In the last few years we were involved in the preparation of polysubstituted heterocycles starting with readily obtainable nitriles [1—3]. As a part of this program we investigated the reaction of cyanothioacetamide 1 with the cinnamalonitriles 2a—c. In the last decade, reports have appeared describing the reaction of 1 with active methylene reagents that afforded either pyran or pyridine derivatives [4—8]. In our laboratory it has been found that 1 reacts with 2a—c to yield 1:1 adducts. The same products were obtained on reacting malononitrile with the α-cyano-cinnamothioacetamides 3a—c. This finding indicated that the reaction of 1 with 2a—c proceeds via initial addition of the active methylene moiety in 1 to the activated double bond in 2 thus forming either the acyclic Michael adducts 4a—c or their cyclization products 5 or 6. 1H NMR spectra fit the thiopyran form 5 but can scantly be interpreted in favour of the dihydropyridine 6 in the tautomeric form 7. The 13C NMR spectrum established the thiopyran structure 5. Thus, in addition to aryl carbons (and the methoxycarbon in case of reaction of 1 with 2b) 13C NMR showed four signals at δ 41, 72, 118 and 151 ppm. The signals at 41 and 72 showed C—H coupling (Jc—4,H—4 = 133 Hz) whereas the signal at 151 showed C—N coupling (t, J = 5.2 Hz). The presence of not more than 4 signals can be only interpreted in terms of symmetrical structure 5. The reaction of 2a—c with 1 is thus different from its recently reported behaviour towards furan-2-ylidenemalononitrile and thiophen-2-ylidenemalononitrile, with the former products of addition to the cyano group has been formed whereas with the latter ylidene group exchange took place [11].

Compounds 5a—c were converted through refluxing in ethanolic aqueous triethylamine into the pyridinthones 8a—c. Compounds 8a—c were also obtained from the reaction of 2d—f with 1 in refluxing ethanolic aqueous triethylamine. The formation of 8a—c from 5a—c is assumed to be formed via ring opening, recyclization and oxidation of the formed tetrahydropyridine derivative.

Compounds 8a—c are tautomeric with structures 9 and 10. However 13C NMR revealed the absence of any sp3 carbon or CH in the molecule which exclude structure 9. The pyridinthonic form 8 was preferred over the tautomeric 10 based on the existence of two signals at δ 179.4 ppm and 162 ppm. The low field signal can be assigned to thioxo group and is comparable to the signal at δ 176.4 ppm reported for pyridine-
2-thiones whereas the signal at δ 162 can be correlated to that at δ 164.5 for 2-methoxypyridine [12]. This results show that the reactions of 2 with active methylene reagents can be utilised as an excellent approach to synthesis of several, otherwise difficult access heterocycles.

Experimental

All melting points are uncorrected. IR spectra were recorded (KBr) on a Pye Unicam SP-1100 spectrophotometer. 'H NMR spectra were measured in DMSO on a Varian EM-360 spectrometer (60 MHz) using TMS as internal standard and chemical shifts are expressed as δ values. Microanalytical data (C, H, N) were obtained from the microanalytical data unit at Cairo University. MS were recorded on a Mass spectrometer MS 30 and MS 9 (AEI) 70 eV. $^{13}$C NMR were measured at TH Darmstadt.

Compounds 1, 2a–c and 3 were prepared following literature procedures [8, 9].

4-Aryl-2,6-diamino-4H-thiopyran-3,5-dicarbonitriles 5a–c

General procedure:

A suspension of 1 (0.01 mol) in absolute ethanol (50 mol) was treated with an equimolar amount of 2a–c (0.01 mol) and a catalytic amount of triethylamine (0.5 ml). The reaction mixture was warmed till a clear solution was obtained, then left at room temperature for 3 h. The solution was then poured into water. The solid product was collected by filtration and crystallized from ethanol.

2,6-Diamino-4-phenyl-4H-thiopyran-3,5-dicarbonitrile 5a formed colourless crystals from ethanol; m.p. 184 °C, yield 72%. IR: 3440, 3400, 3200 cm$^{-1}$ (two NH$_2$); 3020 cm$^{-1}$ (CH stretch); 2180 cm$^{-1}$ (CN) and 1650 cm$^{-1}$ (C=C; C=N and NH$_2$). $^1$H NMR: 4.23 (s, 1H, thiopyran H-4); 6.52 (s, 4H, two NH$_2$) and 7.4 (s, 5H, C$_6$H$_5$). $^{13}$C NMR: 43.5 (thiopyran C-4; $J$ = 133.6); 72.4 (thiopyran C-3 and C-5); 151.1 (thiopyran C-2 and C-6; $J$ = 5.4); 118.6 (cyanocarbons); 143.3 (phenyl C-1); 126.6 (phenyl C-2 and C-6); 127.0 (phenyl C-4) and 128.6 (phenyl C-3 and C-5).

C$_{13}$H$_{10}$N$_4$S (M.wt. = 254.3; M$^+$ = 254)
Calcd C 61.4 H 3.9 S 12.6,
Found C 61.6 H 3.9 S 12.3.

2.6-Diamino-4-p-methoxyphenyl-4H-thiopyran-3,5-dicarbonitrile 5b formed colourless crystals; m.p. 300 °C, yield 72%. IR: 3390, 3315, 3290 cm$^{-1}$ (two NH$_2$); 2980, 2940 cm$^{-1}$ (CH$_3$); 2230, 2220 cm$^{-1}$ (two CN) and 1650, 1640, 1610 cm$^{-1}$ (C=C; C=N and NH$_2$; not necessarily respectively). $^{13}$C NMR: 42.5 (thiopyran C-4; $J$ = 133.6); 72.6 (thiopyran C-3 and C-5); 150.8 (thiopyran C-2 and C-5; $J$ = 5.4); 55.0 (OCH$_3$; $q$, $J$ = 144.2); 114 (phenyl C-3 and C-5); 127.8 (phenyl C-2 and C-6); 128.3 (phenyl C-5); 158.3 (phenyl C-1).

C$_{14}$H$_{12}$N$_4$OS (M. wt. = 284.3; M$^+$ = 284)
Calcd C 59.1 H 4.2 S 11.3,
Found C 59.0 H 4.1 S 10.9.

2.6-Diamino-4-p-chlorophenyl-4H-thiopyran-3,5-dicarbonitrile 5c formed colourless crystals; m.p. 250–252 °C, yield 75%. IR: 3315, 3200 cm$^{-1}$ (two NH$_2$); 2215 cm$^{-1}$ (CN) and 1650–1620 cm$^{-1}$ (C=C and NH$_2$). $^{13}$C NMR: 151.2 (thiopyran C-2, C-6); 71.4 (thiopyran C-3 and C-5); 42.5 (thiopyran C-4);
118.7 (cyano carbons); 142.3 (phenyl C-1); 128.6 (phenyl C-2 and C-6); 128.5 (phenyl C-3 and C-5) and 131.6 (phenyl C-4).

\[ \text{C}_{13}\text{H}_{16}\text{N}_{4}\text{SCl} \]  
(M. wt. 288.8; M\(^+\) = 288; 290)  
Calcd C 54.0 H 3.1 S 11.1,  
Found C 54.0 H 3.0 S 11.0.

3,5-Dicyano-1,2-dihydro-6-hydroxy-2-thioxo-4-arylpyridines 8a–c

**Method A:**

To a solution of 6a–c (0.01 mol) in ethanol (30 ml) and water (2.0 ml) was added triethylamine (1.0 ml). The reaction mixture was refluxed for 8 h then left to cool. The solid product, separated on standing was collected by filtration and crystallized from ethanol.

**Method B:**

To a solution of 2d–f (0.01 mol) in absolute ethanol (50 ml) was added cyanothioacetamide 1 (0.01 mol) and 3 drops of triethylamine. The reaction mixture was refluxed for 2 h then left to cool. The solid product, so formed, on standing was separated by filtration and crystallized from ethanol.

3,5-Dicyano-1,2-dihydro-6-hydroxy-2-thioxo-4-phenyl-pyridine 8a formed yellow crystals; m.p. 159 °C, yield 68%. IR: 3420, 3280 cm\(^{-1}\) (NH); 2210 cm\(^{-1}\) (CN), 1660 (ring CO) and 1640–1650 (C = C and NH). 'H NMR: 3.28 (s, 1H, OH); 7.68 (s, 5H, C\(_6\)H\(_5\)) and 7.9 (s, 1H, NH). 13C NMR: 179.4 (pyridine C-2); 157.5 (pyridine C-6); 154.6 (pyridine C-4); 135.8 (phenyl C-1); 133.0 (phenyl C-2 and C-6); 130.6 (phenyl C-3 and C-5); 127.6 (phenyl C-4); 116.4, 114.5 (CN carbons); 102.2 (pyridine C-3) and 81.3 (pyridine C-5).

\[ \text{C}_{13}\text{H}_{7}\text{N}_{3}\text{O}_{2}\text{S} \]  
(M. wt. 253.3; M\(^+\) = 253)  
Calcd C 61.6 H 2.8 S 12.6,  
Found C 61.4 H 2.7 S 12.3.

3,5-Diamino-1,2-dihydro-6-hydroxy-2-thioxo-4-methoxyphenyl-pyridines 8b formed yellow crystals; m.p. 295–296 °C. IR: 3310, 3200 cm\(^{-1}\) (NH); 2980, 2960 cm\(^{-1}\) (CH\(_3\)); 1650–1625 cm\(^{-1}\) (ring CO and NH). 'H NMR: 3.49 (s, 1H, OH); 3.85 (s, 3H, CH\(_3\)) and 7.12–7.50 (m, 4H, C\(_4\)H\(_4\)) and 12.98 (s, 1H, NH). 13C NMR: 179.3 (pyridine C-2); 158.4 (pyridine C-6); 154.5 (pyridine C-4); 129.8 (phenyl C-1); 126.7 (phenyl C-2 and C-6); 116.6, 114.7 (cyano carbons); 113.9 (phenyl C-3 and C-5); 160.9 (phenyl C-4); 102.4 (pyridine C-3) and 55.3 (OCH\(_3\)).

\[ \text{C}_{14}\text{H}_{9}\text{N}_{3}\text{O}_{2}\text{S} \]  
(M. wt. 283.3; M\(^+\) = 283)  
Calcd C 59.3 H 3.2 S 11.3,  
Found C 59.0 H 3.2 S 11.2.

3,5-Dicyano-1,2-dihydro-6-hydroxy-2-thioxo-4-p-chlorophenyl-pyridine 8c formed yellow crystals from ethanol; yield 70%, m.p. 280–281 °C. IR: 3300, 3195 cm\(^{-1}\) (NH). 'H NMR: 3.49 (s, 1H, pyridine H-3); 7.57–7.73 (m, 4H, C\(_6\)H\(_4\)) and 13.08 (s, br, 1H, NH). 13C NMR: 179.3 (C-2); 157.5 (pyridine C-6); 154.4 (pyridine C-4); 135.2 (phenyl C-4); 129.9 (phenyl C-1); 128.7 (phenyl C-2); 128.7 (phenyl C-3 and C-5); 116.3 (phenyl C-4); 102.4 (pyridine C-3) and 81.4 (pyridine C-5).

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