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E/Z product distribution in the metathesis of allyl alcohol derivatives with a first generation ruthenium-based catalyst

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ABSTRACT

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Olefin metathesis mediated by a ruthenium catalyst has become a standard reaction for the creation of new carbon-carbon bonds.¹ Whereas a Z-geometry for the new double bond can be expected with reactions forming medium-sized rings, an increasing proportion of *E*-alkene is produced as the ring-size increases. Cross-metathesis reactions, which result in acyclic alkenes, typically give mainly E-alkenes. E/Z ratios are believed to be determined largely by equilibration, that is, the ratios are based on the relative stabilities of the isomers.²

Grubbs³ proposed the cross-metathesis reaction of allylbenzene with Z-1,4-diacetoxy-2-butene (3c) as one of six metathesis reactions to be used when evaluating metathesis catalysts. Various catalysts were compared, and a significant difference was noted between 'first generation', for example, 1, and the more active 'second generation' catalysts, for example, 2, which have an



Based on experiments with four simple derivatives of allyl alcohol, it has been shown that the product of cross-metathesis as mediated by a 'first generation' ruthenium catalyst increases in its proportion of the *E*-isomer as the reaction progresses. This increase is due to equilibration, which is also mediated by the ruthenium catalyst.

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N-heterocyclic carbene ligand. Whereas the E/Z ratios of the products using the first generation catalysts changed very little as the reaction progressed, with the second generation catalysts the proportion of the E-isomer increased dramatically as conversions progressed beyond 70%. This was ascribed to the fact that the more active, N-heterocyclic carbene-based catalysts should encourage reversible, 'secondary' metathesis events and lead to a thermodynamic blend with a higher proportion of the *E*-isomer.⁴ In the course of a routine cross-metathesis reaction involving the first generation catalyst **1**, we noted changes in the E/Z ratio of the product. As this seemed at odds with the report that metathesis reactions mediated by **1** would not undergo significant equilibration, we set out to determine whether our reaction was anomalous by examining the cross metathesis reactions of some simple substrates.

The self-coupling reactions of four readily available derivatives (3a-6a) of allyl alcohol were conducted in the presence of 5 mol % of catalyst 1.⁵ The reactions were conducted in benzene at 40 °C under an atmosphere of slow-moving nitrogen, with the initial concentration of the alkene being 0.10 M (Scheme 1).



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Table 1Isolated yields and E/Z ratios from the metathesis reactions shown in Scheme 1 as afunction of time

Alkene	Yield of cross-metathesis products, <i>E</i> / <i>Z</i> ratio			
	5 min	30 min	4 h	24 h
3a	16%, 4.4:1	27%, 4.6:1	34%, 5.3:1	58%, 5.7:1
4a	68%, 4.4:1	66%, 6.4:1	69%, 7.2:1	62%, 7.6:1
5a	23%, 1.9:1	41%, 3.0:1	66%, 6.4:1	61%, 7.9:1
6a	35%, 7.7:1	46%, 9.7:1	59%, 16:1	51%, 18:1

The acetate **3a** reacted relatively slowly (Table 1). The reaction of **3a** required 24 h for the yield of the 1,4-diacetoxy-2-butenes **3b,c** to surpass 50%, and over that time the ratio of the *E*- and *Z*-isomers increased modestly from 4.4:1 after 5 min up to $5.7:1.^{6}$ In contrast, the benzyl ether **4a** underwent metathesis quickly, and the isolated yield after 5 min was the same as after 4 h. The yield after 24 h was a little lower, which likely reflected some destruction of the products. In spite of little change in the combined yield of the 2-butene products **4b,c**, the *E*/*Z* ratio rose from an initial ratio of 4.4:1 up to 7.6:1.

The tritylated derivative **5a** and the *tert*-butyldimethylsilyl derivative 6a both reacted more slowly than did 4a, and the isolated yields of the 2-butene products **5b,c** and **6b,c** were at their highest after 4 h. However, with these substrates the E/Z ratios continued to increase over the next 20 h. After 24 h the ratio of tritylated products 5b/5c had risen from 1.9:1 to 7.9:1. The idea that a product of direct decomposition of the catalyst, which would accumulate with time while the reaction was heated, was responsible for E/Z isomerization was not consistent with the following experiment. A solution of 1 was heated in benzene to 40 °C for 5 h. Then, 5a was added, and the mixture was heated for 30 min under conditions that were the same as used for the results in Table 1. The yield of **5b,c** was 29%, as opposed to 41% with 'fresh' catalyst, and so heating the catalyst had clearly degraded some of the catalyst. However, the **5b/5c** ratio was only 2.2:1, as opposed to 3.0:1 with 'fresh' catalyst: therefore, a decomposition product was not enhancing the ratio of E/Z in this instance.⁷ Carrying out the reaction of **5a** in the presence of 2.5 mol % of **1** resulted in no significant differences in the evolution of the E/Z ratios.⁸

The silylated derivatives **6b**,**c** were obtained with a **6b**/**6c** ratio of 18:1 after 24 h. It seemed that the bulkier derivatives led to a greater preponderance of the *E*-isomer after time. The increases in *E*/*Z* ratios over time did not appear to be due, to a significant extent, to a selective degradation of the *Z*-isomer. This is because the increases in *E*/*Z* ratios between the 30 min and the 4 h reactions were accompanied by increases in the yields of the metathesis products, not decreases. The data are more consistent with equilibration of the products via secondary metathesis from a kinetically derived mixture with a low *E*/*Z* ratio to a thermodynamic mixture with a higher *E*/*Z* ratio.

The yields of the cross-coupled products did not progress beyond 70%. Indeed, prolonging the reaction time resulted in an erosion of yield, which one presumes was due to slow secondary reactions of the products. Two experiments were conducted in which a total of 2.5 mol % of **1** was added using **5a** as the substrate at the same initial concentration in benzene at 40 °C for 48 h. In the first instance, the catalyst was added all at once. In the second, the catalyst was added in four equal portions every 12 h. The yield of the first experiment was 49% and the **5b/5c** ratio was 8.4:1. The yield of the second experiment was 67% and the **5b/5c** ratio was 11:1. The yield of this second experiment was no improvement over the yield after 4 h, but the *E/Z* ratio was significantly enhanced. In contrast with the initial experiments, these experiments had been conducted in sealed vessels from which the byproduct of cross-metathesis, ethene, would not have escaped. Some metathesis reactions, especially enyne metathesis,^{9,10} have been improved in terms of yield and E/Z ratio when the reactions were conducted under an atmosphere of ethene. The rationale¹⁰ for the improved E/Z ratio is that the products of the primary metathesis, that is, kinetic products, undergo further metathesis with ethene to give a terminal alkene, which in turn undergoes metathesis again with the initial alkene substrate to provide, after many cycles, thermodynamic products via secondary metathesis. *N*-Heterocyclic carbene- and phosphine-based ruthenium catalysts have been employed in enyne metathesis under ethene. Thus, the presence of ethene was expected to encourage equilibration of the cross-metathesis products.

When 0.1 M benzene solutions of **5a** with 2.5 mol % of **1** were maintained at 40 °C under an atmosphere of ethene, the **5b/5c** ratio was 11:1 after 2 h, and this did not change over the next 24 h. After 2 h the yield of the self-coupled products was 27%, but after 24 h the yield was still only 32%. It appeared that the thermodynamic E/Z ratio (ca. 11:1) had been reached, but under the ethene atmosphere the equilibrium between **5a** and its cross-metathesis products **5b,c** was favouring **5a**. When a crossmetathesis reaction of **5a** was carried out with 2.5 mol % of **1** as above, but for 3 h under N₂ and then 1 h under ethene, the **5b/5c** ratio of the product was 11:1 and the yield was 45%. The E/Z ratio was larger than the corresponding experiment in Table 1 after 4 h, but the yield was lower. This was presumed to be due to reversion of some of the product to **5a**.

If the E/Z ratios of cross-metathesis reactions are established by equilibration, even with a first generation catalyst such as **1**, then the efficiency of equilibration could be assessed by comparing the equilibration of the *Z*-compounds **3c**-**6c** under the usual conditions for cross-metathesis. Accordingly, benzene solutions of samples highly enriched in **3c**-**6c** were warmed to 40 °C under atmospheres of nitrogen gas and of ethene for 10 min in the presence of catalyst **1**. The results are presented in Table 2.

The implications of the experiments under the nitrogen atmosphere were that the equilibration of the Z-isomers **3c-6c** was rapid. Also, equilibration mediated by **1** did not require the presence of some of the allvl compound **3a-6a**. Nevertheless, the recovery of product was not quantitative in any instance. Equilibration was even more rapid under ethene, which implied that equilibration via the allyl compound is more rapid. The equilibration of the diacetate substrate 3c was anomalous in that the proportion of the E-isomer **3b** was greater under the nitrogen atmosphere than under ethene. This is important because with catalyst 1, substrate **3c** is known to homologate an alkene with higher *E*-selectivity than the more reactive allyl acetate **3a**.¹¹ Our results suggest that the reverse might be true if the acetyl protecting group on the substrate were exchanged for a benzyl, trityl or TBDMS group. In every instance with ethene, the recovery of isomerized products 3b,c-**6b,c** was very poor even after just 10 min with much of the substrate having reverted to the allyl compound **3a-6a**. In a similar way, ring-opening metathesis with 1 under an atmosphere of ethene can provide the ring-opened product without subsequent metathesis reactions taking place.¹²

Table 2

Isolated yields and *E*/*Z* ratios from the treatment of 3c-6c (0.1 M) in benzene in the presence of 1 (2.5 mol %) at 40 °C for 10 min

Alkene	Yields and E/Z ratios		
	N ₂ atmosphere ^a	CH ₂ CH ₂ atmosphere ^b	
3b/c 1:48	90%, 1:5.3	48%, 1:10	
4b/c 1:23	83%, 1:2.9	33%, 3.1:1	
5b/c 1:40	86%, 1:23	21%, 1:5.3	
6b/c 1:13	96%, 1.2:1	20%, 2.6:1	

^a Reaction conducted under a slow stream of dry N₂.

^b Reaction conducted under a slow stream of ethene.

In conclusion, it has been demonstrated that E/Z equilibration is a significant process with a first generation ruthenium catalyst, in contrast with the result of a previous study.³ However, the rate of equilibration becomes competitive with degradation of the product as the product approaches its equilibrium ratio. In other words, the formation of cross-metathesis products with higher E/Z ratios requires longer reaction times, but this is at the expense of the overall yield of the products. Addition of ethene certainly accelerates equilibration, but the effect on yield can be disastrous because the metathesis equilibrium can rapidly move too far towards the starting alkene.

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