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A NEW SYNTHESIS OF 3,4-DIAMINOTHIOPHENES

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3,4-Diaminothiophenes were synthesized by the cleavage of pyridine ring in 3-aminothien-4-yl-pyridinium iodides, which were prepared by the reaction of 1-cyanomethylpyridinium chloride with carbon disulfide and alkylating agents in the presence of alkali, followed by the base-catalyzed interamolecular cyclization.

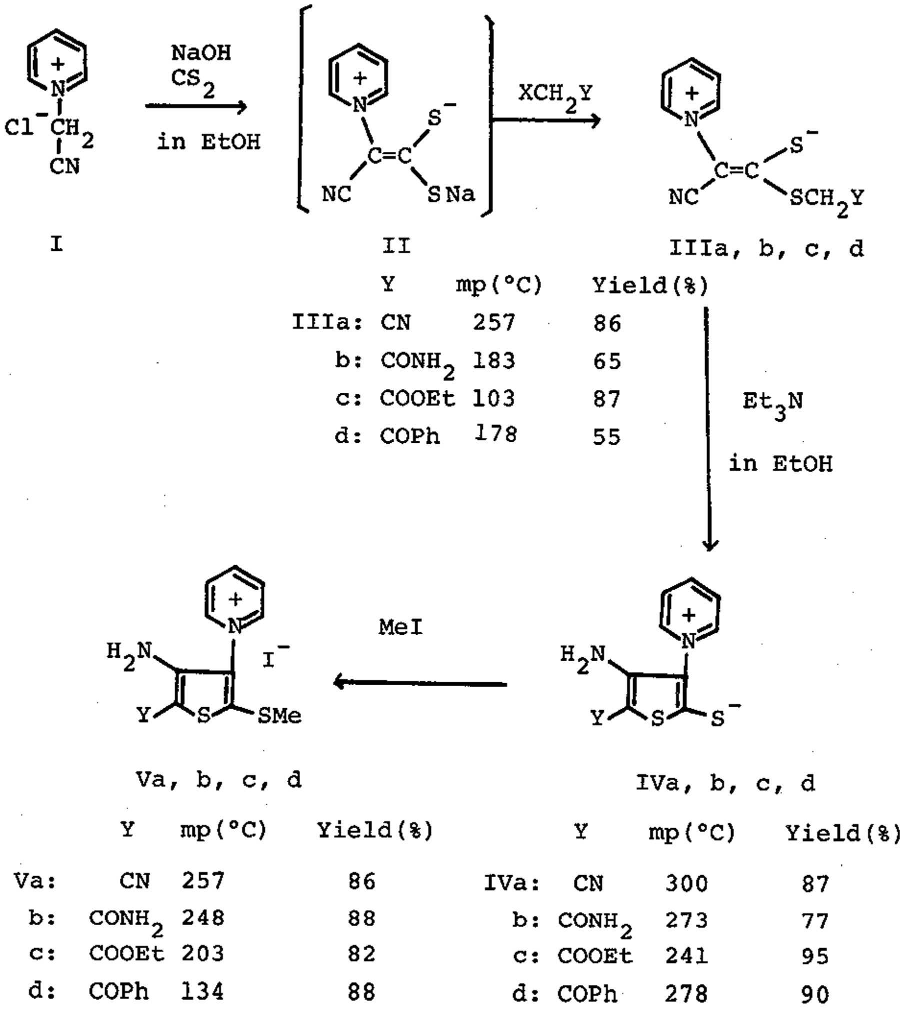
The reaction of 3,4-diaminothiophenes with 1,2-dicarbonyl derivatives gave thieno[3,4-b]pyrazines in a good yield.

Aromatic *o*-diamines are very useful compounds as a synthetic intermediate.¹⁾ Their versatility as synthetic intermediates is principally base on the fact that they may be easily transformed into a variety of condensed heterocyclic systems.

In our present paper, we report the synthesis of heterocyclic diamines, 3,4-diaminothiophenes, by using the ring opening reaction of pyridine ring in 3-aminothien-4-ylpyridinium iodides. Generally, 3,4-diaminothiophenes are obtained by the reaction of 3,4-dinitrothiophenes and they are very labile.(2) Gompper(3) reported the synthesis of thiophenes using ketene dithioacetals as an intermediate. We have recently reported that the reaction of pyridinium ylides with carbon disulfide afforded various stable pyridinium ylides containing (methylthio)thiocarbonyl group in a good yield.(4) We applied the Gompper and our own methods(3,4) to the synthesis of 3-aminothien-4-ylpyridinium salts.

Condensaton of 1-cyanomethylpyridinium chloride (I) with carbon disulfide in the presence of sodium hydroxide in ethanol yielded a sodium salt of the dithiocarboxylate (II) which reacted with 1 mol equivalent of chloroacetonitrile to give IIIa. This compound underwent a Thorpe-Ziegler cyclization by refluxing in the presence of triethylamine in ethanol to give 4-amino-5-cyano-3-(1-pyridinio)thiophene-2-thiolate (IVa) in 85% yield.

Similarly, treatment of II with other alkylating agents (α-chloroacetamide, ethyl α-bromoacetate, α-bromoacetophenone) produced the dithiocarboxylates (IIIb, c, d) which underwent the Thorpe-Ziegler type cyclization to give thiophene derivatives (IVb, c, d) in a good yield. Compounds IVa, b, c, d were easily methylated with methyl iodide to yield the pyridinium salts (Va, b, c, d) in a good yield.



I

II

IIIa, b, c, d

	Y	mp(°C)	Yield(%)
IIIa:	CN	257	86
b:	$CONH_2$	183	65
c:	COOEt	103	87
d:	COPh	178	55

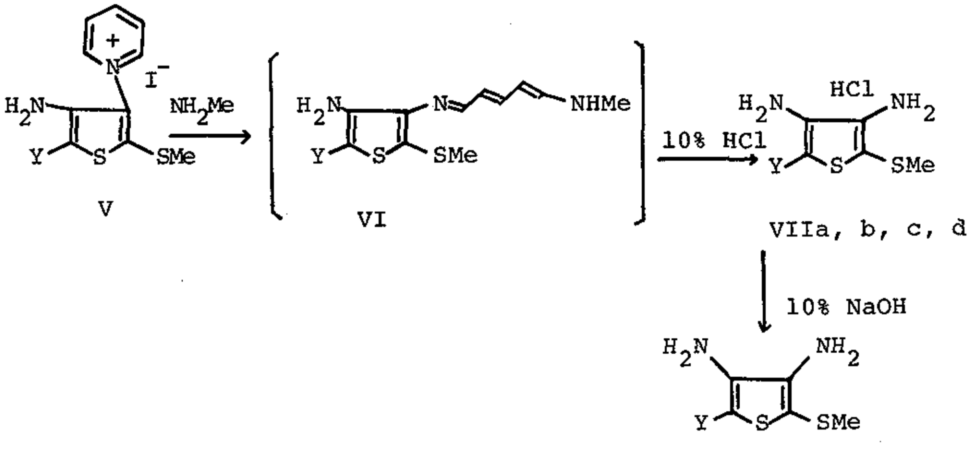
IVa, b, c, d

	Y	mp(°C)	Yield(%)
IVa:	CN	300	87
b:	$CONH_2$	273	77
c:	COOEt	241	95
d:	COPh	278	90

Va, b, c, d

	Y	mp(°C)	Yield(%)
Va:	CN	257	86
b:	$CONH_2$	248	88
c:	COOEt	203	82
d:	COPh	134	88

A number of opening reactions of pyridine ring by amines have been reported.[5] We also examined the synthesis of 3,4-diaminothiophenes by ring cleavage of pyridinium salts by methylamine. Pyridinium salts (Va, b, c, d) reacted with methylamine and treatment of its reaction mixture with 10% hydrochloric acid solution gave 3,4-diamino-2-(methylthio)thiophene mono hydrochlorides (VIIa, b, c, d) which were neutralized by alkali to yield free 3,4-diaminothiophenes (VIIIa, b, c, d) in a good yield.

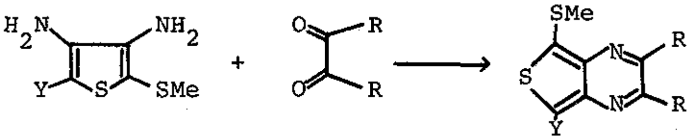


VIIIa, b, c, d

	Y	mp(°C)	Yield(%)(from V)
VIIIa	CN	90	89
VIIIb	$CONH_2$	116	86
VIIIc	COOEt	78	82
VIIId	COPh	143	88

A variety of quinoxaline derivatives have been prepared for the characterization of aromatic *o*-diamines.[1a] These derivatives are widely used because their formation generally takes place very smoothly in a good yield and they are readily isolated as crystalline compounds.

Imoto et al.[2b] reported the synthesis of 2,3-diphenylthieno-[3,4-b]pyrazine by the condensation of 3,4-diaminothiophenes, which are obtained from 3,4-dinitrothiophenes by reduction with tin and hydrochloric acid, with benzil. We examined the synthesis of thieno[3,4-b]pyrazines for synthetic and pharmaceutical interest. Namely, 2-(methylthio)thieno[3,4-b]pyrazines were prepared in a good yield by the condensation of 3,4-diamino-2-(methylthio)thiophenes with 1,2-dicarbonyl compounds (glyoxal, diacetyl, benzil). The reaction progressed very smmothly by refluxing in ethanol or heating at 100°.



IXa, b, c, d, e, f, g

	Y	R	mp(°C)	Yield(%)
IXa:	CN	H	143	97
IXb:	CN	Me	142	64
IXc:	CN	Ph	239	56
IXd:	COOEt	H	118	95
IXe:	COOEt	Ph	211	52
IXf:	COPh	H	160	89
IXg:	$CONH_2$	H	188	67

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6) Structures of all the new compounds were supported by elemental analysis and their spectral (UV, IR, NMR, and mass) data.

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