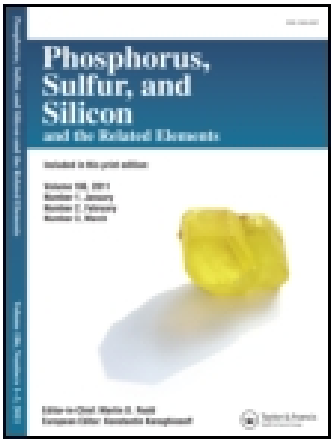

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Substituted Quinolinones, Part 14: Synthesis of Novel Dispiro(heterocycle-N,2′-[1,3]dithietane-4′,3″-quinolinedione) Derivatives Under PTC Conditions

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SUBSTITUTED QUINOLINONES, PART 14: SYNTHESIS OF NOVEL DISPIRO(HETEROCYCLE-*N*,2′-[1,3]DITHIETANE-4′,3′′-QUINOLINEDIONE) DERIVATIVES UNDER PTC CONDITIONS

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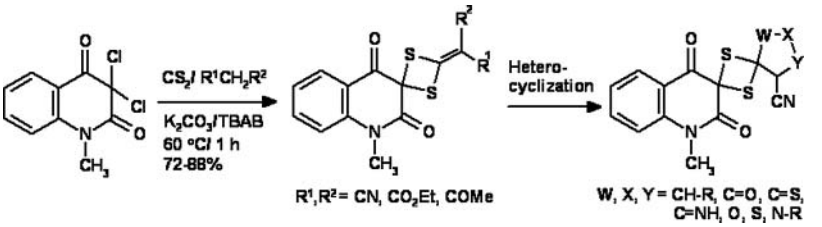
GRAPHICAL ABSTRACT



Abstract *The four-membered spiro-heterocycles ethyl cyano(1-methyl-2,4-dioxospiro{1,3-quinoline-3,4′-[1,3]dithietane}-4′-ylidene)-acetate* ***2a****, -malononitrile* ***2b****, -acetylacetone* ***2c****, and thiazetidine isomer* ***3*** *were prepared under phase transfer catalysis (PTC) conditions. The thermal treatment of dithietanes* ***2a–c*** *led to the bis-quinolinyl sulfide* ***4****. Some interesting nucleophilic additions followed by cyclization reactions were carried out with the dithietane* ***2a*** *to give the corresponding novel dispiro derivatives* ***5–8****,* ***10–13****, and* ***15****.*

Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.*

Keywords Dispiro-heterocycles; 1,3-dithietane; phase transfer catalysis; quinolinone

INTRODUCTION

The heterocyclic synthetic utility of ketene-*S*,*S*-acetals[1–3] as well as ketene-*N*,*S*-acetals[4] has attracted considerable attention. The ketene-*S*,*S*-acetals have been used as starting materials for the synthesis of a wide variety of heterocycles.[5–7] Geminal dihalo compounds, such as 3,3-dichloroquinoline-2,4-diones, have revealed important activity towards nucleophilic substitution with various *N*, *S*, and *O*-nucleophiles, leading to 3,3-disubstituted

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Dedicated to the memory of the late Professor Ahmed K. El-Shafie.
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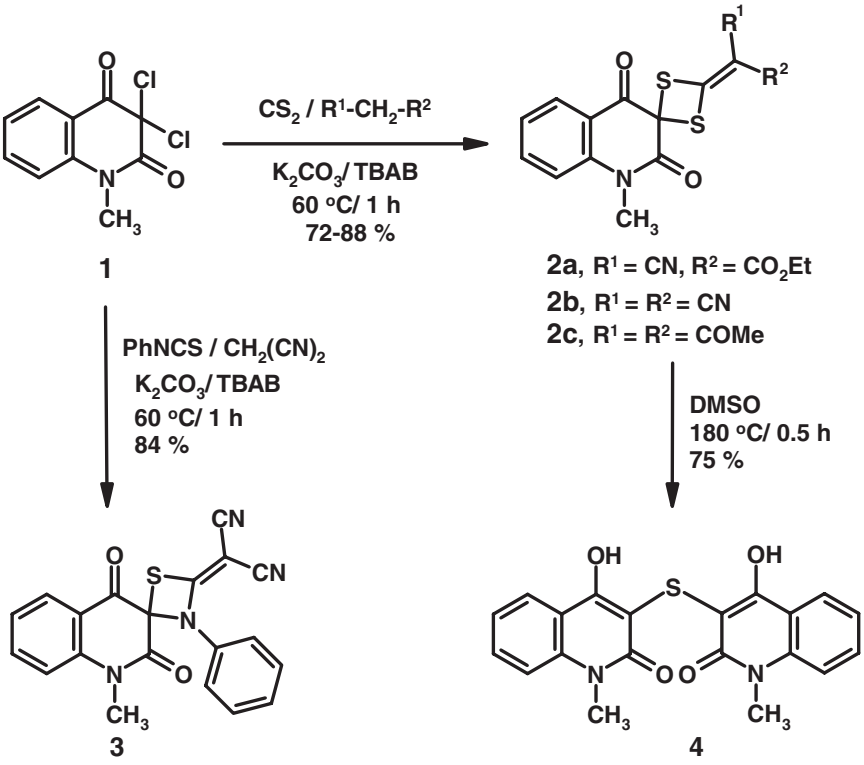


Scheme 1

quinolinediones and/or fused quinolines at face-*c*.[8–11] The interesting structures and properties of 1,3-dithietanes and 1,3-thiazetanes[12,13] prompted our attention to obtain novel spiro-heterocyclic ring systems starting from ketene-*S*,*S*-acetals and 3,3-dichloroquinoline-2,4-dione.[14] Quinolinones are associated with important biological activities,[15–17] and during our recent investigation of new 3-substituted quinolinones, these compounds showed significant antiparasitic activity, especially towards bilharzias. In this article, we report Michael reaction of a spiro[(4-methylidene[1,3]dithietane)-2,3′-quinolinedione] leading to dispiro-dithietane derivatives as novel heterocyclic systems (Scheme 1). Since dithietanes are a four-membered heterocyclic system, which is sensitive to nucleophilic and thermal treatments,[18] the application of phase transfer catalysis (PTC) conditions[19–21] enabled carrying out nucleophilic reactions, such as Michael addition, under mild conditions: temperature, basic catalysis, and solvent.

RESULTS AND DISCUSSION

3,3-Dichloro-1-methylquinoline-2,4(1*H*,3*H*)-dione (**1**)[14] is a geminal dichloro derivative that was subjected to the reaction with a mixture of some active methylene compounds, viz.; ethyl cyanoacetate, malononitrile, and acetylacetone and carbon disulfide, using potassium carbonate as a catalyst in dioxane, under PTC conditions. Tetrabutyl ammonium bromide (TBAB) was selected as a PT-catalyst where experimental results showed the best yield percentage (72–88%) and purity of product in the presence

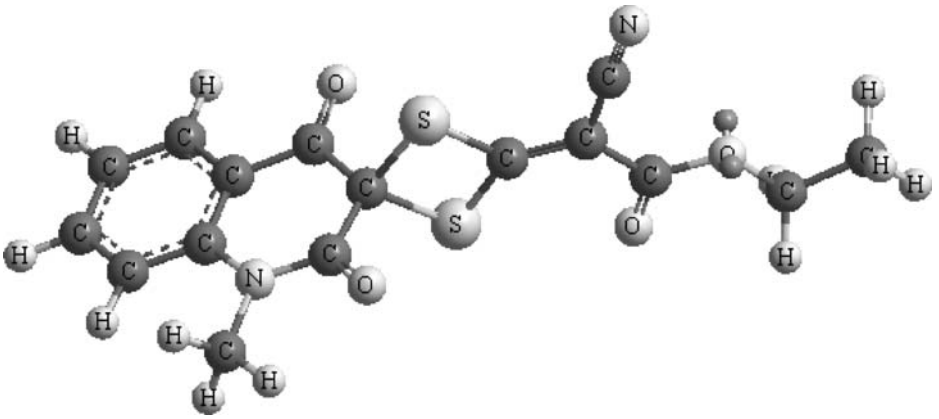


Figure 1 MM2-optimized structure of the spiro compound **2a**.

of TBAB. This reaction led to the formation of novel spiro[1,3-dithietane-2,3′-quinoline] derivatives **2a–c**.

Figure 1 shows MM2-minimized energy 3D-structure[22] of the spiro compound **2a**, which reveals that the dithietane nucleus lies in a plane perpendicular to the quinolinedione nucleus plane. As expected, the molecule of compound **2a** assumed this configuration to avoid repulsion between sulfur atoms of the dithietane ring and oxygen atoms of the quinoline-2,4-dione system.

Similarly, treating the dichloro compound **1** with phenyl isothiocyanate under the above conditions furnished spiro[quinoline-3,2′-[1,3]thiazetidin] **3** in 84% yield (Scheme 1). The structure of these four spiro four-membered 1,3-diaza-heterocyclic derivatives was checked using IR, ^{1}H NMR, and mass spectra. The experimental results revealed relative thermal stability of these small heterocyclic systems. Interestingly, heating of any of the trio **2a–c** in boiling DMSO (179–180°C) led to breaking of the dithietane ring with coupling of two molecules furnishing 4-hydroxy-3-[(4-hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)sulfanyl]-1-methylquinolin-2(1*H*)one (**3**). The structure of the sulfide **4** was supported via its mass fragmentation pattern (Figure S1, Supplemental Materials, available online). Mass spectrum showed the molecular ion peak at m/e 380 (*I*, 24.7%) and the base peak at m/e 175 (*I*, 100%), which is related to 4-hydroxy-1-methylquinolin-2(1*H*)-one cation (Figure 2).

The reaction of the dithietane **2a** with certain cyclic α-active methylene keto-compounds, viz., cyclopentanone, cyclohexanone, cycloheptanone, tetralone, 4-hydroxy-1-methylquinolin-2(1*H*)-one (**9**), cyanoacetamide, and cyanothioacetamide, in presence of piperidine as a catalyst gave rise to seven innovative dispiro dithietane heterocyclic systems. It was found that use of classic base catalyzed reaction conditions (piperidine in dioxane) or phase transfer catalyzed reaction conditions (potassium carbonate/TBAB in dioxane) gave the same products and in nearly the same yields. In this article, we describe the convenient method using piperidine due to its simplicity in working up the products. Spectral characterization of the products illustrated that a Michael-type addition took place between the in situ–formed carbanion and activated exo-cyclic double bond of the dithietane **2a** followed by an intramolecular cyclocondensation leading to the dispiro pyrans **5–8**, **10**, and the dispiro piperidines **11a**,**b** (Schemes 2 and 3).

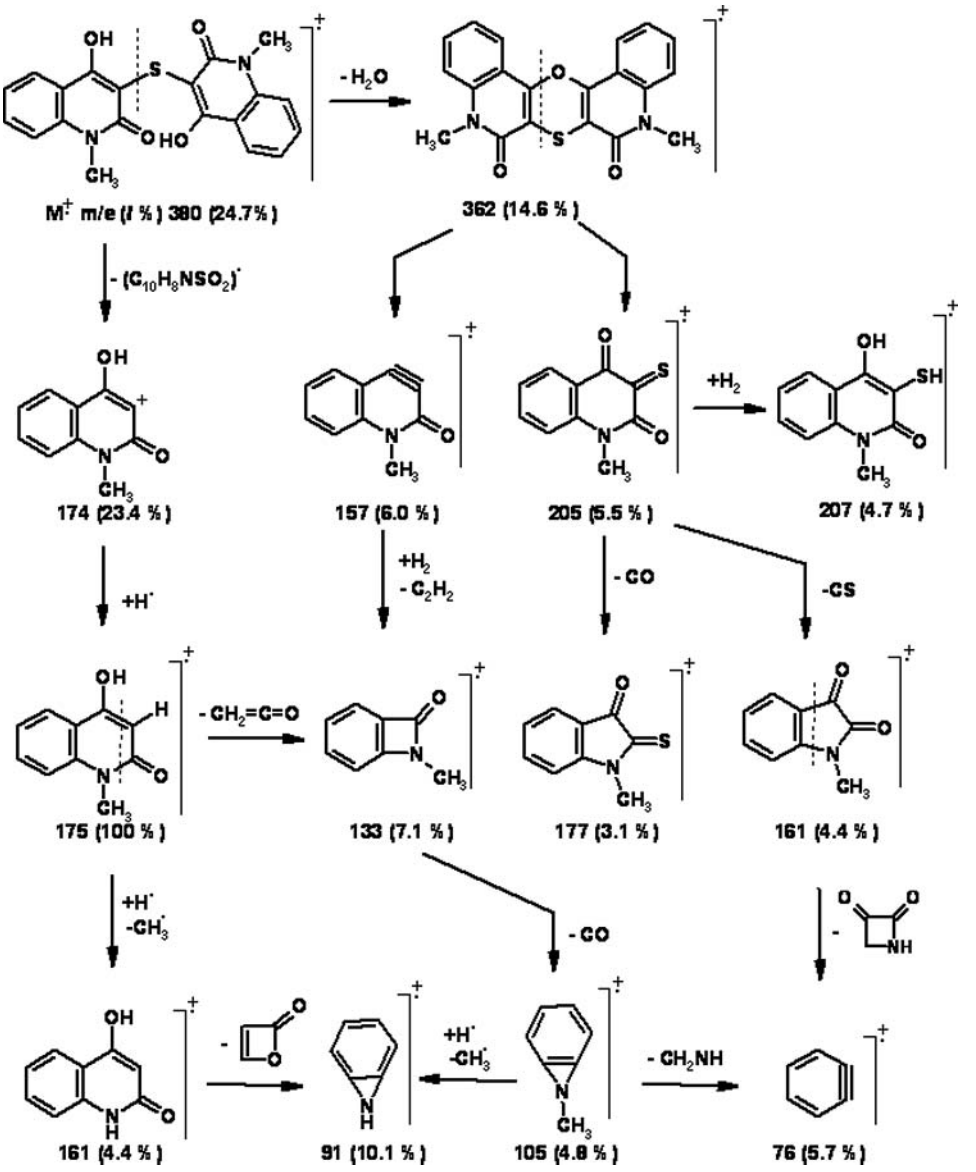
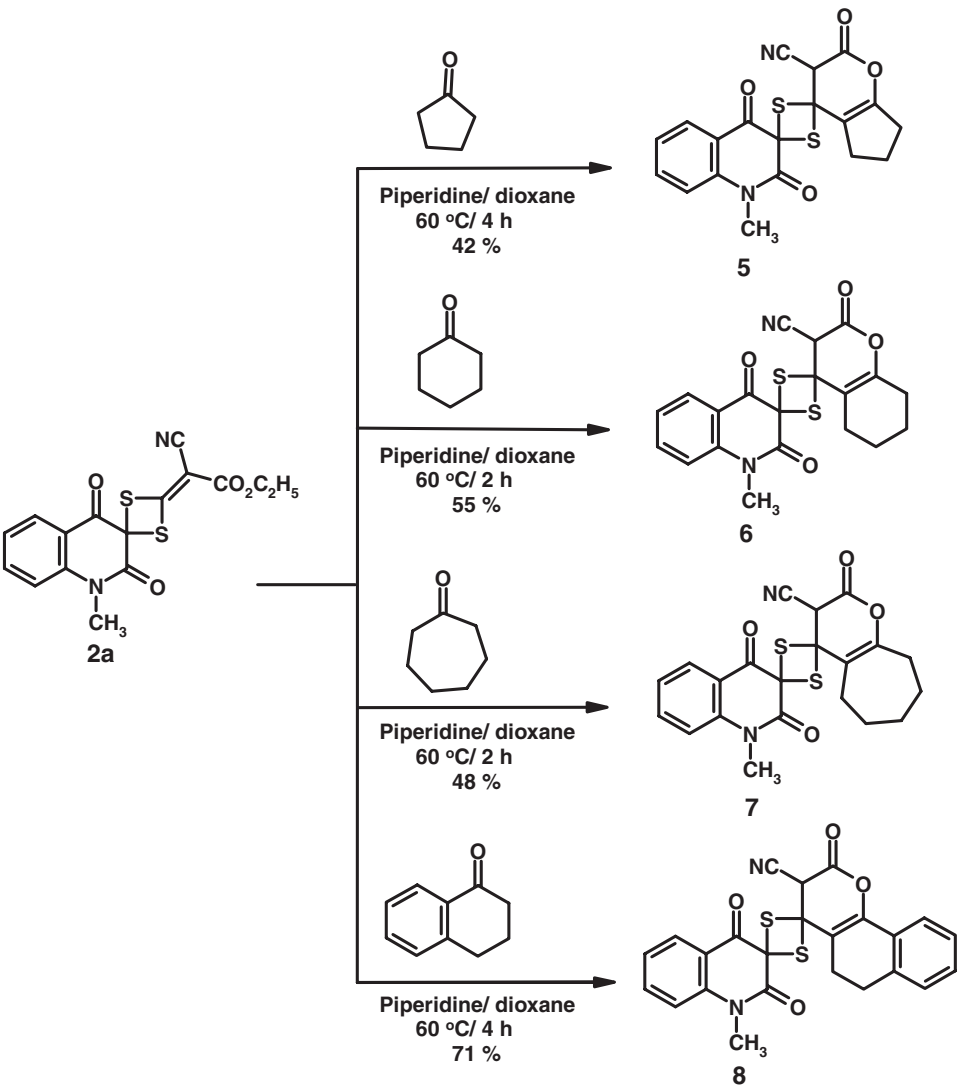


Figure 2

In general, as shown by IR and ^{1}H NMR spectra of the products, it was noted that in these cyclization reactions selectively, the carboxylate group is involved in an addition-elimination (condensation) process, leading to a pyran or a piperidine ring, at the same time the cyano-group remained away from the possible nucleophilic addition. This is just an empirical result, but we have no explanation for this regioselective behavior.

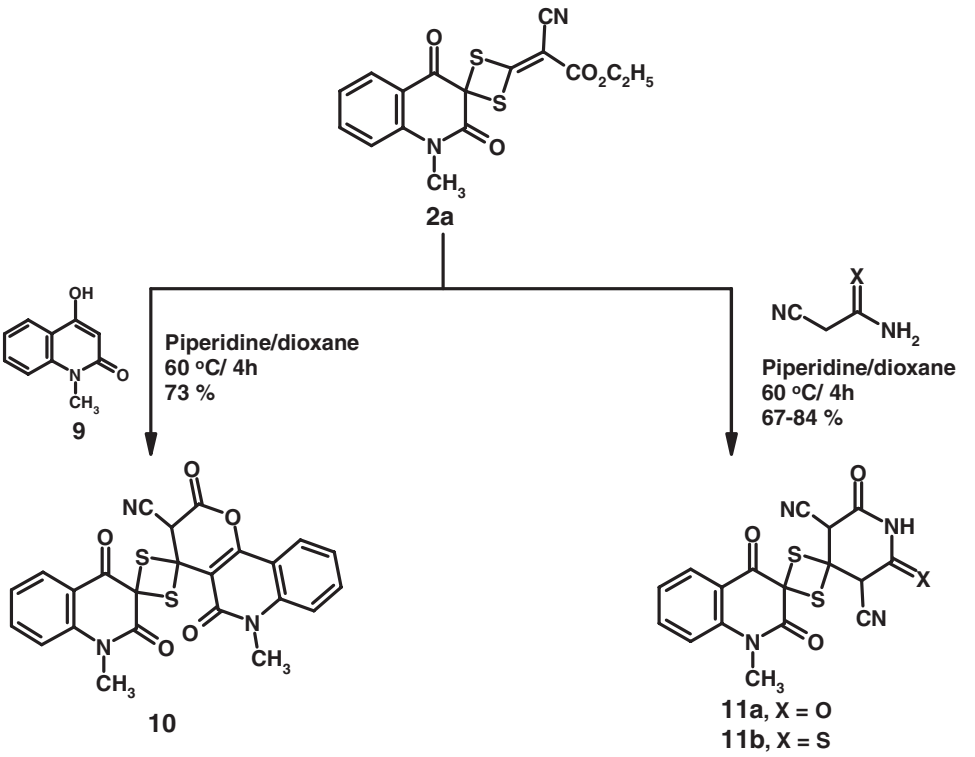
When the dithietane **2a** was treated with certain diaza-binucleophiles, such as guanidine hydrochloride, thiourea, and 4-amino-5-(trifluoromethyl)-4*H*-1,2,4-triazole-3-thiol (**14**)[23] under PTC conditions, some interesting dispiro diaza- and or triaza-heterocyclic



Scheme 2

compounds were obtained. Comparison between use of traditional bases, such as piperidine and PTC systems like potassium carbonate/TBAB to catalyze such addition-cyclization reaction, clearly showed that PTC conditions are more suitable due to significant difference in yield percentage between the two methodologies. While use of piperidine as catalyst led to yields that did not exceed 30%, this PTC reaction afforded the pyrimidine **12**, 1,3-thiazinane **13**, and 1,3,4-thiadiazepine **15** in excellent yields (72–85%) (Scheme 4).

Again the IR spectra of the compounds **12**, **13**, and **15** revealed the presence of a cyano group, showing that it was not included in the reaction course. At the same time, there is no indication for an ethyl set of protons in the ^{1}H NMR spectra of these three compounds, providing clear evidence for its inclusion in the cyclization process. All structures were



Scheme 3

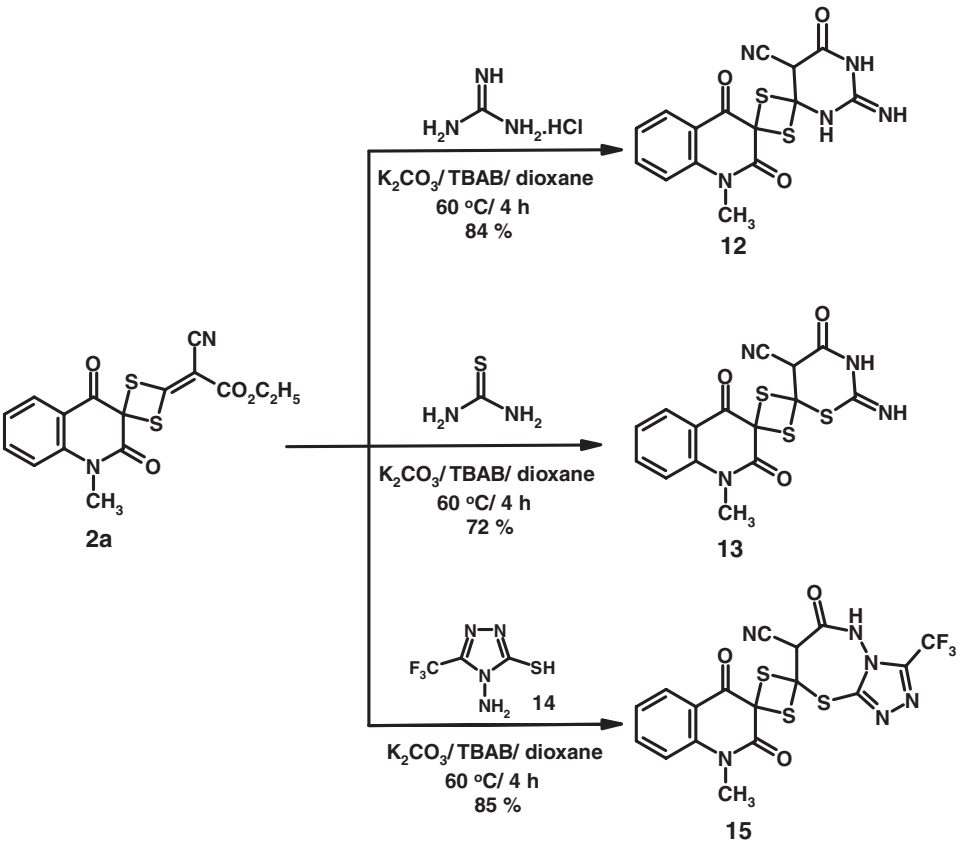
also supported by mass spectrometry along with satisfactory elemental analyses (±0.4%) for carbon, hydrogen, nitrogen, and sulfur.

CONCLUSIONS

Phase transfer catalyzed nucleophilic substitution of geminal dihalo compounds with in situ–prepared ketene-*S,S*-acetals and/or ketene-*N,S*-acetals is an efficient methodology to obtain spiro 1,3-dithietane compounds. Many dispiro heterocyclic compounds including dithietane ring system can be prepared via a convenient method and in excellent yields using piperidine as catalyst especially in the case of addition of α-active methylene keto compounds to 2-methylidine-1,3-dithietanes. Potassium carbonate/TBAB in dioxane proved to be the catalyst of choice when diaza-binucleophiles are reacted with activated exocyclic double bond systems like 2-methylidine-1,3-dithietanes.

EXPERIMENTAL

Melting points were determined in open capillary tubes on a digital Stuart SMP3. IR spectra were taken on a Perkin-Elmer FT-IR 1650 or Nicolet 710 FT-IR spectrometers, using samples in KBr disks. ^{1}H NMR spectra were recorded on Varian Gemini-200 NMR-spectrometer (200 MHz), using DMSO-d_6 or $CDCl_3$ as solvents and TMS as internal reference. Mass spectra were determined on a Carlo-Erba QMD-1000 instrument by direct



Scheme 4

inlet, operating at 75 eV. Elemental microanalyses were performed on a Perkin Elmer CHN-2400 Analyzer at the Microanalytical Center, Cairo University. All reactions were monitored by TLC on 0.2-mm silica gel F-254 (Merck) plates, using UV light (λ = 254 nm) for detection.

3,3-Dichloro-1-methylquinoline-2,4(1H,3H)-dione (1)

This compound was obtained using the method described in the literature.[14]

General Procedure for the PTC-Synthesis of Dithietanes 2a–c

To a stirred mixture of anhydrous potassium carbonate (2.79 g, 20 mmol), TBAB (0.1 g, 0.3 mmol), and an active methylene compound (5 mmol), viz., ethyl cyanoacetate (0.55 mL), malononitrile (0.34 g), and acetylacetone (0.52 mL) in dry dioxane (30 mL), carbon disulfide (0.31 mL, 5 mmol) diluted with dioxane (5 mL) was added dropwise added. The mixture was then stirred at 60°C for 0.5 h. A yellowish-orange precipitate was obtained. Afterwards, a solution of compound **1** (1.22 g, 5 mmol) in dioxane (50 mL) was added to the mixture, and the stirring was continued at 60°C for 1 h. Then the mixture was

filtered off, and the filtrate was evaporated in vacuo. The residual solid that obtained was crystallized to give the dithietanes **2a–c**.

Ethyl 2-cyano-2-(1′-methyl-2′,4′-dioxo-2′,4′-dihydro-1′H-spiro[[1,3]dithietane-2,3′-quinoline]-4-ylidene)acetate (2a). This compound was obtained from ethyl cyanoacetate, yield 1.30 g (72%); mp 253–5°C (dioxane); IR (ν_{max}, cm^{-1}): 2216 (C≡N), 1720 (C=O), 1671–1642 (C=O); ^{1}H NMR (δ): 1.12–1.40 (t, J = 6.2 Hz, 3H, $CO_2CH_2CH_3$), 3.80 (s, 3H, NCH_3), 4.13–4.43 (q, J = 6.4 Hz, 2H, $CO_2CH_2CH_3$), 7.40–7.90 (m, 4H, H_{arom}); Mass (m/z, *I*%): $M^{+\cdot}$ 360 (43%). *Anal.* calcd. for $C_{16}H_{12}N_2O_4S_2$ (360.41): C, 53.32; H, 3.36; N, 7.77; S, 17.79%. Found: C, 53.60; H, 3.50; N, 7.90; S, 17.89%.

2-(1′-Methyl-2′,4′-dioxo-2′,4′-dihydro-1′H-spiro[[1,3]dithietane-2,3′-quinoline]-4-ylidene)malononitrile (2b). This compound was obtained from malononitrile, yield 1.38 g (88%); mp > 300°C (iso-propanol); IR (ν_{max}, cm^{-1}): 2299 (C≡N), 1665–1640 (C=O), ^{1}H NMR (δ): 3.80 (s, 3H, NCH_3), 7.40–7.90 (m, 4H, H_{arom}); Mass (m/z, *I*%): $M^{+\cdot}$ 313 (22.2%). *Anal.* calcd. for $C_{14}H_7N_3O_2S_2$ (313.36): C, 53.66; H, 2.25; N, 13.41; S, 20.46%. Found: C, 53.90; H, 2.41; N, 13.60; S, 20.58%.

4-(2,4-Dioxopentan-3-ylidene)-1′-methyl-1′H-spiro[[1,3]dithietane-2,3′-quinoline]-2′,4′-dione (2c). This compound was obtained from acetylacetone, yield 1.39 g (80%); mp 260–262°C (ethanol); IR (ν_{max}, cm^{-1}): 1682 (C=O), 1660–1643 (C=O); ^{1}H NMR (δ): 2.28 (s, 6H, $COCH_3$), 3.78 (s, 3H, NCH_3), 7.32–7.80 (m, 4H, H_{arom}); Mass (m/z, *I*%): $M^{+\cdot}$347 (36.5%). *Anal.* calcd. for $C_{16}H_{13}NO_4S_2$ (347.41): C, 55.32; H, 3.77; N, 4.03; S, 18.46%. Found C, 55.50; H, 3.50; N, 4.20; S, 18.20%.

2-(1-Methyl-2,4-dioxo-3′-phenyl-2,4-dihydro-1H-spiro[quinoline-3,2′-[1,3]thiazetidine]-4′-ylidene)malononitrile (3)

To a stirred mixture of anhydrous potassium carbonate (2.79 g, 20 mmol), TBAB (0.1 g, 0.3 mmol), and malononitrile (0.34 g, 5 mmol) in dry dioxane (30 mL), phenyl isothiocyanate (0.66 mL, 5 mmol) in dioxane (5 mL) was added dropwise. The mixture was then stirred at 60°C for 0.5 h. A pale yellow precipitate was obtained. Afterward, a solution of compound **1** (1.22 g, 5 mmol) in dioxane (50 mL) was added to the mixture, and the stirring was continued at 60°C for 1 h. Then, the mixture was filtered off, and the filtrate was evaporated in vacuo. The residual solid that was obtained was crystallized from DMF to give the thiazetidine **3**. Yield 1.56 g (84%); mp 290–292°C; IR (ν_{max}, cm^{-1}): 2197 (C≡N), 1660–1642 (C=O); ^{1}H NMR (δ): 3.80 (s, 3H, NCH_3), 7.22–7.95 (m, 9H, H_{arom}); Mass (m/z, *I*%): $M^{+\cdot}$ 372 (66.3%). *Anal.* calcd. for $C_{20}H_{12}N_4O_2S$ (372.41): C, 64.51; H, 3.25; N, 15.04; S, 8.61%. Found: C, 64.76; H, 3.50; N, 15.21; S, 8.77%.

4-Hydroxy-3-[(4-hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)sulfanyl]-1-methylquinolin-2(1H)-one (4)

A solution of the dithietane **2a** (1.08 g, 3 mmol) in DMSO (20 mL) was boiled under reflux at ca. 180°C for 0.5 h. Then, the mixture was left to cool to room temperature and poured onto crushed ice. The precipitate so obtained was filtered and crystallized from DMF, to give the sulfide **4**. Yield 0.5 g (87%); mp >300°C; IR (ν_{max}, cm^{-1}): 3440–2650 (H-bonded-OH), 1654–1642 (C=O); ^{1}H NMR (δ): 3.68 (s, 3H, NCH_3), 3.72 (s, 3H, NCH_3), 7.22–7.95 (m, 8H, H_{arom}), 13.22–13.40 (b, 2H, 2 x OH; exchangeable with D_2O); Mass

(m/z, *I*%): $M^{+\cdot}$ 380 (24.7%). *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, 63.00; H, 3.90; N, 7.20; S, 8.30%.

General Procedure for the Synthesis of Compounds 5–8, 10, and 11a,b

To a mixture of the dithietane **2a** (1.08 g, 3 mmol) and the proper active methylene compound (3 mmol), viz., cyclopentanone (0.3 mL), cyclohexanone (0.35 mL), cycloheptanone (0.4 mL), α-tetralone (0.42 mL), 4-hydroxy-1-methylquinolin-2(1*H*)-one (**9**) (0.53 g), cyanoacetamide (0.26 g), cyanothioacetamide (0.31 g) in dioxane (20 mL), or piperidine (0.2 mL) was added. Then, the mixture was heated at 60°C for 2–4 h. After that, the reaction mixture was treated with icy dilute acetic acid (20 mL, 20%) to give solid precipitates, which were collected by filtration, washed with cold water, dried, and crystallized to give the dispiro compounds **5–8**, **10**, and **11a**,**b**.

Dispiro[(3-cyano-2-oxo-2,3,4,5,6,7-hexahydrocyclopenta[b]pyran)-4,2′-(1,3-dithietane)-4′-3″-(1″-methylquinoline-2″,4″(1″H,3″H)-dione)] (5). This compound was obtained from cyclopentanone, yield 0.5 g (42%); mp 277–278°C (ethanol); IR (ν_{max}, cm^{-1}): 2210 (C≡N), 1682 (C=O), 1668–1640 (C=O); ^{1}H NMR (δ): 1.61–2.03 (m, 6H, 3 x CH_2), 3.60 (s, 3H, NCH_3), 3.96 (s, 1H, H_{pyran}), 7.09–7.81 (m, 9H, H_{arom}); Mass (m/z, *I*%): $M^{+\cdot}$ 398 (24.3%). *Anal.* calcd. for $C_{19}H_{14}N_2O_4S_2$ (398.46): C, 57.27; H, 3.54; N, 7.03; S, 16.09%. Found C, 57.30; H, 3.30; N, 7.20; S, 16.20%.

Dispiro[(3-cyano-2-oxo-3,4,5,6,7,8-hexahydro-2H-chromene)-4,2′-(1,3-dithietane)-4′-3″-(1″-methylquinoline-2″,4″(1″H,3″H)-dione)] (6). This compound was obtained from cyclohexanone, yield 0.68 g (55%), mp 256–258°C (dioxane); IR (ν_{max}, cm^{-1}): 2220 (C≡N), 1680 (C=O), 1660–1632 (C=O), ^{1}H NMR (δ):1.40– 1.80 (m, 8H, 4 x CH_2), 3.68 (s, 3H, NCH_3), 3.88 (s, 1H, H_{pyran}), 7.56–8.13 (m, 4H, H_{arom}); Mass (m/z, *I*%): $M^{+\cdot}$ 412 (20.2%). *Anal.* calcd. for $C_{20}H_{16}N_2O_4S_2$ (412.49): C, 58.24; H, 3.91; N, 6.79; S, 15.55%. Found: C, 58.40; H, 3.60; N, 6.90; S, 15.70%.

Dispiro[(3-cyano-2-oxo-2,3,4,5,6,7,8,9-octahydrocyclohepta[b]pyran)-4,2′-(1,3-dithietane)-4′-3″-(1″-methylquinoline-2″,4″(1″H,3″H)-dione)] (7). This compound was obtained from cycloheptanone, yield 0.61 g (48%), mp 246–248 $^{-}$C (ethanol); IR (ν_{max}, cm^{-1}): 2222 (C≡N), 1683 (C=O), 1656–1634 (C=O); ^{1}H NMR(δ): 1.23–1.96 (m, 10H, 5 x CH_2), 3.70 (s, 3H, NCH_3), 3.86 (s, 1H, H_{pyran}), 7.60–8.10 (m, 4H, H_{arom}); Mass (m/z, I%): $M^{+\cdot}$ 426 (64.7%). Anal. calcd. for $C_{21}H_{18}N_2O_4S_2$ (426.52): C, 59.14; H, 4.25; N, 6.57; S, 15.04%. Found: C, 59.10; H, 4.20; N, 6.60; S, 15.16%.

Dispiro[(3-cyano-2-oxo-3,4,5,6-tetrahydro-2H-benzo[h]chromene)-4,2′-(1,3-dithietane)-4′-3″-(1″-methylquinoline-2″,4″(1″H,3″H)-dione)] (8). This compound was obtained from tetralone, yield 0.98 g (71%), mp 295–296°C (iso-propanol); IR (ν_{max}, cm^{-1}): 2212 (C≡N), 1688 (C=O), 1656–1635 (C=O); ^{1}H NMR(δ): 2.23–2.48 (m, 4H, 2 x CH_2), 3.64 (s, 3H, NCH_3), 3.89 (s, 1H, H_{pyran}), 7.20–8.18 (m, 8H, H_{arom}); Mass (m/z, *I*%): $M^{+\cdot}$ 460 (27.8%). *Anal.* calcd. for $C_{24}H_{16}N_2O_4S_2$ (460.53): C, 62.59; H, 3.50; N, 6.08; S, 13.92%. Found: C, 62.40; H, 3.50; N, 6.10; S, 13.80%.

Dispiro[(2,4-dioxo-1-methyl-1,2,3,4-tetrahydroquinoline)-3,2′-(1,3-dithietane)-4′,4″-(6″-methyl-2″,5″-dioxo-3″,4″,5″,6″-tetrahydro-2″H-pyrano[3,2-c]quinoline-3″-carbonitrile)] (10). This compound was obtained from 4-hydroxy-1-methylquinolin-2(1H)-one (9), yield 1.07 g (73%), mp >300°C (DMF); IR (ν_{max}, cm^{-1}): 2203 (C≡N), 1640 (C=O); ^{1}H NMR (δ): 3.64 (s, 3H, NCH_3), 3.70 (s, 3H, NCH_3), 3.89 (s, 1H, H_{pyran}), 7.20–8.08 (m, 8H, H_{arom}); Mass (m/z, I%): $M^{+\cdot}$ 489 (33.5%). Anal. calcd. for

$C_{24}H_{15}N_3O_5S_2$ (489.53): 58.89; H, 3.09; N, 8.58; S, 13.10%. Found: C, 58.80; H, 3.00; N, 8.70; S, 12.90%.

Dispiro[(3,5-dicyano-2,6-dioxopiperidine)-4,2′-(1,3-dithietane)-4′-3″-(1″-methyl-quinoline-2″,4″(1″H,3″H)-dione)] (11a). This compound was obtained from cyanoacetamide, yield 0.8 (67%), mp >300°C (DMF); IR (ν_{max}, cm^{-1}): 3230–3205 (NH), 2203, 2198 (C≡N), 1680 (C=O) 1652–1646 (C=O); ^1H NMR (δ): 3.28 (s, 1H, $H_{piperidine}$), 3.39 (s, 1H, $H_{piperidine}$), 3.66 (s, 3H, NCH_3), 7.18–7.89 (m, 4H, H_{arom}), 11.40 (s, 1H, NH, exchangeable with D_2O); Mass (m/z, *I*%): $M^{+\cdot}$ 398 (14.6%). *Anal.* calcd. For $C_{17}H_{10}N_4O_4S_2$ (398.42): C, 51.25; H, 2.53; N, 14.06; S, 16.10%. Found: C, 51.30; H, 2.30; N, 14.20; S, 15.80%.

Dispiro[(3,5-dicyano-2-oxo-6-thioxopiperidine)-4,2′-(1,3-dithietane)-4′-3″-(1″-methyl-quinoline-2″,4″(1″H,3″H)-dione)] (11b). This compound was obtained from cyanothioacetamide, yield 1.04 (84%), m.p. 278–279°C (DMF); IR (ν_{max}, cm^{-1}): 3434–3235 (br, NH), 2220 (C≡N), 2192 (C≡N), 1681 (C=O), 1650–1640 (C=O); ^1H NMR (δ): 3.25 (s, 1H, $H_{piperidine}$), 3.33 (s, 1H, $H_{piperidine}$), 3.60 (s, 3H, NCH_3), 7.08–7.80 (m, 4H, H_{arom}), 11.30 (s, 1H, NH, exchangeable with D_2O); Mass (m/z, *I*%): $M^{+\cdot}$ 414 (8.2%). *Anal.* calcd. for $C_{17}H_{10}N_4O_3S_3$ (414.49): C, 49.26; H, 2.43; N, 13.52; S, 23.21%. Found: C, C, 49.50; H, 2.50; N, 13.40; S, 23.40%.

General Procedure for the PTC Synthesis of Compounds 12, 13, and 15

To a stirred mixture of anhydrous potassium carbonate (2.79 g, 20 mmol), TBAB (0.1 g, 0.3 mmol), and the proper binucleophile (5 mmol), viz., guanidine hydrochloride (0.49 g), thiourea (0.39 g), and 4-amino-5-(trifluoromethyl)-4*H*-1,2,4-triazole-3-thiol (**14**) (0.92 g) in dry dioxane (50 mL), a solution of the dithietane **2a** (1.8 g, 5 mmol) in dioxane (50 mL) was added, and the stirring was continued at 60°C for 4 h. Then the mixture was cooled in an ice bath overnight. The mixture was then filtered, and the precipitate that was obtained was washed several times with water to remove water-soluble salts. The residual solid product was crystallized to give the dispiro compounds **12**, **13**, and **15**. The filtrate of the reaction mixture was evaporated in vacuo, and the solid so obtained was crystallized to give an additional amount of the same product.

Dispiro[(5-cyano-2-imino-4-oxohexahydropyrimidine)-4,2′-(1,3-dithietane)-4′-3″-(1″-methylquinoline-2″,4″(1″H,3″H)-dione)] (12). This compound was obtained from guanidine hydrochloride, yield 1.57 (84%), mp 287–289°C (dioxane); IR (ν_{max}, cm^{-1}): 3430, 3324 (N–H), 3150 (N–H), 2210 (C≡N), 1662 (C=O), 1646–1632 (C=O). ^1H NMR (δ): 3.70 (s, 3H, NCH_3), 4.20 (s, 1H, $H_{pyrimidine}$), 7.23–7.90 (m, 4H, H_{arom}), 8.40 (b, 1H, NH, exchangeable with D_2O), 9.00 (b, 1H, NH, exchangeable with D_2O), 10.40 (b, 1H, NH, exchangeable with D_2O); Mass (m/z, *I*%): $M^{+\cdot}$ 373 (16.2%). *Anal.* calcd. for $C_{15}H_{11}N_5O_3S_2$ (373.41) requires C, 48.25; H, 2.97; N, 18.75; S, 17.17%. Found: C, 48.30; H, 2.70; N, 18.60; S, 17.00%.

Dispiro[(5-cyano-2-imino-4-oxo-1,3-thiazinane)-6,2′-(1,3-dithietane)-4′-3″-(1″-methylquinoline-2″,4″(1″H,3″H)-dione)] (13). This compound was obtained from cyanothioacetamide, yield 1.4 g (72%), mp 244–246°C (DMF); IR (ν_{max}, cm^{-1}): 3480–3240 (N–H), 2220 (C≡N), 1664 (C=O), 1653–1627 (C=O); ^1H NMR (δ): 3.67 (s, 3H, NCH_3), 3.98 (s, 1H, $H_{thiazinane}$), 7.25–8.13 (m, 4H, H_{arom}), 9.80 (b, 1H, NH, exchangeable with D_2O), 11.60 (b, 1H, NH, exchangeable with D_2O); Mass (m/z, *I*%):

$M^{+\cdot}$ 390 (10.6%). *Anal.* calcd. for $C_{15}H_{10}N_4O_3S_3$ (390.46): C, 46.14; H, 2.58; N, 14.35; S, 24.64%. Found: C, 46.00; H, 2.60; N, 14.20; S, 24.40%.

Dispiro[(2,4-dioxo1-methyl-1,2,3,4-tetrahydroquinoline)-3,2′-(1,3-dithietane)-4′-8″-(6″-oxo-3″-(trifluoromethyl)-5″,6″,7″,8″-tetrahydro[1,2,4]triazolo[3,4-b]-[1,3,4]thiadiazepine-7″-carbonitrile)] (15). This compound was obtained from 4-amino-5-(trifluoromethyl)-4*H*-1,2,4-triazole-3-thiol (**14**), yield 2.11 g (85%), m.p. 198–200°C (ethanol); IR(ν_{max}, cm^{-1}): 3430–3172 (N–H), 2200 (C≡N), 1678 (C=O), 1654–1636 (C=O). ^{1}H NMR (δ): 3.72 (s, 3H, NCH_3), 4.00 (s, 1H, $H_{thiadiazepine}$), 7.28–8.05 (m, 4H, H_{arom}), 12.50 (s, 1H, NH, exchangeable with D_2O); Mass (m/z, *I*%): $M^{+\cdot}$ 498 (8.4%). *Anal.* calcd. for $C_{17}H_9N_6F_3O_3S_3$ (498.49): C, 40.96; H, 1.82; N, 16.86; S, 19.30%. Found: C, 40.80; H, 2.00; N, 16.50; S, 19.10%.

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