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Aryl Coupling through Borate Complexes with Ethanolamine.

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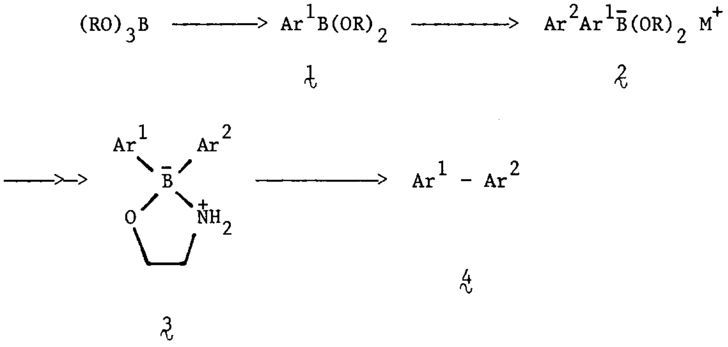
The scope and limitations of aromatic coupling by the action of N-bromosuccinimide on stable diarylethanolamine borate salts are disclosed. The procedure is an excellent, regiospecific procedure for the coupling of furyl and thienyl residues to each other or to aromatic rings in mild conditions and without scrambling.

A recent paper[1] discloses that poly-α-thienyls may be made with reasonable efficiency by aromatic coupling using boron methodoiogy based on the work of Levy[2] and Suzuki.[3] However, in the case of the production of 2,2'-bithienyl, the one compound reported in detail, the reported yield was good (81%) but almost half of the thienyl residues were recovered as thiophene. We are therefore prompted to report on the use of the related but different methodology shown in the Scheme.



Scheme

Our process[4,5] depends on the stepwise addition of aryl units to readily available trialkoxyboranes (we use either trimethoxy- or tri-isobutoxyborane) to give aryldialkoxyboranes, 1 followed by the diaryldialkoxyborates, 2. These can be converted to the borates 3 either directly, or through the diarylhydroxyboranes, by reaction with ethanolamine. The salts 3 are stable compounds that have frequently been used for the characterisation of diorganylboron moieties,[6,7] and they may be stored for long periods in air without special precautions. They also possess the advantage that the aryl residues to be coupled are the only organyl moieties to be bonded to boron.

For investigative purposes we used the production of 2,2'-bithienyl **4a**, from **3a** (Table 2) as a test for successful procedures. Use of iodine in a fashion similar to Suzuki and Levy gave the required product but accompanied by a large amount of 2-iodothiophene, the result of α-attack. Bromine in the presence of base gave 2,2'-bithenyl (40%) but always accompanied by some 4,4'-dibromo-2,2'-bithienyl, **4j**. Use of three equivalents of bromine leads directly to **4j** in 77% isolated yield, this being a useful preparative procedure (Table 2, exp.12). Neither chlorine nor N-chlorosuccinimide are suitable reagents for coupling **3a**. We also tried coupling by use of silver nitrate, potassium ferricyanide and DDQ but without success. However, the use of N-bromosuccinimide in a two phase system consisting of CH_2Cl_2, MeOH and a borax buffer at pH 9 gives **4a** in 90% yield and this system was therefore used extensively thereafter.

We found that replacement of ethanolamine by either N,N-dimethylethanolamine or 8-hydroxyquinoline was disadvantageous (Table 2). Occasionally we were forced to use salts **2**, but yields of coupled products were generally lowered.

The nature of the base used is important, in particular in controlling the proportion of α-attack. The results are shown in Table 1.

Table 1.

Coupling of **3a** with different bases.

System	2-Bromothiophene (%)	2,2'-Bithienyl (%)
Pyridine/Br_2/MeOH	44	28
Dabco/Br_2/MeOH	29	50
K_2CO_3/Br_2/MeOH	11	45
DBU/Br_2/MeOH	trace	25
Dabco/MeOH/NBS	35	53
Proton sponge/MeOH/NBS	0	0

We were unable to induce coupling by alkylation or acylation of the ethanolates or the N,N-dimethylethanolates.

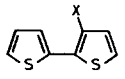
The results of our study of the coupling of aromatic residues is shown in Table 2.

Table 2.

Coupling of diarylethanolamine borates.

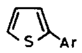
Experiment	Salt	Ar^1	Ar^2	Procedure	Product	Yield %
1	3a	2-Thienyl	2-Thienyl	NBS/Borax/MeOH	4a	90(82)
2	5a	"	"	"	4a	32
3	6a	"	"	"	4a	10
4	3b	"	3-Chlorothienyl	"	4b	(47)
5	3c	"	Phenyl	"	4c	100
6	3d	3-Thienyl	"	NBS/Borax/DMSO[4]	4d	45
7	3e	2-Thienyl	4-Biphenylene	"	4e	40
8	3f	2-Thienyl	2-Furyl	NBS/Borax/MeOH	4f	93
9	3g	Phenyl	2-Furyl	"	4g	35(25)
10	3h	"	3-Methoxyphenyl	"	4h	5
11	3i	"	Phenyl	"	4i	1
12	3j	2-Thienyl	2-Thienyl	$3Br_2$/NaOMe	4j	(77)

[a] Yields are g.c. except those in parentheses which are isolated yields.



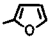
4a X = H

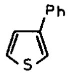
4b X = Cl



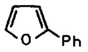
4c Ar = Ph

4e Ar = 

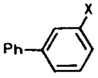
4f Ar = 



4d



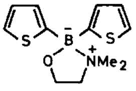
4g



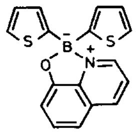
4h X = OMe

4i X = H

4j



5a



6a

We make the following comments.

(1) In the case of unsymmetrical salts, 3, no symmetrical coupled diaryls are detected. Thus the reaction is intramolecular and it is simple by this procedure to couple different types of aromatic residues.

(2) The reactions are regiospecific. In all the cases tested the new carbon-carbon bond is formed between the two carbon atoms originally bonded to boron.

(3) For successful reactions at least one of the two aromatic residues should be reasonably activated. Two phenyl rings will not couple (Table 2, exp.11) but a thienyl and a phenyl residue couple in high yield (Table 2, exp.5). We therefore expect, but have not yet proven, that activation of at least one phenyl residue by two or three methoxy groups, as required for lignan synthesis, will lead to successful coupling reactions.

In some cases we had difficulty in producing the required ethanolamine borate due to hydrolysis in going from **2** to **3**. This was particularly true when one of the aromatic rings was N-methylpyrrole. In such cases we used the salts **2** directly. Thus **2k** (Ar^1 = N-methylpyrrolyl, Ar^2 = Ph) by the action of bromine gave **4k**, 2-phenyl-N-methylpyrrole, in 20% isolated yield together with di- and tri-bromo-N-methylpyrrole.

We also used salts, **2**, to couple aromatic and alkynyl residues, though in disappointing yield. Thus **2l** (Ar^1 = Ph, Ar^2 = PhC C-) gave diphenylethyne in 15% yield on reaction with iodine in sodium methoxide.

Synthesis of 2,2'-Bithienyl. Borinate, **3a**, (0.242 g., 1 mmole) is dissolved in dry methanol (8 ml) in a nitrogen flushed flask and dry dichloromethane (20 ml.) and degassed aqueous borax buffer, pH9[8] is added. The mixture is cooled to 0°C and a solution of NBS (0.18 g., 1 mmole) in dichloromethane (20 ml.) is added with stirring over 10 m. After a further 10 m. the aqueous layer is separated and extracted with dichloromethane (20 ml.). Analysis of the combined organic layers by g.c. shows a 90% yield. After drying ($MgSO_4$) and filtration the solvent is removed and the product separated by elution with light petroleum (60-80°C) on a Kieselgel G60 column to give 2,2'-bithienyl (0.132 g., 82%), identical by m.s., ^1H n.m.r., i.r. and g.c. with an authentic sample.

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