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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF NEW BAYLIS-HILLMAN DERIVED NITRO METHYLENE IMIDAZOLE DERIVATIVES AS INSECTICIDAL AGENTS

Raghavachary Gampa [1, 2], Lavanya Devi Chebrolu [1], Krishna Gudikandula [3], Jayathirtha Rao Vaidya [1], Venkateshwar Rao Ghanakota *[2] and Singara Charya Maringanti [3]

Crop Protection Chemicals Division [1], Indian Institute of Chemical Technology, Uppal Road, Tarnaka, Hyderabad- A.P. 500 607, India
Department of Chemistry [2], Department of Microbiology [3], Kakatiya University, Warangal-506009, A.P. India

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Correspondence to Author:
Dr. V. Jayathirtha Rao

Chief Scientist, Head, Crop Protection Chemicals Division, Indian Institute of Chemical Technology, Uppal Road, Tarnaka, Hyderabad-500 607, India.

E-mail: jrao@iict.res.in

ABSTRACT: A series of Baylis-Hillman derived N-cinnamyl substituted nitro methylene imidazole derivatives **4a-s**were synthesizedfrom Baylis-Hillman acetates and nitro methylene imidazole compoundsand characterised by ^{1}H NMR, IR, Mass and HRMS spectroscopy. Their insecticidal activities were evaluated against *T. Castaneum* and compared with a standard insecticide Permethrane. Preliminary biological activity tests showed that most of the compounds exhibited good insecticidal activity against *T. Castaneum* at 100µg/cm^2 especially compounds 4b, 4g, 4i, 4l, 4n and 4r showed good insecticidal activity against *T. castaneum*, interestingly compound 4b with p-fluoro substitution displayed 75% activity. The structure-activity relationship showed that compounds with electron-with drawing substitutions like -F, -Br, -Cl, -NO_2, -CF_3 at the para position havinggood insecticidal activity and compounds with electron-with drawing groups like -F, -Br at the meta position have shown moderate activity.This work provides some hints for further structural modifications on the Baylis-Hillman derivatives and the enhancement of insecticidal activity.

INTRODUCTION: With the increase of food demands, a safe and efficient way to protect large monocultures in modern agriculture is required.[1, 2] The discovery of highly effective and selective pesticides is still one of the most crucial tools for preventing disease transmission and pest management.

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Extensive studies have been carried out to develop several control programs against the insects. Imidacloprid is the most widely used insecticide. However, it is relatively toxic toward mammals and aquatic species, such as birds, bees, and silkworms. Imidacloprid is obtained by structural modification of the lead compound CH-IMI (**Fig.1**).[3-5]

CH-IMI has been reported as a potential new insecticide, a series of neonicotinoid insecticides that use CH-IMI as a basic unit have been rapidly developed in recent years. These insecticides possess novel structures and various modes of action compared with traditional insecticides, including hexahydronitroimidazopyrimidines,[6-8]

some of which are shown as compounds I to IV **(Fig. 1)**.[9-14]

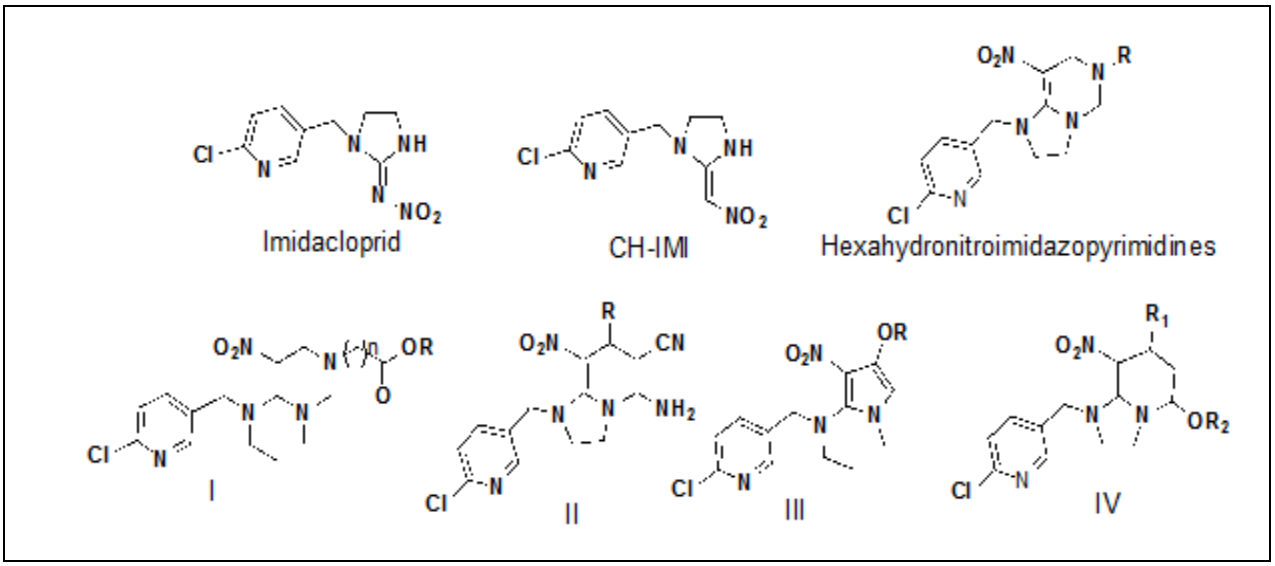


FIG. 1: COMMERCIALIZED NEONICOTINOID INSECTICIDES AND ACTIVE COMPOUNDS

Neonicotinoid insecticides are known to act agonistically and show high selectivity to insect nicotinic acetylcholine receptors (nAChR); they are also relatively safe toward mammals and aquatic species.[15-17] Neonicotinoids are increasingly used in crop protection and animal health care against a broad spectrum of sucking and biting insects.[18-22] Neonicotinoid insecticides have many mutual molecular characteristics. The presence of a strong electron-withdrawing pharmacophoric group, such as CN or NO_2, is an essential structural characteristic of this insecticides.[23, 24]

However, the excessive and frequent use of neonicotinoid pesticides causes significant increases in pest resistance, so there is a need to synthesize new insecticides, to show better results than earlier reported. In the scope of a research program aimed at developing new chemical entities as possible lead compounds, efforts were directed to replace the heterocyclic component of nicotine derivatives to potentiate bioactivity. In this contest by considering nitromethylenyl imidazole group as essential for insecticidal activity we aimed to replace the nicotinyl heterocyclic ring with some Baylis-Hillman derived cinnamyl substituted compounds to findits potentiality as insecticides. The Baylis–Hillman reaction [25-29] has attracted the attention of organic chemists as this reaction provides synthetically useful multifunctional molecules. The develolpment of resistance to imidacloprid by pest insects is a significant concernand therefore, it is an ongoing effort to synthesize new insecticidal agents.

Inspired with the biological profile of nitro methylene imidazole group and their increasing importance in pharmaceutical and biological fields, and in continuation of our research towards the exploitation of the Baylis–Hillman reaction in heterocyclic chemistry, design and synthesis of biologically active and pharmacologically important new heterocycles and their derivatives,[30-37] we have synthesized 19 new Baylis-Hillman derived nitro methylene imidazole derivatives by the reaction of Baylis–Hillman acetates and nitro methylene imidazole and screened for their insecticidal activity.

Experimental:

Materials: All chemicals were of research grade and were used as obtained from commercial source. The reactions were carried out in a round-bottomed flask of 25 ml capacity at room temperature in an efficient fume hood. The progress of all the reactions was monitored by TLC. Melting points were determined on a MEL-TEMP II melting point apparatus and were uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 MHz, 75 MHz spectrometer; TMS was used as an internal standard in DMSO-d_6. Mass spectra were recorded on Thermofinnig an ESI ion trap Mass

Spectrometer and QSTAR XL High resolution mass spectrometer (HRMS). Commercially available organic compounds were used without further purification except for the solvent, which was distilled by known methods before use.

Insecticidal activity studies:

Fumigation bioassay: The susceptibility of *T. castaneum* adults to the fumigant action of all the synthesized compounds (**4a-s**) were investigated according to the method described by Kim and Ahn (2001).[38] Groups of 10 adults were placed in diet cups (3.6 cm diameter x 4 cm) covered with nylon 60 mesh cloth. Each filter paper (Whatman No. 2, 5.0 cm diameter) treated with each test compound (0.35 mg/cm^2) previously dissolved in acetone (100 µl), it was placed in the bottom of a polyethylene cup (5.0cm diameter x 9cm**)**, and a diet cup containing adult insects was put into the polyethylene cup. This prevented direct contact of the test adults with the test compound. Each polyethylene cup was then either sealed with a lid, method A, or left unsealed, method B. Controls received 100µl acetone only. The insects were exposed for 2 days. All treatments were replicated 10 times.

General experimental procedure for the synthesis of Baylis-Hillman adducts:

Aromatic aldehyde (10 mmol) was taken in the 50ml R.B flask and then methyl acrylate (15 mmol) was added. To this reaction mixture DABCO (20 mol% with respect to aldehyde) was added and allowed to stir at room temperature till completion of the reaction (monitored by TLC). After completion, the reaction mixture was diluted with H_2O (50mL) and extracted with ethyl acetate (3 x 50mL). The combined organic layers were dried over Na_2SO_4, concentrated in vacuum and purified by silica gel column chromatography using EtOAc:hexane (1:9) as eluent to afford pure Baylis-Hillman adducts.

General experimental procedure for the synthesis of Baylis-Hillman acetates:

To a well-stirred solution of BH adduct (10 mmol) in dichloromethane (DCM) (20 mL), pyridine (11 mmol) was added and cooled to 0^{o}C. Then acetyl chloride (11mmol) was added slowly at the same temperature under nitrogen atmosphere and allowed to stir at room temperature until the completion of the reaction (TLC). After completion, the reaction mixture was diluted with water (15 mL) and extracted with dichloromethane (2 x 20 mL). The combined organic layers were washed with sat.Na_2SO_4 solution, then separated the organic layers and dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting residue was subjected to silica gel column chromatography using EtOAc:hexane(1:9) as eluent to afford pure compound.

Synthesi of 2-(Nitromethylene)imidazolidine (3):

a. potassium 2-nitroethene-1,1-bis(thiolate) (a):

4g (0.03mol) of nitromethane and 6ml (0.05mol) of carbon bisulfide were placed in a 100 ml three-necked flask and 10ml of ethanol was added as a solvent, and then the solution was stirred. To the resulting solution was added slowly and dropwise the solution of 8g (0.14mol) of potassium hydroxide in 40ml of ethanol at room temperature over nearly 30min. Since the reaction was exothermic, the rate of addition depended on the reaction temperature, which was preferably controlled between 30-35°C. After the addition was complete, the mixture was further stirred for 2 hours, filtered to obtain a crude product, which was a brown yellow powder in 72% yield

b. (2-nitroethene-1,1-diyl)bis(methylsulfane) (b):

To a solution of 2g (0.0094mol) of potassium 2-nitroethene-1,1-bis(thiolate) in 10ml of dried methanol in a round-bottomed flask, 0.0187mol of dimethyl sulphate was added. The mixture was then stirred for 2 hours at room temperature. The precipitated solid was filtered to obtain a crude product, which was a light brown yellow powder in 70% yield.

c. 2-(nitromethylene)imidazolidine (3):

2.5g (0.0178mol) of 1, 1-dimethylthio-2-nitroethene, 3.3g (0.0178mol) of N1-((6-chloropyridin-3-yl) methyl) ethane-1,2-diamine were added to 15ml of ethanol. The resulting mixture was refluxed for 4 hours at 80-90 °C. The mixture was then cooled to reduce solid, concentrated, filtrated and dried to give a light yellow powder in 56% yield**.**

General experimental Procedure for the synthesis of 2-(nitromethylene)imidazolidin-1-yl)methyl)acrylate: To NaH (1.5 mmol) in 10 mL of THF, 2-(nitromethylene)imidazolidine**3** (1.0 mmol) was added at 0^{o}C and stirred for 15 minutes. To the reaction mixture Baylis-Hillman acetate**2a-s** (1.0 mmol) in 5 mL THF was added and stirred at room temperature for 2-4 h. Completion of the reaction was monitored by TLC. After completion of the reaction, the mixture was poured in to NH_4Cl solution and extracted with ethyl acetate. Combined organic layers were washed with brine solution and dried over Na_2SO_4, evaporated and purified by silica gel column chromatography to obtain the desired products; Baylis-Hillman derived *N*-cinnamyl substituted nitro methylene imidazole derivatives **4a-s**.

(E)-methyl 2-(((E)-2-(nitromethylene) imida zolidin-1-yl)methyl)-3-phenylacrylate (4a): Light yellow solid; Yield: 80 %; mp 163-165^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.62(s, 1H), 8.01(s, 1H), 7.45-7.41(m, 3H), 7.31-7.29(d, 2H,*J*=8.21), 6.43(s, 1H), 4.18(s, 2H), 3.85(s, 3H), 3.65-3.62(t, 2H,*J*=8.69),3.54-3.50(t, 2H, *J*=7.47);^{13}C NMR (75 MHz, DMSO-d_6) δ: 166.9, 159.0, 156.8, 144.9, 129.6, 128.9, 128.8, 128.6, 126.8, 125.7, 96.9, 52.3, 49.7, 48.3, 45.2;IR (KBr,cm^{-1}):3438, 2950, 1712, 1585, 1383, 1258, 1142, 700:ESI-MS (m/z): 304 $[M+H]^+$; HRMS (ESI);m/z calculated for $C_{15}H_{18}O_4N_3$; 304.1292, found; 304.1295.

(E)-methyl 3-(4-fluoro phenyl)-2-(((E)-2-(nitro methylene) imidazolidin-1-yl)methyl) acrylate (4b) : Light yellow solid; Yield: 83 %; mp 128-130^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.62(s, 1H), 7.97(s, 1H), 7.33-7.29(m, 3H), 7.18-7.12(t, 2H,*J*=8.30), 6.41(s, 1H), 4.16(s, 1H), 3.85(s, 3H), 3.67-3.64(m, 2H), 3.58-3.55(m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ: 159.0, 159.2, 166.7, 143.3, 136.6, 135.7, 131.9, 130.4, 130.2, 129.1, 129.0, 126.4, 129.8, 128.3, 96.8, 52.4, 48.4, 42.2, 41.8; IR (KBr, cm^{-1}):3354, 3134, 2952, 1708, 1587, 1557, 1430, 1249, 1108, 832, 708; ESI-MS (m/z): 322 $[M+H]^+$; HRMS (ESI);m/z calculated for $C_{15}H_{17}O_4N_3F$;322.11976, found; 322.11872.

(E)-methyl 2-(((E)-2-(nitromethylene) imida zolidin-1-yl)methyl)-3-m-tolylacrylate (4c): Light yellow solid; Yield: 82 %; mp 138-141 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.63(s, 1H), 8.00(s, 1H), 7.35-7.32(t, 1H, *J*=9.08), 7.10-7.08(d, 3H, *J*=9.12), 6.44(s, 1H), 4.18(s, 2H), 3.85(s, 3H), 3.66-3.63(t,2H,*J*=8.39), 3.56-3.52(t, 2H,*J*=9.46), 2.38(s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ: 159.0, 159.2, 166.7, 143.3, 136.6, 135.7, 131.9, 130.4, 130.2, 129.1, 129.0, 126.4, 129.8, 128.3, 96.8, 52.4, 48.4, 42.2, 41.8, 28.2; IR (KBr, cm^{-1});3371, 3139, 2954, 1701, 1579, 1530, 1437, 1247, 1106, 700; ESI-MS (m/z): 318 $[M+H]^+$; HRMS (ESI); m/z calculated for $C_{16}H_{20}O_4N_3$:318.14483, found; 318.14382.

(E)-methyl3 - (3-fluorophenyl) – 2 -(((E)-2-(nitro methylene)imidazolidin-1yl)methyl)acrylate(4d): Light yellow solid; Yield: 76 %; mp 138-140 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.62(s, 1H), 7.95(s, 1H), 7.47-7.40(m, 1H), 7.13-7.07(m, 2H), 7.01-6.98(d, 2H,*J*=9.06), 6.40(s, 1H), 4.16(s, 1H), 3.86(s, 3H), 3.66-3.63(d, 2H, *J*=9.06), 3.56-3.49(d, 2H, *J*=9.82); ^{13}C NMR (75 MHz, DMSO-d_6) δ:166.4, 158.9,156.61, 143.0, 130.7, 130.6, 128.5, 127.0, 124.5, 124.5, 96.7, 52.3, 48.3, 42.1, 41.7; IR (KBr, cm^{-1});3362, 3137, 2928, 1718, 1585, 1526, 1437, 1282, 1109, 760; ESI-MS (m/z): 322 $[M+H]^+$; HRMS (ESI); m/z calculated for $C_{15}H_{17}O_4N_3F$;322.11976, found;322.11885.

(E)-methyl2-(((E)-2-(nitro methylene) imidazoli din-1-yl) methyl) -3-(2-(trifluoromethyl) phenyl) acrylate (4e): Light yellow solid; Yield: 68 %; mp 142-144^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.60(s, 1H), 8.15(s, 1H), 7.77-7.76(d,1H,*J*=7.78), 7.65-7.62(t, 2H,*J*=7.62), 7.56-7.53(t, 1H,*J*=7.32), 7.25-7.23(d,1H,*J*=7.62), 6.33(s, 1H), 4.02(s, 1H), 3.87(s, 3H),3.63-3.59(t, 2H,*J*=8.54), 3.44-3.40(t, 2H,*J*=9.61); ^{13}C NMR (75 MHz, DMSO-d_6) δ: 166.0, 158.9, 141.2, 131.9, 130.7, 129.8, 129.1, 128.8, 126.2, 126.2,128.5, 96.6, 52.4, 48.0, 42.0, 41.8; IR (KBr, cm^{-1}):3365, 3120, 2959, 1719, 1589, 1552, 13151260, 707; ESI-MS (m/z): 372 $[M+H]^+$; HRMS (ESI);m/z calculated for $C_{16}H_{17}O_4N_3F_3$; 372.11657, found;372.11544.

(E)-methyl 3- (2, 4-dichlorophenyl) – 2 - (((E)-2 (nitro methylene) imidazolidin-1-yl) methyl) acrylate (4f): Light yellow solid; Yield: 80 %; mp 156-160 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.60(s, 1H), 7.93(s, 1H), 7.51(s, 1H), 7.35-7.33(d, 1H,*J*=8.91), 7.16-7.15(d, 1H, *J*=9.12), 6.40(s, 1H),

4.04(s, 2H), 3.87(s, 3H), 3.66-3.62(t, 2H, *J*=9.91), 3.49-3.45(t, 2H,*J*=9.46); ^{13}C NMR (75 MHz, DMSO-d_6) δ:166.1, 159.0, 140.6, 136.1, 134.3, 130.9, 130.6, 129.9, 128.7, 127.5, 96.9, 52.7, 48.4, 42.2, 42.4; IR (KBr, cm^{-1}); 3376, 3119, 2923, 1717, 1586, 1553, 1427, 1384, 1263, 1146, 822, 712; ESI-MS (m/z): 372 $[M+H]^+$; HRMS (ESI); m/z calculated for $C_{15}H_{16}O_4N_3Cl_2$;372.0512, found; 372.0520.

(E)-methyl3-(4-bromophenyl)- 2-(((E) - 2 - (nitro methylene) imidazolidin-1-yl) methyl) acrylate (4g): Light yellow solid; Yield: 76 %; mp 116-118^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.63(s, 1H), 7.93(s, 1H), 7.61-7.58(d, 2H,*J*=8.30), 7.19-7.16(d, 2H,*J*=8.30), 6.43(s, 1H), 4.15(s, 2H), 3.85(s, 3H), 3.70-3.63(t, 2H,*J*=10.12), 3.55-3.49(t, 2H,*J*=9.18);^{13}C NMR (75 MHz, DMSO-d_6) δ: 166.7, 159.0, 143.5, 132.4, 132.2, 130.5, 130.1,131.4, 126.5, 124.1, 97.0, 52.5, 48.5, 42.2, 41.9; IR (KBr, cm^{-1});3353, 2950, 1712, 1583, 1435, 1383, 1233, 1110, 1071, 760; ESI-MS (m/z): 382 $[M+H]^+$; HRMS (ESI);m/z $[M+Na]^+$ calculated for $C_{15}H_{16}O_4N_3BrNa$;404.02164, found;404.02108.

(E)-methyl3-(4-isopropylphenyl)-2-(((E)-2-(nitro methylene) imidazolidin-1-yl) methyl) acrylate (4h): Light yellow solid; Yield: 76 %; mp 126-128 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.64(s, 1H), 8.00(s, 1H), 7.32-7.23(m, 4H),6.49(s, 1H), 4.20(s, 2H), 3.85(s, 3H), 3.66-3.63(d,2H, *J*=8.3), 3.57-3.51(d, 2H, J=8.30),2.99-2.90(m, 1H),1.28-1.25(s, 6H); ^{13}C NMR (75 MHz, DMSO-d_6) δ:167.2, 159.1, 151.1, 145.3,140.1, 131.0, 129.3, 127.1, 124.5, 97.0, 52.4, 48.1, 42.2, 42.0, 33.9, 23.6 ; IR (KBr, cm^{-1}):3357, 3116, 2956, 1711, 1579, 1554, 1440, 1272, 1109, 837, 717; ESI-MS (m/z): 346 $[M+H]^+$; HRMS (ESI); m/z calculated for $C_{18}H_{24}O_4N_3$;346.17613, found; 346.17496.

(E)-methyl3 - (4-ethylphenyl) - 2 - (((E)-2-(nitro methylene) imidazolidin-1-yl) methyl) acrylate (4i): Light yellow solid; Yield: 78 %; mp 110-112 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.64(s, 1H), 8.00(s, 1H), 7.29-7.23(m, 4H), 6.47(s, 1H), 4.20(s, 2H), 3.85(s, 3H), 3.67-3.64(d, 2H,*J*=8.39), 3.56-3.53(d, 2H, *J*=9.76), 2.71-2.66(m, 2H), 1.25(s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ:167.2, 159.1, 146.5, 145.3, 140.1, 130.9,130.9, 129.3, 128.5,128.3, 124.5, 97.0, 52.4, 48.2, 42.2, 42.0, 28.6, 15.1; IR (KBr, cm^{-1}):3358, 3296, 3117, 2960, 1709, 1671, 1578, 1393, 1273, 1154, 835, 713; ESI-MS (m/z): 332 $[M+H]^+$; HRMS (ESI); m/z calculated for $C_{17}H_{22}O_4N_3$;332.1605, found; 332.1606.

(E)-methyl 3 - (3-chlorophenyl)-2 - (((E)-2-(nitro methylene) imidazolidin-1yl) methyl) acrylate (4j): Light yellow solid; Yield: 82 %; mp 146-228148 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.6(s, 1H), 7.93 (s, 1H), 7.39(s, 2H),7.20-7.18(m, 3H), 6.42(s, 1H), 4.15(s, 1H), 3.86(s, 3H),3.70-3.63(t, 2H,*J*=10.57), 3.56-3.49(t, 2H,*J*=9.06); ^{13}C NMR (75 MHz, DMSO-d_6) δ:166.5, 159.0, 142.9, 135.3, 134.8, 130.7, 130.2, 129.5, 128.8, 126.9, 96.9, 52.5, 48.5, 42.1, 41.9; IR (KBr, cm^{-1}):3363, 3126, 2956, 1715, 1587, 1426, 1256, 1256, 1113, 832, 711; ESI-MS (m/z): 338 $[M+H]^+$; HRMS (ESI); m/z calculated for $C_{15}H_{17}O_4N_3Cl$; 338.09021, found;338.08943.

(E)-methyl 3 - (3-bromophenyl)-2-(((E)-2-(nitro methylene) imidazolidin-1yl)methyl) acrylate (4k): Light yellow solid; Yield: 72 %; mp 118-120^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.62(s, 1H), 7.93(s, 1H), 7.57-7.54(d, 1H,*J*= 9.12),7.43(s, 1H), 7.36-7.31(t, 1H,*J*=10.13), 7.25-7.23(s, 1H), 6.42(s, 1H),4.15(s, 2H),3.86(s, 3H),3.70-3.63(m, 2H), 3.55-3.50(m, 2H);^{13}C NMR (75 MHz, DMSO-d_6) δ:166.4, 158.9, 142.8, 135.5, 132.3, 131.6, 130.3, 127.3, 127.2, 122.7, 96.8, 52.4, 48.3, 42.1, 41.8; IR (KBr, cm^{-1}):337, 3127, 2922, 1710, 1660, 1584, 1431, 1251, 1106, 826, 720; ESI-MS (m/z):404 $[M+Na]^+$; HRMS (ESI); m/z calculated for $C_{15}H_{16}O_4N_3BrNa$;404.02098, found;404.02164.

(E)-methyl 3 - (4-chlorophenyl) - 2 - (((E)-2-(nitrosomethylene)imidazolidin-1-yl)methyl) acrylate (4l): Light yellow solid; Yield: 81 %; mp 135-137^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.79(s, 1H), 7.97(s, 1H), 7.66(s, 1H), 7.48-7.42(t, 2H,*J*=8.12), 7.35-7.29(t, 2H,*J*=8.49), 6.46(s, 1H), 4.21(s, 1H), 3.87(s, 3H), 3.72-3.66(t, 2H,*J*=8.12), 3.56-3.51(t, 2H, *J*=8.49); ^{13}C NMR (75 MHz, DMSO-d_6) δ:159.0, 159.2, 166.7, 143.3, 136.6, 135.7, 131.9, 130.4, 130.2, 129.1, 129.0, 126.4, 129.8, 128.3, 96.8, 52.4, 48.4, 42.2, 41.8; IR (KBr, cm^{-1}):3389, 3123, 2928, 2864, 1720, 1583, 1432, 1383, 1267, 1118, 878, 759; ESI-MS (m/z): 338

$[M+H]^+$; HRMS (ESI);m/z calculated for $C_{15}H_{17}O_4N_3Cl$;338.09021, found;338.08949.

(E)-methyl 2- (((E)-2- (nitromethylene) imida zolidin-1-yl) methyl)-3-(4-nitrophenyl) acrylate (4m): Light yellow solid; Yield: 62 %; mp 139-141^oC; ^1H NMR (300 MHz, DMSO-d_6) δ: 8.60(s, 1H), 8.33-8.31(d, 1H,*J*=8.31), 8.00(s, 1H), 7.73-7.72(m, 1H), 7.55-7.53(m, 1H), 7.49-7.47(s, 2H), 6.31(s, 1H), 4.14 (s, 1H), 3.88(s, 3H),3.67-3.64(t, 2H,*J*=9.15),3.57-3.53(t, 2H,*J*=9.16);^{13}C NMR (75 MHz, DMSO-d_6)δ: 166.7, 158.0, 142.5, 138.4, 132.2, 130.5, 130.1,131.4, 125.5, 124.1, 97.0, 52.5, 48.5, 42.2, 41.9; IR (KBr, cm^{-1}):3341, 3152, 2951, 1719, 1590, 1509, 1339, 1257, 1108, 863, 716; ESI-MS (m/z): 349 $[M+H]^+$; HRMS (ESI);m/z calculated for $C_{15}H_{17}O_6N_4$; 349.11426, found;349.11385.

(E)-methyl2-(((E)-2-(nitromethylene)imidazolidi din-1-yl)methyl)-3-p-tolylacrylate(4n): Light yellow solid; Yield: 78 %; mp 131-133^oC; ^1H NMR (300 MHz, DMSO-d_6) δ: 8.63(s, 1H), 7.99(s, 1H), 7.25(s, 1H), 7.21-7.20(d, 3H, *J*=8.24), 6.45(s, 2H), 4.19(s, 1H), 3.85(s,3H), 3.67-3.64 (t,2H,*J*=8.54), 3.56-3.53(t, 2H, *J*=9.76), 2.39 (s, 3H); ^{13}C NMR (75 MHz, DMSO-d_6) δ:166.8, 158.7, 144.5, 139.7, 130.3, 129.2, 128.9, 128.3, 130.5, 124.4, 96.5, 51.9, 47.9, 41.9, 41.5, 20.9; IR (KBr, cm^{-1}):3359, 3124, 2955, 2926, 1707, 1582, 1552, 1427, 1385, 1256, 1119, 812, 711; ESI-MS (m/z): 318 $[M+H]^+$; HRMS (ESI);m/z calculated for $C_{16}H_{20}O_4N_3$;318.14483, found; 318.14421.

(E)-methyl2-(((E)-2-(nitromethylene) imidazoli din-1-yl) methyl) – 3 - (3(trifluoro methyl) phenyl) acrylate (4o): Light yellow solid; Yield: 78 %; mp 140-142^oC; ^1H NMR (300 MHz, DMSO-d_6) δ: 8.61(s, 1H), 7.97(s, 1H), 7.25(s, 1H), 7.20-7.20(d, 3H,*J*=8.24), 6.45(s, 1H), 4.19(s, 2H), 3.85(s,3H), 3.67-3.64(t, 2H,*J*=8.54), 3.56-3.53(t, 2H,*J*= 9.76); ^{13}C NMR (75 MHz, DMSO-d_6) δ:171.3, 156.8, 142.6, 138.6, 131.3, 130.9, 130.4, 129.8, 129.2, 123.7, 124.0, 102.8, 52.8, 45.2, 42.4, 41.4; IR (KBr, cm^{-1}):3384, 2957, 2931, 2880, 1732, 1614, 1554, 1460, 1334, 1223, 810, 703; ESI-MS (m/z): 372 $[M+H]^+$; HRMS (ESI);m/z $[M+Na]^+$ calculated for $C_{16}H_{16}O_4N_3F_3Na$;394.09851, found;394.09732.

(E)-methyl 3 - (2-chlorophenyl) - 2- (((E)-2-(nitromethylene) imidazolidin-1-yl) methyl) acrylate (4p): Light yellow solid; Yield: 78 %; mp 142-144^oC; ^1H NMR (300 MHz, DMSO-d_6) δ: 8.60(s, 1H), 8.02(s, 1H), 7.73-7.72(m, 1H), 7.54-7.53(m, 1H), 7.30 -7.33(m, 2H), 7.19-7.17(d, 1H*J*=8.29), 6.38(s, 1H), 4.06(s, 1H), 3.87(s, 3H), 3.63-3.60(t, 2H,*J*=9.12), 3.48-3.44(t, 2H,*J*=9.19); ^{13}C NMR (75 MHz, DMSO-d_6) δ:167.0, 159.8, 142.3, 131.9, 130.7, 129.8, 128.5, 128.1, 127.8, 126.2, 126.2, 95.6, 51.4, 48.0, 42.0, 41.8; IR (KBr, cm^{-1}):3449, 2955, 1717, 1584, 1536, 1436, 1255, 1112, 836, 692; ESI-MS (m/z): 338 $[M+H]^+$; HRMS (ESI);m/z $[M+Na]^+$ calculated for $C_{15}H_{16}O_4N_3ClNa$;360.07215, found;360.07164.

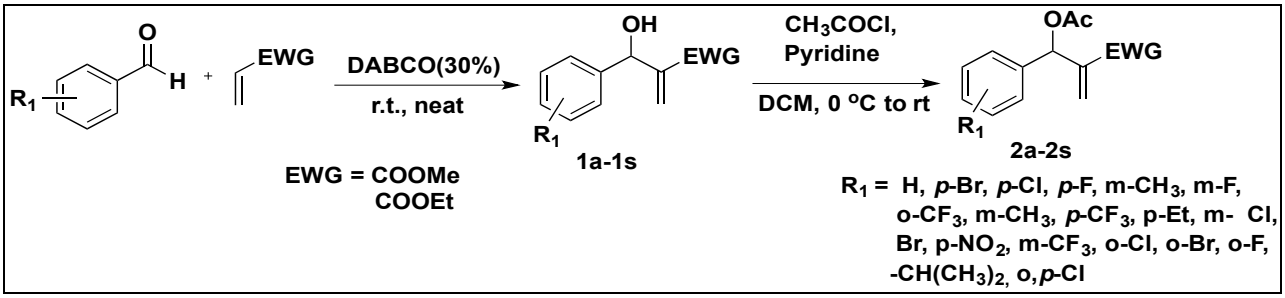
(E)-methyl3-(2-bromophenyl)- 2-(((E) - 2 - (nitro methylene)imidazolidin-1-yl) methyl) acrylate (4q): Light yellow solid; Yield: 72 %; mp 140-142^oC; ^1H NMR (300 MHz, DMSO-d_6) δ: 8.62(s, 1H), 7.97(s, 1H), 7.33-7.26(m, 1H), 7.18-7.12(m, 3H), 6.41(s, 1H), 4.16(s, 2H), 3.85(s, 3H), 3.70-3.62(m, 2H), 3.58-3.52(m, 2H);^{13}C NMR (75 MHz, DMSO-d_6) δ:165.7, 159.0, 158.2, 142.3, 137.6, 135.7, 131.9, 130.4, 130, 129.1, 129.0, 126.4, 129.8, 128.3, 96.8, 52.4, 48.4, 42.2, 41.8; IR (KBr, cm^{-1}):3384, 2957, 2931, 2880, 1732, 1614, 1554, 1460, 1334, 1223, 810, 703;ESI-MS (m/z):404 $[M+Na]^+$; HRMS (ESI);m/z calculated for $C_{15}H_{17}O_4N_3BrNa$;404.02151, found;404.02173.

(E)-methyl 3 - (2-fluorophenyl) - 2 - (((E)-2-(nitro methylene) imidazolidin-1-yl) methyl) acrylate (4r): Light yellow; Yield: 78 %; mp 118-120^oC; ^1H NMR (300 MHz, DMSO-d_6) δ:8.60(s, 1H), 7.91(s, 1H), 7.56-7.54(d, 1H,*J*=9.12),7.42(s, 1H), 7.32-7.31(t, 1H,*J*=9.83), 7.24-7.21(s, 1H), 6.32(s, 1H),4.15 (s, 2H), 3.76(s, 3H),3.70-3.63(m, 2H), 3.55-3.50(m, 2H); ^{13}C NMR (75 MHz, DMSO-d_6) δ:166.4, 158.9, 142.8, 135.5, 132.3, 131.6, 130.3, 127.3, 127.2, 122.7, 96.8, 52.4, 48.3, 42.1, 41.8; IR (KBr, cm^{-1}):337, 3127, 2922, 1710, 1660, 1584, 1431, 1251, 1106, 826, 720; ESI-MS (m/z): 322 $[M+H]^+$; HRMS (ESI);m/z calculated for $C_{15}H_{17}O_4N_3F$;322.11885, found;322.11971.

(E)-methyl 3 - (2,4-dichlorophenyl) – 2 - (((E)-2-(nitro methylene) imidazolidin-1-yl) methyl) acrylate(4s): Light yellow solid; Yield: 82 %; mp 156-160 ^oC; ^1H NMR (300 MHz, DMSO-d_6) δ:

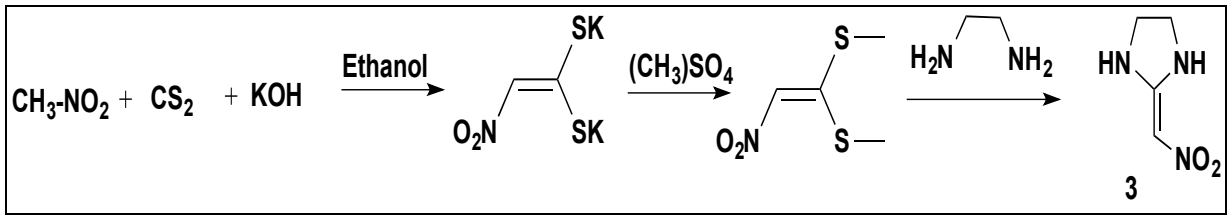
8.50(s, 1H), 7.83(s, 1H), 7.41(s, 1H), 7.25-7.23(d, 1H, *J* = 9.12), 7.16-7.15 (s, 1H), 6.40(s, 1H), 4.04(s, 2H), 3.87(s, 3H), 3.56-3.52(t, 2H,*J*=8.13), 3.49-3.45(t, 2H,*J*=8.27); ^{13}C NMR (75 MHz, DMSO-d_6) δ:166.4, 158.0, 142.6, 136.2, 134.3, 130.8, 130.6, 129.0, 128.7, 127.5, 96.9, 52.6, 47.4, 42.2, 42.3; IR (KBr, cm^{-1}); 3376, 3119, 2923, 1717, 1586, 1553, 1427, 1384, 1263, 1146, 822, 712; ESI-MS (m/z): 372 $[M+H]^+$; HRMS (ESI); m/z calculated for $C_{15}H_{16}O_4N_3Cl_2$;372.0422, found; 372.0430.

RESULTS AND DISCUSSION: Aromatic aldehyde, activated olefin and DABCO were mixed and stirred at r.t under solvent free conditions to get corresponding Baylis-Hillman adducts 1a-s. The BH adducts were acetylated using acetyl chloride/pyridineto get Baylis-Hillman acetates 2a-s[39] (**Scheme 1**).



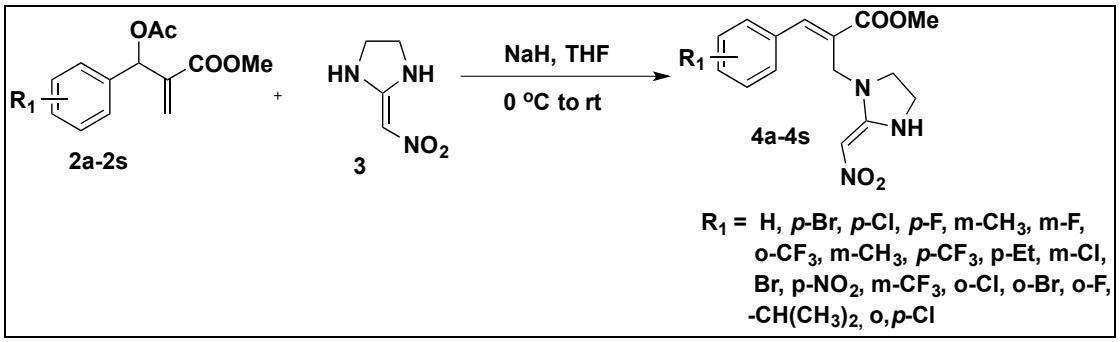
SCHEME 1: SYNTHESIS OF BAYLIS-HILLMAN ACETATES

2-(nitromethylene) imidazolidine **3** was synthesized based on the earlier reports.[40-41] Nitromathane and CS_2 were mixed in ethanol in the prescence of KOH to make bisthiolate and it was methylated using dimethyl sulphate. Thus obtained methylated bisthiolate was mixed with ethylene diamine and refluxed to make 2-(nitromethylene)imidazolidine compound **3** (**Scheme 2**).



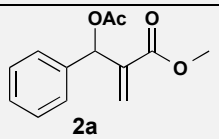
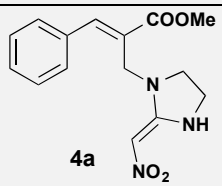
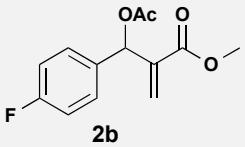
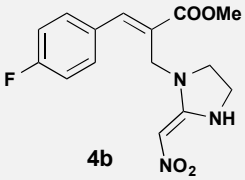
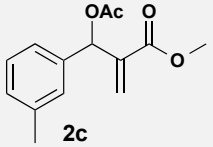
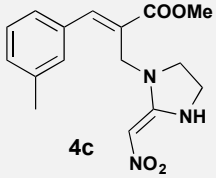
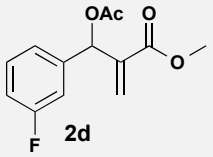
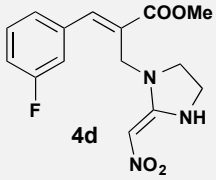
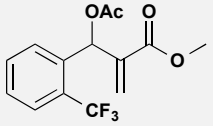
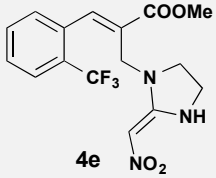
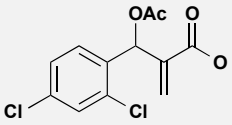
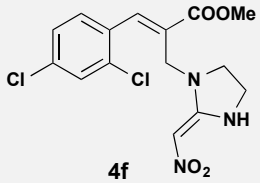
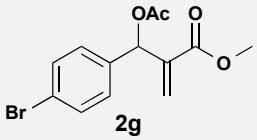
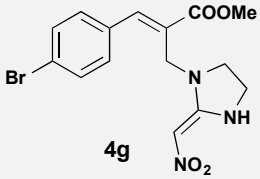
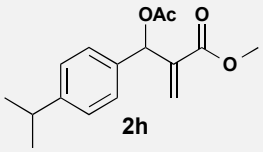
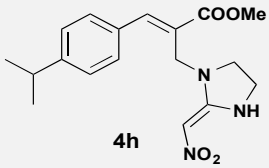
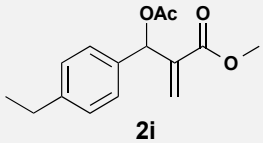
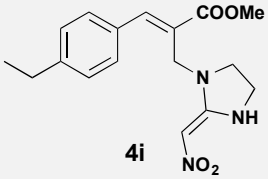
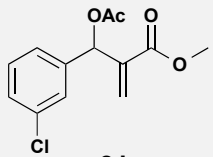
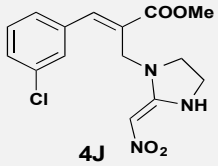
SCHEME 2: SYNTHESIS OF 2-(NITROMETHYLENE)IMIDAZOLIDINE

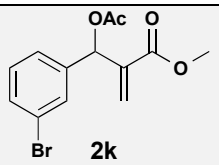
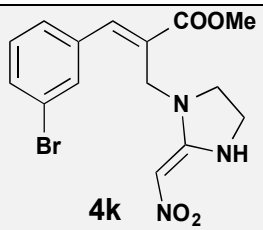
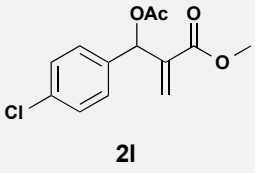
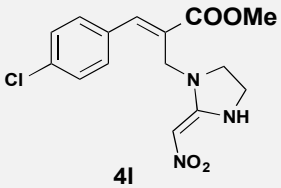
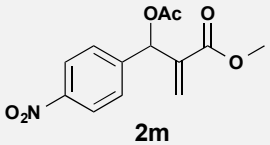
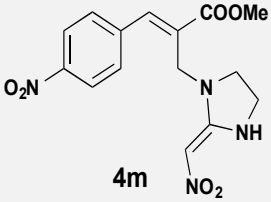
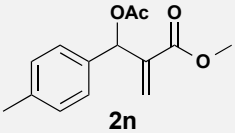
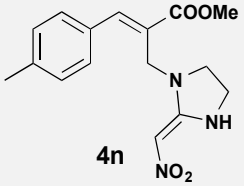
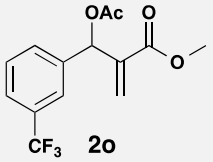
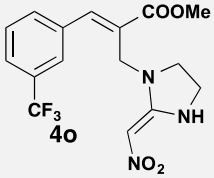
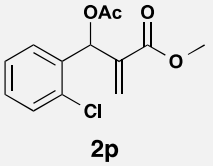
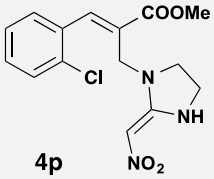
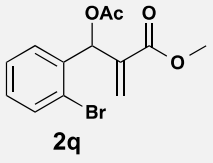
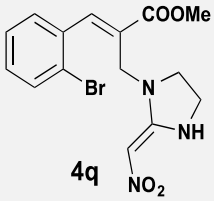
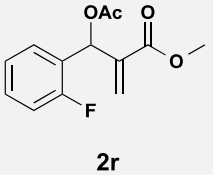
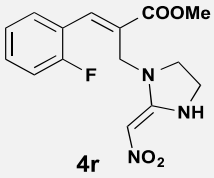
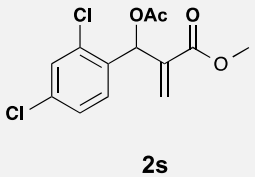
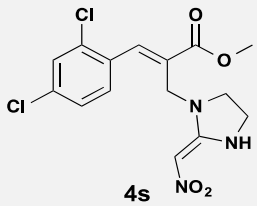
Baylis-Hillman derived *N*-cinnamyl substituted nitro methylene imidazole derivatives were prepared by the reaction between Baylis-Hillman acetate **2a** and 2-(nitromethylene)imidazolidine**3,** in THF solvent in the presence of NaH, at 0 ^{o}C to room temperature for 2-3 h.The desired product**4a** was obtained after column chromatography in good yieldsas shown in **Scheme 3** (**Table 1**). To demonstrate general utility of the method, different Baylis-Hillman derived nitro methylene imidazole derivatives **4b-4s** were prepared. The structures of **4a-s** were firmly established by well-defined ^{1}H-NMR, ^{13}C-NMR, IR and HRMS.



SCHEME 3:SYNTHESIS OF BAYLIS-HILLMAN DERIVED CINNAMYL SUBSTITUTED NITROMETHYLENE IMIDAZOLE DERIVATIVES

TABLE 1:VARIOUS N-CINNAMYL SUBSTITUTED NITRO METHYLENE IMIDAZOLE DERIVATIVESSYNTHESIZED

S. No	BH Acetate	Product	Yield
1	 2a	 4a	80
2	 2b	 4b	83
3	 2c	 4c	82
4	 2d	 4d	76
5	 2e	 4e	68
6	 2f	 4f	80
7	 2g	 4g	76
8	 2h	 4h	76
9	 2i	 4i	78
10	 2J	 4J	82

11	 2k	 4k	72
12	 2l	 4l	81
13	 2m	 4m	62
14	 2n	 4n	78
15	 2o	 4o	78
16	 2p	 4p	78
17	 2q	 4q	78
18	 2r	 4r	87
19	 2s	 4s	82

Insecticidal activity: The insecticidal activity of the title compounds was tested against *T. castaneum* and the bioassay results were given in **Table 2**. The insecticidal activity was compared with a standard insecticide Permethrane. The results of initial screening showed that 100 µg/cm^{2}of the newly synthesized compounds have moderate to potent activities. The mortality rates of compounds 4b(having p-Fluoro substitution), 4g(having p-bromo substitution), 4i(having p-ethyl substitution), 4l(having p-chloro substitution), 4n (having p-nitro substitution) and 4r(having o-Fluoro substitution)exhibited good insecticidal activities against *T. castaneum* and were 75%, 60%, 65%, 60%, 60% and 65%, respectively. Compounds 4d, 4h, 4k, and 4o at a dose of 100 µg/cm^2 exhibited moderate activities against *T. castaneum*, with mortality rates of 50%, 55%, 55%, and 55%, respectively.

As shown in **Table 2**, compounds demonstrated good activities with electron-with drawing groups like -F, -Br, -Cl, -NO_2, -CF_3at the para position and moderate activities with electron-with drawing groups like -F, -Br at the meta position. Compound 4b is having higher inscticidal activity.

TABLE 2: BIOLOGICAL EVALUATION OF COMPOUNDS 3(a-s) ON *T. CASTANEUM*

S. No	Com Compound	Concentration µg/cm^2	Mortality %
1	4a	100	30
2	4b	100	75
3	4c	100	35
4	4d	100	50
5	4e	100	00
6	4f	100	00
7	4g	100	60
8	4h	100	55
9	4i	100	65
10	4J	100	35
11	4k	100	55
12	4l	100	60
13	4m	100	60
14	4n	100	40
15	4o	100	55
16	4p	100	30
17	4q	100	40
18	4r	100	65
19	4s	100	00

CONCLUSION: In conclusion, a series of novel neonicotinoid analogs with Baylis-Hillman derived N-cinnamyl substituted nitro methylene imidazole derivatives were synthesized from Baylis-Hillman acetates and nitro methylene imidazole compounds. The prepared compounds were tested for their insecticidal activity against *T. Castaneum* and compared with a standard insecticide Permethrane. Most of the compounds exhibited good insecticidal activity against *T. castaneum*. Compounds4b, 4g, 4i, 4l, 4n and 4r showed higher insecticidal activities than other compounds.Compound 4b is having higher inscticidal activity. These primary results are promising and beneficial for further research on the development of new and more effective insecticides based on Baylis-Hillman derivatives.

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