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Regiochemical Aspects in the Reaction of 2,3,5-Tri-O-benzoyl-D-ribofuranosyl Acetate with Silyl Enol Ethers Catalyzed by Stannic Chloride

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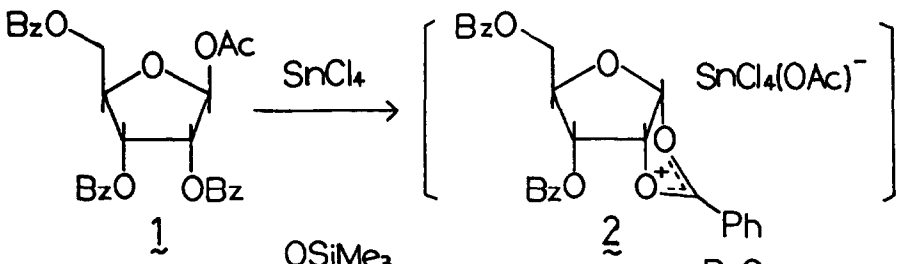
Summary: In the reaction with silyl enol ethers catalyzed by stannic chloride, 2,3,5-tri-O-benzoyl-D-ribofuranosyl acetate behaves as an ambident electrophile; silyl enol ethers of ketones having α-hetero substituents afford C-1 adducts, whereas those of usual acyclic ketones give products arising from attack on C-2 benzoxyl group.

Recently, synthetic studies on C-nucleoside antibiotics such as formycin,[2] showdomycin,[3] pyrazomycin,[4] and their analogues[5] have been much interested. For their synthesis, one of the most important processes is how to introduce carbon chain on C-1 position of ribose nucleus. 1-Halo ribose derivatives are usually used for this purpose.

2,3,5-Tri-O-benzoyl-D-ribofuranosyl acetate 1 is also employable for such carbon chain elongation. Although most of the nucleophiles react with 1 on carbonyl carbon of C-2 benzoxyl group under basic conditions,[5c,6] it has been described that the reaction with olefinic[7] or aromatic substrates[8] proceeds selectively on C-1 site of 1 under the influence of Lewis acid. According to this method, we previously reported synthesis of showdomycin[3a] which involves the reaction of 1 with 1,2-bis(trimethylsiloxy)cyclobutene as a key step.

In the present, we have examined on the reaction of 1 with a variety of silyl enol ethers for the preparation of useful precursors of C-nucleosides. In contrary to the reported examples,[3a,7] it is found that the silyl enol ether has a remarkable influence to decide the reaction site of 1. As shown in the Table, regiochemistry of the reaction appears to be definitely determined by the silyl enol ether and no regio-isomer could be detected under standard conditions (1 eq of $SnCl_4$, CH_2Cl_2, r.t.) in every case. Silyl enol ethers of usual acyclic ketones[9] 3a-b and of esters 3c-d gave the products 4a-d arising from attack on C-2 benzoxyl. On the other hand, the reaction took place selectively on C-1 site with enols of ketones 3e-g having α-hetero substituents to afford the desired 5e-g.

Since the phenylthio group can easily be removed by reduction, the use of such silyl enol ethers is generally feasible for introduction of 2-ketoalkyl



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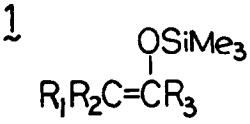
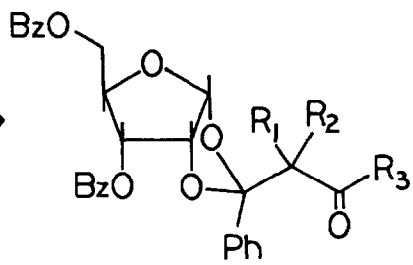
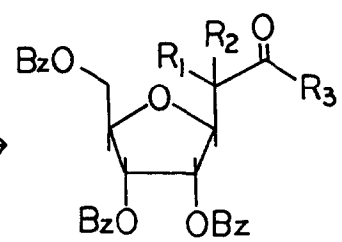


3 a-g

3	R_1	R_2	R_3	yield (%) [a] 4	5
a	Me	H	Et	88	—
b	H	H	^{t}Bu	55	—
c [b]	H	H	OEt	32	—
d	SPh	H	OEt	82	—
e	SPh	H	Me	—	83
f	SPh	H	^{t}Bu	—	45
g	$OSiMe_3$	$-(CH_2)_2-$		—	92

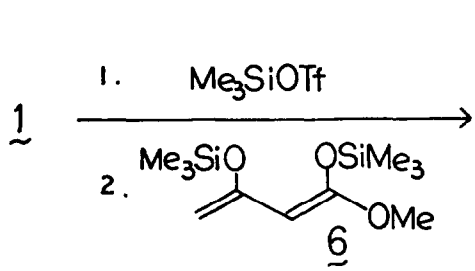


4 a-d [10]



5 e-g [10]

a) Isolated yield
b) tert-Butyldimethylsilyl enol ether was used.



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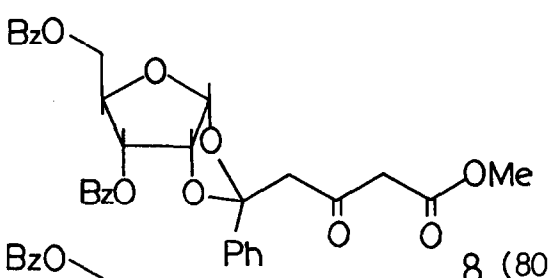
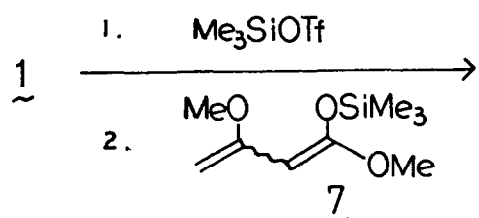


8 (80%) [10]



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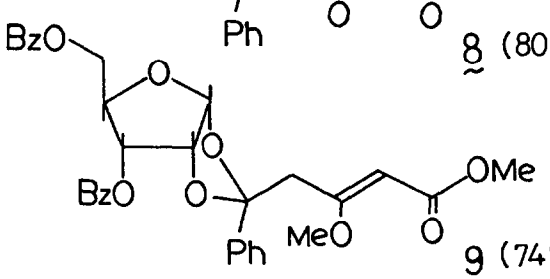

9 (74%)

group on C-1 site of 1. For example, 5e gave the corresponding desulfurization product [70% yield, ^{1}H NMR(CCl_4) δ 2.10 (3H, s), 2.79 (2H, d-like, J = 7.0 Hz] by treating with Raney nickel.

These regiochemical aspects may be in part attributable to the difference of actual nucleophlic species. ^{1}H NMR studies have revealed that 3a reacts rapidly with stannic chloride at room temperature to yield the corresponding α-trichlorostannyl carbonyl compound, but 3e is quite stable in the presence of stannic chloride. These observations have suggested that α-hetero substituents may prevent silyl-stannyl group exchange and 3e-g react with well precedented intermediate 2 in a similar manner with olefinic or aromatic substrates, whereas, with regard to 3a-d, actual nucleophiles seem to be α-stannyl carbonyl compounds which may react on C-2 benzoxyl group selectively.[9,11]

Reactions of dienol ethers (6 and 7) with 1 have also been examined, but they reacted on C-2 benzoxyl group selectively to yield 8 and 9 under the influence of trimethylsilyl trifluoromethanesulfonate.

Typical procedure is as follows. A mixture of 2,3,5-tri-O-benzoyl-D-ribofuranosyl acetate (1, 40 mg, 0.08 mmol) and stannic chloride (0.09 mmol) in dichloromethane (2 ml) was stirred for 5 min at room temperature, and the silyl enol ether (3e, 0.09 mmol) was added to it. After stirring for 1.5 h at room temperature, aq K_2CO_3 solution was added to the reaction mixture and was extracted with ether. Combined extracts were washed with satd aq NaCl, dried, and concentrated. Silica gel column chromatography of the residue gave 5e (40.2 mg, 83% yield).[10]

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9) 1-Trimethylsiloxycyclohexene is an exceptional example. Although it reacts with stannic chloride to yield α-stannylcyclohexanone, the corresponding C-1 adduct was obtained exclusively. See ref 7.
10) NMR and IR spectra are in good agreement with its structure. Spectroscopic data for typical products are as follows:
4a: The product was obtained as a mixture of the following two separable diastereomers; IR(neat) 1730, 1715 cm^{-1}; NMR(CCl_4) δ 7.84 (4H, m), 7.30 (11H, m), 5.90 (1H, d, J = 4.0 Hz), 5.10 (1H, dd, J = 5.0 and 4.0 Hz), 4.76 (1H, dd, J = 9.0 and 5.0 Hz), 4.17 (2H, m), 3.40 (1H, m), 2.93 (1H, q, J = 7.0 Hz), 2.21 (2H, q, J = 7.0 Hz), 0.99 (3H, d, J = 7.0 Hz), 0.87 (3H, t, J = 7.0 Hz): and IR(neat) 1730, 1715 cm^{-1}; NMR(CCl_4) δ 7.78 (4H, m), 7.30 (11H, m), 6.05 (1H, d, J = 4.0 Hz), 4.70 (2H, m), 4.18 (2H, m), 3.45 (1H, m), 2.90 (1H, q, J = 7.0 Hz), 2.36 (2H, q, J = 7.0 Hz), 0.97 (3H, t, J = 7.0 Hz), 0.94 (3H, d, J = 7.0 Hz).
5e: IR(neat) 1730, 1715 cm^{-1}; NMR(CCl_4) δ 7.85 (6H, m), 7.25 (14H, m), 5.68 (2H, m), 4.50 (4H, m), 3.92 (1 x 5/9H, d, J = 4.0 Hz), 3.75 (1 x 4/9H, d, J = 8.0 Hz), 2.27 (3 x 4/9H, s), 2.17 (3 x 5/9H, s).
8: IR(neat) 1730 cm^{-1}; NMR(CCl_4) δ 7.93 (4H, m), 7.38 (11H, m), 6.18 (1H, d, J = 4.0 Hz), 5.26 (1H, dd, J = 5.0 and 4.0 Hz), 4.92 (1H, dd, J = 9.0 and 5.0 Hz), 4.22 (1H, dd, J = 12.0 and 4.0 Hz), 3.64 (3H, s), 3.61 (1H, m), 3.41 (2H, s-like), 3.06 (2H, s-like).
11) The ester 3d also reacts with stannic chloride, but identification of the corresponding product is quite difficult.

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