

The Study of α and β Furanboronic Acids

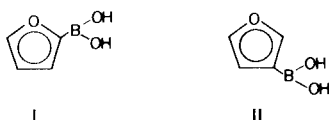
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Kuivila (1) and Brown *et al.* (2) have shown that quantitative data concerning the relative reactivities for electrophilic substitution can be derived from studies of protodeboronation in aromatic and heteroaromatic systems. Therefore the differences in the rates of hydrolysis for benzene (1) and thiophene (2) boronic acids have been measured. At the moment, little is known about the reactivity of the furan ring because of the difficulty of synthesis in the β substituted compounds. In this paper, the preliminary results for α and β furanboronic acids in comparison with the benzene and thiophene derivatives are reported.

The α furanboronic acid I has been prepared by the reaction of methyl borate with α -furyl magnesium iodide (3), the method first requires the synthesis of α iodofuran and unfortunately cannot be used for the preparation of the β isomer because the corresponding β -furyl magnesium iodide does not exist.



Compounds I and II have been synthesized by the reaction of the corresponding lithium derivatives on butyl borate.

α And β furyllithium are obtained respectively by direct metallation of furan in the case of the former (4) and the latter (5) by Ralogen/metal exchange between β -bromofuran and ethyllithium.

β -Furanboronic acid closely resembles the α isomer in its chemical behaviour (3), similarly so do the benzene and thiophene analogues. The $B(OH)_2$ function is readily substituted by the chloromercury group or by iodine, but the reaction of both α and β boronic acids with ammoniacal silver oxide or hydrogen peroxide do not yield the corresponding hydroxy furans.

In order to study electrophilic substitution a quantitative knowledge of the acidity is essential. Ultra violet spectrophotometric monitored titration of I and II gave the

pK_a values reported in Table I and these are listed with the literature values for furancarboxylic acids, and benzene and thiophene boronic and carboxylic acids.

Good correlation is obtained between the pK_a 's of the two series (Figure 1). This result shows that the acidity of the carboxylic and boronic groups is affected by the same factors. The slightly higher acidity of the furan acids may be due to the stronger electronegativity of the oxygen atom, in spite of the smaller resonance energy of the furan ring compared to the thiophene ring.

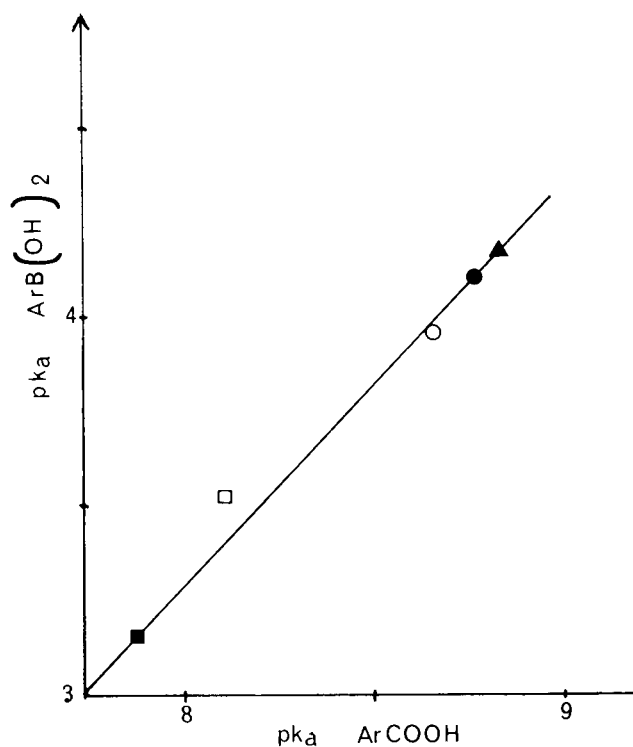


Figure 1. Correlation between the carboxylic acid pK_a 's and the boronic acid pK_a 's (■ α -furan, □ α -thiophene, ○ β -furan, ● β -thiophene, ▲ benzene).

Table I

	Benzene	α -Thiophene	β -Thiophene	α -Furan	β -Furan
Boronic acids pKa	8.83	8.11	8.77	7.88	8.65
Carboxylic acids pKa	4.18	3.53	4.10	3.16	3.95

Table II

Rate Constants and Relative Rates for Protodeboronation of Boronic Acids at 68.5° in 1M Perchloric Acid

	Benzene	α -Thiophene	β -Thiophene	α -Furan	β -Furan
λ nm	218	250	250	233	230
Rate constants k (sec ⁻¹) (pseudo first order)	1.01x10 ⁻⁹	5.56x10 ⁻⁴	5.56x10 ⁻⁶	9.19x10 ⁻⁴	7.12x10 ⁻⁶
Relative rates	1	5.5x10 ⁵ (a)	5.5x10 ³ (a)	9.1x10 ⁵	7.05x10 ³

(a) Lit. values (2): α -thiophene 8.5x10⁵, β -thiophene 7.1x10³.

The conventional aqueous perchloric acid method was used for determining the protodeboronation of the two furan boronic acids as well as the benzene and thiophene derivatives. All the kinetic measurements naturally being performed in the uv.

Table II re-emphasizes the similarities in behaviour between the α derivatives and the β derivatives.

A slight increase in the reactivity of the α and β positions on the furan ring compared to the thiophene ring in respect to ease of electrophilic substitution was observed. Thus the results allow the quantitative assignment of the reactivities of the two rings when the following sequence maintains: α -furan > α -thiophene > β -furan > β -thiophene. Good correlations between these results and recent reports of measurements on reactivities of heterocyclic rings (6) (7) are in accordance with the postulate of an electrophilic mechanism for the protodeboronation reaction. Now it should be possible to evaluate the directing effects of the several substituents on the α and β positions of the furan ring.

EXPERIMENTAL

α -Furanboronic Acid.

An ethereal solution of 110 ml. of 1M ethyllithium at -40° was added to a solution of 6.8 g. (0.1 mole) of furan in 50 ml. of anhydrous ether over twenty minutes under a nitrogen blanket. The reaction mixture was left at ambient temperature for two hours, then refluxed for thirty minutes. A solution of 25.3 g. (0.11 mole) of butyl borate in 100 ml. of ether was added at -30° and the mixture was refluxed for a further three hours.

The reaction solution was hydrolysed at 0° stirring for one hour with a 1N hydrochloric acid solution. The ethereal layer was extracted twice with a saturated solution of sodium carbonate.

The alkaline phase was acidified (pH \cong 1) and extracted with ether. The ether phase was dried over sodium sulfate.

Fractionation yielded 6 g. (53%) of α -furanboronic acid, m.p. 110° dec., which is in accord with the literature value (3).

β -Furanboronic Acid.

An ethereal solution of 110 ml. of 1M ethyllithium was added in a slow stream to a stirred solution of 14.7 g. of β -bromofuran in 50 ml. of ether at -70°. The mixture was stirred for 1 hour at this temperature and a solution of 25.3 g. of butyl borate in 100 ml. of ether was added, then stirred for 3 hours at -40°. After warming to 0°, the reaction mixture was hydrolysed and the product isolated as described above.

Fractionation yielded 7.3 g. (65%) of β -furanboronic acid m.p. 126-128°; nmr (DMSO/TMS): H₂ 7.81 ppm; H₄ 6.63 ppm; H₅ 7.53 ppm.

Anal. Calcd. for C₄H₅O₃B: C, 42.94; H, 4.51; B, 9.66. Found: C, 42.93; H, 4.50; B, 9.47.

The kinetic procedure was similar to that described by Kuivila and Nahabedian (1).

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