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LETTERS

A New Route to C-Glycosylidene Compounds Mediated by Olefin Metathesis

Olivier Dirat, Thierry Vidal, Yves Langlois*
Laboratoire de Synthèse des Substances Naturelles
Associé au CNRS, ICMO, bâtiment 410, Université de Paris-sud, 91405 Orsay, France.

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Abstract: Various 1-methylene glucose derivatives afforded after ring closure olefin metathesis cyclic polyethers and C-glycoside precursors. © 1999 Published by Elsevier Science Ltd. All rights reserved.

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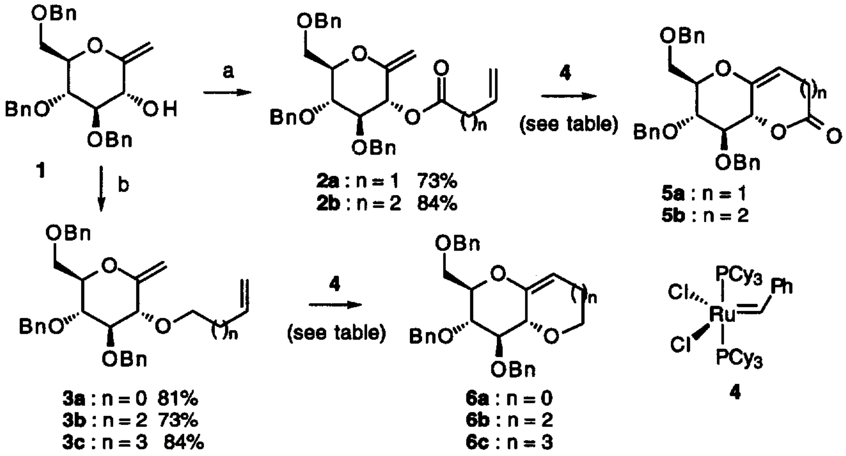
The discovery of versatile olefin metathesis catalysts by Schrock[1] and Grubbs[2] induced the conception of new strategies in synthesis[3]. Particularly, recent applications of this method to various enol ethers gave a new access to C-1 glycal derivatives[4], to fused ether ring systems[5] and to dihydropyrans[6]. An alternative to these approaches is presented in this preliminary communication using 1-exomethylene glucose derivatives as starting materials[7].

The glucose derivative **1**, obtained in 68% overall yield from 2,3,5-tri-*O*-benzyl-D-arabinofuranose by a known sequence of reactions[8,9], was classically esterified or etherified affording respectively compounds **2a**-**2b** and **3a**-**3c** in good yields (Scheme).

The olefin metatheses were performed under argon on esters and ether derivatives **2a**-**2b** and **3a**-**3c** in the presence of the Grubbs catalyst **4** in refluxing dichloromethane[10] for three days and gave rise respectively to compounds **5a**-**5b** and **6a**-**6c**[11].



Scheme : a : $CH_2CH(CH_2)_nCO_2H$, DCC, DMAP, 0°C, 15 min, 1h, R.T. b : NaH, $CH_2CH(CH_2)_nCH_2Br$, DMF, 0°C, 15 min, 1h, R.T.

E-mail : langlois@icmo.u-psud.fr

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The results are summarised in the table. Several experiments showed that the reaction was totally inhibited in toluene (see for instance, entry 2). In dichloromethane, five, six, seven and eight membered rings were obtained under these conditions. With ester derivatives **2a**, the use of sub-stoichiometric amounts of titanium tetra*iso*propoxide had little influence (entries 1 and 3), whereas an excess of this reagent decreased the yield (entry 4). Better yields were observed in seven and eight membered ring formation (entries 5, 7 and 8). The use of the commercially available Grubbs catalyst **4**, despite the density of ether functional groups, is worthy of note. In previous examples[4,5] either the use of the Schrock catalyst was necessary or the reaction was very sensitive to the presence functional groups[6].

Entry	Starting material	4 %	Ti(OiPr)4 equiv	Product	Yield %
1	**2a**	20	0	**5a**	30
2	**2a**	20	0		0 (toluene)
3	**2a**	20	0.3	**5a**	35
4	**2a**	20	3	**5a**	<10
5	**2b**	20	0	**5b**	51
6	**3a**	15	0	**6a**	20
7	**3b**	10	0	**6b**	62
8	**3c**	15	0	**6c**	54

Applications of this methodology to the synthesis of fused oxygenated heterocycles and C-glycosides are in current development.

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10) Concentrations of 1.5 x 10^{-3} M in starting material were used for these reactions.
11) Dissolution of the crude reaction products in toluene followed by evaporation under vacuum made the chromatographic purification easier, the Ru catalyst being retained at the top of the column chromatography.