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Antibacterial studies of newly synthesized β-ketoesters

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Abstract
In this paper, antibacterial studies of newly synthesized β-ketoesters have been reported. Afetr the synthesis of β-ketoesters, antibacterial studies have been completed by using disc diffusion method. During the antibacterial studies the antibiotic ciprofloxacin was used as standard drug. The disc diffusion method for the antibacterial was used against four bacteria say E. coli (ATTC-25922), S. aureus (ATTC-25923), P. aeruginosa (ATTC-27853) and K. pneumonia.

Keywords: Keto esters, bacteria, antibiotics, disc diffusion method

Introduction
In order to antibacterial studies two gram positive [1] and two gram negative [2] bacteria have been selected say Gram positive; E. coli and S. aureus and Gram negative; P. aeruginosa (ATTC-27853) and K. pneumonia.
Most types of E. coli are harmless [3]. However, sometypes can cause diarrhea. One ypes causes traveler's diarrhea. The worst type of E. coli causes bloody diarrhea and can sometimes cause kidney failure and even death. These problems are most likely to occur in children and in adults with immune systems. The bacterium S. aureus is the cause of enteric fever. The bacterium K. pneumoniae is the cause of pneumonia [4].

Antibacterial Activity
Evaluation of Antibacterial Activity
In the present research work, activities of the all synthesized compounds have been evaluated by disc diffusion method[15]. The aim of these studies was to study the changes in the activity with the complexation of the ligand quinoline-2-carbaldehyde benzoyl hydrazone with metal ions.
All the synthesized complexes of metal ions with the ligands have been screened against the following four bacteria.

- Escherichia coli,
- S. aureus,
- P. aeruginosa and
- K. pneumonia.

The newly synthesized β-ketoesters for their antibacterial activity against E. coli (ATTC-25922), S. aureus (ATTC-25923), P. aeruginosa (ATTC-27853) and K. pneumonia (recultured) bacterial strains by the disc diffusion method [5]. The discs measuring 6.25 mm in diameter were punched from Whatman No. 1 filter paper (GE Healthcare, Little Chalfont, UK). Batches of 100 discs were dispensed to each screw-capped bottle and sterilized by dry heat at 140°C for an hour. The test compounds were prepared with different concentrations using DMF. One milliliter containing 100 times the amount of chemical in each disc was added to each bottle, which contains 100 discs. The discs of each concentration were placed in triplicate in a nutrient agar medium separately seeded with fresh bacteria. The incubation was carried out at 37°C for 24 h. Solvent and growth controls were kept, and the zones of inhibition and minimum inhibitory concentrations (MIC) were noted. Results of these studies were given in following table and compared with the standard ciprofloxacin.

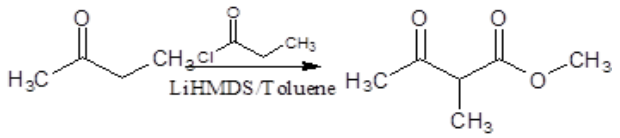
Table 1

Compounds	E. coli	K. pneumonia
Ofloxacin	16(6.25)	21(6.25)
1	17(6.25)	20(6.25)
2	18(6.25)	21(6.25)
3	19(6.25)	22(6.25)
4	17(6.25)	19(6.25)
5	17(100)	14(100)
6	17(100)	15(100)

Newly synthesized pyrazoles were screened for their antifungal activity against *Aspergillus flavus* (NCIM no. 524), *Aspergillus fumigates* (NCIM no. 902), *Penicillium marneffei* (recultured) and *Trichophyton mentagrophytes* (recultured) in dimethylsulfoxide (DMSO) by the serial plate dilution method [6]. Sabouraud agar media was prepared by dissolving peptone (1 g), d-glucose (4 g) and agar (2 g) in distilled water (100 mL), and the pH was adjusted to 5.7. Normal saline was used to make a suspension of spores of fungal strain for lawning. A loopful of particular fungal strain was transferred to 3 mL of saline to get a suspension of corresponding species. Agar media of 20 mL was poured into each Petri dish. An excess of suspension was decanted, and the plates were dried by placing them in an incubator at 37°C for 1 h. Using an agar, punch wells were made on these seeded agar plates, and 10 to 50 µg/mL of the test compounds in DMSO were added into each labelled well. A control was also prepared for plates in the same way using solvent DMSO. The Petri dishes were prepared in triplicate and maintained at 37°C for 3 to 4 days. Antifungal activity was determined by measuring the inhibition zone. The results of these studies were given in Table 2 and compared with the standard ciclopiroxolamine.

Synthesis
The formation of β-keto ester was found to be in better yield when LiHMDS was used as a base. When other bases are

used, the formation of β-keto ester intermediate from ketones was very slow, and the reactions were also found to be incomplete even after 4 to 5 h of stirring at r.t. The addition of hydrazine hydrate to the latter reaction mixtures gave the desired product in low yield (Table 8), and the corresponding hydrazone of ketones was isolated as the major product. After finding the suitable base, the reaction conditions were optimized further by varying the solvents to improve the yield. It was found that the hydrocarbon solvent (toluene) produced better yield compared to the cyclic ether solvent (THF). This may be due to the possible destabilization of formed intermediate with charge in the case of hydrocarbon solvent like toluene, and hence, the formed enolate reacts with ethyl chloroformate smoothly.



Conclusion

The β-keto esters from ethyl chloroformate was successfully attempted, and the developed method is simple, fast and applicable to the ketones having the alkyl halogens, protecting groups like Boc and Cbz that were tolerated and proved to be useful in the synthesis of fused bicyclic and tricyclic pyrazolones efficiently using cyclic ketones. Since this method is successful for different ketones, it can be useful for the synthesis of pharmaceutically important pyrazolones also. The synthesized pyrazolones were subjected to antimicrobial, docking and cytotoxicity assay against ACHN (human renal cell carcinoma), Panc-1 (human pancreatic adenocarcinoma) and HCT-116 (human colon cancer) cell line, and lead molecules have been identified. Some of the compounds are found to have promising activity against different bacterial and fungal strains tested.

References

1. Ueda TH, Mase N, Oda II. Synthesis of β-ketoesters derivatives. Chem Pharm Bull. 1981; 3:3522-3528. Doi: 10.1248/cpb.29.3522.
2. Hukki J, Laitinen P, Alberty JE. Preparation and pharmacological activity of β-ketoesters derivatives with potential antihistaminic properties II. Pharm Acta Helv. 1968; 3:704-712.
3. Nakagawa H, Ohyama R, Kimata A, Suzuki T, Miyata N. Hydroxyl radical scavenging by edaravone derivatives: Bioorg Med Chem Lett. 2006; 3:5939-5942.
4. Kawai H, Nakai H, Suga M, Yuki S, Watanabe T, Saito KI. Effects of a novel free radical scavenger, MCI-186, on ischemic brain damage in the rat distal middle cerebral artery occlusion model. J Pharmacol Exp Ther. 1997; 3:921-927.
5. Watanabe T, Yuki S, Egawa M, Nishi H. Protective effects of MCI-186 on cerebral ischemia: possible involvement of free radical scavenging and antioxidant actions. J Pharmacol Exp Ther. 1984; 3:1597-1604.
6. Wu TW, Zeng LH, Wu J, Fung KP. Myocardial protection of MCI-186 in rabbit ischemia-reperfusion. Life Sci. 2002; 3:2249-2255. Doi: 10.1016/S0024-3205(02)01965-3.