



# Suzuki coupling reaction of 6-iodo- or 6,8-diiodospiropyran: synthesis of spiropyran analogs

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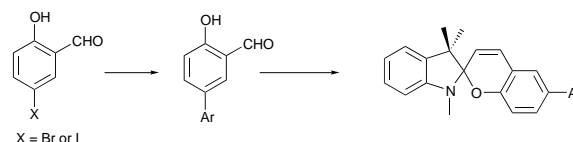
Received 4 September 2001; revised 17 September 2001; accepted 19 September 2001

**Abstract**—6-Iodospiropyrans and 6,8-diiodospiropyran were coupled with arylboronic acids in the presence of palladium acetate and sodium carbonate in DMF to give the corresponding spiropyrans in high yields. © 2001 Published by Elsevier Science Ltd.

Photochromic indolinobenzopyran dyes have been paid considerable attention, due to their potential application in many new technologies,<sup>1–3</sup> including the area of rewritable optical memory and optical switching, non-linear optics, and real-time holography. Since the stability of the spiropyran structure, the absorption associated with the merocyanine chromophore and other physical properties are strongly dependent on the substituent, it is of interest and important to investigate the influence of structural changes of the parent spiropyran, especially for a ferroelectric liquid crystal optical switch based on the principle of photoresolution.<sup>4–6</sup> Transition metal-catalyzed cross-coupling reaction between organometallic species and aryl halides is a powerful synthetic tool and represents one of the most straightforward methods for aryl–aryl carbon–carbon bond formation.<sup>7</sup> The main advantage of this reaction is its tolerance of a broad range of functional groups and its non-toxic by-products.<sup>7c,d</sup>

Herein, we wish to report Suzuki reaction of 6-iodospiropyran and 6,8-diiodospiropyran with arylboronic acids as one of the structural modifications of spiropyrans. In the beginning, we planned to synthesize spiropyrans by the Suzuki coupling of 5-iodo(or 3,5-diiodo)salicylaldehyde with arylboronic acid followed by the condensation with Fischer's base in refluxing ethanol (Scheme 1). However, the reaction of 5-iodo(or 5-bromo)salicylaldehyde with phenylboronic acid under various Suzuki conditions was in vain. The reaction even under the reported conditions<sup>8</sup> resulted in the formation of the expected product in low yield due to

the remaining substrate and the unidentified side product.



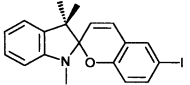
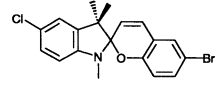
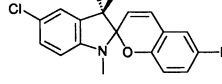
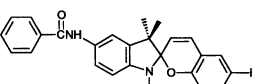
Scheme 1.

Therefore, we changed our strategy to get 6-monoaryl (or 6,8-diaryl) substituted spiropyrans by the direct coupling reaction of 6-iodo- or 6,8-diiodospiropyran with arylboronic acids. 6-Iodospiropyran, 6-bromospiropyran and 6,8-diiodospiropyran used were prepared by the reaction of corresponding salicylaldehydes and Fischer's base in refluxing ethanol, respectively.<sup>9</sup> Phenylboronic acid and 6-iodospiropyran were chosen for the coupling study (entry 1, Table 1). The reaction of 6-iodospiropyran with phenylboronic acid was tried under several reaction conditions<sup>10</sup> to give the coupling product in high isolated yields, respectively (Scheme 2). The choice of reagents and solvent is palladium acetate, sodium carbonate and DMF due to the personal preference and economic reason.<sup>11</sup> The reaction of 6-iodospiropyran having substituents with phenylboronic acid gave the corresponding coupling products in high yields under reaction conditions as shown in Table 1. The substituents (chloro or benzamido) and double bond of spiropyran remained intact under the reaction conditions. 6-Bromospiropyran seemed to be less reactive under the conditions and the reaction gave the coupling product in 63% yield due to incomplete reaction, even in the extended reaction time (entry 3, Table 1).

**Keywords:** iodospiropyran; dyes; Suzuki coupling; arylboronic acid; salicylaldehyde.

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**Table 1.** The reaction of 6-halospiropyrans with phenylboronic acid

Entry	Substrate	Time	Yield <sup>a)</sup>	Entry	Substrate	Time	Yield <sup>a)</sup>
1		2.5h	89%	3		7h	63%
2		2h	87%	4		2.5h	92%

a) Isolated yields. b) Reaction conditions: boronic acid (1.5 equiv.), Pd(OAc)<sub>2</sub> (5 mol%), Na<sub>2</sub>CO<sub>3</sub> (2 equiv.) in DMF (5 ml) at 80 °C.

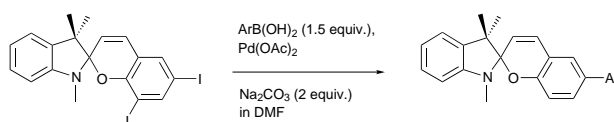
The reaction of 6-iodospiropyran with various arylboronic acids under the reaction conditions gave the corresponding coupling products in high yields except for that of 2-thiopheneboronic acid (Table 2). The reaction of thiopheneboronic acid gave a product in 41% yield due to incomplete reaction even in the extended reaction time and even in the presence of additional catalyst and reagent (entry 6).

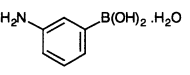
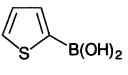
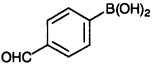

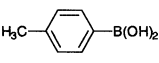
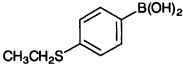
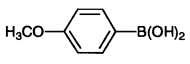
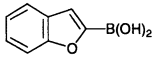
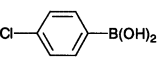
The coupling of 6,8-diiodospiropyran with various arylboronic acids gave the corresponding coupling products in high yields except for that of 2-thiopheneboronic acid and the results are shown in Table 3 (Scheme 3). The reaction of 2-thiopheneboronic acid with 6,8-diiodospiropyran gave the coupling product in 47% yield due to incomplete reaction. Any difference in reactivity of two iodo groups of 6,8-diiodospiropyran under the reaction conditions was not observed by TLC

during the reaction. Trials to get monophenylspiropyrans by the reaction of 6,8-diiodospiropyran with 1 equiv. of phenylboronic acid in various temperatures failed.

A spiropyran was subjected to the ozonolysis<sup>12</sup> in methanol and methylene chloride (2:1) to give salicylaldehyde derivative in 76% isolated yield (Scheme 4). This might be an alternative efficient route for the preparation of salicylaldehyde derivatives by Nguyen group,<sup>8</sup> which are substrates for salen type ligand in coordination as a scaffold for asymmetric catalysis,<sup>13</sup> specific DNA cleavage,<sup>14</sup> liquid crystalline properties<sup>15</sup> and NLO properties.<sup>16</sup>

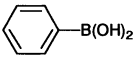
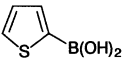
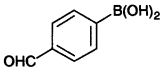

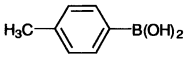
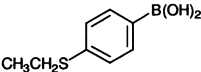
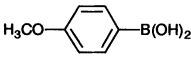
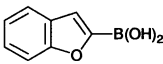
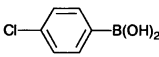
In conclusion, monoaryl (or diaryl) substituted spiropyrans were prepared by the reaction of 6-iodospiropyran or 6,8-diiodospiropyran with arylboronic acid under

**Scheme 2.****Table 2.** The reaction of 6-iodospiropyran with various boronic acids

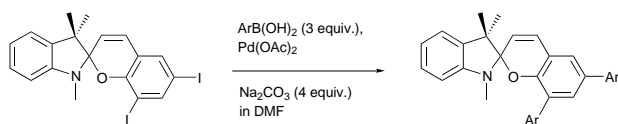
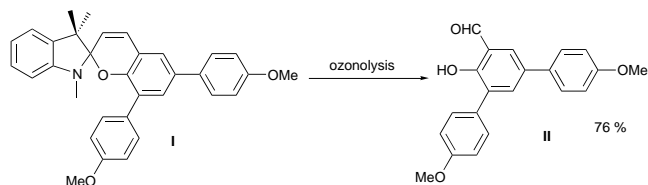
Entry	Boronic acid	Time	Yield <sup>a)</sup>	Entry	Boronic acid	Time	Yield <sup>a)</sup>
1		1h	95%	6		4h	41%
2		1.5h	86%	7		1.5 h	86%
3		2.5h	86%	8		2.5h	79%
4		2h	89%	9		1.5h	71%
5		1.5h	79%				

a) Isolated yields. b) Reaction conditions: boronic acid (1.5 equiv.), Pd(OAc)<sub>2</sub> (5 mol%), Na<sub>2</sub>CO<sub>3</sub> (2 equiv.) in DMF (5 ml) at 80 °C.

**Table 3.** The reaction of 6,8-diiodospiropyran with various boronic acids

Entry	Boronic acid	Time	Yield <sup>a)</sup>	Entry	Boronic acid	Time	Yield <sup>a)</sup>
1		1.5 h	91%	6		3.5h	47%
2		2h	80%	7		0.5h	79%
3		1.5h	98%	8		1h	72%
4		1.5h	72%	9		0.5h	80%
5		1h	68%				

a) Isolate yields. b) Reaction conditions: boronic acid (3 equiv.), Pd(OAc)<sub>2</sub> (5 mol%), Na<sub>2</sub>CO<sub>3</sub> (4 equiv.) in DMF (5 ml) at 80 °C.

**Scheme 3.****Scheme 4.**

one of Suzuki reaction conditions. This is a very useful method for the structural modification of spiropyrans themselves as well as the synthesis of salicylaldehyde analogs for various purposes.

### Acknowledgements

This work was supported by a Korea University Grant.

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- The reaction of 6-iodospiropyran and phenylboronic acid under several conditions:

Entry	Catalyst(Pd)	Base	Salt	Solvent	Yield
1	Pd(PPh <sub>3</sub> ) <sub>4</sub> 10 mol%	Na <sub>2</sub> CO <sub>3</sub> 0.4 M	.	MeCN:2ml, H <sub>2</sub> O: 2ml	88%
2	Pd(OAc) <sub>2</sub> 5 mol%	KOAc 2 equiv	LiCl 1 equiv.	DMF 5ml	84%
3	Pd(OAc) <sub>2</sub> 5 mol%	Na <sub>2</sub> CO <sub>3</sub> 2equiv.	LiCl 1 equiv.	DMF 5ml	82%
4	Pd(OAc) <sub>2</sub> 5 mol%	Na <sub>2</sub> CO <sub>3</sub> 2equiv.	.	DMF 5ml	89%

11. A representative example: To a solution of 6-iodospiropyran (70 mg, 0.17 mmol) in DMF (5 ml) was added palladium acetate (2 mg, 5 mol%), anhydrous sodium carbonate (37 mg, 0.34 mmol) and phenyl boronic acid (33 mg, 0.26 mmol) and the resulting solution was heated at 80°C. The reaction was followed by TLC using a solution of ethyl acetate and hexane (1:10). After 2.5 h of heating, the reaction was concentrated and chromatographed on silica gel using a solution of ethyl acetate and hexane (1:10). Concentration gave the coupling product in 89% yield in colorless oil.
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