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Synthesis and Spectroscopy Characterizations of Some New Bis 1,3-thiazolidin-4-ones Derived from 4-hydroxybenzaldehyde Substrate

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ABSTRACT

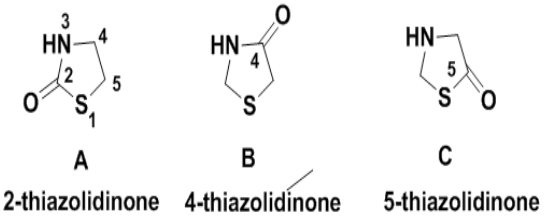
Over three major convenient steps, a series of some novel Bis-Schiff bases, and Bis 1,3-thiazolidin-4-one derivatives have been synthesized: Firstly, the etherification process through the reaction of the 4-hydroxybenzaldehyde substrate with *o-*, *m-*, and *p*-chlorobenzylchlorides under mild circumstances. Secondly, the condensation reaction between 4-((chlorobenzyl)oxy)benzaldehyde compounds with a number of aromatic diamines in an acidic environment produces the required Bis-schiff intermediates. Finally, the practical cyclization step was finished by synthesizing the required Bis 1,3-thiazolidin-4-one products with 79-97% yields through refluxing reaction in benzene with thioglycolic acid.

Keywords: 1,3-thiazolidin-4-ones, Cyclization process, Bis-Schiff bases, Thioglycolic acid, Heterocyclic compounds, 4-((chlorobenzyl)oxy)benzaldehyde, Etherification process.

INTRODUCTION

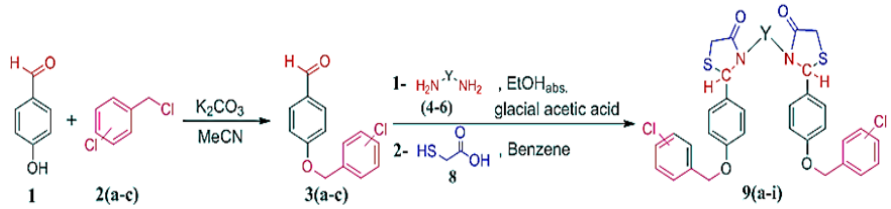
Heterocyclic compounds have been classified as one of the most significant classes of organic molecules as a result of their use in industrial and pharmaceutical applications.[1-13] The most significant of them are thiozolidinones (Scheme 1), which are thiazolidine compounds and are described as doubly unsaturated five-membered heterocyclic compounds having an S atom at position 1, an N atom at position 3, and a C=O group at position 2, 4, or 5.[14-15]

The 1,3-thiazolidin-4-one moiety (wonder nucleus) is a magic moiety with a wide range of biological characteristics, including anti-inflammatory[16-17], oncological activity[18], wound healing[19], anticonvulsant[20], anti-biofilm[21], Tyrosine inhibition[22], antibacterial[23], anti-HIV[24], etc. In 1961, Brown thoroughly examined the chemistry of 1,3-thiazolidin-1-one.[25] The major synthetic pathways for 1,3-thiazolidin-4-one derivatives require 3 components (an aldehyde, an amine, and thioglycolic acid), which are combined in one or two steps.[26] Because of the relevance of thiazolidinone derivatives, various helpful synthetic processes for their manufacture have since been devised.[27-30]



Scheme 1. Structures of the various thiazolidinone derivatives

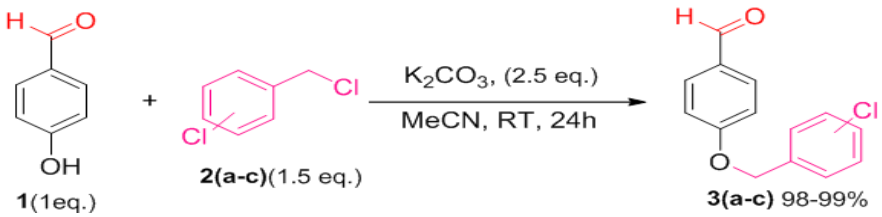
As a result, the production and biological effects of 1,3-thiazolidin-4-one derivatives are receiving a lot of interest, and our present research is a continuation of our ongoing work on the invention, synthesis, and characterization of novel Bis 1,3-thiazolidin-4-one derivatives using three critical approaches: Etherification[31], condensation[28,32], and finally cyclization reaction processes[33] (Scheme 2).



Scheme 2. Synthetic route of thiazoledenone derivatives from 4-hydroxybenzaldehyde

RESULTS AND DISCUSSION

In this approach, we reported a novel synthesis of Bis-1,3-thiazolidin-1-one compounds, which could have significant pharmacological properties. This work's framework established the etherification of the OH and transformed it into the OR group. This step was done by the reaction of p-hydroxybenzaldehyde with the *o-*, *m-*, and *p*-chloro substituted of benzyl chloride in the presence of anhydrous K_2CO_3 and MeCN as a solvent, at room temperature Typically, after the workup process step, the corresponding 4-((chlorobenzyl)oxy)benzaldehyde products 3(a-c) were prepared with higher yields (98-99%) (Scheme 3, and Table 1). FT-IR for the prepared 3(a-c) compounds exhibit a strong peak at (1255, 1261, 1269) cm^{-1} in the fingerprint area for the arC-O-alC group and these indicated the formation of the expected products.

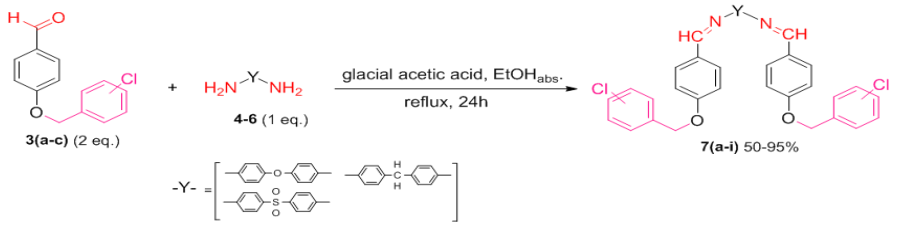


Scheme 3. Synthetic route of 4-((chlorobenzyl)oxy)benzaldehyde derivatives from 4-hydroxybenzaldehyde

Table 1: The physical properties of 4-((chlorobenzyl) oxy)benzaldehyde products 3(a-c)

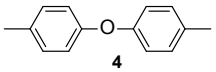
Products No	Chloro sub.	m.p. (°C)	Color	R_f	Yield%
3a	*o*-Cl	44-48	Pale yellow	0.7	98
3b	*m*-Cl	50-52	White	0.6	98
3c	*p*-Cl	64-66	Pale yellow	0.6	99

While the second step involved the synthesis of Bis-Schiff base compounds 7(a-i) through the condensation reaction. This reaction was forwarded by the treatment of 4-((chlorobenzyl)oxy)benzaldehyde 3(a-c) intermediates with aromatic diamines (4-6) with adding a few drops of glacial acetic acid by refluxing reaction in ethanol absolute for 24 hours. This step (Bis-Schiff bases synthesis) showed a prosperous method and awarded the pure desired products (50-95%) after the purification through the recrystallization from ethanol absolute (Scheme 4 and Tables (2, 3)). The ^{1}H-NMR spectra of compounds 7(a-i) showed extra protons signal peaks in the aromatic region with the chemical shifts at (7.92-6.94) ppm and a novel imine signal peaks with the chemical shifts at (8.61–8.40) ppm, both of which were consistent with the aromatic structural in these substances.



Scheme 4: Synthesis of Bis-Schiff bases from 4-((chlorobenzyl)oxy)benzaldehydes

Table 2: The physical properties or Bis-Schiff base products 7(a-i)

Pro. No.	-Y-	Chloro sub.	M.wt (gm/mol)	m.p.(°C)	Color	R*f*	Yield%
7a		*o*-Cl	657.591	134-138	Orange	0.8	76
7b		*m*-Cl	657.591	219-220	White	Invisible	----------
7c		*p*-Cl	657.591	250-254	White	0.9	50

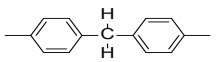
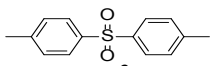
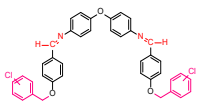
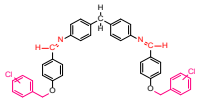
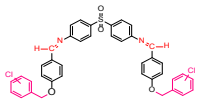
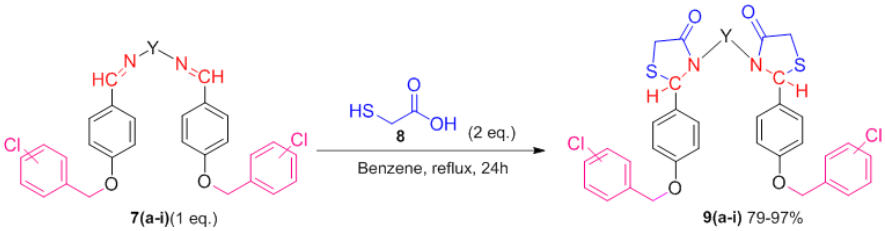
							75
7d		*o*-Cl	655.619	114-118	Yellow	0.8	85
7e		*m*-Cl	655.619	158-160	White	----------	----------
7f		*p*-Cl	655.619	220-222	White	Invisible	56
						----------	----------
						0.9	60
7g		*o*-Cl	705.65	170-172	Yellow	0.8	95
7h		*m*-Cl	705.65	98-100	Red	---------	----------
7i		*P*-Cl	705.65	252-255	Pale yellow	Invisible	58
						---------	----------
						0.9	50

Table 3: The physical properties of the synthesized Bis 1,3-thiazolidin-4-ones 9(a-i) from 4-((chlorobenzyl)oxy)benzaldehyde substitutes

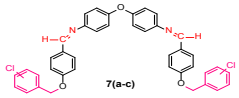
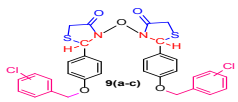
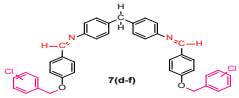
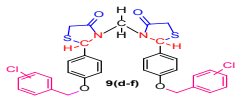
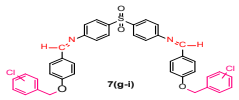
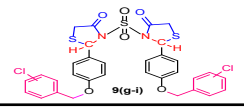
Pro. No.	Bis-Schiff bases	Chloro Sub.	M.wt (g/mol)	m.p. (°C)	Color	R_f	Yield%
9a		*o*-Cl	805.785	145-147	Pale-yellow	0.3	96
9b		*m*-Cl	805.785	198-200	Yellow	0.2	80
9c		*p*-Cl	805.785	258-260	white	0.2	82
9d		*o*-Cl	803.813	98-100	Dark yellow	0.2	97
9e		*m*-Cl	803.813	58-61	Yellow	0.2	86
9f		*p*-Cl	803.813		White	0.2	81
9g		*o*-Cl	853.844	178-179	Pale yellow	0.2	93
9h		*m*-Cl	853.844	105-108	Orange	0.3	79
9i		*p*-Cl	853.844	257-259	white	0.3	89

Lastly, the Bis 1,3-Thiazolidin-4-ones 9(a-i) products were produced in the final step by refluxing Bis-imines 7(a-i) with thioglycolic acid in dry benzene as solvent. Following the purification approach, this stage (cyclization process) yielded the anticipated products 9(a-i) with good yields (79-97%) (Tables 3, 4 and Scheme 5). The ^{1}H-NMR spectra revealed a further set of proton signal peaks with the chemical shifts at (3.97-3.07) and (6.68-6.02) ppm, which correspond to the aromatic 4-thiazolidinone framework's CH_2-S and CH-S, respectively. Furthermore, the formation of new additional carbon signal peaks with the chemical shifts at (173.3-170.82) ppm for C=O of amide, as well as two signals in ^{13}C-NMR spectra with the chemical shifts at (71.59-69.25) and (35.6-29.72) ppm attributed to C-C=O and C-S, respectively, supported the structures of the products that were wanted 9(a-i).



Scheme 5. Synthesis of Bis 1,3-thiazolidin-4-one derivatives from Bis Schiff bases

Table 4: The Bis 1,3-thazolidin-4-ones 9(a-i) derived from Bis-Schiff bases intermediates

Entry	Chloro sub.	Bis-Schiff bases	Bis-4-thiazolidin-3-ones
1	*o*-Cl *m*-Cl *p*-Cl		
2	*o*-Cl *m*-Cl *p*-Cl		
3	*o*-Cl *m*-Cl *p*-Cl		

EXPERIMENTAL

MATERIALS AND METHODS

Table 5: Chemicals used and their suppliers

Chemicals	Companies
4-hydroxy benzaldehyde.	SIGMA-ALDRICH
4-chlorobenzyle chloride.	SIGMA-ALDRICH(99%)
3-chlorobenzyle chloride.	SIGMA-ALDRICH(99%)
2-chlorobenzyle chloride.	SIGMA-ALDRICH(99%)
4,4-oxydianiline.	SIGMA-ALDRICH(97%)
4,4-aminophenyl sulfone.	TCI
4,4-diamino diphenyl methane.	Alfa Aesar (97%)
Glacial acetic acid.	Hanover Riedel-De Hean AG (99.8%)
Acetonitrile.	Sharlau
Ethanol absolute.	Sharlau (99.9%)
Benzene.	BDH (99.7%)
Dichloromethane.	ReAgent
Petroleum ether.	ROTH
Ethyl acetate.	BDH (99.5%)

All reactions took place in anhydrous, dry conditions with the use of solvents. Commercial reagents weren't purified before usage. As an absolute solvent, ethanol was utilized. Electrothermal apparatus have been used for melting points determination, which maybe uncorrected. Bruker DPX-300FT-NMR spectrometers have been used to generate ^{1}H- and ^{13}C-NMR spectra at 400 and 100.2 MHz. The Spectrum was recorded in $CDCl_3$. IR spectra were recorded using a 1710-FTIR Perkin-Elmer spectrometer. Merck Kiese gel 60 F254 Thin Layer Chromatography (TLC) on aluminum foil from Macherey-Nagel. UV light at 254 & 365 nanometers was used for detection.

General procedure for syntheses of 4-((chlorobenzyl) oxy)benzaldehyde Compounds 2(a-c)

In dry acetonitrile (150 mL) chloro substitutions of benzyl chloride 2(a-c) (3.96 g, 0.025 mol, 1.5 eq.) with anhydrous K_2CO_3 (5.6 g, 0.04 mol, 2.5 eq.) were added to a solution of p-hydroxy benzaldehyde (2 g, 0.016 mol, 1 eq.) The reaction mixture was stirred at ambient temperature for 24 hours. TLC (PE/ EtOAc 80:20) was utilized to track the reaction's progress. The crude reaction mixture had been concentrated by vacuum. DCM was used to extract the mixture, after which the organic layer was brine-washed and dried on Magnesium sulfate. Then the solvent was vacuum evaporated to generate crude products, which were subsequently refined by recrystallization from ethanol absolute to produce the necessary pure products 5(a-c) (Table 1).[31]

4-((2-chlorobenzyl)oxy)benzaldehyde (3a)

Pall yellow solid, (98%), R_f = 0.7, (44-48)°C. IR ν_{max} (cm^{-1}): 2924, 2825, 1689, 1255.

4-((3-chlorobenzyl)oxy)benzaldehyde (3b)

White solid, (98%), R_f = 0.6, (50-52)°C. IR ν_{max} (cm^{-1}): 2924, 2854, 1689, 1269.

4-((4-chlorobenzyl)oxy)benzaldehyde (3c)

Pall yellow solid, (99%), R_f = 0.6, (64-66)°C. IR ν_{max} (cm^{-1}): 2924, 2850, 1688, 1261.

General procedure for preparation of Bis-Schiff Bases 7(a-i) from 4-((chlorobenzyl)oxy) benzaldehyde 3(a-c)

A solution of 4-((chlorobenzyl)oxy) benzaldehyde substitutes 3(a-c) (2 eq.) was added to a solution of aromatic di-amines (4-6) (1 eq.) with stirring in ethanol absolute (40 mL) at room temperature. The mixture was then treated with some drops of glacial acetic acid and refluxed overnight. TLC (DCM/MeOH 98:2 and 2 drops of 10% NH_4OH solution) was used to monitor the reaction development. Hot filtration, ethanol washing, and recrystallization by ethanol process were applied to obtain the desired Bis-Schiff products 7(a-i) (Table 2).[34,8]

N-(4-(4-((4-((2-chlorobenzyl)oxy)benzylidene) amino)phenoxy)phenyl)-1-(4-((2-chlorobenzyl) oxy)phenyl)methanimine (7a)

Orange solid, (76%), R_f=0.8, (134–138)°C. ^{1}H-NMR: δ (ppm) = 8.56 (d, *J* = 15.2 Hz, 2H, 2(N=CH)), 7.89 (t, *J*=8 Hz, 6H, $CH_{aromatic}$), 7.64-7.61 (m, 4H, $CH_{aromatic}$), 7.55-7.53 (m, 4H, $CH_{aromatic}$), 7.33-7.153 (m, 10H, CHaromatic), 5.24 (d, *J* = 4 Hz, 4H, 2(O-CH_2)).

N-(4-(4-((4-((3-chlorobenzyl)oxy)benzylidene) amino)phenoxy)phenyl)-1-(4-((3-chlorobenzyl) oxy)phenyl)methanimine (7b)

White solid, (50%), R_f = invisible, (219-220)°C. ^{1}H-NMR: δ (ppm) = 8.50 (s, 2H, 2(N=CH)), 7.52 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 7.44-7.43 (m, 2H, $CH_{aromatic}$), 7.27-7.20 (m, 10H, $CH_{aromatic}$), 7.00-6.95 (m, 8H, CHaromatic), 5.23 (s, 4H, 2(O-CH_2)).

N-(4-(4-((4-((4-chlorobenzyl)oxy)benzylidene) amino)phenoxy)phenyl)-1-(4-((4-chlorobenzyl) oxy)phenyl)methanimine (7c)

White solid, (75%), R_f = 0.9, (250-254)°C. ^{1}H-NMR: δ (ppm) = 8.61 (s, 2H, 2(N=CH)), 7.57 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 7.32-730 (m, 4H, $CH_{aromatic}$), 7.21 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 7.02 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 6.95 (d, *J* = 6Hz, 6H, $CH_{aromatic}$), 5.20 (s, 4H, 2(O-CH_2)).

N-(4-(4-((4-((2-chlorobenzyl)oxy)benzylidene) amino)benzyl)phenyl)-1-(4-((2-chlorobenzyl)oxy) phenyl)methanimine (7d)

Yellow solid, (85%), R_f = 0.8, (114-118)°C. ^{1}H-NMR: δ (ppm)=8.50 (s, 2H, 2(N=CH)), 7.54 (d, *J* = 6.1 Hz, 4H, $CH_{aromatic}$), 7.31-7.14 (m, 16H, $CH_{aromatic}$), 6.94 (d, *J* = 6.4 Hz, 4H, $CH_{aromatic}$), 5.23 (s, 4H, 2(O-CH_2)), 3.82 (s, 2H, -CH_2-).

N-(4-(4-((4-((3-chlorobenzyl)oxy)benzylidene) amino)benzyl)phenyl)-1-(4-((3-chlorobenzyl)oxy) phenyl)methanimine (7e)

White solid, (56%), R_f = invisible, (158-160)°C. ^{1}H-NMR: δ (ppm) = 8.40 (s, 2H, 2(N=CH)), 7.45 (d, *J* = 4.5 Hz, 4H, $CH_{aromatic}$), 7.36-7.33 (m, 6H, $CH_{aromatic}$), 7.23-7.18 (m, 8H, CHaromatic), 7.14-7.12 (m, 2H, $CH_{aromatic}$), 7.00 (d, *J* = 4.5 Hz, 4H, $CH_{aromatic}$), 5.20 (s, 4H, 2(O-CH_2)), 3.74 (s, 2H, -CH_2-).

N-(4-(4-((4-((4-chlorobenzyl)oxy)benzylidene) amino)benzyl)phenyl)-1-(4-((4-chlorobenzyl)oxy) phenyl)methanimine (7f)

White solid, (60%), R_f = 0.9, (220-222)°C. ^{1}H-NMR: δ (ppm) = 8.54 (s, 2H, 2(N=CH)), 7.56 (d, *J* = 6.4 Hz, 4H, $CH_{aromatic}$), 7.31-7.20 (m, 16H, $CH_{aromatic}$), 6.98 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 5.19 (s, 4H, 2(O-CH_2)), 3.81 (s, 2H, -CH_2-).

N-(4-((4-((4-((2-chlorobenzyl)oxy)benzylidene) amino)phenyl)sulfonyl)phenyl)-1-(4-((2-chlorobenzyl)oxy)phenyl)methanimine (7g)

Yellow solid, (95%), R_f = 0.8, (170-172)°C. ^{1}H-NMR: δ (ppm) 9.90 (s, 2H, 2(N=CH)), 7.96 (d, *J* = 8.8 Hz, 4H, $CH_{aromatic}$), 7.86 (d, *J* = 8.8 Hz, 4H, $CH_{aromatic}$), 7.66 (d, *J* = 8.4 Hz, 2H, $CH_{aromatic}$), 7.55-7.52 (m, 4H, $CH_{aromatic}$), 7.44-7.41 (m, 4H, $CH_{aromatic}$), 7.11-7.09 (m, 6H, $CH_{aromatic}$), 5.26 (s, 4H, 2(O-CH_2)).

N-(4-((4-((4-((3-chlorobenzyl)oxy)benzylidene) amino)phenyl)sulfonyl)phenyl)-1-(4-((3-chlorobenzyl)oxy)phenyl)methanimine (7h)

Red solid, (58%), R_f = invisible, (98-100)°C. ^{1}H-NMR: δ (ppm)=8.53 (s, 2H, 2(N=CH)), 7.92 (d, *J* = 6 Hz, 4H, CHaromatic), 7.53 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 7.48 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 7.21 (m, 8H, $CH_{aromatic}$), 6.95 (s, 4H, $CH_{aromatic}$), 5.22 (s, 4H, 2(O-CH_2)).

N-(4-((4-((4-((4-chlorobenzyl)oxy)benzylidene) amino)phenyl)sulfonyl)phenyl)-1-(4-((4-chlorobenzyl)oxy)phenyl)methanimine (7i)

Pale-yellow solid, (50%), R_f = 0.9, (252-

255)°C. ^{1}H-NMR: δ (ppm) = 8.53 (s, 2H, 2(N=CH)), 7.92 (d, *J* = 5.6 Hz, 4H, $CH_{aromatic}$), 7.86 (d, *J* = 8.8 Hz, 4H, $CH_{aromatic}$), 7.66 (d, *J* = 8.4 Hz, 2H, $CH_{aromatic}$), 7.55-7.52 (m, 4H, $CH_{aromatic}$), 7.44-7.41 (m, 4H, $CH_{aromatic}$), 6.95 (m, 4H, $CH_{aromatic}$), 5.22 (s, 4H, 2(O-CH_2)).

General procedure for preparation of Synthesis of Bis 1,3-thiazolidin-4-ones 9(a-i) from Bis limine 7(a-i)

A dropwise addition of thioglycolic acid 8 (10 mg, 2 eq.) have been added to a (1eq.) of Bis-Schiff Bases 7(a-i) solution in present of dry benzene (30 mL) with refluxing the mixture for twenty-four hours. TLC was used to monitor the reaction progress (DCM/ MeOH 98:02 and 2 drops of 10% NH4OH solution). Rotary evaporation was used to evaporate the extra solvent. The solid chemicals that remained were neutralized through the addition of a cold 10% NaHCO solution till CO_2 bubbles were evaluated and left to stand overnight. The solid products have been separated through filtration, water cold washing, dried, and recrystallized twice using EtOH absolute. The physical characteristics of Bis 1,3-thiazolidin-4-ones 9(a-i) are synthesized in (Table 3).[35,36]

3,3'-(oxybis(4,1-phenylene))bis(2-(4-((2-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9a)

Pale-yellow solid, (96%), R_f = 0.3, (145-147)°C. ^{1}H-NMR: δ (ppm) = 7.59 (m, 4H, $CH_{aromatic}$), 7.46-7.41 (m, 4H, $CH_{aromatic}$), 7.32 (d, *J* = 3.6 Hz, 2H, $CH_{aromatic}$), 7.13-7.06 (m, 8H, $CH_{aromatic}$), 7.02 (d, *J* = 8.8 Hz, 2H, $CH_{aromatic}$), 6.95- 6.90 (m, 4H, $CH_{aromatic}$), 6.02 (d, *J* = 6.8 Hz, 2H, 2(CH-S)), 5.28 (d, *J* = 2.4 Hz, 4H, (O-CH_2)), 3.92 (d, *J* = 5.2 Hz, 2H, (CH_2-S)), 3.98 (dd, *J* = 1.6 and 6.8 Hz, 2H, (CH_2-S)). ^{13}C-NMR: δ (ppm) = 171.05(2C=O), 158.98 (2C_{ar}), 153.92 (2C_{ar}), 134.32 (2C_{ar}), 132.70 (2C_{ar}), 131.09 (2C_{ar}),129.57 (2C_{ar}), 129.25 (4C_{ar}), 128.81 (4C_{ar}), 127.64 (2C_{ar}), 127.06 (2C_{ar}), 122.37 (4C_{ar}), 117.26 (4C_{ar}), 115.16 (4C_{ar}), 67.21 (2C-C=O), 61.32 (2O-C), 29.72 (2C-S).

3,3'-(oxybis(4,1-phenylene))bis(2-(4-((3-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9b)

Yellow solid, (80%), R_f = 0.2, (198-200)°C; ^{1}H-NMR: δ (ppm) = 7.34 (s, 2H, $CH_{aromatic}$), 7.29-7.24 (m, 8H, $CH_{aromatic}$), 7.11-7.06 (m, 10H, $CH_{aromatic}$), 6.98 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 6.68 (s, 2H, 2(CH-S)), 5.13 (s, 4H, (O-CH_2)), 3.77 (dd, *J* = 15.6 and 15. 3, 4H, 2(CH_2-S)). ^{13}C-NMR: δ (ppm) = 173.3 (2C=O), 160.4 (2C_{ar}), 154.5 (2C_{ar}), 140.4 (2C_{ar}), 135.1 (2C_{ar}), 134.1 (2C_{ar}), 133.0 (2C_{ar}), 128.8 (4C_{ar}), 128.6 (4C_{ar}), 128.0 (2C_{ar}), 126.7 (2C_{ar}), 126.6 (2C_{ar}), 124.6 (2C_{ar}), 122.6 (2C_{ar}), 116.1 (2C_{ar}), 71.5 (2C-C=O), 66.9 (2O-C), 35.6 (2C-S).

3,3'-(oxybis(4,1-phenylene))bis(2-(4-((4-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9c)

White solid, (82%), R_f = 0.2, (258-260)°C; ^{1}H-NMR: δ (ppm) = 7.87 (d, *J* = 8.8 Hz, 2H, $CH_{aromatic}$), 7.49-7.43 (m, 10H, CHaromatic), 7.27 (m,4H, $CH_{aromatic}$), 6.99 (d, *J* = 8.4 Hz, 2H, $CH_{aromatic}$), 6.91 (appearant t, *J* = 8.8 and 6.8 Hz, 4H, $CH_{aromatic}$), 6.84 (d, *J* = 9.2 Hz, 2H, $CH_{aromatic}$), 6.39 (d, *J* = 6.4 Hz, 2H, 2(CH-S)), 5.03 (d, *J* = 5.2 Hz, 4H, (O-CH_2)), 3.92 (dd, *J* = 5.2 and 4 Hz, 4H, 2(CH_2-S)). ^{13}C-NMR: δ (ppm) = 170.85 (2C=O), 158.64 (2C_{ar}), 148.00 (2C_{ar}), 132.92 (4C_{ar}), 132.48 (2C_{ar}), 132.40 (2C_{ar}), 128.96 (4C_{ar}), 128.90 (8C_{ar}), 120.32 (4C_{ar}), 115.58 (4C_{ar}), 115.25 (4C_{ar}), 68.82 (2C-C=O), 63.80 (2O-C), 33.15 (2C-S).

3,3'-(methylenebis(4,1-phenylene))bis(2-(4-((2-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9d)

Dark-yellow solid, (97%), R_f = 0.2, (98-100)°C; ^{1}H-NMR: δ (ppm) = 7.91-7.86 (m, 4H, $CH_{aromatic}$), 7.57-7.56 (m, 2H, $CH_{aromatic}$), 7.32-7.29 (m, 6H, $CH_{aromatic}$), 7.24-7.20 (m, 4H, $CH_{aromatic}$), 7.14-7.07 (m, 8H, $CH_{aromatic}$), 6.62 (dd, *J* = 8.4 and 18.4 Hz, 2H, 2(CH-S)), 5.26 (d, *J* = 6 Hz, 4H, (O-CH_2)), 4.02 (s, 2H,-CH_2-), 3.90 (d, *J* = 6.4 Hz, 2H, (CH_2-S)), 3.79 (d, *J* = 7.2 Hz, 2H, (CH_2-S)). ^{13}C-NMR: δ (ppm)= 170.99 (2C=O), 159.19 (2C_{ar}), 138.88 (2C_{ar}), 132.75 (2C_{ar}), 132.06 (4C_{ar}),130.45 (2C_{ar}), 129.70 (4C_{ar}), 129.43 (4C_{ar}), 128.78 (2C_{ar}), 128.51 (4C_{ar}), 127.00 (2C_{ar}), 125.87 (2C_{ar}), 121.06 (2Car), 115.37 (4C_{ar}), 67.39 (2C-C=O), 65.37 (2O-C), 40.93 (-C-), 29.72 (2C-S).

3,3'-(methylenebis(4,1-phenylene))bis(2-(4-((3-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9e)

Yellow solid, (86%), R_f = 0.2, (58-61)°C; ^{1}H-NMR: δ (ppm) = 7.86 (m, 4H, $CH_{aromatic}$), 7.53 (d, *J* = 9.2 Hz, 4H, $CH_{aromatic}$), 7.43 (s, 2H, $CH_{aromatic}$), 7.36 (s, 6H, $CH_{aromatic}$), 7.30-7.28 (m, 4H, $CH_{aromatic}$), 7.06 (d, *J* = 8.8 Hz, 4H, $CH_{aromatic}$), 6.39 (s, 2H, 2(CH-S)), 5.03 (s, 4H, (O-CH_2)), 3.96 (s, 4H, 2(CH_2-S)), 3.84 (s, 2H, -CH_2-). ^{13}C-NMR : δ (ppm) = 171.28 (2C=O), 158.51 (2C_{ar}), 147.14 (2C_{ar}), 140.10 (2C_{ar}), 136.13 (2C_{ar}), 130.82 (4C_{ar}), 129.33 (2C_{ar}), 128.79 (4C_{ar}), 128.26 (2C_{ar}), 127.83 (4C_{ar}), 126.81 (2C_{ar}), 126.66 (2C_{ar}), 126.14 (2C_{ar}), 121.53 (2C_{ar}), 115.23 (4C_{ar}), 68.71 (2C-C=O), 63.65 (2O-C), 52.62 (-C-), 33.17 (2C-S).

3,3'-(methylenebis(4,1-phenylene))bis(2-(4-((4-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9f)

White solid, (88%), R_f= 0.2, (175-177)°C; ^{1}H-NMR: δ (ppm) = 7.89-7.84 (m, 2H, $CH_{aromatic}$), 7.48-7.46 (m, 3H, $CH_{aromatic}$), 7.35-7.27 (m, 6H, $CH_{aromatic}$), 7.21-7.12 (m, 8H, $CH_{aromatic}$), 7.06 (d, *J* = 8.4 Hz, 2H, $CH_{aromatic}$), 7.87 (d, *J* = 8.8 Hz, 2H, $CH_{aromatic}$), 6.38 (s, 2H, 2(CH-S)), 5.01 (s, 4H, (O-CH_2)), 3.97 (d, *J* = 15.2 Hz, 4H, 2(CH_2-S)), 3.84 (s, 2H, (-CH_2-)). ^{13}C-NMR: δ (ppm) = 170.82 (2C=O), 158.56 (2C_{ar}), 139.45 (2C_{ar}), 136.36 (4C_{ar}), 136.13 (2C_{ar}), 132.92 (2C_{ar}), 132.62 (2C_{ar}), 130.00 (8C_{ar}), 129.34 (4C_{ar}), 129.01 (2C_{ar}), 128.84 (4C_{ar}), 115.22 (4C_{ar}), 69.25 (2C-C=O), 68.78 (2O-C), 34.48 (-C-), 33.16 (2C-S).

3,3'-(sulfonylbis(4,1-phenylene))bis(2-(4-((2-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9g)

Pale-yellow solid, (93%), R_f= 0.2, (178-179)°C; ^{1}H-NMR: δ (ppm) = 7.81-7.74 (m, 4H, CHaromatic), 7.67 (d, *J* = 8.8 Hz, 2H, $CH_{aromatic}$), 7.51 (t, *J* = 8.8 Hz, 4H, $CH_{aromatic}$), 7.45-7.40 (m, 4H, $CH_{aromatic}$), 7.34 (d, *J* = 6 Hz, 3H, $CH_{aromatic}$), 7.31 (appearant t, *J* = 3.2 and 3.6 Hz, 3H, $CH_{aromatic}$), 6.99 (d, *J* = 8.8 Hz, 4H, $CH_{aromatic}$), 6.50 (s, 2H, 2(CH-S)), 5.13 (d, *J* = 4 Hz, 4H, (O-CH_2)), 3.19 (d, *J* = 8.4 Hz, 2H, (CH_2-S)), 3.07 (d, *J* = 15.6 Hz, 2H, (CH_2-S)).

^{13}C-NMR : δ (ppm) = 171.19 (2C=O), 158.84 (2C_{ar}), 150.09 (2C_{ar}), 141.01 (2C_{ar}), 140.29 (2C_{ar}), 134.20 (2C_{ar}), 133.44 (2C_{ar}), 132.43 (4C_{ar}), 131.91 (4C_{ar}), 129.21 (4C_{ar}), 128.99 (4C_{ar}), 126.89 (4C_{ar}), 126.81 (4C_{ar}), 67.17 (2C-C=O), 64.61 (2O-C), 33.25 (2C-S).

3,3'-(sulfonylbis(4,1-phenylene))bis(2-(4-((3-chlorobenzyl)oxy)phenyl) thiazolidin-4-one) (9h)

Orang solid, (79%), R_f= 0.3, (105-108)°C; ^{1}H-NMR: δ (ppm) = 7.92 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 7.33-7.15 (m, 16H, $CH_{aromatic}$), 6.94 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 6.60 (s, 2H, 2(CH-S)), 5.18 (s, 4H, (O-CH_2)), 3.71 (dd, *J* = 15.6 and 15.6 Hz, 4H, 2(CH_2-S)). ^{13}C-NMR: δ (ppm) = 170.99 (2C=O), 160.74 (2C_{ar}), 139.78 (2C_{ar}), 136.48 (2C_{ar}), 133.64 (2C_{ar}), 133.54 (4C_{ar}), 130.78 (6C_{ar}), 128.99 (2C_{ar}), 128.84 (2C_{ar}), 128.15 (2C_{ar}). 127.88 (2C_{ar}), 127.70 (2C_{ar}), 126.50 (2C_{ar}), 115.03 (4C_{ar}), 68.66 (2C-C=O), 60.98 (2O-C), 31.16 (2C-S).

3,3'-(sulfonylbis(4,1-phenylene))bis(2-(4-((4-chlorobenzyl)oxy)phenyl)thiazolidin-4-one) (9i)

White solid, (89%), R_f= 0.3, (257-259)°C; ^{1}H-NMR: δ (ppm) = 7.81 (d, *J* = 6 Hz, 4H, $CH_{aromatic}$), 7.39-7.22 (m, ^{13}H, $CH_{aromatic}$), 7.11-7.04 (m, 6H, $CH_{aromatic}$), 6.94 (d, *J* = 6 Hz, 2H, $CH_{aromatic}$), 6.32 (s, 2H, 2(CH-S)), 5.18 (s, 4H, (O-CH_2)), 3.75 (dd, *J* = z 15.6 and 15.6 Hz, 4H, 2(CH_2-S)). ^{13}C-NMR: δ (ppm) = 173.3 (2C=O), 160.4 (2C_{ar}), 145.9 (2C_{ar}), 137.1 (2C_{ar}), 135.2 (2C_{ar}), 135.1 (4C_{ar}), 134.2 (2C_{ar}), 134.1 (4C_{ar}), 129.3 (4C_{ar}), 128.7 (2C_{ar}). 128.3 (4C_{ar}), 128.1 (4C_{ar}), 127.3 (2C_{ar}), 126.7 (2C_{ar}), 123.8 (2C_{ar}), 116.1(2C_{ar}),70.9 (2C-C=O), 66.9 (2O-C), 35.6 (2C-S).

CONCLUSION

In conclusion, we have reported a practical method towered the synthesis of 1,3-Thiazolidin-4-ones derivatives. This process started with the etherification step between p-hydroxy benzaldehyde substrate and *o-, m-*, and *p*-chloro substitution of benzyl chloride at room temperature, followed by appropriate synthesis of various new Bis-Schiff bases derivatives through the reaction of 4-((chlorobenzyl) oxy)benzaldehyde with some aromatic di-amine substrates under the condensation reaction conditions. Lastly the cyclization process between Bis-Schiff bases and thioglycolic acid afforded the desired 1,3-Thiazolidin-4-one's products over three functional and efficient steps.

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Conflict of interest

The author declare that we have no conflict of interest.

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