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Ruthenium catalysed cross metathesis with fluorinated olefins

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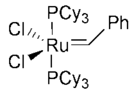
The *E*-selective cross metathesis (CM) of fluorinated olefins with various functionalised alkenes in good to excellent yields is reported.

In the last decade ruthenium catalysed olefin metathesis has emerged as a powerful synthetic tool for the formation of carbon–carbon bonds.[1] There is growing interest in fluorinated molecules, with their particularly interesting chemical, biological and physical properties.[2] For instance, a high electronegativity together with an atomic size close to hydrogen have made these compounds useful components of both pharmaceuticals and agrochemicals. This, in addition to the selective solubilities of perfluorinated molecules and the advent of new possibilities with fluorinated phases,[3] encouraged us to prepare fluorine-substituted olefins *via* a CM methodology. There has been one report concerning this subject, however the yield of the cross product was modest.[4] Recently we have demonstrated[5,6] that reactivity and selectivity in Ru-catalysed CM reactions depend strongly on the electronic properties of both the ligand and Ru–carbene complex. In line with this earlier work, we expected that phosphine-free catalyst **3**[6,7] would show superior activity and stability in CM reactions involving electron deficient fluoroalkenes than either **1** or **2**.[8]



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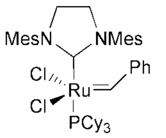

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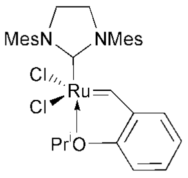

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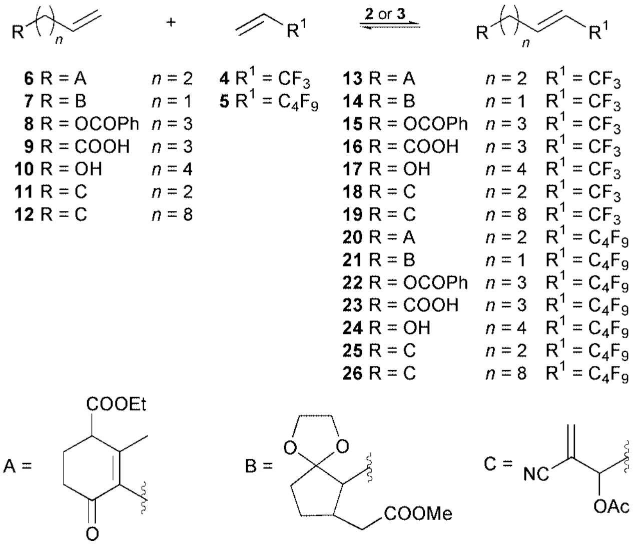
Cy = cyclohexyl   Mes = 2,4,6-trimethylphenyl

Herein we report the CM of various functionalised olefins with 3,3,3-trifluoropropene **4**† and 3,3,4,4,5,5,6,6,6-nonafluorohexene **5**,‡ as models for molecules with varying degrees of fluorine substitution using catalysts **1**, **2** and **3**. Preliminary experiments using terminal olefins **6**–**12**[9] (Scheme 1) with up to five equivalents of **4** in a closed flask at 45 °C under atmospheric pressure, resulted in quantitative dimerisation of the more electron rich substrates. In order to suppress the dimerisation reaction in the presence of **4**, the flask was equipped with a balloon containing 10 equivalents of **4**. In the case of **5**, 10 equivalents of nonafluorohexene were used as a solvent to achieve good yields of the products **20**–**26**. It was found that α,α,α-trifluorotoluene could be used successfully as an additive to overcome the insolubility of **1**, **2** and **3** in **5**. Using **2**, best results were achieved stirring the reaction mixture at 60 °C for 4 h, whereas reactions catalysed by **3** gave higher yields of CM products under milder conditions (45 °C, 3 h). The results of these experiments are presented in Table 1.

Using substrates **6**–**10** with ester, carboxylic acid, ketone and hydroxy functionalities (Scheme 1), general conversions to CM products (**13**–**17** and **20**–**24**) and dimers were good to excellent. CM reactions with the fluoroolefin were generally favoured over dimerisation, except where the substrate contained a hydroxy group; this effect could be due to the poor solubility of these substrates in the fluorinated media. The nitrile derivatives **11** and **12**, which contain both electron deficient and relatively electron rich terminal double bonds, were chosen to investigate chemoselectivity. Irrespective of the catalyst, fluoroalkene substrates or reaction conditions, the nitrile derivatives with an unprotected hydroxy group were not converted to CM products, giving only starting materials in all cases. The corresponding acetylated derivatives **11** and **12** gave good to excellent conversions, however **11** showed disappointing yields of CM products (**18**, **25**) due to competitive ring-closing metathesis (RCM), giving a ratio of about 50% of RCM in three cases and 6% of RCM using the combination of catalyst **2** and fluorinated olefin **5**. In the case of the larger homologue **12**, formation of the eleven membered RCM product is unfavourable, and hence



Scheme 1

Table 1 CM reactions of fluorinated olefins using **2** and **3**

		Yield[a] (%)		Dimer[a] (%)	
Substrate	Product	Cat. 3	Cat. 2	Cat. 3	Cat. 2
6	**13**	⩾95[b]	41	0	33
7	**14**	⩾95[b]	77	0	10
8	**15**	⩾95[b]	85	0	5
9	**16**	70	58	19	23
10	**17**	75	50	18	50
11	**18**	50	16	0	19
12	**19**	⩾95[b]	⩾95[b]	0	0
6	**20**	90	40	10	45
7	**21**	79	38	21	42
8	**22**	⩾95[b]	⩾95[b]	0	0
9	**23**	59	42	41	56
10	**24**	7	21	79	73
11	**25**	57	13	0	47
12	**26**	⩾95[b]	24	0	35

[a] CM product and dimer yields determined by ^{1}H NMR. [b] Only CM product detected by ^{1}H NMR.

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higher yields of the CM products **19** and **26** could be obtained.

These CM reactions proved to be chemoselective, *i.e.* only coupling between the fluorinated olefins and the more electron rich, monosubstituted double bond was observed in all cases.

No difference in reactivity or selectivity was found when the fluoroolefin was varied from **4** to **5**, with the exception of when **10** was used as the CM partner. In this case the poor solubility of **10** in **5** (also observed with the unprotected forms of **11** and **12)** possibly explains the lack of activity with this substrate.

Consistent with our earlier findings,[6] **3** gave superior conversions and higher yields of CM products than **2**. Bisphosphine complex **1** proved inactive in these systems, giving neither CM nor dimerisation products regardless of the reaction conditions.

CM processes are generally known to exhibit a moderate *E*-selectivity,[10] favoured when the substrates contain bulky substituents.[4] We found that all CM products (**13–26**) had an *E*/*Z* ratio of $\geqslant 20:1$. The stereoselectivity of fluorinated olefins with a variety of functionalised alkenes should further increase the synthetic utility of this reaction.

In summary, we have shown that stereoselective CM reactions between **4** and **5** with a variety of alkenes are possible in good yields. With the exception of hydroxy substrates, catalysts **2** and **3** both gave good conversions to CM, dimerisation and RCM products, whereas **1** proved unsuitable for these purposes. Product ratio analyses show that **3** is a better catalyst for CM than **2** in this system.[6]

Further studies in the use of selective CM reactions are underway in our laboratories. The results of these investigations will be reported in due course.

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Notes and references

† Procedure for CM reactions with **4** and **2** or **3**: to a solution (0.05 M) of **6** (78 mg, 0.410 mmol) and catalyst **3** (12.6 mg, 5 mol%) in trifluorotoluene (10 mL) under N_2 was added gaseous **4** (100 mL, 4.46 mmol) *via* a needle, the atmosphere being maintained by a balloon. The resulting solution was stirred at 45 °C for 3 h (60 °C for 4 h for **2**). Removal of the solvent *in vacuo* gave a brown oil which could be purified by flash chromatography (hexane–EtOAc).

‡ Procedure for CM reactions with **5** and **2** or **3**: to a mixture of **6** (80 mg, 0.420 mmol) and **5** (1.033 g, 4.200 mmol) was added catalyst **3** (12.9 mg, 10 mol%) in trifluorotoluene (61.3 mg, 0.420 mmol) under N_2. The resulting solution was stirred at 45 °C for 3 h (60 °C for 4 h for **2**). Removal of the solvent *in vacuo* gave a brown oil which could be purified by flash chromatography (hexane–EtOAc). The excess of **5** could be recovered by distillation.

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