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Isoeugenol Ester Derivatives as Future Potential Drug

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Abstract: ***Isoeugenol has wide medical applications. It is used in manufacturing perfumeries, flavorings, essential oils (odour description: Clove, spicy, sweet, woody) and in medicine (local antiseptic and analgesic). Its analogues also show various biological activities which prompted us to synthesize few more analogues for their future applications as bioactive molecules. These were synthesized by coupling isoeugenol with benzoyl chloride / substituted benzoyl chloride / acetyl chloride using pyridine as a base in dichloromethane as a solvent at 15^{0}C to RT for 8hrs. These synthesized analogues were unambiguously characterized by ^{1}H NMR, elemental analysis and Mass spectral data. Few of them showing promising antibacterial activity.***
Keywords: Isoeugenol, substituted benzoyl chloride, pyridinene, dichloromethane, ^{1}H NMR, antibacterial activity, ^{1}HNMR, TOF MS ES, Gram + ve, Gram – ve cultures.

I. INTRODUCTION

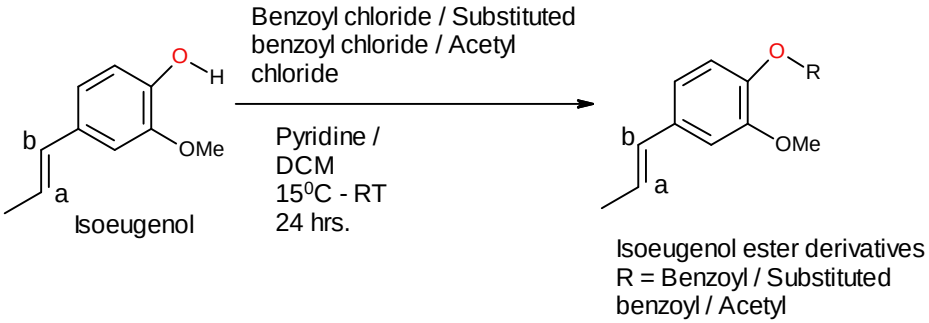
Phenolic compounds exist in most plant tissues as secondary metabolites *i.e*. they are not essential for growth, development or reproduction but may play roles as antioxidants and in interactions between the plant and its biological environment. Phenolics are also important components of the human diet due to their potential antioxidant activity[1], their capacity to diminish oxidative stress induced tissue damage resulted from chronic diseases[2], and their potentially important properties such as anticancer activities[3-5]. In continuation to our earlier work on phenolic compounds, Isoeugenol is a phenylpropene, a propenyl substituted guaiacol. It occurs in the essential oils of plants such as ylang–ylang. It can be synthesized from eugenol and had been used in the manufacture of vanillin. It may occur as either the cis (*Z*) or trans (*E*) isomer. Trans (*E*) isoeugenol is crystalline while cis (*Z*) isoeugenol is a liquid[6]. Since it is a naturally occurring active compound having antioxidant and antimicrobial properties, we decided to make a library of compounds using various permutation and combinations to come up with novel ester derivatives of isoeugenol using conventional method. The objective of this study is to condense two molecules of the same disease domain to produce more potent candidate in the same disease domain or to condense two molecules of different disease domain to produce mixed variety of those disease domain or to have drug candidate with entirely different disease domain.

II. RESULTS AND DISCUSSION

Isoeugenol is condensed with benzoyl / substituted benzoyl / acetyl chloride in dichloromethane using pyridine as a base at 15^{0}C – RT for 24 hrs. to yield respective ester derivatives. The crude reaction mixture obtained in each stages were purified by column, radial and preparative thin layer chromatographic techniques and unambiguously characterized by various spectroscopic techniques.
General method for the preparation of compounds (I - V) :- These were prepared by following general method as depicted below.
To a stirred solution of Isoeugenol (1 eq.) in dichloromethane (30 mL) was added pyridine (2.5 eq.) and cool the reaction in ice bath at 15^{0}C. Clear solution of reaction mixture was obtained. To this, was added benzoyl chloride / substituted benzoyl chloride / acetyl chloride (2 eq.) at 15 – 20^{0}C and stirred, allowed to attain room temperature and stirring was continued for next 8 hrs (TLC). The organic layer was concentrated under reduced pressure to minimum to yield crude mass which was preadsorbed on silica gel and purified by column chromatography (SiO_2, 100 – 200 mesh) with increase in concentration of ethyl acetate in petroleum ether to yield pure compound. The purified compounds were unambiguously characterized by ^{1}H NMR, elemental analysis and Mass spectroscopic techniques. The general yields of these reactions were ranges between 60 – 80 %.
The most significant features of this methodology are (a) good accessibility of the reagent and its stability (b) a stoichiometric amount of reagent can be used by direct weighing, avoiding excess (c) no evolution of hazardous vapors during the reaction (d) the total elimination of the use of toxic organic solvents (e) a simple experimental procedure (g) good control over the outcome of the reaction by varying the amount of reagent (h) less expensive (i) Avoidance of DCC and DMAP which is quite a costlier reagents. The aforesaid protocol thus provides an improved procedure for the synthesis of useful ester derivatives having important pharmaceutical, agricultural and other physicochemical properties.

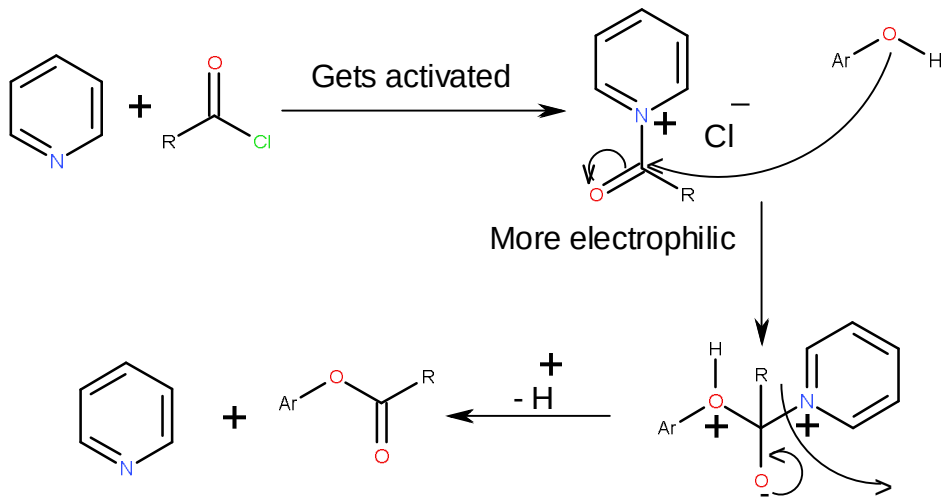
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Reaction Scheme :



Compound No.	R
1	Benzoyl
2	2-Methyl benzoyl
3	Acetyl
4	4-Methyl benzoyl
5	4-Methyl benzene sulphonyl

Probable mechanism for Esters :



1) Compound 1 : 2-methoxy-4-[(1E)-prop-1-en-1-yl]phenyl benzoate

1H NMR (400 MHz, CDCl3) δppm : 1.87 (d, 3H, J = 7.8 Hz, terminal methyl from isoeugenol moiety), 3.80 (s, 3H, Ar x –OCH3), 6.0 – 6.25 (m, 1H, olefinic proton 'a'), 6.39 (d, J = 15.8 Hz, 1H, olefinic proton 'b'), 6.8 – 7.2 (m, 3H, ArH from isoeugenol moiety), 7.4 – 8.3 (m, 5H, ArH from benzoyl moiety). TOF MS ES: 269 (M + H), 291 (M + Na). Molecular formula C17H16O3. Pure viscous mass (1.34 gms, 82 %). Anal. Calcd. for C17H16O3 : C 76.10 H 6.01 O 17.89 Found C 76.13 H 6.04 O 17.86;

2) Compound 2 : 2-methoxy-4-[(1E)-prop-1-en-1-yl]phenyl 3-methylbenzoate

1H NMR (400 MHz, CDCl3) δppm : 1.87 (d, 3H, J = 7.8 Hz, terminal methyl from isoeugenol moiety), 2.42 (s, 3H, Ar-CH3 from m-toluoyl moiety) , 3.80 (s, 3H, Ar x –OCH3), 6.1 – 6.25 (m, 1H, olefinic proton 'a'), 6.37 (d, J = 15.6 Hz, 1H, olefinic proton 'b'), 6.8 – 7.2 (m, 3H, ArH from isoeugenol moiety), 7.25 – 8.50 (m, 4H, ArH from m-toluoyl moiety). TOF MS ES: 283 (M + H), 305 (M + Na). Molecular formula C18H18O3. Pure viscous mass (1.30 gms, 76 %). Anal. Calcd. for C18H18O3 : C 76.57 H 6.43 O 17.0 Found C 76.54 H 6.40 O 17.04;

3) Compound 3 : 2-methoxy-4-[(1E)-prop-1-en-1-yl]phenyl acetate

1H NMR (400 MHz, CDCl3) δppm : 1.85 (d, 3H, J = 7.8 Hz, terminal methyl from isoeugenol moiety), 2.28 (s, 3H, -CO-CH3 from acetyl moiety) , 3.81 (s, 3H, Ar x –OCH3), 6.0 – 6.25 (m, 1H, olefinic proton 'a'), 6.34 (d, J = 15.6 Hz, 1H, olefinic proton 'b'), 6.75 – 7.0 (m, 3H, ArH from isoeugenol moiety). TOF MS ES: 207 (M + H), 229 (M + Na). Molecular formula C12H14O3. Pure viscous mass (0.86 gms, 68 %). Anal. Calcd. for C12H14O3 : C 69.88 H 6.84 O 23.27 Found C 69.85 H 6.81 O 23.30;

4) Compound 4 : 2-methoxy-4-[(1E)-prop-1-en-1-yl]phenyl-4-methylbenzoate

1H NMR (400 MHz, CDCl3) δppm : 1.87 (d, 3H, J = 7.8 Hz, terminal methyl from isoeugenol moiety), 2.43 (s, 3H, Ar-CH3 from p-toluoyl moiety) , 3.79 (s, 3H, Ar x –OCH3), 6.0 – 6.25 (m, 1H, olefinic proton 'a'), 6.37 (d, J = 15.6 Hz, 1H, olefinic proton 'b'), 6.8 – 7.2 (m, 3H, ArH from isoeugenol moiety), 7.2 – 8.2 (m, 4H, ArH from p-toluoyl moiety). TOF MS ES: 283 (M + H), 305 (M + Na). Molecular formula C18H18O3. Pure viscous mass (1.24 gms, 76 %). Anal. Calcd. for C18H18O3 : C 76.57 H 6.43 O 17.0 Found C 76.54 H 6.41 O 17.04;

5) Compound 5 : 2-methoxy-4-[(1E)-prop-1-en-1-yl]phenyl 4- methylbenzenesulfonate.

1H NMR (400 MHz, CDCl3) δppm : 1.83 (d, 3H, J = 7.6 Hz, terminal methyl from isoeugenol moiety), 2.43 (s, 3H, Ar-CH3 from p-toluoyl sulphonyl moiety) , 3.53 (s, 3H, Ar x –OCH3), 6.0 – 6.25 (m, 1H, olefinic proton 'a'), 6.30 (d, J = 15.8 Hz, 1H, olefinic proton 'b'), 6.7 – 7.2 (m, 3H, ArH from isoeugenol moiety), 7.2 – 7.82 (m, 4H, ArH from p-toluoyl moiety). TOF MS ES: 319 (M + H), 341 (M + Na). Molecular formula C17H18O4S. Pure viscous mass (1.20 gms, 68 %). Anal. Calcd. for C17H18O4S : C 64.13 H 5.70 O 20.10 S 10.07 Found C 64.10 H 5.67 O 20.12 S 10.10;

III. EXPERIMENTAL

MPS. are uncorrected. 1H NMR spectra were recorded at 400 MHz on a Varian spectrometer and Mass spectra on TOF MS ES mode. Elemental analysis was carried out as a percentage on a Thermo finnigan, Flash EA 1112 series, Italy.

A. Chromatographic System

1) *Column Chromatography:* For column chromatography 100 – 200 mesh Acme grade silica gel is used. The crude reaction mixture is concentrated under reduced pressure to yield crude mass which is preadsorbed on silica gel and purified by column chromatography with increase in concentration of Ethyl acetate in Petroleum ether. The fractions having similar 'rf" values were pooled together, concentrated and subjected for characterization using various spectroscopic techniques.
2) *Thin layer Chromatography:* TLC plates were prepared using silica gel G (ACME, BOMBAY). Pet. ether: EtOAc (85:15) was used as the solvent system.
3) *Radial Chromatography:* The circular glass plates of thickness 1 mm, were prepared by using silica gel (PF254, E. MERCK, 50 g) in cold distilled water (105 ml). For elution, gradually increasing concentrations of EtOAc in pet ether were employed

IV. BIOLOGICAL ACTIVITY

Antibacterial Activity using agar diffusion method7:- Conc 100 µm

The synthesized molecules were screened for their antibacterial activity using agar diffusion method at 100 µm concentration against Gram positive (Staphylococcus aureus) and Gram negative (Escherichia coli) bacterial species qualitatively. The results of the antibacterial activities are summarised in Table 1.

Table 1: Antibacterial Activity Results

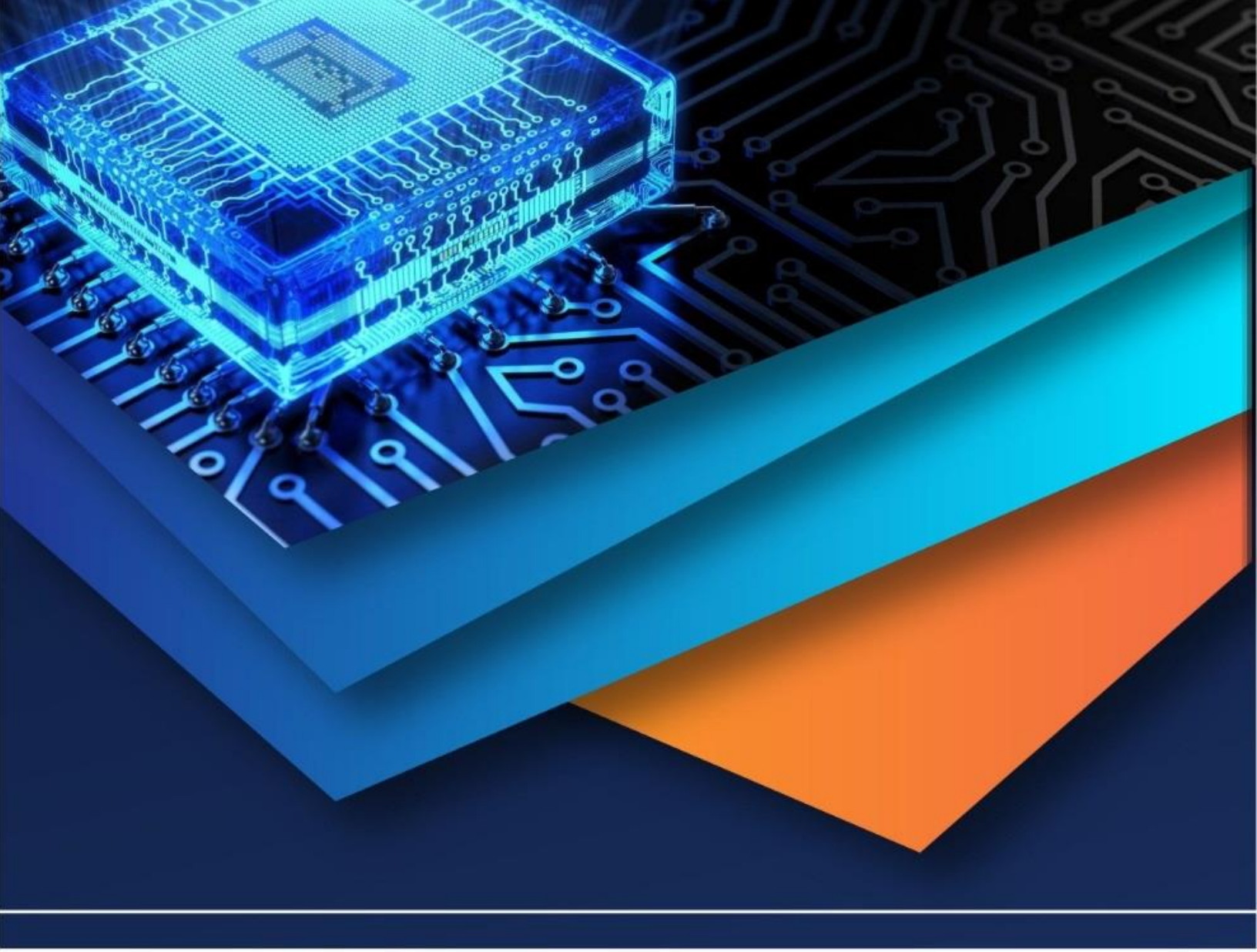
Sr. No	Compound No.	Antibacterial Activity	
		Against Gram - ve bacteria species (*Escherichia coli*)	Against Gram +ve bacterial species (*Staphylococcus aureus*)
1	Isoeugenol	+	+
2	1	-	-
3	2	-	-
4	3	+	-
5	4	-	-
6	5	-	+

The above results shows that the base molecule, isoeugenol has antibacterial activity against both the bacterial cultures. Its derivatives viz. 3 and 5 were active against Escherichia coli (Gram negative bacterial species) and Staphylococcus aureus (Gram positive bacterial species) respectively. Thus, acetyl and 4-methyl benzene sulphonyl derivatives were potential antibacterial candidates. In depth analysis of these compounds through structure activity relationship studies would provide further insight and can be an interesting topic of future studies.

REFERENCES

[1] Martin, K. R.; Appel, C. I. Polyphenols as dietary supplements: A double–edged sword. Nutr. Dietary Suppl. 2010, 2, pp. 1 – 12.
[2] Bravo, L. Polyphenols: Chemistry, dietary sources, metabolism and nutritional significance. Nutr. Rev. 1998, 56, pp. 317 – 333.
[3] Harris, C. S.; Mo, F.;Migahed L.;Chepelev, L.; Haddad, P. S.; Wright, J. S.; Willmore, W. G.; Arnason, J. T.; Bennett, S. A. L. Plant phenolics regulate neoplastic cell growthand survival :a quantitative structure-activity and biochemical analysis. Can. J. Physiol. Pharmacol. 2007, 85, pp. 1124 – 1138.
[4] Huang, W. Y.; Cai, Y. Z.; Zhang, Y. B. Natural phenolic compounds from medicinal herbs and dietary plants : Potential use for cancer prevention. Nutr. Cancer 2010, 62, pp. 1 – 20.
[5] Liu, R. H.; Potential synergy of phytochemicals in cancer prevention: Mechanism of action. J. Natr. 2004, 134, pp. 3479S – 3485S.
[6] The Merck Index, 12th edition, Merck & Co., Whitehouse Station, New Jersey, USA, 1996.
[7] Finn, R. K. Theory of Agar Diffussion Methods for Bioassay. Anal. Chem. 1959, 31 (6), pp. 975 – 977.

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