Synthetic approach toward bioactive quinazolinone and derivatives

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Introduction

- Quinazolinone has wide range of pharmaceutical activities
- Neglected Disease initiative (DNDi) have discovered that substituted quinazolinones exhibit activity against T. cruzi.
- Chagas disease is a lifelong parasitic infection that caused by T. cruzi and was discovered in 1909
- Chagas disease is transmitted to human being and to more than 150 species of domestic animals.

Methods & Materials

- Using eMolecule.com to make sure the availability of starting materials/reagents and to look up pricing
- Using scientific research paper to propose the synthetic pathway of target compound
- Using several techniques NMR, IR, and Thin Layer Chromatography (TLC) to assess the differences between starting product ( initial quinazolinone compound) and final products to confirm formation of desired products
- Using SDS safety guideline to make sure that how to handle reagents (such as NaOH) and proper way to handling the techniques.

Objective

- To establish a synthetic pathway toward bioactive quinazolinone using various/differing substituent R groups

Approach

- Reaction start from initial compound (e) to target compound (a)
- Step 1: Chlorination of 2,4 (1H,3H) -quinazolinone(e) with POCl3 to yield 2,4 -dichloroquinazolinone (d)
- Step 2: Hydrolysis with NaOH to yield initial quinazolinone core
- Step 3: undergo coupling/substitution reaction with various R1 and R2 substituent derivate
- Step 4: Transformation will start with coupling/substitution reaction of Various R1 substituent derivatives to yield compound (a)

Figure 1: Triatomine insect takes blood meal → Human stages → Amastigotes multiply by binary fission in cells of infected tissue → intracellular amastigotes transform and enter the bloodstream → Triatomine bug takes a blood meal (again) → Parasites multiply and differentiate in the midgut → Metacyclic trypanosomes in hindgut

Figure 2: Retrosynthesis of Quinazolinone from target compounds (a) to initial compound (e).

Figure 3: Proposed synthesis of quinazolinone compounds j, k, l with reagents that can be perform in the proposal experiment

Results/Expected significance

- Should shows aromatic amine group In NMR around 7-8 ppm.
- Aromatic amine group – two aromatic ring
- Should shows amine (NH) group In NMR around 6-7 ppm
- Aromatic amine group
- Should shows tertiary amine, lack NH
- Aliphatic amine group
- HNMR signal for ethyl group – downfield quartet and up field triplet

Conclusion

- Synthetic approach toward quinazolinone derivatives will inform future design of therapeutics for Chagas disease
- This proposal would help to make medicine for chagas disease in the lab
- Once prepared, these proposal of new derivative can be a great opportunity to see how they react with Chagas disease and how the bioactive of these compounds turn out to design new anti-parasite drugs.

References


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