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 H₂S 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. In connection with the general study of enamino-nitriles corresponding to structures (I) or (II), we attempted to prepare the corresponding thioamides. When treated under such conditions, 3-aminocrotononitrile (Ia) afforded the thioamide in high-yield (70%)

The others compounds did not react successfully, but high-melting, sparingly soluble by-products are formed. We then tried the method described by Cassar, which proceeds via phase-transfer catalysis; thioamides were obtained in good yields (15-75%). 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 synthesis6). 4-Thioxothiopyran (IV) is obtained as from (Ia), in equivalent yield.

Scheme 1 outlines the above experimental results.

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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 C3 is more easily attacked by the "bare" ion than the functional carbon C1 of the nitrile group.

Nevertheless, this behaviour is not observed when R1 is a phenyl group; as a result of steric and electronic effects, the sulfhydric ion attacks in C1, and 3-aminocinnamnitrile leads to the corresponding thioamide, using the above conditions13.
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 tetramethysilane was the internal reference standard.
Synthesis of 2,6-dimethyl-3-cyano-4-oxothiopyran (compound III)

A solution of nitrile (1a) (100 moles) in benzene (150 ml) is added to an aqueous solution (50 ml) of 50 moles of Na2S, 2 moles of KOH and 25 moles of catalyst (Bu3N)4H+X- (X = Br, CN). The heterogeneous 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): 2210 (CN); 1655 (C=O); 1590 (C=C); 680 (C-S-C). 1H-nmr (CDCl3): 6.4 (s, 1H, CH=C); 2.7 (s, 3H, CH3); 2.4 (s, 3H, -CH3). Anal. Calcld. for C8H7NS2: C 54.07; H 3.86; N 10.21. Found: C 54.07; H 4.10; N 9.23.

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 (CH3(NH2)C=C-CN)2Na+, (100 moles, 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). 1H-nmr (CDCl3): 7.3 (s, 1H, CH=C); 2.6 (s, 3H, -CH3); 2.3 (s, 3H, -CH3). Anal. Calcld. for C8H7NS2: C 50.3; 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 P4S10. 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 1H-nmr data are in accordance with structure (III)).

Synthesis of 2,6-dimethyl-3-cyano-4-pyrrone (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=O). 1H-nmr (DMSO d6): 6.12 (s, 1H, -CH=C); 2.38 (s, 3H, -CH3); 2.2 (s, 3H, -CH3). Anal. Calcld. for C8H7NO2: C 64.42; H 4.69; N 9.39. Found: C 63.30; H 4.83; N 10.21.

REFERENCES

7. S. Coen, unpublished results.

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