Reactions of Aroylthioureas with Acetylenic Esters and Dibenzoyl Ethylene. Selectivity towards the formation of New 1,3-Thiazines

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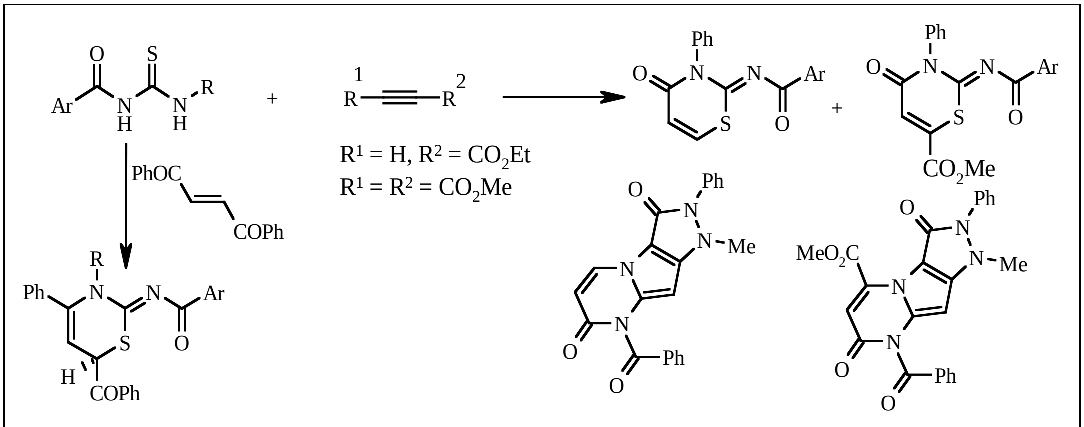

A series of 1,3-thiazines has been synthesized by the reactions of *N*-aroylsubstituted thioureas with ethyl propiolate, dimethyl but-2-ynedioate and (*E*)-1,4-diphenyl-but-2-ene-1,4-dione. The reaction of antipyrinylphenyl thiourea with π-deficient acetylenic reagents did not afford the corresponding 1,3-thiazines, whereas pyrrolo-pyrazolopyrimidines were obtained.

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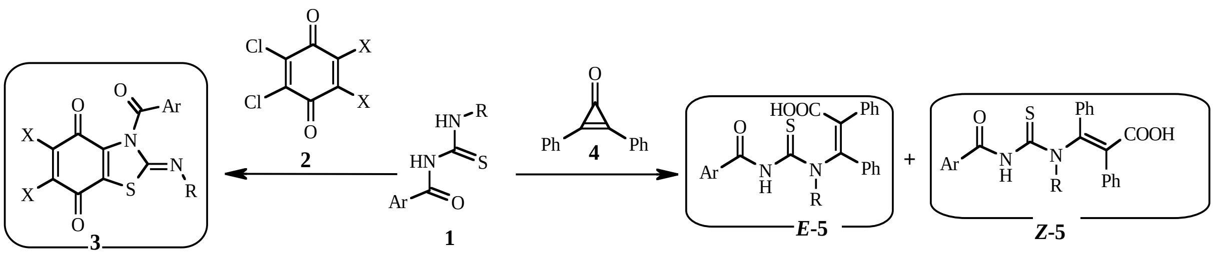
INTRODUCTION

Five membered ring systems such as imidazolidin-2-thiones were obtained from the oxidative cyclization of 1-dibenzoyl-3-aryl-thioureas with bromine-acetophenone in the presence of excess triethylamine [1,2]. Manaka [3] reported on the one-pot condensation of aroylthiourea with α-halocarbonyl derivatives to afford 2-acylimino-3-alkyl-3*H*-thiazolines. 1,2,4-Triazoles were synthesized by the direct reaction of *N*-aryl-*N*'-benzoylthioureas with hydrazine hydrate [4]. To the best of our knowledge, six memberd ring systems were only synthesized as salts from the reaction of aroylthioureas with $SOCl_2$ in $ClCH_2$-CH_2Cl followed by 70% $HClO_4$ to give 31-94% diaminoaryl-oxadiazinium perchlorates, whereas 1,3,5-thiadiazinium salts were prepared by cyclization of aroyl-thioureas with $POCl_3$ [5]. Recently, Aly and his group have demonstrated a very convenient procedure to synthesize fused thiazoles **3** from the reaction of aroyl-phenyl thioureas with π-acceptor quinones (**2**, 2,3,5,6-tetrachloro-1,4-benzoquinone, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and 2,3-dichloro-1,4-naphthoquinone, Scheme 1) [6]. However, the reactions of compounds **1** with 2,3-diphenylcyclopropenone (**4**) in acetic acid afforded the *E* and *Z* mixtures of 3-(3'-aroyl-1-substituted-thioureido)-2,3-diphenylcinnamic acids (**5**, Scheme 1) [7]. It was reported that 1-benzoyl-3-(4-hydroxy-phenyl)-urea reacted, in presence of sodium hydroxide, with benzoyl chloride to provide 1-(3-hydroxyphenyl)-6-oxo-1,6-di-hydro-2-thiomethyl-pyrimidine-4-carboxylic acid methyl ester [8]. Additionally, it was known that the reaction of amidinothioureas, imidoylthioureas, thioacylamidines, *O*-methyl-1-aryl-2-thioisobiurets, and 1-aryl-isodithiobiurets with diethyl azodicarboxylate gave the corresponding thiadiazoles by the oxidative cyclic S-N bond formation [9]. A series of 3-alkyl-5-methylene-2-arylimino-1,3-thia-zolidin-4-ones was obtained from the reaction of *N*-alkyl-*N*'-arylthioureas with dimethyl but-2-ynedioate [10a]. Hyrazinothioureas represented by 1-acylthiosemicarbzides reacted with phenyl propiolate in acetic acid under reflux to afford traizolothiazines [10b]. In light of the afore-mentioned, it appears that the tendency of substituted-thioureas, as simple molecules, is variable from one reagent to another. The efficiency of our synthetic program has been concerned with the use of facile and elegant methods for the preparation of novel heterocycles rather than those suffering from low yields due to the multiple steps described in their preparation [11]. Herein we report on our findings for the synthesis of various novel thiazinones, during the reaction of various *N*-aroyl thioureas with ethyl propiolate, dimethyl but-2-ynedioate and (*E*)-1,4-diphenyl-but-2-ene-1,4-dione. It is note worthy to mention that 1,3-thiazines have their broad spectrum as anti-microbial agents [12,13].

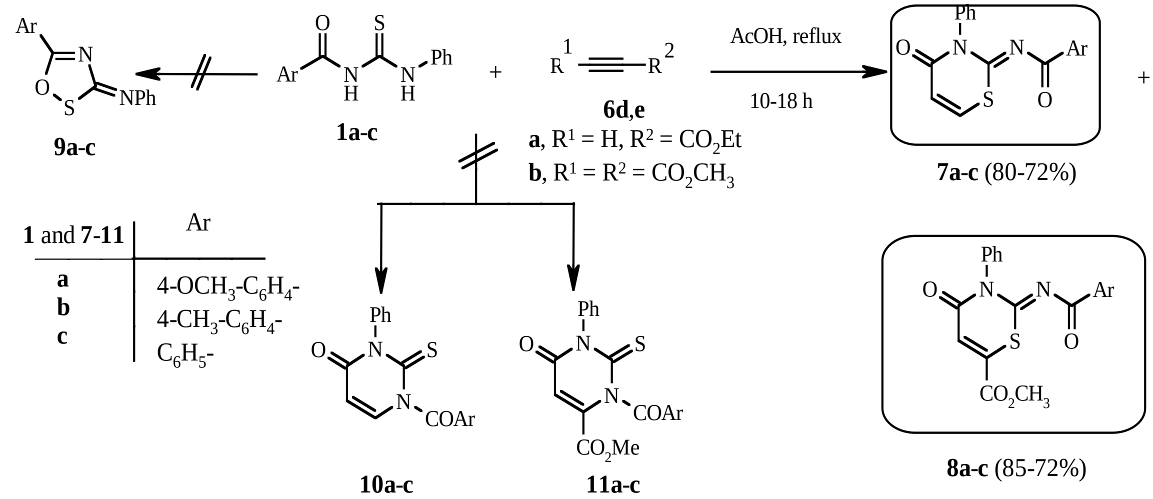


Scheme 1. Reactions of aroylsubstituted thioureas **1** with π-quinones **2** and 2,3-diphenylcyclopropenone (**4**)

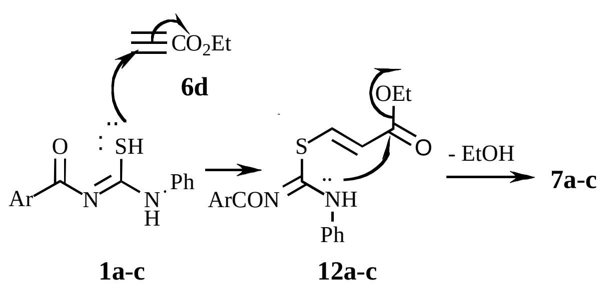
RESULTS AND DISCUSSION

In the present protocol as exhibited in Scheme 2, the reaction of *N*-aroyl-phenyl thioureas **1a-c** with ethyl propiolate (**6d**) and dimethyl but-2-ynedioate ethyl ester (**6e**) under reflux in acetic acid yielded the corresponding 1,3-thizinones **7a-c** and **8a-c**. Generally, it must be pointed out that the ^{1}H nmr spectra of **7a-c** did not reveal any proton resonances related to the NH- or –SH groups. Besides, the ^{13}C nmr spectra did not show any significant carbon signal related to the presence of the *C*=S. The carbon signals related to carbonyl of both the N*C*OAr and *C*-4 absorbed at δ_C 166.0-167.0 and 170.8-172.0 ppm, respectively were observed. The ir spectra indicated the presence of another carbonyl group at ν_{max} 1700-1680 cm^{-1}. The ^{1}H nmr spectra of **7a-c** showed the presence of 6- and 5-H protons at δ_C 6.50-6.60 and 7.00-7.15 ppm, respectively (see the Experimental Section). The ^{13}C nmr spectra showed the presence of *C*-5 and *C*-6 at δ_C 118.0-118.8 and 125.8-126.2 ppm, respectively. Besides, the azomethine carbon (*C*-2), in the ^{13}C nmr spectra, absorbed at δ_C 156.8-158.0 ppm. The ir spectra of compounds **8a-c** revealed brood absorption bands at ν_{max} 1680-1720 cm^{-1} corresponding to the carboamide, *C*-4 and ester groups. The ^{1}H nmr spectrum for **8a**, as an example, revealed only one singlet at δ_H 7.10 ppm related to 5-H. The ^{13}C nmr spectrum showed *C*H-5 at δ_C 135.0 ppm, whereas the methyl-carboxylate and methoxy protons absorbed at δ_C 52.6 and 50.8 ppm (see the Experimental Section). The spectral data from nmr, mass and ir as well as the elemental analyses supported that compounds **7a-c** and **8a-c** have the structure of 4-substituted-*N*-(4-oxo-3-phenyl-3,4-dihydro-[1,3]thiazin-(2*Z*)-ylidene)-benzamides and 2-[(*Z*)-4-substituted-benzoyl-imino]-4-oxo-3-phenyl-3,4-dihydro-2*H*-[1,3]thiazine-6-methyl esters. From the aforementioned we excluded any other suggestions such as formation of products **9a-c** (resulting from the oxidative process), **10a-c** or **11a-c** (Scheme 2). The reaction mechanism depends on the presence of a tautomerism between the NH and the C=S into the N=C-SH groups in **1a-c** (Scheme 3). It is believed that attachment by the SH group proceeds faster compared to the aromatic amine (Scheme 3) [6a,14]. Therefore, reaction of **1a-c** with **6d** can be described as due to nucleophilic attack of the thiol group to the acetylenic carbon to form the intermediate **12a-c**. Thereafter another nucleophilic attack from the NH electron lone pair to the carbonyl in **12a-c** accompanied with ethanol elimination affords the heterocyclic compounds **7a-c** (Scheme 3).

Surprisingly, on reacting 1-benzoyl-1'*H*-pyrazol-4'-yl-thiourea (**1d**) with **6d** or **6e**, the reaction proceeded to give mainly the corresponding fused pyrolopyrimidines **13** and **14** (Scheme 4). Furthermore, the ir and nmr spectra of **13** and **14** supported the disappearance of any thione, thiol, and NH groups or protons. Moreover, the ^{1}H nmr spectra did not show the presence of the methyl group in position-5 of **1d**, whereas the pyrrole-CH appeared as a singlet at δ_H 7.96 ppm in case of **13**. Mass spectrum and elemental analysis confirmed the molecular formula of **13** as $C_{22}H_{16}N_4O_3$. The ^{1}H nmr spectrum of **13** revealed two doublets of the pyrimidine ring at δ_H 6.00 (5-H, J = 8.0 Hz) and 6.60 ppm (6-H, J = 8.2 Hz). The ^{13}C nmr spectrum of **13** showed the appearance of several distinctive carbon signals as shown in Figure 1. On the other hand, mass spectrum and elemental analysis supported the molecular formula of **14** as $C_{24}H_{18}N_4O_5$. The ^{1}H nmr spectrum of compound **14** revealed two singlets at δ_H 7.40 and 7.90 ppm, which were in accord to 6-H and –9, respectively. The ^{13}C nmr spectrum confirmed the ^{1}H nmr spectral data by the appearance of *C*H-6 and –9 at δ_C 127.4 and 128.4 ppm, respectively. Additionally, the absorptions of numerous carbon signals in the ^{13}C nmr spectrum of **14** could be distinguished as shown in Figure 1. Two methyl groups resonated as two singlets, in the ^{1}H nmr of **14**, at δ_H 3.36 and 3.98 ppm corresponding to the *N*CH$_3$ and CH$_3$-ester protons. The complete spectral data is in good agreement with the structures of either **13** or **14** (see Figure 1 and the Experimental Section). The NOE experiments of compounds **13** and **14** supported their proposed structures. Hence, irradiation of the 9-H resonance in either **13** or **14**, caused strong enhancement of the *ortho*-proton resonances of the benzoyl group (δ_H 7.70-7.74), whereas that irradiation slightly affected the *N*-CH$_3$ protons signal (Figure 1).



Scheme 2. Reaction of ethyl propiolate (**6d**) and dimethyl but-2-ynedioate ester (**6e**) with aroyl-substituted thioureas **1a-c**; synthesis of 1,3-thiazin-4-ones **7a-c** and **8a-c**.



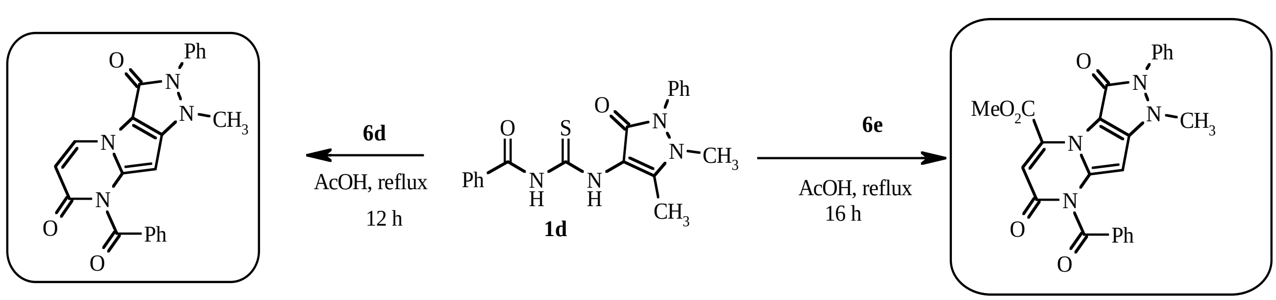
Scheme 3. Rationale formation of compounds **7a-c**

Furthermore, irradiation of the resonances 5-H (or 6-H) of **13** caused mutual strong saturation with 6-H (or 5-H) (Figure 1). Besides, NOE experiment where the 5-H (δ_H 6.60 ppm) signal is saturated in **13** affected moderately the 9-H (δ_H 7.96 ppm) signal, whereas irradiation of 6-H (δ_H 6.00 ppm) in **14** slightly affected of methyl-ester protons.

Interestingly, irradiation of the *N*-CH_3 protons in either **13** or **14** slightly caused enhancement to both the *ortho-N*-Ph protons and 9-H. Figure 1 shows some distinctive δ' values of the NMR spectra for compounds **13** and **14** along with their distinguished NOE experiments.

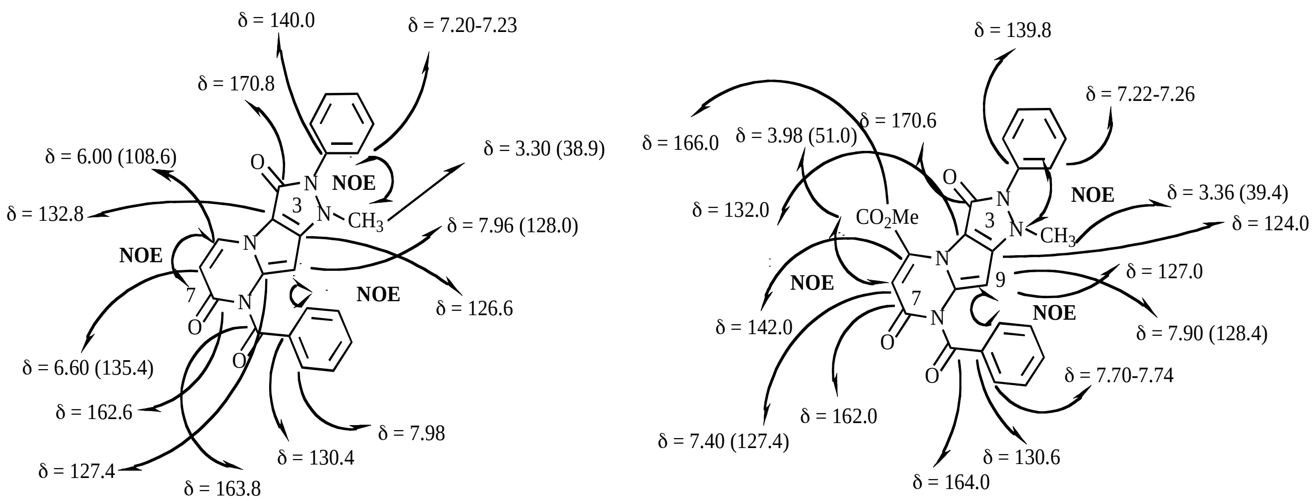
Since, the calculated bond distance [15] between the carbonyl group and the thiol group is found to be 1.6 Å, we can suggest a type of hydrogen bond is formed between them. Consequently, this hydrogen bond can offer the formation of another seven member ring (Figure 2), which indicates high reactivity of the NH group in **1d** compared with the thiol group.

The reaction mechanism, in case of the formation of **13**, can be simply described by nucleophilic attacking of N^3 on terminal acetylenic-CH to form intermediate **15**. Thereafter, the other nitrogen (N^1) undergoes nucleophilic attack on the carbonyl ester to form the salt **16** (Scheme 5). Tautomerization of the CH_3–C=C-C=O group in **16** to typical CH_2=C-C=C-OH group occurred *via* proton transfer process (Scheme 5). Spontaneously, cyclization process is occurred *via* nucleophilic addition of the exocylic-CH_2 on the thiol carbon accompanied by elimination of ethanol and hydrogen sulfide (Scheme 5) to give **17**. Ultimately, elimination of the catalyzed proton affords directly compound **13** (Scheme 5).



13 (85%) **14** (90%)

Scheme 4. Reaction of *N*-benzoyl-antipyrinyl thioureas **1d** with π-dificient acetylenes **6d,e**



13

14

Figure 1. Distinctive δ's values and NOE experiments of compounds **13** and **14**

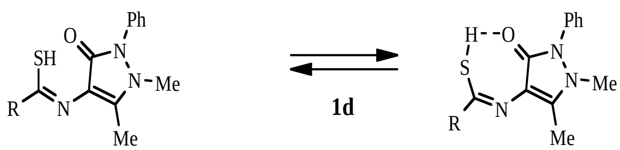
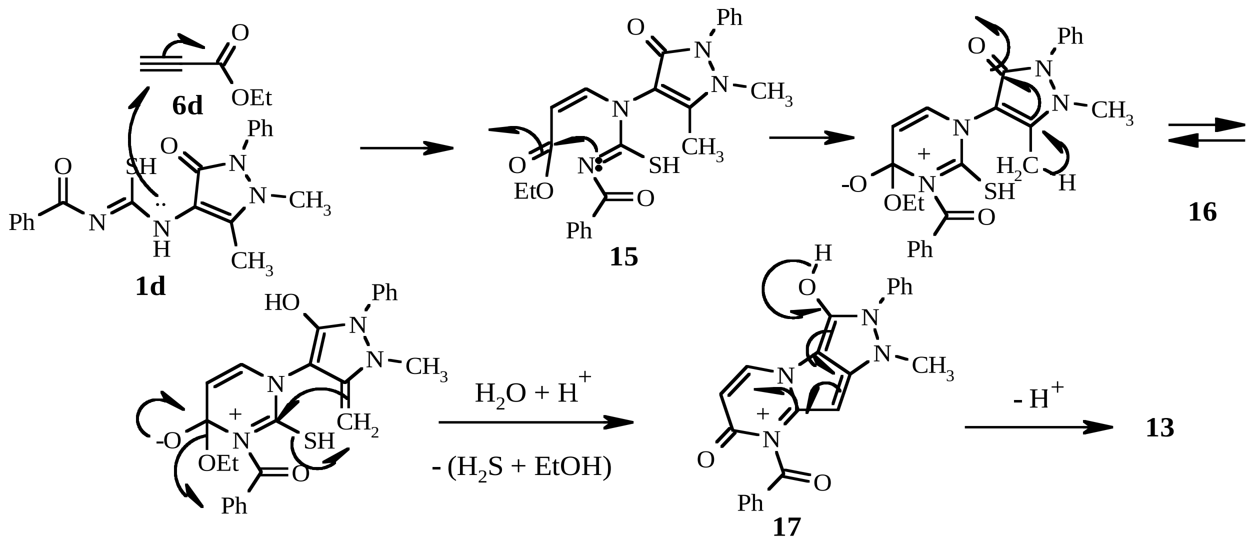


Figure 2. Hydrogen bond formed between the thiol and carbonyl groups in **1d**

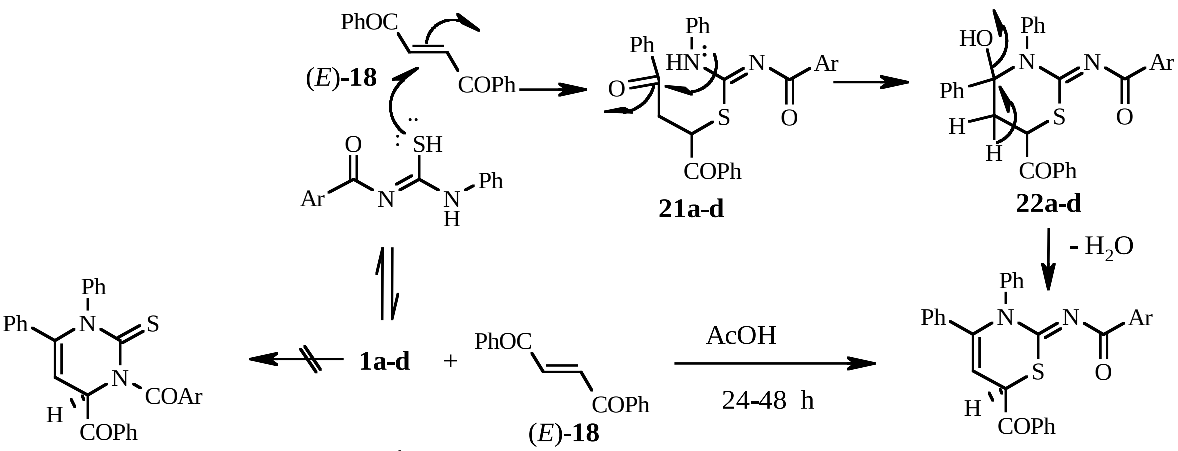
In order to explore the above mode of synthesis for another class of heterocycles, under similar reaction conditions, the reaction of (*E*)-1,4-diphenyl-but-2-ene-1,4-dione (*E*-**18**) with thioureas **1a-d** successfully proceeded to afford the corresponding 1,3-thiazines **19a-d** (Scheme 6). The ^{1}H nmr spectrum of **19a**, as an example, revealed the presence of O*C*H$_3$, *C*-6 (thiazine), *C*-5 (thiazine) and *N*-Ph 2 CH$_2$ at δ_H 3.94, 4.80 ppm (1 H, d, J = 11.5 Hz), 6.30 (1 H, d, J = 11.4 Hz) and 6.70 (dd, J = 8.0, 1.2 Hz) ppm. The ^{13}C nmr spectrum supported the ^{1}H nmr spectroscopic data by the distinctive appearance of the carbon signals represented the thiazine skeleton and its environments at δ_C 44.4 (*C*H-6), 54.0 (O*C*H$_3$), 100.0 (*C*H-5), 115.0 (*N*-Ph 2 *C*H2'), 116.2 (Ph 2 CH2'), 142.6 (*C*-4), 144.2 (*N*-Ph*C*), 160.8 (CH$_3$OAr*C*), 162.8 (C=N, *C*-2), 168.0 (*N*-*C*=O) and 180.0 ppm (*C*OPh). The ^{1}H nmr spectrum of **19a** apparently supported the (*R*)-configuration due to the presence of H-6 in *trans*-form (J = 11.5 Hz) in relation to H-5 (J = 11.4 Hz). In the case of **19d**, the ^{13}C nmr spectrum revealed several distinctive carbon signals such as at δ_C 15.7, 35.8, 45.2, 93.0, 106.0, 130.0, 130.4, 142.0, 143.4, 160.0, 162.0, 166.6, and 179.2 ppm corresponding to *C*H$_3$-pyrazole, pyrazole *N* *C*H$_3$, *C*H 6, *C*H 5, pyrazole *C*-4, pyrazole *C*-3, thiazine *C*-3, thiazine *C*-4, *N*-Ph *C*, pyrazole-*C*O, thiazine *C*-2, *N*-C=O and *C*=O, respectively (see the Experimental Section). Compound **1d** did not show any abnormal reactivity during its reaction with (*E*)-**18** and *N*-[(*R*)-6-benzoyl-3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl]-4-phenyl-3,6-dihydro-[1,3]-thiazin-(2*Z*)-ylidene]-4-methyl-benzamide (**19d**) was obtained (Scheme 6). The difference in reactivity during the reaction of **1d** with either **6d** and/or **18** might be attributed to the steric effect. In other meaning, the combination between **1d** and **18** might constitute a type of steric that enables the thiol group to react more easily compared with NH group. The spectral data along with the elemental analysis excluded the suggested formation of other products such as **20a-d** (Scheme 6). The reaction mechanism can be simply outlined as shown in Scheme 6. In conclusion, we have thus demonstrated a very convenient procedure to synthesize of 1,3-thiazines by the reaction of but-2-ynedioic acid, propynoic acid ethyl ester, and (*E*)-1,4-diphenyl-but-2-ene-1,4-dione with aroyl-substituted thioureas under reflux in acetic acid.

EXPERIMENTAL

General Consideration. All mps were recorded on a Gallenkamp apparatus. ^{1}H NMR and ^{13}C NMR spectra (Bruker AM 400, ^{1}H: 400.13 MHz, ^{13}C: 100.6 MHz); s = singlet, d = doublet, dd = double-doublet and m = multiplet. The NMR samples were dissolved in dimethyl sulfoxide-d$_6$ solutions. Coupling constants were expressed in Hz. Elemental analyses were carried at the Assuit Microanalysis Center of Assiut University. Mass spectroscopy was performed with a Finnigan MAT 8430 spectrometer at 70 eV, Institute of Organic Chemistry, Technical University-Braunschweig, Germany. IR spectra were run on a Shimadzu 470 spectrometer using potassium bromide pellets.



Scheme 5. Mechaistic pathway of the reaction of **1d** and acetylenic carboxylate **6d**



20a-d

19a-d (80-90%)

1, **19** and **20**	Ar
a	4-OCH_3-C_6H_4-
b	4-CH_3-C_6H_4-
c	C_6H_5-
d	antipyrinyl-

Scheme 6. Reactions of aroyl-substituted thioureas **1a-d** with *E*-1,4-diphenyl- but-2-ene-1,4-dione (*E*-**18**); synthesis of 1,3-thiazines **19a-d**.

Starting materials. Aroylthioureas **1a-c** and **1d** were prepared according to literatures [14] and [7], respectively.

Reaction of 1a-d with 6d,e and (*E*)-18, General procedure. Into a 250 cm^3 two-necked round bottom flask containing a solution of **1a-d** (2 mmol) in glacial acetic acid (50-80 mL), a solution of 2 mmol of either **6d**,**e** (or *E*-**18**) in glacial acetic (20 mL) was dropwisely added with stirring. The mixture was stirred at room temperature for 1 h and then gently refluxed with stirring (the reaction was monitored by TLC analyses). In the case of products **7a**-**d** and **8a**-**d**, the solvent was evaporated under vacuum and the formed solid products were purified by dissolving in dry acetone (30-50 mL) and subjected to preparative plates chromatography (silica gel), toluene: ethyl acetate (10:1). In the case of reaction of **1a**-**d** with (*E*)-**18**, the formed solid products **19a**-**d** were collected by filtration and the precipitates were washed with water and ethanol until the odor of acetic acid disappeared. The obtained products were recrystallized from the stated solvents.

4^1-Methoxy-*N*-[4-oxo-3-phenyl-3,4-dihydro-[1,3]-thiazin-(2*Z*)-ylidene]-benzamide (7a) was obtained as yellow crystals (0.54 g, 80%), mp 260 °C (ethanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.90 (3 H, s, OCH_3), 6.60 (1 H, d, J = 7.0 Hz, 6-

H), 6.92 (2 H, dd, J= 8.0, 1.4 Hz, Ar H), 7.10 (1 H, d, J = 7.2 Hz, 5-H), 7.34-7.42 (4 H, m, Ar H), 7.75-7.90 (3 H, m, Ar H) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 53.0 (O*C*H$_3$), 118.8 (*C*H-6), 126.2 (*C*H-5), 126.8 (Ph *C*H, *C*H4$^/$), 127.0, 127.6, 128.0, 130.0 (Ar 2 *C*H), 133.8 (Ar C-*C*O), 138.9 (*N*-Ar *C*), 150.0 (H$_3$COAr *C*), 158.0 (*C*-2), 167.0 (= N*C*OAr), 172.0 (*C*-4) ppm; ir (potassium bromide): 3060-2980 (Ar CH, w), 2930-2860 (aliph. CH, m), 1700-1680 (C=O, s), 1600 (C=N, s), 1496 (C=C, m), 1450 (s), 920 (m) cm^{-1}; uv (CH$_3$CN); λ_{max} nm (log ε) 420 (3.90); ms (electron impact, 70 eV): m/z (%) 339 ([M+1], 24%), 338 ([M$^+$], 100), 323 (14), 307 (28), 230 (40), 202 (54), 152 (26), 136 (82), 86 (24), 77 (40). *Anal*. Calcd. for $C_{18}H_{14}N_2O_3S$ (338.39): C, 63.89; H, 4.17; N, 8.28; S, 9.48. Found: C, 63.75; H, 4.10; N, 8.20; S, 9.40.

4'-Methyl-*N*-[4-oxo-3-phenyl-3,4-dihydro-[1,3]-thiazin-(2*Z*)-ylidene]-benzamide (7b) was obtained as yellow crystals (0.48 g, 75%), mp 298°C (ethanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 2.34 (3 H, s, CH$_3$), 6.58 (1 H, d, J = 7.2 Hz, 6-H), 7.15 (1 H, d, J = 7.0 Hz, 5-H), 7.28-7.36 (4 H, m, Ar H), 7.60-7.80 (5 H, m, Ar H) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 32.8 (*C*H$_3$), 118.4 (*C*H-6), 126.2 (*C*H-5), 126.6 (Ph-*C*H, *C*H-4$^/$), 127.0, 127.4, 127.8, 129.6 (Ar 2*C*H), 133.6 (Ar *C*-CO), 134.6 (CH$_3$Ar *C*), 138.2 (*N*-Ar*C*), 157.2 (*C*-2), 166.6 (=N*C*OAr), 171.2 (C-4) ppm; ir (potassium bromide): 3050-2986 (Ar CH, w), 2930-2860 (aliph. CH, m), 1700-1685 (C=O, s), 1596 (C=N, s), 1494 (C=C, m), 1450 (s), 918 (m) cm^{-1}; uv (CH$_3$CN) λ_{max} nm (log ε) 418 (3.80); ms (electron impact, 70 eV): m/z (%) 322 ([M$^+$], 100), 306 (30), 230 (34), 202 (50), 188 (12), 152 (26), 144 (20), 136 (82), 120 (24), 86 (24), 77 (30). *Anal*. Calcd. for $C_{18}H_{14}N_2O_2S$ (322.39): C, 67.06; H, 4.38; N, 8.69; S, 9.95. Found: C, 67.12; H, 4.34; N, 8.62; S, 9.90.

***N*-[4-Oxo-3-phenyl-3,4-dihydro-[1,3]-thiazin-(2*Z*)-ylidene]-benzamide (7c)** was obtained as pale yellow crystals (0.44 g, 72%), mp 238 °C (ethyl acetate/benzene); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 6.50 (1 H, d, J = 7.0 Hz, 6-H), 7.00 (1 H, d, J = 7.0 Hz, 5-H), 7.10-7.26 (5 H, m, Ph H), 7.54-7.76 (5 H, m, Ph H) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 118.0 (*C*H-6), 125.8 (*C*H-5), 126.0, 126.8 (Ph-*C*H, *C*H-4$^/$), 128.2, 128.6, 128.8, 129.2 (Ph 2*C*H), 133.8 (Ar *C*-CO), 138.0 (*N*-Ph *C*), 156.8 (*C*-2), 166.0 (= N*C*OPh), 170.8 (*C*-4) ppm; ir (potassium bromide): 3040-2980 (Ph CH, w), 1700-1682 (C=O, s), 1600 (C=N, s), 1496 (C=C, m), 1450 (s), 918 (s) cm^{-1}; uv (CH$_3$CN) λ_{max} nm (log ε) 410 (3.60); ms (electron impact, 70 eV): m/z (%) 308 ([M$^+$], 100), 230 (26), 202 (48), 188 (16), 150 (24), 142 (20), 136 (32), 105 (60), 86 (20), 77 (26). *Anal*. Calcd. for $C_{17}H_{12}N_2O_2S$ (308.36): C, 66.22; H, 3.92; N, 9.08; S, 10.40. Found: C, 66.12; H, 3.89; N, 9.00; S, 10.30.

2-[(*Z*)-4-Methoxy-benzoylimino]-4-oxo-3-phenyl-3,4-dihydro]-2*H*-[1,3]thiazine-6-carboxylic acid methyl ester (8a) was obtained as yellow crystals (0.67 g, 85%), mp 212 °C (ethanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.90 (3 H, s, ester OCH$_3$), 3.96 (3 H, s, OCH$_3$), 6.85 (1 H, s, J = 7.0 Hz, 5-H), 7.35-7.42 (2 H, m, Ar H), 7.48-7.60 (5 H, m, Ar-H), 7.96-7.98 (2 H, dd, J = 8.0, 1.2 Hz, Ar H) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 50.8 (O*C*H$_3$), 52.6 (ester O*C*H$_3$), 125.8 (Ph *C*H, *C*H-4$^/$), 128.9, 130.5, 131.8.8, 132.8 (Ar 2*C*H), 132.8 (Ar *C*-CO), 133.8 (*C*H-5), 136.4 (*N*-Ar *C*), 152.0 (CH$_3$OAr *C*), 155.0 (*C*-6), 158.4 (*C*-2), 165.4 (*C*=O-ester), 167.8 (=N*C*OAr), 171.4 (*C*-4) ppm; ir (potassium bromide): 3080-2990 (Ar CH, m), 2960-2870 (aliph. CH, m), 1720-1680 (C=O, br, s), 1610 (C=N, s), 1500 (C=C, s), 1460 (m), 920 (s) cm^{-1}; uv (CH$_3$CN) λ_{max} nm (log ε) 3.9 (3.60); ms (electron impact, 70 eV): m/z (%) 396 ([M$^+$], 100), 135 (64), 107 (16), 92 (10), 77 (26), 64 (14). *Anal*. Calcd. for $C_{20}H_{16}N_2O_5S$ (396.42): C, 60.60; H, 4.07; N, 7.07; S, 8.09. Found: C, 60.75; H, 4.00; N, 7.00; S, 8.02.

2-[(*Z*)-4-Methyl-benzoylimino]-4-oxo-3-phenyl-3,4-dihydro]-2*H*-[1,3]thiazine-6-carboxylic acid methyl ester (8b) was obtained as yellow crystals (0.61 g, 80%), mp 198 °C (methanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 2.34 (3 H, s, CH$_3$), 3.94 (3 H, s, ester OCH$_3$), 7.06 (1 H, s, J = 7.2 Hz, 5-H), 6.95-7.30 (7 H, m, Ar H), 7.60 (2 H, dd, J = 8.2, 1.2 Hz, Ar H) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 32.8 (*C*H$_3$), 50.4 (ester O*C*H$_3$), 125.5 (Ph *C*H, *C*H-4$^/$), 126.8, 127.2, 127.6, 128.2 (Ar 2*C*H), 130.4 (Ar *C*-CO), 135.4 (*C*H-5), 137.8 (H$_3$C-Ar *C*), 138.0 (*N*-Ar *C*), 155.2 (*C*-6), 158.2 (*C*-2), 165.5 (*C*=O-ester), 167.6 (=N*C*OAr), 173.4 (*C*-4) ppm; ir (potassium bromide): 3084-3005 (Ar CH, m), 2980-2890 (aliph. CH, m), 1716-1684 (C=O, br, s), 1608 (C=N, s), 1520 (C=C, s), 1460 (s), 918 (s) cm^{-1}; uv (CH$_3$CN) λ_{max} nm (log ε) 3.7 (3.50); ms (electron impact, 70 eV): m/z (%) 380 ([M$^+$], 100), 365 (20), 288 (60), 260 (54), 135 (64), 120 (24), 112 (34), 77 (40). ***Anal.*** Calcd. for $C_{20}H_{16}N_2O_4S$ (380.43): C, 63.15; H, 4.24; N, 7.36; S, 8.43. Found: C, 63.05; H, 4.20; N, 7.34; S, 8.42.

2-[(*Z*)-Benzoylimino]-4-oxo-3-phenyl-3,4-dihydro-2*H*-[1,3]-thiazine-6-carboxylic acid methyl ester (8c) was obtained as yellow crystals (0.52 g, 72%), mp 210 °C (methanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.94 (3 H, s, ester O*C*H$_3$), 6.95 (1 H, s, J = 7.0 Hz, 5-H), 6.94-7.20 (6 H, m, Ph H), 7.40-7.50 (2 H, m, Ph H), 7.66 (2 H, dd, J = 8.0, 1.2 Hz, Ph H) ppm; ^{13}C NMR (dimethyl sulfoxide-d_6): δ 50.2 (ester-O*C*H$_3$), 125.0, 125.8 (Ph *C*H, *C*H4$^/$), 126.8, 127.6, 128.0, 128.2 (Ph 2 *C*H), 130.0 (Ph *C*-CO), 134.2 (*C*H-5), 138.6 (*N*-Ph *C*), 155.0 (*C*-6), 158.0 (*C*-2), 165.8 (*C*=O-ester), 167.0 (=N*C*OPh), 172.6 (*C*-4) ppm; ir (potassium bromide): 3070-3008 (Ph CH, m), 1718-1680 (C=O, br, s), 1610 (C=N, m), 1560 (C=C, m), 1450 (m), 916 (s) cm^{-1}; uv (CH$_3$CN) λ_{max} nm (log ε) 3.6 (3.40); ms (electron impact, 70 eV): m/z (%) 366 ([M$^+$], 100), 288 (54), 260 (64), 126 (22), 112 (32), 77 (50). *Anal*. Calcd. for $C_{19}H_{14}N_2O_4S$ (366.40): C, 62.29; H, 3.85; N, 7.65; S, 8.75. Found: C, 65.15; H, 3.80; N, 7.64; S, 8.70.

8-Benzoyl-1-methyl-2-phenyl-1*H*-pyrazolo-[3',4':4,5]pyrrolo-[1,2-*a*]-pyrimidine-3,7-(2*H*,8*H*)-dione (13) was obtained as pale brown crystals (0.70 g, 85%), mp 242 °C (ethanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.30 (3 H, s, *N*CH$_3$), 6.00 (1 H, d, J = 8.0 Hz, 5-H), 6.60 (1 H, d, J = 8.2 Hz, 6-H), 7.00-7.30 (6 H, m, Ph H), 7.60-7.70 (2 H, m), 7.96 (1 H, s, pyrrole-H-9), 7.98 (2 H, dd, J = 8.0, 1.4 Hz, CO-Ph CH2'). 7.96 (1 H, s, pyrrole-H-9) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 38.9 (*N*CH$_3$), 108.6 (*C*H-5), 126.6 (*C*-9a), 126.8, 127.2 (Ph *C*H, *C*H-4$^/$), 127.4 (*C*-8a), 128.0 (*C*H-9), 128.4, 128.6, 128.8, 129.0 (Ph 2*C*H), 130.6 (Ph-*C* CO), 132.8 (*C*-3a), 135.4 (*C*H-6), 140.0 (*N*-Ph *C*), 162.6 (*C*-7), 163.8 (benzoyl-CO), 170.8 (*C*-3) ppm; ir (potassium bromide): 3060-2990 (Ar CH, m), 2960-2840 (aliph. CH, m), 1710 (CO, s), 1680 (C=O, s), 1600 (C=N, m), 1498 (C=C, m), 1450 (m), 922 (m) cm^{-1}; uv (CH$_3$CN) λ_{max} nm (log ε) 390 (3.82). MS (electron impact, 70 eV): m/z (%) 384 ([M$^+$], 100), 368 (20), 306 (34), 292 (36), 278 (40), 196 (18), 170 (26), 105 (64), 91 (38), 56 (60). *Anal*. Calcd. for $C_{22}H_{16}N_4O_3$ (384.40): C, 68.74; H, 4.20; N, 14.58. Found: C, 68.69, H, 4.30; N, 14.50.

Methyl 8-benzoyl-1-methyl-3,7-dioxo-1-phenyl-2,3,7,8-tetra-hydro-1*H*-pyrazolo-[3',4':4,5]pyrrolo-[1,2-*a*]-pyrimidine-5-carboxylate (14) was obtained as pale brown crystals (0.83 g, 90%), mp 202 °C (methanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.36 (3 H, s, *N*CH$_3$), 3.98 (3 H, s, *C*H$_3$-ester), 7.10-7.30 (6 H, m, Ph H), 7.40 (1 H, s, 6-H), 7.60-7.64 (2 H, m), 7.70-7.74 (2 H, m, CO-Ph CH2'), 7.90 (1 H, s, 9-H) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 39.4 (*N*CH_3), 51.0 (*C*H_3-ester), 124.0 (*C*-9a), 127.0 (*C*-8a), 127.4 (*C*H-6), 127.6, 127.8 (Ph-*C*H, *C*H-4$'$), 128.4 (*C*H-9), 128.0, 128.4, 128.6, 128.8 (2 Ph *C*H), 130.6 (Ph *C*-CO), 132.0 (*C*-3a), 139.8 (*N*-Ph *C*), 142.0 (*C*-5), 162.0 (*C*-7), 164.0 (benzoyl-*C*O), 166.0 (*C*O ester), 170.6 (*C*-3) ppm; ir (potassium bromide): 3060-2990 (Ar CH, m), 2960-2840 (aliph. CH, m), 1716 (CO, s), 168.0 (C=O, s), 1600 (C=N, m), 1498 (C=C, m), 1450 (m), 922 (m) cm^{-1}; uv (CH_3CN) λ_{max} nm (log ε) 430 (4.24); ms (electron impact, 70 eV): m/z (%) 442 ([M$^+$], 100), 410 (18), 365 (40), 366 (60), 245 (38), 228 (66), 186 (44), 119 (44), 105 (82), 91 (38), 77 (62), 56 (46). *Anal.* Calcd. for $C_{24}H_{18}N_4O_5$ (442.43): C, 65.15; H, 4.10; N, 12.66. Found: C, 65.30, H, 4.10; N, 12.60.

***N*-[(*R*)-6-Benzoyl-3,4-diphenyl-3,6-dihydro-[1,3]thiazin-(2*Z*)-ylidene]-4'-methoxy-benzamide (19a)** was obtained as pale brown crystals (0.91 g, 90%), mp 312 °C (ethanol); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 3.94 (3 H, s, OCH_3), 4.80 (1 H, d, J = 11.5 Hz, H-6), 6.30 (1 H, d, J = 11.4 Hz, H-5), 6.70 (2 H, dd, J = 8.0, 1.2 Hz), 6.90 (2 H, dd, J = 8.2, 1.4 Hz), 7.00-7.20 (5 H, m), 7.30-7.35 (1 H, m), 7.45-7.64 (7 H, m), 7.80 (2 H, dd, J = 8.2, 1.4 Hz) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 44.4 (*C*H-6), 54.0 (O*C*H_3), 100.0 (*C*H-5), 115.0 (*N*-Ph 2 *C*H2'), 116.2 (CH_3OPh 2*C*H2'), 118.8 (*N*-Ph *C*H4'), 126.0, 126.6 (Ph *C*H *C*H4'), 127.4, 128.0, 128.2, 128.6, 129.4 (Ph 2*C*H), 132.0, 134.6 (Ph *C*), 135.6 (CH_3OPh-2 *C*H3'), 136.8 (Ph *C*-CO), 142.6 (*C*-4), 144.2 (*N*-Ph *C*), 160.8 (CH_3O-Ph *C*), 162.8 (*C*=N, *C*-2), 168.0 (*N*-*C*=O), 180.0 (*C*OPh) ppm; ir (potassium bromide): 3072-2980 (Ar CH, m), 2970-2880 (aliph. CH, m), 1700-1690 (C=O, s), 1598 (C=N, m), 1496 (C=C, m), 1452 (m), 920 (m) cm^{-1}; uv (CH_3CN) nm λ_{max} nm (log ε) 420 (3.83); ms (electron impact, 70 eV): m/z (%) 504 ([M$^+$], 30), 398 (12), 324 (10), 310 (12), 105 (100), 99 (24), 57 (16). *Anal.* Calcd. for $C_{31}H_{24}N_2O_3S$ (504.61): C 73.79, H 4.79, N 5.55, S 6.35. Found C, 73.86; H, 4.80; N, 5.50; S, 6.35.

***N*-(*R*)-6-Benzoyl-3,4-diphenyl-3,6-dihydro-[1,3]thiazin-(2Z)-ylidene)-4'-methyl-benzamide (19b)** was obtained as pale brown crystals (0.83 g, 85%), mp 330 °C (ethyl acetate); ^{1}H NMR (dimethyl sulfoxide-d_6): δ 3.38 (3 H, s, CH_3), 4.72 (1 H, d, *J* 13.7 Hz), 5.45 (1 H, d, J = 13.8 Hz), 6.60 (2 H, dd, J = 8.2, 1.2 Hz), 6.95-7.25 (8 H, m), 7.30-7.70 (9 H, m) ppm; ^{13}C NMR (dimethyl sulfoxide-d_6): δ 32.8 (*C*H_3), 44.0 (*C*H-6), 92.6 (*C*H-5), 114.8 (*N*-Ph 2 *C*H2'), 118.4 (*N*-Ph *C*H4'), 126.0, 126.6 (Ph CH *C*H4'), 127.2, 127.6, 128.0, 128.2, 128.4, 128.6, 128.8 (Ph 2*C*H), 132.2, 132.6 (Ph *C*), 134.8 (CH_3CPh *C*), 136.6 (Ph *C*-CO), 142.4 (*C*-4), 143.8 (*N*-Ph *C*), 162.2 (*C*=N, *C*-2), 166.8 (N-*C*=O), 179.5 (*C*OPh) ppm; ir (potassium bromide): 3060-2990 (Ar CH, m), 2980-2886 (aliph. CH, m), 1700-1692 (C=O, s), 1595 (C=N, s), 1496 (C=C, m), 920 (m) cm^{-1}; uv (CH_3CN) λ_{max} nm (log ε) 416 (3.6); ms (electron impact, 70 eV): m/z (%) 488 ([M$^+$], 28), 472 (20), 396 (40), 368 (24), 324 (20), 312 (24), 172 (24), 108 (38), 91 (30), 77 (100). *Anal.* Calcd. for $C_{31}H_{24}N_2O_2S$ (488.61): C, 76.20; H, 4.95; N, 5.73; S, 6.56. Found C, 76.00; H, 4.90; N, 5.70; S, 6.50.

***N*-[(*R*)-6-Benzoyl-3,4-diphenyl-3,6-dihydro-[1,3]thiazin-(2*Z*)-ylidene]-benzamide (19c)** was obtained as pale brown crystals (0.74 g, 80%), mp 320 °C (acetone). ^{1}H nmr (dimethyl sulfoxide-d_6): δ 4.70 (1 H, d, J = 13.8 Hz), 5.50 (1 H, d, J = 13.8 Hz), 6.62 (2 H, dd, J = 8.2, 1.2 Hz), 6.95-7.25 (8 H, m), 7.30-7.70 (9 H, m) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 44.2 (*C*H-6), 92.2 (*C*H-5), 115.2 (*N*-Ph 2 *C*H2'), 118.0 (*N*-Ph *C*H4'), 125.8, 126.2, 126.8 (Ph *C*H 4'), 127.4, 128.2, 128.6, 129.0, 129.6, 130.2, 131.0 (Ph 2*C*H), 132.4, 132.8 (Ph *C*), 136.3 (Ph *C*-CO), 142.0 (*C*-4), 143.4 (*N*-Ph *C*), 162.0 (*C*=*N*, C-2), 166.6 (*N*-*C*=O), 179.2 (*C*OPh) ppm; ir (potassium bromide): 3080-2996 (Ar CH, m), 1696-1690 (C=O, s), 1600 (C=N, s), 1500 (C=C, w), 918 (s) cm^{-1}; uv (CH_3CN) λ_{max} (log ε) 410 (3.4); ms (electron impact, 70 eV): m/z (%) 474 ([M$^+$], 32), 396 (38), 368 (34), 264 (34), 186 (20), 105 (100), 91 (24), 77 (60). *Anal.* Calcd. for $C_{30}H_{22}N_2O_2S$ (474.59): C, 75.93; H, 4.67; N, 5.90; S, 6.76. Found C, 76.10; H, 4.70; N, 5.82; S, 6.72.

***N*-[(*R*)-6-Benzoyl-3-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazol-4-yl]-4-phenyl-3,6-dihydro-[1,3]thiazin-(2*Z*)-ylidene]-4-methyl-benzamide (19d)** was obtained as pale brown crystals (1.0 g, 87%), mp 342 °C (acetone); ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.68 (3 H, s, pyrazole CH_3), 2.50 (3 H, s, *N*-pyrazole CH_3), 4.68 (1 H, d, J= 13.8 Hz), 5.40 (1 H, d, J = 13.9 Hz), 6.70 (2 H, dd, J = 8.0, 1.2 Hz, *N*-pyrazole-Ph 2CH 2'), 6.95-7.60 (10 H, m), 7.80-7.98 (8 H, m) ppm; ^{13}C nmr (dimethyl sulfoxide-d_6): δ 15.7 (*C*H_3 pyrazole), 35.8 (*C*H_3-*N* pyrazole), 45.2 (*C*H-6), 93.0 (*C*H-5), 106.0 (pyrazole *C*-4), 114.2 (*N* pyrazole Ph 2*C*H2'), 118.0 (*N* pyrazole-Ph*C*H 4'), 126.8, 127.0, 127.2 (Ph*C*H 4'), 127.6, 128.0, 128.4, 128.6, 129.0, 129.6, 130.2 (Ph 2 *C*H), 130.8 (pyrazole *C*-3), 132.4, 132.8 (Ph *C*), 136.3 (Ph *C*-CO), 142.0 (*C*-4), 143.4 (*N*-Ph *C*), 160.0 (pyrazole *C*O), 162.0 (*C*=*N*, C-2), 166.6 (*N*-*C*=O), 179.2 (*C*OPh) ppm; ir (potassium bromide): 3080-2994 (Ar CH, m), 2990-2894 (aliph. CH, m), 1706-1692 (C=O, s), 1600 (C=N, s), 1500 (C=C, s), 918 (s) cm^{-1}; uv (CH_3CN) λ_{max} nm (log ε) 435 (3.81); ms (electron impact, 70 eV): m/z (%) 584 ([M$^+$], 40), 568 (14), 554 (16), 506 (18), 478 (42), 402 (24), 396 (30), 296 (30), 186 (20), 105 (100), 91 (24), 77 (54). *Anal.* Calcd. for $C_{35}H_{28}N_4O_3S$ (584.70): C, 71.90; H, 4.83; N, 9.58; S, 5.48. Found C, 72.10; H, 4.80; N, 9.50; S, 5.40.

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