International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2019): 7.583

The Efficiency and Pharmacokinetics of "DBore-Covidesivir" for the Treatment of COVID-19 Virus Infection; Proved as Theoretical and Structural Pattern

Covidesivir Dronadula Borraiah

Abstract: ***An outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and its caused coronavirus disease 2019 (COVID-19) have been reported in China since December 2019. To date, there are no approved therapeutics or vaccines for covid-19 disease (CVD). Covid-19 is an infectious disease which causes significant morbidity and mortality. Although Covid-19 often causes a simple respiratory infection, it mostly causes disorders affecting several organs including the lungs, headache, brain, muscle pain, shortness of breath (breathing problems), runny nose, fatigue and serious life-threatening primary viral or secondary bacterial pneumonia. Currently, covidesivir is the most important and effective drug for severe. Covidesivir is Chloramphenicol "it is used to treat meningitis, plague, cholera and typhoid fever" and (+)-artemisinin "it is used as an antimalarial for the treatment of multi-drug resistant strains of falciparum malaria" derivative synthesized in 2020,is a new antiviral compound. Covidesivir may also assist in decreasing morbidity associated with antimalarial and antiviral infections.***

Keywords: Chloramphenicol, wacker oxidation, Dess-Martin oxidation, Pictet-Spengler reaction, A-313675, 2,2-dimethyl-1,3-dioxane-4,6-dione, (2S)-3-methyl-2-(2-oxo-1,3-diazinan-1-yl)butanoic acid, 1-bromo-1-butene, n,n-Carbonyldiimidazole, Ammonia, Methanol, Hydrogen Chloride, Ethyl Acetate, Ammonium chloride, Ethanol, Water, DMP, DCM, Boron trichloride, Dimethyl sulfide, 1,2-dichloroethane, Diphenyl ether, Potassium hydride,N,N'- Dicyclohexylcarbodiimide, Dioxane, Dimethyl zinc, Copper(ll) triflate, Toluene, Trimethyl orthoformate, p-Tolunesulfonyl hydrazide, n-Butyllithium, Tetramethylethylenediamine, Dimethyl formamide, Dichloromethane, Palladium(ll) chloride, Hydrogen peroxide, (+)-Artemisinin.

1. Introduction

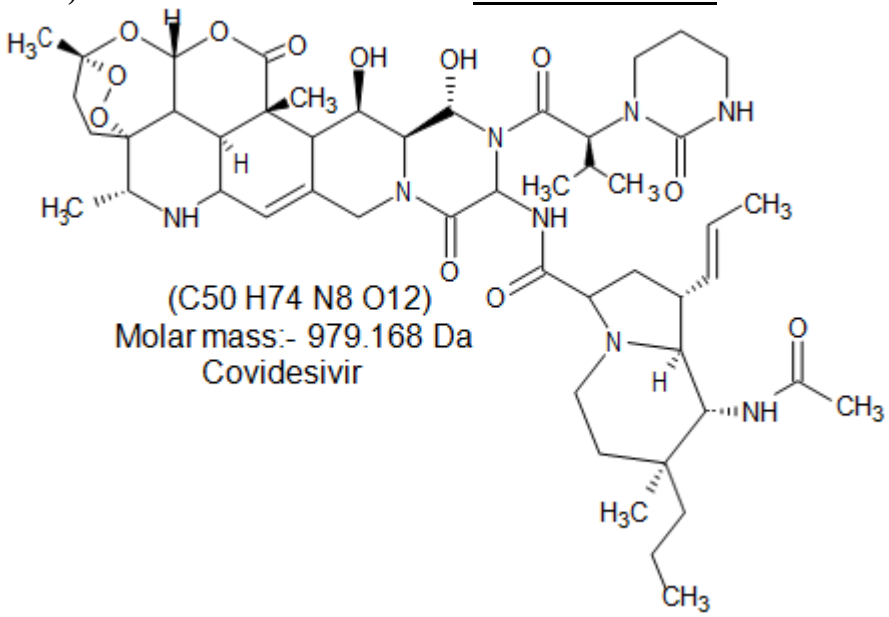
December 2019, a rapid and widespread outbreak of a novel coronavirus designated COVID-19, emerged in the city of Wuhan, China. According to the World Health Organization (WHO) surveillance draft in January 2020, any traveler to Wuhan City in Hubei Province 2 weeks before the onset of the symptoms is suspected to be infected with COVID-19. Additionally, the WHO distributed interim guidance for laboratories that carry out the testing for the newly-emerged outbreak, as well as infection prevention and control guidance. The COVID-19 pneumonia is suspected of having originated in a seafood market, with an unknown animal being responsible for the emergence of the novel virus. There are now surveillance borders around the globe, attempting to prevent the spread of the new mysterious coronavirus. Just three months ago, in mid-January, only 41 cases had been confirmed to be COVID-19 positive, leaving one person dead and 7 in critical care. These numbers are continually increasing each day, and the number of confirmed cases at the time of this writing has now exceeded 24,76,916 with 1,70,297 confirmed deaths and 6,46,739 recovered, mostly in United states, Spain, Italy, Germany, United kingdom, France, Turkey, Iran, China, On 20 January 2020, the National Health Commission of China confirmed human-to-human transmission of the COVID-19 outbreak. The WHO declared COVID-19 to be a Public Health Emergency of International Concern (PHEIC), then COVID-19 is declared WHO. The symptoms of COVID-19 include fever, malaise, dry cough, shortness of breath, and respiratory distres "This article starts from the structure, immunogenicity and pathogenesis of infection of the SARS-CoV-2,and then analyzes the feasibility of conducting biosynthesis and putting into Chloramphenicol and (+)-artemisinin use of Covidesivir from the pharmacological characteristics and successful explanation of Covidesivir.

Family of Coronaviruses

Viruses classified under the Coronaviridae family are enveloped positive-sense, single-stranded RNA viruses that exhibit high genetic diversity. Within the Orthocoronavirinae subfamily, there are four genera: alphacoronavirus, betacoronavirus, gammacoronavirus, and deltacoronavirus. Viruses in this family can infect a wide variety of host species, such as birds, humans, and non-human mammals, including dromedary camels, alpacas, domestic pigs, dogs, cats, ferrets, minks, and bats. However, to our knowledge, only viruses of the alpha- and betacoronavirus genera infect humans, though those in the gamma- and deltacoronavirus genera have indirect effects through economic impacts on the agricultural production of poultry and pigs. Host specificity is believed to be largely dependent upon variation in the CoV spike attachment glycoprotein. Although the infectivity of most strains is host species-specific, host range is wide across different CoVs, and some bat CoVs rely on the same host receptor (angiotensin-converting enzyme-2; ACE-2) as human CoVs to facilitate entry into cells. It has been hypothesized that the CoV propensity for host-switching may partly be attributable to recombination events that alter the spike protein, which, in turn, affects interactions with host receptors (e.g., ACE-2) .Historically, HCoVs were largely considered to be relatively low virulence viruses that produced less severe, self-limiting disease, and were predominantly known as the second most prevalent cause of colds and upper respiratory infections (URIs), after rhinoviruses. The endemic human CoVs that cumulatively

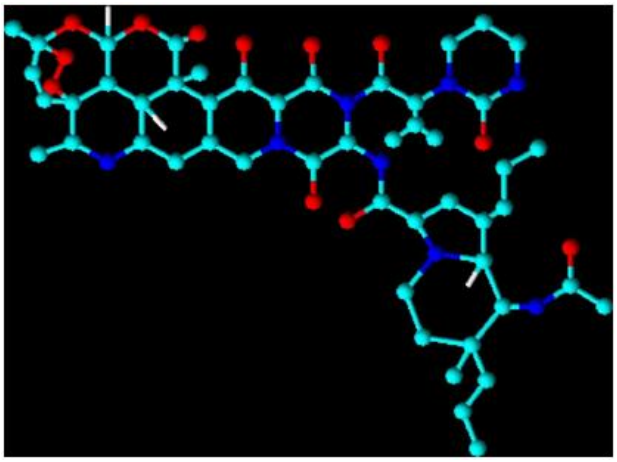
account for about 10–30% of URIs are HCoV-229E and HCoV-NL63, which are both alpha coronaviruses, and HCoV-OC43 and HCoV-HKU1, which are both beta coronaviruses. Among patients with URIs severe enough to warrant hospitalization, one study found that approximately 5% of cases were attributable to rhinoviruses or HCoVs, but a substantial proportion of these hospitalized patients had underlying pulmonary or cardiac comorbidities that may have exacerbated their conditions. The virus underlying COVID-19 (SARS-CoV-2) is a betacoronavirus that is closely related to SARS-CoV. These CoVs share ~80% RNA sequence identity. The similarity is even greater between the viruses when comparing the sequences specific to a key drug target, the RNA-dependent RNA polymerase (RdRP) (>90% sequence identity). By contrast, MERS-CoV shares about 50% genomic sequence identity with SARS-CoV-2, and with the exception of some bat strains, many animal CoVs are even less similar.

Covidesivir structure



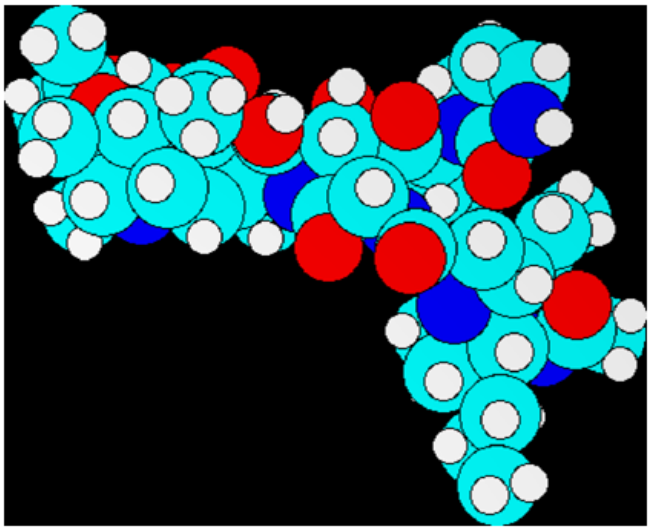
CC(=O)N[C@H]1[C@@H]2[C@@H](\C=C\C)CC(N2CC[C@]1(C)CCC)C(=O)NC1C(=O)N2CC3=CC4N[C@H](C)[C@]56CC[C@@](C)(O[C@@H]7OC(=O)[C@](C)(C3[C@@H](O)[C@H]2[C@H](O)N1C(=O)[C@H](C(C)C)N1CCCNC1=O)[C@@H]4C76)OO5

Graphical structure of Covidesivir

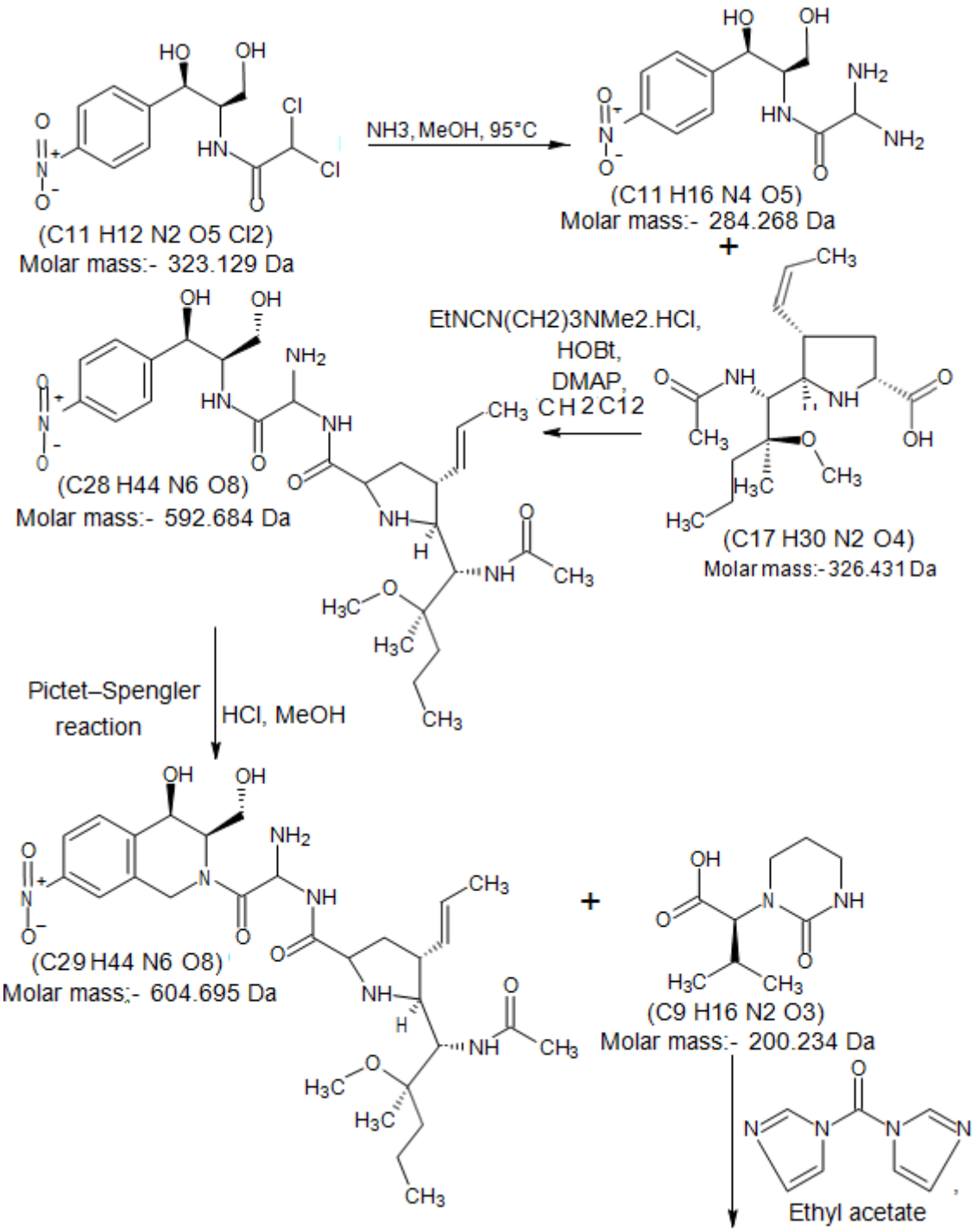


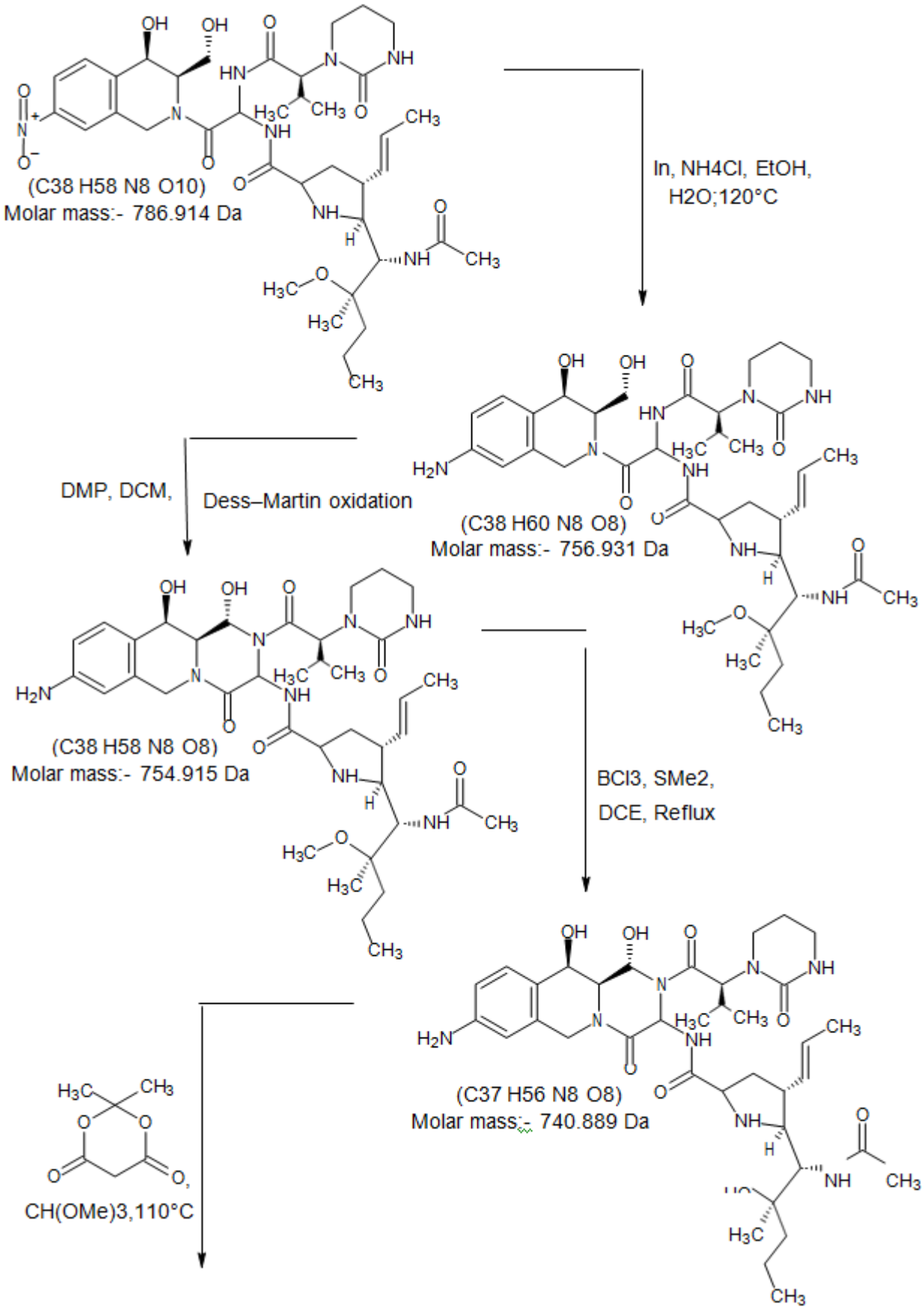
Molecular Formula: $C_{50}H_{74}N_8O_{12}$
Formula Weight: 979.16896
Composition: C(61.33%) H(7.62%) N(11.44%) O(19.61%)
Molar Refractivity: 253.29 ± 0.4 cm^3
Molar Volume: 701.9 ± 5.0 cm^3
Parachor: 2027.2 ± 6.0 cm^3
Index of Refraction: 1.641 ± 0.03
Surface Tension: 69.5 ± 5.0 dyne/cm
Density: 1.39 ± 0.1 g/cm^3
Dielectric Constant: Not available
Polarizability: 100.41 ± 0.5 $10^{-24}cm^3$

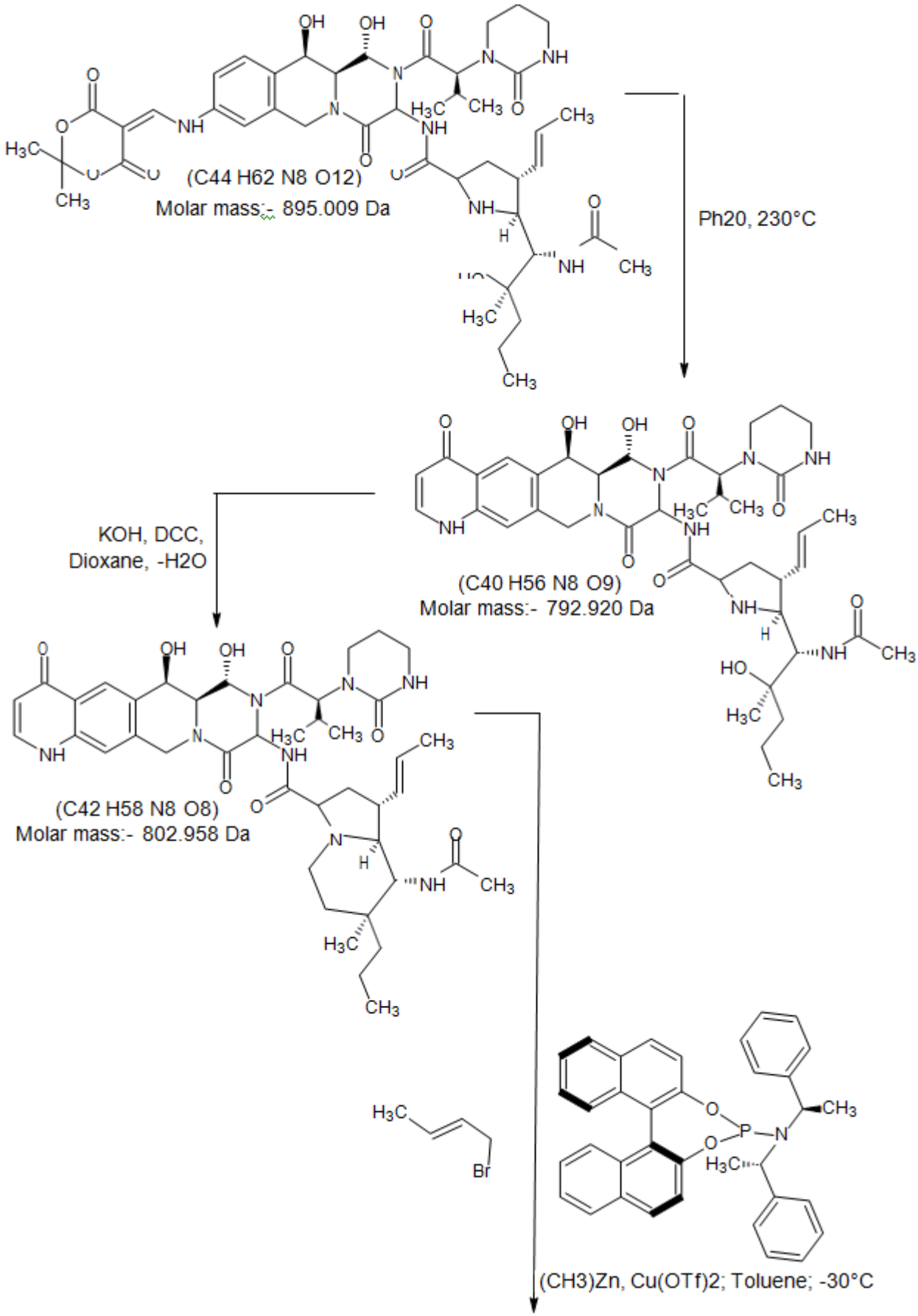
RDBE: 18
Monoisotopic Mass: 978.54262 Da
Nominal Mass: 978 Da
Average Mass: 979.169 Da
M+: 978.542071 Da
M-: 978.543168 Da
[M+H]+: 979.549896 Da
[M+H]-: 979.550993 Da
[M-H]+: 977.534246 Da
[M-H]-: 977.535343 Da

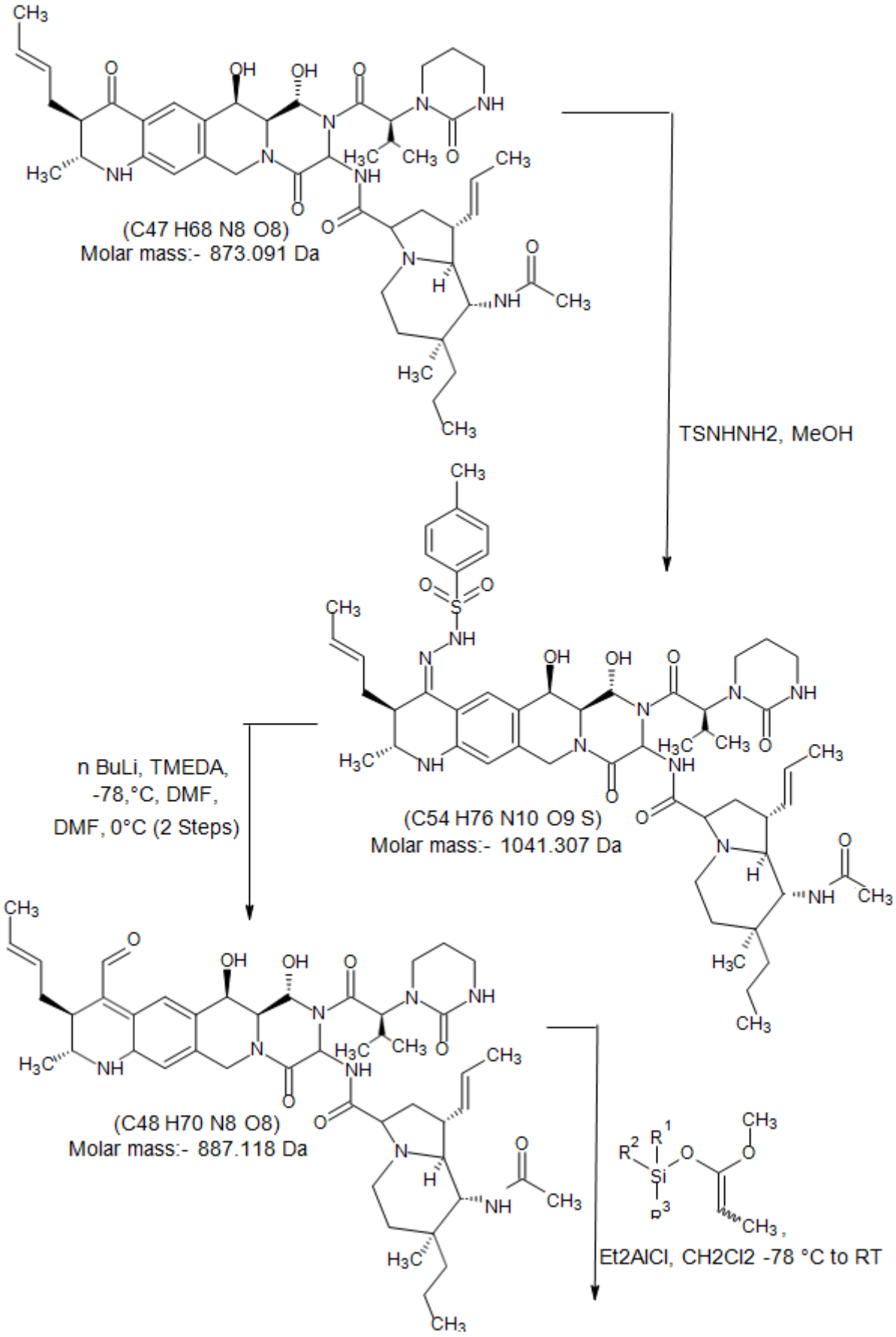


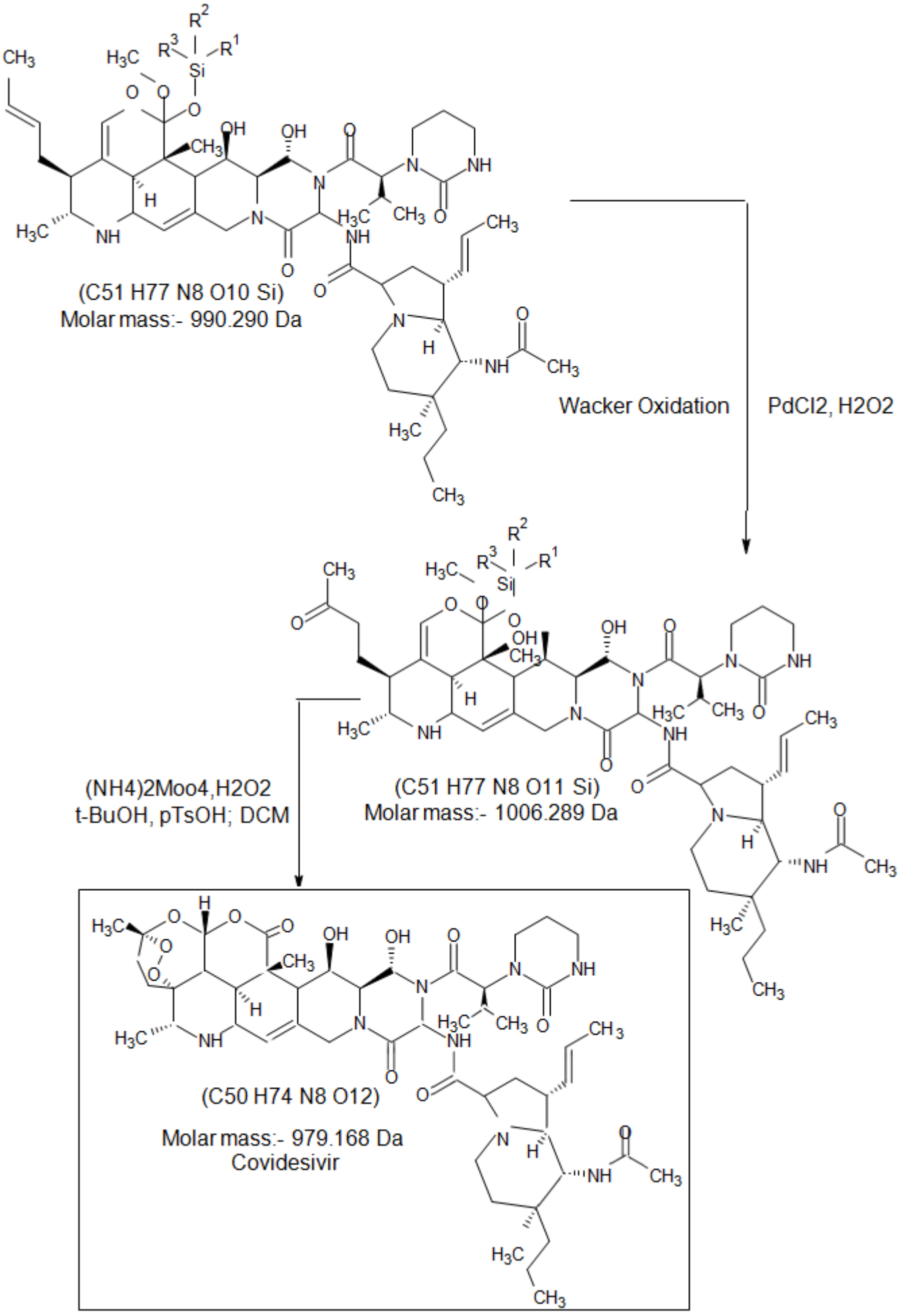
Bio synthesis:-







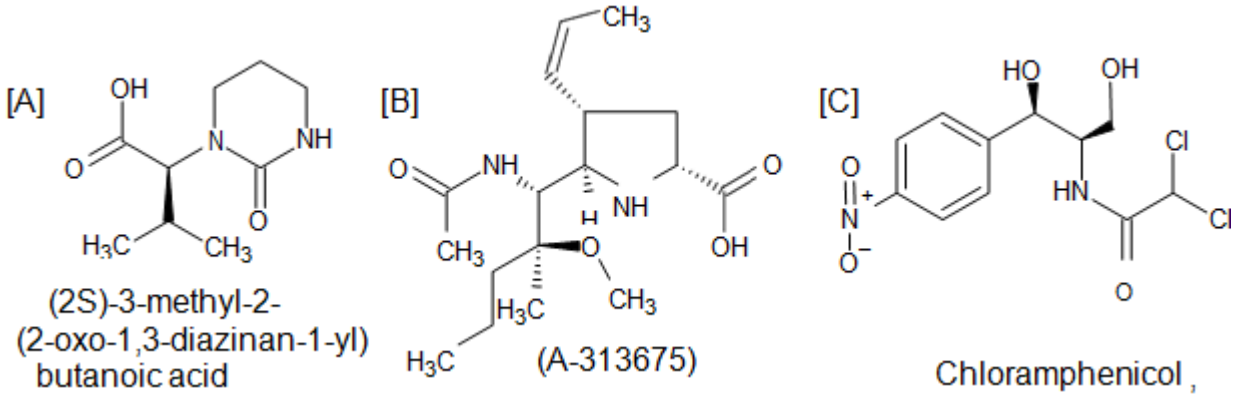




2. Preparation of Bio synthesis

2,2-dichloro-N-[(1R,2R)-1,3-dihydroxy-1-(4-nitrophenyl) propan-2-yl] acetamide in the presence of ammonia, methanol at 95 °C to produce 2,2-diamino-[(1R,2R)-1,3-dihydroxy-1-(4-nitrophenyl)propan-2-yl]acetamide in the presence of (A-313675), EDC (1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride, hydroxybenzotriazole, 4-dimethylaminopyridine, dichloromethane to produce (5R)-N-(1-amino-2-{[(2R,3R)-1,3-dihydroxybutan-2-yl]amino}-2-oxoethyl)-5-methylpyrrolidine-2-ca rboxamide in the presence of hydrogen chloride, methanol to produce 2,2-diamino-1-[(3R,4R)-4-hydroxy-3-(hydroxymethyl)-7-nitro-3,4-dihydroisoquinolin-2(1H)-yl]ethan -1-one in the presence of (2S)-3-methyl-2-(2-oxo-1,3-diazinan-1-yl)butanoic acid,1,1'-carbonyldiimidazole, ethyl acetate to produce (2S)-N-(aminomethyl)-3-methyl-2-(2-oxo-1,3-diazinan-1-yl)butanamide in the presence of ln, ammonium chloride, ethanol, water at 120 °C to produce 2,2-diamino-1-[(3R,4R)-7-amino-4-hydroxy-3-(hydroxymethyl)-3,4-dihydroisoquinolin-2(1H)-yl]eth an-1-one in the presence of dess martin periodinane, dichloro methane, dess-martin oxidation to produce (1S,11R,11aS)-3,8-diamino-1,11-dihydroxy-1,2,3,6,11,11a-hexahydro-4H-pyrazino[1,2-b]isoquino lin-4-one in the presence of boron trichloride, dimethyl sulfide,1,2 dichloro ethane at reflux to produce N-[(1S,2R)-2-hydroxy-2-methyl-1-{(2S,3R)-3-[(1E)-prop-1-en-1-yl]pyrrolidin-2-yl}pentyl]acetamide in the presence of trimethyl orthoformate, 2 2-dimethyl-1 3-dioxane-4 6-dione at 110 °C to produce 5-(anilinomethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione in the presence of diphenyl ether at 230 °C to produce quinolin-4(1H)-one in the presence of potassium hydride, n,n'-dicyclo hexyl carbodiimide, dioxane to produce N-{(1R,7S,8R,8aS)-7-methyl-1-[(1E)-prop-1-en-1-yl]-7-propyloctahydroindolizin-8-yl}acetamide in the presence of dimethyl zinc, copper(ll)triflate, toluene at -30 °C to produce (2R,3R)-3-[(2E)-but-2-en-1-yl]-2-methyl-2,3-dihydroquinolin-4(1H)-one in the presence of p-toluenesulfonyl hydrazide, methanol to produce N'-{(2R,3R,4E)-3-[(2E)-but-2-en-1-yl]-2-methylpiperidin-4-ylidene}-4-methylbenzene-1-sulfonohyd razide in the presence of n-butylithium, tetramethyl ethylenediamine at -78 °C ,dimethylformamide at 0 °C to produce (2R,3S)-3-[(2E)-but-2-en-1-yl]-2-methyl-1,2,3,8a-tetrahydroquinoline-4-carbaldehyde in the presence of dichloromethanediethylaluminum chloride at -78 °C to RT to produce (2R,3S,6aR,9bS)-3-[(2E)-but-2-en-1-yl]-6-methoxy-2,6a-dimethyl-2,3,6a,7,9a,9b-hexahydro-1H,6 H-pyrano[3,4,5-de]quinoline in the presence of palladium(ll)chloride,hydrogen peraxide, wacker oxidation to produce 4-[(2R,3S,9bR)-6-methoxy-2-methyl-2,3,6a,7,9a,9b-hexahydro-1H,6H-pyrano[3,4,5-de]quinolin-3- yl]butan-2-one in the presence of hydrogen peraxide, tert butyl alcohol, p-toluenesulfonicacid,dichloromethane, ammonium molybdate to produce DBore - Covidesivir.

Covidesivir biosynthesis involve these major compounds:-



3. Conclusion

While previous theoretical studies on covidesivir are promising, there is no clinical triles. Therefore, postulating on expected results of the trials is extremely challenging. Nonetheless, there are hundreds of clinical trials ongoing internationally on different drugs that utilize various mechanisms of action, including trials on other nucleosides inhibitors (e.g., ribavirin), protease inhibitors (e.g., lopinavir/ritonavir),and interleukin-6 receptor inhibitors (e.g., sarilumab). Another well-known candidate that is being evaluated in multiple trials against COVID-19 is chloroquine (or hydroxychloroquine), which is already approved as an antimalarial (and for extra intestinal amebiasis). If the trial findings are ultimately positive for covidesivir with help of biosynthesis, it will be imperative to ensure that the drug is produced on a commercial scale capable of meeting the demand generated by both the current pandemic and future outbreaks. Such a change in production may also allow for the added benefit of the drug becoming more available for agricultural and veterinary use for relevant indications.

4. Funding Statement

This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

5. Declaration of Competing Interest

The authors report no relevant conflicts of interest. Dronadula Borraiah was employed in Divis Laboratory, as chemist in research and development However, none of these studies involved Gilead Sciences.

6. Acknowledgements

The authors acknowledge Dr. Tasinm Munshi for her technical assistance.

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[20] Organization (WHO), World Health (28 March 2020). "FACT: #COVID19 is NOT airborne". @WHO. Retrieved 3 April 2020. These droplets are too heavy to hang in the air. They quickly fall on floors or surfaces.