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Preliminary communication

Double asymmetric induction in the catalytic osmylation of some α,β-unsaturated octuronic acid derivatives

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In the Kishi model[1] **1** used to rationalise the diastereofacial selectivities resulting from catalytic osmylation of chiral allylic alcohols and their derivatives, OsO_4 is considered to approach the olefinic double-bond from the direction *anti* to the oxygen function at the adjacent stereocentre when the molecule adopts the least compressed, eclipsed conformation. Other models[2] predict the same qualitative results. Sharpless and co-workers[3] have recently produced a face-selection model **2** for the *catalytic* asymmetric osmylation of prochiral olefins, using either dihydroquinidine *p*-chlorobenzoate (**3**) or dihydroquinine *p*-chlorobenzoate (**4**) as the chiral ligand in the osmylating agent **5**. By combining the two models, there is every likelihood of the inherent diastereofacial selectivity of the chiral allylic system **1** towards catalytic osmylation being enhanced in the presence of **4**, whereas it would diminish with **3** as the chiral ligand in the osmylating agent **5**. We have used the "matching" osmylation reaction[4] to enhance the diastereofacial selectivities of several α,β-unsaturated uronic acid derivatives used in the synthesis of higher-carbon sugars[5–7].

Unlike a previous report[8], we found that catalytic osmylation in the presence of the appropriate alkaloid ester worked well for such (*E*)-conjugate esters as **6**, **9**, and **12**. Both (*E*)-octenopyranosiduronate derivatives **6**[7] and **9**[7] showed enhanced diastereofacial selectivities when catalytic osmylation was carried out at 0° in the presence of the "matching" dihydroquinine ester **4**, whereas there was a significant decrease in their diastereofacial selectivities in the presence of the "mismatching" dihydroquinidine ester **3**. For each set of results, the stereoisomer (**7**, **10**, and **13**) predicted by Kishi's empirical rule[1] is given first. Likewise, the diastereofacial selectivity of the (*E*)-octenofuranuronate **12**[7], which preferentially undergoes catalytic osmylation in an anti-Kishi sense, more than doubled in the presence of

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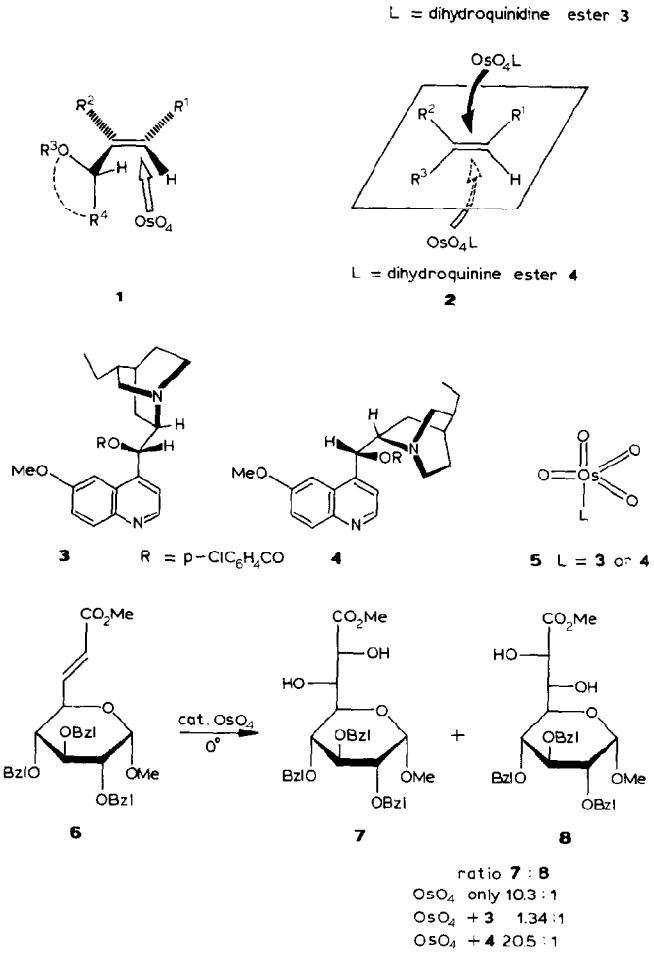
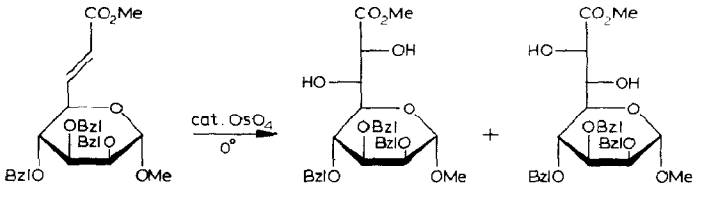


the "matching" dihydroquinidine ester **3***. By contrast, there was little change in the inherent anti-Kishi selectivity[9] of the (*Z*)-octenopyranuronate derivative **15** towards catalytic osmylation in the presence of either **3** or **4** under our conditions (see below). It is significant that osmylations of (*Z*)-conjugate esters often exhibit poor stereoselectivities in the corresponding stoichiometric procedure[8†] and provide[1,5] most of the exceptions to Kishi's empirical rule[1].

The following procedure proved to be useful for small-scale experiments and could be scaled-up as required. To a well-stirred and cooled (0°) solution of the

*Expressed in a more graphic way, the diastereoisomeric excess (d.e.) of **14** increased from 36.5 to 68% through the simple expedient of adding the dihydroquinidine ester **3** (0.27 equiv./substrate) to the reaction mixture.

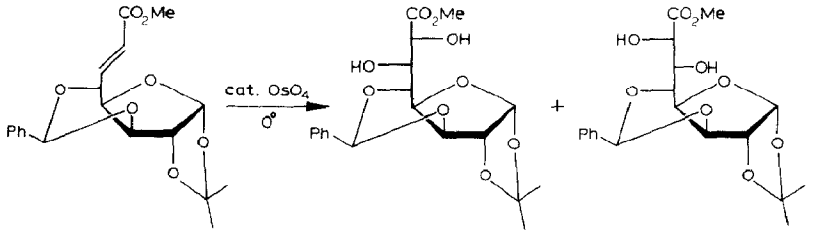
†Stoichiometric asymmetric osmylation establishes the highest diastereofacial selectivity that can be reached or approached with a chiral substrate using the catalytic procedure[10,11].



9 **10** **11**

ratio **10** : **11**

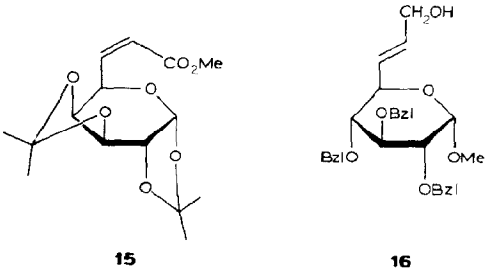
OsO_4 only 7.4 : 1
OsO_4 + **3** 3.45 : 1
OsO_4 + **4** 15.9 : 1



12 **13** **14**

ratio **13** : **14**

OsO_4 only 1 : 2.15
OsO_4 + **3** 1 : 5.3
OsO_4 + **4** 1 : 1.6



15 **16**

(*E*)-conjugate ester (0.55 mmol), *N*-methylmorpholine *N*-oxide monohydrate (0.67 mmol, 1.2 equiv.), and either **3** or **4** (0.15 mmol, 0.27 equiv.) in acetone–water (5.2:1 v/v, 1.55 mL) was added 0.055M OsO_4 in toluene (0.1 mL, 0.01 equiv.), whereafter the reaction mixture was stirred for 4–6 h at 0° and then kept in a refrigerator (0–4°) overnight before being processed in the usual way[7,9]. The ratios of the osmylation products were determined by 300-MHz ^{1}H-n.m.r. spectroscopy (see ref. 7 for details) on the crude reaction mixtures prior to chromatography, which furnished the products in combined yields of ≥90%. Previous work[7] had established the identities of **7, 8, 10, 11, 13,** and **14**.

Since the completion of this work, Sharpless and co-workers[10,11] have introduced a new experimental procedure for catalytic asymmetric osmylation which

significantly improves the facial selectivities of substrates that previously showed a poor response. This procedure might well enhance the diastereofacial selectivity of substrates such as the octenopyranose derivative[6] **16**, which showed no improvement in the "matching" reaction incorporating **4** under the experimental conditions described above.

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