

# NMR spectroscopic study of the formation of borate esters ascorbic acid and isoascorbic acid

Naoki Obi,<sup>a\*</sup> Masatoshi Katayama,<sup>a</sup> Junko Sano,<sup>a</sup> Yasuhiko Kojima,<sup>a</sup> Yasuo Shigemitsu,<sup>b</sup> Kanako Takada<sup>a</sup>

<sup>a</sup> Dainippon Ink and Chemicals, Inc., 631 Sakado, Sakura-shi, Chiba-ken, Japan

<sup>b</sup> Kawamura Institute of Chemical Research, 631 Sakado, Sakura-shi, Chiba-ken, Japan

Letter

The favorable positions for borate ester formation of ascorbic acid are 3,5-OH groups which yields a 6-membered ring, even though <sup>13</sup>B NMR chemical shifts of the borate ester of ascorbic acid suggested the existence of a 5-membered ring.

The reactions of boric acid and aromatic boric acid with polyhydroxy compounds have recently gained attention in the medical and pharmaceutical areas.<sup>1</sup> Recently, we discovered a new photographic developing system by using ascorbic acid as a developing agent,<sup>2</sup> and found that borate plays an important role in a nucleation reaction leading to high contrast.<sup>3</sup>

It is well known that the borate ion, B(OH)<sub>4</sub><sup>-</sup>, can react with polyhydroxy compounds in aqueous solution to afford borate esters.<sup>4</sup> However, there has been no structural study on the borate ester formation of ascorbic acid and isoascorbic acid.<sup>5</sup> Here, we provide the first structural study of borate ester formation of ascorbic acid and isoascorbic acid. Furthermore, we present the first experimental evidence that ascorbic acid and isoascorbic acid have different favorable positions for borate ester formation.

We used <sup>11</sup>B NMR and <sup>13</sup>C NMR spectroscopy to identify borate esters of ascorbic acid and related compounds. The <sup>11</sup>B NMR study showed that ascorbic acid, isoascorbic acid, and magnesium ascorbyl-2-phosphate form the borate ester. On the other hand, 5,6-*o*-isopropylideneascorbic acid does not readily form the borate ester (Table 1). <sup>13</sup>C NMR spectra of ascorbic acid in the presence of boric acid showed no additional signals at C(1) (δ 180), C(2) (δ 116) and C(6) (δ 66) upon borate ester formation, whereas, for C(4) (δ 81) and C(5) (δ 73), additional signals which were *ca.* 2 ppm lower were observed. The linewidth for C(3) (δ 178) became broader upon ester formation (Fig. 1). From these results, it was found that 3- and 5-OH groups rather than 2,3-OH or 5,6-OH groups of ascorbic acid are involved in the borate ester formation and that ascorbic acid forms a 5-membered ring by borate ester formation (Fig. 1).

<sup>13</sup>C NMR spectra of isoascorbic acid in the presence of boric acid showed no additional signals at C(1) (δ 180), C(3) (δ 178) and C(2) (δ 116) upon borate ester formation, whereas,

for C(5) (δ 74) and C(6) (δ 63), additional signals were observed. The linewidth for C(4) (δ 83) became broader upon ester formation (Fig. 3). Therefore, it is expected that, in contrast to ascorbic acid, the favorable OH-groups for borate ester formation of isoascorbic acid are 5,6-OH groups rather than 3,5-OH groups and that isoascorbic acid forms a 5-membered ring by borate ester formation.

Because of the characteristic difference of the chemical shifts between α,β-bidentate and α,γ-bidentate structures,<sup>6-8</sup> it is generally believed that the existence of 5- and 6-membered ring complexes can be distinguished by <sup>11</sup>B NMR spectroscopy. However, ascorbic acid gave an unexpected <sup>11</sup>B NMR chemical shift. Even though ascorbic acid forms a 6-membered ring, it showed the same <sup>11</sup>B NMR chemical shifts as the borate ester of α,β-diols which produces 5-membered rings such as ethylene glycol and *cis*-1,2-cyclopentanediol.

Results of the calculation of the minimum-energy structure using Mopac(AM1) showed that the O—B—O angle for the ethylene glycol borate ester (5-membered ring) and 1,3-propandiol borate ester (6-membered ring) were 105 and 109°,

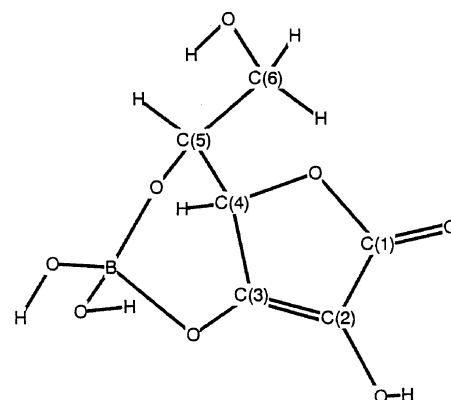


Fig. 1 Proposed structure of borate ester of ascorbic acid

Table 1 <sup>11</sup>B NMR spectroscopic data for boric acid–ascorbic acid derivative solutions at pH = 11<sup>a</sup>

	Boric acid concn./M	Ligand concn./M	Chemical shift/ppm			Peak area/%		
			B <sup>0</sup> + B <sup>-</sup>	BL	BL <sub>2</sub>	B <sup>0</sup> + B <sup>-</sup>	BL	BL <sub>2</sub>
Ascorbic acid	0.2	0.2	-16.71	-13.47	-9.62	59	39	2
Isoascorbic acid	0.2	0.2	-16.50	-13.66	-9.72	42	53	5
5,6- <i>o</i> -isopropylidene ascorbic acid	0.2	0.2	-16.94	-13.45	—	96	4	0
Magnesium ascorbyl-2-phosphate	0.1	0.1	-16.81	-13.62	-9.5	64	34	2

<sup>a</sup> B<sup>0</sup> = B(OH)<sub>3</sub>; B<sup>-</sup> = B(OH)<sub>4</sub><sup>-</sup>; BL = monoester; BL<sub>2</sub> = diester.

respectively. These values are in good agreement with the published data.<sup>9</sup> Calculated values of the O—B—O angle of the ascorbic acid borate monoester were 104(2,3-OH), 113(2,5-OH), 113(2,6-OH), 103(3,5-OH), 107(3,6-OH), 105°(5,6-OH). Results of this calculation showed that the O—B—O angle for borate esters of 3,5-OH groups of ascorbic acid is closer to that for a 5-membered ring than for a 6-membered ring, which may be one of the reasons why <sup>11</sup>B NMR chemical shifts of the borate ester of ascorbic acid agreed with those of borate esters of  $\alpha$ ,  $\beta$ -diols.

In summary, we have shown that the favorable positions for borate ester formation of ascorbic acid and isoascorbic are 3,5-OH groups which yield 6-membered rings and 5,6-OH groups which yield 5-membered rings.

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