CROATICA CHEMICA ACTA CCACAA 59 (1) 313—326 (1986)

CCA-1645

YU ISSN 0011-1643
UDC 547.836.3
Original Scientific Paper

On the Synthesis of Isomeric Dithiophene Analogues of Phenathridine-*N*-oxides

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Received August 7, 1985

Six of nine *o,o'*-formylnitrobithienyls have been synthesized by the tetrakis(triphenylphosphine)palladium(0)-catalyzed coupling of the three *o*-bromonitrothiophenes with two of the three *o*-formylthiopheneboronic acids with sodium carbonate or sodium bicarbonate as base and an ethylene glycol dimethyl ether-water mixture as solvent. In the reaction with 3-formyl-2-thiopheneboronic acid, the coupling was carried out by using triethylamine as base and *N,N*-dimethylformamide as solvent in an attempt to avoid the facile deboronation of 3-formyl-2-thiopheneboronic acid, but without success.

Reduction of the *o,o'*-formylnitrobithienyls gave high yields of the *N*-oxides of the six isomeric dithienopyridines, which are analogues of phenanthridine-*N*-oxide. A direct synthesis of one of the dithienopyridines, dithieno[2,3-c:2',3'-c]-pyridine, was achieved by the palladium(0)-catalyzed coupling of 2,3-dibromothiophene with 2-formyl-3-thiopheneboranic acid to 3-bromo-2'-formyl-2,3'--bithienyl, which was transformed to the 3-azido-2'-formyl-2,3'--bithienyl, which upon reduction with hydrogen sulfide underwent ring closure to the phenanthridine analogue.

INTRODUCTION

We have recently been interested in the chemistry and pharmacological properties of tricyclic aromatic systems derived from the corresponding benzenoid compounds by changing one or two rings by thiophene rings. Thus, methods have been developed for the synthesis of various dithienotropylium ions,[1–5] and some of their chemical reactions[6] and spectral properties,[7] as well as the pharmacological properties of some derivatives, have been studied.[8] A general method for the synthesis of benzodithiophenes, thiophene analogues of phenanthrene, has ben worked out.[9] In addition, electrophilic substitution reactions[10] and UV spectra[11] of these systems were studied. We were specially interested in understanding the effect of the mode of anellation of the thiophene rings on the chemical and physical properties.

As a continuation of this work, we became interested in studying the thiophene analogues of phenanthridine, which chould also be of potential pharmaceutical interest. The chemistry of phenanthridine is still being studied very actively and has been reviewed in Ref. 12. Well-established routes for

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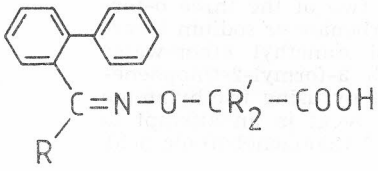
their preparation involve the cyclization of 2-substituted biphenyls, for example the cyclization of 2-acylaminobiphenyls with phosphorus oxychloride or polyphosphoric acid. Friedel-Crafts cyclization of *o*-biphenylaminoacetic acid chloride has also been used to prepare the phenathridine system. Other well-investigated methods involve Beckmann rearrangement of *o*-phenylbenzophenone oxime or the related reactions of fluorenone oxime, both leading to the phenanthridine system. Phenanthridone is also obtained in high yield by treating fluorenone with hydrazoic acid (Schmidt reaction). *o*-Biphenylcarboxylic acid azides undergo Curtius rearrangement to the isocyanate, which upon ring closure leads to the phenanthridine. Recently, additional methods based on 2-substituted biphenyls have been developed. Thus, oxidation of biphenyl-2-yl(phenyl)-mtehylene aminooxyacetic acid, I, with persulfate gave the iminyl, II, which is readily transformed to phenanthridines. Alternatively, the corresponding *t*-butyl peresters could be thermolyzed.[13] A similar route, but using the radical III, obtained by oxidation of the corresponding Schiffs base, has been suggested as a convenient synthesis of phenanthridines.[14]



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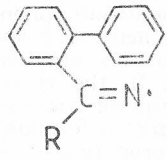

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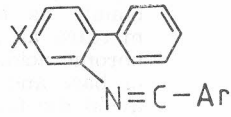
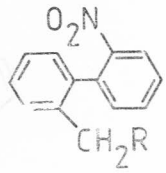


(III)

Another recent approach is the metalation of 2-amino-3',4'-dimethoxybiphenyl with a tenfold excess of butyllithium to give the 2'-lithio derivative, which upon reaction with *N*,*N*-dimethyl formamide and hydrolysis gave 7,8-dimethoxyphenanthridine.[15] A rather special synthesis of phenanthridine was achieved by photoisomerization of 2-isocyanobiphenyl.[16] The methods based on 2-substituted biphenyls and fluorenones have of course the disadvantage that, in unsymmetrical cases, mixtures may be obtained. This can be avoided by using appropriate 2,2'-disubstituted biphenyls, like in the classical syntheses of phenanthridones from diphenic acid via Hofmann or Curtius rearrangements.[12] Reduction of 2'-nitrobiphenyl-2-carboxylic acid with ammoniacal ferrosulfate,[17] or with zinc and hydrochloric acid,[18] also gives phenanthridone. An interesting synthesis of phenanthridine-*N*-oxides is the base-catalyzed condensation of certain 2-substituted 2-nitrobiphenyls, IV, to give V.[19] Thermal or photochemical decomposition of 2-azido-2'-methylbiphenyl led to phenanthridine in very low yield.[20] Important methods for the synthesis of phenanthridines have also been developed from systems without the biphenyl link. A classical case is the Pschorr reaction, i. e. the decomposition of diazonium salts such as VI in the presence of copper powder to give VII.[12] However, the reaction does not give as good yields as when stilbenes are used, and frequently several other products are also formed.

Formation of the biphenyl bond by photochemical coupling has also been successfully used for the synthesis of phenanthridine derivatives in modest yields.[12,21–23] Since dilute solutions must be employed in order to



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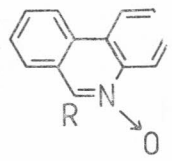

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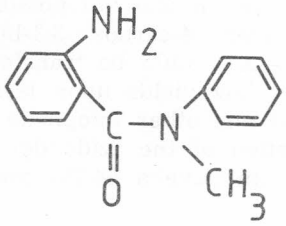

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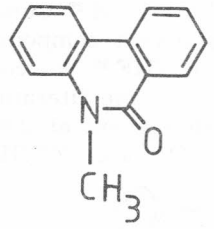
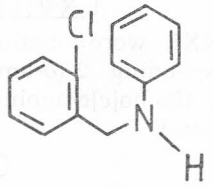


(VII)

minimize dimerization of the reactants, the photochemical route is usually convenient only for the preparation of relatively small amounts of material.

Cyclodehydration reactions leading to hydrophenanthridines,[12] followed by aromatization, have also been used in some cases for the syntheses of phenanthridines.[24] Several reactions involving benzyne intermediates have been employed for the synthesis of phenanthridines.[12] Thus, benzyne reacts with phenylisocyanate to give phenanthridone.[25] The reaction of VIII with potassium amide in liquid ammonia gave the 5,6-dihydrophenanthridine, IX, in high yield.[26,27] Some other methods are also discussed in Ref. 12.



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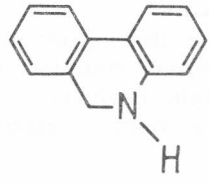

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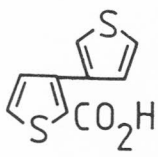
Thiophene analogues of the phenanthridine system, which should be of potential pharmacological interest, have hitherto attracted little interest, probably due to synthetic difficulties. Attempts to prepare dithienopyridones by the Beckmann rearrangement of cyclopentadithiophenones were unsuccessful.[28] However, by applying the Curtius reaction to the azides derived from 2-carboxy-3,3'-bithienyl, X, 3-carboxy-2,3'-bithienyl, XI and 3-carboxy--2,2'-bithienyl, XII, oxo-8-dihydro-7,8-dithieno[2,3-c:3',2-c]pyridine, XIII, oxo--8-dihydro-7,8-dithieno[3,2-c:2',3'-c]pyridine, XIV, and oxo-4-dihydro-4,5-dithieno[3,2-c:2',3'-c]pyridine, XV, respectively, were obtained in high yield upon



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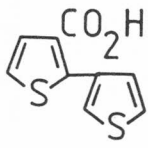

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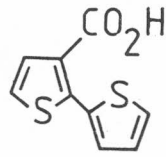
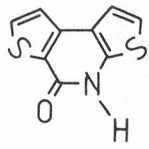


(XII)

heating in boiling diphenylmethane.[29] However, it was not possible to obtain the pyridones by this method starting from 4-carboxy-3,3-bithienyl and 2-carboxy-2,3'-bithienyl.[29] Compounds XIII—XV could be transformed to the corresponding parent compounds in rather low yields upon treatment with $LiAlH_4/AlCl_3$ in THF.[30] We could only find one other thiophene analogue of phenanthridine in the literature. The reaction of the azido derivative, XVI, in tetrachlorothiophene at 230 °C for 10 min gave a 64.5% yield of XVII, together with 22.5% of XVIII.[20]



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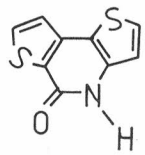

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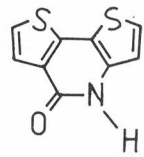

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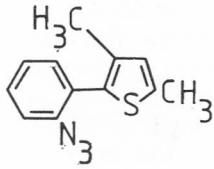

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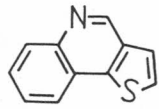

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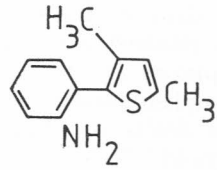
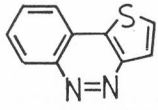


(XVIII)

The tricyclic thieno[c]cinnolines, XIX—XXI, were obtained by diazotisation and internal coupling to the corresponding 2-(*o*-aminophenyl)thiophenes. To obtain derivatives of the three thieno[*c*]cinnolines, this direct diazotisation procedure is capable of extension.[31]



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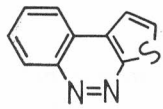

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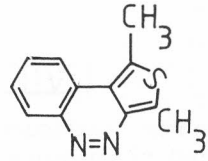
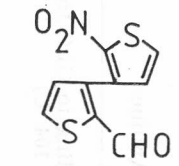


(XXI)

RESULTS AND DISCUSSION

Analyzing the different approaches to the synthesis of phenanthridines, it appeared to us that the ring closure of *ortho*-substituted 2-acylaminobithienyls would be difficult, due to the known instability of aminothiophenes

and the possibility of obtaining isomer mixtures in certain cases. It, therefore, seemed more reasonable to start from an *o,o'*-substituted bithienyl, especially as we recently developed a very useful and general method for the preparation of unsymmetrical bithienyls containing a variety of substituents, i. e. Pd(0)-catalyzed coupling of aromatic halogen compounds with thiopheneboronic acids.[32,33] All six isomeric thienylpyridines have also recently been prepared by this method.[34] Its great advantage lies in the fact that various functional groups, such as the formyl and nitro group, are tolerated, and that the coupling is carried out in aqueous medium. Coupling of the easily available 2-formyl-3-thiopheneboronic acid[35,36] with 3-bromo-2-nitrothiophene,[37] 2-bromo-3-nitrothiophene[38] and 4-bromo-3-nitrothiophene,[39] using tetrakis(triphenylphosphine)palladium(0) as catalyst, sodium carbonate or sodium bicarbonate as base, and a mixture of ethylene glycol dimetyl ether and water as solvent, gave 2-formyl-2'-nitro-3,3'-bithienyl, XXII,[33] 2-formyl-3'--nitro-3,2'-bithienyl, XXIII, and 2-formyl-4'-nitro-3,3'-bithienyl, XXIV, respectively, in high yields. Similarly, the reaction of 4-formyl-3-thiopheneboronic acid with the same three *o*-nitrobromothiophenes gave 4-formyl-2'-nitro-3,3'-bithienyl, XXV,[33] 4-formyl-3'-nitro-3,2'-bithienyl, XXVI, and 4-formyl-4'--nitro-3,3'-bithienyl, XXVII



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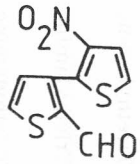

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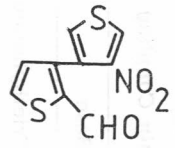

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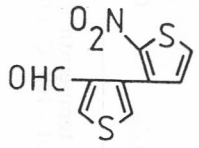

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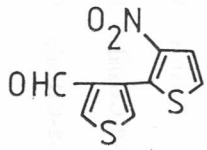

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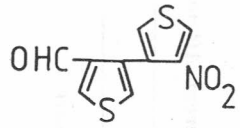


(XXVII)

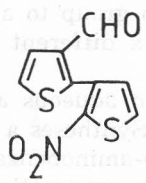
Due to the facile hydrolysis of 3-formyl-2-thiopheneboronic acid under the alkaline conditions used, only very low yields of the desired bithienyls were obtained.[33] Before we were able to modify the reaction conditions, a paper appeared by Thompson and Gardino,[40] who, by using *N,N*-dimethylformamide as solvent and triethylamine as base, successfully coupled arylboronic acids with 5-bromonicotinates to 5-arylnicotinates. However, this modification and some other presented in Table I for the coupling between the 3-formyl-2-thiopheneboronic acid and 2-nitro-3-bromothiophene or 3-nitro--2-bromothiophene did not encourage us to continue the work with the three missing bithienyls, XXVIII—XXX. When aniline was used both as base and solvent, the nucleophilic substitution of 2-nitro-3-bromothiophene was the main reaction, giving *N*-phenyl(2-nitro-3-thienyl)amine. Interestingly enough, 3-formyl-2-thiopheneboronic acid could be coupled under anhydrous conditions

TABLE I

Reaction Conditions in Different Attempts to Obtain Coupling with 3-Formyl-2-thiopheneboronic Acid

Halide	Catalyst	mole-%	Base	Solvent	Result
3-Nitro-2-bromothiophene	$Pd[P(C_6H_5)_3]_4$	0.03	Triethylamine	Ethyleneglycol dimethylether[a]	No coupling product
3-Nitro-2-bromothiophene	$Pd[P(C_6H_4\text{-}2\text{-}CH_3)_3]_2$	0.03	Triethylamine	Dimethylformamide[b]	Traces of coupling product
2-Nitro-3-bromothiophene	$Pd[P(C_6H_5)_3]_4$	0.03	Sodium bicarbonate	Ethyleneglycol dimethylether[a]	No coupling product
2-Nitro-3-bromothiophene	$Pd[P(C_6H_4\text{-}2\text{-}CH_3)_3]_2$	0.03	Triethylamine	Dimethylformamide[b]	No coupling product
2-Nitro-3-bromothiophene	$Pd[P(C_6H_4\text{-}2\text{-}CH_3)_3]_2$	0.03	Triethylamine	Dimethylformamide[b]	Traces of coupling product
2-Nitro-3-bromothiophene	$Pd[P(C_6H_4\text{-}2\text{-}CH_3)_3]_2$	0.03	Triethylamine	Dimethylformamide[c]	Traces of coupling product
2-Nitro-3-bromothiphene	$Pd[P(C_6H_4\text{-}2\text{-}CH_3)_2]$	0.09	Triethylamine	Dimethylformamide[b]	Desired bithienyl[d] 3,3-Diformyl-2,2'--bithienyl 3-formylthiophene
2-Nitro-3-bromothiophene	$Pd[P(C_6H_5)_3]_4$	0.03	Aniline	Aniline[b]	*N*-Phenyl(2-nitro--3-thienyl)amine 64%[e]

[a] Reflux temperature; [b] 100 °; [c] Romm temperature; [d] According to GLC the areas for the three components were 9 : 6 : 35; [e] Isolated yield M Wt = 220, m. p. 101—103 °C (lit. value[48] 104 °C).



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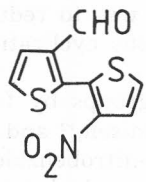

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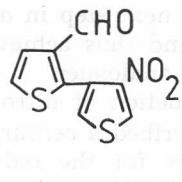


(XXX)

with *o*-bromoaniline and 5-methyl-3-bromo-2-aminopyridine.[41] The yields obtained, melting points, elemental analyses and the ^{1}H NMR data of the six isomeric *o,o'*-formylnitro-bithienyls are given in Tables II, III and IV.

TABLE II

Melting Points, Yields, Molecular Weights and Elemental Analyses for Some o,o'-Formylnitrobithienyls

Compound	M.p. (°C)	Yield %	MWt	C	H	N	S	Ref.
XXII	73—74	82						33
XXIII	128—130	81	239	45.0	2.11	5.88	27.0	
XXIV	152—153	53	239	45.2	2.10	5.84	26.9	
XXV	164—165	58	239					33
XXVI	149—150	84	239	45.5	2.08	5.85	27.0	
XXVII	201—202	65	239	45.0	2.04	5.85	26.6	
Elemental analyses calculated for $C_9H_5NO_3S_2$ (239.27)				45.18	2.11	5.85	26.80	

TABLE III

^{1}H NMR Chemical Shifts (ppm) in Deuteriochloroform Solution for Some o,o'-Formylnitrobithienyls

Compound	2H	4H	5H	2'H	4'H	5'H	CHO	Ref.
XXII		7.21	7.80		7.08	7.62	9.72	33
XXIII		7.24	7.87		7.57	7.72	9.77	
XXIV		7.15	7.77	8.50		7.37	9.73	
XXV	7.34		8.21		6.99	7.50	9.82	33
XXVI	7.42		8.22		7.31	7.69	9.78	
XXVII	7.31		7.25	8.20		8.41	9.82	

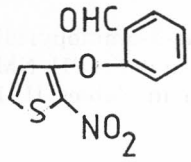
TABLE IV

^{1}H NMR Coupling Constants (Hz) in Deuteriochloroform Solution for Some o,o-Formylnitrobithienyls

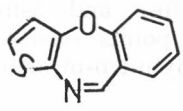
Compound	J_{23}	J_{25}	J_{CHO}	$J_{2'3'}$	$J_{2'5'}$	Ref.
XXII	4.94		1.21	5.47		33
XXIII	5.05		1.25	5.65		
XXIV	4.95		1.22		3.67	
XXV		3.34	0.60	5.41		33
XXVI		3.35	0.60	5.65		
XXVII		3.55	0.73		3.54	

The next step in our strategy was to reduce the nitro group to an amino group, and thus achieve spontaneous cyclization to the six different phenanthridine analogues.

Reduction of nitro to amino groups by ferrosulfate in aqueous ammonia was described a century ago by Claisen,[42] and in Organic Syntheses a detailed procedure for the reduction of *o*-nitrobenzaldehyde to *o*-aminobenzaldehyde is given.[43] This method has also recently been used for the preparation of the tricyclic thieno[3,2-b] [1,4]benzoxazepine system, XXXII, from XXXI.[44]

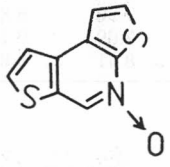


(XXXI)



(XXXII)

The reduction of the six *o,o'*-nitroformylthiophenes went smoothly, and in most cases in very high yields. However, in all cases the *N*-oxides of the dithienopyridines were obtained. Obviously, ring closure from the hydroxylamine intermediate occurred faster than the reduction of the hydroxylamine function to the amine, in spite of the use of the excess reducing agent. The formation of *N*-oxides was evident from the elemental analysis and IR spectra which showed absorption in the 1200—1235 cm^{-1} region, considered to be characteristic of *N*-oxides.[45] ^1H NMR spectra also support the proposed structures, since the azomethine proton shifts are at somewhat higher field than in the corresponding known dithieno-pyridines.[29] The mass spectra of the dithieno pyridine-*N*-oxides at 70 eV were found to be the same as those of the parent compound, showing no molecular peak, which first led to some confusion. However, recording the mass spectrum at 18 eV gave the molecular ions at *m/e* 207. Upon chemical ionization in an atmosphere of ammonia, the $(M^+NH_4)^+$ peak could also be observed. The six *N*-oxides XXXIII—XXXVIII with yields obtained, melting points and the elemental analyses are given in Table V. Chemical shifts, coupling constants and characteristic IR frequencies are given in Tables VI and VII.



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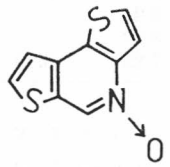

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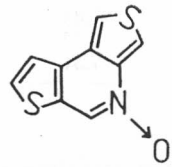
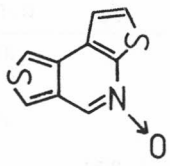
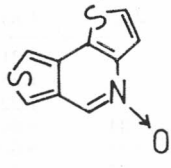


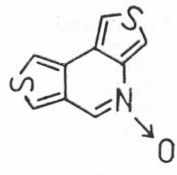
(XXXV)



(XXXVI)



(XXXVII)



(XXXVIII)

TABLE V

Melting Points, Yields, Molecular Weigths and Elemental Analyses for Some Dithienopyridine-N-oxides

Compound	M.p. (°C)	Yield (%)	MWt	C	H	N	S
Dithieno[2,3-c:3',2'-e]pyridine-N-oxide XXXIII	201—203	58	207	52.0	2.33	6.85	31.3
Dithieno[2,3-c:2',3'-e]pyridine-N-oxide XXXIV	209—211	95	207	51.4	2.36	6.74	30.8
Dithieno[2,3-c:3',4'-e]pyridine-N-oxide XXXV	188—190	92	207	52.1	2.42	6.79	31.1
Dithieno[3,4-c:3',2'-e]pyridine-N-oxide XXXVI	185—187	90	207	52.1	2.46	6.91	30.7
Dithieno[3,4-c:2',3'-e]pyridine-N-oxide XXXVII	185—187	88	207	52.1	2.35	6.77	31.1
Dithieno[3,4-c:3',4'-e]pyridine-N-oxide XXXVIII	177—179	98	207	52.0	2.44	6.76	29.7
Elemental analyses calculated for $C_9H_5NOS_2$ (207.26)				52.15	2.43	6.76	30.94

TABLE VI

^{1}H NMR Chemical Shifts (ppm) in Deuteriochloroform Solution and Characteristic IR N—O Stretching Frequences (cm^{-1}) of Some Dithienopyridine-N-oxides

Compound	2H	4H	5H	2'H	4'H	5'H	CH=N	N→O
XXXIII		7.63	7.77		7.62	7.66	8.81	1245
XXXIV		7.49	7.74		7.62	7.88	8.79	1235
XXXV		7.67	7.71	8.40		7.95		1230
XXXVI	7.87		7.85		7.57	7.60	8.62	1210
XXXVII	7.74		7.81		7.47	7.87	8.56	1215
XXXVIII	7.81		7.68	8.25		7.84	8.37	1220

TABLE VII

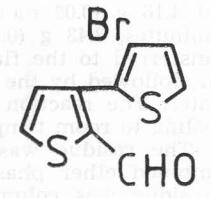
^{1}H NMR Coupling Constants (Hz) in Deuteriochloroform Solution for Some Dithienopyridine-N-oxides

Compound	J_{23}	J_{25}	$J_{2'3'}$	$J_{2'5'}$	$J_{CH=N}$
XXXIII	5.25		5.70		0.75(3)
XXXIV	5.25		5.60		0.75(3)
XXXV	5.15			3.65	0.50(3)
XXXVI		3.10	5.55		0.30(5)
XXXVII		3.10	5.50		0.90(5)
XXXVIII		2.70		3.40	0.50(5)

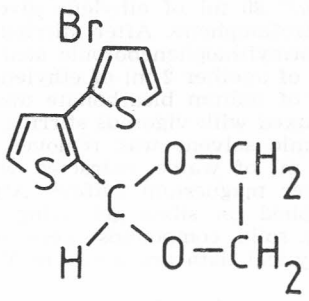
Work on the reduction of these *N*-oxides by standard methods, to give the parent compounds, is in progress, as well as attempts to prepare the parent compounds directly by using other reduction methods on the *o,o'*-nitroformylthienyls.

We have also worked out another approach to the thiophene analogues of phenanthridine using the azido group instead of the nitro group as precursor for the amino function.

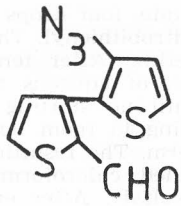
Pd(0)-catalyzed coupling between 2-formyl-3-thiopheneboronic acid and 2,3-dibromothiophene, which occurs in the 2-positon, was used for the preparation of 3-bromo-2'-formyl-2,3'-bithienyl, XXXIX. It is important to add the solution of base rapidly to the mixture of the halide, the formylboronic acid and the catalyst. Otherwise, as much as 10% of 2,2'-diformyl-3,3'-bithienyl was obtained as a by-product in a self-coupling of the 2-formyl-3-thiopheneboronic acid. This side-reaction reminds of the coupling of benzeneboronic acid to biphenyl using palladium acetate in acetic acid-perchloric acid.[46] Protection of the formyl group of XXXIX as the acetal, XL, halogen-metal exchange with butyllithium, followed by the reaction with *p*-toluenesulfonylazide and thermal decomposition of the intermediate triazene salt, yielded 3-azido-2-formyl-2,3'-bithienyl, XLI. This route has been extensively used for the preparation of azidobithienyls and aminobithienyls.[47] The compound XLI was transformed without purification to dithieno[2,3-c : 2',3'-e]pyridine, XLII. Application of this route to 2,3- and 3,4-dibromothiophene and the three *ortho*-formylthiopheneboronic acids should make six of the nine dithienophenanthridines available. The use of 2-bromo-3-iodothiophene should give the



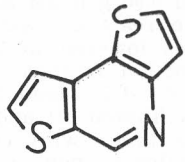
(XXXIX)



(XL)



(XLI)



(XLII)

remaining three, as it is known that 2-bromo-3-iodothiophene undergoes Pd-catalyzed coupling in the 3-position.[32] However, on the azido route, protection of the formyl group and further reaction on the bithienyl derivative is necessary, although obviously the two dibromothiophenes are much more easily available than the bromonitrothiophenes. On the other hand, on the nitro route, only the final reduction of the *N*-oxide is required. In addition, due to the instability of azido derivatives the yields can be expected to be lower. We, therefore, believe that the nitro route should, in most cases, be the most conveninent one for preparing the six isomeric dithienopyridines of phenanthridine type described in this paper.

It is obvious that the most rapid and convenient route would be the coupling of the formylthiopheneboronic acids with *ortho*-aminobromothiophenes. Due to the well-known instability of simple aminothiophenes, this route did not seem feasible. However, we have used it for the preparation of phenanthridine itself and pyridine analogues of this ring system.[41]

EXPERIMENTAL

Melting points are uncorrected. The ^{1}H NMR spectra were recorded with Jeol MH-100 and Varian XL-300 spectrometers. The MS were recorded on a Finnigan 4021 spectrometer. GLC analyses were carried out on a Varian 3700 gas chromatograph using a Dexil 300, 3%, 3 m column.

General Procedure for the Coupling Reaction Giving Unsymmetrical Bithienyls

A 250-ml three-necked flask, equipped with condenser, stirrer and nitrogen inlet, was charged with 0.69 g (0.0003 mol) of tetrakis(triphenylphosphine) pal-

ladium(0),[49] 80 ml of ethylene glycol dimethyl ether and 4.16 g (0.02 mol) of the bromonitrothiophene. After stirring the mixture for 20 minutes, 3.43 g (0.022 mol) of the formylthiopheneboronic acid was quantiatively transferred to the flask with the help of another 2 ml of ethylene glycol dimethyl ether, followed by the addition of 5.1 g of sodium bicarbonate dissolved in 50 ml of water. The reaction mixture was refluxed with vigorous stirring for one hour. After cooling to room temperature, the organic solvent was removed at reduced pressure. The residue was diluted with 10 ml of water, extracted with ether and the combined ether phases were dried over magnesium sulfate. After evaporation, the residue was column chromatographed on silica gel using ethyl acetate/cyclohexane, 1 : 1, as eluent. The resulting solid compounds were recrystallized. Six *o,o'*-formylnitrobithienyls and their physical data are given in Tables II, III and IV.

*General Procedure for Preparation of Dithienopyridine-*N*-oxides From* o,o'-*Formylnitrothiophenes*

A 250 ml three-necked flask equipped with condenser and stirrer was charged with 25 ml of water, 10.56 g (0.038 mol) of ferrous sulfate, four drops of 2 N hydrochloric acid and 0.96 g (0.004 mol) of the *o,o'*-formylnitrobithienyl. The stirring was started and the reaction mixture was heated to reflux. After ten minutes, the temperature was lowered to 70 °C, whereupon 11 ml of aqueous ammonia were added. The reaction mixture was then refluxed until no starting material was left according to GLC, about 30 minutes. After cooling to room temperature, the black solid was filtered off and washed with chloroform. The resulting filtrate was extracted three times with chloroform. The combined chloroform phases were treated with active carbon and dried over sodium sulfate. After evaporation the solid residue was column chromatographed on silica gel using ethanol as eluent. Six dithienopyridine-*N*-oxides and their physical data are given in Tables V, VI and VII.

2-Formyl-3'-bromo-3,2'-bithienyl was prepared according to the general procedure described above from 3.5 g (0.003 mol) of tetrakis(triphenylphosphine)palladium(0),[49] 400 ml of ethylene glycol dimethyl ether and 24.2 g (0.10 mol) of 2,3-dibromothiophene,[50] 17.1 g (0.11 mol) of 2-formyl-3-thiopheneboronic acid[35] and 25.2 g of sodium bicarbonate dissolved in 220 ml of water. Upon work-up the residue was distilled at reduced pressure giving 17.7 g (65%) of the title compound, b. p. 144—146 °C/6.7 Pa, m. p. 56—58 °C.

NMR, ($CDCl_3$): δ 7.25 (H4), 7.74 (H5), 7.11 (H4'), 7.43 (H5'), 9.91 (CHO), $J_{45} = 4.95$ Hz, $J_{4'5'} = 5.25$ Hz, $J_{H5-CHO} = 1.30$ Hz.

Anal. $C_9H_5BrOS_2$ (273.16): calc'd.: C 39.57; H 1.85; Br 29.25; S 23.47
found: C 39.6; H 1.87; Br 29.6; M Wt 272/274

3'-Bromo-2-[2-(1,3-dioxolanyl)]-3,2'-bithienyl

A 250 ml round-bottomed flask equipped with water separator and condenser was charged with 8.2 g (0.03 mol) of 2-formyl-3'-bromo-3,2'-bithienyl, 3 ml (0.05 mol) of ethylene glycol, 50 ml of toluene and a few crystals of *p*-toluenesulfonic acid. The reaction mixture was refluxed until no more water separated. Upon cooling, the reaction mixture was washed with sodium bicarbonate and water, dried and evaporated. The solid residue was recrystallized from ethanol giving 8.1 g (85%) of the title compound, m. p. 98.5—100.0 °C.

NMR, ($CDCl_3$): δ 7.00 (H4), 7.47 (H5), 7.04 (H4), 7.30 (H5'), (CH), 6.05, $(CH_3)_2$ 4.05, $J_{45} = 5.05$ Hz, $J_{4'5'} = 5.30$ Hz.

Anal. $C_{11}H_9BrO_2S_2$(317.22):
calc'd.: C 41.65; H 2.86; Br 25.19; S 20.21.
found: C 41.5; H 2.85; Br 26.1; S 20.2; M Wt 316/318.

Dithieno[2,3-c : 2',3'-e]pyridine

To a solution of 15.86 g (0.05 mol) of 3'-bromo-2-[2-(1,3-dioxolanyl)]-3,2'-bithienyl in 40 ml of dry ether in a 500 ml three-necked flask, equipped with stirrer, dropping funnel, condenser and nitrogen inlet, 36.1 ml of 1.47 N butyllithium in

hexane was added dropwise at —70 °C. The reaction mixture was stirred for five hours, whereupon 10.85 g (0.055 mol) of *p*-toluenesulfonylazide[51] dissolved in 50 ml of dry ether was added dropwise. After the addition was complete, the reaction mixture was stirred for another five hours at —70 °C. When the temperature reached —10 °C, the resulting triazene salt was filtered rapidly, washed with dry ether and suspended in 150 ml of dry ether. To this suspension, a solution of 22.3 g (0.05 mol) of tetrasodiumpyrophosphate in 200 ml of distilled water was added dropwise at 0 °C. The mixture was stirred at room temperature overnight. The phases were separated and the aqueous phase was extracted twice with ether. The combined ether phases were washed with water and dried over sodium sulfate. After evaporating the solvent, a brown oil was obtained, which was immediately added to a solution of 30 ml of ether and 30 ml of 2 N hydrochloric acid at 0 °C. The reaction mixture was stirred for five hours at room temperature, whereupon the phases were separated and the water phase extracted twice with ether. The combined ether phases were washed with a sodium bicarbonate solution and water, decoloured with active carbon and dried over sodium sulfate. The brown oil, obtained upon removal of the solvent, was dissolved in 20 ml of methanol and 20 ml of ether, cooled to 10 °C and treated with four drops of piperidine. Hydrogen sulfide was bubbled through the reaction mixture under cooling until an exothermic reaction was observed, whereupon the stream of hydrogen sulfide was adjusted so that the temperature was kept below 20 °C. After one hour when the evolution of nitrogen had ceased, the solution was cooled to 0 °C and the precipitated sulfur was filtered off. The filtrate was poured into 100 ml of water and the resulting water solution was extracted five times with chloroform. The combined chloroform phases were dried over magnesium sulfate and evaporated giving a brown residue, which was column chromatographed on silica gel using ethanol as eluent. 0.83 g (9%) of dithieno[2,3-c:2',3-e]-pyridine was obtained, m. p. 72—73 °C after sublimation at 50 °C/0.5 mmHg (Lit. value[30]: 76—78 °C.)

Acknowledgements. — This work was completed during the stay of S. G. as Michael Visiting Professor at The Weizmann Institute of Science, Rehovot, Israel, which is gratefully acknowledged. S. G. and A.-B. H. also acknowledge a grant from The Swedish Natural Science Research Council. The stay of Y. Y. in Lund was within the framework of the Swedish-Chinese exchange program.

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POVZETEK

Sinteze izomernih ditiofenovih analogov fenantridin *N*-oksidov

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Sintetizirali smo šest od devet *o,o'*-formilnitrobitienilov iz treh *o*-bromonitrotiofenov in dveh od treh *o*-formiltiofenboronskih kislin. Reakcija je potekala ob prisotnosti tetrakis(trifenifosfin)paladaija(0) kod katalizatorja in natrijevega karbonata ali natrijevega bikarbonata kot baze v zmesi etilenglikol dimetiletra in vode. Po redukciji *o,o'*-formilnitrobitienilov smo dobili z visokimi izkoristki *N*-okside šestih izomernih ditienopiridinov, analogov fenantridin *N*-oksida. Sinteza ditieno 2,3-c:2',3'-c piridina je potekala iz 2,3-dibromotiofena in 2-formil-3-tienoboronske kisline ob prisotnosti (Pd(0) katalizatorja in nastali 3-bromo-2'-formil-2,3'-bitienil smo pretvorili v 3-azido-2'-formil-2,3'-bitienil, ki je po redukciji s H_2S cikliziral v analog fenantridina.