

ACTIVATED NITRILES IN HETEROCYCLIC SYNTHESIS :

NOVEL SYNTHESIS OF THIOPYRANO[2,3-d]THIAZOLES

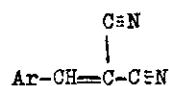
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Abstract - A novel synthesis of thiopyrano[2,3-d]thiazoles is reported via the reaction of arylmethylenemalononitriles with thiazolidin-2-one-4-thione and thiazolidin-2,4-dithione.

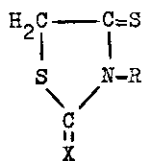
As a part of our interest for developing some new simple and efficient routes for the synthesis of fused thiazoles of probable biological activities,¹⁻³ we report here on the utility of the reaction of arylmethylenemalononitriles with thiazolidin-2-one-4-thione, its N-phenyl derivative and thiazolidin-2,4-dithione for the synthesis of thiopyrano[2,3-d]thiazoles. The work offers a potential new approach for the synthesis of such fused ring system.

The reaction between equimolecular amounts (20 mmol) of arylmethylenemalononitriles (1a,b) and/or thiazolidin-2-one-4-thione⁴ (2a), its 3-phenyl derivative⁵ (2b) or thiazolidin-2,4-dithione⁶ (2c), at room temperature in absolute ethanol (30 ml) in the presence of a few drops of triethylamine for 3 h, afforded colourless products (3a-f) which were crystallised from ethanol. The molecular formulae of these products correspond to addition of (1a,b) to each of (2a-c). Two alternative theoretically possible structures 3 and 4 were considered for the adducts. Structure 3 was assigned for the reaction products based on their ¹H NMR and IR spectra. The IR spectrum of 3a as a typical example for the adducts 3a-f showed the presence of ν_{NH} at 3220 cm⁻¹, a strong $\nu_{\text{C=N}}$ at 2240 cm⁻¹ and a strong $\nu_{\text{C=O}}$ at 1680 cm⁻¹. The ¹H NMR of 3a showed the signals at δ (ppm, CDCl₃) 9 (s, 1H, NH), 8 (s, 5H, Ph), 4.2 (d, 1H, H-C-C=S), 3.7 (t, 1H, Ar-CH-) and 2.7 (d, 1H, -CH-C=N). Furthermore, the adduct 3a was found to be identical (mp and mixed mp) with the product obtained by the reaction between equimolecular amounts (20 mmol) of malononitrile and 5-benzylidenethiazolidin-2-one-4-thione (5) in absolute ethanol in the presence of triethylamine at room



1a, Ar = C₆H₅

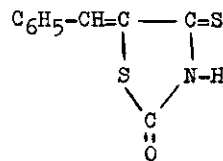
b, Ar = C₆H₄OCH₃-p



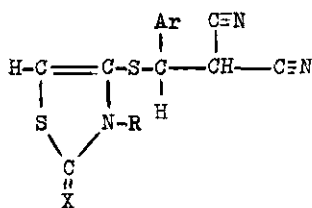
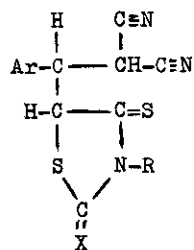
2a, R=H, X=O

b, R=C₆H₅, X=O

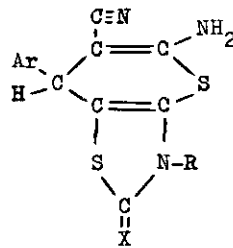
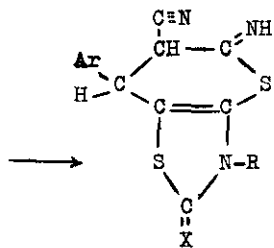
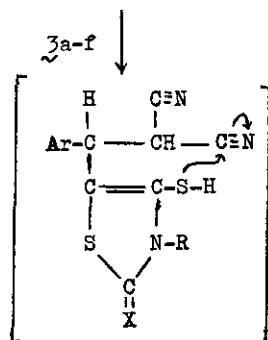
c, R=H, X=S



5



4



6a-f

List for 5[Aryl(dicyanomethyl)methyl]-1,3-thiazolidin-2,4-dione derivatives (3a-f) and thiopyrano[2,3-d]thiazole derivatives (6a-f).

Compd.*	Ar	R	X	M.P. (°C)	Yield (%)	Compd.*	Ar	R	X	M.P. (°C)	Yield (%)
3a	C ₆ H ₅	H	O	195	70	6a	C ₆ H ₅	H	O	275	55
3b	C ₆ H ₄ OCH ₃ -p	H	O	199	76	6b	C ₆ H ₄ OCH ₃ -p	H	O	260	50
3c	C ₆ H ₅	C ₆ H ₅	O	184	68	6c	C ₆ H ₅	C ₆ H ₅	O	260	60
3d	C ₆ H ₄ OCH ₃ -p	C ₆ H ₅	O	197	75	6d	C ₆ H ₄ OCH ₃ -p	C ₆ H ₅	O	272	52
3e	C ₆ H ₅	H	S	205	65	6e	C ₆ H ₅	H	S	230	52
3f	C ₆ H ₄ OCH ₃ -p	H	S	190	72	6f	C ₆ H ₄ OCH ₃ -p	H	S	245	55

*Satisfactory elemental analyses for the newly synthesised compounds were obtained.

temperature. When the reaction between arylmethylenemalononitriles (1a,b) and the thiazolidinone derivatives (2a-c) was carried out in refluxing absolute ethanol in the presence of a few drops of triethylamine for 1h, 1:1 adducts were obtained. Structure (6a-f) or its tautomer was assigned for these adducts based on ^1H NMR and IR data. The IR spectrum of 6a as a typical example for (6a-f) showed the presence of a strong ν_{NH_2} at 3420, 3320 cm^{-1} , ring ν_{NH} at 3200 cm^{-1} , strong $\nu_{\text{C}\equiv\text{N}}$ at 2220 cm^{-1} , ring $\nu_{\text{C}=\text{O}}$ at 1650 cm^{-1} and a strong $\nu_{\text{C}=\text{C}}$ at 1610 cm^{-1} . The ^1H NMR spectrum of 6a revealed the presence of a low field absorption for NH_2 at δ (ppm, CDCl_3) 11.2 (b, 2H, NH_2), due to the anisotropy of the $\text{C}=\text{C}$ group, 8.1 (s, 1H, NH), 7.7 (s, 5H, Ph) and 3.8 (s, 1H, $\text{Ar}-\text{CH}-$). Besides, refluxing the products (3a-f) in absolute ethanol containing a few drops of triethylamine for 1h afforded (6a-f) respectively. The formation of the adducts 6 is assumed to proceed via initial Michael addition to yield acyclic adducts 3 which when heated in refluxing ethanol in the presence of triethylamine cyclised via the attack of the mercapto group on the cyano group affording the cyclic products 6.

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