SYNTHESIS OF HETEROCYCLIC COMPOUNDS XXXV[1]

THIOPYRIDONES FROM α-BENZOYLCINNAMONITRILES

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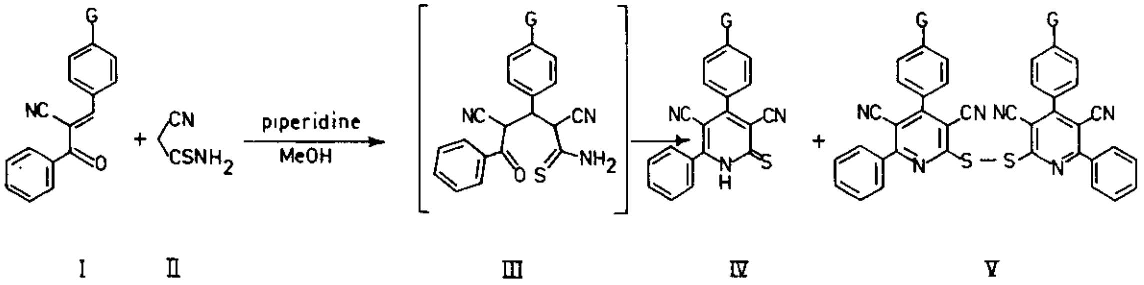
Abstract- 2-Pyridothiones (IV) are obtained from the reaction of α-benzoylcinnamonitriles (I) with cyanothioacetamide (II). Disulphides V result as well from the reaction. Transformation of IV into V and of V into IV, as well as methylation of IV and their hydrolytic conversion into pyridones VI are also described. Pyridones VI can also be obtained from methylthiopyridines VIII.

In a previous paper published in this journal[2], the synthesis of 4,6-diaryl-3,5-dicyano-2-pyridones from α-benzoylcinnamonitriles was described. We now report the results obtained when α-benzoylcinnamonitriles (I)[3] were used as starting materials for the preparation of thiopyridones, using cyanothioacetamide as the other reactant. The reaction of cyanothioacetamide (II) with I is very simple to carry out in alcoholic solution at room temperature and in the presence of a catalytic amount of piperidine as a basic catalyst. In these conditions, the spontaneous cyclization of the adduct (III) resulting from the conjugated addition of cyanothioacetamide (II)[4] to the double bond of I leads to a 2-pyridothione ring (IV) which is obtained from the reaction together with its oxidative dimerization product, bis-pyridyl disulphide V (Scheme I).



SCHEME I

The fact that the heterocyclic ring is obtained in a fully aromatized state is in contrast with the results obtained in the reaction of cyanoacetamide (VII) (see Scheme II) with α-benzoylcinnamonitriles. In this reaction[2], the nitrogen ring is isolated as a fully saturated piperidone and the final pyridones have to be prepared from it by means of dehydration and dehydrogenation.

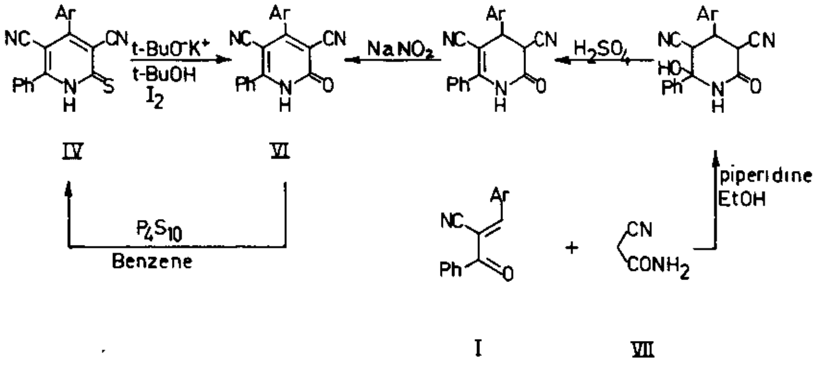
Compounds IV and V can be isolated from the reaction mixture by means of column chromatography on silica gel, but the reaction can also be compelled to yield only either IV or V. If the reaction mixture is treated with 2-hydroxyethanethiol, the thiopyridone IV is the only product isolated. Using this method, the yields are as indicated in table I. The compounds IV thus obtained, in which the thiocarbonyl tautomer is expected to be the main one[5,6], show the NH stretching bands at 3300-2700 cm^{-1}, together with the band due to the thiocarbonyl group at 1190-1200 cm^{-1}. On the other hand, the addition of iodine-potassium iodide to the mixture leads to disulphides V as the only products (Table I).

TABLE I[*]

		IV		V		VI		VIII	
	G	M.P.(°C)	Yield (%)	M.P.(°C)	Yield (%)	M.P.(°C)	Yield (%)	M.P.(°C)	Yield (%)
a	H	250-2 (Ethanol)	50	246-8 (Acetone)	46	262-3 (lit 262)[7] (Et.acetate)	92	151-2 (Ethanol)	47
b	CH_3	250-1 (Ethanol)	66	226-8 (Acetic a.)	55	309 (lit 308-10)[7] (Acetone)	67	222-3 (Ethanol)	54
c	CH_3O	246-8 (Ethanol)	56	244 (Acetone)	39	325-6(lit 325-6)[7] (Et. acetate)	90	210-11 (Ethanol)	51
d	Cl	250-1 (Ethanol)	46	258-60 (Acetone)	40	337-8(lit 337-8)[7] (Methanol)	90	275-7 (Ethanol)	59
e	NO_2	204-6 (Ethanol)	27	296-8 (Acetone)	26			284-6 (Ethanol)	30

[*] All melting points were determined in capillary and are uncorrected. Satisfactory analytical and mass spectral data were obtained for the new compounds.

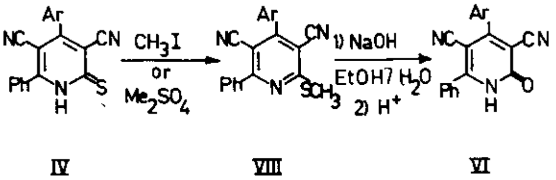
Treatment of thiopyridones IV with potassium tert-butoxide in the presence of iodine brings about the transformation of the thiocarbonyl group into a carbonyl group and pyridones VI are formed. These compounds are identical with the pyridones obtained from the reaction of cyanoacetamide (VII) with α-benzoylcinnamonitriles (I), followed by dehydration and aromatization (Scheme II)[2], and from a recently reported ring transformation of 4,6-diaryl-3,5-dicyano-2-amino-4H-pyrans[7].



SCHEME II

The reverse transformation, VI into IV, can also be achieved by using phosphorus pentasulphide, according to a recently reported procedure[8], but the reaction yield is only moderate and an equilibrium is achieved in which some starting material is still present.

Methylation of thiopyridones IV with either methyl iodide or dimethyl sulphate affords methylthiopyridines VIII (Scheme III), all of which show the methyl group as a sharp singlet at 2.70-2.75 ppm in the NMR spectra. The yields shown (Table I) are those obtained when methyl iodide is used as the methylation reagent. Similar results are obtained with dimethyl sulphate.



SCHEME III

Basic hydrolysis of methylthiopyridines VIII with sodium hydroxide in aqueous ethanol yields pyridones VI in almost quantitative yield.

Work in progress indicates that these syntheses can also be applied to different kinds of unsaturated ketones, other than α-benzoylcinnamononitriles and that thiopyridones IV can be used in the preparation of bicyclic ring systems.

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REFERENCES

1. Previous paper in this series: J.L. Soto, C. Seoane, N. Martín and L. A. Blanco, *Heterocycles*, accepted for publication.
2. C. Seoane, J. L. Soto, and M.P. Zamorano, *Heterocycles*, 1980, **14**, 639.
3. H. Kaufman, *Ber.*, 1917, **50**, 5150; M. Quinteiro, C. Seoane and J.L. Soto, *J. Heterocyclic Chem.*, 1978, **15**, 57; D. Drapkina, V. Brudz and B. Bolotin, Tr. Vses. Nauch.- Isled Inst. Khim. Reactivou Osobo Chist. Khim. Vesehehestr., 1967, Nº 30, 333. *Chem. Abstr.*, 1968, **69**, 6727p.
4. E. Howarol, A. Kotch, R. V. Lindsey, and R.E. Putnam, *J. Am. Chem. Soc.*, 1958, **80**, 3924.
5. A.R. Katritzky and J.M. Lagowsky, *Adv. Heterocyclic Chem.*, 1962, **1**, 131.
6. J. Elguero, C. Marzin, A.R. Katritzky and P. Linda. "The Tautomerism of Heterocycles", Academic Press, 1976.
7. C. Seoane, J.L. Soto, M.P. Zamorano, and M. Quinteiro, *J. Heterocyclic Chem.*, 1981, **18**, 309.
8. J. S. Davies, K. Smith, and J. Turner, *Tetrahedron Letters*, 1980, **21**, 2191.

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