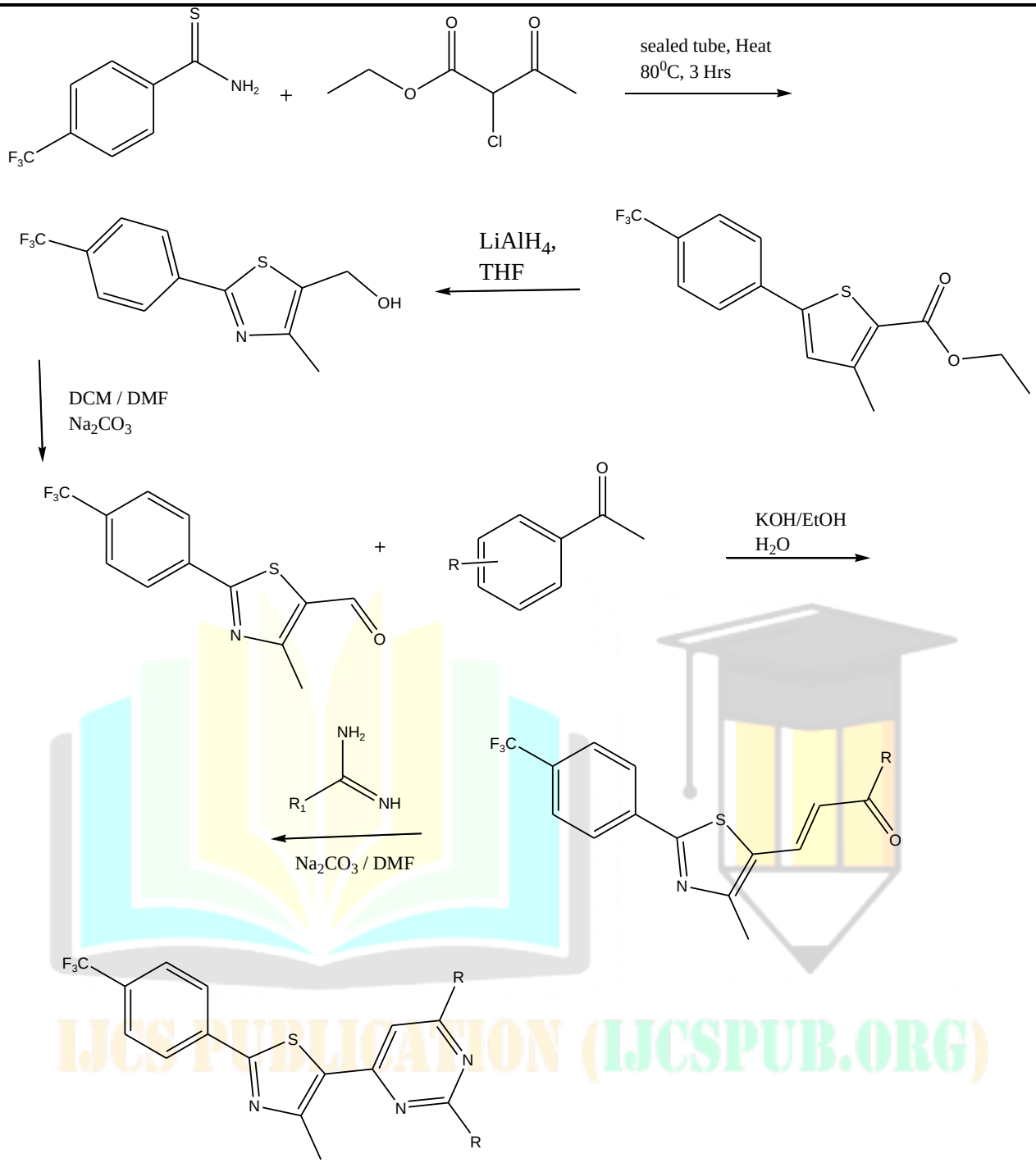
Ruxelitinib



Erlotinib

Biological activity : At first, thiazole derivatives and well-known drugs (Ruxolitinib and Erlotinib) at 10 nm were checked for cytotoxicity versus TF1 and HEL cell lines that expressed EGFR. These tests were done in a lab. They discovered that HEL erythroleukemia cell line was vulnerable to compounds, but the A431 lung cancer cell line was susceptible to derivatives. Two cell lines weren't responsive to our thiazole bases. They were TF1 and A549 cells, though. Compounds were also analysed in terms of their cytotoxicity to normal kidney cells, vero cells. Ruxolitinib and Erlotinib are two drugs that are already on the sector.

ChekrapaniKesari et.al(Kesari et al., n.d.)were constructed a sequence of 4-amino -5-cinnamoylthiazoles that have almost been made and tested for anti-cancer properties. Cell lines from three different types of cancer have been used to evaluate the cytotoxicity (breast carcinoma MCF-7, human liver cancer HepG-2 and human colon adencarcinomaSW480). (E)-1-(4-amino -2-(pyrolidin-1-yl)thiazol-5-yl) The most influential compound found during the in vitro structure-activity relationship (SAR) study we describe here was -3-(2,4-dichloropenyl)prop-2-en-1-one. This compound was found during the preparation and anticancer activity of a new series of structural analogues. € -3-(4-methyl-2-(4-(trifluoromethyl)phenyl)thiazol-5-yl)-1-phenyl prop-2-en-one derivatives as part of our work on anticancer agents.



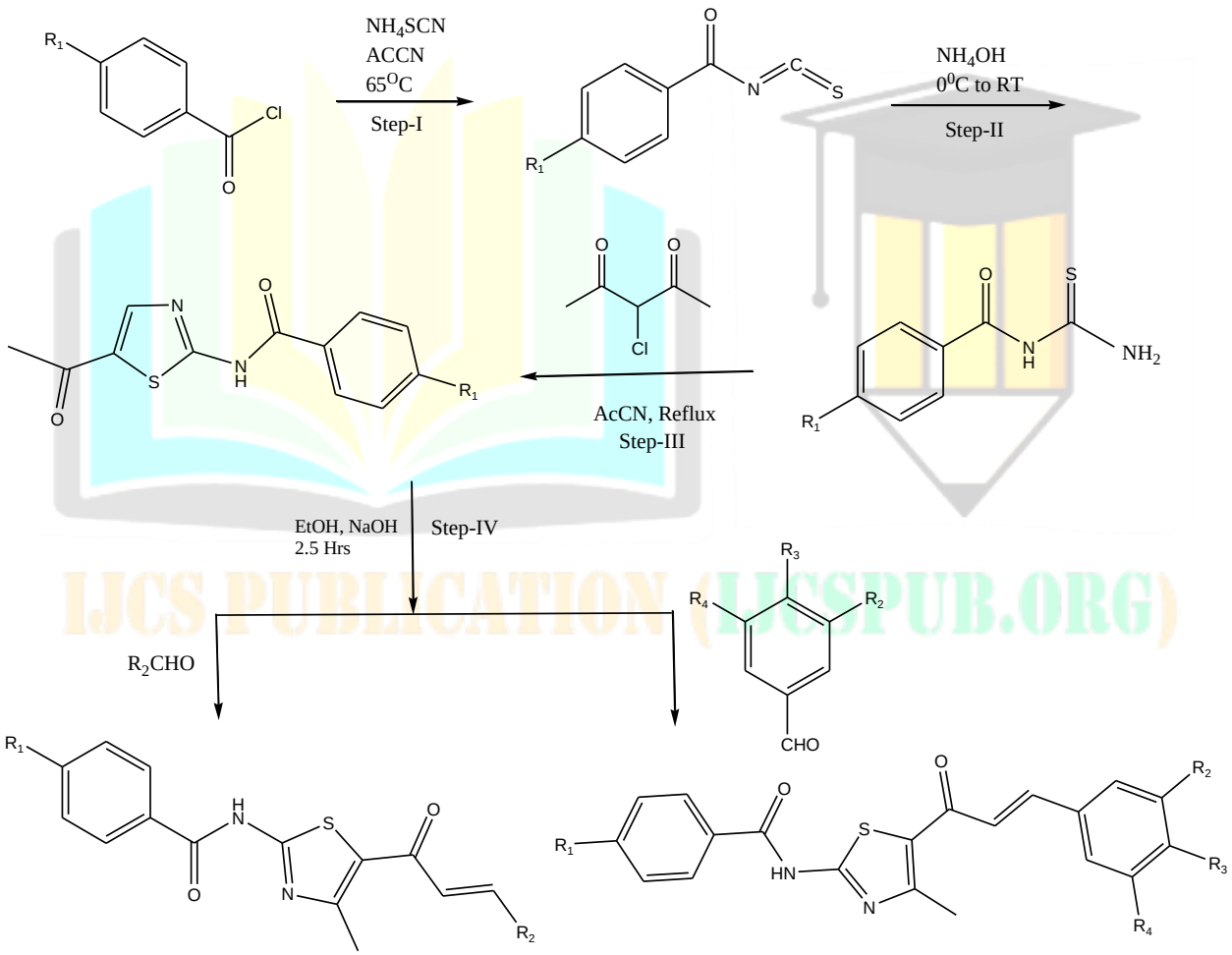
Biological activity: First, thiazole compounds and quite well drugs (ruxolitinib and erlotinib) at 10 nm were tested for cytotoxicity against TF1 and HEL cell lines that had JAKZ and A549 and A431 cell lines that had EGFR. They found that HEL erythroleukemia cell lines were vulnerable to compounds, but A431 lung cancer cell lines were not. However, TF1 and A549 cells were not responsive to our thiazole-based chalcones. This is why we didn't use them. Another thing that was glanced at was how bad the compounds were for normal kidney cells called Vero. Ruxolitinib and Erlotinib are two well-known drugs that do this**.**

2. Claisen-Schmidth condensation Reaction

Shweta Sinha et al.(Sinha et al., n.d.) a series of benzo[d]imidazo[2,1-b]thiazole-chalcone conjugates (5a-aa) were designed, synthesized and evaluated for their cytotoxic potency against a panel of human cancer cell lines like lung (A-549), breast (MDA MB-231), prostrate (DU-145) and colon cancer (HT-29). Preliminary results revealed that some of these conjugates like 5d and 5u exhibited significant antiproliferative effect against human breast cancer (MDA MB-231) with IC50 values of 1.3 and 1.2 mM respectively. To investigate the mechanistic aspects underlying the activity, the detailed biological studies of these promising conjugates (5d and

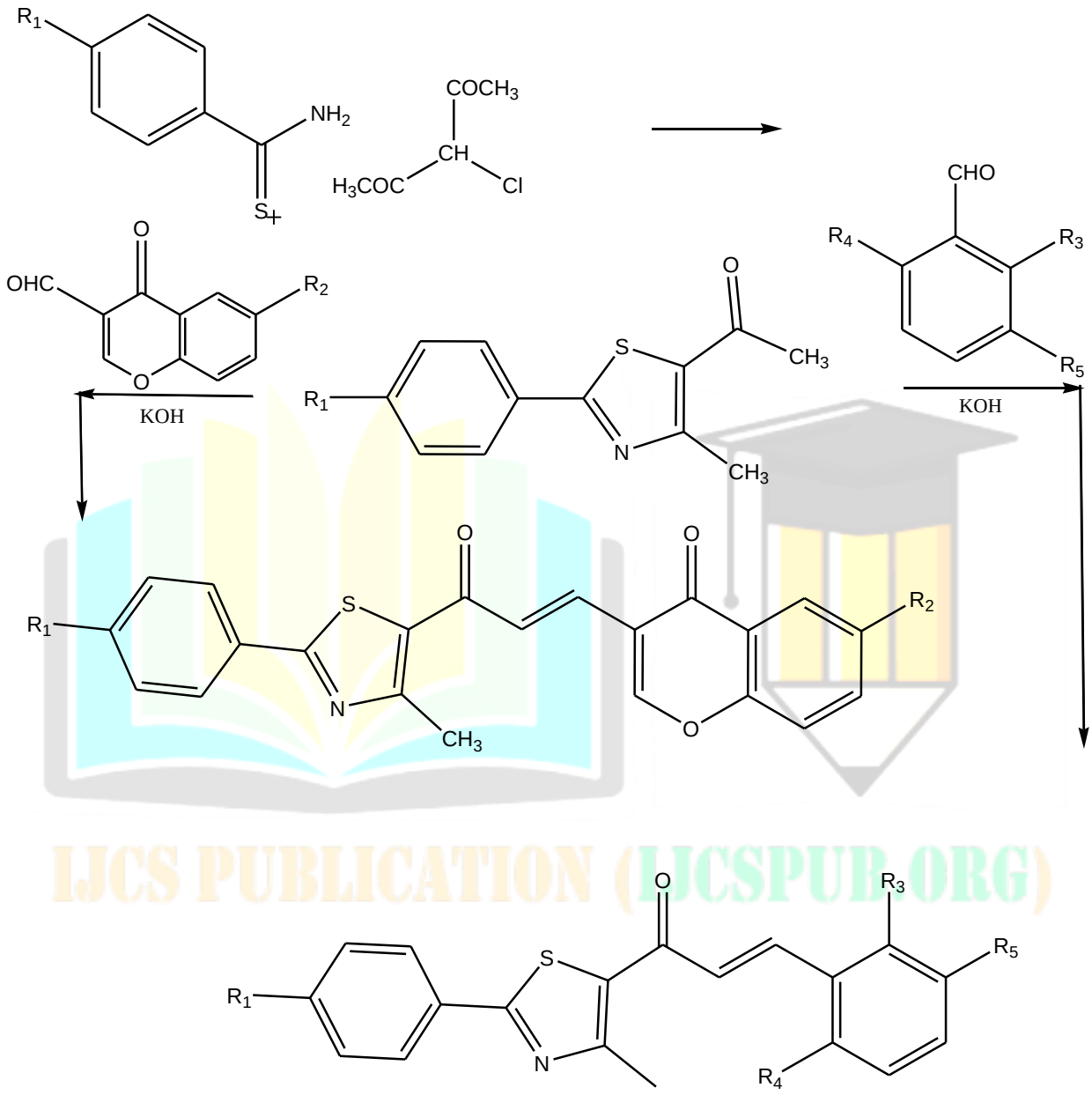
5u) were carried out on the MDA MB-231 cancer cells. Flow cytometric analysis revealed that these conjugates induce cell-cycle arrest in the G2/M phase. The tubulin polymerization assay suggests that these conjugates effectively inhibit microtubule assembly. In addition, morphological changes, reactive oxygen species (ROS) detection by 20, 70–dichlorofluorescindiacetate (DCFDA) and annexin V–FITC/PI assays indicate that 5d and 5u induces apoptosis. Furthermore, in silico computational studies, including molecular docking studies have been carried out to rationalise the binding modes of these conjugates with the tubulin protein.

Sinh et al.(Sinha et al., n.d.) were made some new chalconethiazoles, which have been the main precursors and can be made as before. This is how you made the first step of the process: You mixed benzoyl chloride with acetonitrile, which has ammonium thiocyanate. In the second step, the product in acetonitrile is blended with the proper quantity of ammonium hydroxide at 0 degrees Celsius. When making the third step, 3-chloropentane-2,4-dione was placed into the intermediate from the second step. N-Carbamothiolyl substituted benzamides were reacted with reflux to produce the intermediates we wished. N-(5-Acetyl-4-methylthiazol-2-yl) substituted benzamide was manufactured by Hantzschthiazole synthesis, and the Claisen-Schmidt condensation reaction was used to make the hybrids.



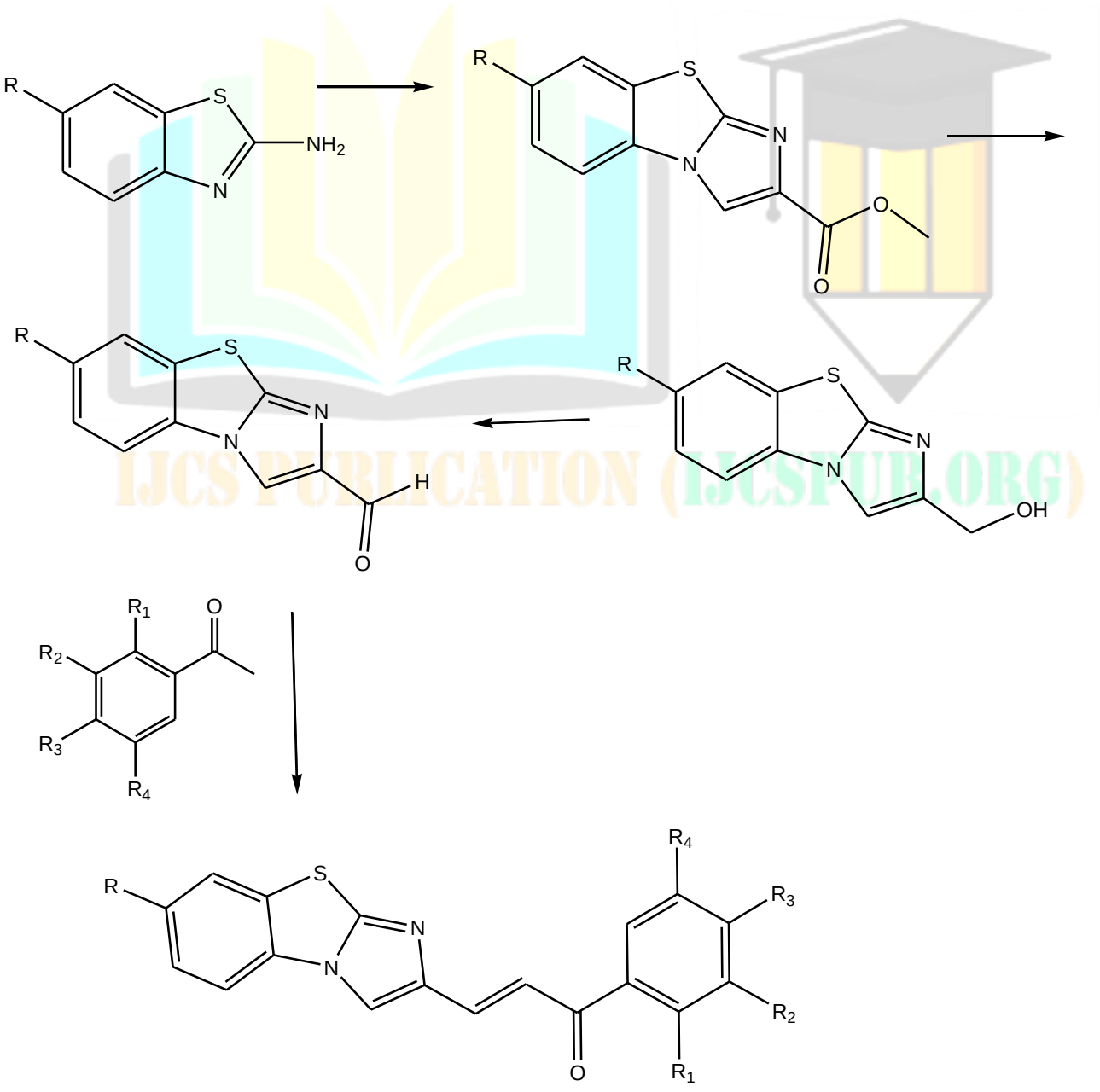
Biological activity: Tests were done in vitro with zileuton as the "reference drug" in a cell-free system with a human recombinant 5-lox enzyme. All the compounds at a concentration of 10 micrometres were inspected. At -236, the inhibition was assessed by looking at the conversion of substrate AA to the product, 5 HPETE. DMSO was used as a negative control, which didn't show any inhibition. The reference drug Zileuton had an IC50 of 1.05=+ 0.03 micrometers, which the literature said was expected**.**

DagobertTazoo et al. (Tazoo et al., n.d.) were made **e**ighteen chalcones were constructed by Claisen-Schmidt condensation. The beginning for 2-aryl-4-methyl -5-acetylthiazole(1-3) was formed by blending some aryl thioamides (Hantzsch reaction) with 3-chloroacetyl acetone in ethanol at a low temperature with good yields. The response of 2-aryl-4-methyl -5-acetylthiazole with various chromones and aldehydes in the presence of solid KOH in ethanol led to an excellent result of the compounds.



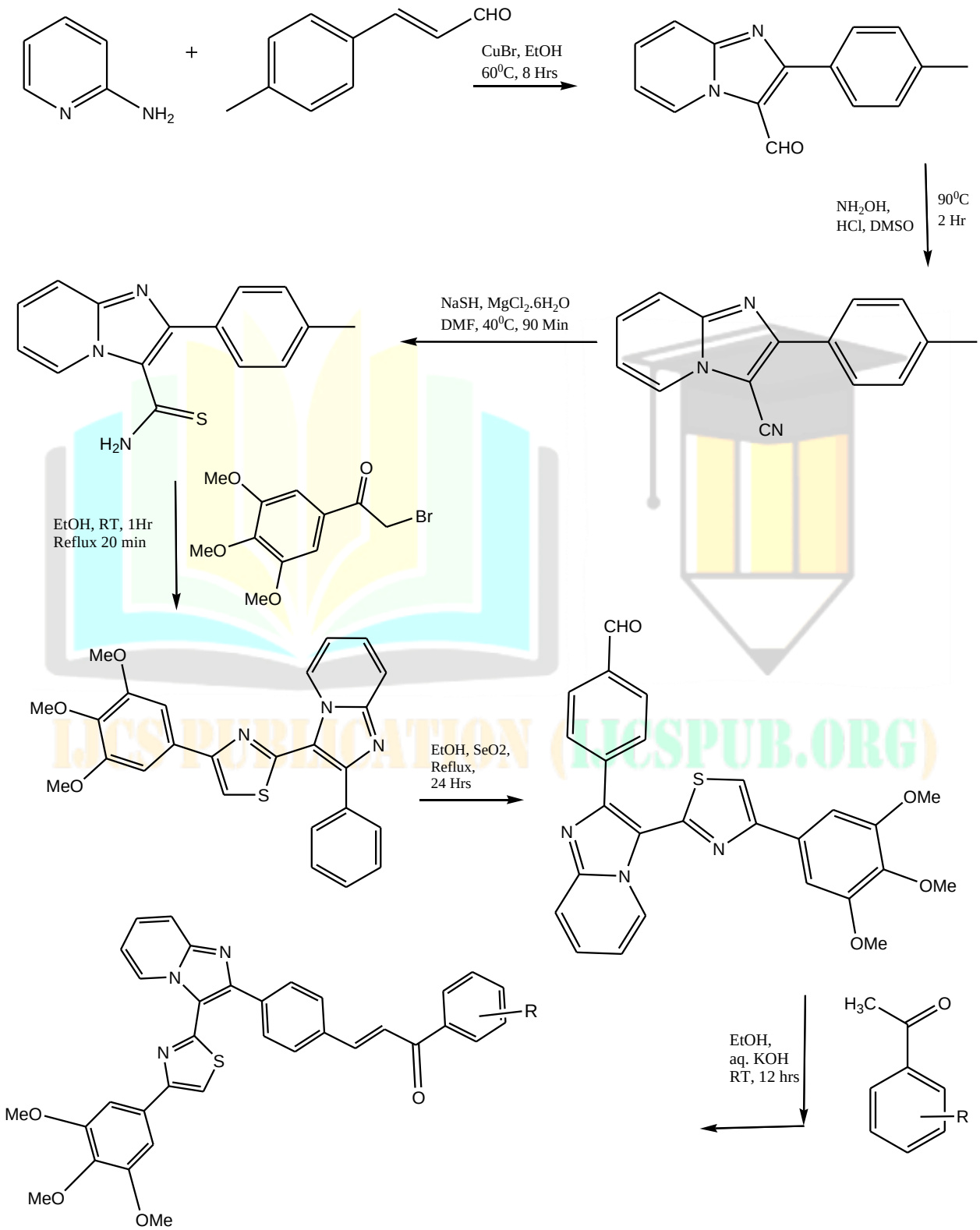
Biological activity : The therapies for infectious diseases and the growing number of microbial pathogens are difficult to treat drugs. Hospitalized patients, persons with AIDS, and people who have had organ transplants or anticancer therapies were becoming more and more likely to have a therapeutic problem. There were a lot of antibiotics and chemotherapeutics that could be used. Still, the chalcones (1,3-diarylpropenone or 1,3-diphenyl-2-propen-1-one) are an essential group of natural products with a wide range of biological effects, including antibacterial, antitumor, antioxidant, antifungal, antiviral, and anti-inflammatory effects.

Faria Sultana et al. (Sultana, 2018)chalconebenzo[d]imidazo[2,1,b]thiazole conjugates were made from the substituted ethylbenzo[d]thiazole. imidazo[2,1,b] Substituted 2-aminobenzothiazoles were easily made into thiaazole-2-carboxylates by combining them with ethyl bromopyruvate. These were then reduced with $LiAlH_4$ to make substituted benzo[d]thiazoles, which can be used to make other things. It started with imidazo[2,1,b]thiazol-2-ylmegthanol, which was then oxidised by Dess Martin over and over again to make benzoylmegthanol. [d] imidazo[2,1,b] This is thiazole-2-carbaldehyde and chalconebenzo[d]. imidazo[2,1,b] Claisen-Schmidt reactions made thiazole conjugates. Acetophenones with the appropriate substituents were blended with benzo[d]imidazole-2-carbaldehyde.



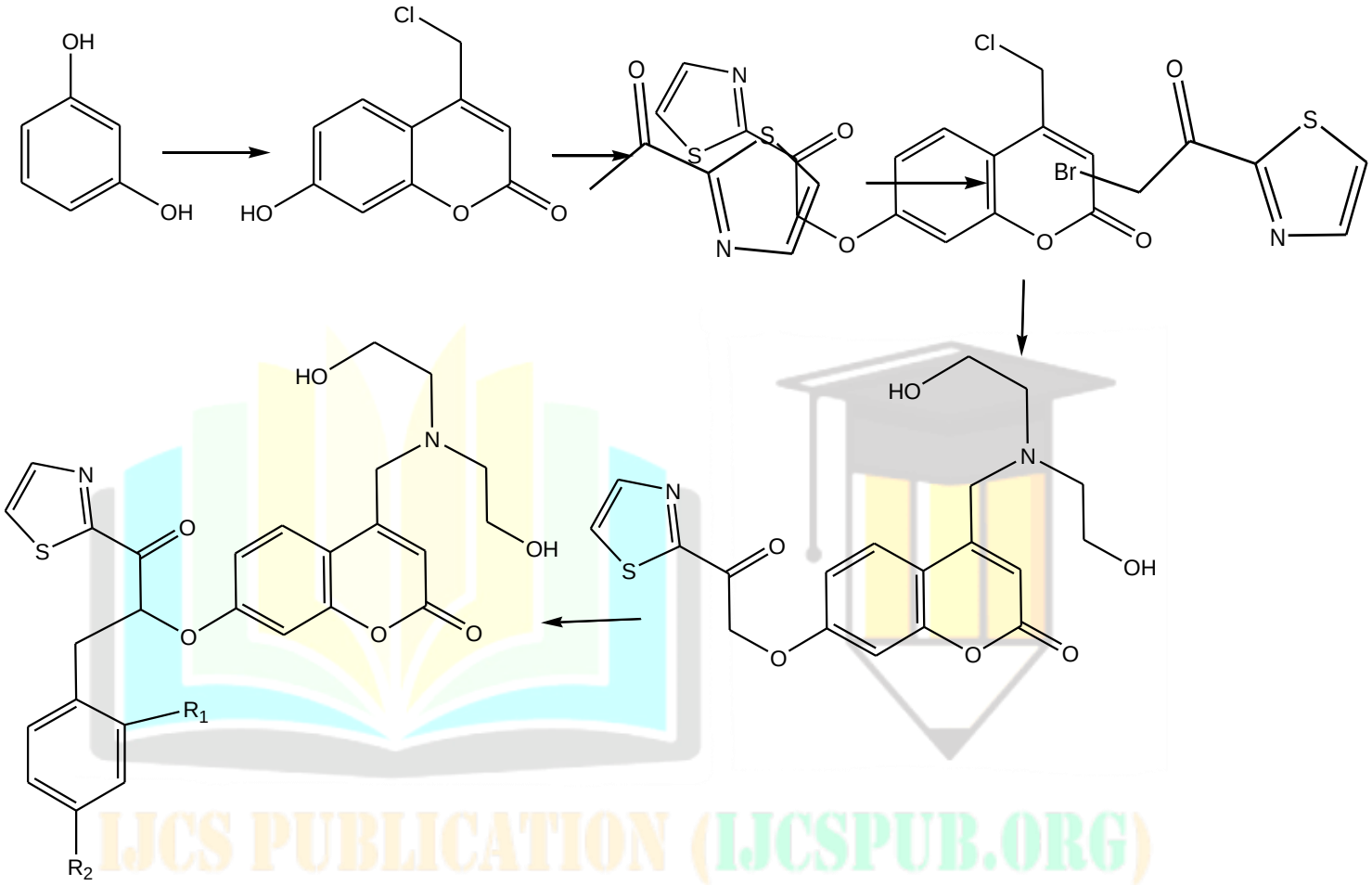
Biological activity: MTT was used to see how well chalcone-linked benzo[d]imidazo[2,1,b]thiazole conjugates worked against a variety of different types of human cancer cells, including lung, breast, prostate, and color cancer cells. Doxorubicin and nocodazole were used as the standard compounds and IC50 values. The chalcone-linked thiazoleconjugates formed also had moderate to excellent antiproliferative action, with IC50 values ranging from 1.28 to 50 micrometers.

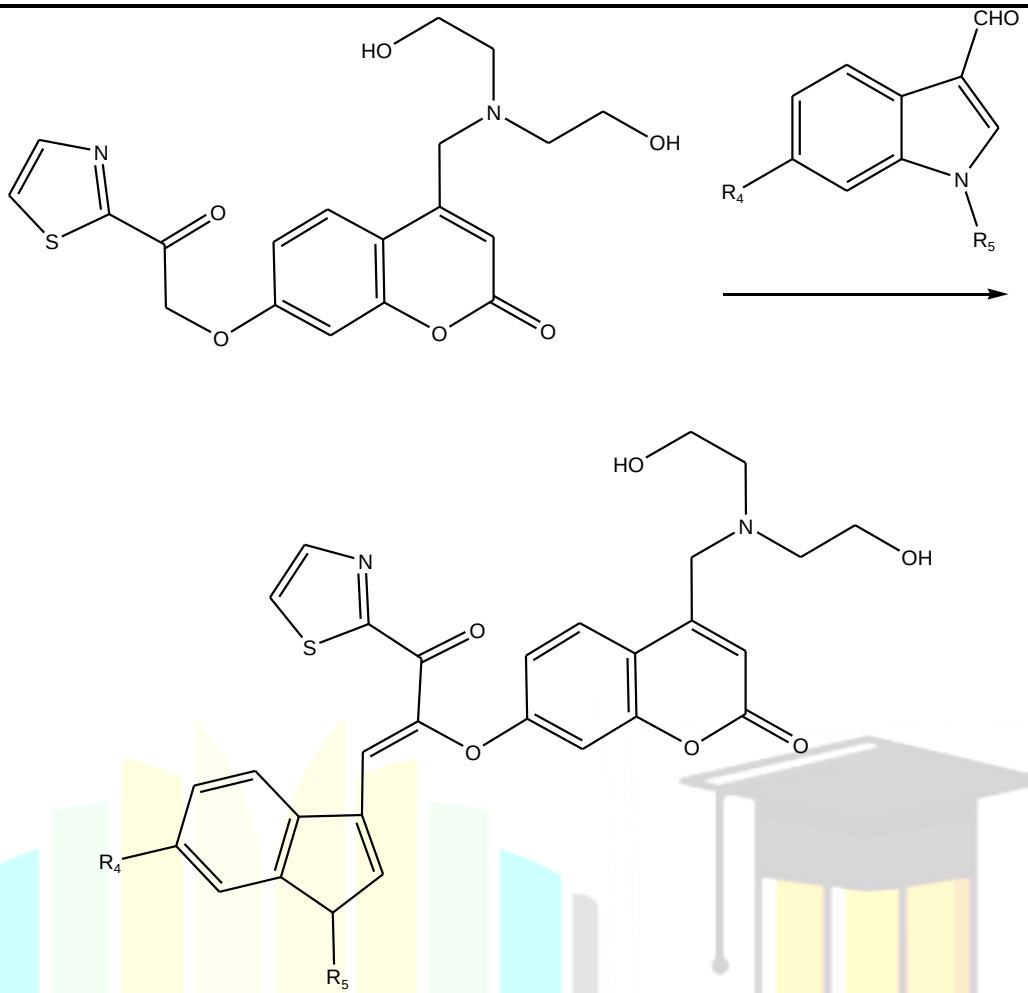
VellankiRagha Suma et al.(Suma, n.d.)were prepared different chalcone substituents of imidazopyrimidenes with aldehydes.



Biological activity: The molecules were tested for their anticancer action versus four human cancer cells lines i.e. MCF-7C (breast carcino), A549 (lung carcinoma), DU-145 (prostate carcinoma) and MDA MB-231 (breast carcinoma) via MTT method and clinical drug etoposide was used as the positive control. The etoposide was used in chemotherapy medication for the cure of various types of cancer etoposide as reference drug.

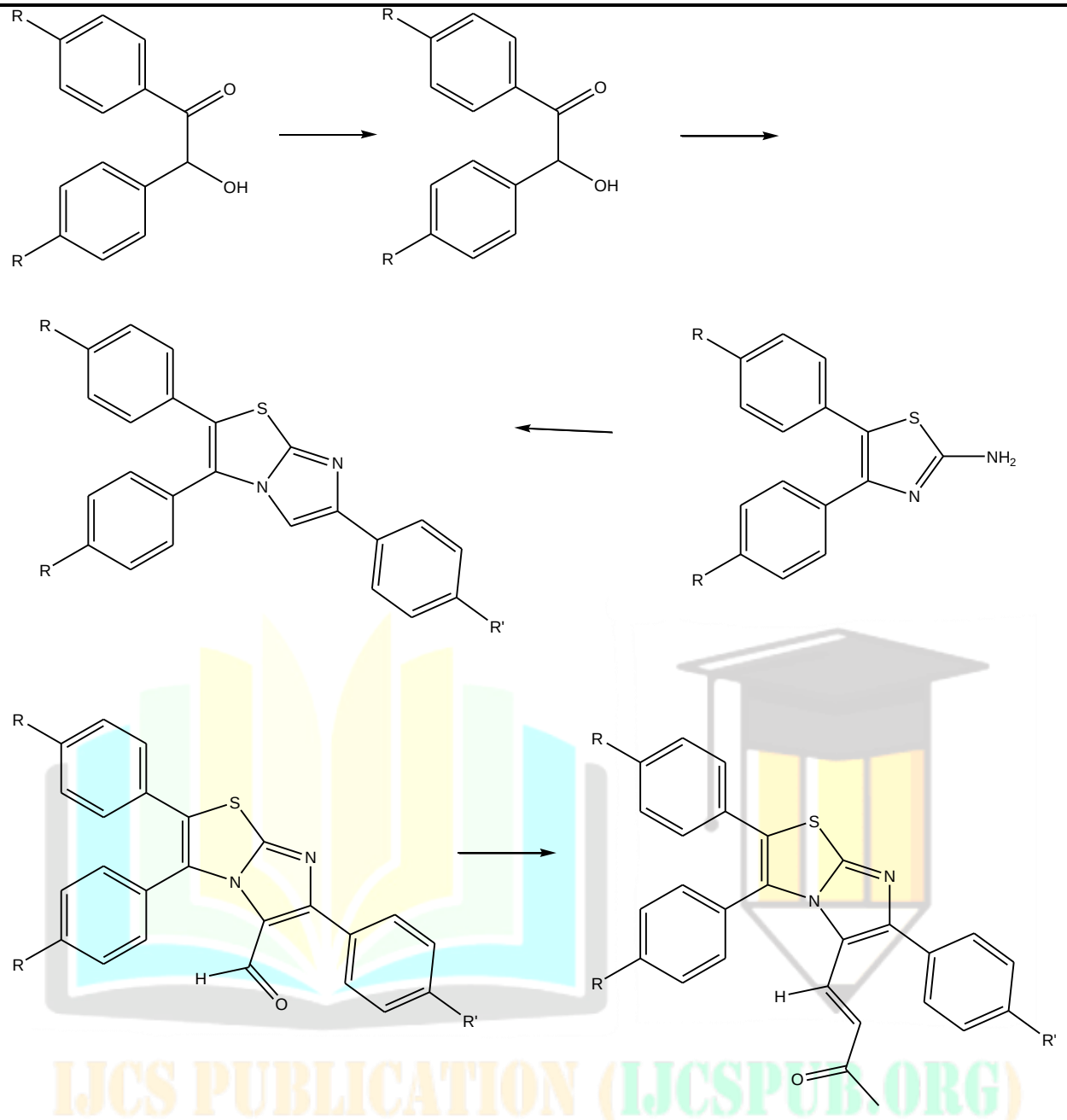
Yuanyuan Hu et al.(Hu, 2021)were made a series of novel chalcone conjugated coumarinthiazole hybrids was designed and synthesized using the synthetic routes outlined.





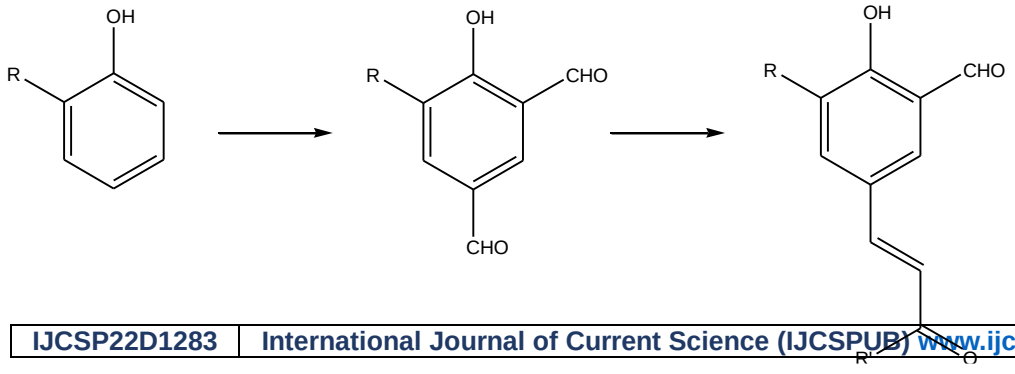
Biological activity: Antibacterial activity:The newly derivedcoumarinthiazole derivatives in vitro Norfloxacin a widely used clinically effective antimicrobial agent was employed to compared the antibacterial activity the less inhibitory concentration (MIC) was the minimum concentration (mM)at which target compounds could fully resist bacterial growth a good knowledge of structure activity relationship (SAR) of chalcone conjugated coumarinthiazole hybrids the series of phenyl derived coumarinthiazole hybrids could be observed that series of derivatives showed obvious selectivity towards MRSA strains.Themethoxy benzene modified hybrid showed high resistence versus MRSA compared with other products with a MIC value of 0.004 mM was 6 times higher compared to standardnorfloxacin (0.025Mm)

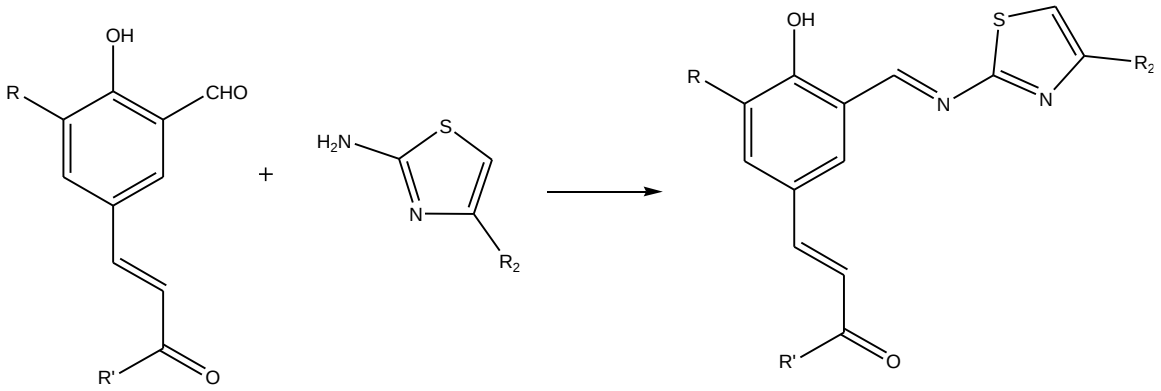
Ahmed Kamal et al.(Kamal et al., 2014)were synthesized series of novel chalconeimidazo [1,2,b] thiazole from commercially available benzoin and anisoin under the claisenschmidt condensation to imidazo [1,2,b]thiazolechalcone conjugates.



Biological activity: Antiproliferative action of five human cancer cell lines i.e. MCF-7 (breast),A549(lung),Hela (cervix),DU-145 (prostrate),HT-29 (colon) by employing and MT cell viability assay with doxorubicin as a stnadardantiproliferative activity with IC50 values ranging from 0.64 to 30.9 micrometer versus checked cell lines.The IC50 values of 0.64 micrometer most sensitive A549 cells was selected a model cell line for subsequent experiment.

KoneniV.Sachidhara et al.(Sashidhara et al., n.d.)were made a series of novel hybrids possessing chalcone and thiazole moieties.

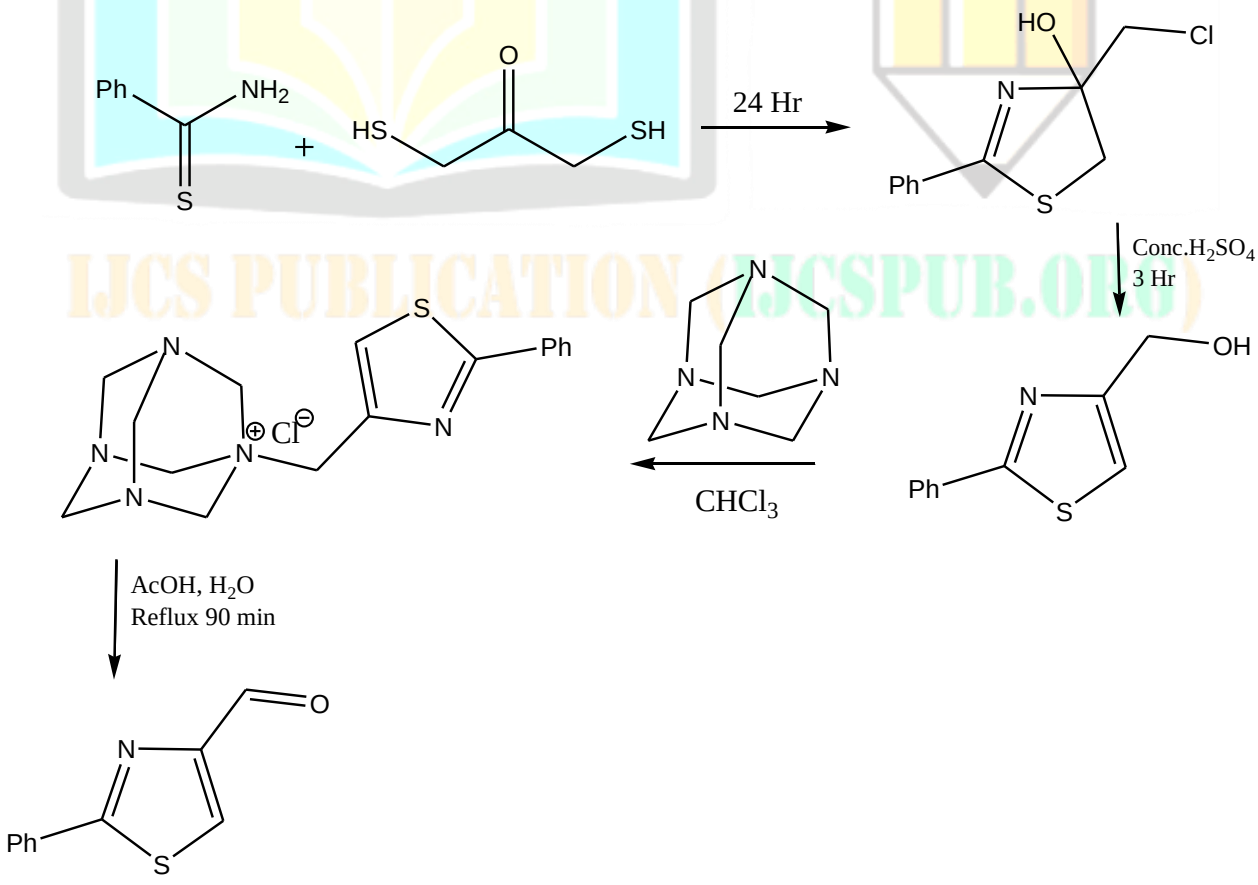


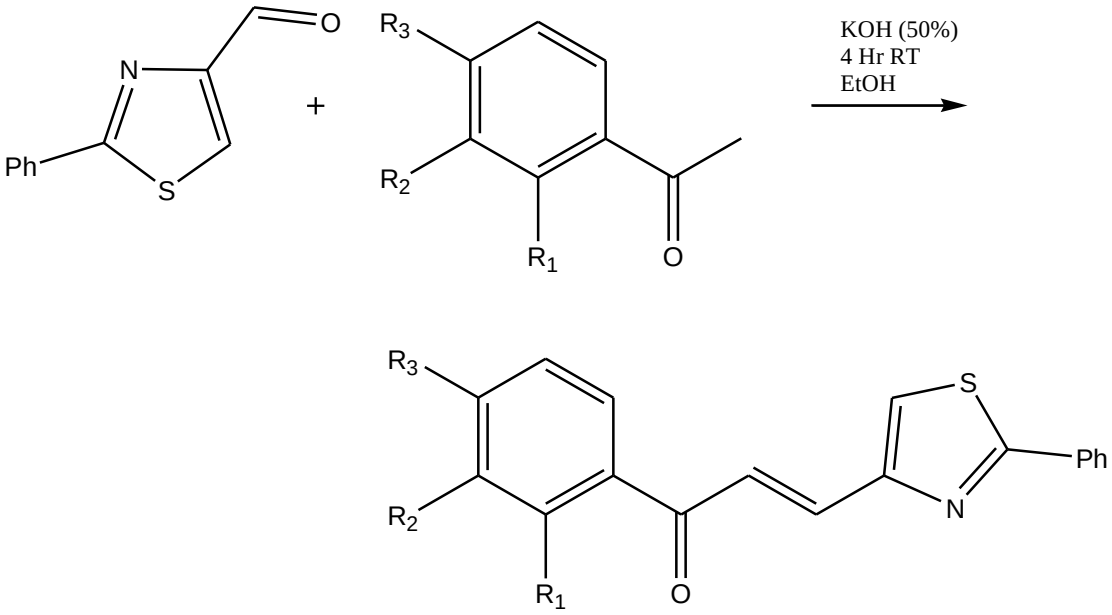


Biological activity: All of the hybrids that were made were evaluated to kill bacteria in the lab, using norfloxacin and gentamycin as a guide. The chalconethiazole hybrids were efficient against various strains of Staphylococcus aureus. Using human RBC hemolytic activity, an image of the preliminary structure-activity relationship (SARS) will be shown. The molecules seemed to have reduced MIC values and no hemolytic behavior, so they were selected to screen in the MTT**.**

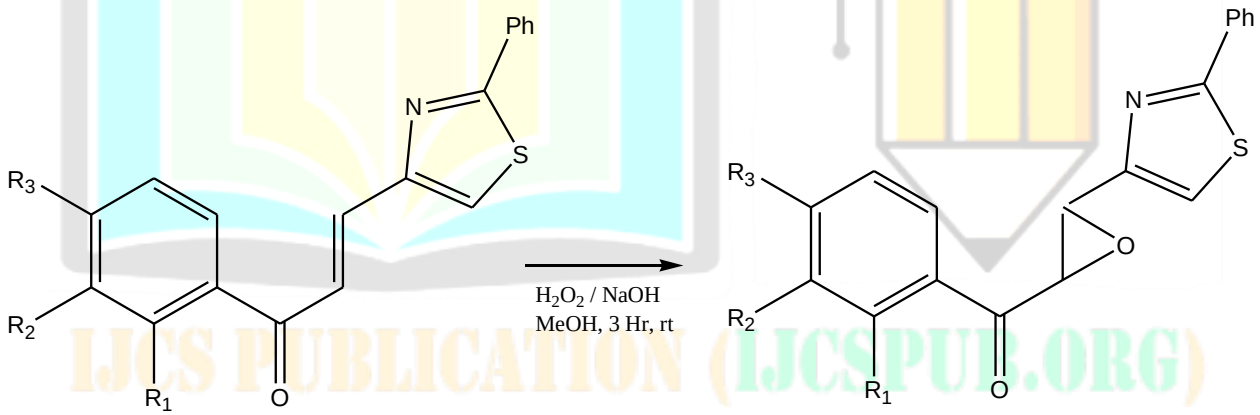
3. Hantzsch-Sommlet Reaction

Irederic Nana et al.(Nana et al., 2020)were prepared thiazolylchalcones via classic reactions of Hantzsch and Somelet reaction.

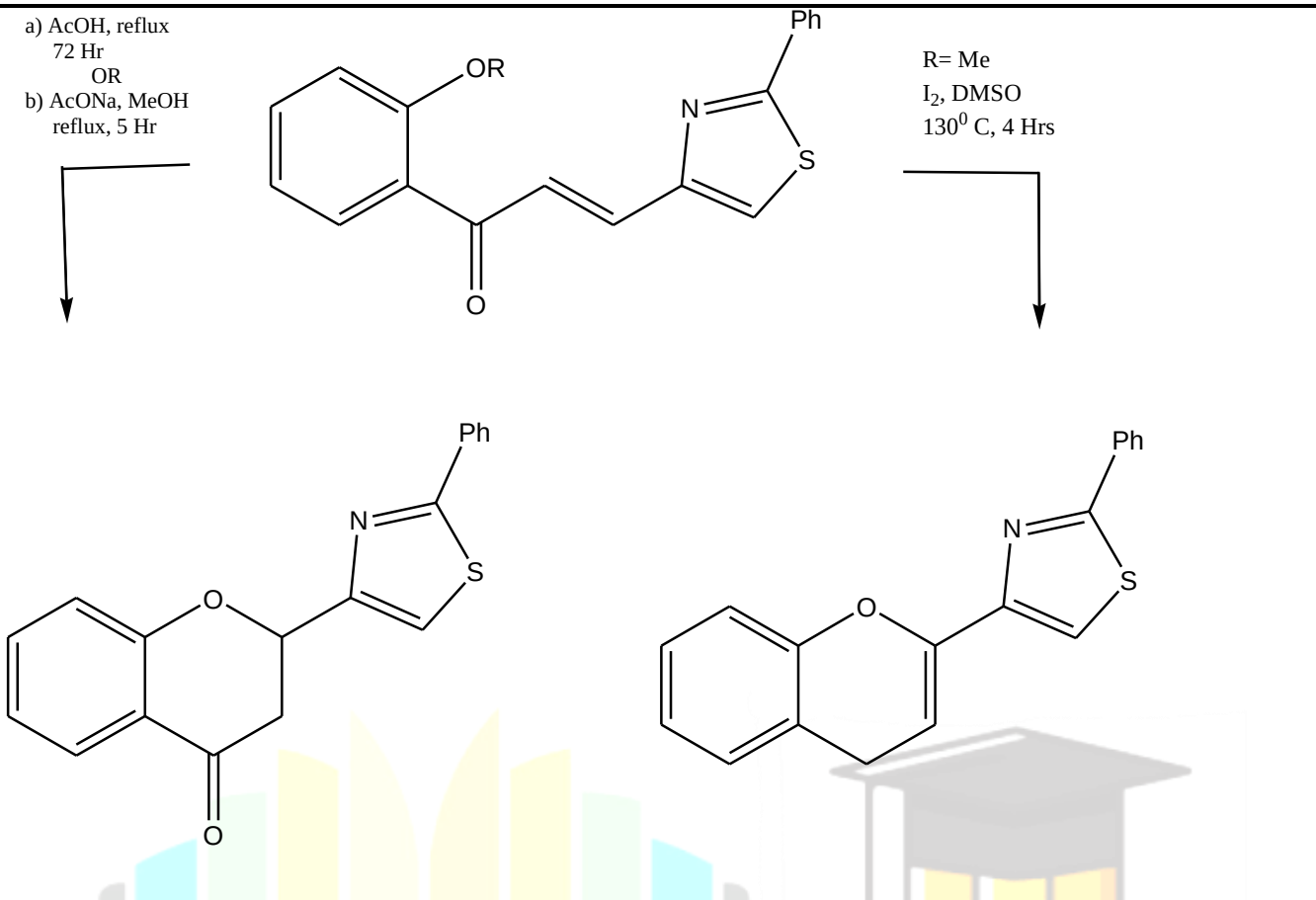




Biological activity:CCRF-CEM leukemia cells seemed to have IC50 values of 0.25 micrometer and their MDR subline CEM/ADR5000 had IC50 values of 0.47 micrometer and 0.62 micrometers, respectively, against the MDR U87 EGFR glioblastoma cells (0.75 micrometers). The nine cancer cells with promising IC50 values (10 micrometers) of other thiazolicchalcones were part of the study.



Biological activity : They got the cell lines HCT116 and HT29 from the NCI, and LoVo arrived from the American Tissue Culture Collection. Cells were constant at 37C and 5% CO2 in RPMI1640+ Glutamax development medium with 10% Fetal Calf Serum. The compounds were mixed with a growth medium at a suitable scale right before they were used.



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