**Synthesis and biological activity of 2-(2-substiuted benzylidenehydrazinyl)-4-(methoxy methyl)-5-phenylthiazole derivatives**

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**Abstract**

Acetophenone (**35**) on reaction with dimethyl carbonate (**36**) in the presence of sodium hydride as a base in toluene solvent gave methyl 3-oxo-3-phenylpropanoate (**37**). This reaction mixture was used in the next step without purification. These on reaction with thiosemicarbazide (**38**) in presence of NBS in toluene solvent gave Methyl 2-hydrazinyl-5-phenylthiazole-4-carboxylate (**39**). This intermediate on reaction with LAH in THF solvent gave (2-hydrazinyl-5-phenylthiazol-4-yl)methanol (**40**). This was purifierd by column chromatography and characterized from its spectral data.





In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **39,** the -NH2 protons appeared as a broad singlet at δ 4.34, The –NH proton appeared as a broad singlet at δ 11.06, -CH3 protons appeared as singlet at δ 4.03 and the aromatic protons are appeared as follows 7.34 (m, 1H), 7.56 (m, 2H),7.82 (m, 2H).

In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **40,** the -NH2 protons appeared as a broad singlet at δ 4.42, The –NH proton appeared as a broad singlet at δ 11.12, -OCH2 proton appeared as a broad singlet at δ 3.72 and the remaining aromatic protons appeared as follows 7.52 (m, 1H), 7.64 (m, 2H),7.86 (m, 2H).

(2-(2-benzylidenehydrazinyl)-5-phenylthiazol-4-yl) methanol **(42a-e)** were prepared by the reaction of (2-hydrazinyl-5-phenylthiazol-4-yl)methanol **(40)** with different aromatic Benzaldehyde (**41a-e**) in the presence of sodium sulphate in ethanol solvent at 65oC about 1.5 hour gave title compounds.





In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **42c, -NH** proton appeared as a singlet at δ 11.95, imine proton resonated at δ 8.59 as a singlet,-OCH2 proton observed at δ 5.53 as a singlet, two methyl protons observed at δ 2.35, 1.97as a singlets and the remaining aromatic protons appeared as follows: δ 7.67 (d, J=8.0Hz, 1H), 7.47, (d, J=8.2Hz, 1H), 7.42 (d, J=7.2Hz, 1H), 7.32 (m, 4H), 7.10 (t, J=7.5, 15.0Hz, 1H). The carbon signal assignments of **42c** as follows: δ 160.9, 142.0, 138.4, 137.4, 136.2, 132.1, 131.1, 126.7, 126.6, 126.1, 124.8, 123.9, 122.08, 122.02, 112.5, 108.3, 57.4, 19.8, 13.9. The ESI (MS) of **42c** showed the quassimolecuklar ion peak at 338.1 (M+1).

(2-(2-benzylidenehydrazinyl)-5-phenylthiazol-4-yl)methanol (**44a-e**) on reaction with methyl iodide in sodium hydride in ethanol solvent at reflux temperature about 1.5 hour gave the title compounds.These compounds were purified by recrystallisation method and characterized from spectral data.





In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **44c,** the-OCH3 proton appeared at δ 3.3, **, -NH** proton appeared as a singlet at δ 11.94, imine proton resonated at δ 8.92 as a singlet,-OCH2 proton observed at δ 5.51 as a singlet, two methyl protons observed at δ 2.37 (6H) as a singlet and the remaining protons appeared as follows : δ 7.67 (d, J=7.7Hz, 1H), 7.56 (s, 2H), 7.47, (d, J=7.7Hz, 1H), 7.27 (d, J=15.3Hz, 2H), 7.14 (m, 2H). The carbon signal assignments of **44c** as follows: δ 160.8, 139.3, 137.5, 136.4, 130.0, 126.6, 124.8, 122.9, 122.0, 120.2, 117.7, 112.5, 108.4, 57.4, 55.2, 20.79. The ESI (MS) of **44c** showed the quassi molecular ion peak at 352.3 (M+1).

The newly synthesized schiffbase derivatives were found to display good to moderate antibacterial activity and the chances of becoming these compounds as a potential active pharmachopore is high. A further structural activity studies and exploring the various biological activities is the future scope of the work.

**Introduction**

Chemistry of pyrazolothiazoles is well known. Some pyrazolothiazoles are used as drugs and some are known for their herbicidal1, antibacterial2 and anti-inflammatory3 activity.

The following are few interesting examples of the pyrazolothiazoles from the survey of the literature.

Novel 2-pyrazolinylthiazoles4 (**1a**) (eg. R = COOEt, Ar = 2-Naphthyl) were prepared regioselectively by cyclocondensation of 4-substituted-2-hydrazinothiazoles with 1,3-dicarbonyl compounds (CF3COCH2COAr). The aromatisation of (**1a**) via dehydration to give 2-(3-aryl-5-trifluoro-methylpyrazol-1-yl)thiazoles (**1b**). The compounds (**1b**) were obtained from (**1a**) by boiling with acetic anhydride. The molecular structure of (**1b**) (R = 4-F-C6H4, Ar = 4-Cl-C6H4) was determined by X-ray crystallography.



Ravinder *et al.*5 have reported the synthesis of pyrazolo coumarin derivatives (**1c)** by the cyclocondensation of 1-thiocarbamyl-3,5-dimethylpyrazole with 3-(2-bromoacetyl) coumarins.



Rao and Srimanth6 have reported the synthesis of 3-[2-(3,5-dimethyl-1H-pyrazol-1-yl)-4-thiazolyl]-2H-1-benzopyran-2-ones (**2**) by the cyclocondensation of appropriate 3,4,5-trisubstituted-1-thiocarbamylpyrazoles with various 3-(2-bromoacetyl)coumarins.



The 1-(1,3-thiazol-2-yl)pyrazolin-3-ones7 were prepared by reaction of thiocarbamylpyrazolidinones with α-haloacetal, ketal or appropriate carbonyl compounds. Dimeric products were prepared by reaction of pyrazolidinones with appropriate thiocyanates.



Kreutzberger2 synthesized 4-antipyrinyl-5-ethyl-2-[(4-pyrrolidinyl) methyleneamino] thiazole (**7**) by reacting 2-amino-4-antipyrinyl-5-ethylthiazoles (**6**) with S-triazine and pyrrolidine.



In another communication, Buzas*et al.*8 reported the synthesis of a number of pyrazolidine diones (**8**). They were converted into metal salts. These metal salts were found to be anti-inflammatory agents.



Condensation of 2-hydrazinothiazole with several unsymmetrical-1,3-diketones leads to the formation of single isomer9 (**9**).



Harode and Sharma10 could synthesize 2-[3'-methylpyrazol-5-one-1'-yl)-4-arylthiazoles (**10**) by treating α-haloketones with 3-methyl-1-thiocarbomyl pyrazol-5-ones.



Kalluraya*et al*.11 have reported the preparation of some 4-(substituted)-2-(4-arylhydrazono-3-methyl-5-oxo-2-pyrazolin-1-yl)thiazoles (**13**) by the Hantzsch condensation of 1-thiocarbomyl-3-methyl-4-(arylhydrazono)-2-pyrazolin-5-one (**12**) with 6-substituted-3-(2-bromoacetyl)coumarin (**11**).



Bharati Badami *et al*.12 synthesized 3-aryl-4-[2-(3,5-dimethyl phenyl pyrazol-1-yl)thiazol-4-yl]sydnones (**14**) by treating 3-aryl-4-(2-hydrazino-4-thiazolyl]sydnones with 1,3-dicarbonyl compounds.



**PRESENT WORK:**

Synthesis of 2-(2-benzylidenehydrazinyl)-4-(methoxymethyl)-5-phenylthiazole involves five steps:

1) Synthesis of methyl 3-oxo-3-phenylpropanoate (3).

2) Synhthesis of methyl 2-hydrazinyl-5-phenylthiazole-4-carboxylate (5).

3) Synthesis of (2-hydrazinyl-5-phenylthiazol-4-yl)methanol (6).

4) Synthesis of (2-(2-benzylidenehydrazinyl)-5-phenylthiazol-4-yl)methanol (8).

5) Synthesis of (E)-2-(2-benzylidenehydrazinyl)-4-(methoxymethyl)-5-phenylthiazole (10).

**1) Synthesis of methyl 3-oxo-3-phenylpropanoate (3).**

Acetophenone (**1**) on reaction with dimethyl carbonate (**2**) in the presence of sodium hydride as a base in toluene solvent gave methyl 3-oxo-3-phenylpropanoate (**3**). This crude reaction mixture was used in the next step without purification.



**2) Synhthesis of methyl 2-hydrazinyl-5-phenylthiazole-4-carboxylate (5).**

Methyl 2-hydrazinyl-5-phenylthiazole-4-carboxylate **(5)** was synthesized by the reaction of methyl 3-oxo-3-phenylpropanoate (**3**) and Hydrazinecarbothioamide (**4**) in the presence of NBS in toluene. This was purifierd by column chromatography and characterized from its spectral data.



In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **5,** the -NH2 protons appeared as a broad singlet at δ 4.34, The –NH proton appeared as a broad singlet at δ 11.06, -CH3protons appeared as singlet at δ 4.03 and the aromatic protons are appeared as follows 7.34 (m, 1H), 7.56 (m, 2H),7.82 (m, 2H).

**3) Synthesis of (2-hydrazinyl-5-phenylthiazol-4-yl)methanol (6).**

(2-hydrazinyl-5-phenylthiazol-4-yl)methanol **(6)** was synthesized by the reaction of Methyl 2-hydrazinyl-5-phenylthiazole-4-carboxylate **(5)** with LAH in THF solvent. This was purifierd by column chromatography and characterized from its spectral data.



In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **6,** the -NH2 protons appeared as a broad singlet at δ 4.42, The –NH proton appeared as a broad singlet at δ 11.12, -OH proton appeared as a broad singlet at δ 3.72 and the remaining aromatic protons appeared as follows 7.52 (m, 1H), 7.64 (m, 2H),7.86 (m, 2H).

**4) Synthesis of (2-(2-benzylidenehydrazinyl)-5-phenylthiazol-4-yl)methanol (8a-e).**

(2-(2-benzylidenehydrazinyl)-5-phenylthiazol-4-yl)methanol**(84a-e)** were prepared by the reaction of (2-hydrazinyl-5-phenylthiazol-4-yl)methanol **(6)** with different aromatic Benzaldehyde (**7a-e**) in the presence of sodium sulphate in ethanol solvent at 65oC about 1.5 hour gave title compounds.





In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **8c, -NH** proton appeared as a singlet at δ 11.95, imine proton resonated at δ8.59 as a singlet,-OCH2 proton observed at δ 5.53 as a singlet, two methyl protons observed at δ 2.35, 1.97as a singlets and the remaining aromatic protons appeared as follows: δ7.67 (d, J=8.0Hz, 1H), 7.47, (d, J=8.2Hz, 1H), 7.42 (d, J=7.2Hz, 1H), 7.32 (m, 4H), 7.10 (t, J=7.5, 15.0Hz, 1H). The carbon signal assignments of **8c**as follows: δ160.9, 142.0, 138.4, 137.4, 136.2, 132.1, 131.1, 126.7, 126.6, 126.1, 124.8, 123.9, 122.08, 122.02, 112.5, 108.3, 57.4, 19.8, 13.9. The ESI (MS) of **8c** showed the quassimolecuklar ion peak at 338.1 (M+1).

**5) Synthesis of 2-(2-benzylidenehydrazinyl)-4-(methoxymethyl)-5-phenylthiazole (10a-e).**

(2-(2-benzylidenehydrazinyl)-5-phenylthiazol-4-yl)methanol (**8a-e**) on reaction with methyl iodide in sodium hydride in ethanol solvent at reflux temperature about 1.5 hour gave the title compounds.These compounds were purified by recrystallisation method and characterized from spectral data.





In the 1H-NMR (DMSO-d6, 400MHz) spectrum of **10c,** the-OCH3 proton appeared at δ 3.3, **, -NH** proton appeared as a singlet at δ 11.94, imine proton resonated at δ 8.92 as a singlet,-OCH2 proton observed at δ 5.51 as a singlet, two methyl protons observed at δ 2.37 (6H) as a singlet and the remaining protons appeared as follows : δ7.67 (d, J=7.7Hz, 1H), 7.56 (s, 2H), 7.47, (d, J=7.7Hz, 1H), 7.27 (d, J=15.3Hz, 2H), 7.14 (m, 2H). The carbon signal assignments of **10c** as follows: δ 160.8, 139.3, 137.5, 136.4, 130.0, 126.6, 124.8, 122.9, 122.0, 120.2, 117.7, 112.5, 108.4, 57.4, 55.2, 20.79. The ESI (MS) of **10c** showed the quassimolecuklar ion peak at 352.3 (M+1).

**EXPERIMENTAL:**

**1) Synthesis of methyl 3-oxo-3-phenylpropanoate (3).**



To a dried 250-mL RBF were added NaH (3.7 g, 60% in mineral oil, 92 mmol), dimethyl carbonate (5.9 g, 66 mmol) and toluene (33 mL) under nitrogen. After the mixture was heated to reflux, a solution of acetophenone (33 mmol) in toluene (17 mL) was added dropwise over 0.5 h. After the evolution of hydrogen ceased (20 min), the reaction was cooled down to room temperature. Glacial acetic acid (10 mL) was added dropwise and a heavy pasty solid separated. Ice-cold water was slowly added until the solid was dissolved completely. Then, the reaction system was dilute with 200 mL of EtOAc. The organic layer was separated, washed with water (20 mL) and brine (20 mL) and dried over Na2SO4. After the solvent was evaporated, the residue was purified by flash chromatography on silica gel with EtOAc/Hexaness (1:3) as eluent to give compound **3**as a colorless oil (5.70 g, 97% yield).

**2) Synhthesis of methyl 2-hydrazinyl-5-phenylthiazole-4-carboxylate (5).**



To a mixture of Methyl 3-oxo-3-phenylpropanoate (8.90 g, 0.05 mol) in water (50.0 mL) and THF (20.0 mL) below 0°C was added NBS (10.70 g, 0.06 mol, 1.20 equiv.). The reaction mixture was stirred at room temperature for 2 h and thin-layer chromatography (TLC, petroleum ether–ethyl acetate 2:1, on silica gel plate, UV lamp λ = 254 nm, Rf = 0.71) showed disappearance of 1.Hydrazinecarbothioamide (4.55 g, 0.05 mol, 1.00 equiv.) was added and the reaction mixture was heated to 80°C for 2 hrs. After cooling to r.t., the reaction mixture was filtered to get free of the insoluble substance, then ammonia solution (8.0 mL) was added to the filtrate. The resulting yellow solid were stirred at room temperature for 10 min and filtered. The obtained solid was washed with water (100 mL × 3) and recrystallized with ethyl acetate, then dried to give the target compound.

|  |  |
| --- | --- |
| Yield | 65% |
| Mp | 186-188oC |
| Physical status | solid |
| 1H-NMR | δ 4.03 (s, 3H, COOC***H***3), 4.34 (br, N*H*2), 7.34 (m, 1H), 7.56 (m, 2H),7.82 (m, 2H) and 11.06 (br, 1H, N***H***-NH2). |
| ESI MS: | 250.1 (M+1) |

**3) Synthesis of (2-hydrazinyl-5-phenylthiazol-4-yl) methanol (6).**



To a solution of Methyl 2-hydrazinyl-5-phenylthiazole-4-carboxylate (4.42.0 g, 0.02 mol) in dry THF (50.0 mL) below -20°C was added LAH (0.95 g, 0.025 mol, 1.25 equiv.). The reaction mixture was temperature raised slowly and stirred at room temperature for 4 h and thin-layer chromatography (TLC, petroleum ether–ethyl acetate 3:2, on silica gel plate, UV lamp λ = 254 nm, Rf = 0.45) showed disappearance of 2. Then, the Na2SO4 paste was added to the reaction mixture for quenching reaction. The resulting mixture was washed with water ethyl acetate, and organic layer was separated dried on ah. MgSO4. Then the solvent was evaporated to get crude solid and recrystallized solid with ethanol to pure product. (3.3 g, 74%), m.p.203–205 °C, 1H-NMR (CDCl3, 400 MHz): δ 3.72 (br, 1H,O***H***), 4.42 (br, N*H*2), 7.52 (m, 1H), 7.64 (m, 2H),7.86 (m, 2H) and 11.12 (br, 1H, N***H***-NH2).

|  |  |
| --- | --- |
| Yield | 74% |
| Mp | 203-205oC |
| Physical status | solid |
| 1H-NMR (CDCl3, 400 MHz) | δ 3.72 (br, 1H,O***H***), 4.42 (br, N*H*2), 7.52 (m, 1H), 7.64 (m, 2H),7.86 (m, 2H) and 11.12 (br, 1H, N***H***-NH2). |

**4) Synthesis of substituted (2-(2-benzylidenehydrazinyl)-5-phenylthiazol-4-yl)methanols (8a-e).**

*i) Synthesis of (E)-(2-(2-benzylidenehydrazinyl)-4-phenylthiazol-5-yl)methanol* (**8a**).



|  |  |
| --- | --- |
| Yield | 68% |
| Mp | 280-283oC |
| Physical status | solid |
| 1H-NMR | 11.96 (s, 1H), 8.54 (s, 1H), 7.96 (d, J= 7.9Hz, 2H), 7.82 (d, J=8.2Hz, 2H), 7.59 (d, J=7.8Hz, 2H), 7.51 (d, J=8.2Hz, 2H), 7.49 (m, 1H), 7.46 (m, 1H), 5.51 (s, 2H). |
| 13C-NMR | 160.8, 142.0, 137.5, 136.0, 133.6, 131.9, 128.9, 128.6, 126.9, 126.6, 124.8, 122.0, 120.2, 118.8, 112.5, 108.4, 57.3. |
| ESI MS: | 310.2 (M+1) |

*ii) (E)-(4-phenyl-2-(2-(pyridin-2-ylmethylene)hydrazinyl)thiazol-5-yl)methanol* (**8b**).



|  |  |
| --- | --- |
| Yield | 72% |
| Mp | 260-265oC |
| Physical status | solid |
| 1H-NMR | 11.92 (s, 1H), 8.84 (s, 1H), 7.87 (d, J=8.9Hz, 2H), 7.4 (d, J=8.2Hz, 1H), 7.41 (d, J=8.1Hz, 1H), 7.22 (t, J=7.2, 15.8Hz, 1H), 7.27 (d, J=2.6Hz, 1H), 7.18 (d, J=9.2Hz, 2H), 7.13 (t, J=7.2, 15.3Hz, 1H), 5.50 (s, 2H). |
| 13C-NMR | 160.2, 159.6, 142.1, 137.8, 129.2, 126.2, 124.1, 123.3, 122.6, 121.2, 120.5, 114.2, 112.6, 108.8, 57.3. |
| ESI MS: | 311.8 (M+1) |

*iii) (E)-(2-(2-(3,5-dimethylbenzylidene)hydrazinyl)-4-phenylthiazol-5-yl)methanol* (**8c**).



|  |  |
| --- | --- |
| Yield | 77% |
| Mp | 270-273oC |
| Physical status | solid |
| 1H-NMR | 11.95 (s, 1H), 8.59 (s, 1H), 7.67 (d, J=8.0, 1H), 7.47, (d, J=8.2Hz, 1H), 7.42 (d, J=7.2Hz, 1H), 7.32 (m, 4H), 7.10 (t, J=7.5, 15.0Hz, 1H), 5.53 (s, 2H), 2.35 (s, 3H), 1.97 (s, 3H). |
| 13C-NMR | 160.9, 142.0, 138.4, 137.4, 136.2, 132.1, 131.1, 126.7, 126.6, 126.1, 124.8, 123.9, 122.08, 122.02, 112.5, 108.3, 57.4, 19.8, 13.9. |
| ESI MS: | 338.2 (M+1) |

iv) (E)-(2-(2-(4-butylbenzylidene)hydrazinyl)-4-phenylthiazol-5-yl)methanol (**8d**).



|  |  |
| --- | --- |
| Yield | 69% |
| Mp | 241-245oC |
| Physical status | solid |
| 1H-NMR | 11.94 (s, 1H), 8.93 (s, 1H), 7.83 (d, J=8.2Hz, 2H), 7.67 (d, J=8.0Hz, 1H), 7.48 (d, J=8.2Hz, 1H), 7.42 (d, J=8.2Hz, 2H), 7.29 (m, 2H), 7.10 (t, J=7.2, 14.8Hz, 1H), 5.52 (s, 2H), 2.6 (t, J=7.5, 15.3Hz, 2H), 1.6 (m, 2H), 1.34 (m, 2H), 0.92 (t, J=7.2, 14.8Hz, 3H). |
| 13C-NMR | 160.8, 143.2, 137.5, 134.4, 129.5, 126.6, 124.7, 123.0, 122.0, 120.2, 120.1, 112.5, 108.4, 57.4, 34.2, 32.8, 21.6, 13.7. |
| ESI MS: | 366.12 (M+1) |

*vi) (E)-(2-(2-(3-fluorobenzylidene)hydrazinyl)-4-phenylthiazol-5-yl)methanol* (**8e**).



|  |  |
| --- | --- |
| Yield | 78% |
| Mp | 234-237oC |
| Physical status | solid |
| 1H-NMR | 11.97 (s, 1H), 8.73 (s, 1H), 7.94 (d, J=7.5Hz, 1H), 7.69 (m, 4H), 7.49 (d, J=8.2Hz, 1H), 7.29 (t, J=7.2, 15.0Hz, 1H), 7.23 (s, 1H), 7.10 (7.2, 14.8Hz, 1H), 5.56 (s, 2H). |
| 13C-NMR | 160.8, 142.0, 137.5, 136.0, 133.6, 133.4, 131.9, 129.1, 128.9, 128.6, 126.9, 126.6, 124.8, 122.0, 120.2, 118.8, 112.5, 108.4, 57.3. |
| ESI MS: | 328.2 (M+1) |

**5) Synthesis of (E)-2-(2-benzylidenehydrazinyl)-4-(methoxymethyl)-5-phenylthiazole (10a-i).**

*i) Synthesis of (E)-2-(2-benzylidenehydrazinyl)-5-(methoxymethyl)-4-phenylthiazole* (**10a**).



|  |  |
| --- | --- |
| Yield | 69% |
| Mp | 285-288oC |
| Physical status | solid |
| 1H-NMR | 11.94 (s, 1H), 8.51 (s, 1H), 7.92 (d, J= 7.9Hz, 2H), 7.79 (d, J=8.2Hz, 2H), 7.51 (d, J=7.8Hz, 2H), 7.40 (d, J=8.2Hz, 2H), 7.42 (m, 1H), 7.38 (m, 1H), 5.51 (s, 2H), 3.8 (s, CH3). |
|  | 160.2, 141.7, 137.8, 136.4, 133.1, 131.2, 128.7, 128.4, 126.6, 126.4, 124.2, 121.7, 120.4, 118.2, 112.1, 108.8, 64.3, 57.7. |
| ESI MS: | 324.2 (M+1) |

*ii) (E)-5-(methoxymethyl)-4-phenyl-2-(2-(pyridin-2-ylmethylene)hydrazinyl)thiazole* **(10b).**



|  |  |
| --- | --- |
| Yield | 71% |
| Mp | 265-268oC |
| Physical status | solid |
| 1H-NMR | 11.93(s, 1H), 8.87 (s, 1H), 7.84 (d, J=9.0Hz, 2H), 7.6 (d, J=8.0Hz, 1H), 7.47 (d, J=8.5Hz, 1H), 7.28 (t, J=7.0, 15.3Hz, 1H), 7.22 (d, J=2.2Hz, 1H), 7.16 (d, J=9.0Hz, 2H), 7.10 (t, J=7.0, 15.0Hz, 1H), 5.50 (s, 2H), 3.83 (s, 3H). |
| 13C-NMR | 160.8, 159.3, 142.8, 137.5, 129.9, 126.6, 124.8, 123.0, 122.0, 121.8, 120.2, 114.8, 112.5, 108.3, 57.4, 55.5. |
| ESI MS: | 325.1 (M+1) |

*iii)(E)-2-(2-(3,5-dimethylbenzylidene)hydrazinyl)-5-(methoxymethyl)-4-phenylthiazole* (**10c**).



|  |  |
| --- | --- |
| Yield | 64% |
| Mp | 275-279oC |
| Physical status | solid |
| 1H-NMR | 11.94 (s, 1H), 8.92 (s, 1H), 7.67 (d, J=7.7Hz, 1H), 7.56 (s, 2H), 7.47, (d, J=7.7Hz, 1H), 7.27 (d, J=15.3Hz, 2H), 7.14 (m, 2H), 5.51 (s, 2H), 2.37 (s, 6H). |
| 13C-NMR | 160.8, 139.3, 137.5, 136.4, 130.0, 126.6, 124.8, 122.9, 122.0, 120.2, 117.7, 112.5, 108.4, 57.4, 55.2, 20.79 |
| ESI MS: | 352.1 (M+1) |

*iv) (E)-2-(2-(4-butylbenzylidene)hydrazinyl)-5-(methoxymethyl)-4-phenylthiazole***(10d)**.



|  |  |
| --- | --- |
| Yield | 74% |
| Mp | 248-252oC |
| Physical status | solid |
| 1H-NMR | 11.94 (s, 1H), 8.93 (s, 1H), 7.83 (d, J=8.2Hz, 2H), 7.67 (d, J=8.0Hz, 1H), 7.48 (d, J=8.2Hz, 1H), 7.42 (d, J=8.2Hz, 2H), 7.29 (m, 2H), 7.10 (t, J=7.2, 14.8Hz, 1H), 5.52 (s, 2H), 2.26 (t, J=7.5, 15.3Hz, 2H), 1.6 (m, 2H), 1.34 (3, 2H), 0.92 (t, J=7.2, 14.8Hz, 3H). |
| 13C-NMR | 160.8, 143.2, 137.5, 134.4, 129.5, 126.6, 124.7, 123.0, 122.0, 120.2, 120.1, 112.5, 108.4, 57.4, 55.1, 34.2, 32.8, 21.6, 13.7. |
| ESI MS: | 380.2 (M+2) |

*v) (E)-2-(2-(3-fluorobenzylidene)hydrazinyl)-5-(methoxymethyl)-4-phenylthiazole* (**10e)**.



|  |  |
| --- | --- |
| Yield | 77% |
| Mp | 240-243oC |
| Physical status | solid |
| 1H-NMR | 11.92 (s, 1H), 8.77 (s, 1H), 7.91 (d, J=7.2Hz, 1H), 7.61 (m, 4H), 7.41 (d, J=8.0Hz, 1H), 7.21 (t, J=7.6, 15.2Hz, 1H), 7.21 (s, 1H), 7.11 (J=7.1, 14.2Hz, 1H), 5.52 (s, 2H), 3.81 (s, 3H). |
|  | 160.2, 142.7, 137.1, 136.5, 133.1, 133.1, 131.2, 129.7, 128.1, 128.1, 126.5, 126.1, 124.2, 122.6, 120.1, 118.1, 112.1, 108.3, 57.3, 55.3. |
| ESI MS: | 342.1 (M+1) |

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