

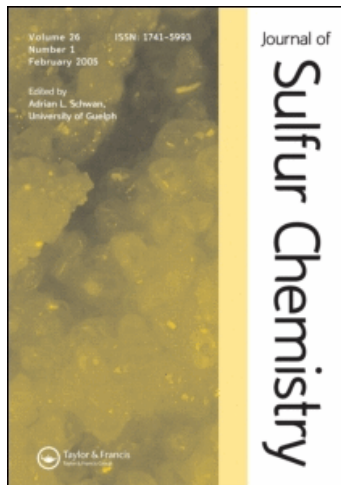
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Ketene *N,S*-acetals in heterocyclic synthesis: Part 1: Synthesis of *N*-phenyl-2-ylidene and 2,5-diylidene-4-thiazolidinone derivatives

M. F. Farhat^a; A. M. M. El-Saghier^b; M. A. Makhlouf^b; K. M. Kreddan^c; A. B. Elmezoughi^a

^a Chemistry Department, Faculty of Science, Al-Fateh University, Tripoli, Libya ^b Chemistry Department, Faculty of Science, Seventh of April University, Al-Zawia, Libya ^c Libyan Petroleum Institute, Tripoli, Libya

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RESEARCH ARTICLE

Ketene *N,S*-acetals in heterocyclic synthesis: Part 1: Synthesis of *N*-phenyl-2-ylidene and 2,5-diylidene-4-thiazolidinone derivatives

M. F. FARHAT*[†], A. M. M. EL-SAGHIER[‡], M. A. MAKHLOUF[†], K. M. KREDDAN[§]
and A. B. ELMEZOUHGI[†]

[†]Chemistry Department, Faculty of Science, Al-Fateh University,
PO Box 13494, Tripoli, Libya

[‡]Chemistry Department, Faculty of Science, Seventh of April University,
Al-Zawia, Libya

[§]Libyan Petroleum Institute, PO Box 3064, Tripoli, Libya

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Ketene *N,S*-acetal potassium salts (**2a–g**), prepared via reaction of active methylenes (**1a–g**) with phenyl isothiocyanate in the presence of potassium hydroxide, were allowed to react with ethyl chloroacetate or chloroacetamide to afford the corresponding 2-ylidene-4-thiazolidinones (**3a–g**) in good yields. Compounds (**3a–g**) reacted with a variety of aromatic aldehydes to afford the corresponding 5-arylidene-2-ylidene-4-thiazolidinone derivatives (**10a–e**). Reaction of compound (**3a**) with triethylorthoformate afforded 5-ethoxymethylene-2-ylidene-4-thiazolidinone derivative (**7**), which was allowed to react with ammonia or phenyl hydrazine to give the corresponding enamino or hydrazino derivatives (**8a**) or (**8b**), respectively.

Keywords: Ketene *N,S*-acetal; 2-Ylidene-4-thiazolidinone; Active methylene; 2,5-Diylidene-4-thiazolidinone; Thiazolidinone

1. Introduction

α -Oxo- and α -cyanoketene-*N,S*-acetals have been used as versatile three-carbon synthons for the synthesis of various heterocyclic compounds [1–9]. Heteroaryl substituted 1,3-thiazolidin-4-ones containing imidazole [10], thiazole [11], benzimidazole [12], acridine [13], quinazolin-4(3H)-one [14], *syn*-triazine [15], pyridine, or diazine [16–18] fragments show high antibacterial [19], antimicrobial, antitumor, or anti-HIV activity, and also have effects on the CNS.

4-Thiazolidinones are a topic of numerous reports concerning their synthesis, chemistry and applications [20, 21]. Nevertheless, synthesis and reactions of 2-ylidene-4-thiazolidinones

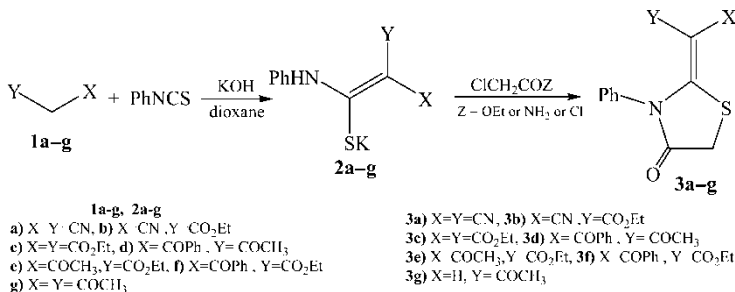
*Corresponding author. Email: mf_farhat@yahoo.com

[22–26] have received comparatively less attention. In our continuous work on the use of ketene-*S,S*- and *N,S*-acetals in the synthesis of heterocyclic compounds [27–38], we report here the development of a simple and general method to synthesize 2-ylidene- and 2,5-diylidene-4-thiazolidinone derivatives.

2. Results and discussions

Syntheses of 4-thiazolidinones (**3a–g**) were successfully carried out using two methods, both of which involve the formation of ketene-*N,S*-acetals (**2a–g**), followed by reaction with ethyl chloroacetate, chloroacetamide or chloroacetylchloride, and subsequent ring closure to the desired products.

In the first method, the active methylene compounds (**1a–g**), phenylisothiocyanate and potassium hydroxide were allowed to react to produce the ketene-*N,S*-acetals (**2a–g**) in high yields. These ketene-*N,S*-acetal salts (**2a–g**) were isolated and made to react with ethyl chloroacetate, chloroacetamide or chloroacetyl chloride in aqueous ethanol to give the 4-thiazolidinones (**3a–g**) (*cf.* scheme 1).



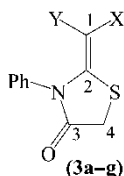
SCHEME 1

Spectral data were in agreement with the proposed structures, and are shown in table 1. In our pursuit of investigating this new route for the synthesis of 2-ylidene-4-thiazolidinones (**3a–g**), we found an interesting reaction of compound (**2g**) with ethyl chloroacetate, the product of this reaction was 2-(1-acetylmethylene)-4-thiazolidinone (**3g**) instead of the expected 2-(1,1-diacetylmethylene)-4-thiazolidinone (**3h**) (*cf.* scheme 2). The deacetylation is believed to proceed through enolization of the carbonyl group of the acetyl group facing the phenylamino side, followed by elimination of ketene.

In the second method, the active methylene compounds were allowed to react with dried K₂CO₃ in DMF followed by addition of phenylisothiocyanate. The resulting solutions were treated individually with ethyl chloroacetate to give the thiazolidinone derivatives (**3a–d**) or *N*-formyl thiophene derivatives (**5a–d**). Spectral data of compounds (**3a–d**) and (**5a–d**) were in agreement with the proposed structures and are shown in table 2.

The formation of 4-thiazolidinones (**3a,b**) and the *N*-formyl thiophene derivatives (**5a–d**) contradict the results reported by Kirsh *et al.* [34], who claimed in obtaining the thiophene derivatives **4**. It seems that the substituents on the active methylene compounds control the reaction both ways. Whereas the more active ketonic carbonyl encourages cyclization of intermediate (**6**) to form thiophenes (**5a–d**) [30–33], cyano and ester groups direct the reaction to form thiazolidinones (**3a,b**) (*cf.* scheme 3).

The dicyano derivative (**3a**) was refluxed in acetic anhydride with triethylorthoformate for three hours to give 2-(1,1-dicyanomethylene)-5-ethoxyethylene-3-phenylthiazolidin-4-one (**7**) in a high yield.

Table 1. Characterization for synthesized compounds (**3a-g**).

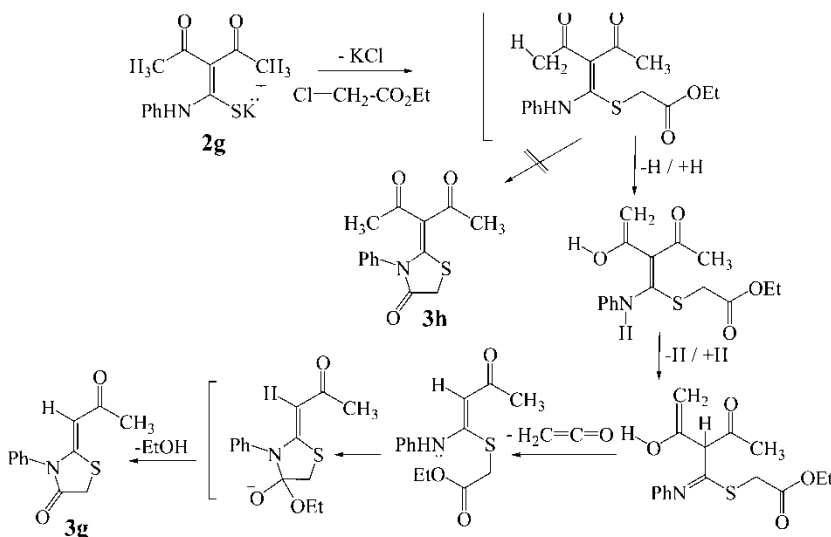
Compound ^a no.	M.p. (° C) yield(%)	I R (cm ⁻¹)	¹ H-NMR (ppm)	¹³ C-NMR (ppm)
3a X=Y=CN	273–275 (76.0)	2213 (CN), 1743 (C=O)	7.59–7.45(m, 5H, arom.), 4.35 (s, 2H, CH ₂ -S).	174.67(CO), 172.36(C ₂), 133.98, 131.74, 130.21, 129.76(C _{arom.}), 114.11, 109.77(2CN), 53.36(C ₁), 33.87(C ₄).
3b X=CN, Y=CO ₂ CH ₂ CH ₃	208–210 (72.6)	2206 (CN), 1749, 1681 (2 C=O _r)	7.61–7.24 (m, 5H, arom.), 4.25 (q, 2H, CH ₂ , J=7.1) _{ester} , 3.90 (s, 2H, H ₄), 1.30 (t, 3H, CH ₃ , J=7.1) _{ester} .	172.45(CO _{amide}), 169.95(CO _{ester}), 165.45(C ₂), 134.24, 131.29, 129.95, 128.87(C _{arom.}), 111.69(CN), 79.50(C ₁), 62.03(CH ₂), 31.78(C ₄), 14.19(CH ₃).
3c X=Y=CO ₂ C ₂ H ₅	112–114 (55.7)	1720, 1683 (3 CO)	7.48–7.20 (m, 5H, arom.), 4.20 (q, 2H, CH ₂ , J=7.1), 3.85 (s, 2H, H ₄), 3.40 (q, 2H, CH ₂ , J=7.1), 1.22 (t, 3H, CH ₃ , J=7.1), 1.05 (t, 3H, CH ₃ , J=7.1).	172.58(CO _{amide}), 165.17(CO _{ester}), 163.51(CO _{ester}), 157.69(C ₂), 134.28, 129.31, 128.20(C _{arom.}), 102.05(C ₁), 61.16(CH ₂), 61.08 (CH ₂), 31.51 (C ₄), 13.71(CH ₃), 13.12(CH ₃).
3d X=COPh, Y=COCH ₃	264–267 (57.4)	1733, 1661, 1642 (3 CO)	7.60–6.70 (m, 10H, arom.), 3.95 (s, 2H, H ₄), 1.81 (s, 3H, CH ₃).	193.51(CO _{ketone}), 192.31(CO _{ketone}), 173.64(CO _{amide}), 160.70(C ₂), 137.17, 134.44, 133.55, 129.87, 128, 128.33, 128.22, 128.03(C _{arom.}), 113.33(C ₁), 30.81(C ₄), 28.22(CH ₃).
3e X=COCH ₃ , Y=CO ₂ Et	148–150 (33.2)	1715, 1638 (3 C=O)	7.50–7.15 (m, 5H, arom.), 3.80 (s, 2H, H ₄), 3.35 (q, 2H, CH ₂ , J=7.1), 2.15 (s, 3H, CH ₃), 1.05 (t, 3H, CH ₃ , J=7.1).	193.56(CO _{ketone}), 173.31(CO _{amide}), 166.15(CO _{ester}), 160.89(C ₂), 135.18, 130.18, 129.10, 128.09(C _{arom.}), 110.37(C ₁), 61.27(CH ₂), 31.36(C ₄), 28.24(CH ₃), 13.61(CH ₃) _{ester} .

(continued)

Table 1. Continued.

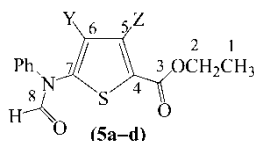
Compound ^a no.	M.p. (°C) yield(%)	IR (cm ⁻¹)	¹ H-NMR (ppm)	¹³ C-NMR (ppm)
3f X=COPh, Y=CO ₂ Et	189–191 (54.2)	1745, 1692, 1665 (3 C=O)	7.50–6.80 (m, 10H, arom.), 4.10 (q, 2H, CH ₂), 3.90 (s, 2H, H ₄), 1.00 (t, 3H, CH ₃).	190.55(CO _{ketone}), 173.10(CO _{amide}), 166.31(CO _{ester}), 158.57(C ₂), 137.38, 134.58, 133.03, 129.51, 129.05, 128.84, 128.06, 127.93(C _{arom.}), 106.31(C ₁), 60.39(CH ₂), 31.70(C ₄), 13.96(CH ₃).
3g X=H, Y=COCH ₃	192–195 (36.9)	1722, 1642 (2 C=O)	7.65–7.30 (m, 5H, arom.), 5.59 (s, 1H, H ₁), 3.90 (s, 2H, H ₄), 2.00 (s, 3H, CH ₃).	195.18(CO _{ketone}), 173.23(CO _{amide}), 160.90(C ₂), 136.83, 130.77, 130.26, 129.19 (C _{arom.}), 100.77(C ₁), 32.05 (C ₄), 30.00(CH ₃).

^aSatisfactory microanalysis obtained C; ±0.35, H; ±0.4, N; ±0.2.



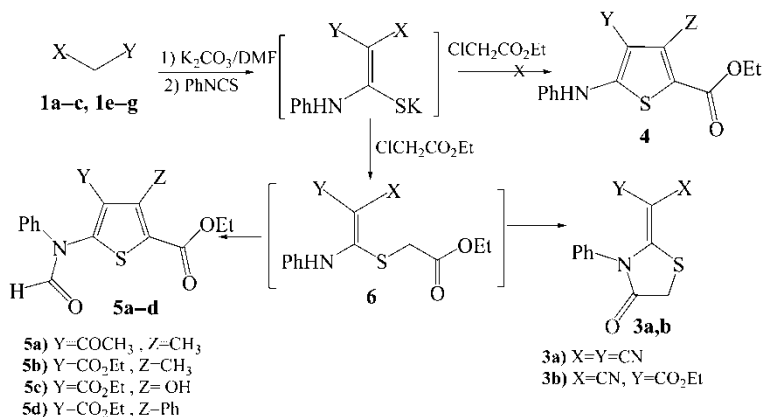
Compound (7) when reacted with ammonia or phenylhydrazine yielded 2-(1,1-dicyanomethylene)-5-aminomethylene-3-phenylthiazolidine-4-one (**8a**) or 2-(1,1-dicyanomethylene)-5-phenylhydrazono-methylene-3-phenylthiazolidine-4-one (**8b**). Spectral data were in agreement with the proposed structure and are shown in table 3.

Condensation reaction of compound (**3a–e**) with various aromatic aldehydes (**9a–e**) in refluxing dioxane in the presence of triethylamine, afforded 5-arylidene-2-(1,1-dicyanomethylene)-3-phenyl-thiazolidine-4-ones (**10a–e**). Spectral data were in agreement with the proposed structures and are shown in table 4. The same product (**10a**) was also obtained by reaction of thiazolidinone (**3a**) with benzylidenemalononitrile and benzylidene ethyl cyanoacetate in the presence of triethylamine (TEA).

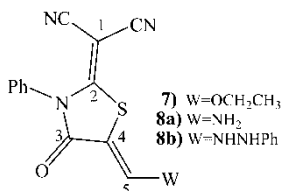
Table 2. Characterization for synthesized compounds (**5a-d**).

Compound ^a no.	M.p.(°C) yield(%)	I R (cm ⁻¹)	¹ H-NMR (ppm)	¹³ C-NMR (ppm)
5a Y=COCH ₃ Z=CH ₃	120–122(82.5)	1699,1655, 1614 (3C=O)	12.06 (s, 1H, CHO), 7.45– 7.14 (m, 5H, arom.), 4.28 (q, 2H, CH ₂ , J=7.1), 2.85 (s, 3H, CH ₃), 2.82 (s, 3H, CH ₃), 1.35 (t, 3H, CH ₃ , J=7.1).	195.90(CO _{ketone}), 163.68(CO _{amide}), 162.88(CO _{ester}), 145.93(C ₇), 145.93(C ₄), 139.74– 120.78(C _{arom.}), 119.36(C ₆), 109.12(C ₅), 60.61(CH ₂), 31.43(CH ₃), 16.66(CH ₃), 14.46 (CH ₃).
5b Y=CO ₂ CH ₂ CH ₃ Z=CH ₃	114–116 (70.2)	1694, 1658 (3C=O)	10.60 (s, 1H, CHO), 7.45 –7.10 (m, 5H, arom.), 4.40 (q, 2H, CH ₂ , J=7.1), 4.30 (q, 2H, CH ₂ , J=7.1), 2.80 (s, 3H, CH ₃), 1.40 (t, 3H, CH ₃ , J=7.1), 1.05 (t, 3H, CH ₃ , J=7.1).	166.95(CO ⁸), 162.90(CO) _y , 162.40(CO ³), 147.57(C ₇), 147.56(C ₄), 139.91– 119.97(C _{arom.}), 109.24(C ₆), 108.66(C ₅), 60.47(CH ₂) _y , 60.46 (CH ₂) ₂ , 16.03(CH ₃) ₂ , 14.47(CH ₃) _y , 14.34(CH ₃) ₁ .
5c Y=CO ₂ CH ₂ CH ₃ Z=OH	108–110 (67.5)	16.83, 1623 (3C=O)	10.80 (s, 1H, CHO), 10.50 (s, 1H, OH), 7.50–7.25 (m, 5H, arom.), 4.40 (q, 2H, CH ₂ , J=7.1) _y , 4.25 (q, 2H, CH ₂ , J=7.1), 1.40 (t, 3H, CH ₃ , J=7.1) _y , 1.30 (t, 3H, CH ₃ , J=7.1) ₁ .	166.26(CO ⁸), 165.73(CO) _y , 163.87(CO ³), 162.43(C ₇), 162.42(C ₄), 139.03– 120.74(C _{arom.}), 98.54(C ₆), 86.38(C ₅), 60.81(CH ₂) _y , 60.62 (CH ₂) ₂ , 14.46(CH ₃) _y , 13.91(CH ₃) ₁ .
5d Y=CO ₂ CH ₂ CH ₃ Z=Ph	110–113 (77.2)	1712, 1664 (3 CO)	10.60 (s,1H,CHO), 7.50 –7.10 (m, 5H, arom.), 4.10 (q, 2H, CH ₂ , J=7.1) _y , 3.90 (q 2H, CH ₂ , J=7.1), 1.05 (t, 3H, CH ₃ , J=7.1) _y , 0.70 (t, 3H, CH ₃ , J=7.1) ₁ .	166.40(CO) ⁸ , 162.02(CO) _y , 161.93 (CO) ³ , 148.63(C ₇), 148.60(C ₄), 139.85– 119.93(C _{arom.}), 110.63(C ₆), 109.37(C ₅), 60.48(CH ₂) ₂ , 59.89(CH ₂) _y , 13.95(CH ₃) _y , 13.18(CH ₃) ₁ .

^aSatisfactory microanalysis obtained C; ±0.35, H; ±0.4, N; ±0.2.



SCHEME 3

Table 3. Spectral data of compounds (**7**, **8a**, **b**).

Compound ^a no.	M.p. (°C) yield(%)	IR (cm ⁻¹)	¹ H-NMR (ppm)	¹³ C-NMR (ppm)
7 W=OCH ₂ CH ₃	256–258 (84.8)	2213 (CN), 1722 (C=O)	8.30 (s, 1H, CH), 7.60– 7.45 (m, 10H, arom.), 4.40 (q, 2H, CH ₂ , J=7.1), 1.35 (t, 3H, CH ₃ , J=7.1).	167.40(CO), 165.15(C ₂), 158.15(C ₄), 133.20, 131.05, 129.43, 129.16(C _{arom.}), 114.35, 110.20(CN), 97.87(C ₅), 72.81(C ₁), 52.93(CH ₂), 15.27 (CH ₃).
8a W=NH ₂	296–298 (81.8)	3400–3188 (NH ₂) 2220 (CN), 1695 (C=O).	8.25 (br, 2H, NH ₂), 7.85 (s, 1H, H ₅), 7.60–7.49 (m, 5H, arom.).	167.08(CO), 165.76(C ₂), 146.05(C ₄), 133.98, 130.47, 129.19, 129.14(C _{arom.}), 115.64, 111.33(2CN), 84.64(C ₅), 48.82(C ₁).
8b W=NHNHPh	224–226 (71.9)	3297 (NHNHPh), 2213 (CN), 1695 (C=O).	10.20 (br, 1HNH), 8.55 (br, 1H, NH), 8.10 (s, 1H, H ₅), 7.60–6.85 (m, 10H, arom.).	168.72(CO), 166.46(C ₂), 146.85(C ₄), 133.91, 130.41, 129.18, 113.73 (C _{arom.}), 115.53, 111.51(2CN), 83.64(C ₅), 47.74(C ₁).

^aSatisfactory microanalysis obtained C; ±0.35, H; ±0.4, N; ±0.2.

3. Experimental section

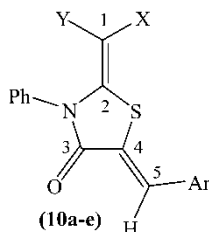
All melting points were determined on a Koffler melting points apparatus and are uncorrected. ¹H-NMR spectra were recorded on a Bruker avance 300 MHz spectrometer using TMS as internal reference (chemical shifts in δ, ppm), ¹³C-NMR spectra were recorded on a Bruker avance 75 MHz spectrometer using TMS as internal reference (chemical shifts in δ, ppm) and IR in KBr were obtained on a Bruker FT-IR ISS 25 spectrophotometer (ν_{max} in cm⁻¹).

3.1 General procedure (I)

3.1.1 Potassium salts of ketene *N,S*-acetals (2a–g**)(typical procedure).** A solution of active methylene compound (**2a**) (0.033 mol) in dioxane (20 ml) was cooled to 0°C, and then added dropwise to a stirred mixture of phenylisothiocyanate (0.033 mol) and dry KOH powder (0.033 mol) in dioxane (50 ml), which was previously cooled to 0°C, keeping the temperature of the stirred mixture at 0–5°C during the addition. The precipitated solid formed was filtered off, washed with cold dioxane and used immediately or kept in a desiccator. Yields of (**2a–g**) are: 87.50%, 92.50%, 82.41%, 99.07%, 82.82%, 89.95%, 69.80%, respectively.

3.2 2-Ylidene-*N*-phenylthiazolidine-4-one (**3a–g**)

3.2.1 Method A: typical procedure. A solution of the salt (**2a**) (0.02 mol) in distilled water (20 ml) was stirred at room temperature and ethyl chloroacetate or chloroacetamide

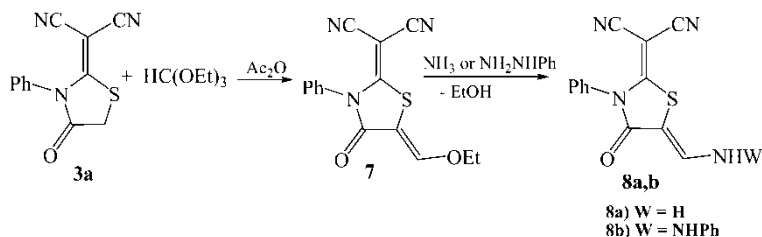
Table 4. Spectral data of compounds (**10a–e**).

Compound ^a no.	M.p. (°C) yield(%)	I R (cm ⁻¹)	¹ H-NMR (ppm)	¹³ C-NMR (ppm)
10a Ar = C ₆ H ₅	304–306 (58.8)	2213 (CN), 1733 (C=O).	8.01 (s, 1H, CH), 7.70–7.25 (m, 10H, arom.).	165.86(CO), 165.60(C ₂), 137.23(C ₅), 132.60, 132.35, 131.90, 131.83, 130.70, 130.27, 129.70, 128.71(C _{arom.}), 116.70(C ₄), 112.88, 109.17 (2CN), 58.40(C ₁).
10b Ar = <i>p</i> -ClC ₆ H ₄	288–290 (44.4)	2220 (CN), 1715 (C=O).	8.10 (s, 1H, CH), 7.84–7.61 (m, 9H, arom.).	167.06(CO), 166.71(C ₂), 134.81(C ₅), 134.45, 132.98, 132.58, 132.24, 130.74, 130.64, 130.14, 129.15(C _{arom.}), 119.81(C ₄), 114.25, 110.33(2CN), 57.93(C ₁).
10c Ar = <i>p</i> -BrC ₆ H ₄	294–296 (73.8)	2220 (CN), 1736 (C=O).	7.99 (s, 1H, CH), 7.87–7.60 (m, 9H, arom.).	167.04(CO), 166.71(C ₂), 134.81 (C ₅), 134.45, 133.75, 133.08, 132.94, 132.24, 130.64, 130.13, 129.15, 126.13 (C _{arom.}), 119.81(C ₄), 114.25, 110.33 (2CN), 57.93(C ₁).
10d Ar = <i>p</i> -NO ₂ C ₆ H ₄	284–286 (56.9)	2213 (CN), 1736 (C=O).	8.01 (s, 1H, CH), 7.70–7.25 (m, 9H, arom.).	167.00(CO), 166.50(C ₂), 149.50 (C ₅), 140.00, 134.50, 133.35, 133.21, 132.28, 130.70, 130.11, 125.45(C _{arom.}), 123.10(C ₄), 114.00, 110.10(2CN), 59.00(C ₁).
10e Ar = <i>p</i> -OCH ₃ C ₆ H ₄	275–278 (55.9)	2214 (CN), 1722 (C=O).	7.95 (s, 1H, CH), 7.70– 7.02 (m, 12H, arom.), 3.90 (s, 3H, CH ₃).	166.12(CO), 165.18(C ₂), 162.60, 133.03, 132.75, 131.80, 130.21, 128.74, 124.98, 115.28(C _{arom.}), 137.20(C ₅), 113.34(C ₄), 113.15, 109.41(2CN), 57.58(C ₁), 55.69(CH ₃).

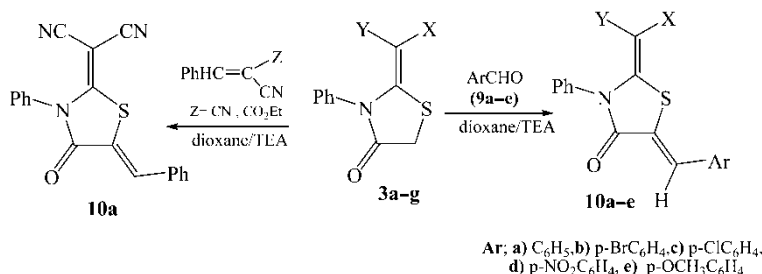
^aSatisfactory microanalysis obtained C; ±0.35, H; ±0.4, N; ±0.2.

or chloroacetyl chloride (0.02 mol) in ethanol was added. The reaction mixture was heated at 60–70°C for about two hours. The precipitated 2-ylidene-3-phenylthiazolidin-4-one (**3a**) was filtered off, dried and crystallized from ethanol. Compounds (**3b–g**) were prepared in a similar way. Melting points, yields, and spectral data of the thiazolidinones (**3a–g**) are shown in table 1.

3.2.2 Method B: typical procedure (II). To a solution of the active methylene compounds (**1a**) (0.01 mol) in DMF (30 ml) in 100 ml three-necked round bottom flask was added anhydrous potassium carbonate (0.01 mol) and the mixture was magnetically stirred for one hour



SCHEME 4



SCHEME 5

at room temperature. Phenylisothiocyanate (0.01 mol) was then added dropwise and the reaction mixture was stirred for two hours at room temperature. An equimolar quantity of ethyl chloroacetate was added and the reaction mixture was stirred at room temperature for another four hours to give a solid product. The obtained products were found to be the same as the 4-thiazolidinones (**3a–c**) obtained by method A (ir and mp's proof).

3.3 *N*-Formylthiophene derivatives (**5a–d**)

3.3.1 Typical procedure. To a solution of the active methylene compounds (**1d**) (0.01 mol) in DMF (30 ml) in 100 ml three-necked round bottom flask was added anhydrous potassium carbonate (0.01 mol) and the mixture was magnetically stirred for one hour at room temperature. Phenylisothiocyanate (0.01 mol) was then added dropwise and the reaction mixture was stirred for two hours at room temperature. An equimolar quantity of ethyl chloroacetate was added and the reaction mixture was stirred at room temperature for another four hours. The obtained product were filtered off, crystallized and found to be the *N*-formylthiophene derivative (**5a**). The *N*-formylthiophene derivatives (**5b–g**) were prepared similarly. Melting points, yields and spectral data of these compounds are shown in table 2.

3.4 *2-(1,1-dicyanomethylene)-5-ethoxymethylene-3-phenylthiazolidinone (7)*

A mixture of compound (**3a**) (0.00147 mol) and triethylamine (2 ml) was heated under reflux in acetic anhydride (15 ml) for three hours. The reaction mixture was cooled and the solid product was collected and recrystallized from ethanol to give orange crystals. M.p., yield, and spectral data of compound (**7**) are shown in table 3.

3.5 2-(1,1-Dicyanomethylene)-5-amino-methylene-3-*N*-phenylthiazolidine-4-one (8a)

A mixture of compound (7) (0.001 mol) and ammonia solution (3 ml) was stirred in absolute ethanol (20 ml) at room temperature for 24 hours. The precipitated solid formed was filtered off and recrystallized from ethanol to give a pink crystalline solid; spectral data of compound (8a) are shown in table 3.

3.6 2-(1,1-Dicyanomethylene)-5-phenylhydrazonomethylene-3-*N*-phenylthiazolidine-4-one (8b)

A solution of compound (7) (0.0034 mol) and phenylhydrazine (10 drops) in absolute ethanol (10 ml) was heated under reflux for four hours. The product formed was filtered off and recrystallized from ethylacetate-petroleum ether mixture to give a brick crystalline solid; spectral data of compound (8b) are shown in table 3.

3.7 5-arylidene-2-(1,1-dicyanomethylene)-3-*N*-phenyl-thiazolidine-4-ones (10a-e)

3.7.1 Typical procedure. A solution of compound (3a) (0.01 mol), and benzaldehyde (0.01 mol) in dioxane (30 ml) was refluxed for about three hours in the presence of triethylamine. The precipitated solid was collected by filtration and recrystallized. The other 5-arylidene-thiazolidinone-4-ones (10b-e) were prepared similarly. Melting points and spectral data of compounds (10a-e) are shown in table 4.

References

- [1] H. Junjappa, H. Ila, C.V. Asokan. *Tetrahedron*, **46**, 5423 (1990).
- [2] L.-B. Wang, C.-Y. Yu, Z.-T. Huang. *Synthesis*, 1441 (1994).
- [3] C.-Y. Yu, L.-B. Wang, W.-Y. Li, Z.-T. Huang. *Synthesis*, 959 (1996).
- [4] Z.-J. Li, Q. Yang, X.-M. Chen, Z.-T. Huang. *Synthesis*, 231 (1999).
- [5] X.-P. Nie, M.-X. Wang, Z.-T. Huang. *Synthesis*, 1439 (2000).
- [6] O. Barun, P.K. Mohanta, H. Ila, H. Junjappa. *Synlett* 653 (2000).
- [7] Z.-H. Xu, Y.-F. Jie, M.-X. Wang, Z.-T. Huang. *Synthesis*, 523 (2002).
- [8] S. Chakrabarti, K. Panda, H. Ila, H. Junjappa. *Synlett*, 309 (2005).
- [9] H. Loghmani-Khouzani, M.M. Sadeghi, M.H. Ghorbani. *J. Iranian Chem. Soc.*, **3**, 360 (2006).
- [10] K.N. Batt, A.M. Dave, N.K. Undavia, P.B. Trivedi. *J. Indian Chem. Soc.*, **66**, 181 (1989).
- [11] S.V. Patel, J.N. Vasavada, G.B. Joshi. *J. Indian Chem. Soc.*, **61**, 560 (1984).
- [12] G.C. Kamdar, D.J. Bhatt, A.R. Parikh. *J. Indian Chem. Soc.*, **65**, 67 (1988).
- [13] C.L. Patel, H. Parekh. *J. Indian Chem. Soc.*, **65**, 282 (1988).
- [14] M.I. Hussain, S. Shukla. *Indian J. Chem.*, **25B**, 549 (1986).
- [15] L. Mehta, H. Parekh. *J. Indian Chem. Soc.*, **65**, 178 (1988).
- [16] A. Rao, A. Carbone, A. Chimirri, E. De Clercq, A.M. Monforte, P. Monforte, C. Pannecouque, M. Zappala. *Il Farmaco*, **57**, 747 (2002).
- [17] A. Rao, A. Carbone, A. Chimirri, E. De Clercq, A.M. Monforte, P. Monforte, C. Pannecouque, M. Zappala. *Il Farmaco*, **58**, 115 (2003).
- [18] A. Rao, J. Balzarini, A. Carbone, A. Chimirri; E De Clercq, A. M. Monforte, P. Monforte, C. Pannecouque, M. Zappala. *Il Farmaco*, **59**, 33 (2004).
- [19] M. Sayyed, S. Mokle, M. Bokhare, A. Mankar, S. Surwase, S. Bhusare, Y. Vibhute. *Arkivoc*, (ii), 187 (2006).
- [20] F.C. Brown. *Chem. Rev.*, **61**, 463 (1961).
- [21] G.R. Newkome, A. Nayak. In *Advances in Heterocyclic Chemistry*, A.R. Katritzky (Ed.) Vol. 25, pp. 88-112 Academic Press: New York (1979).
- [22] N. Hamza, A. Giath, M.N. Ibrahim. *Asian J. Chem.*, **14**, 1760 (2002).
- [23] F. Aydogan, N. Ocal, Z. Turgut, C. Yolacan. *Bull. Korean Chem. Soc.*, **22**, 476 (2001).
- [24] A.M. Asiri. *Molecules*, **6**, M213 (2001).
- [25] I. Vazzana, E. Terranova, F. Mattioli, F. Sparatore. *Arkivoc (Electronic Conference Online 2004 www.arkat_usa.org)*.
- [26] A. Rao, A. Chimirri, S. Ferro, A.M. Monforte, P. Monforte, M. Zappalá. *Arkivoc (Electronic Conference Online 2004)*.
- [27] A.K. El-Shafei, A.M.M. El-Saghier, E.A. Ahmed. *Synthesis*, 152 (1994).

- [28] A.M.M. El-Saghier. *Molecules*, **7**, 756 (2003).
- [29] A.M.M. El-Saghier, M.A. Makhlouf, M.F. Farhat. *Phosphorus, Sulfur Silicon*, **181**, 1569 (2006).
- [30] A.M.M. El-Saghier. *Bull. Chem. Soc. Jpn*, **66**, 2011 (1993).
- [31] A.M.M. El-Saghier. *Phosphorus, Sulfur Silicon*, **179**, 1237 (2004).
- [32] A.M.M. El-Saghier. *Phosphorus, Sulfur Silicon*, **177**, 1213 (2002).
- [33] A.K. El-Shafei, H.A. Abdel-Ghany, A.A. Sultan, A.M.M. El-Saghier. *Phosphorus, Sulfur Silicon*, **73**, 15 (1992).
- [34] G. Sommen, A. Comel, G. Kirsch. *Int. Elect. Conf. On Synth. Org. Chem.*, (2001).
- [35] E. Koltai, J. Nyitrai, K. Lempert. *Tetrahedron*, **29**, 2781(1973).
- [36] T. Srivastava, W. Haq, S.B. Katti. *Tetrahedron*, **58**, 7619 (2002).
- [37] S.S. Bhattacharjee, H. Ila, H. Junjappa. *Synthesis*, **4**, 301 (1982).
- [38] M. Chandrasekaram, H. Ila, H. Jujappa. *Synth. Commun.*, **28**, 3073 (1998).