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SYNTHESIS AND BIOLOGICAL EVALUATION OF SOME 2, 4, 5 TRIPHENYL IMIDAZOLE DERIVATIVES

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ABSTRACT

A series of 1-substituted 2, 4, 5 triphenyl imidazoles were synthesized by the reaction equimolar mixture of 2, 4, 5 triphenyl imidazole with chloro compound in the presence of anhydrous potassium carbonate. The newly synthesized compounds were characterized on the basis of UV, IR and H^1 NMR spectra. The synthesized compounds were screened for antiinflammatory, antimicrobial activities. Antiinflammatory activity was screened by carageenan induced rat paw oedema method. Compounds T_4 & T_5 showed highly significant activity. Antimicrobial activity was screened by disc-plate method. All the compounds showed mild to moderate activities.

KEY WORDS: Antiinflammatory activity, Antimicrobial activity, 2, 4, 5 triphenyl imidazole, chloro compound.

INTRODUCTION

Imidazoles are probably the most well known heterocycle which is common and important feature of a variety of natural products and medicinal agents.

Derivatives of imidazole were reported for anti-inflammatory[1-4], analgesic[5], anti-convulsant[6-7], tuberculostatic[8,] antimicrobial[9] and anticancer[10] activities. Prompted by the broad spectrum activities of 2, 4, 5 triphenyl imidazole derivatives, it was decided to synthesize various 2, 4, 5 triphenyl-1-substituted imidazoles and to evaluate them for their pharmacological activities. Here we are presenting our findings in this paper.

MATERIALS AND METHODS

All melting points were taken in open capillaries on a veego VMP-1 apparatus and are uncorrected. The purity of the synthesized compounds was checked by TLC, UV/VIS spectra were taken in a Schimadzu UV/VIS 1700 spectro photometer. IR spectra were recorded as KBr pellets on Perkin Elmer 1600FT spectrophotometer. H^1 NMR spectra in $CDCl_3$ on a Bracker, 200MHz spectrometer. Chemical shifts were reported as parts per million (δ ppm) with tetramethyl silane (TMS) as an internal standard. All chemicals and reagents used in the synthesis were obtained from Aldrich (USA), Spectrochem (India) and were used without purification.

Synthesis of 2, 4, 5 triphenyl imidazole[11]

2, 4, 5 triphenyl imidazole was prepared from the reaction between benzil and benzaldehyde with ammonium acetate in acetic acid medium. Benzoyl chloride, benzyl chloride, p-methyl benzyl chloride, phenacyl chloride, benzene sulphonyl chloride and tosyl chloride were purified by distillation before use.

Synthesis of 1-substituted 2, 4, 5 triphenyl imidazoles

An equimolar solution of 2, 4, 5 triphenyl imidazole and chloro compound (10mmol, 30ml) in acetone with anhydrous potassium carbonate was refluxed for 7-8 hrs. The product was isolated, dried and recrystallized from ethanol. The purity was tested by TLC using $CHCl_3$: CH_3OH (9:1v/v) binary solvents.

Compound No: T_1

IR (KBr) υmax in cm^{-1} 1722(C=O), 1594(C=N) st, 1676(C=C), 3062(C-H Ar)st.
H^1 NMR ($CDCl_3$) δ ppm: 7.5-8.2 (m, 20H, Ar-H).

Compound No: T_2

IR (KBr) υmax in cm^{-1} 2920(C-H aliphatic), 1593(C=N), 1678(C=C), 3062(C-H Ar) st.

H^1 NMR ($CDCl_3$) δ ppm: 7.4-7.7 (m, 20H, Ar-H).

Compound No: T_3

IR (KBr) υmax in cm^{-1} 1592(C=N), 1658(C=C), 3061(C-H Ar) st.

H^1 NMR ($CDCl_3$) δ ppm: 2.29 (S, 3H, CH_3), 5.6 (S, 2H, -CH2), 7.2-7.9 (m, 19H, Ar-H).

Compound No: T_4

IR (KBr) υmax in cm^{-1} 1594(C≡N), 1659(C=C), 3063(C-H Ar) st, 2924(C-H aliphatic).

H^1 NMR ($CDCl_3$) δ ppm: 5.6 (S, 2H, -CH_2), 7.2-7.9 (m, 20H, Ar-H).

Compound No: T_5

IR (KBr) υmax in cm^{-1} 1593(C≡N), 1659(C=C), 3006-3063(C-H Ar) st, 1324(S=O).

H^1 NMR ($CDCl_3$) δ ppm: 7.4-7.7 (m, 20H, Ar-H).

Compound No: T_6

IR (KBr) υmax in cm^{-1} 1593(C=N), 1658(C=C), 3063(C-H Ar) st, 1325(S=O).

H^1 NMR ($CDCl_3$) δ ppm: 2.4-2.5 (S, 3H, CH_3), 7.2-7.8 (m, 19H, Ar-H).

Anti-inflammatory Screening

The compounds synthesized were evaluated for their antiinflammatory activity using carageenan induced paw oedema method. Albino rats of either sex weighing 150-200g were divided into eight groups, of six each. They were starved over night with water prior to the day of the experiment. Group I served as control and received vehicle (0.5% CMC). Group II received Indomethacin (100 mg/kg). Group III, IV, V, VI, VII and VIII received test compound (200 mg/kg) T1, T2, T3, T4, T5 and T6 respectively. All the drugs were suspended in normal saline and were administered orally 30 mins before the carageenan injection. Acute inflammation was induced each group by injecting 0.1 ml of 1% carageenan into the sub-plantar region of right hind paw. The thickness of the right hind paw was measured with the help of vernier at the end of the 60 min, 120 min, 180 min. The percentage increase in paw oedema of the treated group was compared with that of the control at the inhibitory effect of the drugs were studied. The results are given in table 2.

Antimicrobial Screening

The antibacterial activity of the synthesized compounds were tested by cup plate method against gram (+) bacteria (staphylococcus aureus) and gram (-) bacteria (pseudomonas aureginosa) using nutrient agar medium. The antifungal activity was tested against fungi (candida albicans) using sabourand dextrose medium.

By pouring the sterile agar into petridishes in aseptic conditions, 0.1 ml of each standardized test organism culture was spread onto agar plates. The test compounds (30μg/ml), the standard drug solutions and the solvent control chloroform were placed in the cavity separately. Then the plates were maintained at room temperature for 2 hrs to allow the diffusion of solution into the medium. All the bacterial plates were incubated at 37°c for 24 hrs and fungal plates were incubated at 28°c for 48 hrs. The zone of inhibition was measured in mm. The results are given in table 3

RESULTS AND DISCUSSION

The substituted triphenyl imidazoles were synthesized by refluxing 2, 4, 5 triphenyl imidazole with the different chloro compounds in the presence of anhydrous potassium carbonate. The yield was found to 70-85%. The structures of the synthesized compounds were characterized by UV, IR, H^1 NMR, spectral analysis.

Antiinflammatory activity was screened by carageenen induced paw oedema method. All of them gave remarkable response with that of the standard drug Indomethacin. The synthesized compounds were administered

Table 1. Physical parameters for the synthesized 1-substituted 2, 4, 5 triphenyl imidazoles

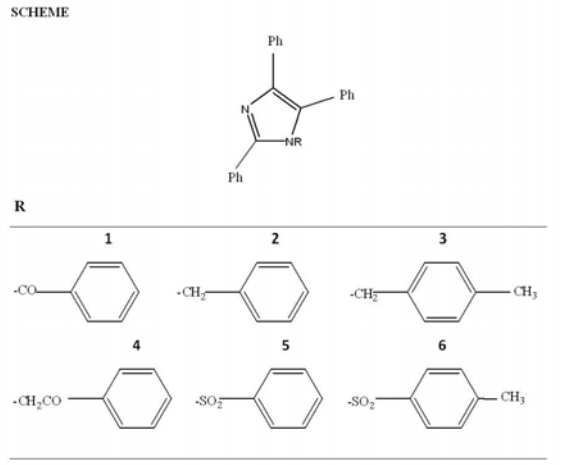
Compound	Yield (%)	Melting Point (°c)	λ_{max} (nm)	Molecular Formula
T_1	85	80	261	$C_{28}H_{20}N_2O$
T_2	82	58	255	$C_{28}H_{22}N_2$
T_3	77	87	261	$C_{29}H_{24}N_2$
T_4	80	90	261	$C_{29}H_{22}N_2O$
T_5	75	93	261	$C_{27}H_{20}N_2O_2S$
T_6	70	96	261	$C_{28}H_{22}N_2O_2S$

Table 2: Anti-inflammatory activity of the synthesized compounds

Compound	Percentage increases in hind paw thickness (mean±SE)			
	60 min	120 min	180 min	240 min
Control	63.46±0.06	86.53±0.07	100±0.04	108.6±0.05
Indomethacin	15.09±0.05	18.86±0.06	22.64±0.04	22.64±0.07
T_1	39.95±0.04	43.55±0.03	43.77±0.05*	44.97±0.03
T_2	42.34±0.05	43.77±0.05	44.73±0.05*	44.25±0.05
T_3	39.95±0.04	43.77±0.05	43.55±0.03*	43.55±0.03
T_4	14.52±0.01	16.46±0.01	16.44±0.01**	18.88±0.001
T_5	23.21±0.03	21.37±0.03	22.06±0.04**	22.52±0.04
T_6	32.77±0.03	49.52±0.03	49.52±0.03*	49.52±0.03

Table 3. Antimicrobial activity of synthesized compounds

Compound (100µg/ml)	Zone of Inhibition (mm)		
	Gram positive *S.Aureus*	Gram negative *P.Aeruginosa*	Antifungal *C.Albicans*
T_1	32	16	24
T_2	14	9	19
T_3	13	32	32
T_4	15	11	20
T_5	31	18	23
T_6	33	15	21
Std drug (100µg/ml)	38	36	35
Solvent control (DMSO)	–	–	–



orally at dose of 5 mg/kg. The triphenyl imidazoles bearing phenacyl group (compound no.T_4), benzene sulphonyl group (compound no.T_5) have showed highly significant activity, where as other compounds showed significant action. All the compounds have showed mild to moderate antimicrobial activities at 30μg/ml.

REFERENCES

[1] J.Fatimi., J.F.Lagorce and J.L.Durox., *Chem.Pharm.Bull*, 42(1994), 698.
[2] SUZUKI F., Kurodat., Tamurat., *J.med-chem* 1992., 35(15)., pp 2863-2870.
[3] SUZUKI M., Maedas., Matsumotok., *Chem.Pharm.Bull* 1986., 34(8)., 3111-3120.
[4] Abignente E., Arenaf., Decaprariisp., F armaaco (sci) 1981., 36(1)., 61-80.
[5] G.I.Isikda., V.Vcucu and Oxdermir., *Chem.Pharm.Bull*., 42(1994), 698.
[6] Ozakanli F., Dalkara S., Calis V., Arzneimittel-For Schung 1994, 44(8)., 920-924.
[7] Pinzam., Farinaz., Cerri A., *J.Med.Chem* 1993, 36(26), 4214-4220
[8] Bukowski., M.Janouice., *Pharmazice*, 45(1990), 904.
[9] Takeuchi I., Sugiura M., Yamamoto K., Ito T., Yakugaku Zasshi 1985., 105 (6)., 554-561
[10] Abdel-Rahman RM., Seeda M., El-Baz I., *Pharmazie* 1994., 49 (11)., 811-814
[11] L.M.Harwood., C.J.Moody and J.M.Percy., *Experimental Organic Chemistry*, 2nd Ed, Blackwell Sceintific Publications, London, (1994), 644.