Stereoselective Samarium(II)-induced Coupling of β-Silylacrylic Esters: a Synthesis of (±)-2-Deoxyribonolactone

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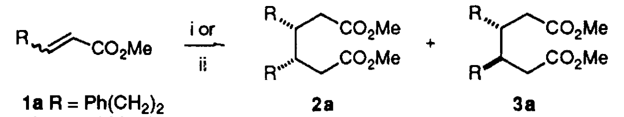
Samarium iodide converts the β-silylacryalte **1c** with high stereoselectivity into the racemic diester **2c**, from which (±)-deoxyribonolactone **11** can be prepared.

We have already shown that a stereogenic centre carrying a silyl group can control the development of new stereogenic centres with 1,2 and 1,3 relationships to it. Using the S_E2' reaction and the hydroboration of allylsilanes, together with enolate alkylations of β-silyl esters and the stereospecific conversion of the phenyldimethylsilyl group into a hydroxy group,[1] we have carried out several stereocontrolled syntheses of small molecules with three or four stereogenic centres.[2] In order to extend the power of this method to target molecules having more than three or four stereogenic centres, we need to be able to set up starting materials possessing another stereogenic centre already related to the silicon-bearing centre. We now report our first candidate having this feature.

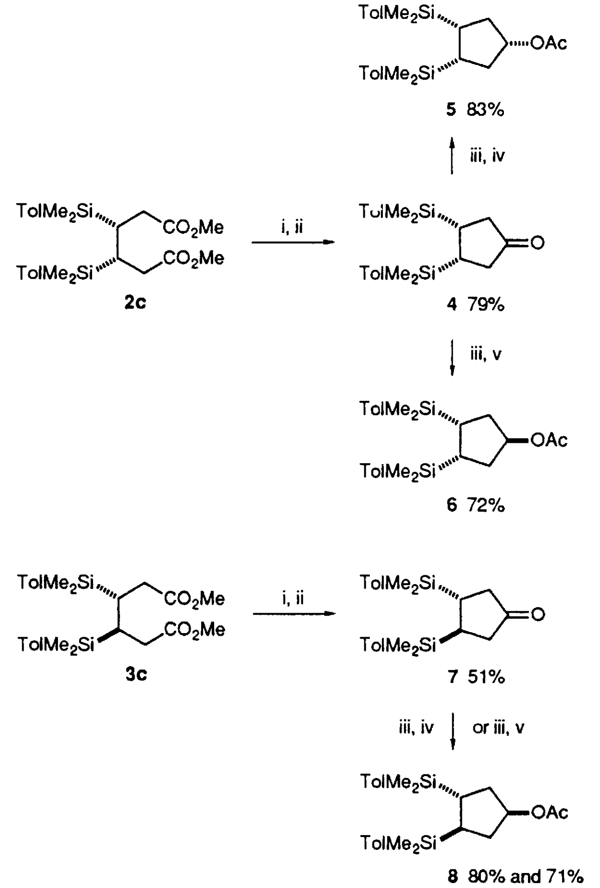
Inanaga[3] reported that samarium(II) iodide in THF–HMPA (tetrahydrofuran–hexamethylphosphoric triamide) containing one equivalent of Bu^{t}OH induces the reductive coupling of β-substituted acrylic acid derivatives such as **1a**, giving mainly the corresponding racemic diastereoisomer **3a** of 3,4-disubstituted adipic acid derivatives. More recently, Alper has reported that he sees no reductive coupling in HMPA alone, only reduction of the C=C double bond.[4] We find, in agreement with Inanaga, that under his conditions applied to β-silylacrylic esters the major product is that of reductive coupling, and in part agreement with Alper, there is also some apparently unavoidable reduction of the C=C double bond (Scheme 1). However, in contrast to Inanaga, the β-silylated acrylic esters **1b** and **1c** give mainly the *meso* diastereoisomers **2b** and **2c**. The phenyldimethylsilyl-containing product **2b** was crystalline, but of low melting (m.p. 41–42 °C), and we have therefore used in all our subsequent work the tolyldimethyl-



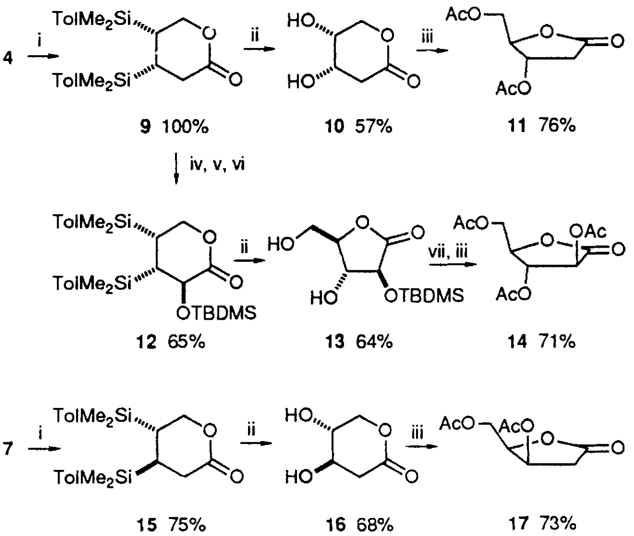
1a R = Ph(CH$_2$)$_2$ **2a** **3a**
1b R = PhMe$_2$Si **2b** **3b**
1c R = TolMe$_2$Si **2c** **3c**

Starting material	Conditions	**2**:**3**	Yield
1a	ii	34:66[3]	70%[3]
(*E*)-**1b**	ii	76:24	65%
(*E*)-**1c**	ii	82:18	65%
(*Z*)-**1c**	i	100:0	72%
(*Z*)-**1c**	ii	70:30	60%

Scheme 1 *Reagents*: i, SmI$_2$, THF, DMPU, dimethyl malonate; ii, SmI$_2$, THF, HMPA, Bu^{t}OH (Tol = *p*-MeC$_6$H$_4$; DMPU = 1,3-dimethyl-3,4,5,6-tetrahydropyrimidine-2(1*H*)-one; dimethylpropylene urea)



Scheme 2 *Reagents*: i, LDA; ii, NaCl, DMSO; iii, NaBH$_4$; iv, Ac$_2$O; v, AcOH, DEAD, Ph$_3$P (LDA = lithium diisopropylamide; DMSO = dimethyl sulfoxide; DEAD = diethyl azodicarboxylate)



Scheme 3 *Reagents*: i, MCPBA, Na$_2$HPO$_4$; ii, KBr, NaOAc, AcOOH; iii, Ac$_2$O, HClO$_4$; iv, NaHMDS, THF; v, 2-phenylsulfonyl-3-phenyloxaziridine; vi, TBDMSCl, imidazole; vii, TBAF, THF (MCPBA = *m*-chloroperbenzoic acid; NaHMDS = sodium hexamethyldisilazide; TBDMS = *tert*-butyldimethylsilyl; TBAF = tetrabutylammonium fluoride)

silyl group. In our experience, this group has the advantage over the phenyldimethylsilyl group of imparting higher melting points to those compounds that crystallise, and of being somewhat easier to remove in our silyl-to-hydroxy conversion. It has the disadvantage that we have been unable to make the corresponding silyllithium reagent from the chloride,[5] but we did not need a silyllithium or cuprate reagent for the preparation of either the *cis*- or the *trans*-acrylic esters **1c**. The *trans*-acrylic ester **1c** (77%) was prepared by hydrosilylation of methyl acrylate with tolyldimethylsilane using octacarbonyldicobalt as the catalyst,[6] and the *cis*-ester by silylation (86%) of ethynylmagnesium bromide with tolyldimethylsilyl chloride followed by methoxycarbonylation (88%) and catalytic hydrogenation (92%) using palladium on barium sulfate. Of all the combinations of solvent, geometry of starting material, and conditions of coupling that we tried, the best was to use the *cis*-ester **1c** in 6:1 THF–DMPU and one equivalent of freshly prepared SmI$_2$ at 20 °C, with three equivalents of dimethyl malonate as the proton source, which gave the easily purified *meso*-diester **2c**, m.p. 96–97 °C, in 72% yield, together with 24% of methyl 3-dimethyl(*p*-tolyl)silylpropanoate but with no trace of the racemic diastereoisomer **3c**, even in the crude reaction mixture. We were not able to find conditions in which the liquid diastereoisomer **3c** was the major product—at best we could obtain it in 14% isolated yield using 6:1 THF–HMPA, with one equivalent of Bu^{t}OH as the proton source, which gave 60% of the two adipic esters in a ratio of 70:30, and 32% of the β-silylpropanoate.

We proved the relative stereochemsitry of the major **2c** and minor **3c** diastereoisomers by the sequence of reactions in Scheme 2. Dieckmann cyclisation and Krapcho demethoxycarbonylation[7] gave the cyclopentanones **4** (m.p. 80–81 °C) and **7**. The cyclopentanone **4** gave a 93:7 mixture of two acetates **5** and **6** on reduction with sodium borohydride followed by acetylation. Alternatively, reduction with sodium borohydride, followed by Mitsunobu reaction[8] using acetic acid, gave the acetates **5** and **6** in a ratio of 7:93. In contrast, the cyclopentanone **7** gave a single acetate **8** on reduction with sodium borohydride followed by acetylation, and Mitsunobu reaction on the intermediate alcohol returned the same acetate.

We have used the cyclopentanones **4** and **7** to synthesise (±)-deoxyribonolactone and its acetate **11**, the acetate **14** of (±)-arabononolactone, and the acetate **17** of (±)-deoxyxylonolactone, as shown in Scheme 3. For this purpose, we prepared the cyclopentanone **4** in a slightly better overall yield (57%) by carrying out the samarium coupling on the (*E*)-acrylic ester (*E*)-**1c** in 6:1 THF–DMPU in the absence of a proton source, but quenching with Bu^{t}OH. This gave a mixture of the Dieckmann cyclisation product and the diester **2c**, directly in 70% yield in a ratio of 8:2, which we submitted to the conditions of the Krapcho reaction to get the ketone **4**, now easily separable from the diester. Baeyer–Villiger reaction on the ketones **4** and **7** gave the lactones **9** (m.p. 72–73 °C) and **15** (m.p. 95–96 °C), respectively. Conversion of the silyl to hydroxy groups using potassium bromide in buffered peracetic acid[1] gave the lactone alcohols **10** and **16**, which rearranged in acid to give the corresponding γ-lactones. Acetylation gave the known acetates **11** and **17**[9] with ^1H NMR spectra identical with those reported. Davis hydroxylation[10] of the lactone **9** followed by silylation gave the lactone **12** (m.p. 93–94 °C), which we converted to the arabononolactone acetate **14**, with a ^{13}C NMR spectrum identical with that reported,[11] by way of the γ-lactone **13** (m.p. 107–108 °C). By a suitable combination of protection and Mitsunobu or equivalent reactions, all the pentose lactones and 2-deoxypentose lactones, and hence pentoses, are, in principle, available from the diol **10** and the triol **13**. Our attempt to find a more elegant route to the other pentose lactones by way of the diol lactone **16**, avoiding the low yield of the ketone **7**, was thwarted by the unexpected observation described in the following paper.

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