



Synthesis, Characterization and Antibacterial Activity of Some Prop-2-ynyl 2-[[2-((E)-(benzoylhydrazono)methyl)phenyl]sulfanyl]acetate Derivatives

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Received: 26 August 2015;

Accepted: 12 October 2015;

Published online: 30 January 2016;

AJC-17746

A series of eleven new hydrazone-hydrazone derivatives (**7a-7k**) have been synthesized from prop-2-ynyl-2-(2-formylphenylthio)acetate (**5**) which was derived by condensation of 2-mercaptobenzaldehyde (**1**) with prop-2-ynyl-2-bromoacetate (**4**). Structures of synthesized compounds have been established by spectral analysis. The synthesized prop-2-ynyl 2-[[2-((E)-(benzoylhydrazono)methyl)phenyl]sulfanyl]acetate derivatives (**7a-7k**) were tested against Gram-positive strains of (i) *Staphylococcus aureus* (MTCC 96) and (ii) *Streptococcus pyogenes* (MTCC 442) and Gram-negative strains of (iii) *Escherichia coli* (MTCC 443) and (iv) *Pseudomonas aeruginosa* (MTCC 424) using agar well diffusion method. Norfloxacin was used as the reference antibacterial drug. Compounds **7i** (R = 4-SO₂Me) and **7j** (R = 2,5-difluoro) showed excellent activity with zone of inhibition 29 and 30 mm, respectively, while the compounds **7h** (R = 4-CN) and **7k** (R = 3-NO₂) showed good antibacterial activity with zone of inhibition 23 and 22 mm, respectively against *E. coli*. The compounds showed similar trends against *P. aeruginosa*, *S. aureus* and *S. pyogenes*.

Keywords: Antibacterial activity, Acetylene compounds, Hydrazones, 2-Mercaptobenzaldehyde, Propargyl alcohol.

INTRODUCTION

Acid hydrazides and the corresponding hydrazones are well known as a class of compounds with diverse biological activities [1-3]. N-acylhydrazone (NAH) subunit has occupied a prominent place in the pharmacophoric framework of agents especially as potent antinociceptive [4-6], antiplatelet [7-9], anti-inflammatory [10] and cardiac stimulant activities [11-13]. Infectious diseases caused by microorganisms are one of the main reasons of death in the world. The search for new antibacterial and antifungal drugs has become a continuous exploration because of the increasing resistance of microbial pathogens. It is enviable to find drugs with improved potency and wide activity spectrum.

Acetylenic metabolites belong to a class of molecules containing triple bond(s). They are found in plants, fungi, microorganisms and marine invertebrates. Although acetylenes are common as components of terrestrial plants, fungi and bacteria, it is only within the last 30 years that biologically active polyacetylenes having unusual structural features have been reported from plants, cyanobacteria, algae, invertebrates and other sources. Alkynes or acetylenic compounds play an important role as building blocks in many synthetic trans-

formations and in new materials. In addition, acetylenic group is common structural motif found in various natural products and also of great interest in medicinal chemistry and the pharmaceutical industry [14]. It moreover functions as a key pharmacophoric unit in acetylenic antibiotics [15] and its presence in anticancer [16] and antitubercular [17] agents is noteworthy. The aim of the present study was to synthesize a set of new hydrazone-hydrazone derivatives (**7a-7k**) from prop-2-ynyl-2-(2-formylphenylthio)acetate and evaluation of their anti-bacterial activity.

EXPERIMENTAL

Chemicals and solvents were purchased from Sigma-Aldrich and Merck. All the reagents were of analytical grade. Thin-layer chromatography (TLC) was performed on E. Merck AL silica gel 60 F254 plates and visualized under UV light. IR spectra were recorded as KBr pellets with Perkin-Elmer Spectrum GX FTIR instrument and only diagnostic and/or intense peaks were reported. ¹H NMR spectra were recorded in DMSO-*d*₆ with Varian Mercury plus 400 MHz instrument and in CDCl₃ + 1 drop DMSO-*d*₆ with Bruker BioSpin GmbH 300 MHz instrument. Signals due to the residual protonated solvent (¹H NMR) served as the internal standard. All the chemical shifts were reported in δ (ppm) using TMS as internal

standard. The ^1H NMR chemical shifts and coupling constants were determined assuming first-order behaviour. Mass spectra were recorded with a PE Sciex model API 3000 instrument. All the reactions were carried out under nitrogen atmosphere.

Synthesis of prop-2-ynyl-2-bromoacetate (4): A mixture of 4-N,N-dimethylaminopyridine (DMAP) (100 mg, 0.820 mmol) and propargyl alcohol (**3**) (2 g, 35.68 mmol) was added to a stirred solution of 2-bromoacetic acid (**2**) (4.95 g, 35.68 mmol) in anhydrous dichloromethane (20 mL). Dicyclohexylcarbodiimide (DCC) (8.83 g, 42.82 mmol) was added at 0 °C to the reaction mixture, which was then stirred for 5 min at 0 °C and for 3 h at 20 °C. The dichloromethane layer solution was washed twice with 0.5 N HCl and with saturated sodium bicarbonate solution and then dried over MgSO_4 . The solvent was removed by evaporation, to obtain prop-2-ynyl-2-bromoacetate (**4**) as a pale yellow liquid. Yield: 4.50 g, 72 %. The crude compound was taken to next step without further purification.

Synthesis of prop-2-ynyl-2-(2-formylphenylthio)acetate (5): To a stirred mixture of 2-mercaptobenzaldehyde (**1**) (1 g, 7.25 mmol) and potassium carbonate (1.2 g, 8.70 mmol) in DMF (15 mL), prop-2-ynyl-2-bromoacetate (**4**) (1.35 g, 7.60 mmol) was added and heated at 70 °C for 2 h. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with dichloromethane (50 mL) followed by water (50 mL). The organic layer was separated, washed with water followed by brine solution, dried over sodium sulphate and evaporated to obtain pale compound (**5**) as a yellow solid. Yield: 1.3 g, 78 %; m.p.: 79–80 °C. ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 10.18 (s, 1H), 7.94 (dd, $J = 1.6, 7.6$ Hz, 1H), 7.63 (td, $J = 7.6, 1.6$ Hz, 1H), 7.47–7.40 (m, 2H), 4.75 (d, $J = 2.4$ Hz, 2H), 4.07 (s, 2H), 3.58 (t, $J = 2.4$ Hz, 1H); ESI-MS: m/z , 234.8 (M+1).

General experimental procedure for the synthesis of hydrazide-hydrazone derivatives (7a–7k): To a stirred solution of compound **5** (100 mg, 0.427 mmol) in ethanol (2 mL) was added corresponding benzohydrazides **6a–6k** (1 mmol) and refluxed for 1 h. The reaction mass was washed with petroleum ether, filtered and dried under vacuum to obtain the pure hydrazone compounds. Yields of the products varied between 75 and 90 %.

Prop-2-ynyl-2-((2-((E)-(benzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7a): White solid; Yield: 80 %; m.p.: 77–78 °C; IR (KBr, ν_{max} , cm^{-1}): 3322 ($\equiv\text{C-H}$ str), 3166 (N-H str), 2112 ($\text{C}\equiv\text{C}$), 1713 (C=O , ester), 1686 (C=O , CONH), 1651 (C=N), 1531 (N-H bend); ^1H NMR (300 MHz, CDCl_3 + DMSO): δ 11.80 (s, 1H), 9.06 (s, 1H), 8.16 (t, $J = 3.0$ Hz, 1H), 8.08 (d, $J = 6.2$ Hz, 2H), 7.52 (m, 5H), 7.37 (d, $J = 4.9$ Hz, 1H), 4.66 (d, $J = 2.5$ Hz, 2H), 3.68 (s, 2H), 2.66 (t, $J = 2.5$ Hz, 1H); ESI-MS: m/z , 352.8 (M+1).

Prop-2-ynyl-2-((2-((E)-(4-chlorobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7b): White solid; Yield: 86 %; m.p.: 106–108 °C; IR (KBr, ν_{max} , cm^{-1}): 3252 ($\equiv\text{C-H}$ str), 3213 (N-H str), 2126 ($\text{C}\equiv\text{C}$), 1727 (C=O , ester), 1649 (C=O , CONH), 1594 (C=N), 1545 (N-H bend); ^1H NMR (300 MHz, CDCl_3 + DMSO): δ 11.70 (s, 1H), 9.06 (s, 1H), 8.16 (t, $J = 3.0$ Hz, 1H), 7.98 (d, $J = 6.0$ Hz, 2H), 7.53 (t, $J = 3.0$ Hz, 1H), 7.44 (d, $J = 6.0$ Hz, 2H), 7.35 (t, $J = 3.0$ Hz, 2H), 4.65 (d, $J = 2.5$ Hz, 2H), 3.65 (s, 2H), 2.55 (t, $J = 2.5$ Hz, 1H); ESI-MS: m/z , 386.7 (M+1).

Prop-2-ynyl-2-((2-((E)-(3-chlorobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7c): White solid; Yield: 80 %; m.p.: 122–123 °C; IR (KBr, ν_{max} , cm^{-1}): 3266 ($\equiv\text{C-H}$ str), 3221 (N-H str), 2123 ($\text{C}\equiv\text{C}$), 1730 (C=O , ester), 1655 (C=O , amide), 1597 (C=N str), 1548 (N-H bend); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO}-d_6$): δ 11.70 (s, 1H), 9.07 (s, 1H), 8.16 (t, $J = 4.7$ Hz, 1H), 8.03 (s, 1H), 7.93 (d, $J = 7.7$ Hz, 1H), 7.74–7.05 (m, 5H), 4.66 (d, $J = 2.5$ Hz, 2H), 3.68 (s, 2H), 2.63 (t, $J = 2.6$ Hz, 1H); ESI-MS: m/z , 386.7 (M+1).

Prop-2-ynyl-2-((2-((E)-(2,4-dichlorobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7d): White solid; Yield: 84 %; m.p.: 128–130 °C; IR (KBr, ν_{max} , cm^{-1}): 3299 ($\equiv\text{C-H}$ str), 3208 (N-H str), 2131 ($\text{C}\equiv\text{C}$), 1750 (C=O , ester), 1665 (C=O , CONH), 1587 (C=N), 1537 (N-H bend); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO}-d_6$): δ 11.70 (*11.62, s, 1H), 8.92 (*8.59, s, 1H), 8.22–8.13 (m, 1H), 7.60–7.42 (m, 4H), 7.37 (d, $J = 7.3$ Hz, 2H), 4.66 (s, 2H), 3.65 (*3.59, s, 2H), 2.60 (d, $J = 3.7$ Hz, 1H) (*peak of minor rotamer); ESI-MS: m/z , 420.7 (M+1).

Prop-2-ynyl-2-((2-((E)-(3,5-dichlorobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7e): White solid; Yield: 84 %; m.p.: 118–119 °C; IR (KBr, ν_{max} , cm^{-1}): 3292 ($\equiv\text{C-H}$ str), 3282 (N-H str), 2130 ($\text{C}\equiv\text{C}$), 1731 (C=O ester), 1651 (C=O , CONH), 1566 (C=N); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO}-d_6$): δ 11.42 (s, 1H), 9.08 (s, 1H), 8.17 (dd, $J = 6.6, 3.0$ Hz, 1H), 7.97 (d, $J = 2.2$ Hz, 2H), 7.59–7.50 (m, 2H), 7.38–7.33 (m, 2H), 4.66 (d, $J = 2.6$ Hz, 2H), 3.67 (s, 2H), 2.57 (t, $J = 2.5$ Hz, 1H); ESI-MS: m/z , 420.7 (M+1).

Prop-2-ynyl-2-((2-((E)-(4-methoxybenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7f): Off white solid; Yield: 82 %; m.p.: 68–69 °C; IR (KBr, ν_{max} , cm^{-1}): 3251 ($\equiv\text{C-H}$ str), 3214 (N-H str), 2126 ($\text{C}\equiv\text{C}$), 1727 (C=O ester), 1649 (C=O , CONH), 1594 (C=N), 1546 (N-H bend); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO}-d_6$): δ 11.34 (s, 1H), 9.06 (s, 1H), 8.15 (t, $J = 3.0$ Hz, 1H), 7.99 (d, $J = 7.1$ Hz, 2H), 7.60–7.50 (m, 1H), 7.45 (d, $J = 8.2$ Hz, 2H), 7.36 (dd, $J = 10.1, 4.4$ Hz, 2H), 4.65 (d, $J = 2.5$ Hz, 2H), 3.67 (s, 2H), 3.06 (s, 3H), 2.62 (t, $J = 2.5$ Hz, 1H); ESI-MS: m/z , 386.7 (M+1).

Prop-2-ynyl-2-((2-((E)-(3,4,5-trimethoxybenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7g): Off white solid; Yield: 80 %; m.p.: 105–107 °C; IR (KBr, ν_{max} , cm^{-1}): 3236 (N-H str), 2129 ($\text{C}\equiv\text{C}$), 1736 (C=O ester), 1646 (C=O , CONH), 1583 (C=N), 1549 (N-H bend); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO}-d_6$): δ 11.80 (s, 1H), 9.05 (s, 1H), 8.11 (t, $J = 3.0$ Hz, 1H), 7.55–7.48 (m, 1H), 7.37 (dd, $J = 6.9, 3.5$ Hz, 2H), 7.31 (s, 2H), 4.66 (d, $J = 2.5$ Hz, 2H), 3.94 (s, 6H), 3.86 (s, 3H), 3.72 (s, 2H), 2.81 (d, $J = 2.5$ Hz, 1H); ESI-MS: m/z , 442.8 (M+1).

Prop-2-ynyl-2-((2-((E)-(4-cyanobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7h): White solid; Yield: 75 %; m.p.: 113–115 °C; IR (KBr, ν_{max} , cm^{-1}): 3317 ($\equiv\text{C-H}$ str), 3247 (N-H str), 2229 ($\text{C}\equiv\text{N}$), 2127 ($\text{C}\equiv\text{C}$), 1721 (C=O , ester), 1646 (C=O , CONH), 1613 (C=N), 1549 (N-H bend); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO}-d_6$): δ 11.55 (s, 1H), 9.10 (s, 1H), 8.46–7.88 (m, 4H), 7.84–7.48 (m, 2H), 7.38 (dd, $J = 6.6, 3.2$ Hz, 2H), 4.67 (d, $J = 2.6$ Hz, 2H), 3.70 (s, 2H), 2.67 (t, $J = 2.5$ Hz, 1H); ESI-MS: m/z , 377.8 (M+1).

Prop-2-ynyl-2-((2-((E)-(4-(methylsulfonyl)benzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7i): Pale yellow

solid: Yield: 90 %; m.p.: 94 °C; IR (KBr, ν_{\max} , cm^{-1}): 3284 ($\equiv\text{C-H}$ str), 3186 (N-H str), 2129 ($\text{C}\equiv\text{C}$), 1746 (C=O ester), 1651 (C=O , CONH), 1589 (C=N), 1558 (N-H bend), 1311 & 1147 (SO_2); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO-}d_6$): δ 11.78 (s, 1H), 9.09 (s, 1H), 8.24 (d, J = 6.0 Hz, 2H), 8.14 (dd, J = 3.0, 6.0 Hz, 1H), 8.03 (d, J = 6.0 Hz, 2H), 7.53 (dd, J = 3.0, 6.0 Hz, 1H), 7.42-7.34 (m, 2H), 4.66 (d, J = 2.6 Hz, 2H), 3.71 (s, 2H), 3.16 (s, 3H), 2.72 (t, J = 2.5 Hz, 1H); ESI-MS: m/z , 430.8 ($\text{M}+1$).

Prop-2-ynyl-2-((2-((*E*)-(2,5-difluorobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7j): Grey solid: Yield: 84 %; m.p.: 118-119 °C; IR (KBr, ν_{\max} , cm^{-1}): 3336 ($\equiv\text{C-H}$ str), 3185 (N-H str), 2111 ($\text{C}\equiv\text{C}$), 1720 (C=O , ester), 1682 (C=O , CONH), 1624 (C=N), 1541 (N-H bend), 1115 (C-F str); ^1H NMR (300 MHz, CDCl_3 + $\text{DMSO-}d_6$): δ 11.42 (*11.03, s, 1H), 8.96 (*8.62, s, 1H), 8.18 (t, J = 3.0 Hz, 1H), 7.71-7.51 (m, 2H), 7.50-7.35 (m, 2H), 7.20 (m, 2H), 4.66 (d, J = 2.6 Hz, 2H), 3.66 (*3.59, s, 2H), 2.55 (t, J = 2.6 Hz, 1H) (*peak of minor rotamer); ESI-MS: m/z , 388.7 ($\text{M}+1$).

Prop-2-ynyl-2-((2-((*E*)-(3-nitrobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (7k): Yellow solid: Yield: 88 %; m.p.: 87-88 °C; IR (KBr, ν_{\max} , cm^{-1}): 3296 ($\equiv\text{C-H}$ str), 3255 (N-H str), 2128 ($\text{C}\equiv\text{C}$), 1737 (C=O , ester), 1655 (C=O , CONH), 1615 (C=N), 1556 (N-H bend), 1526 & 1345 (NO_2); ^1H NMR (400 MHz, $\text{DMSO-}d_6$): δ 12.34 (s, 1H), 9.0 (s, 1H), 8.79 (s, 1H), 8.45 (d, J = 6.8 Hz, 1H), 8.40 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 6.8 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.45-7.36 (m, 2H), 4.71 (d, J = 2.0 Hz, 2H), 4.01 (s, 2H), 3.57 (t, J = 2.0 Hz, 1H); ESI-MS: m/z , 397.9 ($\text{M}+1$).

Antibacterial assay: The synthesized prop-2-ynyl-2-((2-((*E*)-(benzoylhydrazono)methyl)phenyl)sulfanyl)acetate derivatives (**7a-7k**) were tested against Gram-positive strains of (i) *Staphylococcus aureus* (MTCC 96) and (ii) *Streptococcus pyogenes* (MTCC 442) and Gram-negative strains of (iii) *Escherichia coli* (MTCC 443) and (iv) *Pseudomonas*

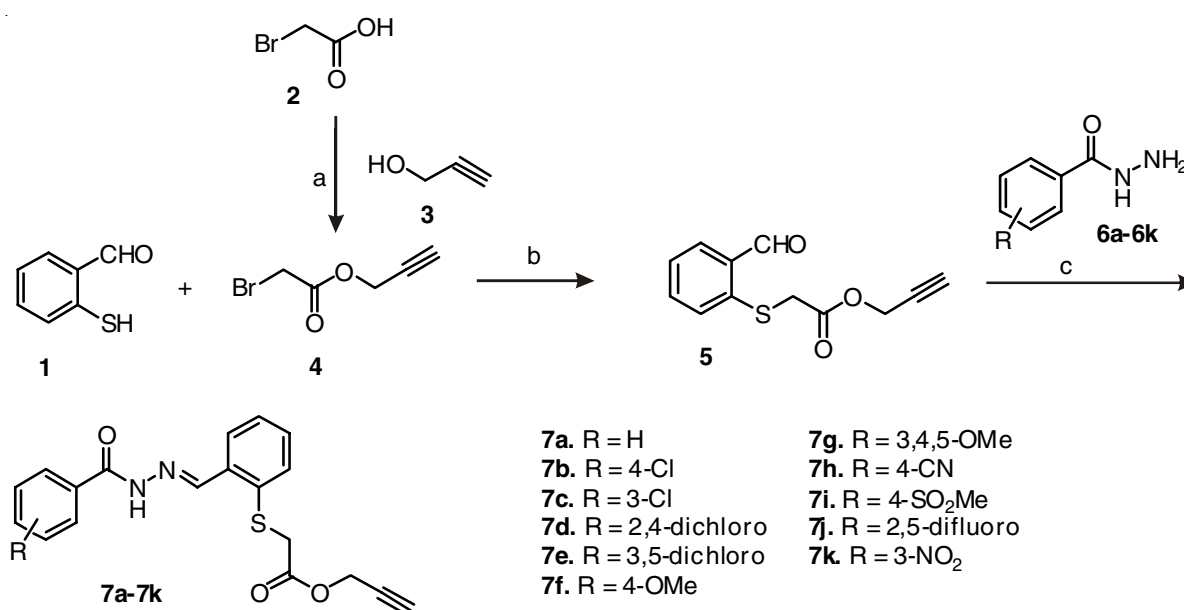
aeruginosa (MTCC 424) using agar well diffusion method according to the literature protocol [18,19]. The compounds were dissolved in dimethyl sulphoxide at 100 $\mu\text{g/mL}$ concentration and norfloxacin was used as the reference antibacterial drug. Antibacterial activity of the compounds was determined by zones showing complete inhibition (mm). Growth inhibition was calculated with reference to positive control. All the samples were taken in triplicate.

RESULTS AND DISCUSSION

The synthetic sequence for the preparation of prop-2-ynyl-2-((2-((*E*)-(benzoylhydrazono)methyl)phenyl)sulfanyl)acetate derivatives (**7a-7k**) is presented in **Scheme-I**. The key intermediate, prop-2-ynyl-2-(2-formylphenylthio)acetate (**5**) was prepared in two steps from commercially available 2-mercaptobenzaldehyde (**1**), 2-bromoacetic acid (**2**) and propargyl alcohol (**3**). The condensation of 2-bromoacetic acid (**2**) and propargyl alcohol (**3**) in the presence of DCC in anhydrous dichloromethane at 20 °C for 3 h resulted in the formation of prop-2-ynyl-2-bromoacetate (**4**). The alkylation of 2-mercaptobenzaldehyde (**1**) with prop-2-ynyl-2-bromoacetate (**4**) was done in the presence of potassium carbonate in DMF at 70 °C for 2 h to obtain prop-2-ynyl-2-(2-formylphenylthio)acetate (**5**). Condensation of aldehyde (**5**) with benzohydrazides (**6a-6k**) in ethanol at reflux for 1 h resulted in the formation of hydrazide-hydrazone derivatives (**7a-7k**) in quantitative yields.

The structural assignment of the synthesized hydrazide-hydrazone derivatives was done by ^1H NMR, MS and IR spectral data. The mass spectra of the compounds showed ($\text{M}+1$) peaks and are in agreement with their molecular formulae.

In general, the IR spectra of the compounds **7a-7k** represented the following characteristic peaks: Acetylene moiety ($\text{C}\equiv\text{C-H}$) gave one sharp band each in the regions 3336-3251 and 2131-2111 cm^{-1} . The strong bands in the region 3282-3167 cm^{-1} were due to secondary N-H stretching vibrations.



Experimental conditions: (a) DCC, DMAP, CH_2Cl_2 , 20 °C, 3 h (b) K_2CO_3 , DMF, 70 °C, 2 h; (c) benzohydrazides **6a-6k**, Ethanol, reflux, 1 h

Scheme-I: Synthesis of novel prop-2-ynyl-2-((2-((*E*)-(benzoylhydrazono)methyl)phenyl)sulfanyl)acetate derivatives (**7a-7k**)

Two very strong characteristic bands in the regions 1750-1713 cm^{-1} and 1682-1645 cm^{-1} were due to the C=O stretching vibrations of ester and hydrazone moieties, respectively. The strong band in the region 1556-1531 cm^{-1} was due to secondary N-H bending vibrations.

The ^1H NMR spectral details of the prop-2-ynyl-2-((2-((E)-(3-nitrobenzoylhydrazono)methyl)phenyl)sulfanyl)acetate (**7k**) are as follows: The protons resonating at 12.34 and 9.0 ppm as singlets with one proton integration, correspond to the groups $-\text{Ph}-\text{CO}-\text{NH}$ and $-\text{N}=\text{CH}-\text{Ph}$, respectively. The protons resonating at 8.79 ppm (singlet), 8.45 ppm (doublet), 8.40 ppm (doublet) and 7.94 ppm (doublet) with one proton integration correspond to the 3-nitro phenyl group while the protons resonating at 7.86 ppm (triplet), 7.53 ppm (doublet) and 7.45-7.36 ppm (multiplet) correspond to the phenyl ring flanked with the sulfanyl acetate group. The signals at 3.55 ppm (triplet), 4.01 ppm (singlet) and 4.67 ppm (doublet), correspond to acetylene, $-\text{S}-\text{CH}_2$ and $-\text{O}-\text{CH}_2$ protons, respectively.

Antibacterial activity: The antibacterial evaluation results of prop-2-ynyl-2-((2-((E)-(benzoylhydrazono)methyl)phenyl)sulfanyl)acetate derivatives (**7a-7k**) are presented in Table-1. It is observed that compounds **7b**, **7c**, **7d** and **7e** with mono and di substituted chloride group, on the basic scaffold, did not show any bacterial activity. With the modification of R group in the basic skeleton, a varying pattern of antibacterial potency was observed. Compound **7a** with R = H (parent structure) showed moderate activity and compounds **7f** and **7g** with R = 4-OMe and 3,4,5-OMe displayed weak antibacterial activity against all the tested bacterial strains. In case of *E. coli*, compounds **7i** (R = 4-SO₂Me) and **7j** (R = 2,5-difluoro) showed excellent activity with zone of inhibition 29 and 30 mm, respectively, while the compounds **7h** (R = 4-CN) and **7k** (R = 3-NO₂) showed good antibacterial activity with zone of inhibition 23 and 22 mm. Compounds **7a-7k**, showed a similar trends of antibacterial activity against *P. aeruginosa*, *S. aureus* and *S. pyogenes*.

It is noteworthy to mention that in general, within the series of the synthesized hydrazones, compounds with chloro group did not show the bacterial activity while the compound **7j** with R = 2,5-difluoro indicated excellent activity. This difference in the activity is attributed to the inclusion of fluorine

atom in the main scaffold. The stability of carbon-fluorine bond is high. They have prolonged half-lives and allow for longer times between dosing and activation. Adding fluorine to biologically active organics increases their lipophilicity. This effect often increases drug's availability because of increased cell membrane penetration [20].

The biological inactivity of chloro derivatives may be attributed to the fact that chloro group diminishes the biological activity by minimizing the metabolism and altering chemical changes [21].

Conclusion

The preparation of prop-2-ynyl-2-((2-((E)-(benzoylhydrazono)methyl)phenyl)sulfanyl)acetate derivatives (**7a-7k**) was carried out from the key intermediate, prop-2-ynyl-2-(2-formylphenylthio)acetate (**5**), which was in turn prepared in two steps from commercially available 2-mercaptobenzaldehyde (**1**), 2-bromoacetic acid (**2**) and propargyl alcohol (**3**). The synthesized hydrazone derivatives were screened for antibacterial activity and observed that compounds **7i** (R = 4-SO₂Me) and **7j** (R = 2,5-difluoro) showed excellent activity with zone of inhibition 29 and 30 mm, respectively, while the compounds **7h** (R = 4-CN) and **7k** (R = 3-NO₂) showed good antibacterial activity with zone of inhibition 23 and 22 mm against the tested bacterial strains viz., *E. coli*, *P. aeruginosa*, *S. aureus* and *S. pyogenes*.

ACKNOWLEDGEMENTS

One of the authors (RA) thank Dr. B.V. Subba Reddy, Sr. Principal Scientist, Indian Institute of Chemical Technology, Hyderabad, India and Dr. B. Ram, the Director, Green Evolution Laboratories, Nalgonda, India for their helpful suggestions and constant encouragement.

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TABLE-1
ANTIBACTERIAL ACTIVITY OF COMPOUNDS **7a-k** (CONCENTRATION USED 100 $\mu\text{g/mL}$ OF DMSO)

Compound No.	R	Zone of inhibition ^b (mm)			
		Gram-negative bacteria		Gram-positive bacteria	
		<i>E. coli</i> MTCC 443	<i>P. aeruginosa</i> MTCC 424	<i>S. aureus</i> MTCC 96	<i>S. pyogenes</i> MTCC 442
7a	H	19	17	19	17
7b	4-Cl	–	–	–	–
7c	3-Cl	–	–	–	–
7d	2,4-Dichloro	–	–	–	–
7e	3,5-Dichloro	–	–	–	–
7f	4-OMe	15	10	9	8
7g	3,4,5-OMe	14	10	10	6
7h	4-CN	23	21	23	20
7i	4-SO ₂ Me	29	25	28	24
7j	2,5-Difluoro	30	25	27	25
7k	3-NO ₂	22	20	22	20
^a Standard drug	–	27	23	26	21

^aNorfloxacin (100 $\mu\text{g/mL}$ of DMSO); ^bZone of inhibition - excellent activity: 24-30 mm; good activity: 20-23 mm; moderate activity: 17-19 mm; weak activity: < 17 mm; –: nil activity

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