New Results on the Functionalization of Terminal Alkenes by Cross-metathesis Reactions

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Abstract: The ruthenium-catalyzed reaction of allylbenzene with several types of alkene provides good yields of the cross-metathesis products regardless of the structural characteristics of the alkene.

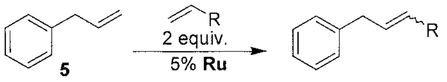
Key words: Cross-metathesis, Ruthenium, allylic bromides.

In the course of our research on sugars we wished to prepare the mannose derivative **4**. Our first approach, involving a Wittig-Horner reaction between the aldehyde **1** and the stabilized anion of phosphonate **2**, afforded very low yields whatever the base and reaction conditions used. We then decided to try an intermolecular cross-metathesis reaction[1], despite the lack of precedents, because the necessary precursors are readily prepared. Compound **3**[2] reacted with acrolein dimethyl acetal in the presence of 5% of Grubbs' catalyst ($Cl_2(PCy_3)_2Ru = CHPh$; **Ru**) to give compound **4** in 77% yield with a 20:1 E/Z ratio (Scheme 1)[3].

There is considerable uncertainty as to the factors that influence the selectivity of intermolecular metathesis reactions: some authors[4–6] suggest that electronic factors predominate, while others[7,8] seem to have found that steric parameters and the influence of neighbouring heteroatoms may be the most important determinants of high selectivity. In view of this, the finding that the reaction of Scheme 1 was highly selective for cross-metathesis, no self-metathesis products having been detected, led us to study this type of process more thoroughly. Using allylbenzene as reference alkene and two equivalents of the alkene partner, we found that the reaction proceeds cross-selectively for a variety of olefins (Table 1)[9]. The results obtained with allyltrimethylsilane and allyloxytrimethylsilane are similar to those previously reported by other authors[10,11]. However, reports that electron-poor olefins do not participate in **Ru**-catalyzed cross-metathesis reactions[12,13] were not corroborated: on the contrary, we found that acrylonitrile and acrolein couple to allylbenzene with high cross-selectivity and in good yield. We also obtained good results with allylalcohol, allylacetamide and in particular allylbromide. The unprecedented achievement of cross-metathesis with this last reagent shows that the presence of a neighboring heteroatom is not strictly necessary for cross-selectivity[9].

Although both allylbenzene and the other olefins underwent self-metathesis when subjected to the reaction conditions in the absence of a partner[14], no significant amounts of self-metathesis products were detected when the two partners were present in the above 1:2 ratio; as expected, when just one equivalent of the second olefin was used, the self-metathesis product of allylbenzene was obtained in 20% yield as well as the cross-metathesis product (39%). In conclusion, the cross-metathesis reaction is favoured under the reaction conditions described above, is not totally dependent on the structural characteristics of the alkenes, and constitutes a simple method for functionalization of a variety of terminal olefins. It should prove particularly useful for obtaining primary allylic bromides, a type of compound of great synthetic value.

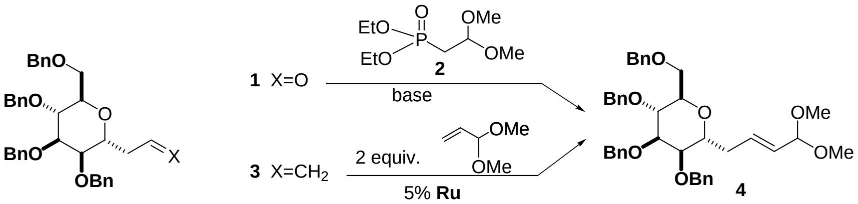
Table 1. Cross-metathesis reactions of allyl compounds.



Entry	R_1	E/Z^a	Yield
1	CN	1:1.5	60
2	CHO	3:1	72
3	$CH(OMe)_2$	20:1	59^b
4	CH_2TMS	1.2:1	64
5	CH_2OTMS	2:1	79
6	CH_2NHAc	9:1	49
7	CH_2Br	3.3:1	65
8	CH_2OH	3:1	72
9	CH_2Ph	4:1	82

[a] *E/Z* ratios were determined by NMR spectroscopy.

[b] 15% yield of unprotected aldehyde was also isolated.



Scheme 1

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(4) 1-α-Allyl-2,3,4,6-tetra-*O*-benzyl mannopyranoside (**3**; 800 mg, 1.42 mmol) and acrolein dimethyl acetal (290 mg, 2.83 mmol) were dissolved in 30 mL of CH_2Cl_2 under argon. $Cl_2(PCy_3)_2Ru = CHPh$ was added (0.07 mmol, 57 mg) and the mixture was refluxed for 16h. The solvent was removed under reduced pressure and the product purified by flash chromatography on silica gel. Compound **4** was obtained in 77% yield (697 mg) and 20:1 E/Z ratio. ^{1}H NMR(250 Hz, $CDCl_3$) (7.27-7.09 (m, 20 H), 5.91-5.81 (dt, J = 15.8, 6.60 Hz, 1H), 5.59-5.50 (dd, J = 15.8, 5.10 Hz, 1H), 4.81-4.72 (dt, J = 7.3, 5.39 Hz, 2H), 4.68-4.57 (m, 7H), 4.17-4.09 (m, 1H), 3.96-3.77 (m, 5H), 3.71-3.67 (dd, J = 4.80, 3.03 Hz, 1H), 3.33 (s, 6H), 2.47-2.39 (dd, J = 10.87, 6.60 Hz, 2H). ^{13}C NMR(128.89-128.03, 103.51, 77.08, 75.70, 75.32, 74.28, 74.17, 73.80, 72.62, 72.52, 71.95, 69.53, 53.33, 53.12, 33.58.

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(10) Metathesis reactions were carried out following the procedure described for compound **4**. All compounds were characterized by ^{1}H and ^{13}C NMR, IR and mass spectrometry. E/Z isomer ratios in the crude final reaction mixture were calculated from 500 MHz NMR integrals, and the major isomer was identified from the coupling constants of the olefinic hydrogens.

(11) For instance, refluxing allylalcohol in dichloromethane for 16 h in the presence of **Ru** gave the dimer in 90% yield.

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