Stereospecific 1,2-Silyl Shift in a Cationic Rearrangement with Retention of Configuration at the Migration Origin

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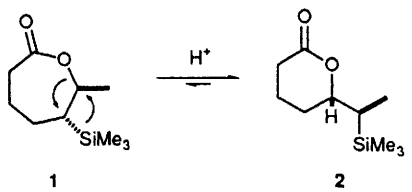
Mitsunobu reaction on the hydroxy acids **5** and **10** stereospecifically gave the lactones **7** and **4**, respectively, with retention of configuration at C-4.

In the preceding paper,[1] we described the synthesis of the acetates of two representative pentose lactones, (±)-deoxyribonolactone and (±)-arabinonolactone, having the (3*RS*,4*SR*) relative configuration, from the lactone **3**, which we had been able to prepare with high stereoselectivity. However, we could only prepare a representative member of the pentose lactone series having the alternative (3*RS*,4*RS*) relative stereochemistry inefficiently, because we had not been able to prepare the corresponding lactone **9** in better than 10% yield.

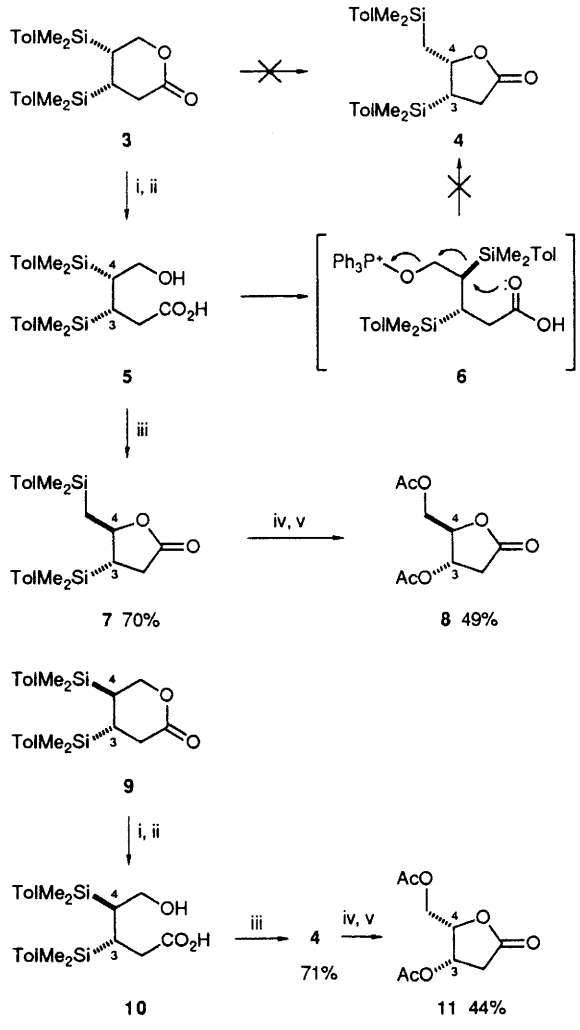
One way of overcoming this limitation might be to take advantage of Hudrlik's observation[2] that lactones with an embedded silylethyl carboxylate group sometimes undergo acid-catalysed rearrangement, with inversion of configuration at both sites, as in the example **1** → **2**. Not too surprisingly, we were not able to persuade the δ-lactone **3** to rearrange to the γ-lactone **4**, presumably because the δ-lactone is thermodynamically the more stable isomer, although we had hoped that steric repulsion between the *cis*-disposed silyl groups in the lactone **3** might have disturbed this pattern. To overcome this difficulty, we opened the lactone to give the γ-hydroxy acid **5**, and submitted it to Mitsunobu conditions without an external nucleophile, hoping that the kinetic preference for five-membered ring-formation might set off the [1,2]-sigmatropic silyl shift, **6** arrows (Scheme 1). We found that the hydroxy acid **5** did indeed give largely (typically 85:15) a γ-lactone in competition with a relactonisation **5** → **3** that we could not completely suppress, but the γ-lactone **7** that we obtained did not have the stereochemistry **4** that we had expectd by analogy with Hudrlik's work.



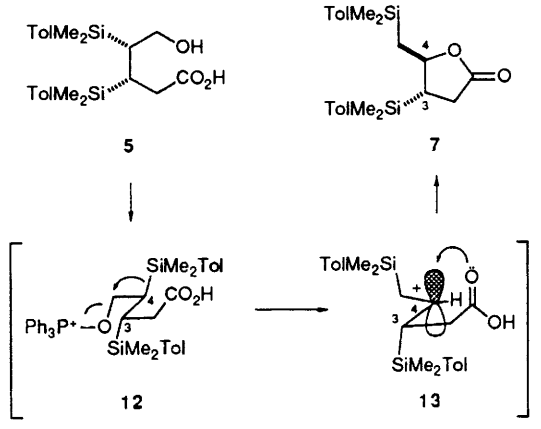
1 **2**

We proved the relative configuration in the lactone **7** by converting the silyl groups to hydroxy groups, in a reaction taking place reliably with retention of configuration,[3] and acetylating the product to give (±)-deoxyribonolactone diacetate **8**, immediately recognisable, and distinguishable from the diastereoisomer **11**, because we had prepared them both before.[1] To test whether we were observing simply the loss of stereochemical integrity at C-4, which does have precedent,[4] we repeated this sequence of reactions using the diastereoisomeric δ-lactone **9**, and obtained, in addition to the usual product of unavoidable (typically 16%) relactonistion **10** → **9**, successively the γ-lactone **4** (m.p. 109–110 °C) and (±)-deoxyxylonolactone diacetate **11**. We did not detect (TLC, ^{1}H NMR) any cross contamination in the two series. Clearly the rearrangement is strictly stereospecific, with retention of configuration at the migration origin, C-4, a remarkable event that is, we believe, without precedent in cationic rearrangements.

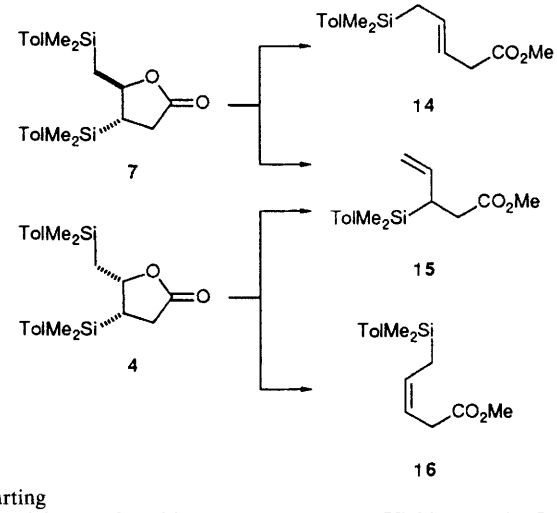
One possible explanation we raise only to dismiss. Hudrlik, knowing the relative configuration in the lactone **1**, had proved the relative configuration in the lactone **2** by converting the hydroxy acid derived from it into the corresponding *trans*-alkene with boron trifluoride–diethyl ether and into the



Scheme 1 *Reagents*: i, KOH, MeOH; ii, citric acid; iii, diethyl azodicarboxylate (DEAD), Ph_3P, CH_2Cl_2; iv, KBr, AcOOH, AcOH; v, Ac_2O, $HClO_4$ (Tol = *p*-MeC_6H_4)



Scheme 2



Starting material	Conditions	Yield	**14**:**15**:**16**
7	i, TBAF, THF, ii, MeI	92%	60:39:1
7	i, BF_3·OEt_2; ii, CH_2N_2	85%	76:19:5
4	i, TBAF, THF, ii, MeI	83%	8:51:41
4	i, BF_3·OEt_2; ii, CH_2N_2	93%	4:6:90

Scheme 3 (THF = tetrahydrofuran)

cis-alkene with potassium hydride, in reactions known to be stereospecifically *anti* and *syn*, respectively. Strictly speaking, this is compatible with double retention as well as with the double inversion shown in **1** → **2**. Dyotropic rearrangements of this type with double retention or double inversion are forbidden to be concerted by the Woodward–Hoffmann rules,[5] and are most likely therefore stepwise ionic processes, as the need for acid catalysis attests. Naturally Hudrlik chose to illustrate his reaction as a double inversion, with which we concur, because it seems extraordinarily unlikely that a nucleophilic displacement of carboxylate at the migration terminus should take place with retention of configuration. How then has our reaction given retention of configuration?

We believe that the silyl groups in the intermediate **6** will be disposed conformationally *anti*, **12**, at the time of rearrangement, and that the cation **13** is an intermediate (Scheme 2). This cation is highly stabilised, with silicon–carbon bonds overlapping with the empty p orbital on both surfaces of the trigonal carbon, thus driving the rearrangement step without any need for nucleophilic participation. Given that a nucleophile could attack this cation *anti* to a silyl group on either surface, it is not at first sight obvious why we observe a high level of stereospecificity rather than a low level of stereoselectivity. We suggest that restricted rotation about the bond between C-3 and C-4 ensures that the carboxylic acid group is held above the plane of the trigonal carbon, as drawn, thus ensuring the delivery of the nucleophile, **13** arrow, to the same surface from which the silyl group had departed. The same argument applied to the hydroxy acid **10** leads to the lactone **4**. The nearest analogy to the event taking place at C-4 in our compounds is the retention of configuration sometimes observed in S_N1 reactions of chiral halides and sulfonates in which the participation of a neighbouring group preserves stereochemical information in the intermediate cation.[6]

With two silyl groups β to the carboxylate group in the lactones **7** and **4**, we wondered which would be captured by fluoride ion on treatment with tetrabutylammonium fluoride (TBAF) or boron trifluoride–diethyl ether. Baldwin's rules suggest that endocyclic elimination ought not to be favoured, since it is the reverse of a 5-*endo-trig* process.[7] We find, however, that the lactone **7** with TBAF gives more endocyclic elimination **7** → **14** than exocyclic **7** → **15**, although the lactone **4** does give marginally more exocyclic elimination (Scheme 3). However, both lactones give mainly endocyclic elimination with boron trifluoride–diethyl ether. We suggest that these eliminations, especially that catalysed by boron trifluoride, are E1 reactions, with a cation like **13** as an intermediate, thus avoiding the strictures of Baldwin's rule. The formation of the more-substituted alkenes **14** and **16** is then unexceptional.[8] This observation is further support for the mechanism in Scheme 2.

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