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PREPARATION OF 1-SUBSTITUTED-3-FORMYL-2(1H)-PYRIDINETHIONES.

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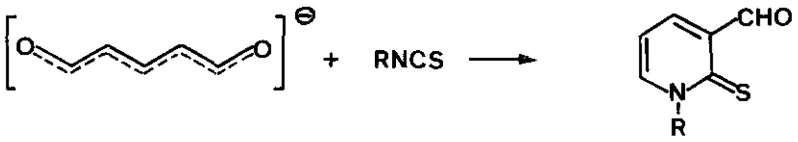
Ring closure reactions of glutacondialdehyde derivatives have been reported[1]. In this paper we report the synthesis of 1-substituted-3-formyl-2(1H)-pyridinethiones 2 from the glutacondialdehyde anion[2] 1 and isothiocyanates:

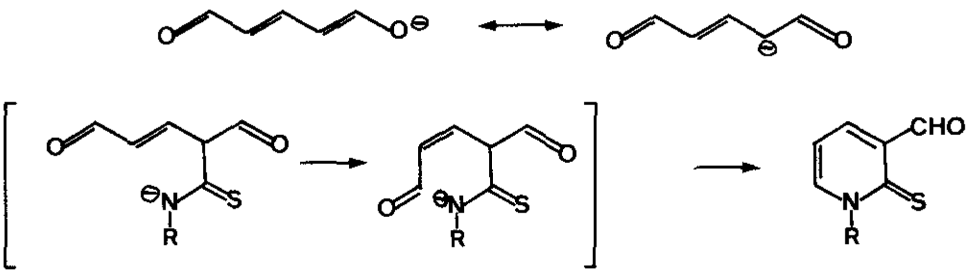


1 2

	R	yield	m.p.		R	yield	m.p.
2a	methyl	58 %	126-8°	2d	phenyl	95 %	180-2°
2b	cyclohexyl	98 %	152-4°	2e	2',6'-dimethylphenyl	79 %	190-2°
2c	*tert*-butyl	38 %	86-7°	2f	2'-naphthyl	94 %	195-6°

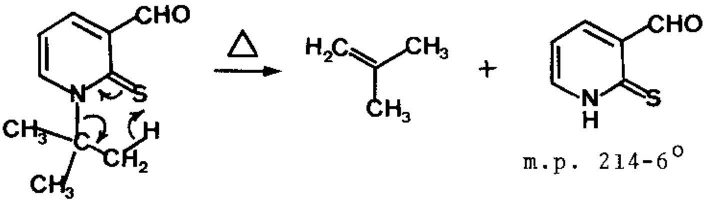
Scheme 1

Due to the low solubility of the glutacondialdehyde anion (sodium or potassium[3] salt) in organic solvents of low polarity, the reactions were run in DMF or DMSO. In the aromatic series the exothermic reactions took place at room temperature, whereas an elevated temperature (ca. 80°C) was necessary to complete the reactions in the aliphatic series.



Scheme 2

The reaction course can be understood on basis of the principle of hard and soft acids and bases (HSAB). In the ambident anion, 1, the carbanion center (C(2)) is a softer base than the oxygen anion center (RO^-, Scheme 2). The thiocarbonyl carbon atom is a soft acid. Consequently, the HSAB principle predicts the reaction to take place at C(2). The subsequent cyclization forming the stable 1-substituted-3-formyl- 2(1H)-pyridinethiones is expectable.



2c 3

Attempts to prepare 3-formyl-2(1H)-pyridinethione, 3, from 1 and reagents such as $(SCN)_2$ and HSCN were unsuccessful. However, 3 was isolated in quantitative yield by thermolyses (ca. 190°C/1atm.) of 2c. Thermal syn-elimination of alkenes from corresponding structural arrangements are well known (e.g. Chugaev reaction).

3-Formyl-2(1H)-pyridinethione may exist in two tautomeric forms. By comparing the UV spectrum of the reaction product with the spectrum of 1-methyl-3-formyl-2(1H)-pyridinethione it can be concluded that the same chromophore is present in both compounds, and consequently, the thioamide form is the principal one. This conclusion is in accordance with results reported for other α- and γ-thionoaza-aromatic compounds.[6]

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