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A Facile Synthesis of 3-(2-Benzyloxy)-5-Chlorophenyl)-1-(3-(4-Chlorophenyl)-5-(P-Tolyl)-4, 5-Dihydro-1h-Pyrazol-1yl)-3-Phenylpropan-1-One from Chalcone And 6-Chloro-4-Phenylchroman-2-One

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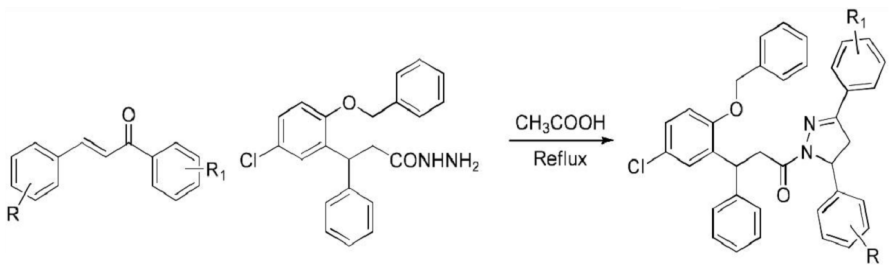
Abstract: ***In present paper, some new dihydropyrazoles have been synthesized and characterization of these synthesized compounds is done by IR, NMR and mass spectral data. A mixture of 3-(2-benzyloxy)-5-chlorophenyl)-3-phenylpropanehydrazide 2 and ifferent substituted chalcones1; 10 ml of glacial acetic acid was added with stirring. The reaction mixture was refluxed on oil bath for 12 hours. After the completion of reaction, the mixture was poured into crushed ice to give desired solid products 3 (P-1 to P-20). (Scheme-1)***
Keywords: Chalcone, phenylhydrazide and pyrazolylchromanone.



1 23 (P-1 to P-20)

Scheme-1

R=H , CH_3.

P-1 to P-20 R 1 = 4-F, 4-CH_3, 3-NO_2, 4-Cl, 4-NO_2, 2-NO_2, 4-Cl, 4-Cl, 4-F, C_6H_5, 4-Cl, C_6H_5,4-Br, 4-Cl, 4-F, 4-F, 4-Cl, 4-Cl, 4-F, C_6H_5.

I. INTRODUCTION

Pyrazoles have been studied extensively because of ready accessibility, diverse chemical reactivity, broad spectrum of biological activity[1-6] and varieties of industrial applications[7].

Different methods are available from the literature for the preparation of 2-pyrazole derivatives[7-9].Much attention was paid to pyrazole as a potential antimicrobial agent after the discovery of the natural pyrazole C-glycoside pyrazofurin which demonstrated a broad spectrum of antimicrobial activity. Literature survey shows that 2-pyrazolines are better therapeutic agents. They possess antiinflammatory[10-12],bactericidal,Fungicidal, nticonvulsant and bercular[10-15] etc.

II. EXPERIMENTAL SECTION

A. Synthesis of substituted chalcones (1)

Substituted aldehydes (0.01 mole) was dissolved in 15 ml of methanol. 0.01 mole of substituted acetophenones and 3-4 drops of saturated sodium hydroxide solution (as a catalyst) was added and the reaction mixture was stirred for 24 hours. After the

completion of reaction, the reaction mass was filtered and washed with chilled methanol. Similarly, other compounds are also prepared using different aldehydes.

B. Synthesis of 6-chloro-4-phenylchroman-2-one

To a mixture of cinnamic acid (0.1 mole), p-chloro phenol (0.1mole), catalytic amount of *p*-TSA was added with stirring and the reaction mixture was heated at 70°-80°C to become clear solution. The temperature was then increased up to 120°-125°C and heating was continued for 3-4 hours. After the completion of reaction, the reaction mixture was cooled up to 80°C. Then 40 ml of toluene and 40 ml of water was added to the reaction mixture and stirred it for 30 minutes. The toluene layer was separated and washed with saturated sodium bicarbonate solution (20 ml) and water (20 ml). The resulting toluene layer was then dried using sodium sulphate under vacuum. 25 ml of isopropyl alcohol added to the resulting oily mass and stirring was done for 30 minutes at 0-5° C. The product was filtered and washed with chilled iso-propyl alcohol (5 ml) and dried to give 6-chloro-4-phenylchroman-2-one

C. Synthesis of methyl 3-(2-(benzyloxy)-5-chlorophenyl)-3-phenylpropanoate

A mixture of 6-chloro-4-phenylchroman-2-one (0.1 mole), potassium carbonate(0.12 mole), benzyl chloride (0.12 mole), sodium iodide (0.05 mole), 100 ml of acetone and 100 ml of methanol was heated with stirring. After the completion of reaction, solvent was removed under vacuum. Then, dichloromethane (100 ml) and water (100 ml) was added to the reaction mixture snd was stirred for 30 minutes. The organic layer was separated and dried using sodium sulphate and distilled completely under vacuum to get oily residue of 3-(2-(benzyloxy)-5-chlorophenyl)-3-phenylpropanoate.

D. Synthesis of 3-(2-(benzyloxy)-5-chlorophenyl)-3-phenylpropanehydrazide (2)

3-(2-(benzyloxy)-5-chlorophenyl)-3-phenylpropanoate (0.01 mole) was dissolved in 20 ml of methanol. 2 ml of hydrazine hydrate (99 %) was added to this solution and the resulting mixture was heated for 10-12 hours at reflux temperature. After the completion of reaction, the reaction mass was filtered and washed with chilled methanol to give pure product.

E. Synthesisof3-(2-benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazol-1yl)-3-phenylpropan-1-one (3 P-1 to P-20)

To a mixture of 3-(2-benzyloxy)-5-chlorophenyl)-3-phenylpropanehydrazide (0.01 mol) and different substituted chalcones (0.01 mol), 10 ml of glacial acetic acid was added with stirring. The reaction mixture was refluxed on oil bath for 12 hours. After the completion of reaction, the mixture was poured into crushed ice to give desired solid products **3** (**P-1 to P-20**). The solid mass was filtered and purified by column chromatography using eluent hexane: ethyl acetate (7:3).

III. MATERIALS AND METHOD

The formation of the compounds was checked by thin-layer chromatography and accomplished on 0.2-mm pre coated plates of silica gel G60 F_{254} (Merck). Visualization was made with UV light (254 and 365nm) or with an iodine vapor.The melting point of all the synthesized compounds was determined in open capillary tubes and was uncorrected.

The characterization of all these compounds was done by IR, NMR and mass spectral data. The IR spectra were recorded on Shimadzu FT-IR-8400 instrument using KBr pellet method. The Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using direct inlet probe technique. ^{1}H NMR and ^{13}C NMR was determined in DMSO solution on a Bruker Ac 400 MHz spectrometer.

A. Spectral data of compounds (P-1 to P-20)

1) 3-(2-benzyloxy)-5-chlorophenyl)-1-(5-(2-chlorophenyl)-3(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1yl)-3-phenylpropan-1-one(P-1):mp 162-164°C; IR (KBr):3030(Ar,C-H), 2956(C-H), 2819(C-H), 1690(C=O), 1616(Ar,C=C), 1563(Ar,C=C), 1535(Ar,C=C), 1478(C-H), 1078(C-O-C), 1030(C-F),736(C-Cl) cm^{-1}; MS: m/z = 623 $[M]^{+}$

2) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-nitrophenyl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-2):mp 154-156°C; IR (KBr): 3026(Ar,C-H), 2914(C-H), 1662(C=O), 1613(Ar,C=C), 1551(Ar,C=C), 1533(Ar,C=C), 1472(C-H), 1076(C-O-C), 732(C-Cl) cm^{-1}; MS: m/z = 630 [M]

3) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-fluorophenyl)-3-(3-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-3):mp 145-147°C; IR(KBr):3061(Ar,C-H),1665(C=O),1624(Ar,C=C),1535(Ar,C=C),1477(C-H), 1020(C-O-C), 1030(C-F), 734(C-Cl) cm^{-1}; MS: m/z = 634 $[M]^{+}$

4) 3-(2-benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(3,4-dimethoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-4):mp 178-180°C; IR (KBr): 3029(Ar,C-H), 2959(C-H), 2829(C-H), 1662(C=O), 1617(Ar,C=C), 1563(Ar,C=C), 1535(Ar,C=C), 1443(C-H), 1078(C-O-C), 1030(C-F),739(C-Cl) cm^{-1}; MS: m/z = 665 $[M]^+$

5) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-fluorophenyl)-3-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-5):mp 170-172°C; IR(KBr):3064(Ar,C-H),1668(C=O),1599(Ar,C=C),1404(C-H),1012(C-O-C),1028(C-F), 734(C-Cl) cm^{-1}; MS: m/z = 634 $[M]^+$

6) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(2-nitrophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-6):mp 149-151°C; IR(KBr): 3069(Ar,C-H), 2969(C-H), 2822(C-H), 1669(C=O), 1616(Ar,C=C), 1539(Ar,C=C), 1476(C-H), 1026(C-O-C), 739(C-Cl) cm^{-1}; MS: m/z = 661 $[M]^+$3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-7): mp 138-140°C; IR (KBr): 3079(Ar,C-H), 2967(C-H), 2842(C-H), 1661(C=O), 1636(Ar,C=C), 1519(Ar,C=C), 1472(C-H), 1023(C-O-C), 750 (C-H), 729(C-Cl) cm^{-1}; MS: m/z = 605 $[M]^+$

7) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(2-nitrophenyl)-4,5-dihydro-1H pyrazol-1-yl)-3-phenylpropan-1-one(P-8):mp 161-163°C; IR(KBr): 3067(Ar,C-H), 1676(C=O), 1636(Ar,C=C), 1532(Ar,C=C), 1473(C-H), 1028(C-O-C), 745(C-H), 734(C-Cl) cm^{-1}; MS: m/z = 650 $[M]^+$

8) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(3,4-dimethoxyphenyl)-3-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-9):mp 140-142°C; IR(KBr): 3025(Ar,C-H), 2956(C-H), 2829(C-H), 1666(C=O), 1617(Ar,C=C), 1573(Ar,C=C), 1532(Ar,C=C), 1453(C-H), 1071(C-O-C), 1023(C-F), 736(C-Cl) cm^{-1}; MS: m/z = 649 $[M]^+$

9) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(2-nitrophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)3-phenylpropan-1-one(P-10):mp 147-149°C; IR (KBr): 3073(Ar,C-H), 2963(C-H), 2862(C-H), 1667(C=O), 1626(Ar,C=C), 1520(Ar,C=C), 1471(C-H), 1025(C-O-C), 750(C-H), 739(C-Cl) cm^{-1}; MS: m/z = 616 [M

B. 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(p-tolyl)-4,5-dihydro-1H-

1) pyrazol-1-yl)-3-phenylpropan-1-one (P-11):mp 167-169°C; IR (KBr): 3043(Ar,C-H), 2922(C-H), 2847(C-H), 1606(C=O), 1529(Ar,C=C), 1466(C-H), 1022(C-O-C), 750 (C-H), 729(C-Cl) cm^{-1}; ^{1}H NMR (400 MHz, DMSO): δ ppm 2.45 (s, 3H, -CH_3), 3.0-3.04 (d, 2H, -CH_2), 3.54-3.59 (d, 2H, -CH_2), 3.93 (t, 1H,-CH), 4.93-5.01(m, 3H, -CH_2-CH),6.58-6.62 (dd, 2H, ArH), 6.84-6.88 (t, 4H, ArH), 6.97-7.35 (m,7H, ArH), 7.42-7.51 (m, 7H, ArH), 8.05 (s, 1H, ArH). 13C NMR (100 MHz, DMSO): δ ppm 20.47, 36.63, 43.41, 44.63, 56.28, 61.64, 108.46, 114.13, 117.43, 119.28, 119.80, 124.11, 129.29, 130.19, 132.77, 134.38, 141.49, 143.20, 152.48,155.79, 168.52. MS: m/z = 619 $[M]^+$

2) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-chlorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-12):mp 164-166°C; IR (KBr): 3069(Ar,C-H), 2967(C-H), 2832(C-H), 1667(C=O), 1631(Ar,C=C), 1519(Ar,C=C), 1474(C-H), 1022(C-O-C), 743(C-H), 732(C-Cl) cm^{-1}; MS: m/z = 605 $[M]^+$

C. 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-bromophenyl)-5-(4-fluorophenyl)-4,5-

1) dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-13):mp 175-177°C; IR(KBr): 3059(Ar,C-H), 2961(C-H), 2822(C-H), 1667(C=O), 1631(Ar,C=C), 1529(Ar,C=C), 1472(C-H), 1032(C-O-C), 1023(C-F), 740(C-H), 733(C-Cl), 575(C-Br) cm^{-1}; MS: m/z = 667 [M]

2) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-14):mp 180-182°C; IR(KBr): 3062(Ar,C-H), 1679(C=O), 1639(Ar,C=C), 1542(Ar,C=C), 1475(C-H), 1029(C-O-C), 741(C-H), 731(C-Cl) cm^{-1}; MS: m/z = 650 $[M]^+$

3) (2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-chlorophenyl)-3-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-15):mp 144-146°C; IR(KBr): 3069(Ar,C-H), 2963(C-H), 2826(C-H), 1677(C=O), 1635(Ar,C=C), 1527(Ar,C=C), 1474(C-H), 1039(C-O-C), 1027(C-F), 740(C-H), 732(C-Cl) cm^{-1}; MS: m/z = 623 $[M]^+$

4) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-fluorophenyl)-5-(4-nitrophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-16):mp 135-137°C; IR(KBr):3052(Ar,C-H), 1677(C=O), 1634(Ar,C=C), 1541(Ar,C=C), 1476(C-H), 1037(C-O-C), 1022(C-F), 743(C-H), 731(C-Cl) cm^{-1}; MS: m/z = 634 $[M]^+$

5) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(4-fluorophenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one (P-17):mp 161-163°C; IR(KBr): 3068(Ar,C-H), 2965(C-H), 2829(C-H), 1674(C=O), 1632(Ar,C=C), 1521(Ar,C=C), 1475(C-H), 1035(C-O-C), 1028(C-F), 742(C-H), 735(C-Cl) cm^{-1}; MS: m/z = 623 $[M]^+$

6) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-chlorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-18):mp174-176°C;IR(KBr):3021(Ar,C-H),2953(C-H),2822(C-H),1662(C=O),1619(Ar,C=C),1579(Ar,C=C), 1531(Ar,C=C), 1455(C-H), 1072(C-O-C), 1021(C-F), 737(C-Cl) cm^{-1}; MS: m/z = 635 $[M]^+$

7) 3-(2-(benzyloxy)-5-chlorophenyl)-1-(3-(4-fluorophenyl)-5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-19):mp 162-164°C; IR(KBr):3029(Ar,C-H),2957(C-H),2826(C-H),1666(C=O),1611(Ar,C=C),1572(Ar,C=C), 1533(Ar,C=C), 1453(C-H), 1071(C-O-C), 1024(C-F), 733(C-Cl) cm^{-1}; MS: m/z = 619 [M]

8) (2-(benzyloxy)-5-chlorophenyl)-1-(5-(4-fluorophenyl)-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl)-3-phenylpropan-1-one(P-20):mp 150-152°C; IR (KBr): 3024(Ar,C-H), 2955(C-H), 2820(C-H), 1660(C=O), 1613(Ar,C=C), 1572(Ar,C=C), 1531(Ar,C=C), 1443(C-H), 1077(C-O-C), 1022(C-F), 731(C-Cl) cm^{-1}; MS: m/z = 589 $[M]^+$

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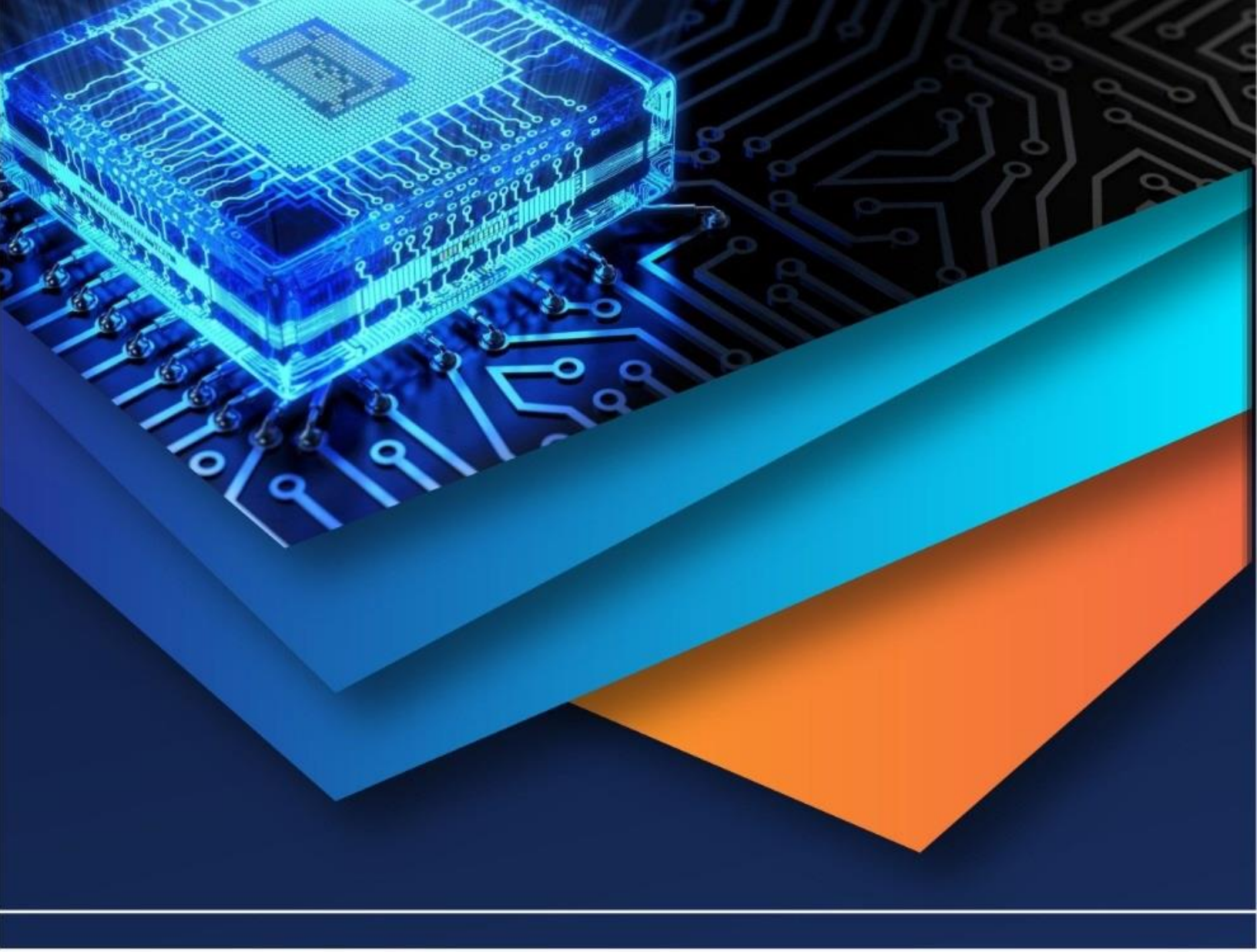

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