Thymine functionalised polymers *via* living ring-opening metathesis polymerisation

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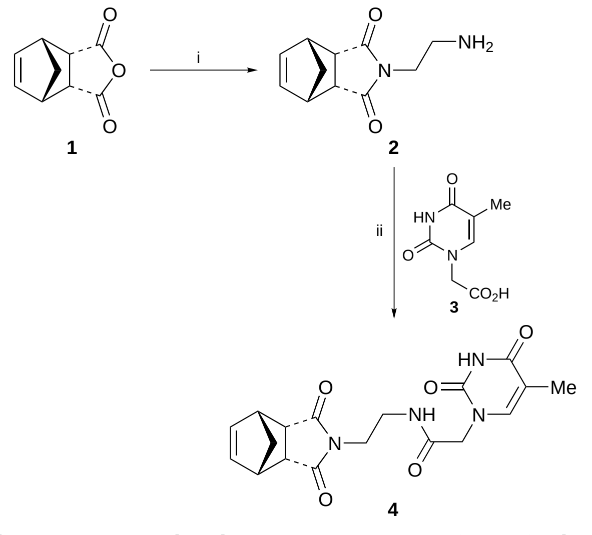
Thymine functionalised poly(norbornene)s are synthesised *via* living ring-opening metathesis polymerisation using the ruthenium initiator $\{RuCl_2(CHPh)[P(C_6H_{11})_3]_2\}$.

In recent years there has been rapid progress in the controlled assembly of polymers *via* living chain-growth polymerisation. Some of the most dramatic advances have occurred in ring-opening metathesis polymerisation (ROMP),[1] where well-defined transition metal initiators allow control over many aspects of the polymer assembly, including its molecular weight and molecular weight distribution,[2] alkene backbone configuration[3] and tacticity.[4] An important recent addition to the armoury of initiators is the ruthenium system introduced by Grubbs,[5] which has been shown to give the widest tolerance yet of key functionalities, including aldehydes, primary amines and most significantly the Brønsted acid groups OH and CO_2H. Thus, it is now possible to address the controlled synthesis of highly functionalised polymers incorporating features of complex biological macromolecules. In a previous report[6] we described the synthesis of polymers derived from amino ester-containing monomers, and the synthesis of polymers from carbohydrate derived monomers has also been disclosed.[7–9] Here, we report the application of ring-opening metathesis polymerisation to the synthesis of nucleotide base functionalised poly(norbornene)s, synthetic macromolecules that may be viewed as a first step *en route* to all-carbon backbone analogues of deoxyribonucleic acid (DNA).

The nucleotide base-substituted monomer **4** was prepared according to Scheme 1. Treatment of himic anhydride **1** with excess ethylenediamine in refluxing toluene gave monoamine **2**‡ in 30% yield. Coupling of amine **2** with thymineacetic acid[10] **3** was achieved using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC, water-soluble carbodiimide) as the coupling agent in DMF and gave monomer **4** as a white solid in 74% yield. The *exo*-isomer of **4** can be obtained by a closely related series of transformations with the exception that it is necessary to protect one end of the ethylenediamine with a triphenylmethyl group prior to its reaction with *exo*-norborn-5-ene-2,3-dicarboxylic anhydride and subsequently to remove the protecting group with trifluoroacetic acid.

Direct evidence that ring-opening occurs in a controlled manner is provided by ^1H NMR spectroscopy and MALDI-TOF mass spectrometry. Fig. 1 shows the crude ^1H NMR spectrum obtained after treatment of $\{RuCl_2(CHPh)[P(C_6H_{11})_3]_2\}$ with 3 equiv. of **4** in $[^2H_8)]$THF in a sealed NMR tube for 90 min. The resonance at δ 20.35 corresponds to the carbene hydrogen of the initiator, while the nearby doublet of doublets resonance at δ 19.09 may be attributed to the carbene hydrogen arising from ring-opening of the first monomer unit, with couplings to the β-hydrogen and the remaining ruthenium-bound tricyclohexylphosphine ligand. Upon standing for several hours this resonance broadens as more monomer is incorporated. In a separate experiment, 3 equiv. of *exo*-**4** were added to the initiator, the mixture stirred for 24 h, and then terminated by addition of ethyl vinyl ether. The MALDI-TOF spectrum of the resultant product [Fig. 2(*a*)] confirms that multiple insertions have occurred to give a narrow molecular weight distribution product (M_n 2340, M_w 2500, M_w/M_n = 1.07).§ The most intense signals are due to protonated oligomers $\{[M + H]^+\}$ with observable minor signals due to sodium $\{[M + Na]^+\}$ and potassium $\{[M + K]^+\}$ salts. The mass of each oligomer confirms the repeat unit (372.38 amu) and the presence of benzylidene and methylidene end-groups arising from the ruthenium initiator and the ethyl vinyl ether terminating agent respectively. The observed M_n is higher than M_n(calc) (1221)



Scheme 1 *Reagents and conditions*: i, $H_2NCH_2CH_2NH_2$ (6 equiv.), toluene, heat; ii, EDC, DMF

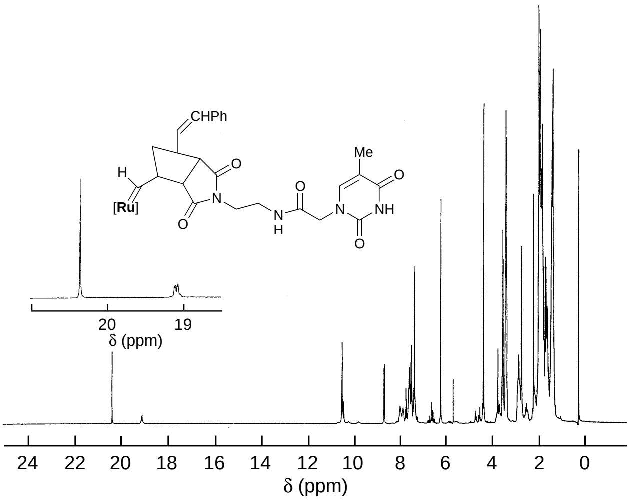


Fig. 1 250 MHz ^1H NMR spectrum ($[^2H_8]$THF) of the products arising from treatment of $\{RuCl_2(CHPh)[P(C_6H_{11})_3]_2\}$ with **4** (2 equiv.); [Ru] = $[RuCl_2(PCy_3)]$

due to the faster rate of propagation *versus* initiation for this monomer–initiator combination.

The MALDI-TOF spectrum of the product mixture prior to the addition of terminating agent is shown in Fig. 2(*b*). In this experiment, which employed indoleacetic acid as the matrix, the oligomers were detected as their sodium salts. The most intense signals are attributable to chains bearing benzylidene and oxo (aldehyde) end-groups, the latter arising from a termination reaction with molecular oxygen.¶ This reaction bears close similarity to that established for well-defined molybdenum initiators.[11] However, unlike the molybdenum system, in which the resultant aldehyde end-capped polymer reacts further with the propagating molybdenum alkylidene species to give a product of twice the anticipated molecular weight, in the case of ruthenium the aldehyde end-groups are tolerated by the ruthenium carbene and thus no further reaction occurs. Interestingly, in the ruthenium-initiated system, signals are also present (indicated by arrows) that correspond to (n − 1) protonated chains that remain attached to the propagating ruthenium centres, *i.e.* [$RuCl_2(PCy_3)$]. The presence of $[M + Na]^+$ and $[M + K]^+$ signals for these species explains the greater multiplicity of signals in Fig. 2(*b*).

Overall, these observations provide direct evidence for a controlled polymerisation of nucleotide base-substituted monomers, and afford insight into a key termination reaction in the ruthenium system. In future publications, extensions of this work to other nucleotide base polymers and copolymers will be described.

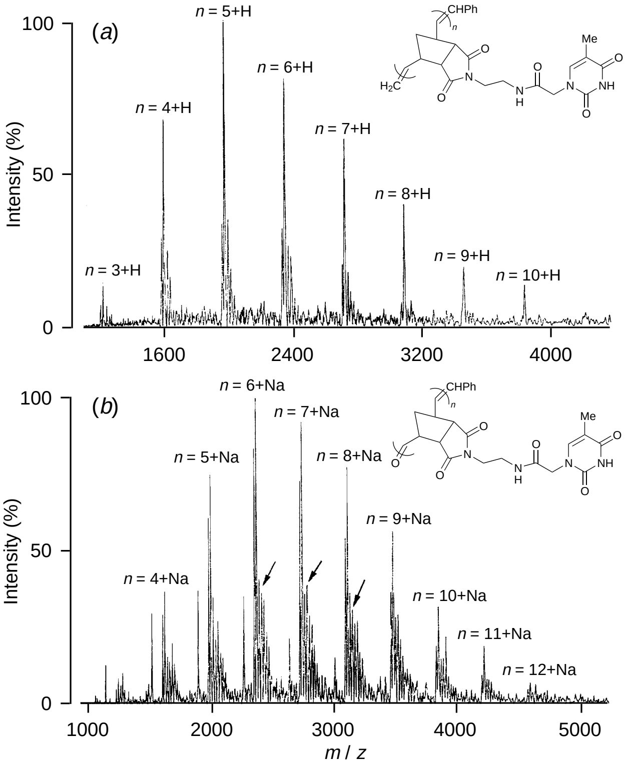


Fig. 2 The MALDI-TOF mass spectrum of poly-*exo*-**4**: (*a*) after termination by ethyl vinyl ether (dihydroxybenzoic acid matrix); (*b*) prior to termination by ethyl vinyl ether but after exposure to atmospheric oxygen (indoleacetic acid matrix)

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Footnotes

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‡ All new compounds gave satisfactory analytical and spectroscopic data.

§ Measured on a Kratos Analytical Kompact MALDI IV spectrometer in linear positive ion mode, accelerating voltage 20 kV, electron multiplier detector. The data presented are a running average of 250 laser shots over the sample position. It should be noted that MALDI-MS has been shown in certain cases to observe components of lower mass preferentially (ref. 12). This results in *M*w being lowered to a greater extent than *M*n, consequently affording a lower molecular weight distribution than the true value. The detector response is also known to affect the measured polymer weight distribution (ref. 13).

¶ Solutions of the ruthenium initiator are known to be sensitive to dioxygen. The reaction observed here occurs upon preparation of the sample slides under non-anaerobic conditions.

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