Arabinose-derived Auxiliaries in Asymmetric Diels–Alder Reaction

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The readily available auxiliary alcohol, benzyl 2,3-O-isopropylidene- β -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,¹ 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 enantiospecific syntheses² 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.³ Now we report our preliminary study on the use of easily accessible arabinose-derived alcohols, benzyl and methyl 3,4-O-isopropylidene- β -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 $(1)^4$ and $(2)^5$ 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)[†] (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 CH₂Cl₂. 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.





† All new compounds gave satisfactory analytical and spectral data.

Hydrolysis of the diastereoisomers to the carboxylic acids of known absolute configuration⁶ 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.⁷ 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-A	Alder	reactions
of (3) an	d of (4) with dier	nes.				

		Cycloadduct				
Diene	Acrylate	Diastereo- selection ^a $[\alpha]_D^{b/^o}$		Isolated yield (%)		
K	(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		
Ľ	(3)	66 : 34	+156.7	51		
	(4)	55 : 45	+ 65.3	39		
$\left \right\rangle$	(3)	85:15	+198.7	48		
	(4)	75:25	+189.9	37		

^a Ratio determined by ${}^{13}C$ n.m.r. spectral analysis. The major adduct has the *R* configuration in each case. ^b In chloroform.





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