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آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Synthesis, Spectral Characterization, *In-vitro* Antibacterial and Antifungal Activities of Novel (2E)-Ethyl-2-(2-(2, 4-Dinitrophenyl) Hydrazono)-4-(Naphthalen-2-yl)-6-Arylcyclohex-3-Enecarboxylates

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**Abstract**

In a search for new leads towards potent antimicrobial agents, an array of novel (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-ene carboxylates 17-24 were synthesized and characterized through their melting point, elemental analysis, MS, FT-IR, one-dimensional NMR (\(^1\)H, \(D_2\)O exchanged \(^1\)H and \(^13\)C), two dimensional HOMOCOR and HSQC spectroscopic data. *In-vitro* microbiological evaluations were carried out for all the newly synthesized compounds 17-24 against clinically isolated bacterial strains namely *Salmonella typhi*, *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, \(\beta\)-Hemolytic streptococcus and *Micrococcus luteus* and also fungal strains namely *Aspergillus flavus*, *Aspergillus niger*, *Mucor*, *Rhizopus* and *Microsporum gypseum* and finally, the results of their structure activity relationship were discussed. The obtained results can be used as the key step for the building of novel chemical compounds with interesting antimicrobial profiles comparable to that of the standard drugs.

**Keywords:** Ethyl 4-(naphthalen-2-yl)-2-oxo-6-arylcyclohex-3-ene carboxylates; (2E)-ethyl-2-(2-(2, 4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-ene carboxylates; 2,4-Dinitrophenyl hydrazine; Antibacterial activity; Antifungal activity.

**Introduction**

Over the past few decades, health-related quality of human life benefits are under threat as many commonly used antibiotics have become less and less effective against certain illnesses, not only because many of them produce toxic reactions but also due to emergence of drug resistant microbes. Hydrazones constitute an important class of compounds for new drug development. Therefore, many researchers have synthesized these compounds as target structures and evaluated their biological activities. These observations have been conducted for the development of new hydrazones that possess varied biological activities (1). Some critical reviews have been published which give an outlook on the developments on antimycobacterial hydrazones (2-5). Hydrazones have been demonstrated to possess varied biological activities (Figure1). For example, isonicotinoyl hydrazones (A) are antitubercular and nifuroxazide (B) is an intestinal antiseptic. Acetylhydrazones (C) provided a good protection against convulsions (6). The 3-Phenyl-5-sulfonamidoindole-2-carboxylic acid 3, 4-methylenedioxy/4-methyl/4-nitrobenzylideny-hydrazide (D) showed antidepressant activity (7). The most
Figure 1. Structurally diverse clinically potent hydrazones that possess varied biological activities.
important anti-inflammatory derivative 2-(2-formylfuryl) pyridyl hydrazone (E) presented a 79% inhibition of pleurisy (8). [(4'-N, N-Dimethylaminobenzylidene-3(3', 4'-ethylenedioxyphenyl) propionylhydrazone] (F) are used as standard antinociceptive drugs (9). The antiplatelet activity of novel tricyclic acylhydrazone derivatives (G) is evaluated by their ability to inhibit platelet aggregation of rabbit platelet-rich plasma (10). The aroylhydrazone chelator 2-hydroxy-1-naphthylaldehyde isonicotinoyl hydrazone (H) showed a greater antimalarial agent activity than desferrioxamine against chloroquine-resistant and sensitive parasites (11). Triazolohydrazones (I) possess a good antibacterial activity (12). A new bioactive compound of N-acylhydrazone class, 3, 4-methylenedioxybenzoyl-2-thienyl hydrazone (J) named LASSBio-294, was shown to have inotropic and vasodilatory effects (13). Triaryl hydrazones (K) exhibit antitumoral activity against MCF-7 and ZR-75-1 human malignant breast cell lines (14).

The 2-Acetyl naphthalene is an interesting starting material which is widely used in perfume formulations (15), mainly in Neroli orange blossom, sweet pea, magnolia, honeysuckle, wisteria, narcissus, jasmine, various exotic florals, etc. In flavor composition, also, the ketone finds a place in imitation of strawberry, grape, various citrus and berry compositions in neroli and other natural flavors, in fruit complexes and in certain types of vanilla flavor. Nowadays, there has been a great deal of interest in exploiting more than one proximal functional groups for designing new structures capable of performing a variety of functions. Synthesis of molecules, which are novel yet resembling known biologically active molecules by virtue of the presence of some critical structural features, is an essential component of the search for new leads in drug designing programme. Taking these considerations into account and as a part of our research program aimed at the synthesis of bioactive novel structurally diverse heterocycles (16-20), herein is reported the molecular conjugation of the naphthyl substituted chalcones moiety with two or more active counterparts which has been designed and synthesized with the hope of producing novel ethyl 4-(naphthalen-2-yl)-2-oxo-6-arylcyclohex-3-ene carboxylates (10-17), an intermediate with three versatile functional groups i.e., ketone, olefin and ester for the synthesis of (2E)-ethyl-2-(2-(2, 4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-ene carboxylates 17-24, a novel hydrazone derivative and to study their in-vitro microbiological evaluation against clinically isolated bacterial and fungal strains.

**Experimental**

**Chemistry**

The progress of the reaction is monitored by TLC analysis. All the reported melting points are taken in open capillaries and are uncorrected. IR spectra are recorded in KBr (pellet forms) on a Nicolet-Avatar–330 FT-IR spectrophotometer and note worthy absorption values (cm⁻¹) alone are listed. ¹H and ¹³C NMR spectra are recorded at 400 MHz and 100 MHz respectively on Bruker Avance II 400 NMR spectrometer using DMSO-d₆ as solvent. Two dimensional HOMOCOR and HSQC spectra are recorded at Bruker DRX 500 NMR spectrometer. The ESI +ve MS spectra are recorded on a Bruker Daltonics LC-MS spectrometer. Satisfactory microanalyses are obtained on Carlo Erba 1106 CHN analyzer.

By adopting the literature precedent (21), (E)-1-naphthalen-2-yl)-3-arylprop-2-en-1-ones 1-8 were prepared.

**General procedure for the synthesis of ethyl 4-(naphthalen-2-yl)-2-oxo-6-arylcyclohex-3-ene carboxylates, compounds 9-16**

To a solution of sodium ethoxide (0.001 mol) in 30 mL of absolute ethanol, freshly distilled ethyl acetocacetate (0.01 mol) and respective (E)-1-naphthalen-2-yl)-3-arylprop-2-en-1-ones (0.01 mol) in absolute ethanol (40 mL) was mixed. This mixture was refluxed in a water bath for 1-3 h by maintaining the temperature around (70-80)°C. The reaction mixture was allowed to be cooled and filtered. Then the crude product was recrystallized from absolute ethanol to afford ethyl 4-(naphthalen-2-yl)-2-oxo-6-arylcyclohex-3-ene carboxylates.
**Ethyl 4-(naphthalen-2-yl)-2-oxo-6-phenylcyclohex-3-ene-carboxylate, compound 9**

IR (KBr) ν (cm⁻¹): 3057, 2987, 2929, 1738, 1659, 1606, 1292, 1155, 847, 816, 766, 704;
1H NMR (δ ppm), (J Hz): 0.92 (3H, t, CH₂CH₃ at C-1, J = 7.1), 3.22-3.28 (2H, H₂α, m), 3.65-3.73 (1H, Hα, m), 3.91 (2H, q, CH₂CH₃ at C-1, J = 7.0), 4.17 (1H, Hβ, d, J = 13.4), 6.73 (1H, s, H₇), 7.24-8.33 (12H, m), 3.92 (2H, q, CH₂CH₃ at C-1, J = 7.0), 4.18 (1H, Hβ, d, J = 14.3), 6.71 (1H, s, H₇), 6.89-8.32 (11H, m, H₁₋₉); 13C NMR (δ ppm): 13.7 CH₂H at C-1, 35.1 C-5, 43.8 C-6, 58.7 CH₂CH₃ at C-1, 59.9 C-1, 123.1 C-3, 169.2 C=O at C-1, 194.2 C-2, 123.4-128.8 -C₆ arom., C-4 carbon may be merged with -C₆ arom™, 132.7, 133.6, 134.3, 141.5 ipso-C’s.

**Ethyl 4-(naphthalen-2-yl)-2-oxo-6-p-tolylcyclohex-3-ene-carboxylate, compound 10**

IR (KBr) ν (cm⁻¹): 3065, 3027, 2979, 2923, 2863, 1740, 1660, 1604, 1148, 897, 849, 816, 753;
1H NMR (δ ppm), (J Hz): 0.96 (3H, t, CH₂CH₃ at C-1, J = 7.1), 2.28 (3H, s, CH₃ at phenyl ring), 3.15-3.17 (2H, H₃, m), 3.62-3.66 (1H, Hα, m), 3.92 (2H, q, CH₂CH₃ at C-1, J = 6.9), 4.11 (1H, Hβ, d, J = 13.3), 6.71 (1H, s, H₇), 7.13-8.30 (11H, m, H₁₋₉); 13C NMR (δ ppm): 14.2 CH₂CH₃ at C-1, 21.0 CH₃ at phenyl ring, 35.7 C-5, 43.8 C-6, 59.2 CH₂CH₃ at C-1, 60.3 C-1, 123.5 C-3, 169.2 C=O at C-1, 194.7 C-2, 123.7-129.2 -C₆ arom., C-4 carbon may be merged with -C₆ arom™, 133.1, 134.0, 134.7, 136.5, 138.9 ipso-C’s.

**Ethyl 6-(4-fluorophenyl)-4-(naphthalen-2-yl)-2-oxocyclohex-3-ene-carboxylate, compound 11**

IR (KBr) ν (cm⁻¹): 3054, 2989, 2925, 1739, 1656, 1603, 1225, 1153, 888, 841, 815, 752;
1H NMR (δ ppm), (J Hz): 0.94 (3H, t, CH₂CH₃ at C-1, J = 7.0), 2.19-2.21 (2H, H₂α, m), 3.68-3.75 (1H, Hα, m), 3.93 (2H, q, CH₂CH₃ at C-1, J = 7.0), 4.06 (1H, Hβ, d, J = 13.3), 7.52 (1H, s, H₂ₚ), 7.16-8.33 (11H, m, H₁₋₉); 13C NMR (δ ppm): 13.8 CH₂CH₃ at C-1, 29.0 C-5, 43.0 C-6, 59.8 CH₂CH₃ at C-1, 59.9 C-1, 123.0 C-3, 169.1 C=O at C-1, 194.1 C-2, 114.9-129.6 -C₆ arom., C-4 carbon may be merged with -C₆ arom™, 132.7, 1333.6, 134.2, 137.7, 160.0 ipso-C’s.

**Ethyl 6-(4-methoxyphenyl)-4-(naphthalen-2-yl)-2-oxocyclohex-3-ene-carboxylate, compound 12**

IR (KBr) ν (cm⁻¹): 3056, 2987, 2932, 2838, 1738, 1657, 1606, 1252, 888, 831, 815, 749; 1H NMR (δ ppm), (J Hz): 0.96 (3H, t, CH₂CH₃ at C-1, J = 7.0), 3.16-3.29 (2H, H₂α, m), 3.59-3.67 (1H, Hβ, m), 3.73 (3H, s, OCH₃ at phenyl ring), 3.92 (2H, q, CH₂CH₃ at C-1, J = 7.0), 4.10 (1H, Hβ, d, J = 14.3), 6.71 (1H, s, H₇), 6.89-8.32 (11H, m, H₁₋₉); 13C NMR (δ ppm): 14.2 CH₂CH₃ at C-1, 35.7 C-5, 43.5 C-6, 55.4 OCH₃ at phenyl ring, 59.5 CH₂CH₃ at C-1, 60.2 C-1, 123.9 C-3, 169.7 C=O at C-1, 194.7 C-2, 129.3 C-2, 133.1 C=O, 134.0, 134.7, 159.1 ipso-C’s.

**Ethyl 6-(4-chlorophenyl)-4-(naphthalen-2-yl)-2-oxocyclohex-3-ene-carboxylate, compound 13**

IR (KBr) ν (cm⁻¹): 3056, 3022, 2978, 2928, 1738, 1658, 1257, 1147, 890, 850, 818, 749;
1H NMR (δ ppm), (J Hz): 0.95 (3H, t, CH₂CH₃ at C-1, J = 7.0), 3.19-3.29 (2H, H₂α, m), 3.68-3.75 (1H, Hα, m), 3.93 (2H, q, CH₂CH₃ at C-1, J = 7.1), 4.18 (1H, Hβ, d, J = 13.4), 6.73 (1H, s, H₂ₚ), 7.40-8.32 (11H, m, H₁₋₉); 13C NMR (δ ppm): 13.8 CH₂CH₃ at C-1, 34.8 C-5, 43.1 C-6, 58.5 CH₂CH₃ at C-1, 60.0 C-1, 123.0 C-3, 169.1 C=O at C-1, 193.9 C-2, 133.3-129.5 -C₆ arom., C-4 carbon may be merged with -C₆ arom™, 132.7, 133.6, 134.2, 134.9, 140.5 ipso-C’s.

**Ethyl 6-(4-bromophenyl)-4-(naphthalen-2-yl)-2-oxocyclohex-3-ene-carboxylate, compound 14**

IR (KBr) ν (cm⁻¹): 3058, 3027, 2977, 2929, 2907, 2863, 1732, 1657, 1598, 1170, 1145, 892, 817, 748, 711; 1H NMR (δ ppm), (J Hz): 0.96 (3H, t, CH₂CH₃ at C-1, J = 7.0), 3.19-3.21 (2H, H₂α, m), 3.67-3.74 (1H, Hα, m), 3.94 (2H, q, CH₂CH₃ at C-1, J = 7.0), 4.18 (1H, Hβ, d, J = 13.4), 6.73 (1H, s, H₂ₚ), 7.42-8.32 (11H, m, H₁₋₉); 13C NMR (δ ppm): 13.8 CH₂CH₃ at C-1, 34.8 C-5, 43.2 C-6, 58.5 CH₂CH₃ at C-1, 60.0 C-1, 123.1 C-3, 169.1 C=O at C-1, 194.0 C-2, 120.1-129.9 -C₆ arom., C-4 carbon may be merged with -C₆ arom™, 131.3, 132.7, 133.6, 134.2, 141.0 ipso-C’s.
Synthesis, Spectral Characterization, In-vitro Antibacterial and Antifungal

Ethyl 6-(3-chlorophenyl)-4-(naphthalen-2-yl)-2-oxocyclohex-3-enecarboxylate, compound 16

IR (KBr) ν (cm⁻¹): 3058, 2977, 2927, 2869, 1658, 1733, 1597, 1170, 1147, 888, 851, 815, 786; ¹H NMR (δ ppm), (J Hz): 0.94 (3H, t, CH₂CH₃ at C-1, J = 7.1), 3.19-3.28 (2H, H₂ at C-1, J = 7.1), 4.16 (1H, H₁, d, J = 13.7), 6.74 (1H, s, H₂ at phenyl ring), 7.25-8.80 (15H, m, H arom).

General method for the synthesis of (2E)-ethyl-2-(2-(2,4-dinitrophenylhydrazono)-4-(naphthalen-2-yl)-6-phenylcyclohex-3-enecarboxylates, compounds 17-24

A solution of ethyl 4-(naphthalen-2-yl)-2-oxo-6-aryl-cyclohex-3-enecarboxylates, compounds 17-24 was treated with 2,4-dinitrophenylhydrazine (0.001 mol) and 2-4 drops of sulfuric acid and refluxed for 2-3 h. The reaction mixture was cooled and then poured over crushed ice. The crude products were recrystallized twice using ethanol as solvent to afford the product.

(2E)-ethyl-2-(2-(2,4-dinitrophenylhydrazono)-4-(naphthalen-2-yl)-6-phenylcyclohex-3-enecarboxylate, compound 17

IR (KBr) ν (cm⁻¹): 3323, 3099, 3060, 2989, 2924, 2847, 1737, 1656, 1512, 1330, 818, 763, 704, 623; ¹H NMR (δ ppm), (J Hz): 0.92 (3H, t, CH₂CH₃ at C-1, J = 7.0), 3.20-3.21 (2H, H₂ at C-1, J = 7.0), 3.66-3.72 (1H, H₁, m), 3.91 (2H, q, CH₂CH₃ at C-1, J = 7.0), 4.16 (1H, H₁, d, J = 13.4), 6.73 (1H, s, H₂ at phenyl ring), 7.25-8.80 (15H, m, H arom). In the D₂O exchanged ¹H NMR spectrum, a broad singlet at 9.97 ppm due to labile NH proton disappeared; ¹³C NMR (δ ppm): 13.8 CH₂CH₃ at C-1, 35.1 C-5, 43.1 C-6, 59.0 CH₂CH₃ at C-1, 115.2 C-3, 169.5 C=O at C-1, 158.8 C-2, 123.1-128.9 -C arom. C-4 carbon may be merged with -C arom 129.5, 132.7, 133.6, 134.3, 141.5, 149.5 ipso-C's.
(2E)-ethyl-2-(2,4-dinitrophenylhydrazono)-6-(4-chlorophenyl)-4-(naphthalen-2-yl)-cyclohex-3-enecarboxylate, Compound 21

IR (KBr) ν (cm⁻¹): 3323, 3088, 2972, 2847, 1736, 1645, 1514, 1326, 823, 744, 629; ¹H NMR (δ ppm), (J Hz): 0.92 (3H, t, CH₃CH₂ at C-1, J = 7.1), 3.15-3.20 (2H, H at phenyl ring), 3.93 (2H, q, CH₂CH₃ at C-1, J = 7.1), 4.17 (1H, H, d, J = 14.4), 6.73 (1H, s, H), 7.42-8.80 (14H, m, H arom.), 9.97 (1H, bs, NH); In the D₂O exchanged ¹H NMR spectrum, a broad singlet at 9.97 ppm due to labile NH proton disappeared; ¹³C NMR (δ ppm): 13.6 CH₃CH₂ at C-1, 35.0 C-5, 43.3 C-6, 60.3 CH₂CH₃ at C-1, 59.2 C-2, 115.7 C-3, 169.8 C=O at C-1, 158.3 C-2, 129.9 C-4, 129.4, 132.3, 133.6, 134.2, 149.1 ipso-C’s.

(2E)-ethyl-2-(2,4-dinitrophenylhydrazono)-6-(3-chlorophenyl)-4-(naphthalen-2-yl)-cyclohex-3-enecarboxylate, Compound 22

IR (KBr) ν (cm⁻¹): 3324, 3097, 2978, 2923, 2847, 1735, 1643, 1514, 1330, 826, 744, 705, 629; ¹H NMR (δ ppm), (J Hz): 0.95 (3H, t, CH₃CH₂ at C-1, J = 7.0), 3.15-3.20 (2H, H, m), 3.57-3.73 (1H, H, m), 3.93 (2H, q, CH₂CH₃ at C-1, J = 7.1), 4.17 (1H, H, d, J = 14.4), 6.73 (1H, s, H, 7.42-8.80 (14H, m, H arom.), 9.97 (1H, bs, NH); In the D₂O exchanged ¹H NMR spectrum, a broad singlet at 9.97 ppm due to labile NH proton disappeared; ¹³C NMR (δ ppm): 13.7 CH₂CH₃ at C-1, 34.7 C-5, 43.3 C-6, 60.2 CH₂CH₃ at C-1, 57.8 C-2, 115.4 C-3, 169.3 C=O at C-1, 158.3 C-2, 129.9-129.1 C arom., 131.3, 132.7, 133.1, 133.6, 134.2, 141.0, 149.1 ipso-C’s.
carbon may be merged with \( -C_{\text{arom}} \) 129.2, 131.4, 132.6, 133.2, 133.7, 134.2, 140.2, 149.3 ipso-C’s.

**Microbiology**

**Materials**

All the clinically isolated bacterial strains namely *Salmonella typhi*, *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, \( \beta \)-Hemolytic streptococcus and *Micrococcus luteus* and also fungal strains namely *Aspergillus flavus*, *Aspergillus Niger*, *Mucor*, *Rhizopus* and *Microsporum gypseum* are obtained from Faculty of Medicine, Annamalai University, Annamalai Nagar, 608 002, Tamil Nadu, India.

**In-vitro antibacterial and antifungal activity**

The minimum inhibitory concentration (MIC) of \( \mu g/mL \) values is carried out by two-fold serial dilution method [22]. The respective test compounds 17-24 are dissolved in dimethyl sulfoxide (DMSO) to obtain 1 \( mg \cdot mL^{-1} \) stock solution. Seeded broth (broth containing microbial spores) is prepared in NB from 24 h old bacterial cultures on nutrient agar (Hi-media, Mumbai) at 37 ± 1 °C while fungal spores from 1 to 7 days old Sabouraud agar (Hi-media, Mumbai) slant cultures were suspended in SDB. The colony forming units (cfu) of the seeded broth are determined by plating technique and adjusted in the range of \( 10^{4}-10^{5} \) cfu/mL. The final inoculums size was \( 10^{5} \) cfu/mL for antibacterial assay and \( 1.1-1.5 \times 10^{2} \) cfu/mL for antifungal assay. Testing is performed at pH of 7.4 ± 0.2 for bacteria (NB) and at a pH of 5.6 for fungi (SDB). Exactly 0.4 mL of the solution of test compound was added to 1.6 mL of seeded broth to form the first dilution. One mL of this was diluted with a further 1 mL of seeded broth to give the second dilution and so on till six of such dilutions are obtained. A set of assay tubes containing only seeded broth was kept as control. The reaction mechanism (Figure 3) involves the formation of Michael addition product by ethyl acetoacetate with (E)-1-(naphthalen-2-
Figure 2. Synthesis of ethyl 4-(naphthalen-2-yl)-2-oxo-6-phenylcyclohex-3-enecarboxylates and (2E)-ethyl 2- (2-(2,4-dinitrophenyl) hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-enecarboxylates.
Table 1. Physical and analytical data of ethyl 4-(naphthalene-2-yl)-2-oxo-6-aryl cyclohex-3-ene-carboxylates 9-16 and (2E)-ethyl-2-(2,2,4-dinitrophenyl)hydrazono)-4-(naphthalene-2-yl)-6-arylcyclohex-3-ene-carboxylates (compounds 9-24).

| Entry | X      | Y      | Reaction time (h) | Yield (%) | m.p. (°C) | C Found (Calculated) | H Found (Calculated) | N Found (Calculated) | m/z (M+1)+ Molecular formula |
|-------|--------|--------|-------------------|-----------|-----------|----------------------|----------------------|----------------------|-----------------------------|
| 9     | H      | H      | 2                 | 80        | 146       | 81.01 (81.06)        | 5.92 (5.99)          | -                    | 371 \[\text{C}_{13}\text{H}_{20}\text{O}_{4}\] |
| 10    | \text{CH}_{3} | H      | 3                 | 78        | 110       | 81.17 (81.22)        | 6.25 (6.29)          | -                    | 385 \[\text{C}_{14}\text{H}_{22}\text{O}_{4}\] |
| 11    | F      | H      | 1                 | 82        | 126       | 77.24 (77.30)        | 5.40 (5.45)          | -                    | 389 \[\text{C}_{14}\text{H}_{18}\text{F}_{2}\text{O}_{4}\] |
| 12    | \text{OCH}_{3} | H      | 3                 | 80        | 122       | 77.91 (77.98)        | 6.00 (6.04)          | -                    | 401 \[\text{C}_{12}\text{H}_{16}\text{O}_{5}\] |
| 13    | Cl     | H      | 1                 | 75        | 114       | 74.12 (74.16)        | 5.20 (5.23)          | -                    | 405 \[\text{C}_{12}\text{H}_{16}\text{Cl}_{2}\text{O}_{4}\] |
| 14    | Br     | H      | 1                 | 78        | 126       | 66.76 (66.82)        | 4.67 (4.71)          | -                    | 449 \[\text{C}_{12}\text{H}_{18}\text{Br}_{2}\text{O}_{4}\] |
| 15    | \text{NO}_{2} | H      | 2                 | 65        | 132       | 72.22 (72.28)        | 5.07 (5.10)          | 3.33 (3.37)          | 416 \[\text{C}_{12}\text{H}_{18}\text{NO}_{4}\] |
| 16    | H      | Cl     | 2                 | 78        | 98        | 74.10 (74.16)        | 5.15 (5.23)          | -                    | 405 \[\text{C}_{12}\text{H}_{16}\text{Cl}_{2}\text{O}_{4}\] |
| 17    | H      | H      | 2                 | 82        | 125       | 67.57 (67.63)        | 4.72 (4.76)          | 10.12 (10.18)       | 551 \[\text{C}_{12}\text{H}_{18}\text{N}_{2}\text{O}_{4}\] |
| 18    | \text{CH}_{3} | H      | 2                 | 85        | 132       | 68.03 (68.07)        | 4.94 (4.99)          | 9.86 (9.92)         | 565 \[\text{C}_{12}\text{H}_{18}\text{N}_{2}\text{O}_{4}\] |
| 19    | F      | H      | 3                 | 75        | 117       | 65.42 (65.49)        | 4.37 (4.43)          | 9.78 (9.85)         | 569 \[\text{C}_{12}\text{H}_{18}\text{F}_{2}\text{O}_{4}\] |
| 20    | \text{OCH}_{3} | H      | 2                 | 80        | 110       | 66.16 (66.20)        | 4.79 (4.86)          | 9.59 (9.65)         | 581 \[\text{C}_{12}\text{H}_{18}\text{O}_{5}\] |
| 21    | Cl     | H      | 3                 | 72        | 128       | 63.59 (63.65)        | 4.29 (4.31)          | 9.52 (9.58)         | 586 \[\text{C}_{12}\text{H}_{16}\text{Cl}_{2}\text{O}_{4}\] |
| 22    | Br     | H      | 3                 | 78        | 176       | 59.08 (59.15)        | 3.94 (4.00)          | 8.88 (8.90)         | 629 \[\text{C}_{12}\text{H}_{18}\text{Br}_{2}\text{O}_{4}\] |
| 23    | \text{NO}_{2} | H      | 3                 | 70        | 164       | 62.47 (62.52)        | 4.19 (4.23)          | 11.72 (11.76)       | 596 \[\text{C}_{12}\text{H}_{18}\text{N}_{2}\text{O}_{4}\] |
| 24    | H      | Cl     | 3                 | 78        | 121       | 63.60 (63.65)        | 4.26 (4.31)          | 9.50 (9.58)         | 586 \[\text{C}_{12}\text{H}_{16}\text{Cl}_{2}\text{O}_{4}\] |

- yl)-3-arylprop-2-ene-1-ones 1-8 in the presence of base, sodium ethoxide. Later, the addition product undergoes intramolecular aldol reaction in the presence of sodium ethoxide base, to give ethyl 4-(naphthalene-2-yl)-2-oxo-6-arylcyclohex-3-ene-carboxylates 9-16. Ethyl 4-(naphthalene-2-yl)-2-oxo-6-arylcyclohex-3-ene-carboxylates 9-16 contain β-dicarbonyl system on reaction with 2,4-dinitrophenylhydrazine in the presence of 2-4 drops of sulfuric acid in refluxing ethanol yields (2E)-ethyl-2-(2,2,4-dinitrophenyl)hydrazono)-4-(naphthalene-2-yl)-6-arylcyclohex-3-ene-carboxylates 17-24. This reaction can be described as a condensation reaction, with two molecules join together with loss of water. It is also called addition-elimination reaction: nucleophilic addition of the α-NH group to the C=O carbonyl group, followed by the removal of a water molecule. In the present reaction, 2, 4-dinitrophenylhydrazine does not react with other carbonyl-containing functional groups such as ester. For ester, there is resonance associated stability as a lone pair of electrons interacts with the p-orbital of the carbonyl carbon resulting in increased delocalization in the molecule. This stability would be lost by addition of a reagent to the carbonyl group. Hence, these compounds are more resistant to addition.

Ethyl 4-(naphthalene-2-yl)-2-oxo-6-phenyl cyclohex-3-ene-carboxylate 9 is chosen as the representative compound to discuss the spectral data of Ethyl 4-(naphthalene-2-yl)-2-oxo-6-arylcyclohex-3-ene-carboxylates 9-16. FT-IR spectrum of Ethyl 4-(naphthalene-2-yl)-2-oxo-6-phenylcyclohex-3-ene-carboxylate 9 shows two strong characteristic absorptions at 1738 and 1659 cm⁻¹ due to ester ketone and carbonyl functional groups respectively. The band at 1606 cm⁻¹ is due to the presence of C=C stretching frequency. The absorption frequency at 3057 cm⁻¹ is assigned to aromatic C-H stretching vibration and the absorption frequencies at 2987 and 2929 cm⁻¹ is assigned to aliphatic C-H stretching vibration. The observed ester carbonyl, ketone and C=C stretching vibrational bands, are supporting evidence for the formation of synthesized compound 9. In the ¹H NMR spectrum of 9, a triplet was observed at 0.92 ppm (J = 7.1 Hz) corresponding to three protons and
Figure 3. Mechanistic pathway for the formation of ethyl 4-(naphthalen-2-yl)-2-oxo-6-phenylcyclohex-3-enecarboxylates and (2E)-ethyl 2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-enecarboxylates.
this signal is due to the ester methyl protons at C-1. A quartet observed at 3.91 ppm \((J = 7.0 \text{ Hz})\) corresponding to two protons and this signal is due to the ester methylene protons at C-1. Two multiplets are obtained in the range of 3.22-3.28 and 3.65-3.73 and they are due to H-5 and H-6 protons. The doublet at 4.17 ppm \((J = 13.4 \text{ Hz})\) has been assigned to H-1 proton. The singlet observed in downfield region at 6.73 ppm is due to H-3 proton. The aromatic protons appeared as a multiplet in the range of 7.24-8.33 ppm. Two \(^{13}\)C resonances at 194.2 and 169.2 ppm are assigned to C-2 carbonyl carbon and ester carbonyl carbon respectively. The \(^{13}\)C resonances at 35.1 and 43.8 ppm are due to the C-5 and C-6 carbons respectively. The \(^{13}\)C resonance observed at 58.7 and 13.7 ppm are assigned to ester methylene and methyl carbons at C-1 respectively. The signal observed at 59.9 ppm is assigned to C-1 carbon, whereas the signal at 123.1 ppm is assigned to C-3 carbon. The aromatic carbons are observed in the range of 123.4-128.8 ppm. C-4 carbon may be merged with the aromatic carbons. The remaining \(^{13}\)C signals at 132.7, 133.6, 134.3 and 141.5 ppm are due to ipso carbons.

In order to discuss the spectral data of (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arlycyclohex-3-ene-carboxylates 17-24, (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalene-2-yl)-6-phenylcyclohex-3-ene-carboxylates 17 is chosen as the representative compound.

FT-IR spectrum of (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-phenylcyclohex-3-ene-carboxylate 17 shows characteristic absorption frequency at 3323 cm\(^{-1}\) which suggests the presence of -NH functional group. The absorption frequency at 1656 cm\(^{-1}\) is assigned to C=N stretching vibration. The band at 1512 cm\(^{-1}\) is due to the presence of C=C stretching frequency. Nitro functional groups show characteristic stretching frequency around 1330 cm\(^{-1}\). Besides these, aromatic CH stretching frequencies are observed at 3099 and 3060 cm\(^{-1}\) and the aliphatic CH stretching frequencies are observed at 2989, 2924 and 2847 cm\(^{-1}\). The observed -NH, C=N, C=C and NO\(_2\) stretching vibrational bands are supporting evidence for the formation of synthesized compound 17. In the \(^1\)H NMR spectrum of 17, a triplet was observed at 0.92 ppm \((J = 7.0 \text{ Hz})\) corresponding to three protons and this signal is due to ester methyl protons at C-1. A quartet observed at 3.91 ppm \((J = 7.0 \text{ Hz})\) corresponding to two protons and this signal is due to ester methylene protons at C-1. Two multiplets are obtained in the range of 3.20-3.21 and 3.66-3.72 and they are due to H-5 and H-6 protons. The doublet at 4.16 ppm \((J = 13.4 \text{ Hz})\) has been assigned to H-1 proton. The singlet observed in downfield region at 6.73 ppm is due to H-3 proton. The aromatic protons appeared as a multiplet in the range of 7.25-8.80 ppm. The aromatic protons due to dinitrophenyl part are observed in the range of 8.12-8.80 ppm. H-3 proton of 2,4-dinitrophenyl part gives signal as a doublet at 8.80 ppm \((J = 2.5 \text{ Hz})\). H-5 proton of 2,4-dinitrophenyl part gives signal as a multiplet around 8.32-8.23 ppm. H-6 proton of 2,4-dinitrophenyl part gives signal as a doublet at 8.12 ppm \((J = 7.3 \text{ Hz})\). The labile NH proton (exchangeable with D\(_2\)O) appears as a broad singlet at 9.97 ppm. In the HOMOCOSY spectrum of 17, the signal at 0.92 ppm shows cross peak with the signal at 3.91 ppm and vice versa. From the above cross peaks, it is confirmed that the triplet observed at 0.92 ppm corresponds to ester methyl protons at C-1, whereas the quartet at 3.91 ppm corresponds to ester methylene protons at C-1. The signal at 4.16 ppm gives cross peak with multiplet at 3.66-3.72. Similarly, the multiplet at 3.66-3.72 gives cross peaks with the signal at 4.16 ppm as well as the signal at 3.20-3.21 ppm. Furthermore, the signal at 6.73 ppm gives correlations with the signal at 3.20-3.21 ppm and vice versa. From the above correlations, it reveals that the singlet at 6.73 ppm corresponds to H-3 proton and the multiplet at 3.66-3.72 ppm corresponds to H-6 proton respectively. The doublet at 4.16 ppm is conveniently assigned to H-1 proton and the multiplet at 3.20-3.21 ppm is unambiguously assigned to H-5 proton.

In the \(^{13}\)C NMR spectrum of 17, five resonances in the aliphatic region at 13.8, 35.1, 43.8, 58.7 and 59.9 ppm are observed. They are all due to CH\(_2\)CH\(_3\) at C-1, C-5, C-6, C-1 and CH\(_2\)CH\(_3\) at C-1 respectively. C-3 carbon resonates at 115.5 ppm. The remaining \(^{13}\)C resonances in quaternary carbon signals at 169.2 and 158.7 ppm are due to C=O at C-1 and C-2 carbon respectively.
The aromatic carbons are observed in the range of 123.1-128.8 ppm. The carbon signals due to aromatic carbons of 2,4-dinitrophenyl part are merged with the aromatic carbons of naphthyl and phenyl rings at the position of 4 and 6 in cyclohexene ring. C-4 carbon may be merged with aromatic carbon signals. The $^{13}C$ resonances at 129.5, 132.7, 133.6, 134.3, 141.5 and 149.5 ppm are due to ipso carbons. In the HSQC spectrum of 17, one bond correlation (13.8/0.92 ppm) is observed between CH$_2$CH$_3$ at C-1 and CH$_2$CH$_2$ at C-1. The $^{13}C$ resonance at 59.9 ppm has correlations with ester methylene protons, CH$_2$CH$_3$ at C-1. Another one-bond correlation (35.1/3.20-3.21 ppm) is observed between C-5 and H-5. The $^{13}C$ resonance at 43.8 ppm has a one-bond correlation with a multiplet around 3.66-3.72 ppm. Hence, the signal at 43.8 ppm corresponds to C-6 carbon whereas the multiplet at 3.66-3.72 ppm is assigned to H-6 proton. The other aliphatic carbon which resonances at 58.7 ppm, shows a one-bond correlation with a doublet at 4.16 ppm. From this correlation, it is revealed that the doublet at 4.16 ppm corresponds to H-1 proton of the cyclohexenone moiety and the $^{13}C$ signal at 58.7 assigned to C-1 carbon. The $^{13}C$ resonance at 115.5 ppm has correlations with singlet at 6.73 ppm. So the signal at 6.73 ppm is conveniently assigned to H-3 proton and the carbon signal at 115.5 ppm is assigned to C-3. In the HSQC, the $^{13}C$ resonances at 169.2 and 158.7 ppm has no correlations with protons and hence it is due to quaternary carbons, ester C=O at C-1 and C=N respectively. The C-4 carbon may be merged with the aromatic carbons. Among the quaternary carbons, the $^{13}C$ resonances at 129.5, 132.7, 133.6, 134.3, 141.5 and 149.5 are due to ipso carbons.

### Antibacterial activity

Novel (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-enecarboxylates 17-24 are tested for their antibacterial activity in-vitro against *S. typhi*, *K.pneumoniae*, *E.coli*, *Paeruginosa*, *S.aureus*, *β-H.streptococcus* and *M.luteus*. Ciprofloxacin is used as standard bactericidal drug. Minimum inhibitory concentration (MIC) in μg/mL values is reproduced in Table 2. A close survey of the MIC values indicates that all the compounds 17-24 exhibited a varied range (6.25-200 μg/mL) of antibacterial activity against all the tested bacterial strains except compounds 18 and 20 against *E.coli* and *K.pneumoniae* respectively which do not have activity even at a maximum concentration of 200 μg/mL. Compounds 18 and 20, which have electron donating methyl/methoxy substituent at the para position of phenyl rings attached to C-6 of cyclohexenone moiety, showed moderate activity against Gram-negative bacteria and showed good activity against Gram-positive bacteria at a MIC value in the range of 6.25-12.5 μg/mL against *S.aureus*, *β.H.streptococcus* and *M.luteus*. Compound 17 which has no substitution at the phenyl ring attached to C-6 of cyclohexenone moiety, exerted excellent activity against Gram-negative bacteria and showed good activity against Gram-positive bacteria at a MIC value of 6.25-12.5 μg/mL against *S.aureus*, *β.H.streptococcus* and *M.luteus*. Compound 19 shows excellent antibacterial activity against *S. typhi*, *K.pneumoniae*, *Paeruginosa* and *β.H.streptococcus* at a MIC value of 6.25 μg/mL which is a four-fold increase in activity with that of Ciprofloxacin. Similarly, compound 21 which has chloro substitution at the *para* position of phenyl rings attached to the C-6 of cyclohexenone moiety, exerted excellent activity against *E.coli* and *M. luteus* at a MIC value of 6.25 μg/mL and exerted a MIC value of 12.5 μg/mL against *S. typhi*, *Paeruginosa* and *S. aureus* respectively. In addition, compound 24, a *meta* chloro substituted compound exhibited good antibacterial activity against *K. pneumoniae* and *S. aureus* at a MIC value of 12.5 μg/mL whereas it showed activity at a MIC of 6.25 μg/mL against *β.H.streptococcus*. Bulky bromo substitution at the *para* position of phenyl rings attached to C-6 of cyclohexenone moiety in compound 22 is active against *P. aeruginosa*. Moreover, compound 23 which has nitro substitution at the *para* position of phenyl rings attached to C-6 of cyclohexenone moiety exerted excellent activity against *P. aeruginosa* and *S. aureus* at a MIC value of 6.25 μg/mL and it showed good activity against *K. pneumonia* at a MIC value of 12.5 μg/mL. All the electron withdrawing substituent namely fluoro, chloro, bromo or nitro compounds such as 19, 21-24 exerted strong antibacterial activity against all the tested strains when compared to standard drug Ciprofloxacin whereas electron...
Table 2. *In-vitro* antibacterial activity (MIC) values for (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-ene carboxylates (compounds 17-24).

| Compounds | Minimum Inhibitory Concentration (MIC) in μg/mL |
|-----------|-----------------------------------------------|
|           | S. typhii | K. pneumoniae | E. coli | P. aeruginosa | S. aureus | β-H. streptococcus | M.luteus |
| 17        | 100       | 100           | 200     | 100          | 50        | 50                | 6.25    |
| 18        | 200       | 100           | 200     | 100          | 12.5      | 12.5              | 12.5    |
| 19        | 6.25      | 6.25          | 25      | 6.25         | 12.5      | 6.25              | 25      |
| 20        | 200       | -             | 200     | 200          | 12.5      | 12.5              | 25      |
| 21        | 12.5      | 25            | 6.25    | 12.5         | 12.5      | 25                | 6.25    |
| 22        | 25        | 25            | 100     | 6.25         | 100       | 25                | 50      |
| 23        | 25        | 12.5          | 50      | 6.25         | 6.25      | 25                | 12.5    |
| 24        | 25        | 12.5          | 25      | 25           | 12.5      | 6.25              | 50      |
| Ciprofloxacin | 25        | 25            | 50      | 25           | 25        | 50                | 25      |

*a* - No inhibition even at higher concentration i.e., at 200 μg/mL.

**Antifungal activity**

The *in-vitro* antifungal activity of (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-ene carboxylates 17-24 was studied against the fungal strains viz., *A. flavus*, *A. Niger*, *Mucor*, *Rhizopus* and *Microsporum gypseum*. Fluconazole was used as a standard drug. Minimum inhibitory concentration (MIC) in μg/mL values is reproduced in Table 3. A close survey of the MIC values indicates that all the compounds 17-24 exhibited a varied range (6.25-200 μg/mL) of antifungal activity against all the tested fungal strains except compounds 17, 21 and 23 which do not have antifungal activity against *M. gypseum*, *Rhizopus* and *A. flavus* respectively even at a high concentration of 200 μg/mL. Compound 17, having no substitution at the phenyl rings attached to C-6 carbon of cyclohexenone moiety exerted moderate activity against all the tested fungal strains, whereas methyl substituted compound 18 exerted good antifungal activities against *Mucor* and *Rhizopus* at a MIC value of 6.25 and 12.5 μg/mL respectively. Similar results are noticed for electron donating methyl or methoxy substituents attached to C-6 of cyclohexenone moiety exerted good antifungal activity against all the tested fungal strains. Although the naphthyl hydrazone derivatives 17-24 were more potent and exerted good antifungal activity when compared to the standard drug Fluconazole. Compounds with electron withdrawing fluoro, chloro, bromo or nitro substituent at the phenyl rings or compounds that having electron donating methyl or methoxy substituents exerted moderate activity against all the tested fungal strains.

**Conclusion**

In crisp, an array of novel of (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-ene carboxylates 17-24 are synthesized and characterized by their physical and analytical data. This reaction may have wide applicability in building a variety of compounds.
of heterocycles by choosing 4-(naphthalen-2-yl)-2-oxo-6-arylcyclohex-3-enecarboxylates as synthon, which has three versatile functional groups i.e., ketone, olefin and ester for the synthesis of structurally diverse organic compounds. The microbiological screening studies carried out to evaluate the antibacterial and antifungal potencies of the newly synthesized (2E)-ethyl-2-(2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-enecarboxylates 17-24 are clearly known from Tables 2 and 3. A close inspection of the in-vitro antibacterial and antifungal activity profile in differently electron donating (CH$_3$ and OCH$_3$) and electron withdrawing (-F, -Cl, Br and –NO$_2$) functional group substituted phenyl rings of novel (2E)-ethyl-2-(2,4-dinitrophenyl)hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-enecarboxylates 17-24 exerted strong anti-bacterial activity against all the tested bacterial strains. Compound 17 against $M$. luteus, compound 18 against $\beta$.H.streptococcus, compound 19 against S. typhi, K.pneumoniae, P. aeruginosa, $\beta$.H.streptococcus and M. luteus, compound 20 against S. aureus, compound 21 against K. pneumoniae and M. luteus, compound 22 against P. aeruginosa, compound 23 against P. aeruginosa and S. aureus and compound 24 against $\beta$.H.streptococcus exerted excellent antibacterial activity at a MIC value of 6.25 μg/mL. Results of the anti-fungal activity study show that electron withdrawing substitutents like fluoro, chloro, bromo and nitro substituted derivatives exerted excellent antibacterial and antifungal activities, since electron withdrawing substituent increases the lipophilicity due to the strong electron withdrawing capability (23). Moreover, electron withdrawing substitutents namely fluorine substitution was commonly used in contemporary medicinal chemistry to improve metabolic stability, bioavailability and protein ligand interactions (24). These observations may promote a further development of our research in this field. Furthermore, the observed marked antibacterial and antifungal activities of this group of naphthyl hydrazone derivatives may be considered as the key steps for the building of novel chemical entities with comparable pharmacological profiles to that of the standard drugs.

Table 3. In-vitro antifungal activity (MIC) values for (2E)-ethyl-2-(2-(2,4-dinitrophenyl) hydrazono)-4-(naphthalen-2-yl)-6-arylcyclohex-3-enecarboxylates (compounds 17-24).

| Compounds | A. flavus | A. Niger | Mucor | Rhizopus | M. gypseum |
|-----------|-----------|---------|-------|----------|-----------|
| 17        | 200       | 100     | 100   | 200      | -         |
| 18        | 25        | 25      |       | 12.5     | 25        |
| 19        | 6.25      | 6.25    | 25    | 12.5     | 6.25      |
| 20        | 25        | 12.5    | 12.5  | 6.25     | 25        |
| 21        | 12.5      | 6.25    | 25    | -        | 6.25      |
| 22        | 6.25      | 6.25    | 25    | 12.5     | 25        |
| 23        | -         | 50      | 6.25  | 100      | 25        |
| 24        | 6.25      | 6.25    | 12.5  | 100      | 25        |
| Fluconazole | 50       | 50      | 25    | 25       | 25        |

*a* - No inhibition even at higher concentration i.e., at 200 μg/mL.
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References

(1) Sevim Rollas S and Kucukguzel G. Biological activities of hydrazono derivatives. Molecules (2007) 12: 19101939.-
(2) Nayyar A and Jain R. Recent advances in new structural classes of anti-tuberculosis agents. Curr. Med. Chem. (2005) 12: 18731886.-
(3) Scior T and Garcés-Eiselle SJ. Isoniazid is not a lead compound for its pyridyl ring derivatives, isonicotinoyl amides, hydrazides and hydrazones: A critical review. Curr. Med. Chem. (2006) 13: 22052219.-
(4) Janin Y. Antituberculosis drugs: Ten years of research. Bioorg. Med. Chem. (2007) 15: 24792513.-
(5) Abassi Nazari M, Kobarfard F, Tabarse P, Azimi M and J Salamzadeh. Effect of antituberculosis regimen containing ethambutol on serum magnesium level in pulmonary tuberculosis patients. Iranian J. Pharm. Res. (2009) 8: 3339.-
(6) Dimmock JR, Vashistha SC and Stables JP. Anticonvulsant properties of various acetylhydrazones, oxamoylhydrazones and semicarbazones derived from aromatic and unsaturated carbonyl compounds. Eur. J. Med. Chem. (2000) 35: 241248.-
(7) Ergenc N and Gunay NS. Synthesis and antidepressant evaluation of new 3-phenyl-5-sulfonamidoindole derivatives. Eur. J. Med. Chem. (1998) 33: 143148.-
(8) Todeschini AR, Miranda AL, Silva CM, Parrini SC and Barreiro EJ. Synthesis and evaluation of analgesic, antiinflammatory and antipatelet properties of new 2-pyridylarylhydrazone derivatives. Eur. J. Med. Chem. (1998) 33: 189199.-
(9) Lima PC, Lima LM, Silva KC, Leda PH, Miranda ALP, Fraga CAM and Barreiro E. Synthesis and analgesic activity of novel N-acetylhydrazones and isosters, derived from natural saffrole. Eur. J. Med. Chem. (2000) 35: 187203.-
(10) Fraga AGM, Rodrigues CR, Miranda ALP, Barreiro EJ and Fraga CAM. Synthesis and pharmacological evaluation of novel heterocyclic acylhydrazone derivatives, designed as PAF antagonists. Eur. J. Pharm. Sci. (2000) 11: 285290.-
(11) Walcourt A, Lovevsky M, Lovejoy BD, Gordeuk VR and Richardson DR. Novel aryl hydrazone and thiosemicarbazide iron chelators with anti-malarial activity against chloroquine-resistant and -sensitive parasites. Int. J. Biochem. Cell Biol. (2004) 36: 401407.-
(12) Kucukguzel SG, Rollas S, Erdeniz H and Kiraz M. Synthesis, characterization and antimicrobial evaluation of ethyl 2-arylhydrazono-3-oxobutyrates. Eur. J. Med. Chem. (1999) 34: 153160.-
(13) Silva AG, Zapata-Suto G, Kummerle AE, Fraga CAM, Barreiro EJ and Sudo RT. Synthesis and vasodilatory activity of new N-acylhydrazine derivatives, designed as LASSBio-294 analogues. Bioorg. Med. Chem. (2005) 13: 34313437.-
(14) Pandey J, Pal R, Dwiwedi A and Hajela K. Synthesis of some new diaryl and triaryl hydrazide derivatives as possible estrogen receptor modulators. Arzneimittelforschung (2002) 52: 3944.-
(15) Arctander S. Perfume and Flavour Chemicals (Aroma Chemicals). Montclair, NJ (1969).
(16) Gopalakrishnan M, Suresh Kumar P, Thanusu J, Kanagarajan V, Govindaraju R and Ezharlasri MR. Microwave-promoted facile and rapid solvent-free procedure for the efficient synthesis of 3,4-dihydropyrimidin-2(1H)-ones and -thiones using ZrO2/SeO2 as a reusable heterogeneous catalyst. Lett. Org. Chem. (2006) 6: 434488.-
(17) Gopalakrishnan M, Suresh Kumar P, Thanusu J and Kanagarajan V. Design, ‘one-pot’ synthesis, characterization, antibacterial and antifungal activities of novel 6-aryl-1,2,4,5-tetrazinan-3-thiones in dry media. J. Sulfur Chem. (2007) 28: 383392.-
(18) Gopalakrishnan M, Thanusu J, Kanagarajan V, Govindaraju R. Design, synthesis and in-vitro microbiological evaluation of 6,6-dimethyl-7,9-diaryl-1,2,4,8-tetrazaothiopir[4,5]decan-3-thiones-A new series of Tailor-made compounds. J. Enz. Inhib. Med. Chem. (2009) 24: 406412.-
(19) Gopalakrishnan M, Thanusu J and Kanagarajan V. Design, synthesis, spectral analysis and in-vitro microbiological evaluation of biolabile 2-phenyl-3-(4,6-diarylpirimidin-2-yl)thiazolidin-4-one. J. Enz. Inhib. Med. Chem. (2009) 24: 10881094.-
(20) Gopalakrishnan M, Thanusu J and Kanagarajan V. Synthesis and biological evaluation of 5,7-diaryl-4,4-dimethyl-4,5,6,7-tetrahydropyrimidin[3,4-d]-1,2,3-thiadiazoles. Med. Chem. Res. (2007) 16: 392401.-
(21) Guthrie W and Wang XP. The aldol condensation of acetophenone with acetone. Can. J. Chem. (1991) 69: 339.-
(22) Dhar MH, Dhar, MM, Dhawan BN, Mehrotra BN and Ray C. Screening of Indian plants biological activity. Part I. Indian J. Exp. Biol. (1968) 6: 232247.-
(23) Lipinski CA, Lombardo F, Dominy BW and Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv. Drug Deliv. Rev. (1997) 23: 325.-
(24) Purser S, Moore PR, Swallow S and Gouverneur V. Fluorine in medicinal chemistry. Chem. Soc. Rev. (2008) 37: 320330.-

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