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Biological Profile and Synthesis of Phenoxyacetic Acid Derivatives: A Review

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ABSTRACT: Phenoxyacetic acid is a monocarboxylic acid that is the *O*-phenyl derivative of glycolic acid with molecular formula $C_8H_8O_3$ and metabolite of 2-phenoxyethanol. It is mostly used in the manufacture of pharmaceuticals, pesticides, fungicides and dyes. Phenoxyacetic acid moiety is present as central structural part in numerous drug classes such as antibacterial, antifungal, anti-inflammatory, anticonvulsant, antihypertensive and antitubercular**.** The commercially existing phenoxyacetic acid containing drugs are Tiaprofenic acid (NSAIDS Non steroidal anti-inflammatory), Tinnelic acid (antihypertensive), flubroprofen (arthritis treatment), Accelofenac (antiinflammatory) and zyertac (antihistaminic).This paper aims to consider the biological profile and synthesis recorded in current literature for phenoxyacetic acid derivatives. The data is taken from various data base 2009-2023. Literature review recognize that the compounds consist of phenoxyacetic acid moiety having a common fundamental feature of a numerous medicinal agents and its derivatives shows miscellaneous pharmacological activities and very easy to synthesize. This vital functional group division has widespread potential.

KEYWORDS: Phenoxyacetic acid, Antimicrobial activity, Anti-inflammatory activity, Anti-cancer, Anti-oxidant and Herbicidal

I. INTRODUCTION

Phenoxy herbicides are a group of chemicals related to the natural growth hormone (IAA) Indole Acetic Acid. Phenoxyacetic acid, aryloxy-phenoxy propanoic acid, and phenoxy propanoic acid are the molecules that contains the key molecular structure of phenoxyherbicides. It is more useful on carlines and leaves, the general

characteristics of these herbicides take account of high selectivity, broad spectrum, low cost and dose safety. It is secure for livestock; humans and the environment after standard dosages are used [1].The chemical structure of phenoxyacetic acid is given in **figure 1**

Phenoxyacetic acid is high melting point (98-99˚C), white or clear crystalline compound. It appears light tan to brown when impure [2]. Its solubility in water is 12 g/L and highly soluble in organic solvents such as ethanol, diethyl ether and benzene. Phenoxyacetic acid is a weak acid and weak base in nature with a pKa of 3.7 [3]. Phenoxyacetic acid is the most important moiety which is associated with potent fungicidal activitiy. Phenoxy acetic acid deivatives possess an extensive diverse natural activities including antimycobacterial, antiinflammatory and antioxidant activities [4].The literature analysis reveals that phenoxyacetic acid derivatives displays numerous properties like antifungal [5], anticancer [6],antioxidant [7],hypoglycemic activity [8],analgesic and antipyretic [9] and cholysistikinin-Breceptor antagonistic activity [10]. Biological profile of phenoxyacetic acid are described in **Fig. 2**

Marketed formulations containing phenoxyacetic acid moiety Tiaprofenic acid (non-steroidal antiiinflammatory) [11], Tienelic acid (Antihypertensive) [12], Flubriprofen (Arithritis treatment) [13], Zyretac/cortisone [14] (antihistaminic), Accelofenac [15] (anti-inflammatory) and Mecroprop (herbicidal) [16], Lumricoxib [17],Metipranolol [18] and Etacrynic acid [19] are presented. The common names, chemical structures and medicinal importance of these compounds are listed in **Figure 3.**

II. LITERATURE REVIEW

Antibacterial activity

Laddha *et al*., [20] synthesized 2-(3, 5-dimethoxyphenoxy)-*N*-(4-(prrrolidin-1-yl) benzylidene) acetohydrazide and evaluated for the antibacterial activity using Ampicillin (25mm) with standard drug. **2-(3, 5-dimethoxyphenoxy)-*N*-(4-(prrrolidin-1-yl)benzylidene)acetohydrazide (21mm)[Structure 1]** showed good antibacterial activity against the strains *E. coli*.

Starcevic *et al*.,[21] The synthesized compounds were investigated for their antibacterial prospective against gram-positive bacteria. **4- Methoxyphenoxyacetic acid[structure 2],** the zone of inhibition for Salmonella paratyphi was (30 mm/ml) at 100 µl.

Chaudhary *et al*., [22] Synthesized *N*-([dibutyl(actetamidooxy)stannyl]oxy}-2-phenoxyacetamide anisole and evaluated for their *in-vitro* antimicrobial activity against gram positive bacteria Bacillus cereus and *Staphylococcus aureus* and Gram-negative bacteria *Salmonella typhimurium* and *Escherichia coli* using Chloramphenicol as standard drug*(*MIC= 3.91–7.80 µg/mL). ***N*-([dibutyl (actetamidooxy) stannyl] oxy}-2-phenoxyacetamide anisole [structure 3] with MIC= 1.56–3.125 µg/mL** range exhibited good antimicrobial activity

Goszczynska *et al*.,[23] synthesized **(*E*)-Methyl 2-(2-methoxy-4-nitro-6-((phenylimino) methyl) phenoxy) butanoate** by reductive amination of alkyl 2-(2-formyl-4-nitrophenoxy) alkanoates with both aniline and 4-methoxyaniline and evaluated for *in-vitro* antibacterial activity against gram positive and gram negative bacteria using ciprofloxacin as reference drug (26mm). **(*E*)-Methyl 2-(2-methoxy-4-nitro-6-((phenylimino) methyl) phenoxy) butanoate (15mm)[Structure 4]** showed significant antibacterial activity.

Subahlaxmi *et al*., [24] synthesized by 2-(4-(3-(2-bromophenyl)-3-oxopropyl) phenoxy) acetic acid by solvent free method and evaluated for their antimicrobial activity using ciprofloxacin as standard drug (MIC=6.67 ± 0.48µL). **2-(4-(3-(2-bromophenyl)-3-oxopropyl) phenoxy) acetic acid** with **MIC=9.66±0.57µL[Structure 5]** showed good antibacterial activity against strain M. *smegmatis*.

Kumar *et al*., [25] synthesized Ethyl 2-[4-{bis(1H-indol-3-yl)methyl}-2-methoxyphenoxy]acetate from 2-methylindole and formylphenoxyaliphatic acid and evaluated for *in-vitro* antimicrobial activity against five different bacterial strains using tetracycline(22mm) as reference drug. **Ethyl 2-[4-{bis (1H-indol-3-yl) methyl}-2-methoxyphenoxy] acetate[Structure 6]** showed good antimicrobial activity against Staphylococcus aureus **(20 mm).**

Chhonker *et al*.,[26] synthesized 2-(2(4-methoxyphenyl) amino) methyl) phenoxy) acetic acid by reacting substituted aldehyde with monochloroacetic acid and screened for the antibacterial activity using ampicillin as reference(23mm). Among all tested compounds **2-(2(4-methoxyphenyl) amino) methyl) phenoxy) acetic acid [Structure 7]** with zone of inhibition **19mm** showed good antibacterial activity against *Staphylococcus aureus.*

Veenubala *et al.,* [27] synthesized (*E*)-4-((2-(carboxymethoxy) benzylidene) amino) benzoic acid by the reaction of 2-formylphenoxyacetic acid with substituted amines and assayed for the antibacterial activity against *E. coli* and *S. aureus* using ampicillin (25mm) as reference. **(*E*)-4-((2-(carboxymethoxy) benzylidene) amino) benzoic acid [Structure 8]** (22mm) demonstrated good antibacterial activity against *E. coli*.

Mcunaus *et al*.,[28] Several 2-(4-(phenyldiazenyl)phenoxy)acetic acid derivatives were prepared by refluxing method in an aqueous medium, and solvent-free and catalyst-free microwave-assisted method. The antibacterial activity was tested against *S. aureus*. **2-(3-chloro-4-(phenyldiazenyl)phenoxy)acetic acid[Structure 9]** showed good antibacterial activity.

Bar et al., [29] Synthesized new substitutes of phenoxy hydrazide analogs and screened for their in vitro anti-bacterial and anti-fungal activities to determine the inhibition zone by using the paper disk agar diffusion technique and evaluate the minimum inhibitory concentration values. **N'-(2-(4-chlorophenoxy)acetyl)-2,3,4,5-tetrafluorobenzohydrazide[Structure 10]** with four fluoro groups showed good inhibition against pathogenic microbes.

Bhat et al.,[30] All the compounds were evaluated for anti-tubercular activity Middle brook 7H9 agar medium against H37Rv Strain. **4-(4-(hydroxymethyl)-5-(4-((4-sulfamoylphenyl)amino)phenyl)-4H-pyrazol-3-yl)phenyl hydrogen carbonate [Structure 11]**shown promising anti-tubercular activity against streptomycin as a standard drug.

Monta *et al*., [31] synthesized 4-(2-methyl-phenylazo)-phenoxyacetic acid by the condensation of sodium azobenzene-4-oxydes with monochloroacetic acid and evaluated for *in-vitro* antimicrobial activity using septonex (17mm) as standard. **4-(2-methyl-phenylazo)-phenoxyacetic acid (20mm) [Structure12]** exhibited better antimicrobial activity against *s. pyogenes.*

More *et al*.,[32] The in vitro activity of synthesized compounds were screened against Mycobacterium tuberculosis H37Rv, and **methyl N'-(4-(1H-pyrrol-1-yl)benzoyl)formohydrazonate[Structure 13.]** have exhibited promising activity. MIC values were determined against M. tuberculosis strain H37Rv using the Microplate Alamar Blue assay (MABA) using isoniazid as the standard drug.

Ashref *et al*., [33] synthesized 2-(4-(1-carbamothioyl-5-(2-chlorophenyl)-4, 5-dihydro-H-pyrazol-3-yl)-2-methoxyphenoxy) acetic acid and they tested for the *in-vitro* activity against M. Tuberculosis H37RV (MTB) and INH-resistant M. Tuberculosis using INH (MIC=1.36µg/ml) as reference drug. **2-(4-(1-carbamothioyl-5-(2-chlorophenyl)-4, 5-dihydro-H-pyrazol-3-yl)-2-methoxyphenoxy) acetic acid[Structure 14]** was found to be more active against M.tuberculosis H_{37}RV (MTB) with minimum inhibitory concentration of **0.06 µg/ml.**

Antifungal activity

Bratulescou [34] synthesized 2-(4-(para-tolyldiazenyl)phenoxy) acetic acid by refluxing method in an aqueous medium, solvent-free and catalyst-free microwave-assisted method and evaluated against two gram-positive bacteria S. *aureus* and S. *pyogenes* and two gram negative bacteria E. *coli* and Salmonella *enteritidis* using Chloramphenicol as reference antibiotic. **2-(4-(para-tolyldiazenyl) phenoxy) acetic acid[Structure 15]** showed more potent antibacterial activity against S. aureus with **70%** effective percentage inhibition

Pucheta *et al*., [35] synthesized Methyl 2-(5-ethyl-4-hydroxy-2-methoxyphenoxy) acetate and evaluated for *in-vitro* anti fungal activity against different pathogenic microbes using Itraconazole (MIC= 0.25µg/ml) as reference drug. **Methyl 2-(5-ethyl-4-hydroxy-2-methoxyphenoxy) acetate (MIC=8µg/ml)[Structure 16]** showed better antifungal activity against *C. utilis*.

Dahiya and mourya [36] synthesized (*S*)-1-((*S*)-1-(2-(2, 6-dibromo-4-formylphenoxy) acetyl) pyrrolidine-2-carbonyl) pyrrolidine-2-carboxylic acid and evaluated for antifungal activities against pathogenic microorganisms using grisofulvin with 20mm zone of inhibition as reference. **(*S*)-1-((*S*)-1-(2-(2,6-dibromo-4-formylphenoxy)acetyl)pyrrolidine-2-carbonyl)pyrrolidine-2-carboxylic acid[Structure 17]** with zone of inhibition 24mm was found to be more potent antifungal agent against pathogenic *Candida albicans.*

Dahiya *et al.*, [37] synthesized (*S*)-2-((*S*)-2-((*S*)-2-amino-3-(2-(2-(4-chloro-3, 5-dimethylphenoxy) acetyl)-1*H*-indol-3-yl) propanamido)-5-guanidino-*N*-nitropentaamido)-3-(1*H*-indol-3-yl) propanoic acid and evaluated antifungal activity against different fungal strains against *C. albicans* using grisofulvin (20mm) as reference drug. **(*S*)-2-((*S*)-2-((*S*)-2-amino-3-(2-(2-(4-chloro-3, 5-dimethylphenoxy) acetyl)-1*H*-indol-3-yl) propanamido)-5-guanidino-*N*-nitropentaamido)-3-(1*H*-indol-3-yl) propanoic acid (24mm)[Structure 18]** showed better antifungal activity.

Nisha et al., 2023 [38] Synthesized 4-Methoxyphenoxyacetic acid and tested for antifbacterial and antifungal properties against strains Streptococcus, Micrococcus, E. coli, Candida albicans, Trichophyton, Fusarium, Enterococcus faecalis, Salmonella typhi, A. niger, Mucor, and Trichoderma. Using gentamycin (20mm) as reference standard**. 4-Methoxyphenoxyacetic acid [structure 19]**showed better antifungal activity (30mm).

Antiviral Activity

Yuanchao *et al.*,[39] synthesized (*E*)-2-(4-((3-(3, 4-dihydrxyphenyl) allyl) amino)-2-(4-methylheptaneamido) phenoxy) acetic and screened for their antiviral activity against influenza virus using Oseltamivir carboxylate (IC_{50} value = 0.0017 µM) as positive control **(*E*)-2-(4-((3-(3, 4-dihydrxyphenyl) allyl) amino)-2-(4-methylheptaneamido) phenoxy) acetic[Structure 20]** acid with **IC_{50} 7.2 µM** and **8.5 µM** possessed good enzyme inhibitory activity against N2 and N1 neuraminidase inhibitors (NAs).

Sahar *et al.*, [40] synthesized revealed (3-(2, 4-dihydroxyphenyl)-5-(4-((2-hydroxyallyl) oxy)-3methylphenyl)-4, 5-dihydro-1H-pyrazol-1-yl) (phenyl) methanone and screened for antiviral activity using Brivudin (MIC 0 .008µM). Literature study revealed **(3-(2, 4-dihydroxyphenyl)-5-(4-((2-hydroxyallyl) oxy)-3methylphenyl)-4, 5-dihydro-1H-pyrazol-1yl) (phenyl) methanone[Structure 21] with MIC 0.032µM** showed significant antiviral activity

Anticancer activity

Adihiti et al.,[41] In the current examination, a novel series of pyridazine analoges was synthesized and evaluated against metastatic neoplastic cells**. 2-(4-chlorophenoxy)-N'-(6-chloropyridazin-3-yl)Acetohydrazide [Structure 22]** has potential cytotoxic efficacy with prolonged activity against various cancer cells, including A549, HepG2, A498.

Acharya et al., [42] For the obtained compounds, in vitro tests were carried out on four melanoma cell lines (A375, G-361, SK-MEL2, SK-MEL28), four prostate cancer cell lines (PC-3, DU-145, LNCaP, VcaP) and a normal human fibroblast cell line (BJ). **1-(4-bromophenyl)-4-(phenoxy)acetylthiosemicarbazide[Structure 23]** is the most active compound.

Sayad et al., 2023[43] New semi-synthetic phenoxy acetamide derivatives, were synthesized, characterized, and screened for their cytotoxic activity against breast cancer (MCF-7) and liver cancer (HepG2) cell lines. When tested against the HepG2 cell line **N-(2-hydrazinyl-2-oxoethyl)-2-(2,4,5-trichlorophenoxy)acetamide [Structure 24]**had significantly increased cytotoxic activity when compared to the reference medication 5-Fluorouracil (5-FU), with IC50 values of 1.43 M, 5.32 M, and 6.52 M

Li et al., 2023[44] A series of novel 1,2,4-triazole-chalcone compounds were designed and synthesized. The anti-proliferative activities of the novel chalcones against four cancer cell lines in vitro were evaluated by MTT, four tumor cell lines including human colon cancer cell SW620, human non-small cell lung cancer cell A549, human cervical cancer cell HeLa, and human breast cancer cell MCF-7. thiophene-2-carbaldehyde compound with **(E)-1-(4-((4-methyl-1,6-dihydropentalen-2-yl)methoxy)phenyl)-3-(4-methylcyclohexa-2,4-dien-1-ylidene)propan-1-one (1:1)[Structure 25]** had good anti-proliferative activity against A549 cells with an IC50 value of 25.58 µM

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Yushun et al., 2023[45] synthesized rel-2-[4-chloro-2-[(5R,6R,7S)-6-[5-(4-methoxyphenyl)-3-(2-naphthyl)- 3,4-dihydropyrazole-2-carbonyl]-5-methyl-2-oxo-3,5,6,7-tetrahydrothiopyrano[2,3-d]thiazol-7-yl] phenoxy]acetic acid and confirmed by 1H, 13C, 2D NMR, and LC-MS spectra. **rel-2-[4-chloro-2-[(5R,6R,7S)-6-[5-(4-methoxyphenyl)-3-(2-naphthyl)- 3,4-dihydropyrazole-2-carbonyl]-5-methyl-2-oxo-3,5,6,7-**

tetrahydrothiopyrano[2,3-d]thiazol-7-yl] phenoxy]acetic acid[Structure 26] Showed a medium impact on leukemia cancer cell line and central nervous system cancer cell lines.

Kozyra et al., [46] synthesized 1-(4-bromophenyl)-4-(phenoxy)acetylthiosemicarbazide and evaluated for in vitro tests were carried out on four melanoma cell lines (A375, G-361, SK-MEL2, SK-MEL28), four prostate cancer cell lines (PC-3, DU-145, LNCaP, VcaP) and a normal human fibroblast cell line (BJ). **1-(4-bromophenyl)-4-(phenoxy)acetylthiosemicarbazide[Structure27]** showed the best activity against melanoma G-361 and prostate LNCaP cell lines with IC50 = 104.86 μM and 145.39 μM, respectively.

Sabatino *et al*., [47] synthesized 2-(4-chlorophenoxy)-5-(4-chlorophenyl) pentatonic acid and analyzed for their ability to reduce colorectal cancer (CRC) cells growth by binding PPARγ. **2-(4-chlorophenoxy)-5-(4-chlorophenyl) pentatonic acid[Structure 28]** showed a significant antiproliferative activity with IC_{50} **=4.8±0.35μM** compared to standard drug RGZ with **IC50= 9.8±0.4 μM** RGZ with **IC50= 9.8±0.4 μM**.

Terenteva *et al*., [48] synthesized 4-chlorophenoxyacetic acid and evaluated for cytotoxic activity using Cisplatin 0.236±0.07μg/ml as standard drug. **4-Cl-phenoxyacetic acid[Structure 29]**demonstrated high cytotoxic activity against breast cancer cells with IC_{50} value of 0.194±0.09μg/ml.

Hu *et al*.,[49] synthesized (5S, 9R)-8-oxo-9(3,4,5-trimethoxyphenyl)-5,5a,7,8,8a,9-hexahydrofluoro[2,3,6,7]naptho[2,3-d][1,3]dioxol-5-yl 2-(2,5-dimethylphenoxy)acetate by acylation of phenoxy acetic acids at C4th-position of podophyllotoxin and evaluated for cytotoxic activity Podophyllotoxin (IC_{50} 6.61 ± 0.69μM) as reference drug. **(5S, 9R)-8-oxo-9(3,4,5-trimethoxyphenyl)-5,5a,7,8,8a,9-hexahydrofluoro[2,3,6,7]naptho[2,3-d][1,3]dioxol-5-yl 2-(2,5-dimethylphenoxy)acetate** with **IC_{50} 1.64+0.41μM [Structure 30]**showed most effective antiproliferative activity against Hela Cells.

Sahar *et al*.,[50] synthesized 2-{4-[3-(2, 4-dihydroxyphenyl)-1-(2-hydroxybenzoyl-4, 5-dihydro-1H-5-pyrazolyl]-2-methoxyphenoxy} acetic acid by the reaction between hydrazides and 2-{4-[3-(2, 4dihydroxyphenyl)-3-oxo-1-propenyl]-2-methoxyphenoxy} acetic acid and evaluated fir cytotoxic activity using Gancyclovir (EC_{50} =100μg/ml) as reference drug. Among all the synthesized compounds **2-{4-[3-(2, 4-dihydroxyphenyl)-1-(2-hydroxybenzoyl-4, 5-dihydro-1H-5-pyrazolyl]-2-methoxyphenoxy} acetic acid[Structure 31]** with a minimum cytotoxic concentration 0.16 **μg/mL** was found to be most active against human embryonic lung (HEL) cell.

Antioxidant activity

Chigurupati *et al*., [51] synthesized 2-(4-(1-benzoyl-3-(1H-indol-3-yl) 4, 5-dihydro1-H-pyrazol-5-yl) phenoxy) acetic acid and evaluated for anti-Alzheimer activity through *in-vitro* Acetylcholinesterase (AChE) inhibition and radical scavenging activity (antioxidant) studies. The *in-vitro* antioxidant activity of synthesized compound was evaluated using DPPH stable free radical and (ABTS) radical cation scavenging assay. **2-(4-(1-benzoyl-3-(1H-indol-3-yl) 4, 5-dihydro1-H-pyrazol-5-yl) phenoxy) acetic acid[Structure 32]** was found to be more potent AChE inhibitor (IC50: 0.68 ± 0.13 lM) with strong DPPH and ABTS radical scavenging activity with IC50: 13.77 ± 0.25 μM and IC50: 12.59 ± 0.21 μM Compared to standard drug **Ascorbic acid** with IC50: 11.5 ± 1.9μM IC50: 11.5 ± 1.9μM

Parsant *et al*., [52] synthesized 2-(4-(4-bromobenzoyl)-2,6-dimethylphenoxy)acetic acid and evaluated for *in-vitro* anti-oxidant activity with the help of DPPH, Nitric oxide (NO) and Hydrogen Peroxide (H_2O_2) radical scavenging assays using ascorbic acid with IC_{50}= 15.73 ± 0.25μg/ml as reference drug. **2-(4-(4-bromobenzoyl)-2, 6-dimethylphenoxy) acetic acid[Structure 33]** with **IC_{50}= 18.94 ±0.24μg/ml** possessed good antioxidant activity.

Wei *et al*., [53] synthesized **2-(2, 4-dichlorophenoxy)-N-nitro-N-(2, 4, 6-tribromophenyl) acetamide** and evaluated for the herbicidal activity using standard 2, 4-D. IC50=0.13 (0.06–0.24). Among all synthesized compounds **2-(2, 4-dichlorophenoxy)-N-nitro-N-(2, 4, 6-tribromophenyl) acetamide [Structure 34]** is more potent herbicidal agent against A. *albus* with IC50= 0.79 (0.37–1.48)

Miscellaneous Activity

Zhang et al.,[54] In vitro studies on the evaluation of red blood cells revealed that **compound 2-(2-methyl-4-(2-oxo-2-(p-tolylamino)ethyl)phenoxy)acetic acid [Structure 35]** (ΔP50 = 45.50 mmHg) and improve the oxygen-releasing property effectively compared to positive control efaproxiral (ΔP50 = 36.40 mmHg).

Shivana *et al.*, [55] synthesized 1-(4-(Methoxy(phenyl)methyl)-2-methylphenoxy)butan-2-one by refluxing a mixture of 4-(methoxy(phenyl)methyl)-2-methylphenol and 1-chlorobutan-2-one in dry distilled acetone and anhydrous potassium carbonate for 4 h and evaluated for in vitro inhibition of α-glucosidase. **1-(4-(Methoxy(phenyl)methyl)-2-methylphenoxy)butan-2-one[Structure 36]** exhibited a significant inhibition of the enzyme (IC50: 10.30 ± 0.25 µg/mL) in comparison with the control, acarbose (IC50: 12.00 ± 0.10 µg/mL).

Bijoux *et al.*, [56] synthesized 2-(4-(3-isopropyl-4-propylbenzyl)-3, 5-dimethylphenoxy) acetic acid and assayed for the relative beneficial effect of each drug analogue against angiogenesis model. **2-(4-(3-isopropyl-4-propylbenzyl)-3, 5-dimethylphenoxy) acetic acid [Structure 37]** was more potent angiogenesis (with Mean 86% stimulation) stimulating agent compared to standard PBS

Mandal *et al.*, [57] synthesized (*Z*)-2-(4-(((2-amino-5-chlorophenyl) amino) methyl) phenoxyacetic acid and analyzed by C-13 NMR and mass spectroscopy. **(*Z*)-2-(4-(((2-amino-5-chlorophenyl) amino) methyl) phenoxyacetic acid [Structure 38]** with **CTC $_{50}$ 15.87 µg/ml** exhibited significant glucose uptake activity. Pioglitazone with **CTC$_{50}$ 15.87µg/ml** used as standard drug.

Mocanu *et al.*, [58] Synthesized 2-(2-chloro-4-(pyrrolidin-1-ylsulfonyl)phenoxy0-N-(2-nitrobenzylidene)acetohydrazide by the condensation of hydrazides with a number of aldehydes, transition metals and evaluated for *in-vitro* antibacterial activites using DMSO(Dimethylsulpoxide) as standard. **2-(2-chloro-4-(pyrrolidin-1-ylsulfonyl)phenoxy0-N-(2-nitrobenzylidene)acetohydrazide[Structure 39]**showed maximum antibacterial activity against *E.coli.* with zone of inhibition **43 mm**.

Wang *et al.*, [59] synthesized 3-(4-((2',6'-dimethyl-4'-(3-(methylsulphonyl)propoxy)-[1,1'biphenyl]-3-yl)methoxy-2-methylphenoxy)prop-1-en-2-ol and evaluated for their hypoglycemic activity using TAK-875 **(EC$_{50}$ = 38.6 nM)** as positive control. **3-(4-((2', 6'-dimethyl-4'-(3-(methylsulphonyl) propox)-[1, 1'biphenyl]-3-yl) methoxy-2-methylphenoxy) prop-1-en-2-ol [Structure 40] EC$_{50}$ = 62.3 nM** very effective drug candidate for the treatment of diabetes mellitus.

Farsa *et al.*, [60] synthesized 2-{-4-[2-(2-oxoperhydroperazin-1-yl) acetamido] phenoxy} acetic and tested *in -vitro* for inhibition of porcine kidney amino peptidase. **2-{-4-[2-(2-oxoperhydroperazin-1-yl) acetamido] phenoxy} acetic acid [Structure 41]** with **IC50=449.5µM** exhibited the highest inhibition activity to AP-M.

Vanzandt *et al.*, [61] synthesized 5-fluoro-2-(4-bromo-2-fluoro-benzylthiocarbamoyl)-phenoxyacetic acid and tested for potency against human aldose reductase (hALR2) and human aldehyde reductase (hALR1). Among all compounds **5-fluoro-2-(4-bromo-2-fluoro-benzylthiocarbamoyl)-phenoxyacetic acid[Structure 42]** (IC50 = 30 nM) with 40% inhibition was most potent in aldose reductase inhibition compared to standard drug tolerestat with 31%inhibtion.

Sato *et al.*, [62] Synthesized [2-[1-[3-*N*, *N*-dimethylcarbomyl)-3, 3-diphenylpropyl]-4-hydroxypiperidin-4-yl] phenoxy] acetic acid and evaluated to determine a peripheral opioid analgesic using standard drug loperamide with potency = 5.436±.68. **[2-[1-[3-*N*, *N*-dimethylcarbomyl)-3, 3-diphenylpropyl]-4-hydroxypiperidin-4-yl] phenoxy] acetic acid [Structure 43]** showed higher analgesic activity with relative potency =54.4±6.6 compared to standard drug loperamide with potency = 5.436±.68.

Brooks et *al.*, [63] synthesized 2-(4-(2-(2-([1, 1':4', 1''-terphenyl]-4-yl)-5-methyloxazol-4-yl) ethoxy) phenoxy)-2- methylpropanoic acid that exhibit significant dual PPAR-alpha and gamma agonist activity. **2-(4-(2-(2-([1, 1':4', 1''-terphenyl]-4-yl)-5-methyloxazol-4-yl) ethoxy) phenoxy)-2- methylpropanoic acid [Structure 44] With** IC$_{50}$ **174±17 nM** showed more efficacy for activating and binding to PPAR alpha receptors. **Rosigiltazone** (IC$_{50}$>**10000nM)** used as reference drug.

Tarun et al.,[64] A series of novel **phenoxy acid hydrazide derivatives[Structure 45]** containing carboxylic moiety such as 4-oxobutanoic acid at 4th position were synthesized, and their antinociceptive, and anti-inflammatory activities were evaluated. Most of the derivatives were found to exhibit peripheral nociceptive effects. The results demonstrated that the presence of acidic moiety increased the peripheral antinociceptive activity and reduced the central antinociceptive activity.

Mode of action: It is explained in Fig. 5

III. SYNTHESIS OF PHENOXYACETIC ACID DERIVATIVES

Abbouchi *et al*., [65] synthesized (2-[2, 3-dichloro-4-(2-methylidenebutanoyl) phenoxy] acetic acid) (**Scheme 1)** and they evaluated for their *in-vitro* anticancer activity against promyelocytic leukemiaity (**HL60)** and human colon carcinoma (**HCT116)** cancer cell lines by the sensitive Cell Titer-Glo **luminescent assay** using doxorubicin as reference standard. Compounds **6 and 7** with IC_{50} 24.8nm and IC_{50} 67.7nm showed good anticancer activity.

Ostoot *et al*., [66] synthesized *N*-(2-(4-chlorophenoxy) acetyl)-2, 3, 4, 5-tetrafluorobenzohydrazide (**scheme 2)** and they evaluated for their anti-microbial activity against many bacterial strains. Compound **6** was found to be most effective antimicrobial drug candidate. The SAR study showed that **6** with four fluoro groups exhibit good inhibition against pathogenic microbes.

Bahakt *et al*., [67] Synthesized 2-(4-(3-(2-oxo-1, 2, 3, 4-tetrahydroquinolin-3-yl) propanoyl) phenoxy) acetic acid (**scheme 3)** and they screened for their antibacterial activity by Agar disc diffusion method using Gatifloxacin as standard drug. Among all the synthesized compounds, **4** exhibited good antibacterial activity against bacterial strain *S. marcescens.*

Nesterkina *et al*, [68] synthesized (E)-2-(4-chlorophenoxy)-N'-((2S, 5R)-2-isopropyl-5-methylcyclohexylidene) acetohydrazide through condensation reaction of (2S, 5R)-2-isopropyl-5methylcyclohexanone with different phenoxyacetic acid hydrazides in the presence of catalyst glacial acetic acid (**scheme 4).** They determined their anticonvulsant activity by pentylenetetrazole model (PTZ) and maximal electroshock (MES) induced seizures in mice. Compound **3** exhibited good anticonvulsant activity.

Lie *et al*., [69] to facilitate the development of a novel herbicide, 4-hydroxyl-3-(2phenoxyacetyl)-pyran-2-one derivatives were designed and synthesized (**scheme 5).** Compound **10** showed a broader spectrum of weed control when compared with a marketable herbicide 2, 4-dichlorophenoxyacetic acid (2, 4-D), and displayed good quality crop safety to Triticum aestivum L. and Zea mays Linn.

Mandal et al., [70] synthesized aniline 2-(2-methoxy-4-((2-methylhydrazono) methyl) phenoxy) acetate and analysed by C-13 NMR and mass spectroscopy **(scheme 6).** Specifically, **4** glitazone candidate exhibited significant glucose uptake activity.

Panczyk K. *et al*., [71] synthesized 1-(2,6-dimethylphenoxy)propane-2-one compound with 2-amino-1-phenylethanol(1:1) **scheme 7** and they subjected for their *in-vivo* anticonvalsant activity by the Epilepsy Therapy Screening Program (ETSP) using MES, 6 Hz, scMET, hippocampal kindling animal models. Results indicated compound **4** was more pharmacologically active.

Hu *et al*., [72] synthesized (5S,9R)-5-hydroxy-9-(3,4,5-trimethoxyphenyl)-5,5a,8a,9-tetrahydrofuro[2',3':6,7]naphtho[2,3-d][1,3]dioxol-8(7H)-one compound with 1-(2,5-dimethylphenoxy)propan-2-one (1:1) podophyllotoxin analogue by acylation of phenoxyacids at C_4-position of podophyllotoxin (**Scheme 8)** and performed their cytotoxic activity. compound **3** with an **IC50 1.64 ± 0.41 µM** showed the more effective antiproliferative activity against Hela cells compared to reference drug Etoposide with **IC50 = 2.45 ± 0.85 µM.**

Wang X *et al*., [73] synthesized 2-(4-((2', 6'-dimethyl-4'-(3-(methylsulfonyl) propoxy)-[1, 1'-biphenyl]-3-yl) methoxy)-2-fluorophenoxy) acetic acid (**scheme 9)**. In this research work compound **8 (EC_{50} = 62.3 nM)** was found as more potent FFA1 agonist based on the structure of phenyl-propanoic acid.

Noolvi *et al*., [74] synthesized 3-(4-((5-amino-1, 3, 4-thiadiazol-2-yl) methoxy)-3-methoxyphenyl)-5-(4-nitrophenyl)-4, 5-dihydro-1H-pyrazole-1-carbothioamide by reaction with thiosemicarbazide and cyclization process in presence of $POCl_3$ (**scheme 10)**. The Synthesized compound evaluated for their *in-vitro* antimicrobial activities against various bacterial strains. Compound **5** showed considerable antimicrobial activitiy.

Wei *et al*., [75] synthesized *N*-(2-bromo-4-chlorophenyl)-2-(2, 4-dichlorophenoxy)-*N*-nitroacetamide (**scheme 11)** and they evaluated for their herbicidal activity. Compound **5** exhibited good herbicidal activity against roots of *A. albus*, *Rape*, and *S. sudanense.*

Mohammed *et al*. [76] synthesized 2-[4-(1-{[bis (prop-1-yn-1-yl)-? ³-chloranyl] carbonyl}-3-(4-chlorophenyl)-4, 5-dihydro-1H-pyrazol-5-yl)-2-hydroxyphenoxy] acetic acid (scheme 12) and they evaluated for their *in-vivo* anti-diuretic activity. Compound **5** showed good antidiuretic activity in comparison to reference drug furasemide. The SAR study revealed that chloro group was better for the activity

Hunsal *et al.*, [77] new caffeic acid derivatives was synthesized by using **scheme 13.** The *in-vivo* anti – inflammatory and analgesic activities were evaluated for all the newly synthesized derivatives. Compound **3** exhibited good anti-inflammatory activity compared to standard drug Aspirin.

Dahiya and Kaur [78] synthesized 2-(4- chloro-3, 5-dimethylphenoxy) acetic acid **scheme 14** and they screened for their antimicrobial activity (Bauer et al.,) against four different bacterial strains *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Bacillus subtilis* and three different fungal strains *Trichophyton mentagrophytes*, *Candida albicans* and Microsporum audouini. Compound **3** displayed better activity against *C. albicans* compared to Grisofulvin as reference drug.

Brooks D *et al.*, [79] synthesized 2-(4-(2-(2-([1, 1':4', 1''-terphenyl]-4-yl)-5-methyloxazol-4-yl) ethoxy) phenoxy)-2-methylpropanoic (**scheme 15)**.Compound **6** with **IC $_{50}$ 548+72nm** showed more activating and binding efficacy to PPAR alpha receptors.

Apaydin *et al.*, [80] Synthesized *N*-(2-methyl-3-oxo-6-(trifluoromethyl)-1-thia-4-azaspiro [4.4] nonan-4-yl)-2-phenoxyacetamide (**scheme 16)** and evaluated for antiviral activity. Compound **5** was found to slow down human corona virus 229E replication.

Chhonaker *et al.*, [81] synthesized 2-(2-((phenylimino) methyl) phenoxy) acetic acid compound with methanol (1:1) by reacting 2-formyl phenoxyacetic acid with substituted aromatic amine. The mixture was dissolved in methanol. The progress of reaction was monitored by using TLC **(scheme -17).** They screened for their antibacterial activity against *E. coli* **(AMJ-2006)** and *S. auerus* **(AMJ-2005)** by disc diffusion method using ampicillin as standard drug. Compound **3** exhibited good antibacterial activity.

IV. CONCLUSION

Literature review recognize that the compounds consist of phenoxyacetic acid moiety having a common fundamental feature of a numerous medicinal agents and its derivatives shows miscellaneous pharmacological activities and very easy to synthesize. This vital functional group division has widespread potential.

CONFLICT OF INTEREST

The author confirms that there is no conflicts of interest.

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AVAILABILITY OF DATA AND MATERIALS

All data are provided in the manuscript or cited in the references.

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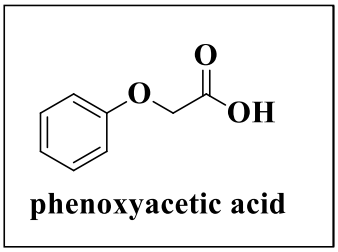


fig. 1: chemical structure of phenoxyacetic acid

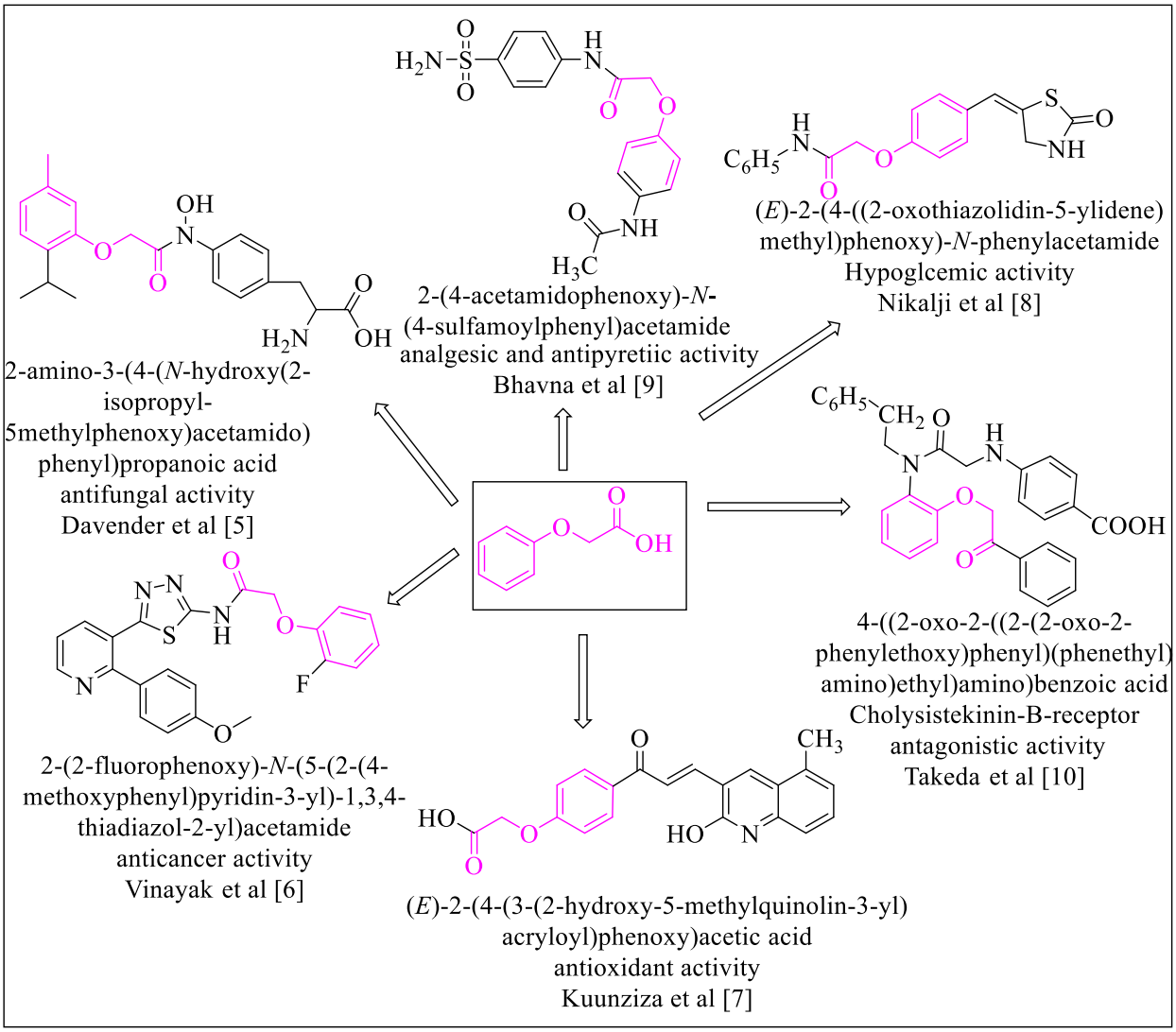


fig. 2: biological profile of phenoxyacetic acid

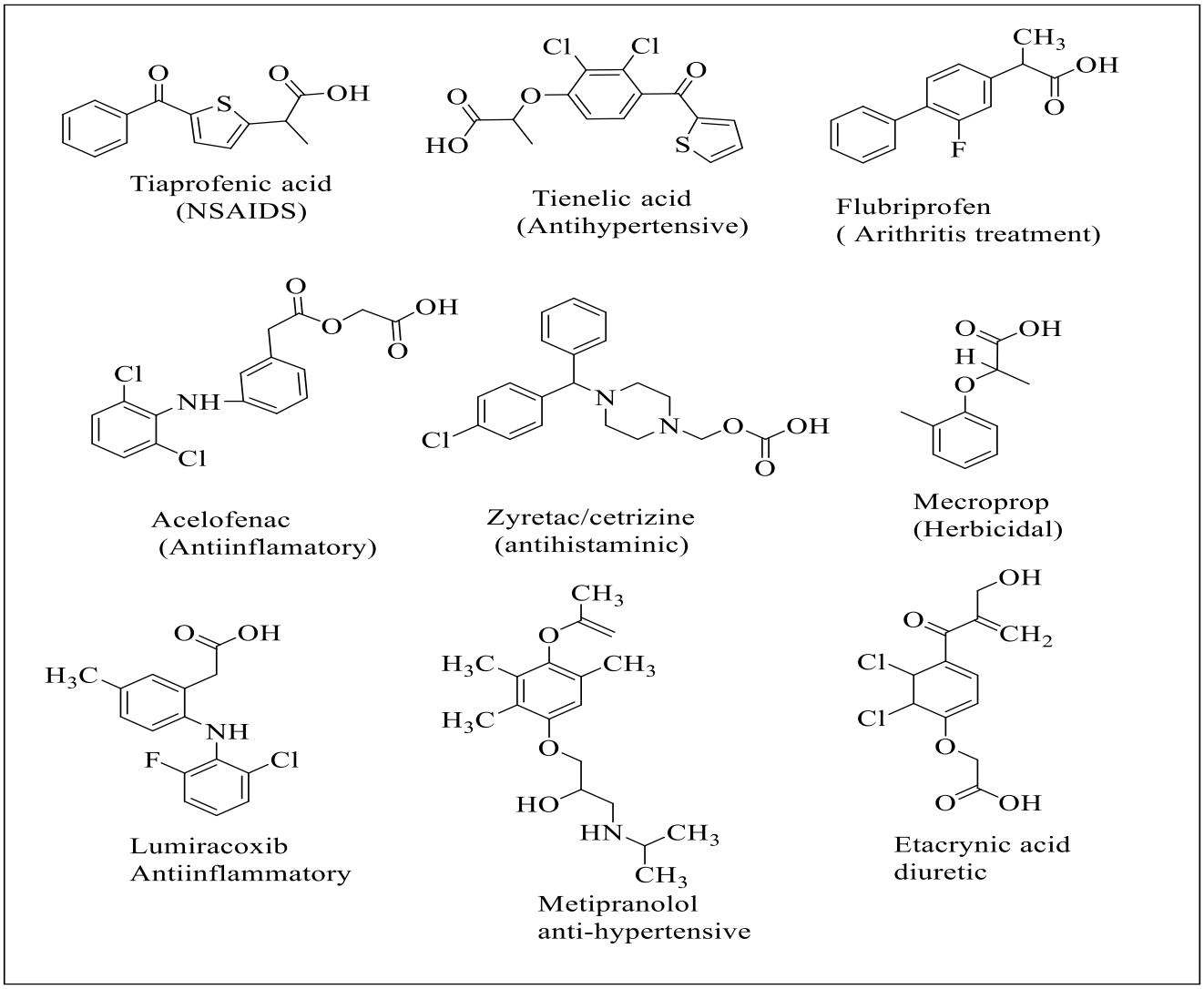
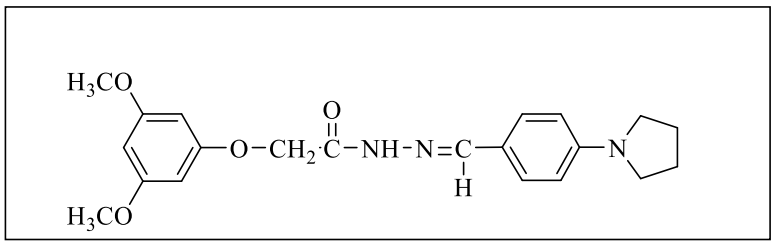
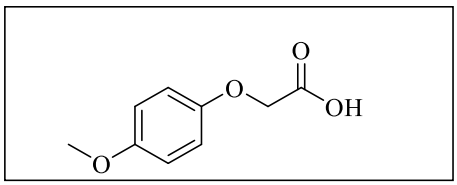


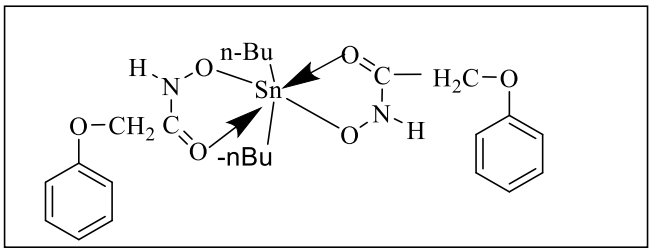
fig. 3:- marketed formulations of phenoxyacetic acid



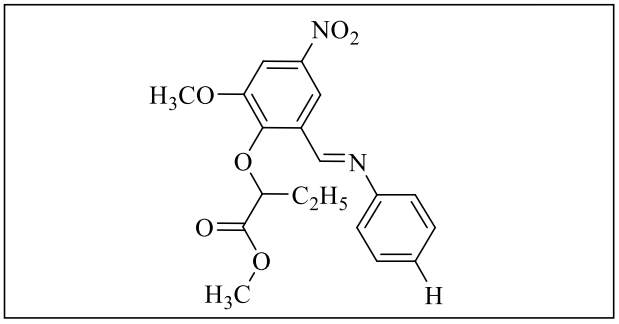
Strucutre 1. 2-(3,5-dimethoxyphenoxy)-N2-(3,5-dimethoxyphenoxy)-N'-(4-(pyrrolidin-1-yl)benzylidene)acetohydrazide
Zone of inhibition 21mm



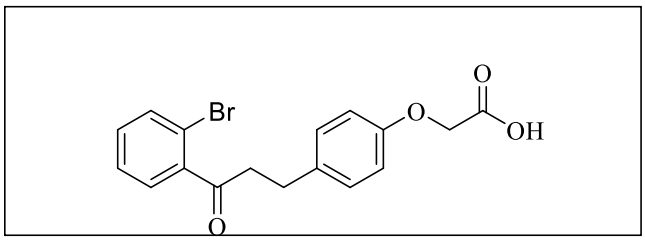
Structure 2. 4-methoxyphenoxyacetic acid



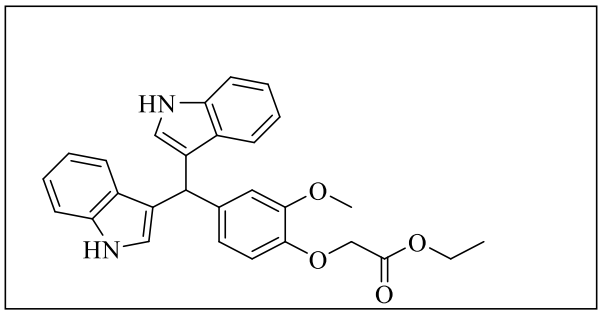
Structure 3. N-{[dibutyl(acetamidooxy)stannyl]oxy}-2-phenoxyacetamide; anisole
MIC=1.56-3.125 microg/mL



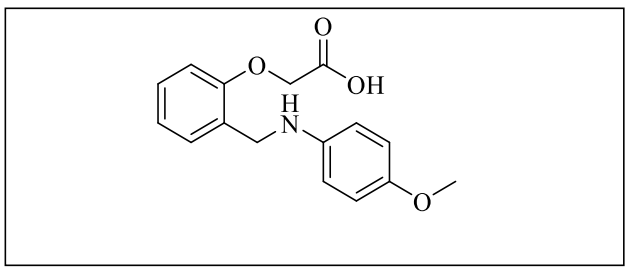
Structure 4. (*E*)-methyl 2-(2-methoxy-4-nitro-6-((phenylimino)methyl)phenoxy)butanoate
Zone of inhibition=15mm



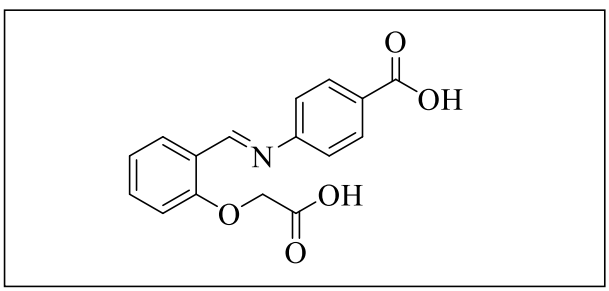
Structure 5. 2-(4-(3-(2-bromophenyl)-3-oxopropyl) phenoxy)acetic acid
MIC=9.66 ± 0.57 µL



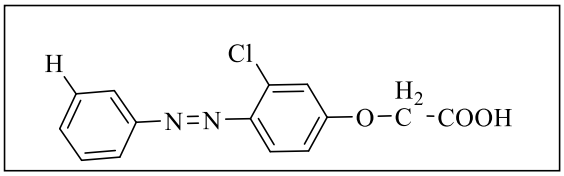
Structure 6 ethyl 2-[4-{bis(1H-indol-3-yl)methyl}-2-methoxyphenoxy]acetate
Zone of inhibition 20mm



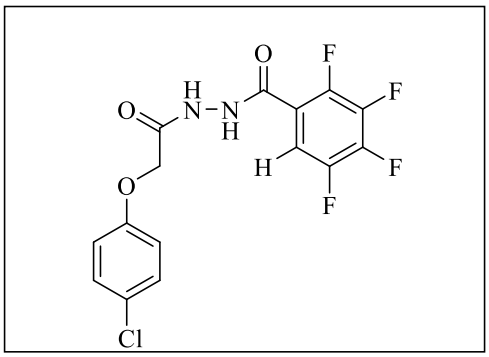
Structure 7. 2-(2-(((4-methoxyphenyl)amino)methyl) phenoxy)acetic acid
zone of inhibition 19mm



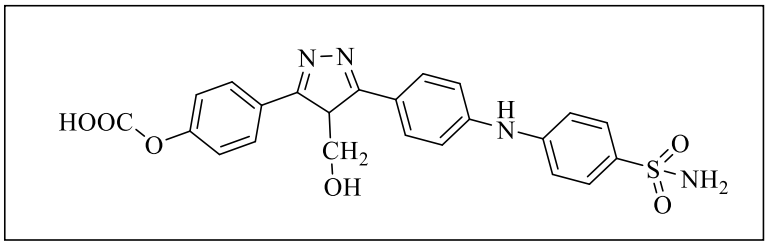
Structure 8. (*E*)-4-((2-(carboxymethoxy)benzylidene) amino)benzoic acid
Zone of inhibition=22mm



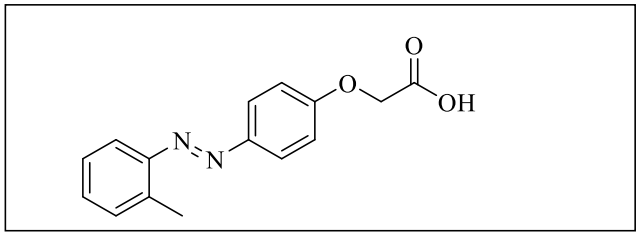
Structure 9. 2-(3-chloro-4-(phenyldiazenyl)phenoxy)acetic acid



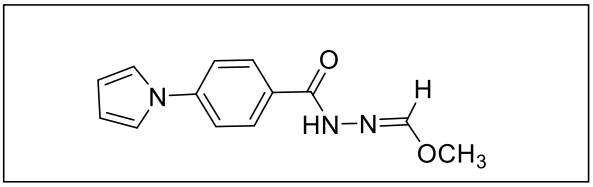
Structure 10. N'-(2-(4-chlorophenoxy)acetyl)-2,3,4,5-tetrafluorobenzohydrazide



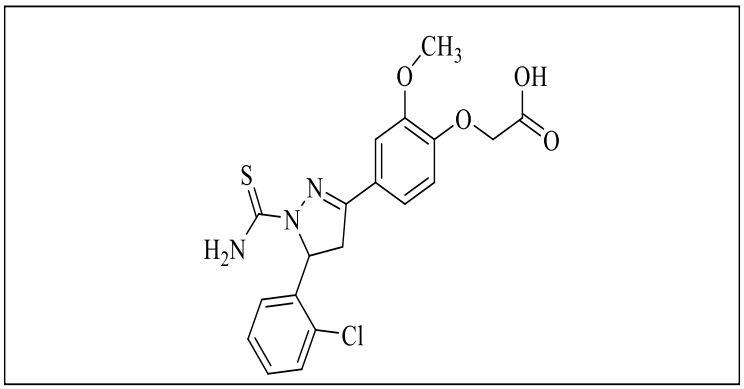
Structure 11. 4-(4-(hydroxymethyl)-5-(4-((4-sulfamoylphenyl)amino)phenyl)-4*H*-pyrazol-3-yl)phenyl hydrogen carbonate



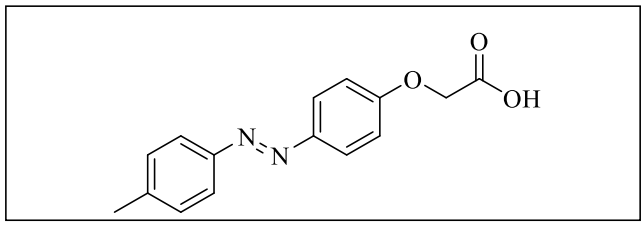
Structure 12.4-(2-Methyl-phenylazo)-phenoxyacetic acid inhibition diameter =20mm



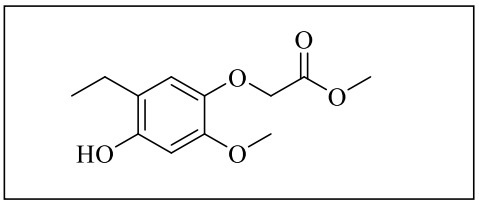
Structure 13. methyl *N*'-(4-(1*H*-pyrrol-1-yl)benzoyl)formohydrazonate



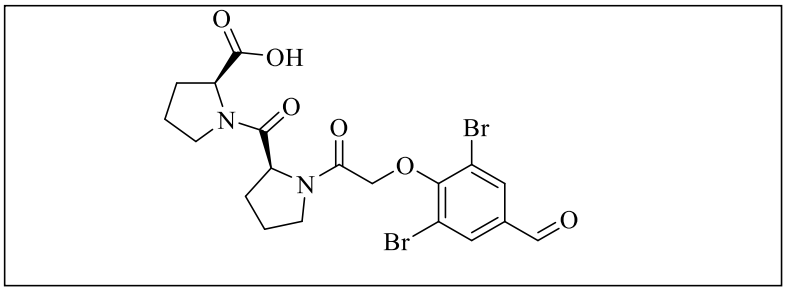
Structure 14. 2-(4-(1-carbamothioyl-5-(2-chlorophenyl)-4,5-dihydro-1*H*-pyrazol-3-yl)-2-methoxyphenoxy)acetic acid MIC:0.06lg/ml



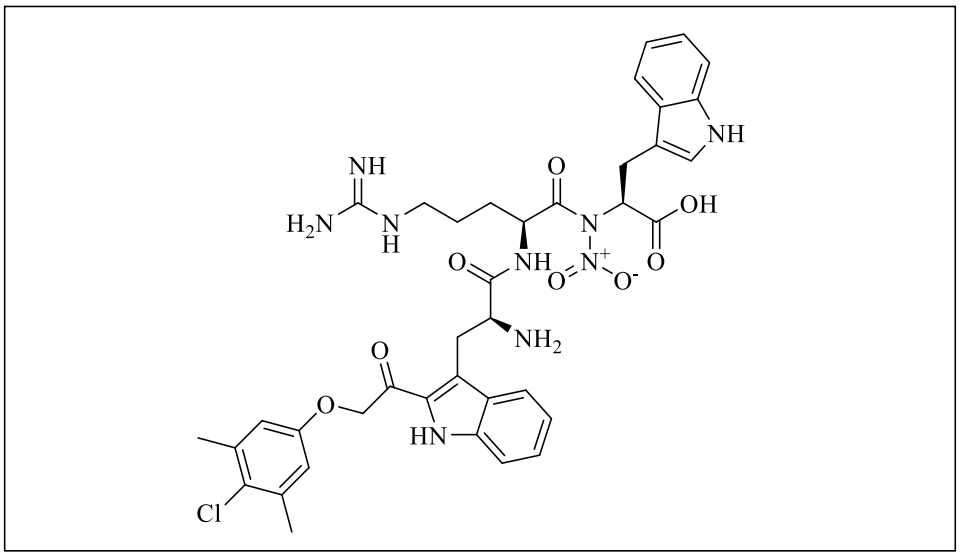
Structure 15. (*E*)-2-(4-(*p*-tolyldiazenyl)phenoxy)acetic acid
Percentage of inhibition 70%



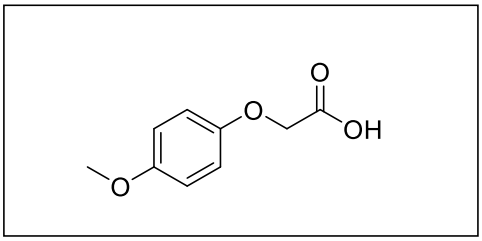
Structure 16. Methyl 2-(5-ethyl-4-hydroxy-2-methoxyphenoxy)acetate
MIC=8 µg/mL



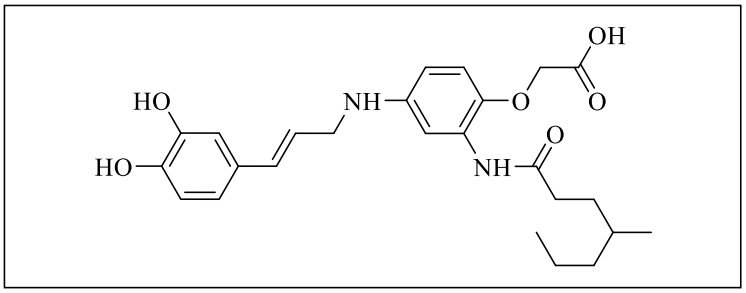
Structure 17. (*S*)-1-((*S*)-1-(2-(2,6-dibromo-4-formylphenoxy)acetyl) pyrrolidine-2-carbonyl)pyrrolidine-2-carboxylic acid



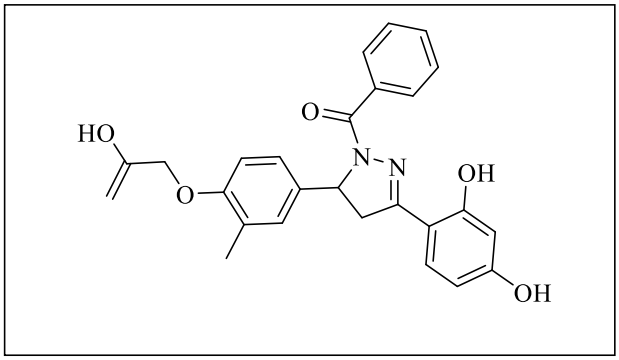
Structure 18. (*S*)-2-((*S*)-2-((*S*)-2-amino-3-(2-(2-(4-chloro-3,5-dimethylphenoxy) acetyl)-1*H*-indol-3-yl)propanamido)-5-guanidino-*N*-nitropentanamido)-3-(1*H*-indol-3-yl)propanoic acid
Zone of inhibition=24mm



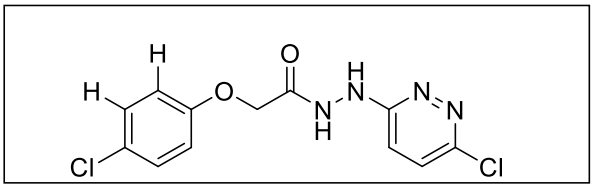
Structure 19. 4-methoxy phenoxyacetic acid
Zone of inhibition=30mm



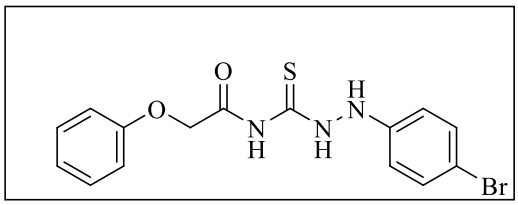
Structure 20. (*E*)-2-(4-((3-(3,4-dihydroxyphenyl)allyl)amino)-2-(4-methylheptanamido)phenoxy)acetic acid
IC_{50}7.2IM and 8.5IM



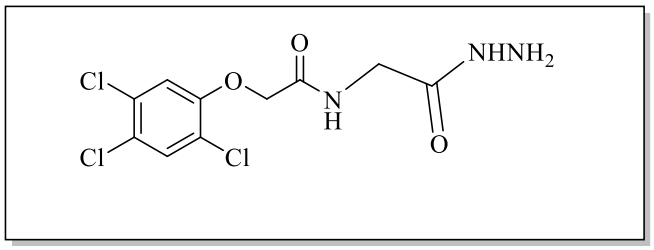
Structure 21. (3-(2,4-dihydroxyphenyl)-5-(4-((2-hydroxyallyl)oxy)-3-methylphenyl)-4,5-dihydro-1*H*-pyrazol-1-yl)(phenyl)methanone
.032microM



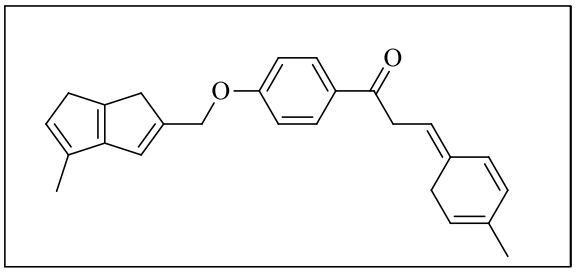
Structure 22. 2-(4-chlorophenoxy)-*N*'-(6-chloropyridazin-3-yl)acetohydrazide



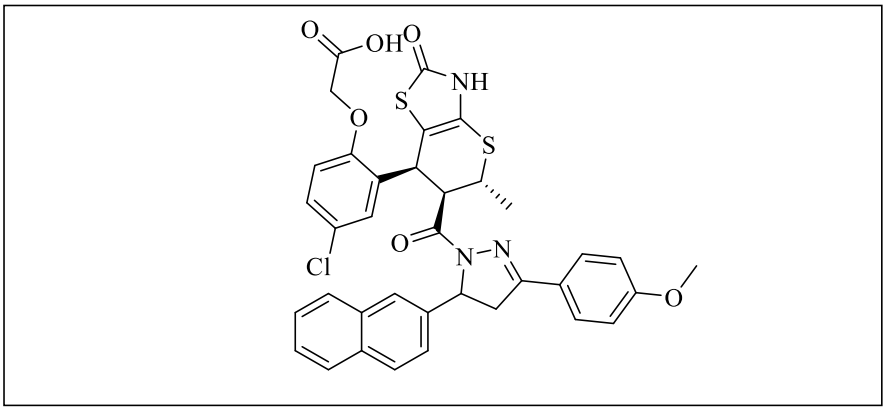
Structure 23. 1-(4-bromophenyl)-4-(phenoxy) acetylthiosemicarbazide



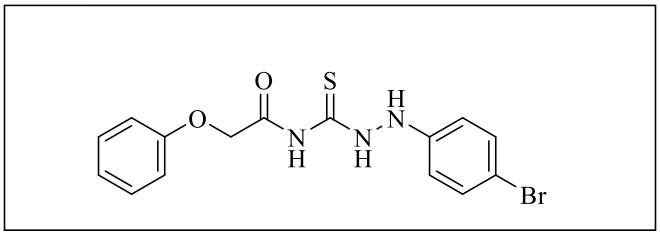
Structure 24. *N*-(2-hydrazinyl-2-oxoethyl)-2-(2,4,5-trichlorophenoxy)acetamide



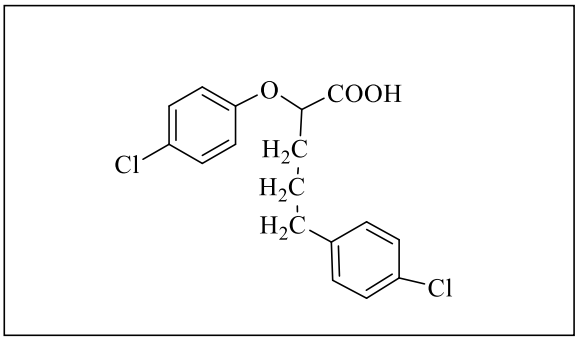
Structure 25: (E)-1-(4-((4-methyl-1,6-dihydropentalen-2-yl)methoxy) phenyl)-3-(4-methylcyclohexa-2,4-dien-1-ylidene)propan-1-one



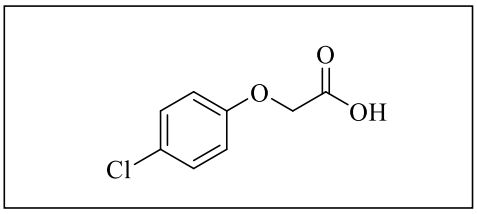
Structure 26. rel-2-[4-chloro-2-[(5R,6R,7S)-6-[5-(4-methoxyphenyl)-3-(2-naphthyl)-3,4-dihydropyrazole-2-carbonyl]-5-methyl-2-oxo-3,5,6,7-tetrahydrothiopyrano[2,3-d]thiazol-7-yl] phenoxy]acetic acid



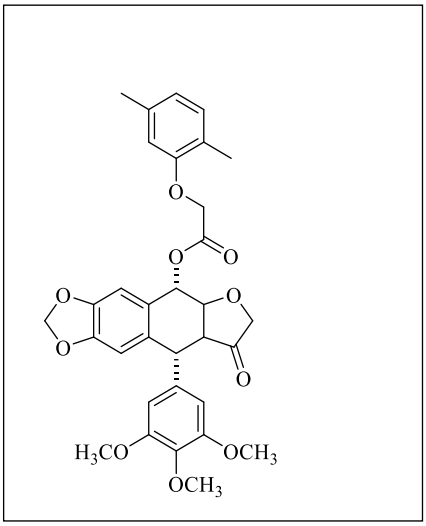
Structure 27. 1-(4-bromophenyl)-4-(phenoxy)acetylthio semicarbazide
IC50 = 104.86 microM and 145.39 microM



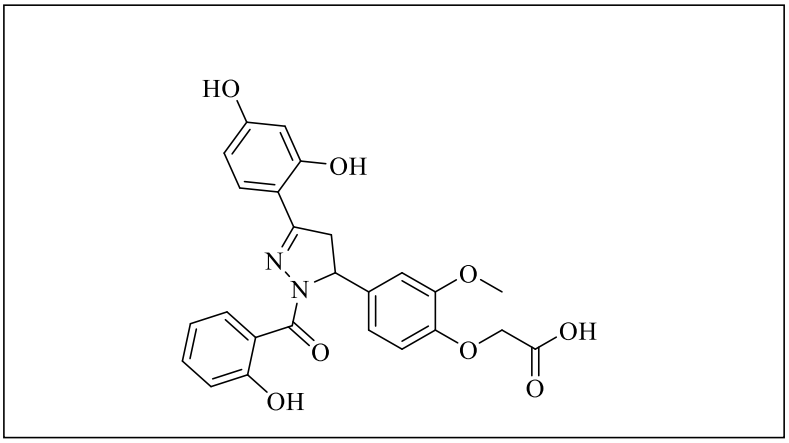
Structure 28. 2-(4-chlorophenoxy)-5-(4-chl orophenyl)pentanoic acid
IC50=4.8±0.35µM



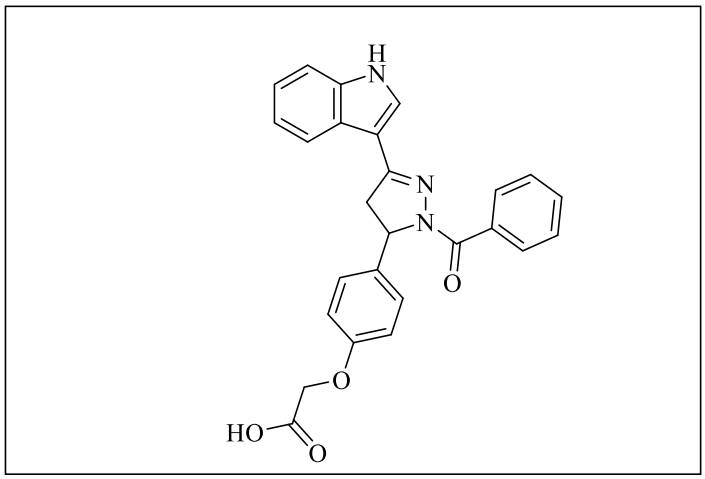
Structure 29. 2-(4-chlorophenoxy)acetic acid
MIC= 0.194±0.09µg/ml



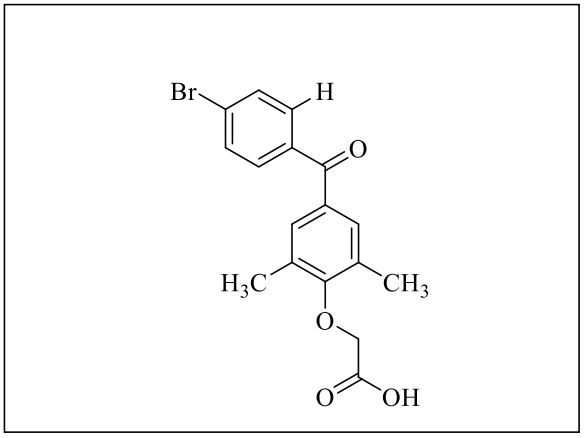
Structure 30. (5*S*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,7,8,8a,9-hexahydrofuro[2',3':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2,5-dimethylphenoxy)acetate IC_{50}1.64+0.41microM



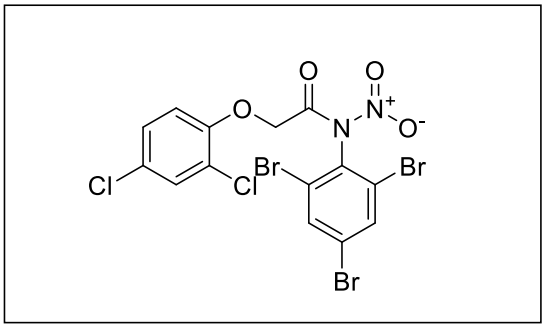
Structure 31. 2-(4-(3-(2,4-dihydroxyphenyl)-1-(2-hydroxybenzoyl)-4,5-dihydro-1*H*-pyrazol-5-yl)-2-methoxyphenoxy)acetic acid
MIC_{50} ; 0.16microgram/ml



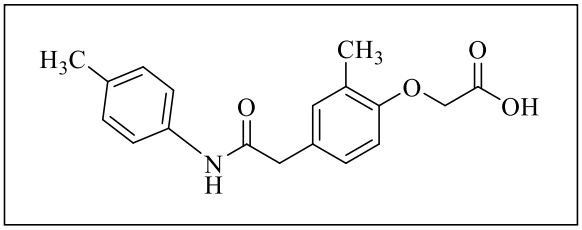
Structure 32. 2-(4-(1-benzoyl-3-(1H-indol-3-yl)-4,5-dihydro-1H-pyrazol-5-yl) phenoxy) acetic acid
IC50: 0.68 ± 0.13 lM



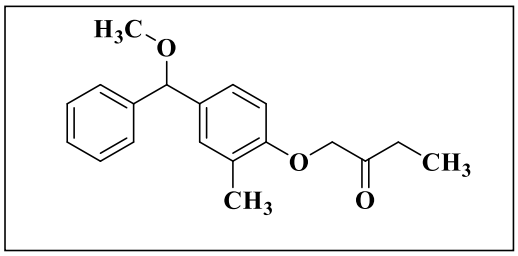
Structure 33. 2-(4-(4-bromobenzoyl)-2,6-dimethyl phenoxy)acetic acid
IC50= 18.94 + 0.24µg/ml



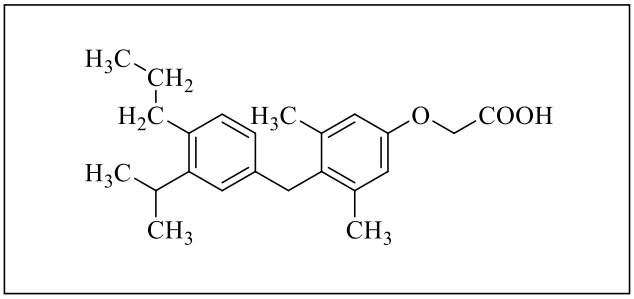
Structure 34. 2-(2,4-dichlorophenoxy)-*N*-nitro-*N*-(2,4,6-tribromophenyl)acetamide



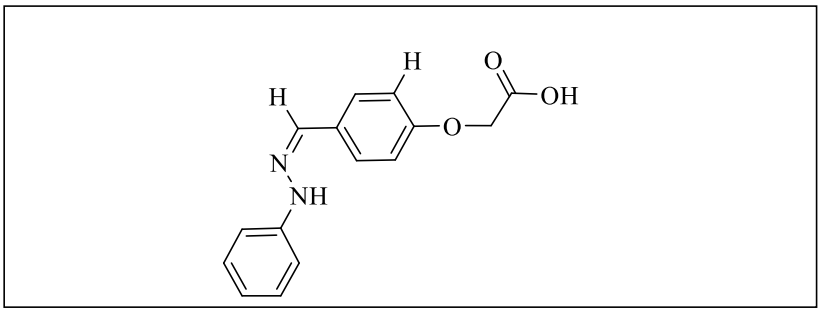
Structure 35. 2-(2-methyl-4-(2-oxo-2-(*p*-tolylamino) ethyl)phenoxy)acetic acid



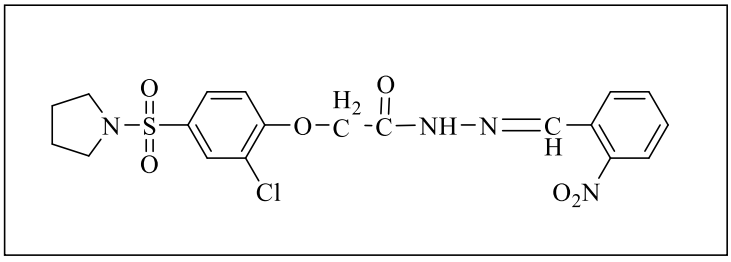
Structure 36. 1-(4-(methoxy(phenyl)methyl)-2-methylphenoxy) butan-2-one(IC50: 10.30 ± 0.25 µg/mL)



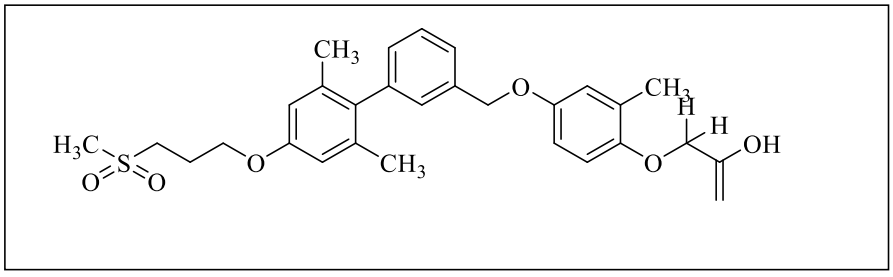
Structure 37. 2-(4-(3-isopropyl-4-propylbenzyl)-3,5-dimethylphenoxy)acetic acid
Mean stimulation=86%



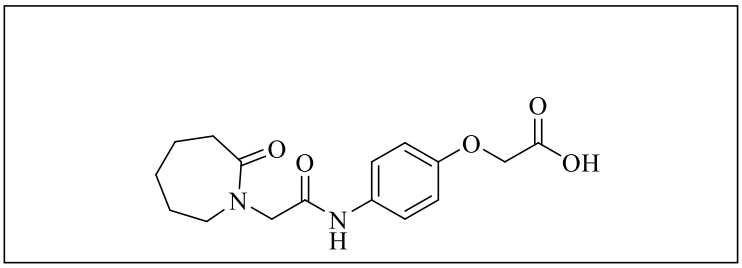
Structure 38. (*Z*)-2-(4-((2-phenylhydrazono)methyl)phenoxy)acetic acid
CTC $_{50}$ 88.87microg/ml



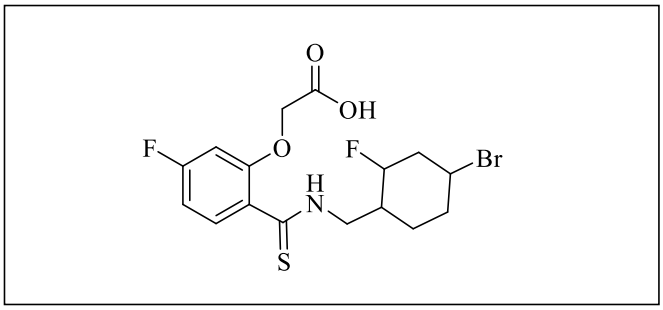
Structure 39. 2-(2-chloro-4-(pyrrolidin-1-ylsulfonyl)phen oxy)-*N*'-(2-nitrobenzylidene)acetohydrazide
Diameter of inhibition= 43mm



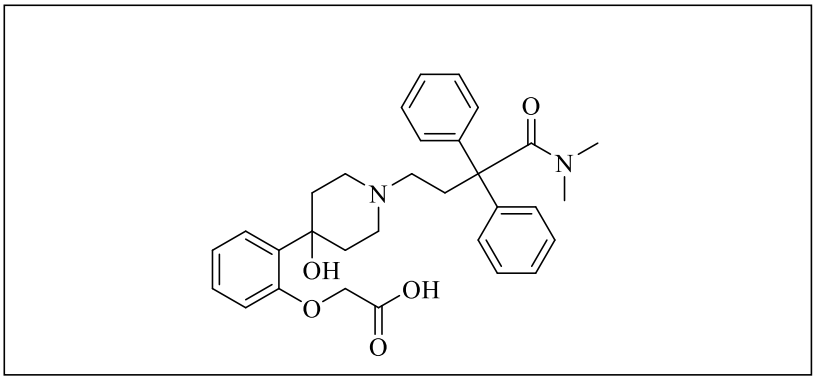
Structure 40. 3-(4-((2',6'-dimethyl-4'-(3-(methylsulfonyl)propoxy) -[1,1'-biphenyl]-3-yl)methoxy)-2-methylphenoxy) prop-1-en-2-olEC$_{50}$ 62.3nM



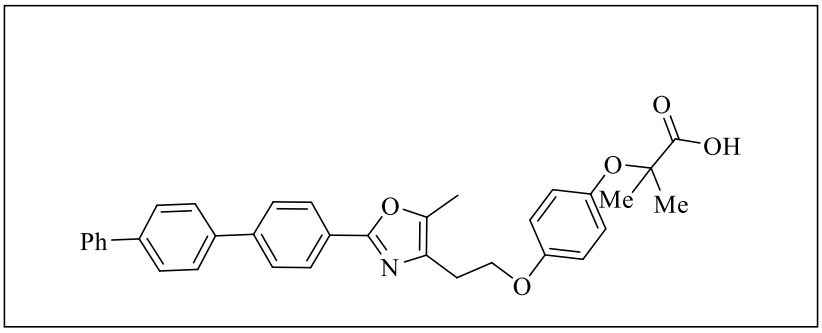
Structure 41. 2-{4-[2-(2-oxoperhydroazepin-1-yl)acetamido] phenoxy}acetic acid IC50= 449.5 microM



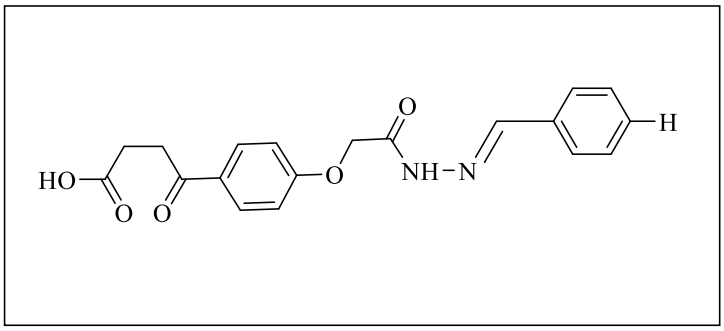
Structure 42. 2-(2-(((4-bromo-2-fluorocyclohexyl)methyl) carbamothioyl)-5-fluorophenoxy)acetic acid IC50=30nM



Structure 43. [2-[1-[3-(N,N-dimethylcarbamoyl)-3,3-diphenylpropyl] -4-hydroxypiperidin-4-yl]phenoxy]acetic acid Relative Potency=54.4+_6.6



Structure 44. 2-(4-(2-(2-([1,1':4',1''-terphenyl]-4-yl)-5-methyloxazol-4-yl) ethoxy)phenoxy)-2-methylpropanoic acid IC $_{50}$ 174+17 microg/ml



(Structure 45. *E*)-4-(4-(2-(2-benzylidenehydrazinyl)-2-oxoethoxy) phenyl)-4-oxobutanoic acid

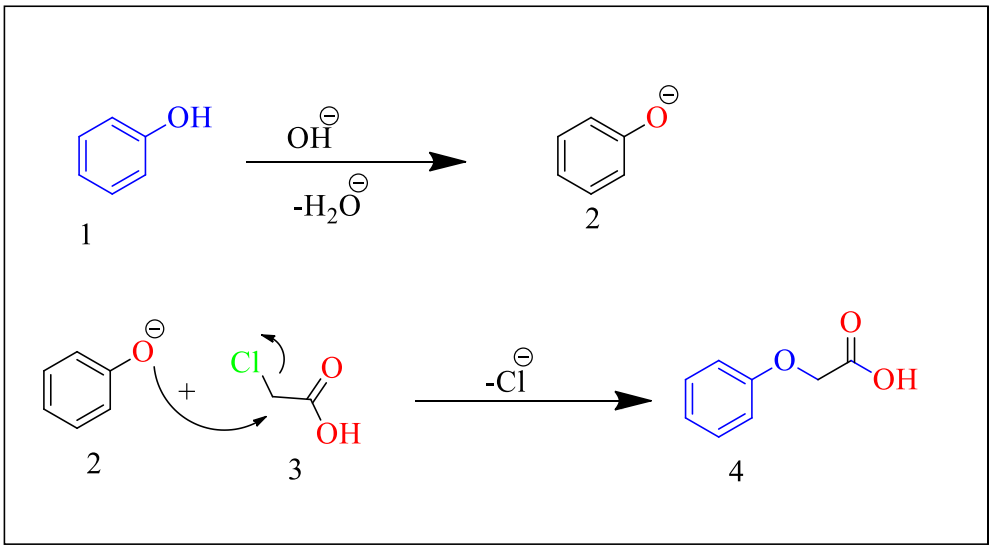


fig. 4 mechanism for the formation of phenoxyacetic acid (48)

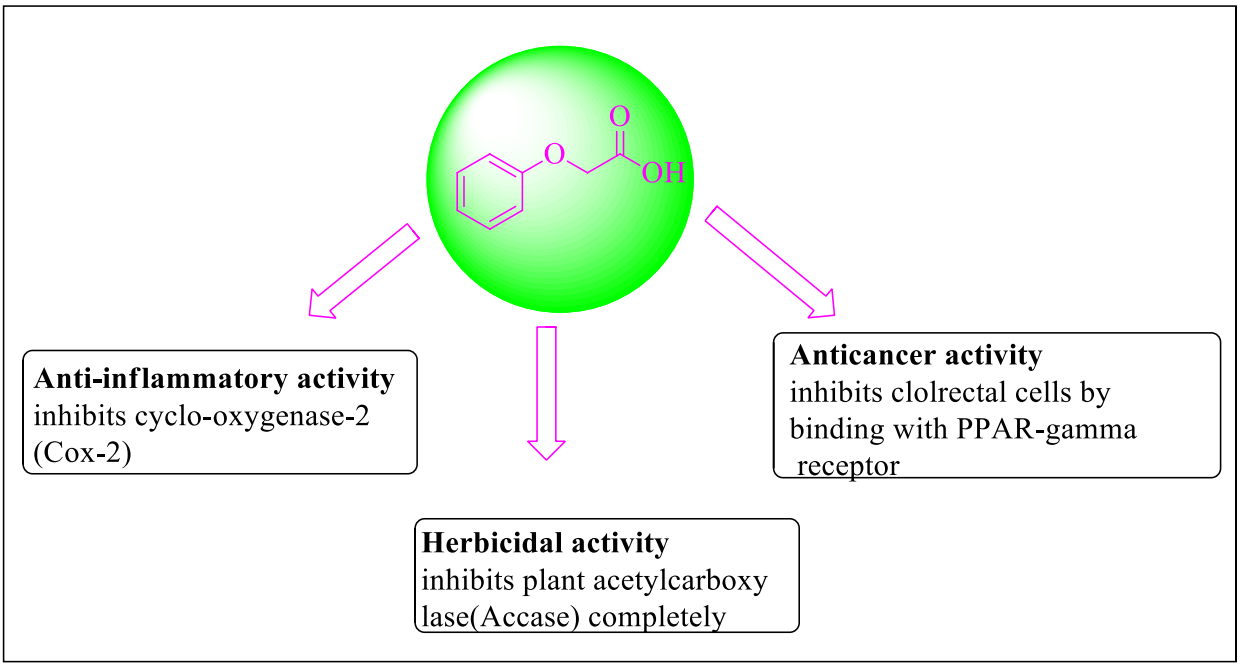
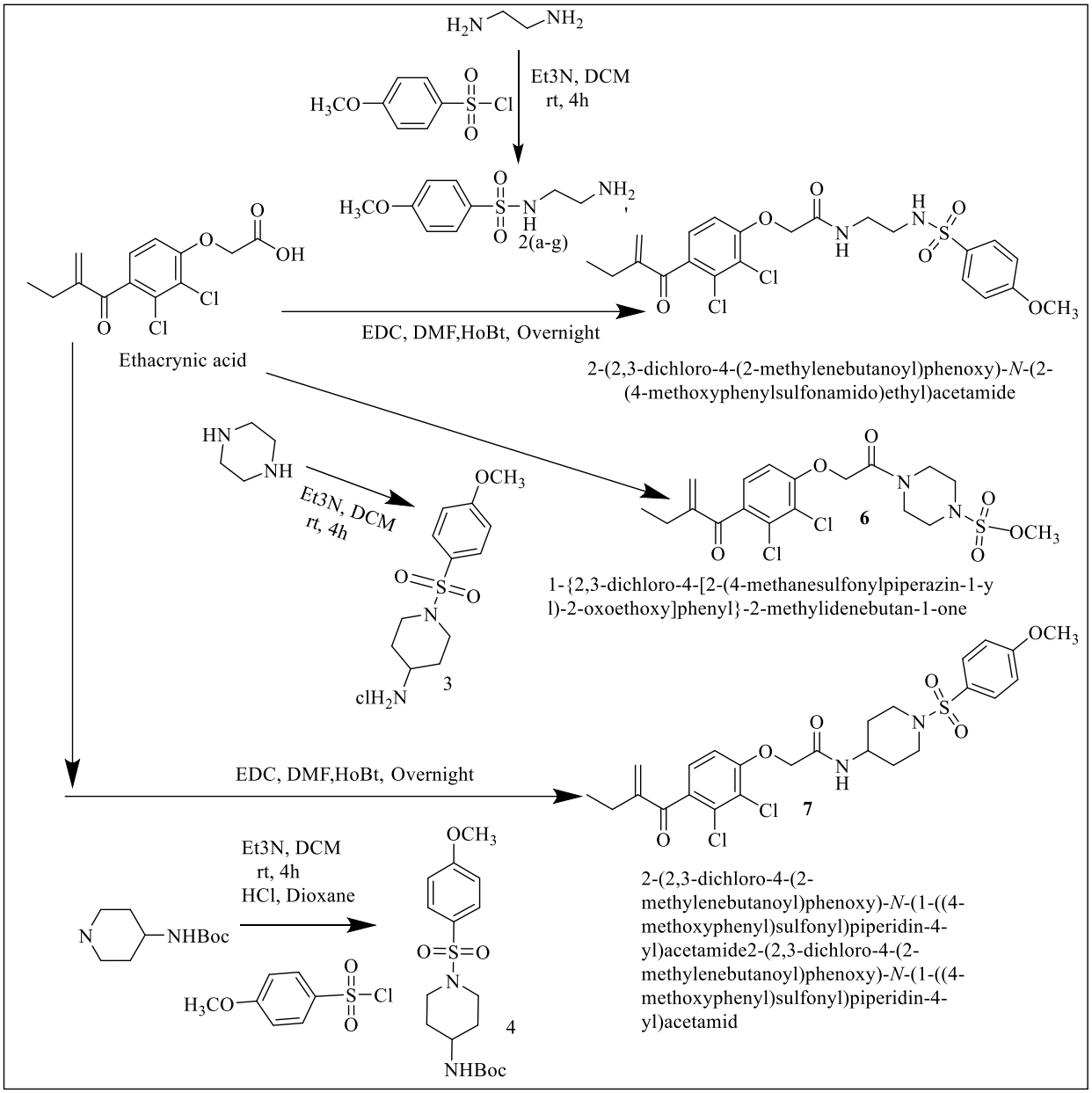
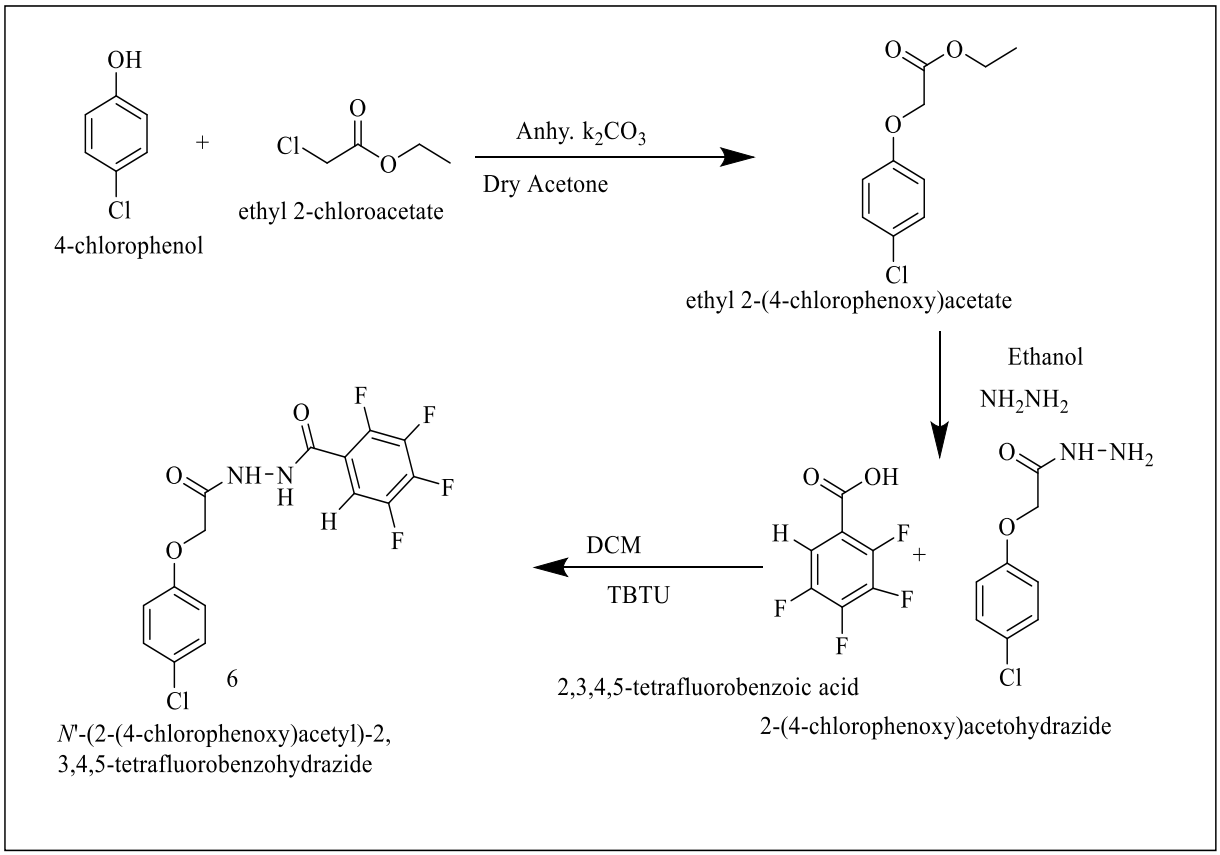


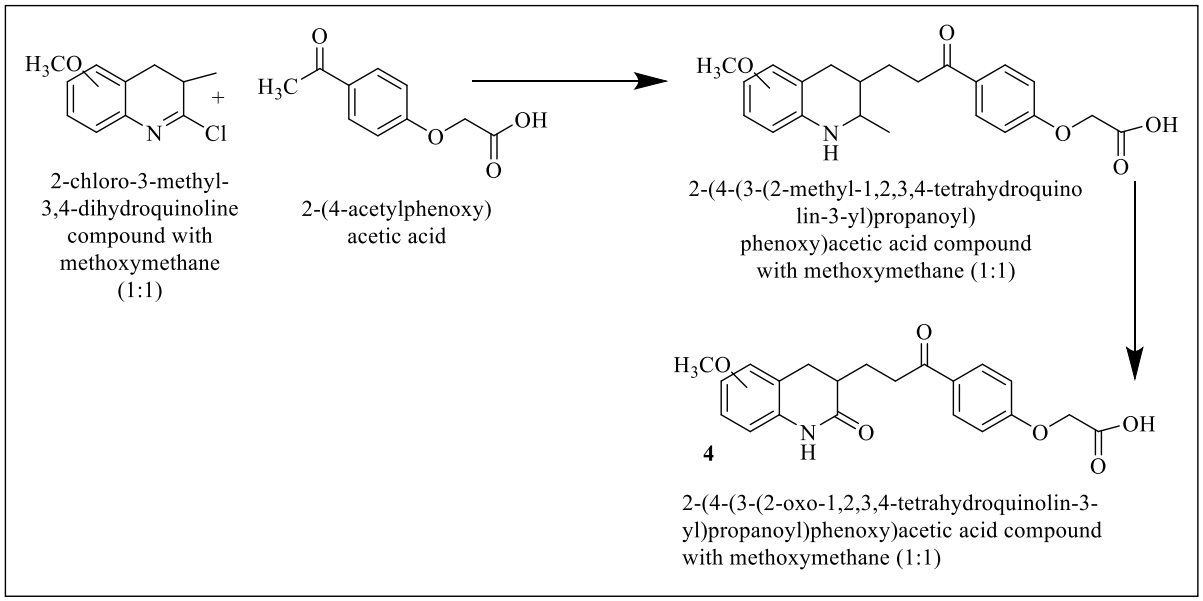
fig. 5 some targeting enzymes inhibiting site of phenoxyacetic acid derivatives



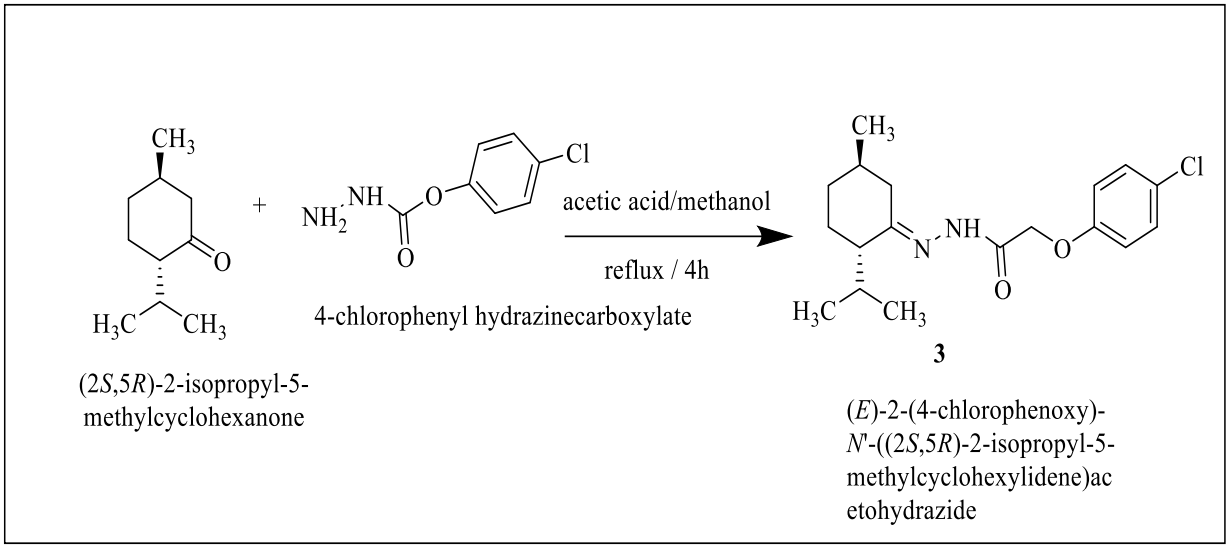
Scheme 1: Synthesis of2-(2,3-dichloro-4-(2-methylenebutanoyl)phenoxy)-*N*-(1-((4-methoxyphenyl)sulfonyl)piperidin-4-yl)acetamide2-(2,3-dichloro-4-(2-methylenebutanoyl)phenoxy)-*N*-(1-((4-methoxyphenyl)sulfonyl)piperidin-4-yl)acetamide



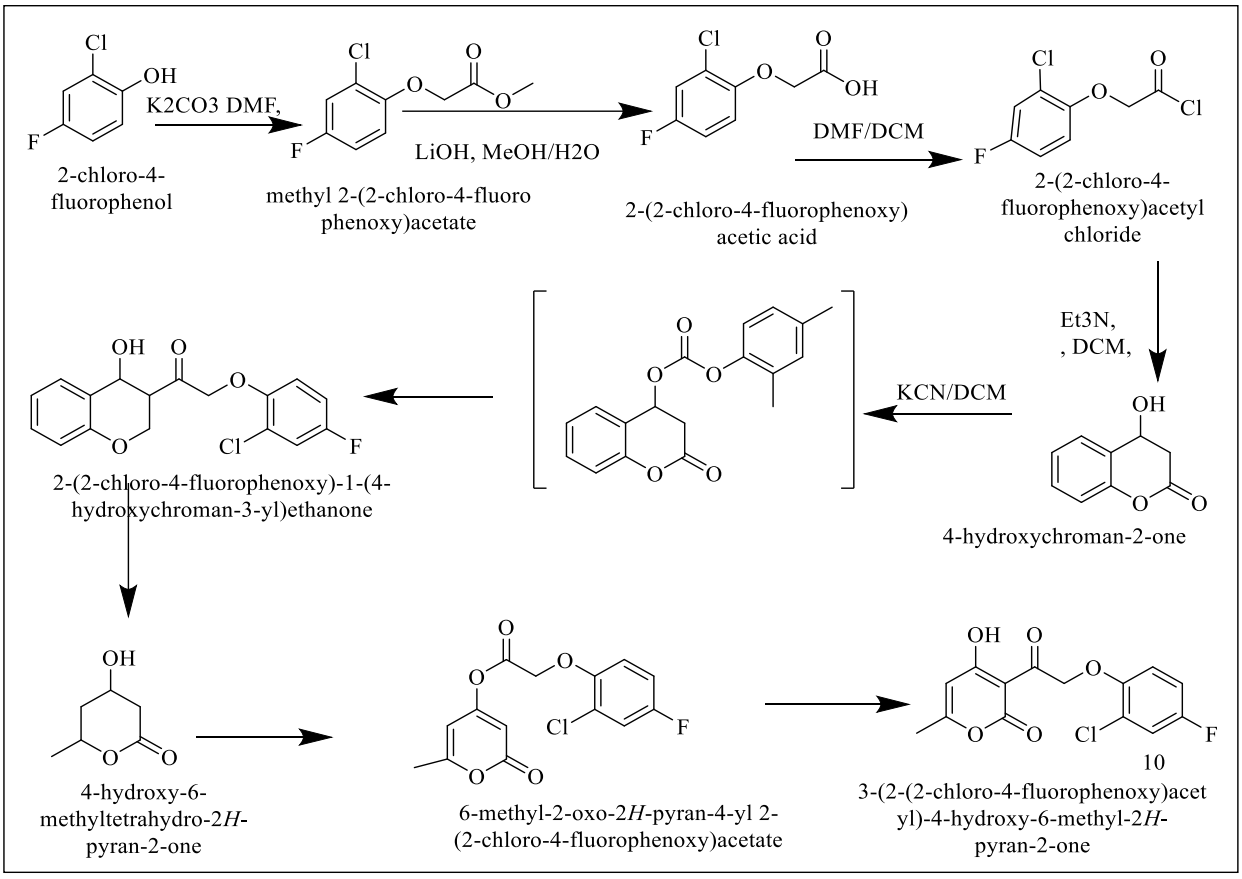
Scheme 2 Synthesis of *N*'-(2-(4-chlorophenoxy)acetyl)-2,3,4,5-tetrafluorobenzohydrazide



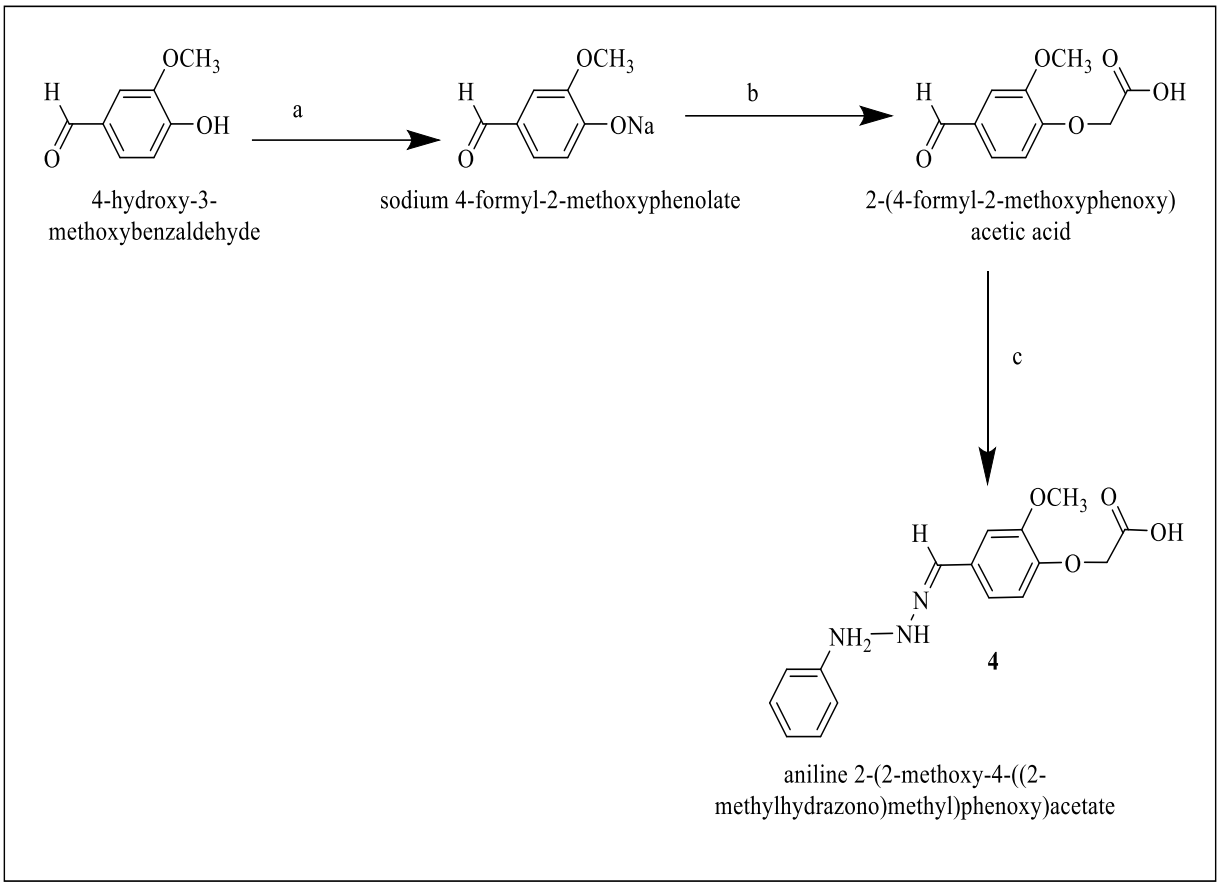
Scheme 3 Synthesis of 2-(4-(3-(2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)propanoyl)phenoxy)acetic acid compound with methoxymethane (1:1)



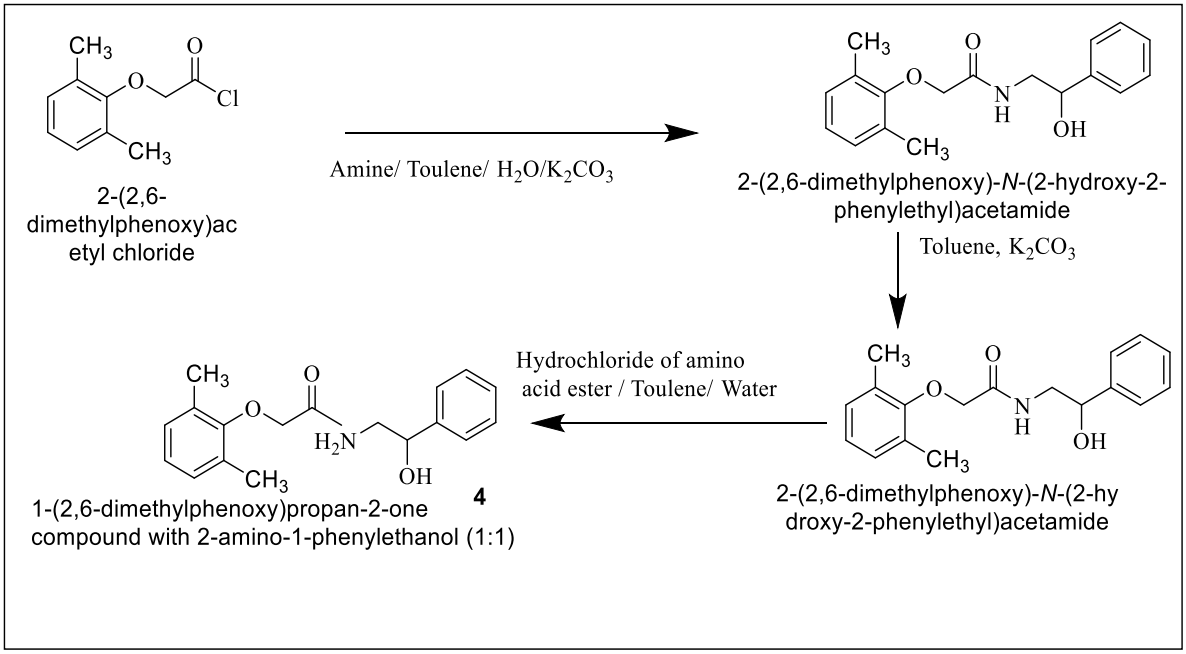
Scheme:-4(*E*)-2-(4-chlorophenoxy)-*N*'-((2*S*,5*R*)-2-isopropyl-5-methylcyclohexylidene)acetohydrazide



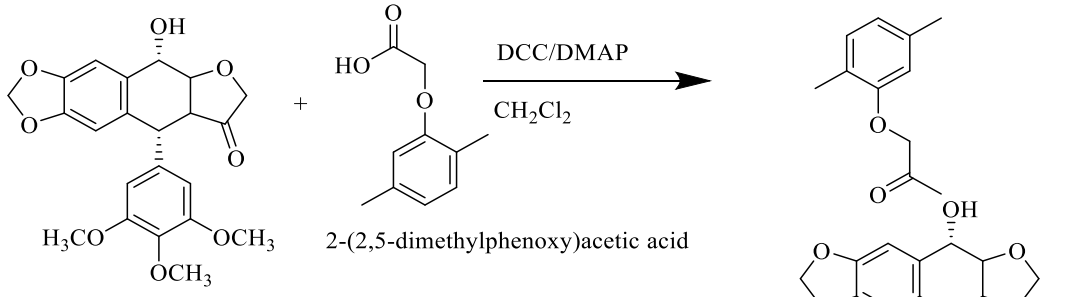
Scheme :5 synthesis of 3-(2-(2-chloro-4-fluorophenoxy)acetyl)-4-hydroxy-6-methyl-2*H*-pyran-2-one



Scheme:-6 Synthesis ofaniline 2-(2-methoxy-4-((2-methylhydrazono)methyl)phenoxy)acetate



Scheme 71-(2,6-dimethylphenoxy)propan-2-one compound with 2-amino-1-phenylethanol (1:1)

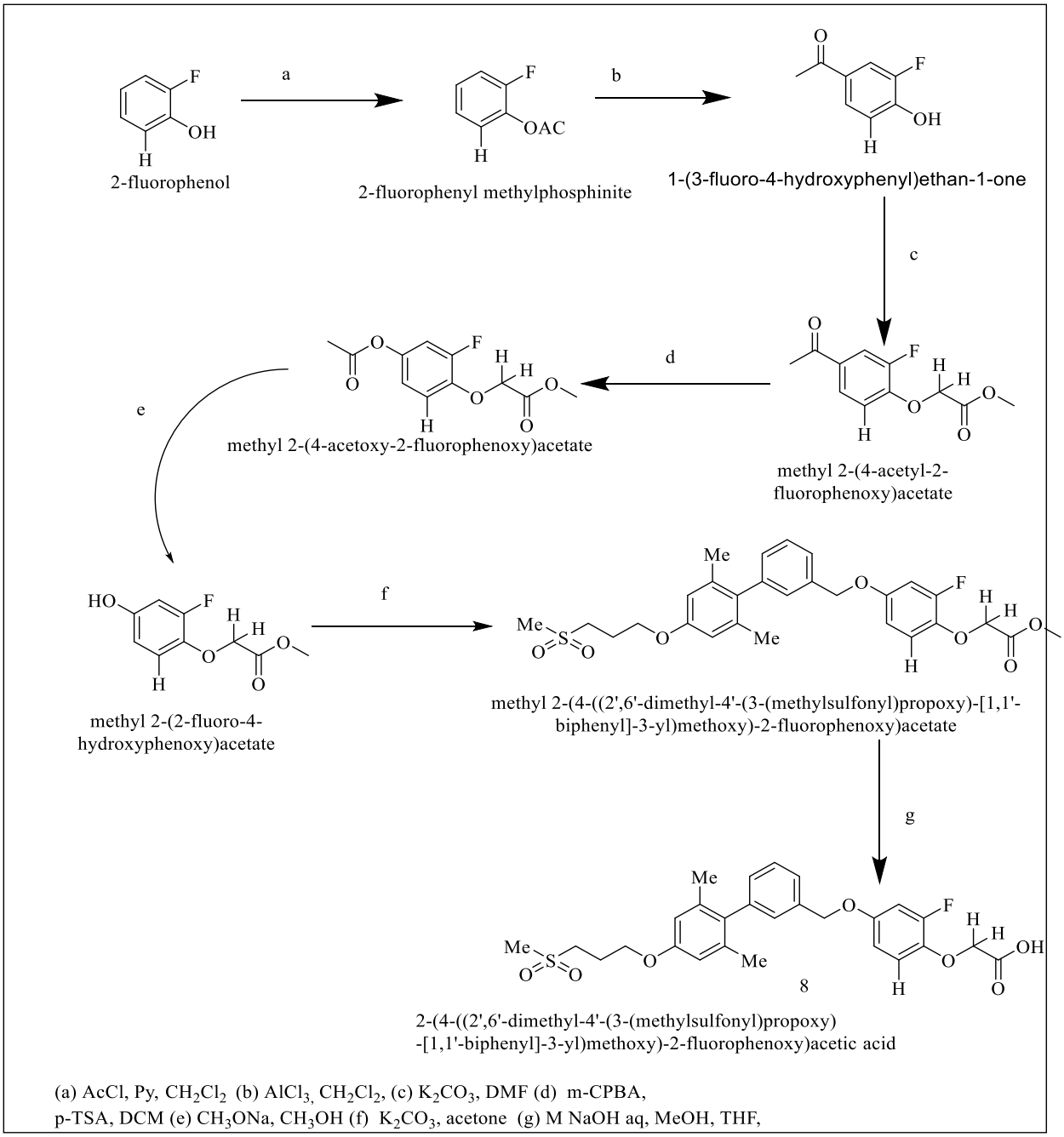


2-(2,5-dimethylphenoxy)acetic acid

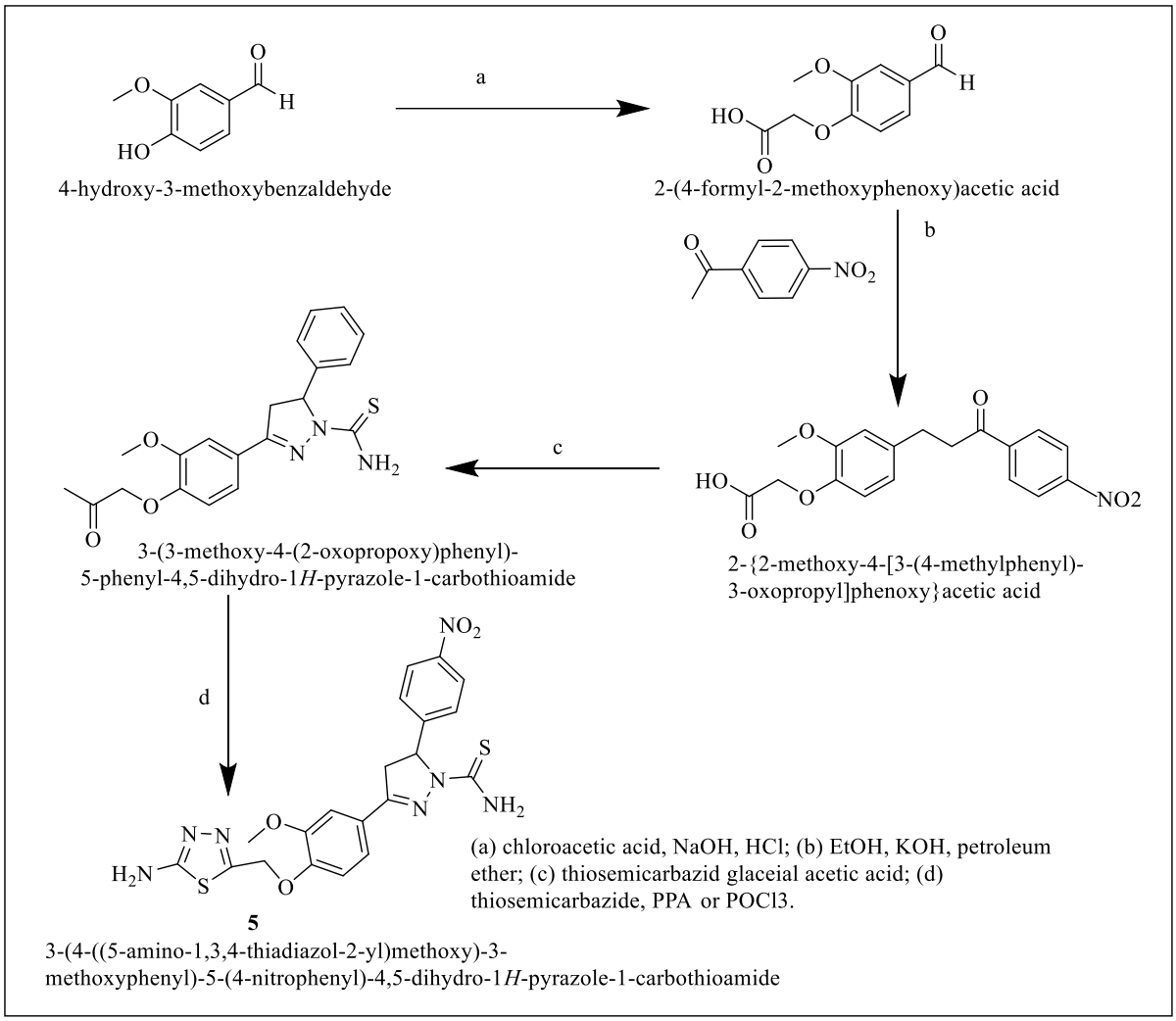
(5*S*,9*R*)-5-hydroxy-9-(3,4,5-trimethoxyphenyl)-5,5a,8a,9-tetrahydrofuro[2',3':6,7]naphtho[2,3-*d*][1,3]dioxol-8(7*H*)-one

(5*S*,9*R*)-5-hydroxy-9-(3,4,5-trimethoxyphenyl)-5,5a,8a,9-tetrahydrofuro[2',3':6,7]naphtho[2,3-*d*][1,3]dioxol-8(7*H*)-one compound with 1-(2,5-dimethylphenoxy)propan-2-one (1:1)

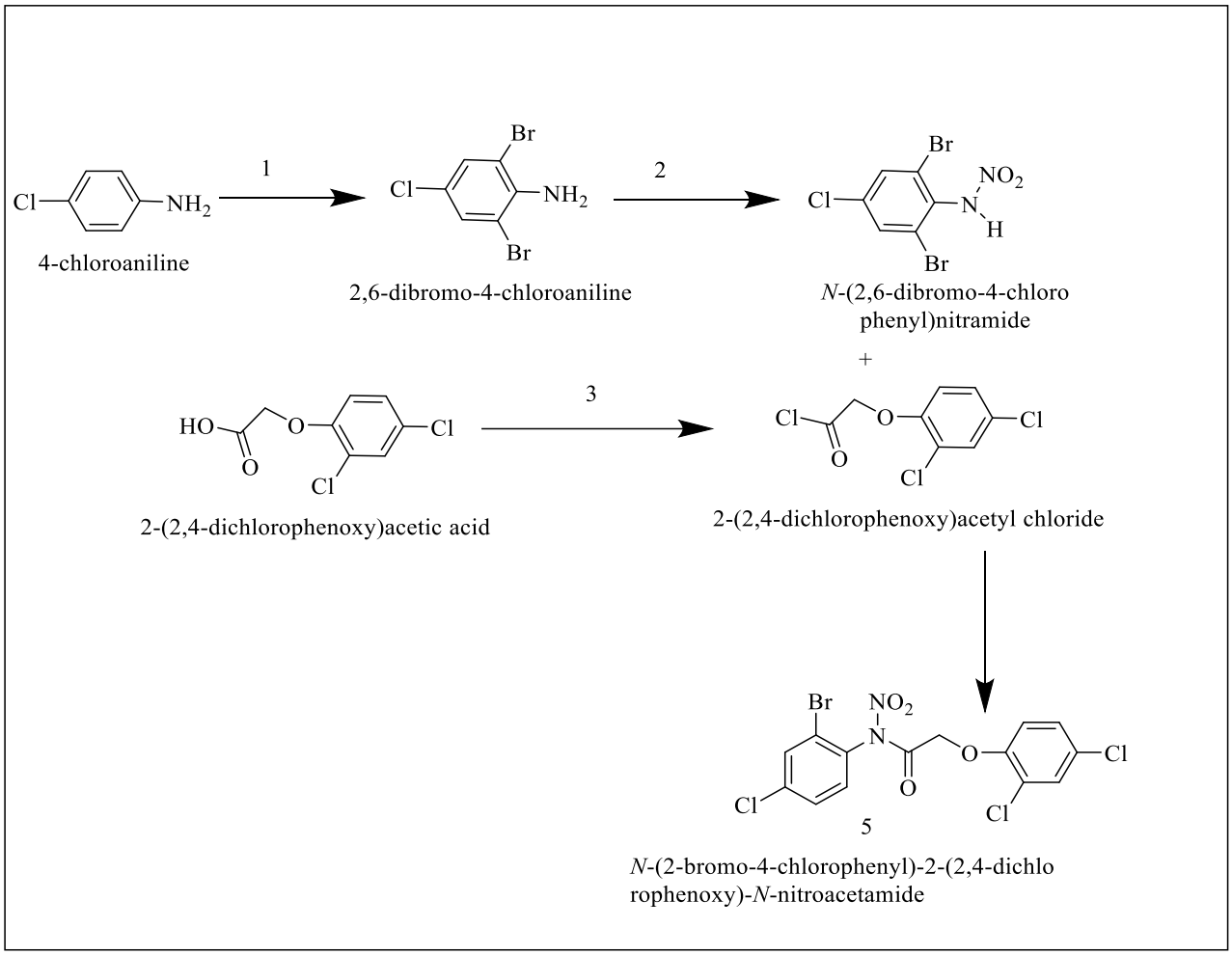
Scheme:- 8 Synthesisof(5*S*,9*R*)-5-hydroxy-9-(3,4,5-trimethoxyphenyl)-5,5a,8a,9-tetrahydrofuro[2',3':6,7]naphtho[2,3-*d*][1,3]dioxol-8(7*H*)-one compound with 1-(2,5-dimethylphenoxy)propan-2-one (1:1)



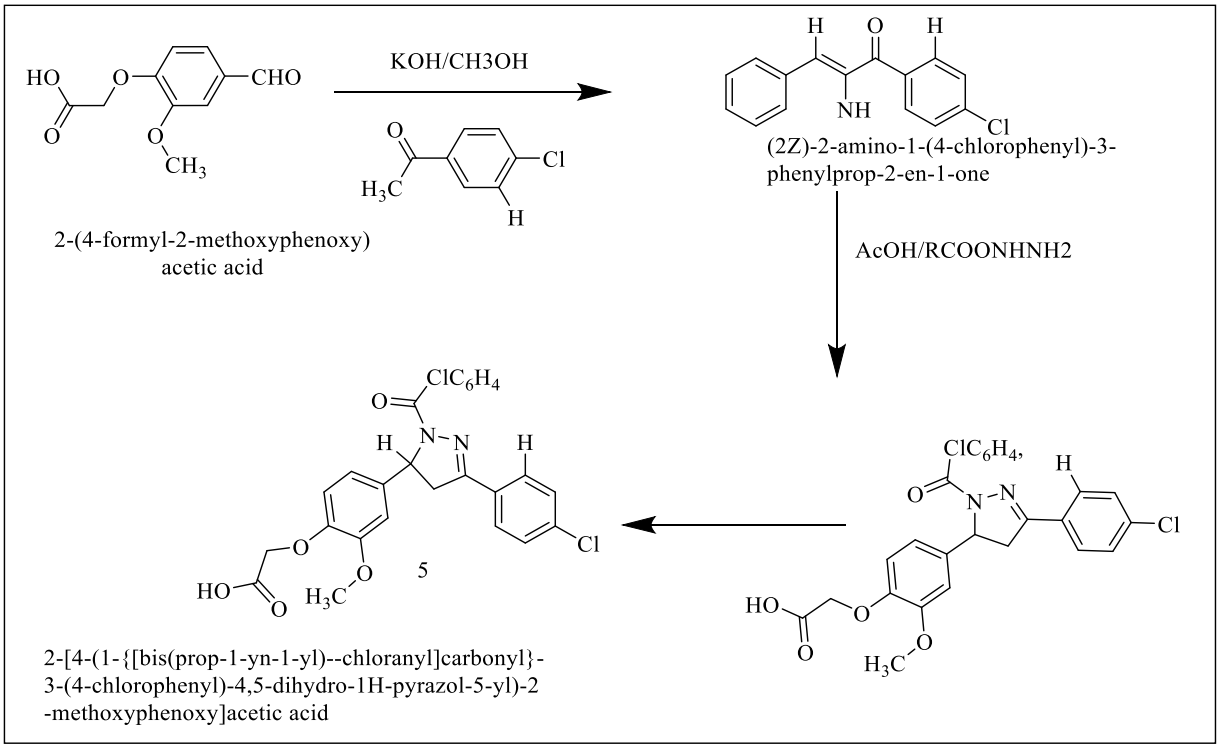
Scheme 9 synthesis of 2-(4-((2',6'-dimethyl-4'-(3-(methylsulfonyl)propoxy)-[1,1'-biphenyl]3yl)methoxy)-2-fluorophenoxy)acetic acid



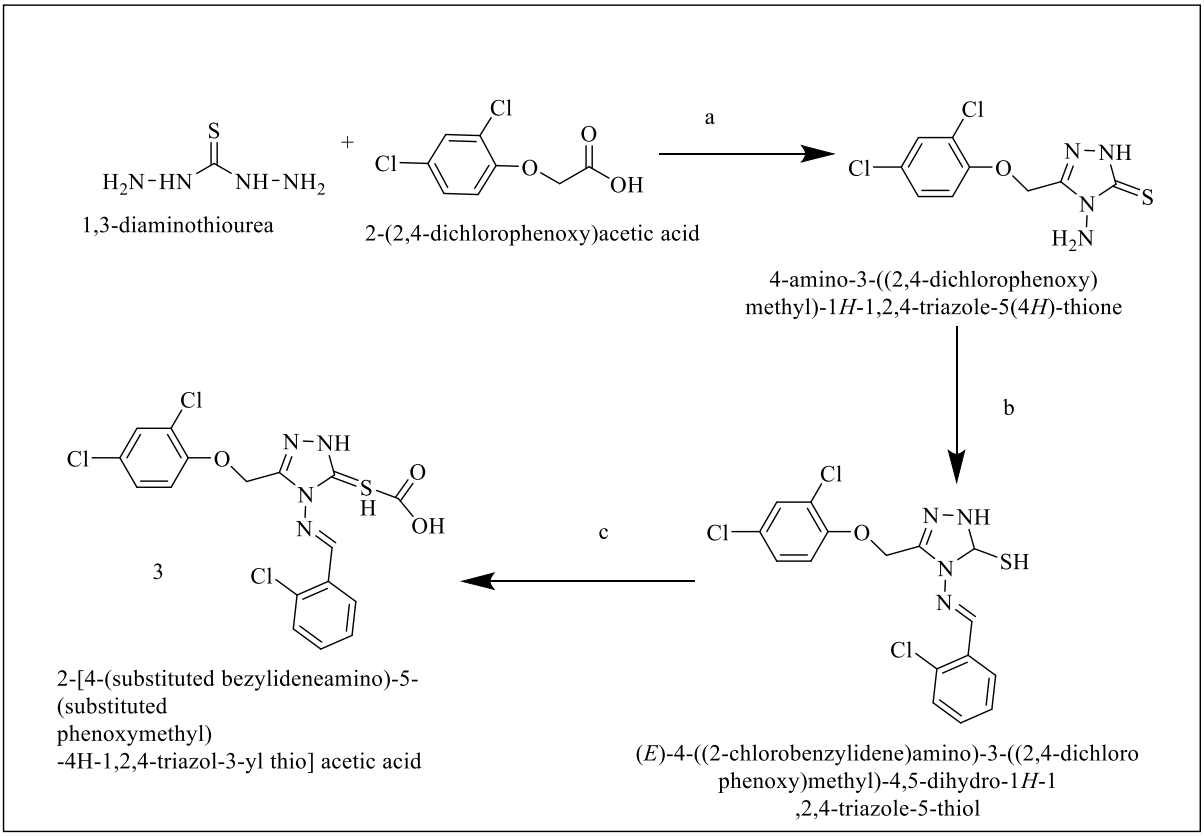
Scheme 10 -3-(4-((5-amino-1,3,4-thiadiazol-2-yl)methoxy)-3-methoxyphenyl)-5-(4-nitrophenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide



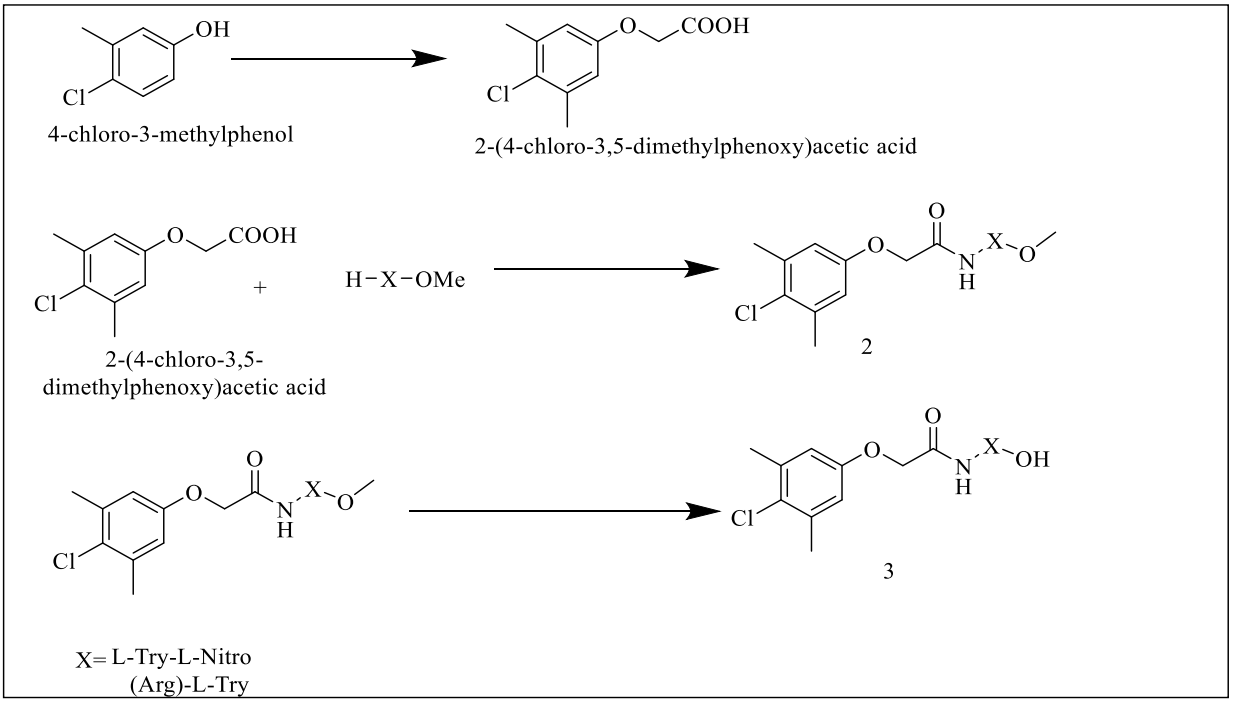
Scheme 11 synthesis of *N*-(2-bromo-4-chlorophenyl)-2-(2,4-dichlorophenoxy)-*N*-nitroacetamide (1)HBr, 30% H_2O_2,H_2O (2 $AcONO_2$, AcOH, Ac_2O, 1–1.5 h. (3) $SOCl_2$ CCl_4,, 0.5 h; (4) Et_2O, 0.5 h



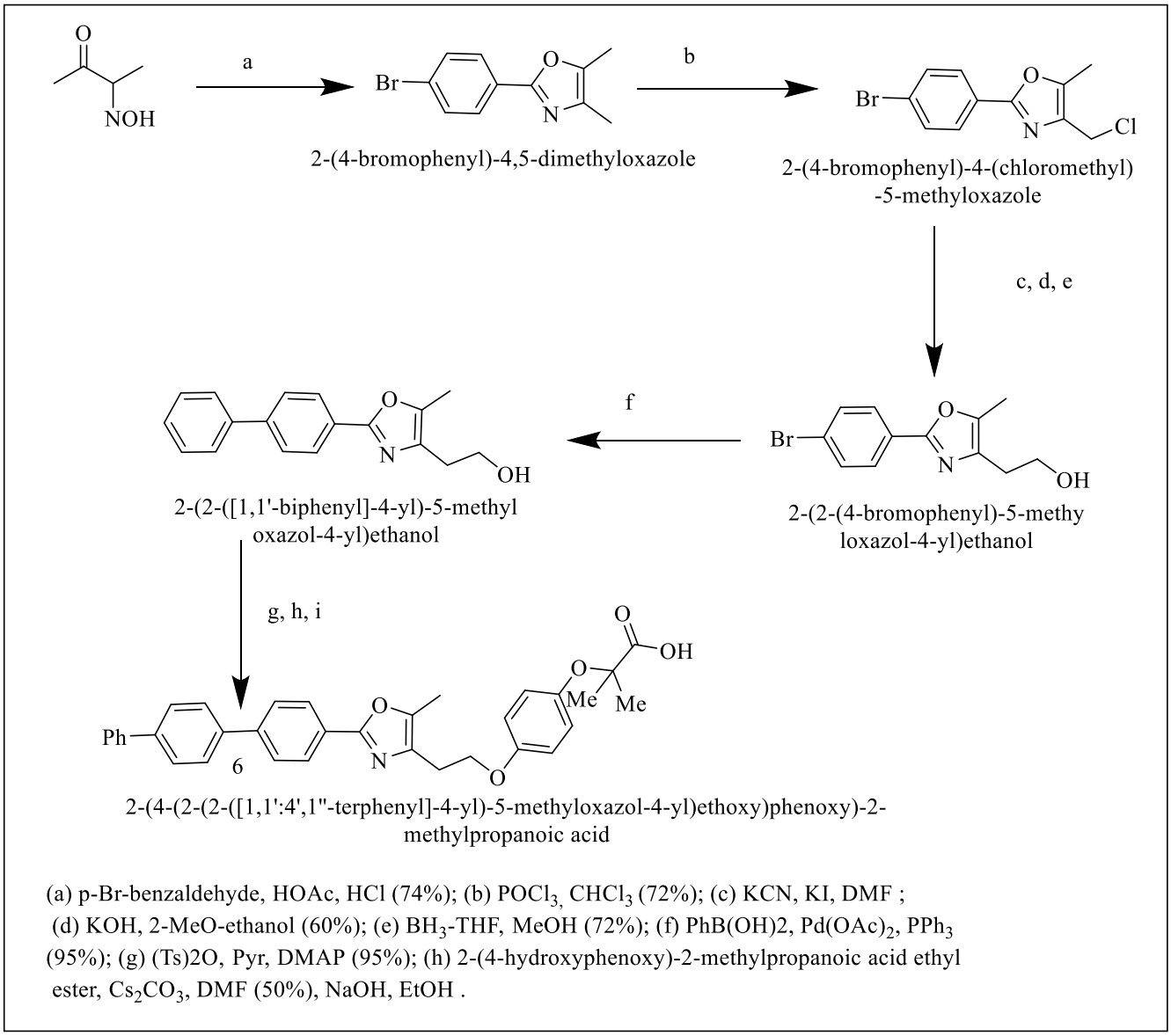
Scheme:-12 Synthesis of 2-[4-(1-{[bis(prop-1-yn-1-yl)-chloranyl]carbonyl}-3-(4-chlorophenyl)-4,5-dihydro-1H-pyrazol-5-yl)-2-hydroxyphenoxy]acetic acid



Scheme 13:= Synthesis of 2-[4-(substituted bezylideneamino)-5-(substituted phenoxymethyl) -4H-1,2,4-triazol-3-yl thio] acetic acid derivative 3 Reagents and conditions: (a) Heat 175–180 C, oil bath, 2–3 h. (b) Aromatic aldehydes, absolute ethanol, re?ux, 2 h. (c) Chloroacetic acid, ethanol, refux, 2–hr

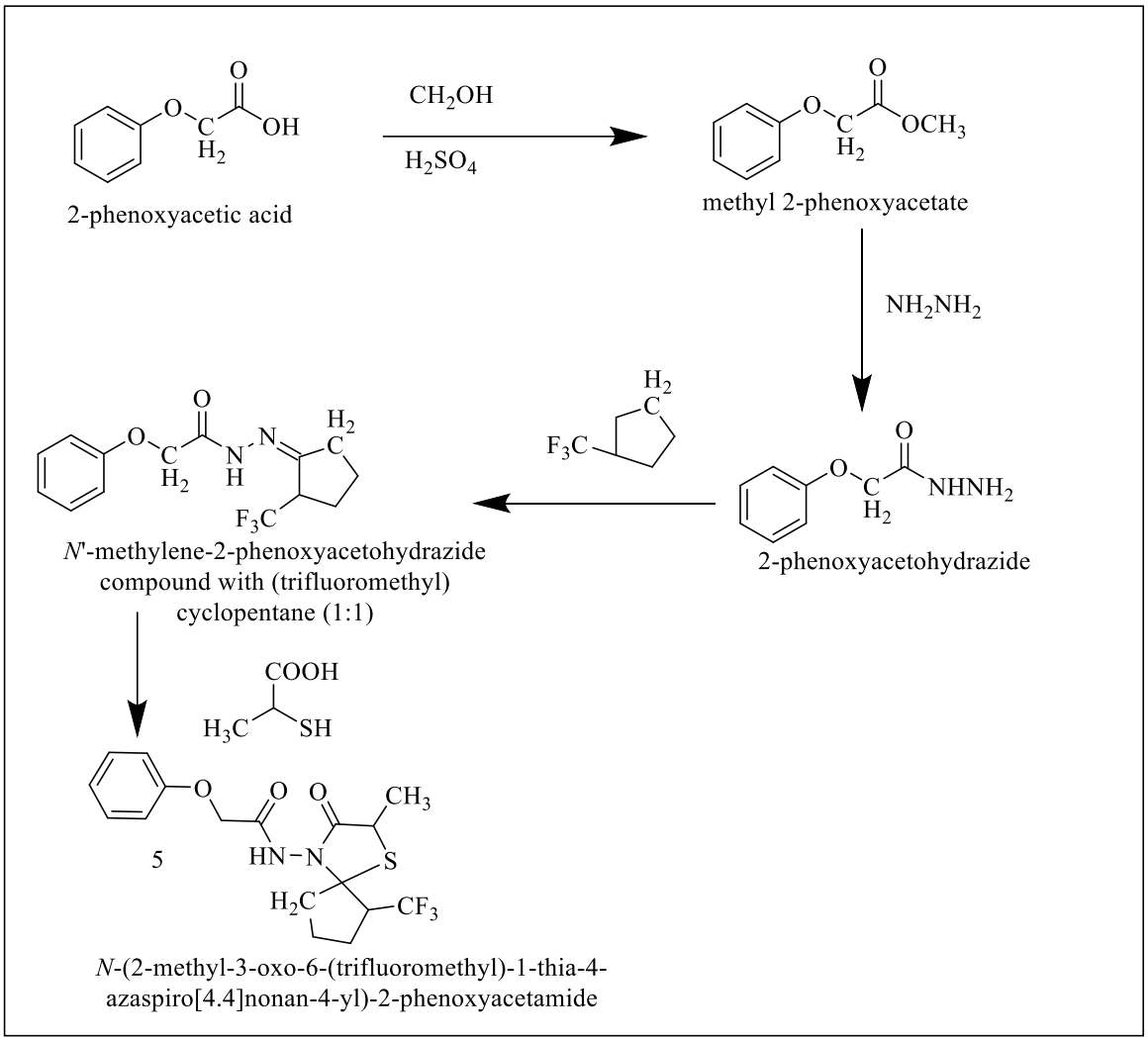


Scheme :14 Synthetic pathway for novel 3,4,5-trisubstituted phenoxyacetic acid analogs.

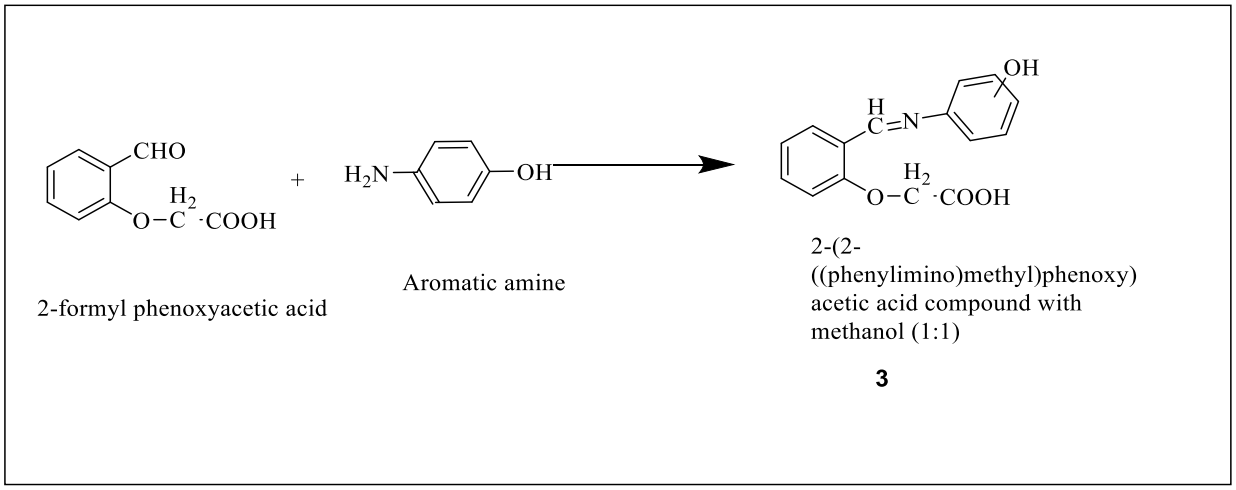


(a) p-Br-benzaldehyde, HOAc, HCl (74%); (b) $POCl_3$, $CHCl_3$ (72%); (c) KCN, KI, DMF ; (d) KOH, 2-MeO-ethanol (60%); (e) BH_3-THF, MeOH (72%); (f) PhB(OH)2, $Pd(OAc)_2$, PPh_3 (95%); (g) (Ts)2O, Pyr, DMAP (95%); (h) 2-(4-hydroxyphenoxy)-2-methylpropanoic acid ethyl ester, Cs_2CO_3, DMF (50%), NaOH, EtOH .

Scheme :- 15 synthesis of 2-(4-(2-(2-([1,1':4',1''-terphenyl]-4-yl)-5-methyloxazol-4-yl)ethoxy)phenoxy)-2-methylpropanoic acid



Scheme: 16 Synthesis of*N*-(2-methyl-3-oxo-6-(trifluoromethyl)-1-thia-4-azaspiro[4.4]nonan-4-yl)-2-phenoxyacetamide



Scheme :-17 synthesis of 2-(2-((phenylimino)methyl)phenoxy)acetic acid compound with methanol (1:1)