

Vacuum-driven anionic ligand exchange in Buchmeiser–Hoveyda–Grubbs ruthenium(II) benzylidenes

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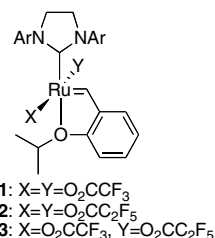
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Abstract—Vacuum-driven anionic ligand exchange of a perfluorocarboxylic acid with ruthenate-bound perfluorocarboxylates is demonstrated and allows for a novel entry to solid-supported ruthenium benzylidenes.
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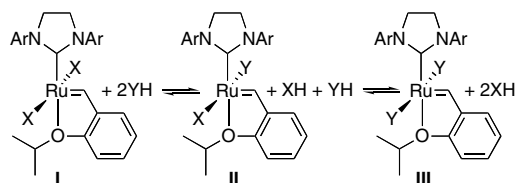
The introduction of well-defined ruthenium benzylidene complexes as pre-catalysts for olefin metathesis has had a tremendous impact on organic synthesis.¹ Subsequently, immobilisation of such complexes on a solid support or to a soluble polymer to reduce both the residual ruthenium content in the organic product and to facilitate recycling has attracted much attention.² A potential additional advantage of immobilisation is to enhance catalyst lifetime by preventing bimolecular decomposition.³ Immobilisation on a solid-support has been variously achieved through a phosphine ligand,⁴ via alkylidene exchange,⁵ or through an *N*-heterocyclic carbene⁶ and the resulting immobilised benzylidenes have been examined for metathesis activity. Immobilisation has also been achieved at the ‘anionic’ position by replacing the ubiquitous chloride ligand with a solid-supported perfluorocarboxylate.⁷ We have recently reported that anionic ligands on Hoveyda–Grubbs benzylidenes are subject to bimolecular ligand exchange.⁸ We now show that ruthenium benzylidene perfluorocarboxylates undergo equilibrium exchange with free perfluorocarboxylic acids also. This leads to a novel protocol for the immobilisation of ruthenium benzylidenes onto a polymer-supported perfluorocarboxylic acid by application of reduced pressure (vide infra).

Keywords: Ruthenium benzylidene; Metathesis; Solid-supported catalyst.

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We have previously shown⁸ that when equimolar quantities of perfluorinated carboxylates **1** and **2** are mixed in THF, an equilibrium is rapidly established (1 h) to give a 1:2:1 mixture of **1**:**3**:**2**. We now further report that when perfluorocarboxylate **2** was treated with trifluoroacetic acid (2 equiv) in THF for 2 h, a 1:2:1 equilibrium mixture of **2**:**3**:**1** was also established, where pentafluoropropanoic acid was liberated (Scheme 1; experiment A).

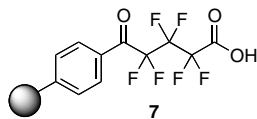


Experiment A: X=C₂F₅CO₂; Y=CF₃CO₂: I = **2**; II = **3**; III = **1**
Experiment B: X=CF₃CO₂; Y=C₇F₁₅CO₂: I = **1**; II = **5**; III = **6**

Scheme 1. Anionic ligand exchange with free perfluorocarboxylic acid.

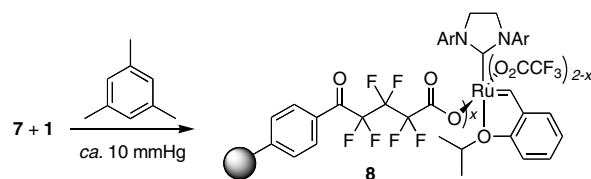
It follows from the above result that such exchange could be driven to completion if a suitable volatile product could be removed from the reaction mixture under reduced pressure. To test this strategy, mesitylene (bp 165 °C) was selected as a non-volatile solvent (relative to THF) and pentadecafluorooctanoic acid (**4**) was selected as a non-volatile (bp 189 °C at 736 mmHg) perfluorinated carboxylic acid. In a control experiment perfluorocarboxylic acid **4** was allowed to exchange with ruthenium trifluoroacetate **1** (Scheme 1; experiment B). The expected 1:2:1 equilibrium position of **1**:**5**:**6** was obtained as determined by inspection of the ¹H NMR spectrum in the benzylidene region: **1** (δ_{H} 17.51 ppm); **5** (δ_{H} 17.59 ppm); **6** (δ_{H} 17.64 ppm). Free trifluoroacetic acid (TFA) (bp 72 °C) was therefore liberated. Conducting the same experiment under reduced pressure (ca. 10 mmHg) resulted in quantitative conversion to the bis-substituted long-chain perfluorinated carboxylate **6**. As predicted and desired, the equilibrium had been driven to the right hand-side by removal of the liberated TFA—the most volatile component of the mixture.

Having shown that it is possible to drive these equilibria under reduced pressure, we used this method to immobilise benzylidene **1** on a solid support. 4-Bromopolystyrene (50–100 mesh, 1% DVB, 1.9 mmol g⁻¹) was converted into an activated organometallic with *i*-Pr(*n*-Bu)₂MgLi following the method of Spring and co-workers.⁹ Subsequent treatment with hexafluoroglutaric anhydride and quenching with TFA gave polymer-supported perfluorocarboxylic acid **7** as an off-white resin with a loading of 1.3 mmol g⁻¹.[†]



[†]Procedure for the preparation of resin **7**: A solution of *i*-Pr(*n*-Bu)₂MgLi (4 mmol, 1.33 equiv 20.0 mL, 0.2 M) in THF:hexanes was added dropwise via syringe over 5 min at 0 °C to pre-swelled 4-bromopolystyrene beads (1606 mg, 3 mmol, 1 equiv, 1.9 mmol g⁻¹, 50–100 mesh, 1% divinylbenzene) in THF (20 mL) under nitrogen. The mixture was allowed to stir at 0 °C for 12 h. The resulting beads were pale yellow in a colourless solution. Freshly distilled hexafluoroglutaric anhydride (1.6 mL, 12 mmol, 3 equiv) was added in portions over 5 min to the stirred resin at 0 °C, taking care to keep the temperature from rising above 2 °C. The mixture was allowed to warm to room temperature over 2 h. The entire mixture was then transferred by wide-bore pipette to a solid-phase-extraction sinter set-up (10 mL volume). The solvent was drained and the solid washed with THF (3 × 10 mL), MeOH–CH₂Cl₂ 1:1 (3 × 10 mL), CH₂Cl₂ (3 × 10 mL), THF (3 × 10 mL) then alternating TFA and THF (both 3 × 10 mL), all under a nitrogen atmosphere with 1 min vacuum assisted nitrogen stream drying between washes. The beads turned a dark orange and exothermed when in TFA. After 16 h drying, the functionalised resin was collected as an off-white solid (2127 mg).

Bromine XRF analysis showed 440 ppm (440 μg g⁻¹) bromine in a sample of 147 mg functionalised resin **7** made up to 3 g with poly-4-vinylpyridine, that is, 1.3 mg (16.5 μmol) bromine in 147 mg functionalised resin indicating therefore that 92% of the original bromine had reacted, giving a loading of 1.3 mmol g⁻¹.



Scheme 2. Vacuum-driven immobilisation.

Vacuum-driven exchange was then utilised for immobilisation on the resin: ruthenium benzylidene **1** and resin **7** were combined in mesitylene and subjected to reduced pressure (ca. 10 mmHg).[§] The characteristic lilac colour of benzylidene **1** in solution was used to monitor the extent of vacuum-driven exchange. After 12 h, the solution was colourless and the resin was dark purple (Scheme 2, Fig. 1). In a control experiment without the application of vacuum, the solution remained lilac. Resin **8** was isolated by simple filtration and analysed for ruthenium loading by XRF.[¶] It is apparent that this novel protocol is an expedient method for the immobilisation of ruthenium benzylidene trifluoroacetates onto a solid-support.

Resin **8** was tested for catalytic activity in the standard¹⁰ ring-closing metathesis of diallylmalonate **9** into cyclopentene **10** with dichloromethane as the solvent at room temperature (Scheme 3, Table 1).

The results show that the polymer-supported catalyst **8** is active for metathesis and that it can be recycled. We calculated a TON of 92 at a loading of 5 mol % at 20 °C. However, the activity is much reduced compared to its homogenous counterpart **1** (TON 590, 0.05 mol %, 20 °C). This is not unexpected, since Mol,^{7a} Buchmeiser^{7c} and Blechert^{7d} have reported metathesis catalysts of reduced activity compared to their homo-

[§]Procedure for immobilisation: Off-white perfluorocarboxylic acid resin **7** (160 mg, approx. 1.3 mmol g⁻¹, 0.2 mmol) was suspended in mesitylene (2 mL). A bright lilac solution of ruthenium benzylidene **1** (31 mg, 0.04 mmol) in THF (1 mL) was added and the mixture subjected to reduced pressure (ca. 20 mm/Hg) with shaking for 16 h. Upon filtering and washing with THF (3 × 30 mL) and CH₂Cl₂ (3 × 30 mL) the product was obtained as lilac-coloured beads (181 mg, 95% of mass gain expected for 100% double immobilisation, that is, $x=2$ in Scheme 2) with a loading of ca. 0.22 mmol g⁻¹. The filtrate was clear and essentially colourless (cf. photographs in Fig. 1).

[¶]An immobilisation run using perfluorinated carboxylic resin **7** (320 mg, approx. 1.3 mmol g⁻¹, 4 equiv 0.42 mmol) and benzylidene **1** (78 mg, 1 equiv 0.1 mmol) gave resin **8** as lilac beads (369 mg). The filtrate was pale lilac, and ruthenium XRF analysis indicated 37 ppm ruthenium in the 40 mL of concentrated filtrate (on calibration against two standards). This corresponds to 1480 μg (14.7 μmol) ruthenium in the filtrate, that is, 15% of the original ruthenium, indicating 85% immobilisation. XRF analysis on the resin gave 2880 ppm (2880 μg g⁻¹, 28.5 μmol g⁻¹) ruthenium content in 361 mg catalyst functionalised resin, made up to 3.17 g with poly-4-vinylstyrene (calibrated against standards at 0 and 2000 ppm). This equates to 9.13 mg (90.3 μmol) ruthenium per 361 mg resin, or 9.33 mg (93.3 μmol) for the total 369 mg resin, that is, 93% of the input ruthenium catalyst had been immobilised. This gives a resin loading of ca. 0.24 mmol g⁻¹.

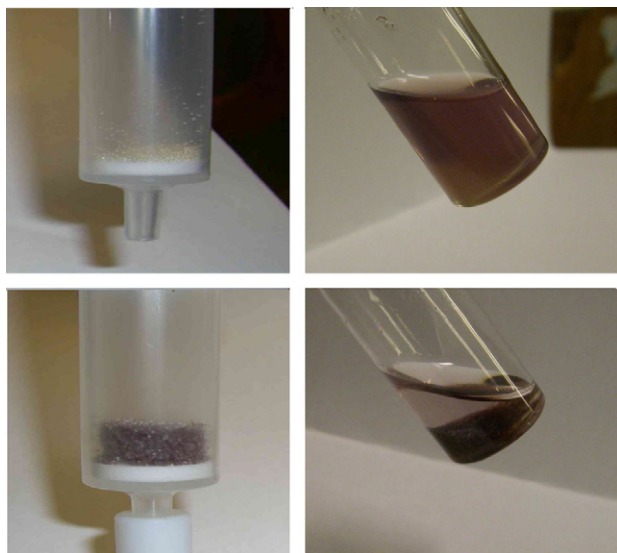
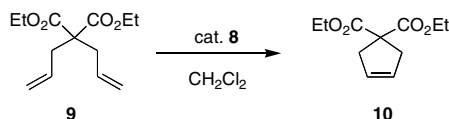


Figure 1. Top-left: resin **7**; top-right: resin **7** and benzylidene **1**; bottom right: after vacuum-driven exchange; bottom-left: the isolated resin **8**.



Scheme 3. Ring-closing metathesis with **8**.

Table 1. Ring-closing metathesis with resin **8**^a

Run	Time (h)	% Conversion ^b
1	48	100
2	48	100
3	96	100
4	96	100
5	96	60

^a Metathesis runs were performed with 80 mg of resin **8** and 100 μL of diallylmalonate **9** (ca. 20 equiv) in CD_2Cl_2 (0.6 mL) at room temperature. After the indicated time the reaction mixture was filtered, and the resin washed with CH_2Cl_2 (3×5 mL). The resin was then re-suspended in CD_2Cl_2 (0.6 mL) and the next batch of malonate (100 μL) added.

^b As determined by ^1H NMR.

geneous variants when immobilised through the ‘anionic’ position. It remains an open question as to why this is so, and should be the direction of further research.

In conclusion, we have shown that free perfluorocarboxylic acids can exchange directly with ruthenate-bound perfluorocarboxylates. By judicious choice of non-volatile solvent and perfluorocarboxylic acid this equilibrium can be driven to a single component by removal of the liberated TFA under reduced pressure. This protocol can be used for the preparation of homogeneous species or for the purpose of immobilisation.

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