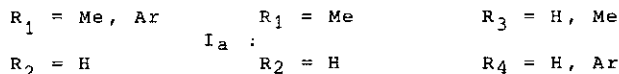
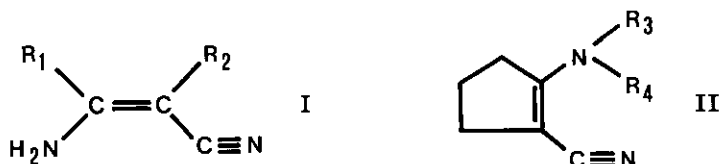


2,6-DIMETHYL-3-CYANO-4-THIOXOTHIOPYRAN AND RELATED MOLECULES FROM ENAMINONITRILES AND HYDROGEN SULFIDE BY PHASE TRANSFER CATALYSIS

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**Abstract** - 3-Aminocrotononitrile reacts with H<sub>2</sub>S in the presence of a phase transfer catalyst to yield 2,6-dimethyl-3-cyano-4-thioxothiopyran (liquid-solid catalysis) or the 4-oxo homolog (liquid-liquid catalysis). In the absence of hydrogen sulfide, 2,6-dimethyl-3-cyano-4-pyrone is obtained. The reaction mechanism is discussed.

Nitriles-thioamides conversion is usually observed in good yields when hydrogen sulfide is passed through a refluxing alcoholic solution of the substrate. The reaction is base-catalysed<sup>1-4</sup>. In connection with the general study of enamino-nitriles corresponding to structures (I) or (II)<sup>5-7</sup> we attempted to prepare the corresponding thioamides. When treated under such conditions, 3-aminocrotononitrile (Ia) afforded the thioamide in high-yield (70%)<sup>8-10</sup>.



The others compounds did not react successfully, but high-melting, sparingly soluble by-products are formed. We then tried the method described by Cassar<sup>11</sup>, which proceeds via phase-transfer catalysis; thioamides were obtained in good yields (15-75%)<sup>12</sup>. However, compound (Ia) showed, when treated by hydrogen sulfide in the presence of a tetraalkyl ammonium salt, a very unexpected reactivity which is the matter of the present note.

3-Aminocrotononitrile reactivity

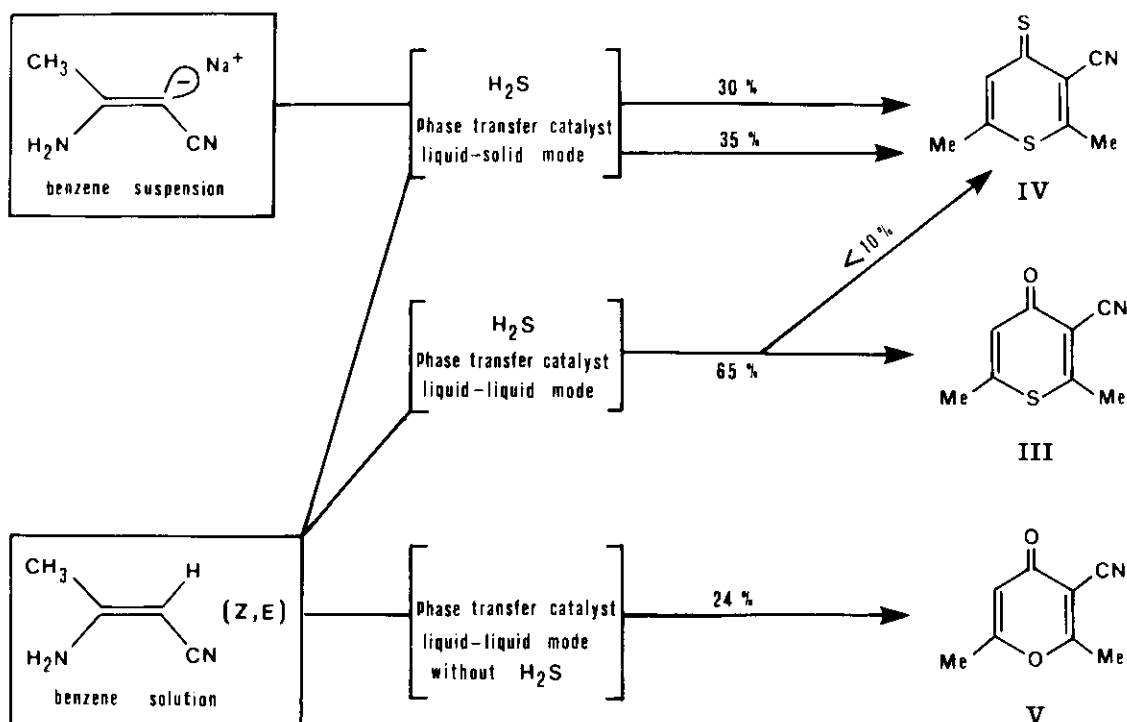
a) The nitrile (Ia), in benzene solution, is allowed to react with hydrogen sulfide, in the presence of an alkaline solution of sodium sulfide and a phase transfer catalyst (liquid-liquid catalysis). The major product (65%) is the 2,6-dimethyl-3-cyano-4-oxothiopyran (III) and a small amount of the 4-sulfurized analog (IV) is formed.

b) If the organic layer is in contact with solid sodium hydroxide and sodium sulfide (when aqueous phase is absent), the only product obtained is the 2,6-dimethyl-3-cyano-4-thioxothiopyran (IV), 35% yield.

c) By liquid-liquid catalysis, but without hydrogen sulfide stream, the 2,6-dimethyl-3-cyano-4-pyrone (V) is formed in lower yield (24%).

d) Likewise, we treated under liquid-liquid phase transfer catalysis a benzene suspension of the sodium salt of (Ia) (which is a precursor in 3-aminocrotononitrile synthesis<sup>6</sup>). 4-Thioxothiopyran (IV) is obtained as from (Ia), in equivalent yield.

Scheme 1 outlines the above experimental results.

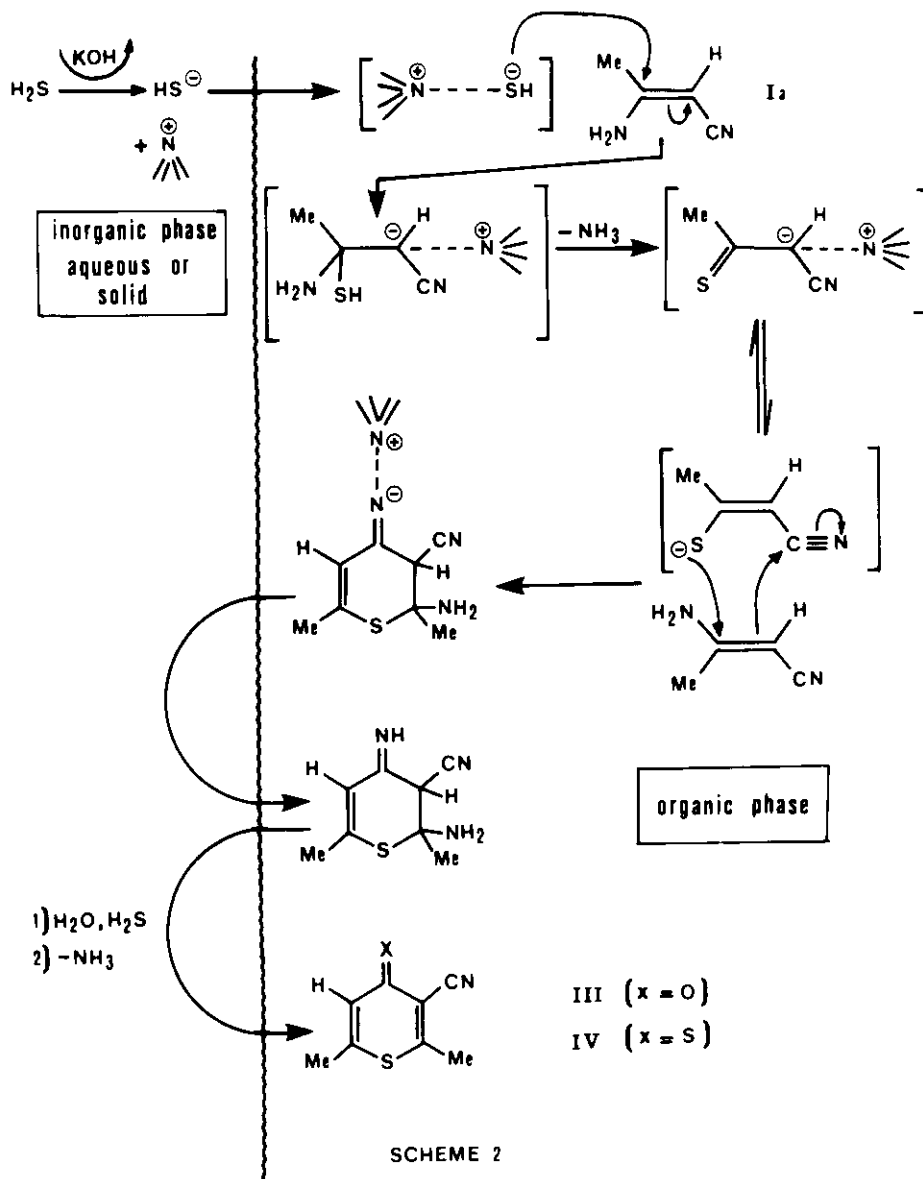


SCHEME 1

In scheme 2 we suggest a reaction mechanism which involves the participation of the two electrophilic centers of (Ia) during the cyclisation step.

When reaction occurs by phase transfer catalysis, it seems that the "hard" center C<sub>3</sub> is more easily attacked by the "bare" ion than the functional carbon C<sub>1</sub> of the nitrile group.

Nevertheless, this behaviour is not observed when R<sub>1</sub> is a phenyl group; as a result of steric and electronic effects, the sulfhydryl ion attacks in C<sub>1</sub>, and 3-aminocinnamionitrile leads to the corresponding thioamide, using the above conditions<sup>13</sup>.



## EXPERIMENTAL

Melting points were measured on a Büchi oil-bath apparatus. Elementary analysis were performed by the microanalytical service of St-Jérôme, Marseille. Infrared spectra were run on a Perkin-Elmer 457 Spectrophotometer. Nmr spectra were recorded on a Bruker CW 80 at 80 MHz. Resonances are quoted in  $\delta$  units, added tetramethylsilane was the internal reference standard.

#### Synthesis of 2,6-dimethyl-3-cyano-4-oxothiopyran (Compound III)

A solution of nitrile (Ia) (100 mmoles) in benzene (150 ml) is added to an aqueous solution (50 ml) of 50 mmoles of Na<sub>2</sub>S, 2 mmoles of KOH and 25 mmoles of catalyst (tBu)<sub>4</sub>N<sup>+</sup>X<sup>-</sup> (X = Br, CN). The heterogenous mixture is stirred under hydrogen sulfide stream (temperature 25°C, reaction time 48 h). The 2,6-dimethyl-3-cyano-4-oxothiopyran crystallizes on cooling after partial solvent evaporation (yield : 65%), mp 134°C; ir (KBr): 2220 (CN) ; 1655 (C=O) ; 1590 (C=C) ; 680 (C-S-C). <sup>1</sup>H-nmr (CDCl<sub>3</sub>): 6.4 (s, 1H, CH=C) ; 2.7 (s, 3H, -CH<sub>3</sub>) ; 2.4 (s, 3H, -CH<sub>3</sub>). Anal. Calcd. for C<sub>8</sub>H<sub>7</sub>NOS (165) : C 58.18 ; H 4.24 ; N 8.48 ; S 19.39 ; found : C 57.01 ; H 4.55 ; N 9.23 ; S 20.66.

#### Synthesis of 2,6-dimethyl-3-cyano-4-thioxothiopyran (compound IV)

The same procedure, carried out without aqueous layer, leads to 2,6-dimethyl-3-cyano-4-thioxothiopyran. Hydrogen sulfide, bubbled through a benzene suspension of the sodium salt (CH<sub>3</sub>(NH<sub>2</sub>)C=C-CN)<sup>-</sup>Na<sup>+</sup>, (100 mmoles, 150 ml), under identical conditions gives the same compound (IV), but in lower yield (30%). mp 150°C; ir (KBr): 2210 (CN) ; 1585 (C=C) ; 1380 (C=S) ; 695 (C-S-C). <sup>1</sup>H-nmr (CDCl<sub>3</sub>): 7.3 (s, 1H, CH=C) ; 2.6 (s, 3H, -CH<sub>3</sub>) ; 2.3 (s, 3H, -CH<sub>3</sub>). Anal. Calcd. for C<sub>8</sub>H<sub>7</sub>NS<sub>2</sub> (181) : C 53.03 ; H 3.86 ; N 7.73 ; S 35.35 ; found : C 54.07 ; H 4.10 ; N 8.05 ; S 33.50.

#### III⇌IV interconversion

A solution of compound (III) (1 g) in benzene (50 ml) is heated for 12 h under vigorous stirring, with an excess of P<sub>4</sub>S<sub>10</sub>. Thin-layer chromatography of the mixture shows that compound (III) disappears ; at the same time, a spot with the same R<sub>f</sub> value as a mark sample of compound (IV) appears. Tlc analysis of compound (IV) solved in acetone-water (95-5) mixture, shows that after a few hours compound (IV) disappears ; a new spot appears which has the same R<sub>f</sub> value as compound (III). This compound is crystallized by partial evaporation of the solvents (ir and <sup>1</sup>H-nmr data are in accordance with structure (III)).

#### Synthesis of 2,6-dimethyl-3-cyano-4-pyrone (compound V)

This compound is likewise obtained by the same procedure followed for the formation of compounds (III) and (IV), but without hydrogen sulfide.

Yield 24%, mp 148°C, ir (KBr): 2210 (CN) ; 1660 (C=O) ; 1565 (C=C) ; 1250 (=C-O-C=). <sup>1</sup>H-nmr (DMSO d<sub>6</sub>): 6.12 (s, 1H, -CH=C) ; 2.38 (s, 3H, -CH<sub>3</sub>) ; 2.2 (s, 3H, -CH<sub>3</sub>). Anal. Calcd. for C<sub>8</sub>H<sub>7</sub>NO<sub>2</sub> (149): C 64.42 ; H 4.69 ; N 9.39 ; O 21.47 ; found : C 63.30 ; H 4.83 ; N 10.21 ; O 21.92.

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