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Comparative Study Between Thermal Heating and Microwave-Assisted Synthesis for New Series of Phenothiazine Derivatives

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Abstract—New and efficient synthetic approaches to phenothiazine derivatives have been developed on the basis of reactions of 1-(10*H*-phenothiazin-2-yl)ethanone hydrazone with isothiocyanates and hydrazonoyl chlorides under conventional thermal heating and microwave irradiation. The structures of the newly synthesized compounds have been confirmed by elemental analyses and spectroscopic data.

Keywords: phenothiazines, hydrazones, thiosemicarbazone, hydrazonoyl halides, thiazoles, microwave assistance.

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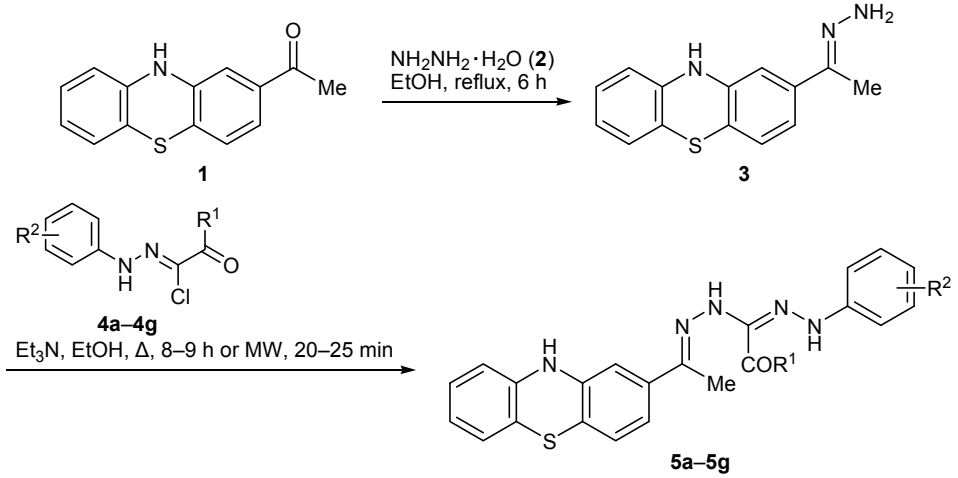
The discovery and innovation of pharmacologically active agents remains an objective target in the search for new medicines and related therapeutic approaches. Many efforts have been made to synthesize novel heterocyclic precursors of chemotherapeutic agents helpful in the treatment of different diseases for the past years. Various phenothiazine derivatives have been reported to possess diverse biological activities. Thus, the significance of phenothiazine compounds as drugs have long been known [1]. They have also been successfully employed as antioxidants in industrial applications [2]. Another bioactive compounds are formazans which have been found to possess wide spectrum of biological activities such as anticonvulsant [3, 4], anticancer [5, 6], antitubercular [7, 8], antifungal [9], antimicrobial [4, 10], anti-inflammatory [11, 12] and anti-HIV [13, 14]. Also, thiazole ring finds applications in many fields such as polymers [15], liquid crystals [16], photonucleases [17], fluorescent dyes [18, 19], insecticides [20], and antioxidants

Scheme 1.



4, **5**, R^1 = Me, R^2 = 3-Me (**a**), 4-Me (**b**), 3-Cl (**c**), 4-O_2N (**d**); R^1 = EtO, R^2 = H (**e**), 3-Me (**f**), 4-O_2N (**g**).

Table 1. Synthesis of formazan derivatives **5a**–**5g** under thermal heating and microwave irradiation

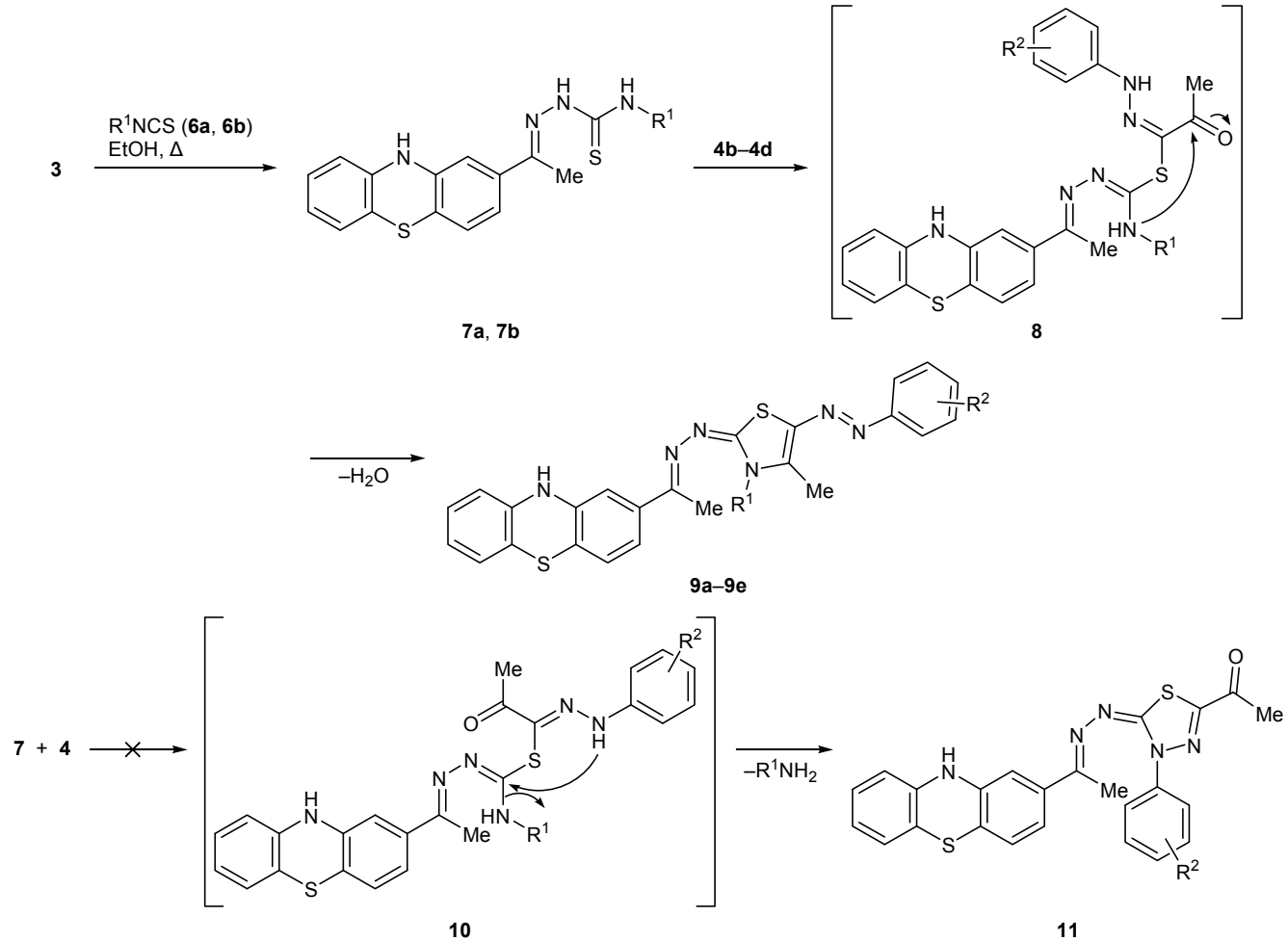
Compound no.	Thermal heating		Microwave irradiation	
	time, h	yield, %	time, min	yield, %
5a	8	72	20	80
5b	9	56	20	82
5c	9	71	25	80
5d	9	63	20	70
5e	8	43	20	50
5f	9	83	25	84
5g	9	47	20	55

[21, 22]. In continuation of our research concerning the synthesis of new heterocyclic compounds [23–28] on the basis of hybridization of biologically active compounds to obtain more effective bioactive derivatives, herein we report the synthesis of new phenothiazine derivatives conjugated with formazan and thiazole fragments under microwave irradiation.

2-Acetylphenothiazine **1** was converted to hydrazone **3** by reaction with hydrazine hydrate (**2**) in ethanol under reflux (Scheme 1). The condensation of **3** with *N*-aryl hydrazonoyl chlorides **4a**–**4g** in the presence of a small amount of triethylamine under reflux or microwave irradiation afforded formazan derivatives **5a**–**5g** (Scheme 1) whose structure was assigned on the basis of all possible spectral data. Expectedly, the reaction between hydrazonoyl halides **4** and hydrazone **3** under microwave irradiation gave better results than under conventional heating with respect to the reaction time and yield (Table 1).

By treatment of hydrazone **3** with phenyl and methyl isothiocyanates **6a** and **6b** in ethanol under reflux we obtained the corresponding *N*-substituted thiosemicarbazones **7a** and **7b** (Scheme 2) which were

Scheme 2.



6, **7**, R^1 = Ph (**a**), Me (**b**); **9**, R^1 = Ph, R^2 = 4-Me (**a**), 3-Cl (**b**); R^1 = Me, R^2 = 4-Me (**c**), 4-O_2N (**d**), 3-Cl (**e**).

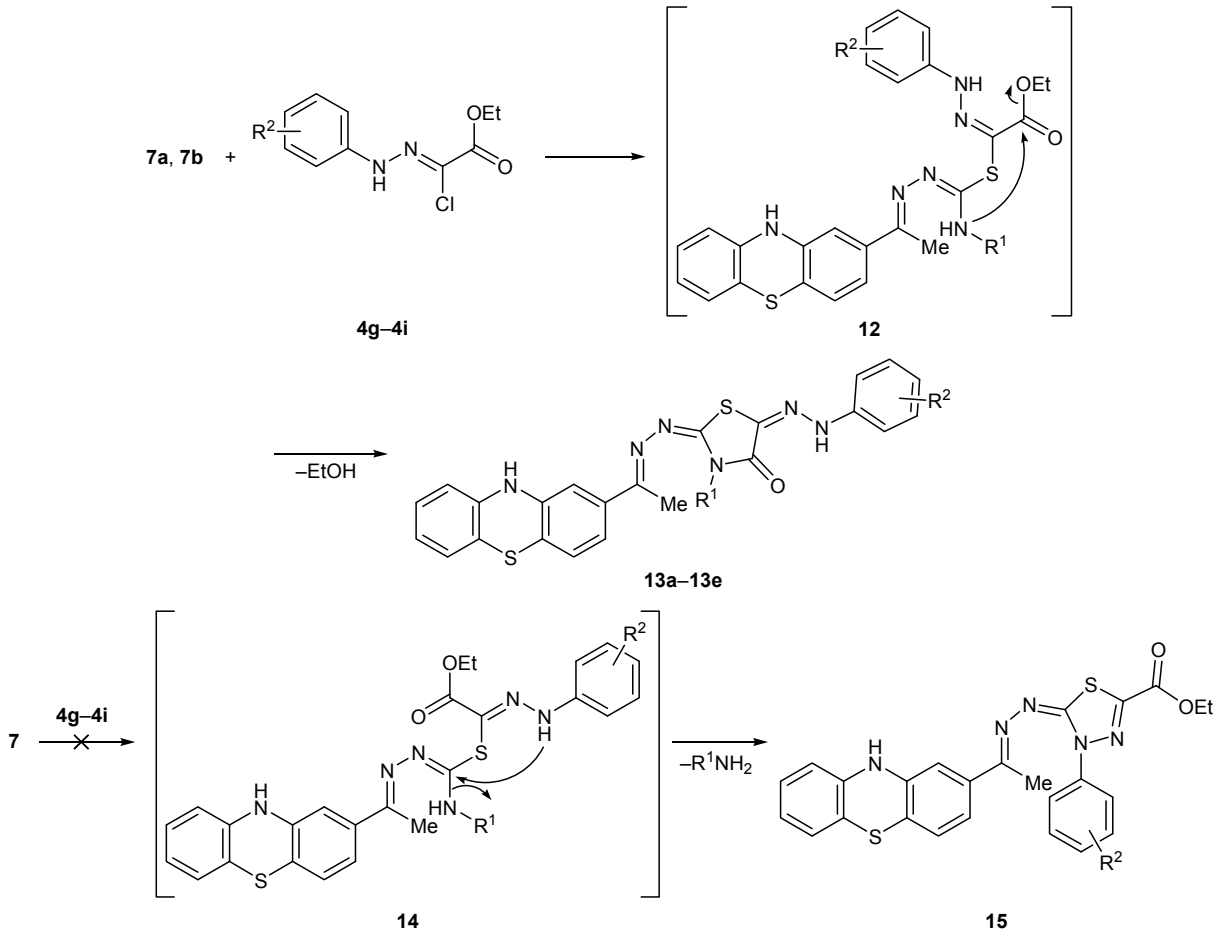
Table 2. Synthesis of thiazole derivatives **9a**–**9e** under thermal heating and microwave irradiation and their UV spectral data

Compound no.	Thermal heating		Microwave irradiation		UV spectrum (dioxane), λ_{max}, nm (log ε)
	time, h	yield, %	time, min	yield, %	
9a	8	63	25	64	474 (2.70), 325 (2.68)
9b	10	68	30	70	480.5 (2.46), 324 (2.74)
9c	10	68	30	75	479.5 (3.03), 324.5 (2.91)
9d	9	55	25	69	475 (3.24), 283 (3.13)
9e	9	70	25	70	488.5 (2.99), 319 (2.92)

brought into condensation with hydrazonoyl chlorides **4b**–**4d** under the same experimental conditions. In all cases, only one product was formed as demonstrated by TLC. The products were identified as thiazole derivatives **9a**–**9e** rather than thiadiazoles **11** on the basis of spectral data and elemental analyses. Furthermore, the UV spectra of **9a**–**9e** displayed an absorption band with its maximum at λ 474–488.5 nm, indicating the presence of an azo group in their molecules (Table 2) [29, 30]. It should be noted that the microwave-assisted reaction between hydrazonoyl halides **4** and thiosemicarbazones **7** provided much shorter reaction time, whereas no appreciable improvement in the yield was observed (Table 2).

In a similar manner, the condensation of **7a** and **7b** with *C*-(ethoxycarbonyl)-*N*-arylhydrazonoyl chlorides

Scheme 3.



4, R^2 = 4-Me (**h**), 3-Cl (**i**); **13**, R^1 = Ph, R^2 = 4-Me (**a**), 3-Cl (**b**); R^1 = Me, R^2 = 4-Me (**c**), 4-O_2N (**d**), 3-Cl (**e**).

Table 3. Synthesis of thiazole derivatives **13a**–**13e** under thermal heating and microwave irradiation and their UV spectral data

Compound no.	Thermal heating		Microwave irradiation		UV spectrum (dioxane), λ_{max}, nm (log ε)
	time, h	yield, %	time, min	yield, %	
13a	8	68	25	80	396 (2.72), 311 (2.87)
13b	10	37	30	60	367.5 (2.43), 310 (2.47)
13c	10	75	30	75	385 (3.07), 299.5 (3.06)
13d	9	66	25	79	396 (3.15), 296 (3.009)
13e	9	79	25	84	375.5 (3.046), 294.5 (3.044)

4g–**4i** afforded thiazole-4(5*H*)-one derivatives **13a**–**13e** while alternative thiadiazole derivatives **15** were ruled out according to the results of spectral analysis (Scheme 3). The ^{1}H NMR of the isolated products lacked triplet and quartet signals typical to ester ethoxy group, so that they were assigned structure **13** rather than **15**. Also, the presence of two NH absorption bands in the IR spectra of **13a**–**13e** in the regions 3393–3336 and 3318–3232 cm^{-1} ruled out the formation of compounds **15**. The UV spectral data for thiazolone derivatives **13a**–**13e** displayed a long-wavelength absorption band with λ_{max} in the region 367.5–396 nm, which indicated the presence of a hydrazone moiety (=N–NH–) (Table 3). The reaction between hydrazonoyl halides **4g**–**4i** and thiosemicarbazones **7a** and **7b** under microwave irradiation was much better than conventional heating in saving reaction time and improving the yield (Table 3).

EXPERIMENTAL

The melting points were measured on a Gallenkamp melting point apparatus in open glass capillaries and are uncorrected. The IR spectra were measured in KBr on a Nicolet 6700 FT-IR spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 400 spectrometer at 400 and 100 MHz, respectively, using DMSO-d_6 as solvent. Elemental analysis (C, H, N) was carried out on a Perkin Elmer 2400 elemental analyzer. Microwave-assisted reactions were performed in a CEM MARS multi-mode microwave system equipped with a magnetic stirring plate and a rotor that allows parallel processing of several vessels per batch. We used 80-mL HP-500 vessels with a Teflon insert (maximum pressure 350 psi, maximum temperature 210°C) for maximum save operation. All chemicals were purchased from Sigma–Aldrich or Fluka and were used without further purification. Hydrazonoyl halides **4a**–**4i** were synthesized as reported previously [31, 32].

1-[(10*H*-Phenothiazin-2-yl)ethylidene]hydrazine (3). A mixture of 2.41 g (0.01 mol) of 1-(10*H*-phenothiazin-2-yl)ethanone (**1**) and 5 mL of hydrazine hydrate in 20 mL of ethanol was refluxed for 6 h. The mixture was allowed to cool down, and the precipitate was filtered off, washed with water, and recrystallized from chloroform. mp 126°C (from $CHCl_3$). IR spectrum, ν, cm^{-1}: 3472–3340, 3190 (NH, NH_2), 1579 (C=N). Mass spectrum, *m*/*z* (I_{rel}, %): 256 (13) $[M + 1]^+$, 255 (71) $[M]^+$, 239 (25), 224 (28), 198 (100), 197 (21), 196 (14), 192 (24), 191 (11), 171 (16), 154 (38), 153 (13), 128 (14), 127 (20), 119 (18), 104 (13), 99 (15), 93 (53), 85 (10), 77 (23). Found, %: C 65.71; H 5.0; N 16.25. $C_{14}H_{13}N_3S$. Calculated, %: C 65.85; H 5.13; N 16.46. *M* 255.34.

Reactions of hydrazone 3 with hydrazonoyl chlorides 4a–4g (*general procedures*). *a*. *Conventional heating*. A mixture of 1 mmol of 1-[(10*H*-phenothiazine-2-yl)ethylidene]hydrazine (**3**), 1 mmol of hydrazonyl chloride **4a**–**4g**, and a catalytic amount of triethylamine in 15 mL of ethanol was refluxed for a period of time indicated in Table 1 or 2. The mixture was then left to cool, and the resulting solid was filtered off, washed with ethanol, and recrystallized to afford the corresponding formazan derivative **5a**–**5g**.

b. *Microwave-assisted reaction*. An HP-500 process vial was charged with a mixture of 1 mmol of hydrazone **3**, 1 mmol of hydrazonoyl chloride **4a**–**4g**, and a catalytic amount of triethylamine in 15 mL of propan-2-ol. The vial was capped properly and irradiated by microwaves at a power of 400 W under pressurized conditions at 110°C for 20–30 min. The mixture was then left to cool, and the resulting solid was filtered off, washed with ethanol, and recrystallized from an appropriate solvent to afford the corresponding formazan derivative **5a**–**5g**.

1-[(3-Methylphenyl)hydrazinylidene]-1-{2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinyl}propan-2-one (5a). mp 178–180°C (from

EtOH). IR spectrum, ν, cm^{-1}: 3389, 3333, 3250 (NH), 1676 (C=O), 1599 (C=N). ^1H NMR spectrum, δ, ppm: 2.17 s (3H, CH_3), 2.26 s (3H, CH_3), 2.33 s (3H, CH_3), 6.59-7.29 m (11H, H_{arom}), 8.92 s (1H, NH), 10.19 s (1H, NH), 11.62 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 18.99, 21.75, 24.03, 110.63, 111.34, 114.13, 114.99, 116.25, 116.42, 118.12, 119.33, 121.58, 122.42, 126.85, 130.83, 132.77, 136.21, 138.01, 139.05, 142.11, 142.78, 144.03, 145.57, 192.47. Mass spectrum, *m*/*z* (I_{rel}, %): 430 (30) $[M + 1]^+$, 429 (100) $[M]^+$, 369 (9), 368 (18), 330 (15), 91 (2). Found, %: C 66.90; H 5.27; N 16.19. $C_{24}H_{23}N_5OS$. Calculated, %: C 67.11; H 5.40; N 16.30. *M* 429.54.

1-[(4-Methylphenyl)hydrazinylidene]-1-{2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinyl}propan-2-one (5b). mp 169–171°C (from EtOH). IR spectrum, ν, cm^{-1}: 3375, 3326, 3271 (NH), 1681 (C=O), 1614 (C=N). ^1H NMR spectrum, δ, ppm: 2.15 s (3H, CH_3), 2.21 s (3H, CH_3), 2.44 s (3H, CH_3), 6.65–7.33 m (11H, H_{arom}), 8.74 s (1H, NH), 8.88 s (1H, NH) 11.53 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 11.57, 24.59, 26.91, 111.01, 113.19, 114.88, 114.99, 115.05, 115.59, 116.69, 118.70, 122.04, 126.56, 126.63, 126.70, 128.09, 141.69, 141.78, 142.20, 142.46, 142.49, 197.33. Mass spectrum, *m*/*z* (I_{rel}, %): 430 (13) $[M + 1]^+$, 429 (33) $[M]^+$, 421 (30), 410 (16), 397 (25), 391 (36), 381 (50), 373 (23), 369 (47), 358 (60), 355 (29), 354 (58), 352 (97), 351 (35), 350 (61), 343 (42), 341 (35), 330 (67), 323 (37), 316 (41), 304 (66), 299 (25), 298 (30), 297 (80), 293 (59), 286 (26), 280 (86), 240 (52), 223 (20), 199 (29), 198 (90), 164 (30), 154 (43), 111 (16), 107 (17), 103 (24), 94 (19), 83 (22), 77 (36). Found, %: C 67.0; H 5.26; N 16.18. $C_{24}H_{23}N_5OS$. Calculated, %: C 67.11; H 5.40; N 16.30. *M* 429.54.

1-[(3-Chlorophenyl)hydrazinylidene]-1-{2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinyl}propan-2-one (5c). mp 179–181°C (from EtOH). IR spectrum, ν, cm^{-1}: 3351, 3220 (NH), 1662 (C=O), 1621, 1596, 1570 (C=N). ^1H NMR spectrum, δ, ppm: 2.19 s (3H, CH_3) 2.48 s (3H, CH_3), 6.65–7.29 m (11H, H_{arom}), 8.71 s (1H, NH), 8.96 s (1H, NH), 11.66 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 12.41, 24.22, 111.40, 112.12, 112.81, 114.96, 115.03, 116.27, 116.44, 118.31, 119.40, 119.43, 122.39, 126.42, 126.72, 126.81, 128.17, 131.35, 133.47, 142.32, 145.59, 146.36, 192.76. Mass spectrum, *m*/*z* (I_{rel}, %): 451 (16) $[M + 2]^+$, 450 (16) $[M + 1]^+$, 449 (63) $[M]^+$, 381 (23), 380 (16), 379 (63), 378 (45), 377 (100), 376 (54), 369 (18), 363 (21), 361 (26), 360 (12), 358 (19), 342 (15), 111 (2), 105 (15), 77 (12). Found, %: C 61.25; H 4.31; N 15.28. $C_{23}H_{20}ClN_5OS$. Calculated, %: C 61.39; H 4.48; N 15.56. *M* 449.96.

1-[(4-Nitrophenyl)hydrazinylidene]-1-{2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinyl}propan-2-one (5d). mp 208–210°C (from EtOH). IR spectrum, ν, cm^{-1}: 3384, 3323, 3287 (NH), 1689 (C=O), 1647, 1608 (C=N). ^1H NMR spectrum, δ, ppm: 2.21 s (3H, CH_3), 2.51 s (3H, CH_3), 6.59–7.29 m (11H, H_{arom}), 8.39 s (1H, NH), 9.03 s (1H, NH), 13.05 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.0, 24.48, 112.36, 114.96, 116.06, 118.72, 119.40, 120.43, 122.29, 122.29, 122.75, 126.16, 126.42, 126.78, 132.59, 136.71, 141.08, 141.17, 142.27, 139.57, 193.72. Mass spectrum, *m*/*z* (I_{rel}, %): 460 (1) $[M]^+$, 363 (15), 327 (23), 326 (100), 325 (69), 294 (20), 243 (33), 240 (57), 225 (20), 198 (53), 197 (30), 192 (13), 171 (11), 167 (13), 166 (11), 154 (16), 138 (48), 108 (17), 92 (23), 86 (15), 80 (15), 77 (16). Found, %: C 59.75; H 4.17; N 18.09. $C_{23}H_{20}N_6O_3S$. Calculated, %: C 59.99; H 4.38; N 18.25. *M* 460.51.

Ethyl 2-{2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinyl}-2-(phenylhydrazinylidene)acetate (5e). mp 174–176°C (from EtOH). IR spectrum, ν, cm^{-1}: 3310 br (NH), 1696 (C=O), 1601 (C=N). ^1H NMR spectrum, δ, ppm: 1.19 t (3H, CH_3, J = 7 Hz), 2.19 s (3H, CH_3), 4.26 q (2H, CH_2, J = 7 Hz), 6.58–7.53 m (12H, H_{arom}), 8.99 s (1H, NH), 10.18 s (1H, NH), 10.96 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 12.79, 26.54, 61.58, 111.47, 112.92, 113.07, 114.96, 116.17, 117.71, 119.35, 122.37, 122.56, 126.51, 126.77, 128.02, 128.19, 129.64, 130.22, 136.23, 142.81, 146.35, 160.75. Mass spectrum, *m*/*z* (I_{rel}, %): 446 (32) $[M + 1]^+$, 445 (100) $[M]^+$, 316 (9), 240 (8), 77 (3). Found, %: C 64.49; H 5.02; N 15.58. $C_{24}H_{23}N_5O_2S$. Calculated, %: C 64.70; H 5.20; N 15.72. *M* 445.54.

Ethyl 2-[(3-methylphenyl)hydrazinylidene]-2-{2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinyl}acetate (5f). mp 156–158°C (from EtOH). IR spectrum, ν, cm^{-1}: 3390, 3336 (NH), 1696 (C=O), 1600 (C=N). ^1H NMR spectrum, δ, ppm: 1.21 t (3H, CH_3, J = 7 Hz), 2.03 s (3H, CH_3), 2.21 s (3H, CH_3), 4.44 q (2H, CH_2, J = 7 Hz), 6.59–7.61 m (11H, H_{arom}), 9.41 s (1H, NH), 10.19 s (1H, NH), 10.98 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 14.57, 21.75, 26.73, 62.73, 112.34, 114.96, 115.12, 117.66, 121.43, 122.55, 122.64, 125.08, 126.73, 127.37, 128.42, 128.51, 130.92, 136.24, 140.47, 141.87, 142.14, 148.08, 155.53, 160.77, 162.60. Mass spectrum, *m*/*z* (I_{rel}, %): 460 (14) $[M + 1]^+$, 459 (51) [*M*]+, 354 (11), 352 (8),

351 (27), 350 (100), 331 (16), 330 (61), 329 (7), 324 (9), 315 (13), 91 (2). Found, %: C 65.16; H 5.34; N 15.21. $C_{25}H_{25}N_5O_2S$. Calculated, %: C 65.34; H 5.48; N 15.24. *M* 459.56.

Ethyl 2-[(4-nitrophenyl)hydrazinylidene]-2-{2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinyl}acetate (5g). mp 193–195°C (from EtOH). IR spectrum, ν, cm^{-1}: 3336, 3228 (NH), 1707 (C=O), 1653, 1599 (C=N). ^{1}H NMR spectrum, δ, ppm: 1.18 t (3H, CH_3, *J* = 7 Hz), 2.23 s (3H, CH_3), 4.30 q (2H, CH_2, *J* = 7 Hz), 6.58–7.32 m (11H, H_{arom}), 8.68 s (1H, NH), 9.49 s (1H, NH), 11.38 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.45, 14.49, 62.27, 111.63, 112.11, 115.02, 116.36, 118.34, 119.64, 120.75, 122.39, 124.89, 126.44, 126.75, 128.19, 133.75, 137.62, 138.96, 142.07, 147.50, 150.46, 162.05. Mass spectrum, *m*/*z* (I_{rel}, %): 490 (20) [*M*]+, 478 (47), 473 (17), 463 (18), 365 (11), 363 (14), 362 (44), 361 (100), 360 (14), 356 (11), 355 (11), 354 (15), 350 (15), 346 (10), 338 (14), 337 (12), 330 (14), 327 (10), 324 (29), 315 (18), 314 (17), 313 (15), 294 (12), 79 (8). Found, %: C 58.54; H 4.37; N 17.0. $C_{24}H_{22}N_6O_4S$. Calculated, %: C 58.76; H 4.52; N 17.13. *M* 490.53.

N-Substituted 2-[1-(10*H*-phenothiazin-2-yl)-ethylidene]hydrazine-1-carbothioamides 7a and 7b (*general procedure*). A mixture of 2.55 g (0.01 mol) of hydrazine **3** and 0.01 mol of phenyl or methyl isothiocyanate in 20 mL of ethanol was refluxed for for 5 h with stirring. When the reaction was complete (TLC), the solid product was filtered off, washed with ethanol, and recrystallized from ethanol.

2-[1-(10*H*-Phenothiazin-2-yl)ethylidene]-*N*-phenylhydrazine-1-carbothioamide (7a). mp 179–180°C (from EtOH). IR spectrum, ν, cm^{-1}: 3306–3177 (NH), 1594 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 6.65–7.59 m (12H, H_{arom}), 8.57 s (1H, NH), 9.89 s (1H, NH), 10.61 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 14.72, 112.51, 114.97, 116.31, 118.88, 120.97, 122.31, 125.78, 125.91, 126.36, 126.69, 128.16, 128.62, 137.26, 139.48, 142.07, 142.23, 148.88, 177.29. Mass spectrum, *m*/*z* (I_{rel}, %): 392 (1) $[M + 1]^+$, 391 (1) $[M]^+$, 350 (10), 324 (18), 316 (43), 301 (22), 278 (27), 255 (19), 240 (32), 239 (29), 225 (21), 224 (49), 223 (37), 198 (42), 197 (28), 192 (27), 191 (18), 154 (13), 105 (100), 83 (12), 77 (56). Found, %: C 64.41; H 4.37; N 14.15. $C_{21}H_{18}N_4S_2$. Calculated, %: C 64.59; H 4.65; N 14.35. *M* 390.52.

***N*-Methyl-2-[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazine-1-carbothioamide (7b).** mp 165–167°C (from EtOH). IR spectrum, ν, cm^{-1}: 3362, 3251, 3143 (NH), 1590 (C=N). Mass spectrum, *m*/*z* (I_{rel}, %): 329 (3) $[M + 1]^+$, 328 (53) $[M]^+$, 297 (47), 239 (44), 224 (52), 198 (100), 197 (46), 196 (26), 192 (35), 180 (15), 171 (27), 166 (22), 165 (19), 154 (39), 153 (24), 140 (14), 139 (15), 127 (18), 126 (19), 102 (14), 91 (16), 89 (15), 77 (25). Found, %: C 58.35; H 4.78; N 16.85. $C_{16}H_{16}N_4S_2$. Calculated, %: C 58.51; H 4.91; N 17.06. *M* 328.46.

Reactions of thiosemicarbazones 7a and 7b with hydrazonoyl chlorides 4b–4d and 4g–4i (*general procedures*). *a*. *Conventional heating*. A mixture of 1 mmol of thiosemicarbazone **7a** or **7b**, 1 mmol of hydrazonyl chloride **4b**–**4d** or **4g**–**4i**, and a catalytic amount of triethylamine in 15 mL of ethanol was refluxed for a period of time indicated in Table 2 or 3. The mixture was then left to cool, and the resulting solid was filtered, washed with ethanol, and recrystallized to afford the corresponding thiazole derivative **9a**–**9e** or **13a**–**13e**.

b. *Microwave-assisted reaction*. An HP-500 process vial was charged with a mixture of 1 mmol of thiosemicarbazone **7a** or **7b**, 1 mmol of hydrazonyl chloride **4b**–**4d** or **4g**–**4i**, and a catalytic amount of triethylamine in 15 mL of propan-2-ol. The vial was capped properly and irradiated at a power of 400 W under pressurized conditions at 90°C for 20–30 min. The mixture was then left to cool, and the resulting solid was filtered, washed with ethanol, and recrystallized from an appropriate solvent to afford the corresponding thiazole derivative **9a**–**9e** or **13a**–**13e**.

2-(1-{[4-Methyl-5-(4-methylphenyldiazenyl)-3-phenyl-1,3-thiazol-2(3*H*)-ylidene]hydrazinylidene}-ethyl)-10*H*-phenothiazine (9a). mp 150–152°C (from EtOH). IR spectrum, ν, cm^{-1}: 3394 br (NH), 1595 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.05 s (3H, CH_3), 2.35 s (3H, CH_3), 2.47 s (3H, CH_3), 6.69–7.64 m (16H, H_{arom}), 8.74 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.45, 14.79, 21.37, 111.80, 114.96, 116.29, 120.60, 122.09, 122.23, 126.37, 126.65, 128.14, 128.84, 129.71, 129.94, 130,10, 130.37, 133.57, 136.21, 137.54, 139.71, 142.17, 142.24, 146.39, 150.68, 158.73, 164.74. Mass spectrum, *m*/*z* (I_{rel}, %): 546 (8) $[M]^+$, 522 (24), 466 (100), 401 (80), 379 (82), 312 (65), 76 (4). Found, %: C 67.87; H 4.54; N 15.54. $C_{31}H_{26}N_6S_2$. Calculated, %: C 68.10; H 4.79; N 15.37. *M* 546.71.

2-(1-{[5-(3-Chlorophenyldiazenyl)-4-methyl-3-phenyl-1,3-thiazol-2(3*H*)-ylidene]hydrazinylidene}-ethyl)-10*H*-phenothiazine (9b). mp 161–163°C (from EtOH). IR spectrum, ν, cm^{-1}: 3397 (NH), 1594 (C=N).

^{1}H NMR spectrum, δ, ppm: 2.05 s (3H, CH_3), 2.42 s (3H, CH_3), 6.66–7.76 m (16H, H_{arom}), 8.74 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.66, 14.85, 111.87, 114.97, 116.26, 119.26, 120.24, 120.65, 122.24, 126.39, 126.68, 128.15, 128.76, 128.94, 129,89, 129.99, 130.22, 131.54, 133.56, 134.56, 136.04, 137.39, 142.26, 142.34, 149.47, 153.85, 159.45, 164.43. Mass spectrum, *m*/*z* (I_{rel}, %): 568 (2) $[M + 1]^+$, 567 (10) $[M]^+$, 528 (14), 501 (39), 453 (100), 376 (28), 342 (42), 90 (14), 84 (14), 78 (9). Found, %: C 63.28; H 3.87; N 14.64. $C_{30}H_{23}ClN_6S_2$. Calculated, %: C 63.53; H 4.09; N 14.82. *M* 567.13.

2-(1-{[3,4-Dimethyl-5-(4-methylphenyldiazenyl)-1,3-thiazol-2(3*H*)-ylidene]hydrazinylidene}ethyl)-10*H*-phenothiazine (9c). mp 253–255°C (from EtOH). IR spectrum, ν, cm^{-1}: 3368 (NH), 1601, 1587 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.34 s (3H, CH_3), 2.47 s (3H, CH_3), 2.68 s (3H, CH_3), 3.58 s (3H, CH_3), 6.69–7.59 m (11H, H_{arom}), 8.75 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 12.50, 14.79, 21.35, 32.06, 111.75, 114.97, 116.31, 118.92, 120.65, 121.90, 122.22, 126.40, 126.65, 128.13, 130.29, 132.80, 137.79, 139.22, 142.19, 142.25, 147.63, 150.71, 158.04, 164.47. Mass spectrum, *m*/*z* (I_{rel}, %): 485 (12) $[M + 1]^+$, 484 (4) $[M]^+$, 428 (19), 374 (16), 312 (33), 251 (41), 181 (14), 93 (34), 62 (100). Found, %: C 64.21; H 4.87; N 17.29. $C_{26}H_{24}N_6S_2$. Calculated, %: C 64.44; H 4.99; N 17.34. *M* 484.64.

2-(1-{[3,4-Dimethyl-5-(4-nitrophenyldiazenyl)-1,3-thiazol-2(3*H*)-ylidene]hydrazinylidene}ethyl)-10*H*-phenothiazine (9d). mp 302–304°C (from EtOH). IR spectrum, ν, cm^{-1}: 3330 (NH), 1600 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.20 s (3H, CH_3), 2.45 s (3H, CH_3), 3.31 s (3H, CH_3), 6.65-7.30 m (11H, H_{arom}), 8.68 s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 516 (9) $[M + 1]^+$, 515 (13) $[M]^+$, 491 (16), 470 (15), 417 (20), 362 (35), 330 (29), 267 (38), 223 (52), 130 (34), 103 (16), 63 (100), 78 (17). Found, %: C 58.06; H 3.87; N 19.14. $C_{25}H_{21}N_7O_2S_2$. Calculated, %: C 58.24; H 4.11; N 19.02. *M* 515.61.

2-(1-{[5-(3-Chlorophenyldiazenyl)-3,4-dimethyl-1,3-thiazol-2(3*H*)-ylidene]hydrazinylidene}ethyl)-10*H*-phenothiazine (9e). mp 214–216°C (from EtOH). IR spectrum, ν, cm^{-1}: 3355 (NH), 1591 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.35 s (3H, CH_3), 2.72 s (3H, CH_3), 3.61 s (3H, CH_3), 6.71–7.66 m (11H, H_{arom}), 8.75 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 12.73, 14.88, 32.29, 111.81, 114.98, 116.28, 119.17, 120.04, 120.72, 121.90, 121.90, 122.25, 126.42, 126.66, 128.16, 128.50, 131.46, 132.79, 134.49, 137.63, 142.27, 150.78, 153.95, 158.91, 164.13. Mass spectrum, *m*/*z* (I_{rel}, %): 506 (5) $[M + 1]^+$, 505 (9) $[M]^+$, 480 (20), 423 (17), 409 (97), 367 (83), 340 (42), 313 (100), 236 (32), 82 (11). Found, %: C 59.21; H 4.03; N 16.43. $C_{25}H_{21}ClN_6S_2$. Calculated, %: C 59.45; H 4.19; N 16.64. *M* 505.06.

5-(4-Methylphenylhydrazinylidene)-2-{[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinylidene}-3-phenyl-1,3-thiazolidin-4-one (13a). mp 195–197°C (from EtOH). IR spectrum, ν, cm^{-1}: 3393, 3277 (NH), 1718 (C=O), 1605, 1590 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.13 s (3H, CH_3), 2.28 s (3H, CH_3), 6.69–7.56 m (16H, H_{arom}), 8.71 s (1H, NH), 10.60 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.13, 21.64, 111.18, 112.2, 112.84, 114.72, 116.15, 118.99, 120.12, 120.89, 122.34, 122.42, 123.56, 126.70, 128.24, 128.58, 129.40, 134.37, 136.82, 137.03, 139.06, 142.06, 142.30, 142.41, 143.17, 158.99, 160.79, 162.46. Mass spectrum, *m*/*z* (I_{rel}, %): 549 (1.32) $[M + 1]^+$, 548 (10) $[M]^+$, 509 (10), 284 (50), 256 (100), 84 (15), 73 (24). Found, %: C 65.39; H 4.24; N 15.11. $C_{30}H_{24}N_6OS_2$. Calculated, %: C 65.67; H 4.41; N 15.32. *M* 548.68.

5-(3-Chlorophenylhydrazinylidene)-2-{[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinylidene}-3-phenyl-1,3-thiazolidin-4-one (13b). mp 240–241°C (from EtOH). IR spectrum, ν, cm^{-1}: 3336, 3318 (NH), 1706 (C=O), 1617, 1600 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.13 s (3H, CH_3), 6.69–7.74 m (16H, H_{arom}), 8.77 s (1H, NH), 10.84 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.45, 112.84, 113.07, 113.75, 114.74, 115.04, 116.16, 119.94, 120.43, 121.66, 122.36, 126.30, 126.40, 126.67, 128.52, 129.19, 129.40, 131.46, 134.30, 135.26, 136.93, 142.10, 142.44, 145.76, 156.74, 162.09, 163.16. Mass spectrum, *m*/*z* (I_{rel}, %): 571 (1.21) $[M + 2]^+$, 570 (2) $[M + 1]^+$, 569 (5) $[M]^+$, 506 (12), 451 (18), 422 (12), 352 (21), 317 (100), 152 (12), 111 (4), 105 (11), 90 (9), 83 (59). Found, %: C 60.97; H 3.54; N 14.66. $C_{29}H_{21}ClN_6OS_2$. Calculated, %: C 61.20; H 3.72; N 14.77. *M* 569.10.

3-Methyl-5-(3-methylphenylhydrazinylidene)-2-{[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinylidene}-1,3-thiazolidin-4-one (13c). mp 240–242°C (from EtOH). IR spectrum, ν, cm^{-1}: 3373, 3245 (NH), 1696 (C=O), 1616, 1597 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 2.40 s (3H, CH_3), 3.34 s (3H, CH_3), 6.68–7.31 m (11H, H_{arom}), 8.71 s (1H, NH), 10.48 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.46, 21.72, 30.12, 111.78, 112.79, 114.68, 115.02, 116.25, 119.78, 120.51, 122.42, 123.03, 126.45, 126.71, 128.25, 129.55, 137.24, 139.02,

142.07, 142.41, 144.13, 156.63, 162.58, 162.94. Mass spectrum, *m*/*z* (I_{rel}, %) 487 (10) $[M + 1]^+$, 486 (16) $[M]^+$, 443 (19), 377 (11), 353 (23), 310 (18), 267 (16), 178 (19), 135 (24), 98 (50), 40 (100). Found, %: C 61.54; H 4.26; N 17.09. $C_{25}H_{22}N_6OS_2$. Calculated, %: C 61.71; H 4.56; N 17.27. *M* 486.61.

3-Methyl-5-(4-nitrophenylhydrazinylidene)-2-{[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinylidene}-1,3-thiazolidin-4-one (13d). mp 290–291°C (from EtOH). IR spectrum, ν, cm^{-1}: 3373, 3232 (NH), 1696 (C=O), 1617, 1598 (C=N). ^1H NMR spectrum, δ, ppm: 2.41 s (3H, CH_3), 3.36 s (3H, CH_3), 6.68–8.20 m (11H, H_{arom}), 8.72 s (1H, NH), 11.16 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.53, 30.33, 112.81, 113.97, 115.02, 116.22, 119.98, 120.52, 122.42, 126.30, 126.46, 126.60, 126.70, 128.26, 129.93, 137.06, 142.03, 142.42, 150.0, 156.11, 162.28, 163.59. Mass spectrum, *m*/*z* (I_{rel}, %): 517 (11) $[M]^+$, 472 (54), 455 (77), 442 (100), 342 (81), 245 (68), 92 (13), 76 (15). Found, %: C 55.53; H 3.61; N 18.78. $C_{24}H_{19}N_7O_3S_2$. Calculated, %: C 55.69; H 3.70; N 18.94. *M* 517.58.

5-(3-Chlorophenylhydrazinylidene)-3-methyl-2-{[1-(10*H*-phenothiazin-2-yl)ethylidene]hydrazinylidene}-1,3-thiazolidin-4-one (13e). mp 259–261°C (from EtOH). IR spectrum, ν, cm^{-1}: 3377, 3241 (NH), 1696 (C=O), 1617, 1597 (C=N). ^1H NMR spectrum, δ, ppm: 2.41 s (3H, CH_3), 3.41 s (3H, CH_3), 6.68–7.33 m (11H, H_{arom}), 8.71 s (1H, NH), 10.66 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 15.50, 30.22, 112.80, 113.01, 113.66, 115.02, 116.24, 118.0, 119.88, 120.50, 121.61, 122.42, 126.46, 126.71, 128.26, 131.47, 134.30, 137.16, 142.05, 142.42, 144.10, 156.37, 162.44, 163.25. Mass spectrum, *m*/*z* (I_{rel}, %): 509 (2) $[M + 2]^+$, 507 (4) $[M]^+$, 415 (10), 374 (8), 326 (14), 270 (9), 235 (100), 210 (60), 150 (63), 112 (11), 103 (31), 91 (31) 77 (25). Found, %: C 56.65; H 3.70; N 16.42. $C_{24}H_{19}ClN_6OS_2$. Calculated, %: C 56.85; H 3.78; N 16.57. *M* 507.03.

CONFLICT OF INTERESTS

The authors declare no conflict of interests.

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