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DESIGN, SYNTHESIS AND ANTIOXIDANT ACTIVITY OF *N, N'*-DIACYLHYDRAZINES CONTAINING 2-(2-ISOPROPYL-5-METHYL PHENOXY) MOIETIES, A SOLVENT FREE GREEN SYNTHETIC APPROACH

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ABSTRACT

A simple and highly efficient process for the synthesis of *N, N'* -Diacylhydrazine derivatives containing 2-(2-isopropyl-5-methyl phenoxy) moieties involving stirring of 2-(2-isopropyl-5-methyl phenoxy) *N, N'* -Diacylhydrazine derivatives and different benzoyl chlorides at room temperature under solvent free conditions has been described. The synthesized compounds were characterized by MASS, FT-IR, ^{1}H and 13C NMR and were assessed for the antioxidant activity using DPPH assay.

KEYWORDS

Diacylhydrazines, Green synthesis, Benzoylation and Antioxidant activity.

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INTRODUCTON

In recent years, acyl hydrazine derivatives have become a center of interest for researchers in the development of agrochemicals due to their elevated biological activities[1-5]. In the mid of 1980s a new non-steroidal insect growth regulator, *N'*-tert-butyl-*N, N'*-diacylhydrazines (RH-5849) was reported as ecdysone agonist. Then subsequently, RH-5992, RH-0345 and RH-2485 were developed[6-13]. These were as molting hormone analogues which have been found to mimic the action of 20-hydroxyecdysone to activate the ecdysone receptor, leading to lethal premature molting[14-16]. *N,N'*-diacylhydrazines possess various biological activities such as fungicidal[17], herbicidal[18], anti-

HIV[19] and antitumor[20]. Diacylhydrazine group is found to be present in many natural products, for example, Elaiomycin isolated from submerged culture filtrates of *Streptomyces gelaticus*; displays strong in vitro inhibition of virulent and avirulent forms of the bovin and human strains of *Mycobacterium tuberculosis*[21]. Montamine, isolated from *C. Montana*, exhibits antioxidant activity[22]. Recent studies report synthesis, biological activities and 3D-QSAR of new *N,N'*-diacylhydrazines possess containing 2,4-dichlorophenoxy moieties[23] as well as larvicidal activity of some the noylhydrazide derivatives[24].

Amongst thyme essential oils thymol and its isomer carvacrol contribute to various biological activities. Thymol (2-isopropyl-5-methylphenol) is the chief phenolic monoterpenoid present in thyme essential oil particularly *thymus vulgaris*[25-27]. Thymol and carvacrol have shown anti-inflammatory, immune modulators, antioxidant, antibacterial and antifungal properties. Similarly many derivatives of thymol and Carvacrol are biologically active[28-31]. In continuation of our work to design novel derivatives of thymol using simple experimental procedures, here in we report a simple green procedure for the synthesis of diacylhydrazines from 2- (2-isopropyl-5-methyl phenoxy) acetohydrazide via benzoylation. Recently an absolutely solvent free green methodology for the benzoylation of both aromatic and aliphatic amines (*primary* and *secondary*) that is devoid of using any alkali and other bases is reported[32]. Generally the benzoylation of aromatic primary or secondary amines, phenols is carried out in the presence of alkali using a method known as Schotten-Baumann reaction[32-36]. However, the product is usually contaminated with traces of benzoyl chloride and requires crystallization from suitable solvent. The solvent free green process affords the product of high purity, in very high yields and in a very short time. In view of these facts, the title compounds were synthesized from 2-(2-isopropyl-5-methyl phenoxy) acetohydrazide using solvent free conditions at room temperature using stirring technique and further they were screened for antioxidant activity.

MATERIAL AND METHODS

General

All chemicals and reagents used in the reactions were procured from Sigma-Aldrich and Fisher with purity 98% and used without further purification. The purification of the synthesized compounds was performed by recrystallization with appropriate solvent system. Melting points of all the synthesized compounds were determined in open capillary tube and were found uncorrected. The purity of the compounds was checked using pre coated TLC plates (MERCK, 60F) with hexane: ethyl acetate (5:5) solvent system. The developed chromatographic plates were visualized under UV at 254 nm. The products were characterized using ^{1}H NMR, ^{13}C NMR, FT-IR and LC-MS. The IR spectra were recorded on FTIR-8400 Shimadzu spectrophotometer using KBr disks. ^{1}H, ^{13}CNMR were recorded on BRUKER 400 MHz using $CDCl_3$ solvent with TMS as internal standard. Mass spectra were recorded in Q-TOF Micro mass (ESI-MS).

Synthesis of ethyl-2-(2-isopropyl- 5-methyl phenoxy) acetate (2)

A mixture of thymol (0.02 M) and anhydrous K_2CO_3 (0.03 M) in an excess of dry acetone (75 mL) was stirred at reflux for 4 hrs. Into the stirred suspension, ethyl chloroacetate (0.02 M) in dry acetone (10 mL) was added drop wise during 1 hr. and stirring was continued for 4 hrs. After keeping the reaction mixture overnight, the excess of solvent was removed and the residue was poured onto crushed ice. Further the contents were stirred for half an hour, extracted with diethyl ether, dried with Na_2SO_4 and solvent was removed under vacuum to obtain yellowish oil, bp: 176 °C, yield: 84 %

Synthesis of 2-(2-isopropyl-5-methyl phenoxy) acetohydrazide (3)

A mixture of ethyl-2-(2-isopropyl-5 methyl phenoxy) acetate (0.015 M) in ethanol (15 mL) and excess of 99% hydrazine hydrate (0.023 M) was refluxed for 2 hrs. The resulting clear solution was concentrated under vacuum. The suspension was poured on crushed ice. The solid separated was filtered, washed thoroughly with cold water, dried and purified by recrystallization in ethanol, m.p 79 °C, yield: 72%.

Synthesis of benzoyl derivative of 2- (2-isopropyl-5-methyl phenoxy) acetohydrazide (4a-4e)

In a typical experimental procedure, exactly equimolar quantities of hydrazide (3) and benzoyl chloride are mixed in neat phase in a small beaker and stirred with a glass rod in a hood. The reaction mixture instantaneously became hot with the evolution of HCl gas and became a solid mass or paste that remains as a complex adhering with and unreacted benzoyl chloride or with any hydrochloride formed in situ. Crushed ice was then added to the contents of the beaker and stirred well with a glass rod. The thick reaction mixture gradually became soft, and product began to deposit on the walls of the beaker by the dissolution of any hydrochloride adhered with the product or by the gradual dispersion of traces of benzoyl chloride in the aqueous phase during stirring, and finally the supernatant aqueous layer became clear when the precipitation of the product was complete as a crystalline product. The product was filtered and washed with water and further recrystallized from ethanol to obtain the benzoylated product in high yield. The reaction time usually varied on an average from 3-5 minutes.

***N*'-(2- (2-isopropyl-5-methyl phenoxy) acetyl) benzohydrazide (4a)**

Color white, mp-124-126°C, yield 95 % Molecular formula - $C_{19}H_{22}O_3N_2$, Molecular weight calculated - 326, LC-MS, m/z: $[M+1]^+$ 327. IR (ν, cm^{-1}) 3275 (-NH), 3026, 2954, 1668 (NH-C=O), 1516, 1431, 1255, 1105, 810, 705. ^{1}H NMR (400 MHz,$CDCl_3$): δ = 1.27 (d, J = 7 Hz, 6H), 2.32 (s, 3H), 3.34 (m, 1H), 4.63 (s, 2H), 6.63 (s, 1H), 6.84 (d, J = 7.72 Hz, 1H), 7.15 (d, J = 7.72 Hz, 1H), 7.42 (t, J= 8 Hz, 2H), 7.52 (t, J = 8 Hz, 1H,), 7.83 (t, J = 8 Hz, 2H,), 9.35 (s, 1H), 9.51 (s, 1H). 13C NMR δ_C 21.86, 22.91, 26.78, 67.21, 123, 126, 127, 128, 131, 132, 134, 136, 154, 164, 165.

2-Fluro-*N*′- (2- (2-isopropyl-5-methyl phenoxy) acetyl) benzohydrazide (4b)

Color white, mp-98-100°C, yield 65 % Molecular formula -$C_{19}H_{21}O_3N_2F$, Molecular weight calculated - 344, LC-MS, m/z: $[M+1]^+$ 345. IR (ν, cm^{-1}) 3317 (-NH), 2947, 2954, 1668 (NH-C=O), 1516, 1431, 1255, 1105, 810, 705. ^{1}H NMR (400 MHz,$CDCl_3$): δ= 1.26 (d, J = 7 Hz, 6H), 2.33 (s, 3H), 3.33 (m, 1H), 4.68 (s, 2H), 6.66 (s, 1H), 6.84 (d, J = 7.72 Hz, 1H), 7.16 (dd, J = 4 and 8 Hz, 2H), 7.27 (dd, J= *4* and8 Hz, 1H), 7.52 (m, 1H,), 8.11 (m, 1H,), 9.35 (s, 1H), 9.51 (s, 1H). ^{13}C NMR (400 MHz, $CDCl_3$): δ= 21.86, 22.87, 26.83, 67.18, 112, 116, 118, 123, 125.04, 125.07, 126, 131.96, 134.87, 134.43, 154, 159, 164.

3-Fluro-*N*′-(2- (2-isopropyl-5-methyl phenoxy) acetyl) benzohydrazide (4c)

Color white, mp-110-112°C, yield 85 % Molecular formula - $C_{19}H_{21}O_3N_2F$, Molecular weight calculated - 344, LC-MS, m/z: $[M+1]^+$IR (ν, cm^{-1}) 3265(-NH), 3049, 1668 (NH-C=O), 1512, 1435, 1259, 1166, 1091, 823, 750. ^{1}H NMR (400 MHz,$CDCl_3$): δ= 1.24 (d, J = 7 Hz, 6H), 2.31 (s, 3H), 3.32 (m, 1H,), 4.62 (s, 2H,), 6.62 (s, 1H,), 6.84 (d, J = 7.72 Hz,1H), 7.19 (d, J = 7.72 Hz, 1H,), 7.23 (d, J= 8 Hz, 1H,), 7.36 (m, 1H), 7.54 (d, J = 8 Hz, 1H), 7.62 (d J = 8H, 1H), 9.33 (s, 1H), 10.0 (s, 1H). ^{13}C NMR (400 MHz, CDCl3): δ= 21.24, 22.89, 26.73, 67.20, 112, 114.74, 114.97, 119, 122, 123, 126, 130, 133, 134, 161, 163, 166.

4-Fluro-*N*′-(2- (2-isopropyl-5-methyl phenoxy) acetyl) benzohydrazide (4d)

Color white, mp-122-124°C, yield 85 % Molecular formula - $C_{19}H_{21}O_3N_2F$, Molecular weight calculated - 344, LC-MS, m/z: 345 $[M+1]^+$ IR (ν, cm^{-1}) 3269(-NH), 2954, 1666(NH-C=O), 1512, 1435, 1247, 1166, 1089, 833, 588,536. ^{1}H NMR (400 MHz,$CDCl_3$): δ= 1.26 (d, J = 7 Hz, 6H), 2.32 (s, 3H), 3.32 (m, 1H), 4.62 (s, 2H), 6.62 (s, 1H), 6.84 (d, J = 7.72 Hz,1H), 7.04 (t, J =2 Hz, 2H), 7.14 (d, J=8 Hz,1H), 7.85(m, 2H), 9.27 (s,1H), 9.83 (s,1H). ^{13}CNMR (400 MHz, $CDCl_3$): δ= 21.25, 22.89, 26.75, 67.23, 112.92, 115.63, 115.90, 123.18, 126.41, 127.23, 129.84, 129.95, 134, 136, 154, 163,166.

2, 6 di-Fluro-*N*′-(2-(2-isopropyl-5-methyl phenoxy) acetyl) benzohydrazide (4e)

Color white, mp-148-150°C, yield 78 % Molecular formula - $C_{19}H_{20}O_3N_2F_2$, Molecular weight calculated - 362, LC-MS, m/z: 363 $[M+1]^+$ IR (ν, cm^{-1}) 3176 (-NH), 3041, 1612 (NH-C=O), 1483, 1240, 1006, 798, 667, 578.^{1}H NMR (400

MHz,$CDCl_3$): δ= 1.24 (d, *J* = 7 Hz, 6H), 2.32 (s, 3H), 3.33 (m, 1H), 4.58 (s, 2H), 6.63 (s, 1H), 6.84 (d, *J* = 7.72 Hz, 1H), 6.97 (t, *J* = 8 Hz, 2H), 7.15 (1H, d, *J*= 8 Hz, 1H), 7.42 (m, 1H), 9.36 (s, 2H). ^{13}C NMR (400 MHz, $CDCl_3$): δ= 21.24, 22.90, 26.73, 67.16, 110.80, 112.08, 112.20, 112.99,123,126, 132, 136, 154, 156, 159.13, 159.21, 161, 165.

Antioxidant Activity

The *In vitro* antioxidant properties of the newly synthesized compounds (4a-4e) at different concentrations were examined by a well-documented reported assay like DPPH free radical scavenging assay. The anti-oxidant activities of the compounds are related to their electron or hydrogen radical releasing abilities to DPPH. Butylated Hydroxy Toluene (BHT) was used as a reference compound. The radical scavenging activity was expressed as % inhibition of DPPH. Fig.1 demonstrates the % radical scavenging against the concentration of entity. Lower absorbance of the reaction mixture indicates higher free radical scavenging activity. DPPH radical scavenging activity of all the compounds were found to be good to moderate as compared to Butylated Hydroxy Toluene. Compound 4b exhibited better antioxidant activity than BHT at concentration 0.5 µg/ml, while at other concentrations compound 4e exhibited comparable antioxidant activity with the BHT. It was observed that presence of ortho substitution in the phenyl ring of benzoyl chloride influenced the antioxidant potency of the molecule. In particular, compound 4b and 4e that is 2-fluro and 2,6-difluro derivatives respectively showed the highest anti-oxidant activity with a remarkable EC_{50} values, 7.9 and 5.52 respectively as compared to standard (2.73), while compounds 4a, 4c and 4d demonstrated decrease in % antioxidant activity with higher EC_{50} values. All EC_{50} values for synthesized derivatives are shown in Table No.1.

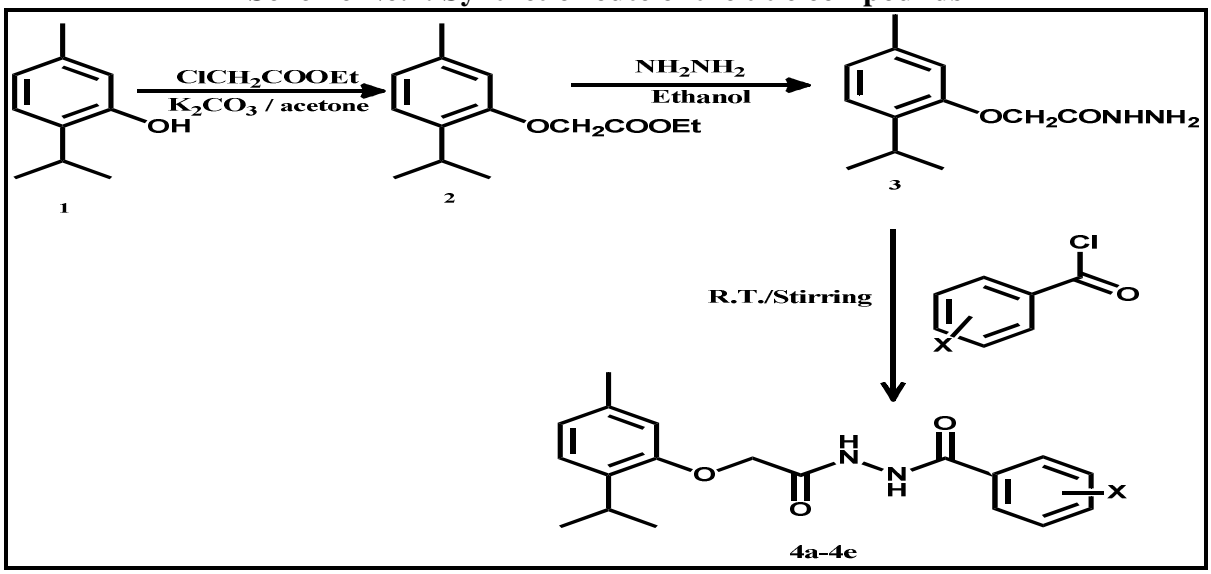
RESULTS AND DISCUSSION

The synthetic part of the work is shown in the scheme No.1. The title compounds (4a-4e) were synthesized in three steps in excellent yields. The overall process afforded the pure product with high yield and short reaction time (3-5 min). Their analytical and spectroscopic data are in agreement with the predicted structures. The synthesis of Ethyl-2-(2-isopropyl-5methyl phenoxy) acetate (2) and 2- (2-isopropyl-5-methyl phenoxy) acetohydrazide (3) was carried out according to the previously reported methods[37]. Finally all the synthesized derivatives were screened for their antioxidant activity using DPPH assay[38].

Table No.1: Anti-Oxidant Activity of synthesized compounds

S.No	Compound	Antioxidant test EC_{50} in µg/ml
1	4a	23.07
2	4b	7.9
3	4c	30.82
4	4d	24.57
5	4e	5.52
6	Standard (BHT)	2.73

Scheme No.1: Synthetic route of the title compounds



[x = a) H, b) 2-fluro, c) 3-fluro, d) 4-fluro, e) 2, 6- difluro]

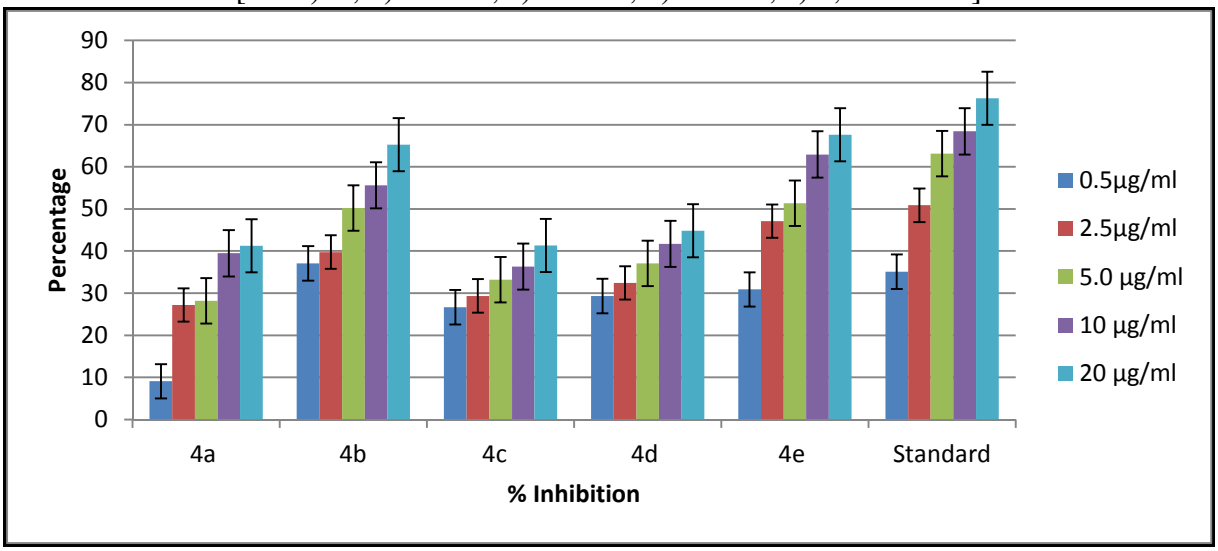


Figure No.1: % radical scavenging at different concentrations

CONCLUSION

In conclusion it can be stated that the present path for the synthesis of diacylhydrazines via benzoylation, without catalyst is simple and highly efficient under solvent free conditions at room temperature using stirring technique. This is mild, rapid and superior method. All the synthesized compounds displayed significant antioxidant activity and play a major role in controlling oxidation.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest

BIBLIOGRAPHY

1. Kadhum A A H, Al-Amiery A A, Musa A Y, Mohamad A B. The antioxidant activity of new coumarin derivatives, *International journal of molecular sciences*, 12(9), 2011, 5747-5761.
2. Wang H, Fu Y F, Fan Z J, Song H B, Wu Q J, Zhang Y J, Bakulev V A. Synthesis, crystal structure and biological activity of N-tert-butyl-N- (4-methyl-1, 2, thiadiazole) -5-yl-N'- (4-methyl-1, 2, 3-thiadiazole) -5-formyl-N'-3, 5-dichloropyridin-2-yl-diacylhydrazine, *Chin J Struct Chem,* 30(412416), 2011, 3.
3. Abdel-Aziz H A, Elsaman T, Attia M I, Alanazi A M. The reaction of ethyl 2-oxo-2H-chromene-3-carboxylatewith hydrazine hydrate, *Molecules,* 18(2), 2013, 2084-2095.
4. Ke S, Qian X, Liu F, Wang N, Fan F, Li Z, Yang Q. Diacylhydrazine derivatives as potential chitin biosynthesis inhibitors: Design, synthesis, and structure-activity relationship, *European journal of medicinal chemistry*, 44(7), 2009, 2985-2993.
5. Zhao Q, Shang J, Liu Y, Wang K, Bi F, Huang R, Wang Q. Synthesis and insecticidal activities of novel N-sulfenyl-N′-tert-butyl-N, N′-diacylhydrazines. 1. N-Alkoxysulfenate derivatives, *Journal of agricultural and food chemistry,* 55(23), 2007, 9614-9619.
6. Wing K D. RH 5849, a nonsteroidal ecdysone agonist: effects on a Drosophila cell line, *Science*, 241(4864), 1988, 467.
7. Wing K D, Slawecki R A, Carlson G R. RH 5849, a nonsteroidal ecdysone agonist: effects on larval Lepidoptera, *Science*, 241(4864), 1988, 470.
8. Heller J J, Klein E, Mattioda H, Sagenmüller A. Field evaluation of RH- 5992 on lepidopterouspests in Europe, *In Brighton Crop Protection Conference Pests and Diseases*, 1,1992, 59-65.
9. Dhadialla T S, Jansson R K. Non-steroidal ecdysone agonists: new tools for IPM and insect resistance management, *Pest Management Science,* 55(3), 1999, 357-359.
10. Cowles R S, Villani M G. Susceptibility of Japanese beetle, Oriental beetle, and European chafer (*Coleoptera: Scarabaeidae*) to halofenozide, an insect growth regulator, *J Econ Entomol,* 89(6),1996, 1356-1365.
11. Cowles R S, Alm S R, Villani, M G. Selective toxicity of halofenozide to exotic white grubs (Coleoptera: Scarabaeidae), *Journal of Economic Entomology*, 92(2), 1999 , 427-434.
12. Le D P, Thirugnanam M, Lidert Z, Carlson G R, Ryan J B. RH-2485: a new selective insecticide for caterpillar control, *Brighton Crop Prot Conf Pests Dis,* 2, 1996, 481-486.
13. Carlson G R, Dhadialla T S, Hunter R, Jansson R K, Jany C S, Lidert Z, Slawecki R A. The chemical and biological properties of methoxyfenozide, a new insecticidal ecdysteroid agonist, *Pest management science*, 57(2), 2001, 115-119.
14. Zhao Q, Ou X, Huang Z, Bi F, Huang R, Wang Q. Synthesis and insecticidal activities of novel *N*-sulfenyl-*N′*-tert-butyl-*N, N′*-diacylhydrazines. 3. N-(alkyldithio), N-(aminothio), and N, N-dithio derivatives, *Journal of agricultural and food chemistry*, 56(22), 2008, 10799-10804.
15. Zhao Q Q, Shang J, Huang Z Q, Wang KY, Bi F, Huang R Q, Wang Q M. Synthesis and insecticidal activities of novel *N*-sulfenyl-*N′*-tert-butyl-*N, N'*-diacylhydrazines. 2. *N*-substituted phenoxysulfenate derivatives, *J. Agric. Food Chem*, 56(13), 2008, 5254-5259.
16. Cui Z, Ling Y, Li B, Li Y, Rui C, Cui J, Yang X. Synthesis and bioactivity of *N* Benzoyl-*N*'- [5- (2'-substituted phenyl)-2-furoyl] semicarbazide derivatives, *Molecules*, 15(6), 2010, 4267-4282.
17. Liu X H, Shi Y X, Ma Y, He G R, Dong W L, Zhang, C Y, Li Z M. Synthesis of Some *N,N′*- Diacylhydrazine Derivatives with Radical-Scavenging and Antifungal

Activity, *Chemical biology and drug design,* 73(3), 2009, 320-327.

18. Xiangyang Z, Yongshu L, Jianquan W, Chengxia T. Synthesis and herbicidal activity of some new diacylhydrazine derivatives fluoride-containing pyrazolyl moiety, *Chinese Journal of Organic Chemistry*, 31(8), 2011, 1295-1299.
19. Zhao H, Neamati N, Sunder S, Hong H, Wang S, Milne G W, Burke T R. Hydrazide-containing inhibitors of HIV-1 integrase, *Journal of medicinal chemistry*, 40(6), 1997, 937-941.
20. Li X, Yang X, Cui Z, Li Y, He H, Ling Y. Synthesis and Bioactivity of Novel N, N′ Diacylhydrazine Derivatives Containing Furan (II). *Chinese Journal of Chemistry,* 28(7), 2010, 1233-1239.
21. Kim B Y, Willbold S, Kulik A, Helaly S E, Zinecker H, Wiese J, Fiedler H P. Elaiomycins B and C. Novel alkylhydrazides produced by Streptomyces sp, BK 190, *Journal of Antibiotics*, 64(8), 2011, 595.
22. Shoeb M, MacManus S M, Jaspars M, Trevidu J, Nahar L, Kong-Thoo-Lin P, Sarker S D. Montamine, a unique dimeric indole alkaloid, from the seeds of Centaurea Montana (Asteraceae), and it's *in vitro* cytotoxic activity against the CaCo2 colon cancer cells, *Tetrahedron*, 62(48), 2006, 11172-11177.
23. Sun G X, Sun Z H, Yang M Y, Liu X H, Ma Y, Wei Y Y. Design, synthesis, biological activities and 3D-QSAR of new N, N'-diacylhydrazines containing 2, 4 dichlorophenoxy moieties, *Molecules*, 18(12), 2013, 14876-14891.
24. Song G P, Hu D K, Tian H, Li Y S, Cao Y S, Jin H W, Cui Z N. Synthesis and Larvicidal Activity of Novel Thenoyl hydrazide Derivatives, *Scientific reports*, 6, 2016, 22977.
25. García-Risco M R, Vicente G, Reglero G, Fornari T. Fractionation of thyme (Thymus vulgaris L.) by supercritical fluid extraction and chromatography, *The Journal of Supercritical Fluids*, 55(3), 2011, 949-954.
26. Thompson J D, Chalchat J C, Michet A, Linhart Y B, Ehlers B. Qualitative and quantitative variation in monoterpene co-occurrence and composition in the essential oil of Thymus vulgar is chemo types, *Journal of Chemical Ecology*, 29(4), 2003, 859-880.
27. Tschiggerl C, Bucar F. Influence of saponin plants on the volatile fraction of thyme in herbal teas, *Fitoterapia*, 82(6), 2011, 903-910.
28. Braga PC, Dal Sasso M, Culici M, Bianchi T, Bordoni L, Marabini L. *Anti-Pharmacology*, 77(3), 2006, 130-136-6.
29. Tian H, Lai D M. Analysis on the volatile oil in Origanum vulgare, Zhongyaocai Zhongyaocai, *Journal of Chinese medicinal materials*, 29(9), 2006, 920.
30. Kumar D, Rawat D S. Synthesis and antioxidant activity of thymol and carvacrol based Schiff bases, *Bioorganic and medicinal chemistry letters,* 23(3), 2013, 641-5.
31. Shen AY, Huang M H, Liao L F, Wang T S. Thymol analogues with antioxidant and L-type calcium current inhibitory activity, *Drug development research*, 64(4), 2005, 195-202.
32. Ghosh S, Das J. Benzoylation of amines sans alkali: a green protocol in neat phase, *Organic Chemistry International*, 743186, 2010, 3.
33. Ando W, Tsumaki H. A facile preparation of aliphatic hydroxamic acid from N, N, O-tris (trimethylsilyl) hydroxylamine and acid chloride, *Synthetic communications*, 13(12), 1983, 1053-6.
34. Taylor E C, McLay G W, McKillop A. Thallium in organic synthesis. II. Acylation, aroylation, andtosylation of phenols and carboxylic acids, *Journal of the American Chemical Society*, 90(9), 1968, 2422-3.

35. Illi V O. Phase transfer catalyzed acylation, *Tetrahedron Letters*, 20(26), 1979, 2431-2432.
36. Furniss B S, Hannaford A J, Smith P W G and Tatchell A R. In Vogel's Text book of Practical Organic Chemistry, *Pearson Education,* 5th Edition, 2006, 916.
37. Said A Said. Synthesis of Some New 2- (2-Isopropyl-5-Methyl Phenoxymethyl)-5-Aryl-1, 3, 4- Ox a diazoles, *Raf. Jour. Sci, Chemistry,* 17(4) 2006, 52-58.
38. Rajput J D, Bagul S D, Bendre R S. Design, synthesis, biological screenings and docking simulations of novel carvacrol and thymol derivatives containing acetohydrazone linkage, *Research on Chemical Intermediates,* 43(8), 2017, 4893-4906.

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