

## Arabinose-derived Auxiliaries in Asymmetric Diels–Alder Reaction

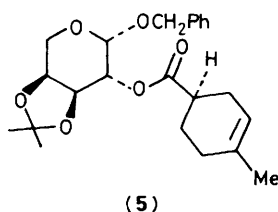
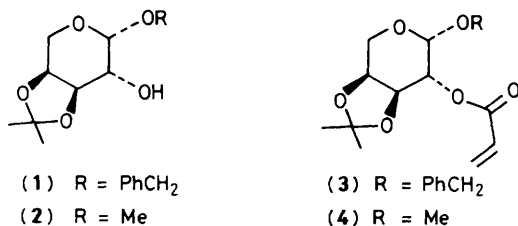
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The readily available auxiliary alcohol, benzyl 2,3-*O*-isopropylidene- $\beta$ -L-arabinopyranoside (**1**), is shown to be superior to its methyl-congener (**2**) in asymmetric induction capacity, attributable to a more efficient shielding by the phenyl ring.

In spite of impressive progress in highly diastereoselective cycloadditions employing chiral dienophiles,<sup>1</sup> issues associated with the rational design of new optically pure auxiliaries to achieve excellent stereocontrol and with the ready availability of these auxiliaries continue to pose a formidable challenge. Carbohydrates may be popular precursors for enantio-specific syntheses<sup>2</sup> of non-racemic natural products containing a great deal of oxygen functionalities, but their use as chiral auxiliaries in asymmetric Diels–Alder reactions is of more recent vintage.<sup>3</sup> Now we report our preliminary study on the use of easily accessible arabinose-derived alcohols, benzyl and methyl 3,4-*O*-isopropylidene- $\beta$ -L-arabinopyranosides (**1**) and (**2**), as *si*-face directing auxiliaries in their acrylates, and show that (**1**) is superior to (**2**) in chiral directing capacity. Arabinose is chosen in this study because it is cheap and commercially available in both enantiomerically pure forms.

Auxiliary alcohols (**1**)<sup>4</sup> and (**2**)<sup>5</sup> could be easily prepared from L-arabinose in high yields and on large scales *via* two well documented steps: glycosidation and acetonation. Esterification of the free hydroxy group in (**1**) and in (**2**) with acryloyl chloride furnished optically pure acrylates (**3**)<sup>†</sup> (m.p. 64–66°C;  $[\alpha]_D^{20} + 190.7^\circ$ ; overall yield from L-arabinose 56%) and (**4**) (m.p. 78–79°C;  $[\alpha]_D^{20} + 204.7^\circ$ ; overall yield 53%) respectively in multi-gram quantities. The ethylaluminium dichloride catalysed Diels–Alder reactions of (**3**) and of (**4**) with a series of dienes were then examined. In a typical experiment, isoprene (10 equiv.) was added to a cold solution (–78°C) of acrylate (**3**) and ethylaluminium dichloride (1 equiv.) in CH<sub>2</sub>Cl<sub>2</sub>. The resulting mixture was then stirred at –20°C for 5 h. Conventional aqueous work-up afforded a mixture of diastereoisomeric adducts in a ratio of 81:19.



Hydrolysis of the diastereoisomers to the carboxylic acids of known absolute configuration<sup>6</sup> established the absolute stereochemistry of the major cycloadduct to be (**5**). Other results are given in Table 1 and show that both auxiliary alcohols (**1**) and (**2**) have *si*-face directing capacity and (**1**) induces asymmetry more efficiently than (**2**). This heightened stereocontrol may be rationalised in terms of the Oppolzer postulate.<sup>7</sup> The anti-periplanar orientation of the carbonyl group and the double bond causes the phenyl ring to shield the *re*-face more effectively, thereby directing the diene addition to the dienophile *si*-face (see Figure 1).

Work is now in progress to improve the diastereoselectivity achieved by acrylate (**3**).

Table 1. Ethylaluminium dichloride catalysed Diels–Alder reactions of (**3**) and of (**4**) with dienes.

Diene	Acrylate	Cycloadduct		
		Diastereo-selection <sup>a</sup>	$[\alpha]_D^{b/c}$	Isolated yield (%)
	(3)	81:19	+195.4	56
	(4)	64:36	+131.3	40
	(3)	73:27	+179.3	68
	(4)	64:36	+128.6	58
	(3)	79:21	+186.0	65
	(4)	68:32	+130.0	50
	(3)	66:34	+156.7	51
	(4)	55:45	+65.3	39
	(3)	85:15	+198.7	48
	(4)	75:25	+189.9	37

<sup>a</sup> Ratio determined by <sup>13</sup>C n.m.r. spectral analysis. The major adduct has the *R* configuration in each case. <sup>b</sup> In chloroform.

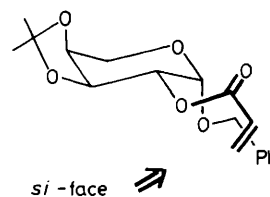


Figure 1

<sup>†</sup> All new compounds gave satisfactory analytical and spectral data.

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