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## DIASTEREOSELECTIVE SYNTHESIS OF 2,3-EPOXYALKYLPHOSPHONATES AND PHOSPHINATES BY EPOXIDATION

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The title compounds were prepared highly diastereoselectively by treatment of 2-alkenylphosphonates and phosphinates with m-chloroperbenzoic acid or MoO<sub>5</sub>·HMPA complex in good yields.

In a previous paper,<sup>1)</sup> we have reported new synthetic route to 2-hydroxyalkylphosphoryl compounds (1) from 2,3-epoxyalkylphosphoryl derivatives (2) and nucleophiles. These 2-hydroxyalkylphosphoryl compounds (1) are converted to the corresponding olefins in moderate to good yields by cesium fluoride induced reaction developed by us 1,2 (Scheme 1). In the case of  $R^3 \neq H$ , the resulting olefins are



usually obtained as a mixture of E- and Z-isomers. When pure E- or Z-olefin is desired, a diastereomer mixture of 1 must be separated by chromatography, recrystallization, and so on. But if 2 can be prepared in a highly diastereoselective manner, it is not necessary to separate diastereomers of 1.

We now report on diastereoselective epoxidation of 2-alkenylphosphonates (3) with two oxidizing reagents.<sup>3)</sup> In the process of this investigation, a possibility of 1,3-asymmetric induction controlled by a chiral center on a phosphorus atom was also studied using racemic 2-alkenylarylphosphinates (4)(Scheme 2).



Diethyl 1-substituted 2-alkenylphosphonates (3) were treated with m-chloroperbenzoic acid (MCPBA) in methanol-free dichloromethane to yield a diastereomer mixture of the corresponding 2,3-epoxyalkylphosphonates (erythro- and threo-2) in good or high yields. The diastereomer ratio was determined by <sup>31</sup>P NMR and <sup>13</sup>C NMR spectroscopies. The results are shown in Table 1.

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| 3   | R <sup>1</sup> | R2 | R3                | Temp /ºC | 2 | Yield/% | Diastereomer Ratio          |
|-----|----------------|----|-------------------|----------|---|---------|-----------------------------|
|     |                |    |                   |          |   |         | (erythro:threo)             |
| a   | Н              | н  | Me                | rt       | a | 94      | 69:31                       |
| b   | н              | Me | Me                | 0        | b | 87      | 69 <b>:</b> 31              |
| с   | н              | Me | Et                | rt       | С | 100     | 72:28                       |
| đ   | Me             | н  | Me                | rt       | d | 85      | 73:27 (from E-3d)           |
|     |                |    |                   |          |   |         | >96: 4 (from Z- <b>3d</b> ) |
| е   | Me             | н  | Et                | 0        | е | 89      | 72:28 (from E- <b>3e</b> )  |
|     |                |    |                   |          |   |         | 88:12 (from Z- <b>3e</b> )  |
| f   | Me             | н  | PhCH <sub>2</sub> | rt       | f | 95      | 76:24 (from E- <b>3f</b> )  |
|     |                |    |                   |          |   |         | 77:23 (from Z- <b>3f</b> )  |
| ga) | н              | Me | PhCH(OH)          | rt       | g | 59      | 84:16                       |
| ha) | Me             | н  | PhCH(OH)          | rt       | h | 87      | 88:12 (from E- <b>3h</b> )  |
|     |                |    |                   |          |   |         | >96: 4 (from Z-3h)          |

Table 1. Epoxidation of 3 with MCPBA

a) Diastereomer ratios of these hydroxyphosphonates were >95:5.

Diastereomer ratio was more than about 70:30 in all cases and the temperaturedependence was observed as usual.<sup>4)</sup> Especially Z-2-butenyl phosphonates series showed higher diastereoselectivity than others. Z-1-Methyl-2-butenylphosphonate (Z-3d) exhibited the highest selectivity and the minor diastereomer from Z-3d could not be detected by <sup>31</sup>P NMR and <sup>13</sup>C NMR spectroscopies, indicating the diastereomer ratio of more than 96:4. The exact stereochemistry of the major epoxide was determined to be erythro by comparison of the diastereomer mixture of diethyl 2hydroxy-1-methylheptylphosphonate prepared by the reaction of **2a** with butylmagnesium bromide in the presence of a catalytic amount of CuI<sup>1</sup>) with the threo predominant mixture obtained by reduction of diethyl 1-methyl-2-oxoheptylphosphonate with sodium borohydride.<sup>5</sup>)



According to these experimental data, the present high diastereoselectivity can be reasonably explained as follows: In the transition state, unexpectedly peracid molecule does not interact with the oxygen atom of phosphoryl group and two transition states **A** and **B** would be imagined. This model is similar to the Felkin's model.<sup>6)</sup> In the present case peracid molecule approaches to the double bond from

the reverse side of the phosphoryl group as shown in A and B. In the transition state B, a large steric repulsion would exist between Z-substituent  $R^1$  and substituent  $R^3$  adjacent to phosphoryl group, but in the transition state A this repulsion no longer exists. Consequently epoxidation would proceed predominantly through the transition state A to produce mainly erythro isomer. When the bulkiness of both  $R^1$  and  $R^3$  increases at the same time, the steric repulsion between  $R^2$  and  $R^3$  could not be ignored and the decrease of diastereoselectivity would be presumed (see 2e and 2f in Table 1). In the case of 2-alkenylphosphonate (3) without any Z-substituents, such a higher selectivity would not be observed because of the absence of the steric repulsion between  $R^1$  and  $R^3$  in B, which was supported experimentally (3a-c and E-3d-f in Table 1). Reactions using 3g and 3h were more diastereoselective than others, because these compounds are considered as homoallyl alcohols,<sup>7</sup> which are well known to be oxidized diastereoselectively by treatment with MCPBA or other oxidants.<sup>8</sup>

| 3 | 2 | Yield/% | Diastereomer Ratio         |  |  |  |
|---|---|---------|----------------------------|--|--|--|
|   |   |         | (erythro:threo)            |  |  |  |
| b | b | 61      | 75:25                      |  |  |  |
| d | d | 31      | 95: 5 (from E- <b>3d</b> ) |  |  |  |
|   |   |         | >96: 4 (from Z-3d)         |  |  |  |
| е | е | 79      | 93: 7 (from E- <b>3e</b> ) |  |  |  |
|   |   |         | 88:12 (from Z- <b>3e</b> ) |  |  |  |
| f | f | 65      | 95: 5 (from E- <b>3f</b> ) |  |  |  |
|   |   |         | >96: 4 (from Z-3f)         |  |  |  |

Table 2. Epoxidation of 3 with MoO<sub>5</sub>•HMPA



In order to investigate 1,3-asymmetric induction based on chirality on a phosphorus atom, we also treated alkyl 2-alkenylarylphosphinates (4) with MCPBA in dichloromethane. The results are summarized in Table 3. Z-Butenyl derivatives afford the corresponding epoxides more diastereoselectively than others. The use of 1-naphthyl group as an aryl moiety gave better results. Although the exact stereochemistry of the major diastereomer has not be determined yet, it can be

O=P(OEt)2

presumed from consideration by molecular model that the reaction would proceed via the transition state C rather than the transition state D, which has large steric repulsion between Z-methyl group and an alkoxyl group.





Table 3. Epoxidation of 2-Alkenylarylphosphinates (4)

| 4 | R1 | R <sup>2</sup> | R  | Ar         | 5 | Yield/% | Diastereomer Ratio                  |
|---|----|----------------|----|------------|---|---------|-------------------------------------|
| a | Me | н              | Et | o-Anisyl   | a | 80      | 53:47 (from E- <b>4a</b> )          |
|   |    |                |    |            |   |         | 73 <b>:</b> 27 (from Z- <b>4a</b> ) |
| b | Me | н              | Et | 1-Naphthyl | b | 91      | 72:28 (from E- <b>4b</b> )          |
|   |    |                |    |            |   |         | 77:23 (from Z- <b>4b</b> )          |
| с | Me | н              | Me | 1-Naphthyl | с | 62      | 57:43 (from E- <b>4c</b> )          |
|   |    |                |    |            |   |         | >96: 4 (from Z-4c)                  |

The present investigation seems to be very important in the following points: (1) Through highly diastereoselective formation of epoxyalkylphosphonate pure Zolefin could be obtained, and (2) 1,3-asymmetric induction based on a chiral center on a phosphorus atom could be shown experimentally.

## References

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- 2) T. Kawashima, T. Ishii, and N. Inamoto, Chem. Lett., 1983, 1375.
- 3) Very recently, McElroy and Warren reported independently on the diastereoselective synthesis of 2,3-epoxyalkylphosphine oxides by the reaction of the corresponding 2,3-alkenylphosphine oxides with MCPBA; A. B. McElroy and S. Warren, Tetrahedron Lett., <u>26</u>, 2119 (1985).
- 4) For example, when the epoxidation of 3e was carried out at room temperature diastereomer ratios (erythro:threo) were 67:33 (from E-3e) and 84:16 (from 2-3e).
- 5) For 2-oxoalkylphosphonic diamides, see: E. J. Corey and G. T. Kwiatkowski, J. Am. Chem. Soc., <u>88</u>, 5653 (1966). For 2-oxoalkyldiphenylphosphine oxides, see:
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- 7) Similar results were observed by McElroy and Warren, see: Ref. 3.
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