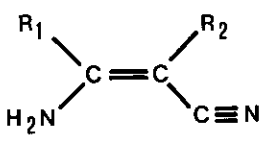
2,6-DIMETHYL-3-CYANO-4-THIOXOTHIOPYRAN AND RELATED MOLECULES FROM ENAMINONITRILES AND HYDROGEN SULFIDE BY PHASE TRANSFER CATALYSIS

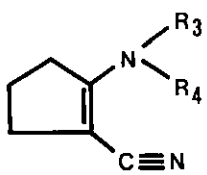
Jean-Pierre Roggero*, Serge Coen, Bernard Ragonnet, and
Catherine Vieillescazes
Faculté des Sciences, Laboratoire de Chimie Organique,
33, rue Louis Pasteur, 84000 - Avignon, France

Abstract - 3-Aminocrotononitrile reacts with H_2S 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[1-4]. In connection with the general study of enamino-nitriles corresponding to structures (I) or (II)[5-7] we attempted to prepare the corresponding thioamides. When treated under such conditions, 3-amino-crotononitrile (Ia) afforded the thioamide in high-yield (70%)[8-10].



I



II

R_1 = Me, Ar; R_2 = H

Ia : R_1 = Me; R_2 = H; R_3 = H, Me; R_4 = H, Ar

The others compounds did not react successfully, but high-melting, sparingly soluble by-products are formed. We then tried the method described by Cassar[11], which proceeds via phase-transfer catalysis ; thioamides were obtained in good yields (15-75%)[12]. 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

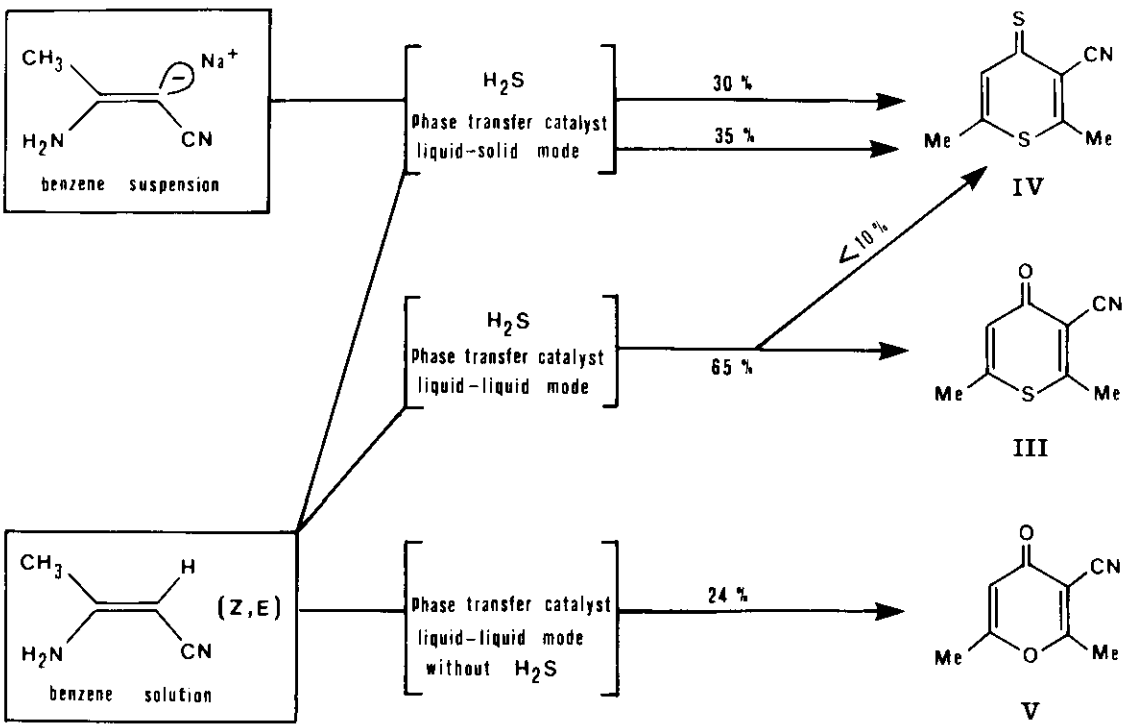
a) The nitrile (Ia), in benzene solution, is allowed to react with hydrogen sulfide, in the presence of an alkaline solution of sodium sulfide and a phase transfer catalyst (liquid-liquid catalysis). The major product (65%) is the 2,6-dimethyl-3-cyano-4-oxothiopyran (III) and a small amount of the 4-sulfurized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

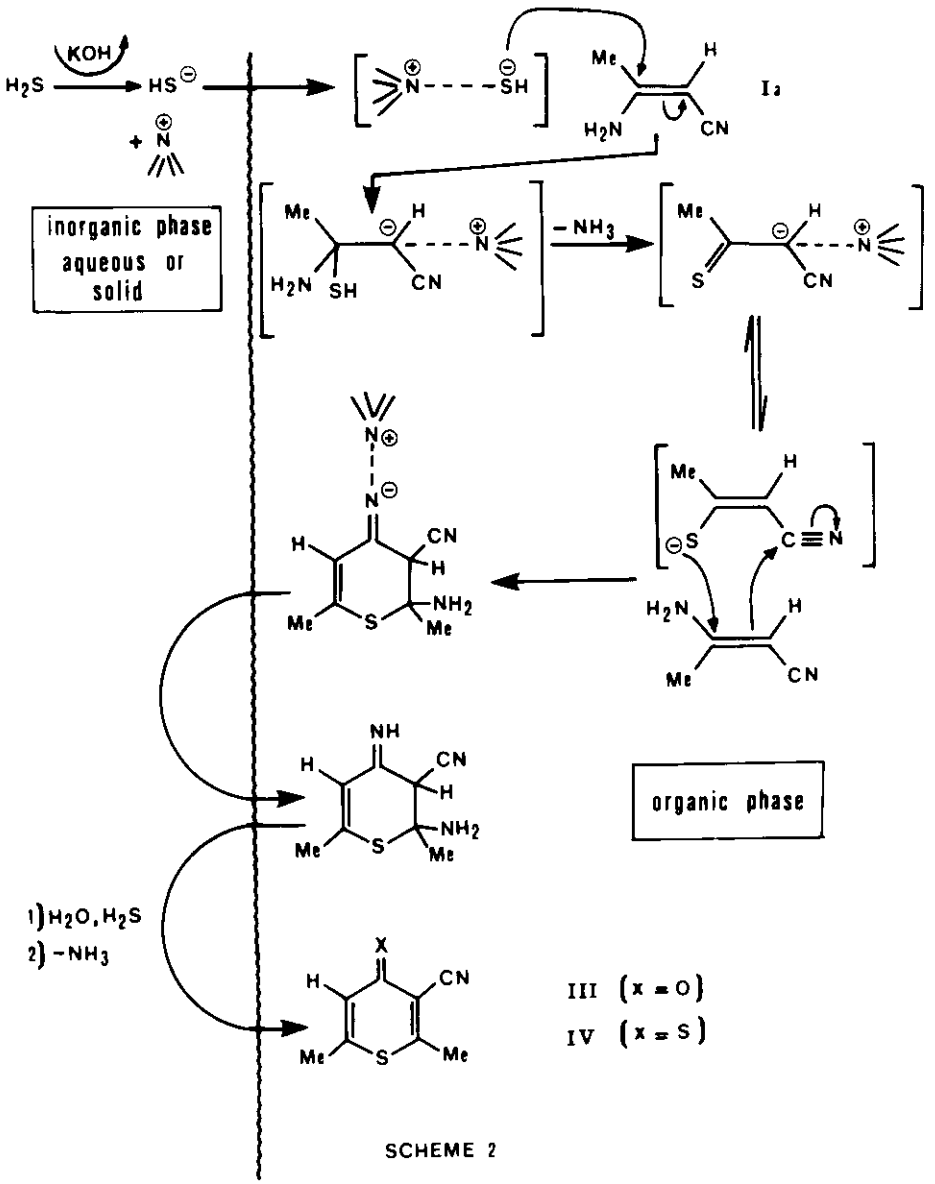
Scheme 1 outlines the above experimental results.



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_3 is more easily attacked by the "bare" ion than the functional carbon C_1 of the nitrile group. Nevertheless, this behaviour is not observed when R_1 is a phenyl group ; as a result of steric and electronic effects, the sulfhydric ion attacks in C_1, and 3-aminocinnamonitrile leads to the corresponding thioamide, using the above conditions[13].



SCHEME 2

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 δ 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_2S, 2 mmoles of KOH and 25 mmoles of catalyst $(tBu)_4N^+X^-$ (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). ^{1}H-nmr ($CDCl_3$): 6.4 (s, 1H, CH-C) ; 2.7 (s, 3H, $-CH_3$) ; 2.4 (s, 3H, $-CH_3$). Anal. Calcd. for C_8H_7NOS (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 $(CH_3(NH_2)C=C-CN)^-Na^+$, (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). ^{1}H-nmr ($CDCl_3$): 7.3 (s, 1H, CH=C) ; 2.6 (s, 3H, $-CH_3$); 2.3 (s, 3H, $-CH_3$). Anal. Calcd. for $C_8H_7NS_2$ (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 vigourous stirring, with an excess of P_4S_{10}. Thin-layer chromatography of the mixture shows that compound (III) disappears ; at the same time, a spot with the same Rf 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 Rf value as compound (III). This compound is crystallized by partial evaporation of the solvents (ir and ^{1}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=). ^{1}H-nmr (DMSO D^6): 6.12 (s, 1H, -CH=C) ; 2.38 (s, 3H, $-CH_3$) ; 2.2 (s, 3H, $-CH_3$). Anal. Calcd. for $C_8H_7NO_2$ (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.

REFERENCES

1. W. Walter and K.D. Bode, Angew. Chem., 1966, 78, 517. Angew Chem., Int. Ed. Eng. 1966, 5, 447.
2. E.E. Reid, "Organic Chemistry of bivalent sulfur", vol. 4, Chemical Publishing Co., New York, 1962.
3. W. Walter, J. Voss and S. Patai, "The Chemistry of amides", J. Zabicky, Ed. Interscience, London, 1970, 383-475.
4. A.E. Fairfull, J.L. Lowe and D.A. Peak, J. Chem. Soc., 1952, 743.
5. C. Vieillescazes, Thèse de Spécialité, Avignon, France, 1983.
6. J.J. Conn and A. Taurins, Can. J. Chem., 1953, 31, 1211.
7. S. Coen, unpublished results.
8. J.C. Poite, D.E.S. Marseille, France, 1965.
9. A. Adams and R. Slack, J. Chem. Soc., 1959, 613, 3061.

10. J. Coerdeler and H.W. Pohland, Chem. Ber., 1961, II, 2950.
11. L. Cassar, S. Panossian and C. Giordano, Synthesis, 1978, 12, 917.
12. S. Coen, personal communication, VII^{e} Int. Conf. on Het. Chem., Marseille, France, 1981.
13. D. Landini and F. Rolla, Synthesis, 1974, 565.

Received, 25th September, 1984