C-Glycopyranosides from the Reaction of Acetylated Glycals with β-Diketones

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Acetylated glycals react with some β-dicarbonyl compounds in the presence of boron trifluoride or bis(benzonitrile)dichloropalladium to give *C*-glycopyranosides.

The boron trifluoride-catalysed reaction of acetylated glycals with protic nucleophiles is known as the Ferrier reaction and is used for the preparation of *O*-glycosides.[1] Recently, the carbonium ion (**1**, R = CH_2OAc), a supposed intermediate in the Ferrier reaction, was trapped with 1-trimethylsilyloxystyrene in order to investigate *C*-glycosidation reactions.[2]

We have found that some β-dicarbonyl compounds react with acetylated glycals in the presence of a boron trifluoride or bis(benzonitrile)dichloropalladium† catalyst to give *C*-glycosides.‡

A solution of di-*O*-acetylxylal (1 mmol) in acetylacetone (4 mmol) was allowed to react in the presence of $BF_3{\cdot}Et_2O$ (0.5 mmol) for 15 min, or in the presence of $Pd(PhCN)_2Cl_2$ (0.004 mmol) for 13 h, at room temperature to give an anomeric mixture (7:1) in 55 or 76% yield, respectively. On hydrogenation, the major product (**2**) gave a dihydro-compound with a $J_{4,5a}$ value of 10.8 Hz in its ^1H n.m.r. spectrum, while the minor product (**3**) gave a dihydro-compound with $J_{4,5a}$ 0.6 Hz. Therefore, the major product has the β-configuration at the anomeric centre and the minor product the α-configuration.

Table 1. The reactions of acetylated glycals with β-dicarbonyl compounds.[a]

β-Dicarbonyl compound	*O*-Acetylated glycal	Catalyst[b] (mol%)	Yield %	α : β Ratio[c]
Acetylacetone	Glycal	A (0.26)	83	4—6 : 1
,,	,,	B (50)[d]	73	5 : 1
,,	Galactal	A (10)	59	α only
,,	,,	B (50)[d]	72	α only
,,	Allal	A (1)	62	5 : 1
,,	,,	B (50)[d]	81	5 : 1
Methyl acetoacetate	Glucal	A (1)	85	4 : 1
,,	Xylal	A (0.1)	65	1 : 4
Ethyl benzoylacetate	Galactal	A (110)	65	α only
,,	,,	B (50)	81	α only
Ethyl 2-oxocyclohexanecarboxylate	Glucal	A (110)	82	[e]
,,	,,	B (50)	82	[e]

[a] The reactions were carried out as described in the text for di-*O*-acetylxylal. [b] A: $Pd(PhCN)_2Cl_2$. B: BF_3. [c] The ratio was estimated by n.m.r. spectrometry. [d] Benzene was added to form a solution. [e] Undetermined.

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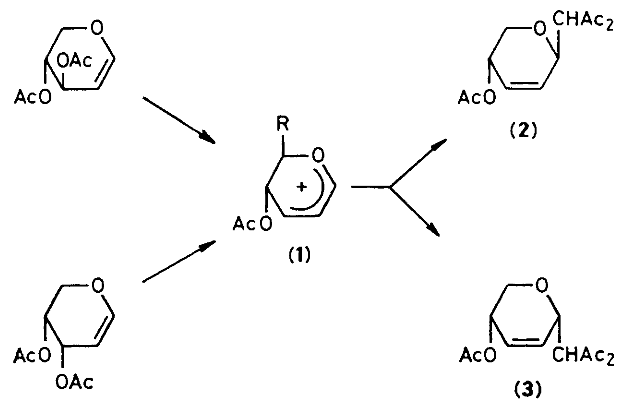
† The palladium complex also catalysed *O*-glycosidation; *e.g.*, allowing di-*O*-acetylxylal (1 mmol) to react with methanol (2 mmol) in benzene in the presence of the Pd complex (0.1 mmol) for 13 h gave 83% of methyl 4-*O*-acetyl-2,3-dideoxy-D-*glycero*-hex-2-enopyranosides[3] (α : β = 1 : 4). $PdCl_2$ was used as a catalyst for *O*-glycosidation.[4]

‡ That *C*-glycosidation has taken place is shown by the absence of the acetal carbon signal in the ^{13}C n.m.r. spectra of the product.



Di-*O*-acetylarabinal reacted similarly with acetylacetone to give the anomeric mixture in the same ratio as the acetylxylal. Consequently, both reactions must proceed *via* a common intermediate (**1**, R = H), the anomeric distribution being controlled by the steric factor.

Other examples are summarised in Table 1. The major products from tri-*O*-acetyl-glucal, -allal, and -galactal were assumed to have the α-configuration at their anomeric centre by analogy with *O*-glycosidation and the parallel result observed for *C*- and *O*-glycosidations in the pentose series.

Ethyl benzoylacetate and ethyl 2-oxocyclohexanecarboxylate did not react with the acetylated glycals in the presence of of a catalytic amount of the Pd complex but did react in the presence of BF_3. However, dipivaloylmethane, hexafluoroacetylacetone, cyclohexane-1,3-dione, isopropylidene, and dimethyl malonate did not react even in the presence of BF_3.

The *C*-glycosidation reactions described here provide a new and simple entry to chiral synthons involving versatile β-dicarbonyl functions.

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