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Exploiting Thermally-Reversible Covalent Bonds for the Controlled Release of Microencapsulated Isocyanate Crosslinkers

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Abstract

The paper reports the successful synthesis of microcapsules that incorporate thermally-reversible Diels-Alder or oxime-urethane bonds within the polymer of the microcapsule shell using an interfacial polymerisation technique. The mechanical strength of these microcapsules was found to be dependent on the structure of the thermally-reversible functionality, thus allowing for the design of strong microcapsules that demonstrated excellent stability in one-pot PU formulations. Release of the encapsulated isocyanate crosslinkers using a thermal stimulus demonstrated the potential of this technology for use in the controlled polymerisation of one-pot PU systems.

Keywords: Microcapsules, controlled release, Diels-Alder cycloadducts, oxime-urethane

1. Introduction

Polyurethane (PU) formulations are used extensively in controlled drug delivery systems, coatings, synthetic rubbers, thermoplastics and foams [1-4] and have a market value of EUR *ca*. 53 billion. [5] The synthesis of PU typically involves the reaction between a polyisocyanate and a polyfunctionalised alcohol in the presence

of a catalyst. However, as a result of the high reactivity of these components such formulations are not stable, polymerising rapidly even under mild conditions. Microcapsule technologies can, potentially, control the release of highly reactive polyisocyanates and allow the release when desired upon exposure to a suitable stimulus, thus improving the stability of PU formulations and the properties of the resultant products. [6,7]

Microcapsules that respond to a range of stimuli have been developed [8] including - pressure, [9] chemical (*i.e*. change in pH or solvent), [10,11] light, [12,13] ultrasound [14,15] and exposure to elevated temperature. [16-24] Release of the core contents from microcapsules using heat can be achieved by heating above the boiling point or degradation temperature of the encapsulated core to increase the internal pressure sufficient to cause rupture of the microcapsule shell. [17,18,22] This approach has been further developed by adhering microcapsules containing blowing agents to magnetic particles - upon application of a magnetic field the particles oscillate creating localised hotspots sufficient to induce degradation of the encapsulated blowing agent, raising the internal pressure and bursting the microcapsules. [21] The contraction of poly(*N*-isopropylacrylamide) (PNIPAM) when exposed to heat has been exploited [16,19] for the thermal release of microcapsules. Upon the application of a thermal stimulus PNIPAM contracts to cause shell wall rupture or exposure of pores within the microcapsule shell wall. A similar strategy has incorporated polymers with low glass transition temperatures (T_g) within the microcapsule shell - upon reaching the T_g, the microcapsule shell collapses and the core is released. [24] More recently, the thermal release of the core from microcapsules has been achieved by incorporating thermally-reversible Diels-Alder adducts within the shell wall of polyelectrolyte microcapsules synthesised using a complex coacervation technique. [20] Polyelectrolyte

microcapsules often exhibit poor stability and mechanical strength. PU microcapsules synthesised using an interfacial polymerisation technique have demonstrated excellent strength and stability properties.

Certain covalent bonds are known to undergo a reverse reaction when exposed to heat. Diels-Alder adducts such as maleimide-furan have been employed as thermally-degradable crosslinkers to bestow controlled-release and healable capabilities in polymer systems. [25]. Oxime-urethane bonds are also reversible at elevated temperatures, regenerating the oxime and isocyanate and have been employed [26] as thermally degradable crosslinks in polymers used for the application of thermally-strippable templates employed in the manufacture of microchips.

Herein we describe the encapsulation of isophorone diisocyanate (IPDI) in PU microcapsules that possess thermally-degradable Diels-Alder and oxime-urethane functionalities within the polymer of the microcapsule shell wall. Stability and release studies of the afforded microcapsules have identified the compatibility of such thermally-degradable crosslinkers with polymer microcapsules. This has allowed for the design of a robust encapsulant system that is capable of releasing IPDI into PU formulations when exposed to a heat stimulus (see Scheme 1).

2. Experimental

2.1. Materials

The chemicals and reagents were either purchased from Sigma Aldrich or supplied by BAE Systems plc. Tetrahydrofuran (THF) was distilled from sodium and benzophenone, dichloromethane was distilled from CaH_2 and tetraethylene glycol dimethylether was distilled under vacuum from CaH_2 (100 °C, 0.1 mmHg). All other

chemicals were used as supplied without further purification. The synthesis of **1**, **2** and **3** was carried out according a literature procedure. [26]

2.2. Chemical and Physical Characterisation

^{1}H and ^{13}C NMR spectra were obtained using a Bruker Nanobay 400 MHz spectrometer. FTIR spectra were obtained using a Perkin Elmer Spectrum 100, using a PE Universal ATR sampling accessory. VTIR spectroscopy was carried out using a Perkin Elmer Spectrum 100 utilising a Specac variable temperature cell holder employing a static liquid sample cell. Mass spectrometry was conducted using a ThermoFisher Scientific Orbitrap XL LCMS operating an electrospray ioniser (ESI). Optical microscopy was carried out using a Leica DM2500M optical microscope employing a Mettler Toledo FP82HT hot stage and images were recorded using an Infinity 1 digital camera. Microcapsule diameters were measured using Leica Interactive Measurement software. Samples analysed using electron microscopy were imaged using an FEI Quanta FEG 600 Environmental Scanning Electron Microscope operating in a thin aqueous atmosphere (0.68 torr). SEM images of microcapsule cross-sections were obtained by first embedding samples in Agar 100 epoxy resin and cured at 70 °C for 48 hours. Thin sections were prepared using a Reichert-Jung Ultracut microtome employing a glass knife. Tensile stress tests were carried out using a single column AML tensiometer stretching the samples at the speed of 10 mm/min.

2.3. Conversion of Protected Maleic Anhydride to Maleimide **4**

Protected maleic anhydride **1** (1.53 g, 9.3 mmol) and 3-amino-1-propanol (0.830 g, 11.1 mmol) were dissolved in MeOH (50 mL) and maintained under reflux for a period of 18 hours. The solvent was removed *in vacuo* to leave a yellow coloured oil that was purified by column chromatography (R_f = 0.29, 2 % MeOH/$CHCl_3$) to afford a white

solid **4** (0.69 g, 36 %) (m.p. 119-124 °C). ^{1}H NMR (400 MHz, Acetone-d_6): δ 1.70 (quint., *J* = 6.5 Hz, 2H), 2.93 (s, 2H), 3.49 (s, 1H), 3.51 (t, *J* = 5.0 Hz, 2H), 3.52 (t, *J* = 7.0 Hz, 2H), 5.15 (s, 2H), 6.59 (s, 2H); ^{13}C NMR (100 MHz, Acetone-d_6): δ 31.6, 36.2, 48.3, 59.7, 81.8, 137.4, 177.4; FTIR (ATR) ν (cm^{-1}): 3511 (O-H), 3099 (C-H), 2952 (C-H), 1691 (C=O), 1405 (C-N), 1158 (C-O); ESIMS calculated mass $(C_{11}H_{14}O_4N)^+$ 224.0917 found 224.0918.

2.4. Deprotection to Form Hydroxy-Functionalised Maleimide **5**

Protected maleimide (0.650 g, 2.9 mmol) **4** was dissolved in toluene (20 mL) and maintained under reflux for a period of 7 hours. The solvent was removed *in vacuo* to leave a pale yellow coloured oil **5** (0.375 g, 83 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.80 (quint. *J* = 6.0 Hz, 2H), 2.60 (br., 1H), 3.59 (br., 2H), 3.69 (t, *J* = 7.0 Hz, 2H), 6.74 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.2, 34.3, 59.1, 134.2, 171.3; FTIR (ATR) ν (cm^{-1}): 3478 (O-H), 3110 (C-H), 2954 (C-H), 1695 (C=O), 1409 (C-N), 1149 (C-O); ESIMS calculated mass $(C_7H_{10}O_3N)^+$ 156.0655 found 156.0654.

2.5. Synthesis of Dihydroxy-Functionalised Diels-Alder Adduct **6**

Hydroxy-functionalised maleimide **5** (0.340 g, 2.19 mmol) and furfuryl alcohol (0.258 g, 2.6 mmol) were dissolved in toluene (40 mL) and maintained at 80 °C for a period of 72 hours. The solvent was removed *in vacuo* to leave a yellow coloured oil that was purified by column chromatography (R_f = 0.15, 5 % MeOH/$CHCl_3$) to afford a colourless oil **6** obtained as a mixture of *exo* and *endo* isomers (7:3) that slowly transformed to the *exo* isomer over a period of several months (0.426 g, 77 %). *Exo*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.76 (quint., *J* = 6.0 Hz, 2H), 3.00 (q, *J* = 6.5 Hz, 1H), 3.49 (m, 1H), 3.49 (m, 1H), 3.54 (t, *J* = 6.0 Hz, 2H), 3.66 (t, *J* = 6.0 Hz, 2H), 4.07 (s, 2H), 6.55 (dd, *J* = 1.0, 6.0 Hz, 1H), 6.62 (d, *J* = 6.0 Hz, 1H), ^{13}C NMR (100 MHz,

$CDCl_3$): δ 30.3, 35.4, 48.1, 50.0, 58.8, 60.6, 80.9, 91.4, 137.0, 138.3, 176.6, 176.7; *Endo*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.65 (quint., *J* = 6.0 Hz, 2H), 3.49 (m, 1H), 3.50 (m, 2H), 3.68 (t, *J* = 6.0 Hz, 2H), 4.21 (m, 1H), 5.29 (s, 2H), 5.31 (d, *J* = 6.0 Hz, 1H), 6.35 (d, *J* = 6.0 Hz, 1H), 6.47 (dd, *J* = 1.0, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.4, 35.1, 46.1, 48.2, 59.0, 61.3, 79.4, 92.1, 134.9, 135.7, 175.5, 175.9; FTIR (ATR) ν (cm^{-1}): 3460 (O-H), 3112 (C-H), 2960 (C-H), 1683 (C=O), 1404 (C-N), 1172 (C-O); ESIMS calculated mass $(C_{12}H_{16}O_5N)^+$ 254.1023 found 254.1025.

2.6. Synthesis of Isocyanate-Terminated Prepolymer **7**

Dihydroxy-functionalised Diels-Alder adduct **6** (0.393 g, 1.6 mmol) and toluene-2,4-diisocyanate (TDI) (0.757 g, 4.4 mmol) were dissolved in tetrahydrofuran (THF) (15 mL) and maintained under reflux for a period of 18 hours under an atmosphere of argon. The solvent was removed *in vacuo* and excess TDI was removed by washing with cyclohexane (3 x 20 mL) at 80 °C to leave a yellow coloured solid **7** (0.926 g, 99%) (125-129 °C). FTIR (ATR) ν (cm^{-1}): 3340 (N-H), 3124 (C-H), 2947 (C-H), 2265 (NCO), 1696 (C=O), 1537 (C-N), 1220 (C-O); ESIMS of 5 derivative from reaction with MeOH, calculated mass $(C_{32}H_{35}O_{11}N_5Na)^+$ 688.2225 found 688.2225.

2.7. Synthesis of oxime-urethane **8**

Protected 4'-hydroxyacetophenone oxime **3** (0.163 g, 0.6 mmol), dibutyltin dilaurate (DBTDL) (0.002 g, 0.003 mmol) and tetramethylxylylene diisocyanate (TMXDI) (0.05 g, 0.2 mmol) dissolved in THF (10 mL) and maintained under reflux for 24 hours. The solvent was removed *in vacuo* to leave a pale yellow oil which was purified by column chromatography (R_f 0.19, 20 % EtOAc/hexane) to give a white solid **8** (0.132 g, 88 %) (m.p. 43-44 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.22 (s, 12H), 0.99 (s, 18H), 1.78 (s, 12H), 2.36 (s, 6H), 6.85 (d, *J* = 9.0 Hz, 4H), 6.88 (m, 2H), 7.35 (m, 3H), 7.54 (m, 1H),

7.56 (d, *J* = 9.0 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ -4.4, 14.2, 18.3, 25.6, 29.1, 56.0, 120.3, 121.2, 123.3, 127.7, 128.1, 128.7, 147.0, 153.5, 158.0, 159.1; FTIR (ATR) ν (cm^{-1}): 2928 (C-H), 2857 (C-H), 1722 (C=O), 1601 (C=N), 1496 (C-N), 1254 (Si-O), 1172 (C-O), 905 (N-O); ESIMS calculated mass $(C_{42}H_{62}O_6N_4Si_2+H)^+$ 775.4281 found 775.4286.

2.8. Deprotection of silyl-ethers to form **9**

Oxime-urethane **8** (0.781 g, 1.0 mmol) was dissolved in THF (20 mL) and tetrabutylammonium fluoride (TBAF) (1.0 M) (1.0 ml, 1.0 mmol) was added and stirred at room temperature for 1 hour. The reaction was quenched with NH_4Cl (20 mL) (saturated) and the product extracted with EtOAc (50 mL). The organic extract was washed with H_2O (3 × 50 mL), dried over $MgSO_4$ followed by filtration and the solvent removed *in vacuo* to give a pale yellow solid which was purified by washing sequentially with Et_2O (3 × 50 mL) and $CHCl_3$ (2 × 50 mL) leaving a white solid **9** (0.490 g, 90 %) (m.p. 92-100 °C). ^{1}H NMR (400 MHz, DMSO-d_6): δ 1.63 (s, 12H), 2.29 (s, 6H), 6.81 (d, *J* = 9.0 Hz, 4H), 7.27 (m, 3H), 7.46 (m, 1H), 7.55 (m, 2H), 7.61 (d, *J* = 8.0 Hz, 4H), 9.93 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.4, 29.3, 55.1, 115.3, 121.2, 122.7, 125.3, 127.8, 128.3, 147.2, 152.8, 159.1, 159.5; FTIR (ATR) ν (cm^{-1}): 3378 (O-H), 3230 (N-H), 2993 (C-H), 2953 (C-H), 1706 (C=O), 1605 (C=N), 1499 (C-N), 1238 (C-O), 911 (N-O); ESIMS calculated mass $(C_{30}H_{34}O_6N_4+Na)^+$ 569.2371 found 569.2367.

2.9. Synthesis of Isocyanate-Terminated Prepolymer **10**

Deprotected oxime-urethane **9** (0.603 g, 1.1 mmol) and TDI (0.538 g, 3.1 mmol) were dissolved in THF (30 mL) and maintained under reflux for 24 hours. The solvent was removed *in vacuo* and excess TDI removed by washing with cyclohexane (3 × 60 mL)

at 80 °C to leave a yellow solid **10** (0.822 g, 84 %) (m.p. 86-91 °C). FTIR (ATR) ν (cm^{-1}): 3357 (N-H), 2979 (C-H), 2924 (C-H), 2255 (NCO), 1723 (C=O), 1593 (C=N), 1505 (C-N), 1193 (C-O), 901(N-O); ESIMS calculated mass 917.3229 $(C_{48}H_{46}O_{10}N_8+Na)^+$ found 917.3233.

2.10. Microencapsulation of Isophorone Diisocyanate

General procedure for synthesis of microencapsulated isophorone diisocyanate (IPDI)

Gum arabic (9 g) was dispersed in H_2O (60 mL) in a 150 mL beaker with the aid of mechanical agitation at a rate of 1000 rpm. Prepolymer and IPDI were dissolved in a hydrophobic solvent. This solution was added to the aqueous solution and the resultant emulsion heated to 70 °C at a rate of 10 °C/minute. When the temperature reached 50 °C, 1,4-butanediol (5.2 g, 56.6 mmol) was added and agitated at the same rate for an additional 30 seconds. The mixture was agitated at a rate of 150 rpm for 45 minutes at 70 °C followed by a further 2 hours at room temperature. After this period, agitation was ceased, H_2O (100 mL) was added and the generated microcapsules allowed to settle at the bottom of the beaker over a period of 1 hour at room temperature. The aqueous solution was decanted to leave polyurethane microcapsules that were collected by vacuum filtration, washed with H_2O and then air dried for a period of 48 hours (0.153 g). For parameters associated with the synthetic process, including – rate of agitation and reaction time, please refer to the Supporting Information (SI).

2.11. Variable Temperature Infrared Spectroscopy

Oxime-urethane **8** was dissolved in dried tetraethylene glycol dimethyl ether to a concentration of 3.0 M. This solution was injected into a variable temperature IR spectroscopy cell utilising NaCl windows separated by a 0.050 mm PTFE spacer. The cell was placed in a variable temperature cell holder and an IR spectrum recorded at

10 °C increments with a FTIR spectrometer and the appearance of an absorption corresponding to the isocyanate functionality formed upon dissociation was observed.

2.12. Preparation and Tensile Testing of Polymer Films

PU-microcapsule **M1** mixture and PU-microcapsule **M2** mixture were prepared by mixing the respective microcapsules (18 mg) with hydroxy-terminated polyalkene (100 mg) and dibutyltin dilaurate (DBTDL) (0.24 mg). PU mixture was prepared by mixing IPDI (11 mg), hydroxy-terminated polyalkene (100 mg) and DBTDL (0.24 mg). The mixtures were pasted in a 1 cm^2 area, 0.5 mm thick, on microscope slides and covered with a second layer of microscope slides. The films were heated to 150 °C for 24 hours followed by a further 24 hours at 60 °C.

Lap shear testing was performed on the samples before and after heating by griping the slides between the tensile tester clamps and pulling them apart at 1 mm/min.

3. Results and Discussion

3.1. Prepolymer Synthesis

PU microcapsules were synthesised using an interfacial polymerisation approach as this route has been shown [6] to afford robust encapsulant systems. This first required the preparation of isocyanate-terminated prepolymers **7** and **10** containing the desired thermally-degradable crosslinkers. To this end a synthetic approach analogous to that developed [26] by Heath *et al*. was employed.

Incorporation of Diels-Alder crosslinkers into a prepolymer **7** first involved the initial protection of maleic anhydride with furan to form a Diels-Alder adduct **1**. The reaction of this adduct with 3-amino-1-propanol followed by deprotection afforded a hydroxy-functionalised maleimide **5**. Subsequent reaction with furfuryl alcohol followed by reaction of excess toluene-2,4-diisocyanate (TDI) led to the formation of an

isocyanate-terminated prepolymer **7** that is capable of further chain extension to form polyurethane microcapsules (Scheme 2). [6,11]

The synthesis of a prepolymer **10** containing an oxime-urethane involved initial protection of a hydroxy-functionalised ketone to give **2** followed by the conversion to the corresponding oxime **3**. The reaction of the generated oxime with tetramethylxylylene diisocyanate (TMXDI) afforded a thermally-reversible oxime-urethane **8**. Deprotection to reveal the hydroxyl functionality **9** then allowed reaction with toluene-2,4-diisocyanate (TDI) to afford the desired isocyanate-terminated prepolymer **10** (Scheme 3).

The presence of the active isocyanate-termini of the prepolymers **7** and **10** was confirmed using FTIR spectroscopy, revealing the presence of a broad absorption at 2268 cm^{-1} corresponding to the isocyanates moiety. This functionality can also be quantified by titrational analysis, [27] which revealed an isocyanate content of 12% and 13% for prepolymers **7** and **10** respectively (see SI file for the calculation).

^{1}H NMR spectroscopy was employed to investigate the potential of the maleimide-furan Diels-Alder adduct to dissociate upon exposure to heat. [28] The dihydroxy-functionalised maleimide furan **6** was dissolved in deuterated DMSO and analysed using ^{1}H NMR spectroscopy before and after exposure to a temperature of 140 °C for 15 minutes (Figure 1). Analysis revealed that after exposure to this temperature the Diels-Alder adduct had almost completely dissociated regenerating the maleimide **5** and furan components.

The dissociation of the thermally-labile oxime-urethane was observed using variable temperature infra-red spectroscopy. [29-31] Figure 2a displays the VTIR spectra of **8**. At 20 °C, an absorbance corresponding to the C=O functionality of the oxime-urethane

at 1757 cm^{-1} was observed. Upon increasing the temperature to 70 °C, an absorbance characteristic of the isocyanate moiety appeared at 2263 cm^{-1}. Further increasing the temperature led to an increase in the intensity of this absorption indicating the dissociation occurred over a broad temperature range. Upon reaching 140 °C an additional absorption at 2337 cm^{-1} is observed which may be attributed to the formation of CO_2, released by reaction of isocyanate and water. This result can be represented quantitatively by measuring the absorption intensities as a function of temperature. A linear increase in absorption intensity of the NCO moiety with increasing temperature is observed between 70-130 °C, after which a small decrease in intensity is observed, likely caused by overlapping with the CO_2 absorption at 2337 cm^{-1}. When compared to the intensity of the NCO absorption, the decrease in intensity of the absorption corresponding to the N-H stretching vibration at 3408 cm^{-1} of the oxime-urethane moiety was much smaller (see Figure 2b) on account of the decarboxylation of carbamic acid which resulted from the reaction of the generated isocyanate and residual water. The resultant amine is capable of reacting with further isocyanate to form urea linkages. To support this observation, pure TMXDI was heated under the same conditions and an analogous result was observed. In this case, at room temperature a characteristic isocyanate vibration was observed at 2271 cm^{-1} and upon further heating to 140 °C, an absorption appeared at 2380 cm^{-1}. In addition, absorptions at 3420 and 1734 correspond to N-H and C=O vibrations, respectively, correlating to the formation of a urea (see SI for further details).

3.2. Microcapsules Synthesis

The microencapsulation of IPDI in polyurethane microcapsules **M1, M2** using the prepolymers **7**, **10** employed an interfacial polymerisation technique similar to that developed by White and co-workers. [6] The prepolymer **7**, **10** and IPDI were dissolved

in a hydrophobic solvent (*o*-methoxyacetophenone and ethyl phenylacetate for **7** and **10** respectively) and emulsified in a surfactant solution of gum arabic with the aid of mechanical agitation. Upon the addition of a water soluble chain extender, 1,4-butanediol, a reaction occurred at the oil-water interface to form a polyurethane shell that contained thermally-degradable crosslinks (Figure 3). The reaction of IPDI was avoided as the high reactivity of TDI-based prepolymers outcompeted the relatively less reactive NCO moieties of IPDI. The generated microcapsules were isolated by filtration, followed by washing with water and allowing to air dry for 48 hours prior to analysis. The properties of the microcapsules were measured using a range of analytical techniques including - optical microscopy, [32] scanning electron microscopy, [33] FTIR spectroscopy [6] and ^{1}H NMR spectroscopy. [34]

Confirmation of the successful microencapsulation of a liquid core was observed by crushing the microcapsules between two microscope slides which reveal the release of a liquid core. Analysis using optical microscopy allowed measurement of the microcapsule diameter which revealed that the average diameter of the microcapsules was 76 µm within a range of 29-138 µm for **M1** and 68 µm within a range of 22-117 µm for **M2**. This result is within the expected literature values for microcapsules synthesised at a rate of agitation of 1000 rpm. [6] The diameter and size distribution of microcapsules can be controlled by changing the rate of agitation and surfactant concentration. [35]

Analysis of the microcapsules using an environmental scanning electron microscope operating in a thin aqueous atmosphere (0.68 torr) revealed that spherical mononuclear microcapsules had been generated and they possessed a smooth external surface along with a rough internal surface and this is in accordance with literature studies. [6] A sample of the microcapsules was embedded in an epoxy resin

and cross-sections prepared using an ultramicrotome employing a glass knife and this was then imaged using the conditions outlined above. [36] An average shell wall thickness of 3.45 µm and 2.45 µm was observed for **M1** and **M2** respectively, within the reported literature range of microcapsules prepared using a similar interfacial polymerisation technique described by Yang *et al.* (SEM images available in SI). [6]

Microcapsules were crushed to release the liquid core and the crushed material was analysed using FTIR spectroscopy. [6,37] A broad absorption at 2255 cm^{-1} was observed characteristic of the isocyanate stretching vibration. This absorption corresponds to the presence of NCO moieties of encapsulated IPDI and prepolymer **7**, **10** (spectra available in SI). [6,37-39] A further notable absorption at 1736 cm^{-1} was observed that is likely to correspond to the urethane carbonyl functional group of the polyurethane microcapsule shell wall

In addition to FTIR spectroscopy, ^{1}H NMR spectroscopic analysis was also employed to confirm the successful encapsulation of IPDI. [31] Microcapsules were crushed and the released core was washed with $CDCl_3$. The washings were filtered to remove the solid shell wall and analysed with ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum was compared to spectra of IPDI and the hydrophobic solvent and a clear overlap between the microcapsule core and the individual components was observed corroborating the observation of the successful microencapsulation of IPDI crosslinker. Chemical shifts corresponding to prepolymers **7**, **10** were not observed in the spectra. This absence is a result of the poor solubility of the prepolymers in $CDCl_3$. Methyl 4-nitrobenzoate was employed as an internal standard since the resonances did not overlap with those of the microcapsule core components. Comparison of the integration of resonances of the internal standard observed at 8.23-8.29 ppm with those of IPDI ppm and the hydrophobic solvents (6.98 ppm and 8.25 ppm for *o*-methoxyacetophenone and ethyl

phenylacetate respectively) allowed the composition of the microcapsule core to be quantified. Analysis of **M1** revealed the core was composed of 80 wt. % IPDI, and 20 wt. % *o*-methoxyacetophenone demonstrating a significantly higher portion of IPDI encapsulated than previously reported [6,37] using an interfacial polymerisation microencapsulation technique. The high percentage of IPDI may be attributed to leaching of the volatile *o*-methoxyacetophenone solvent through the permeable microcapsule shell wall. [40,41] Analysis of **M2** revealed the core was composed of 60 wt/wt % IPDI and 40 wt/wt % ethyl phenylacetate, similar to results previously reported. [6,37]

3.3. Release of Microcapsules with a Heat Stimulus

The capability of these microcapsules to release isocyanate crosslinkers upon exposure to a stimulus of heat was investigated. Microcapsules **M1**, **M2** were heated to 150 °C at a rate of 10 °C/minute and to 200 °C at a rate of 1 °C/minute respectively using a hot stage mounted to an optical microscope and images recorded using a digital camera. In addition to optical microscopy, SEM images were obtained before and after heating. Upon heating **M1** to 125 °C the shell wall of the microcapsules began to dissociate and this dissociation occurred rapidly above this temperature reaching complete dissociation and release of the core from the microcapsules by 140 °C. As expected, SEM analysis of the microcapsules after heating revealed the absence of spherical-shaped microcapsules suggesting complete dissociation of the microcapsules had been achieved (Figure 4). Release of IPDI and TMXDI from **M2** was observed upon reaching a temperature of 150 °C. [42] Upon cooling, a brittle solid material was formed and SEM analysis observed ‘plate-like’ structures (Figure 4f). Microcapsules not containing a thermally-reversible Diels-Alder adduct, designated as ‘control microcapsules’, were also heated to 140 °C. At this temperature the shells of

the control microcapsules began to pucker, suggesting the core had leached from the microcapsules. However, dissociation of the shell wall was not observed.

3.4. Release of Microcapsule Core in PU Formulation

The stability of the microcapsules in PU rubber formulations was investigated. Microcapsules **M1, M2** (18 mg) were mixed with hydroxy-terminated polyalkene (100 mg) and dibutyltin dilaurate (DBTDL) (0.24 mg) designated as **PUM1** mixture and **PUM2** mixture respectively and agitated for 5 minutes with an overhead stirrer. Microcapsules **M1** possessed insufficient mechanical strength to survive the high shear mixing conditions and thus release studies of **M1** were not investigated. The high steric hindrance and non-linear structure of the Diels-Alder prepolymer **7** may have prevented the formation of a strong polymer shell. Conversely, oxime-urethane crosslinkages form strong microcapsules **M2** that demonstrated excellent survivability during mixing. This observation identifies the key structural parameters of prepolymers that are required to form robust microencapsulation systems. A **PU** mixture of IPDI, hydroxy-terminated polyalkene and DBTDL was also prepared and each mixture was placed in 1 cm^2 area between two microscope slides. An application of force was applied to the each of the two slides in opposite directions using a tensometer. The **PU** and **PUM2** mixtures were exposed to 60 °C for a period of 24 hours. Tensile testing after this time revealed that polymerisation of the **PU** mixture had occurred after this time. In contrast, polymerisation was not observed in the **PUM2** mixture, demonstrating how microencapsulation technology can be employed in stable one-pot PU formulations (Figure 5).

The potential of the generated microcapsules **M2** for the controlled delivery of IPDI in PU formulations using an external stimulus of heat was investigated. **PUM2** mixture was placed between two microscope slides and exposed to 150 °C for a period of 24

hours followed by a further 24 hours at 60 °C. Tensile testing was performed before and after heating and revealed that upon exposure to heat an increase in the tensile strength was observed, suggesting that IPDI was successfully released from the microcapsules and polymerisation was achieved (Figure 6).

4. Conclusions

Isocyanate-terminated pre-polymers that incorporating either thermally-reversible Diels-Alder adducts or oxime-urethane bonds have been synthesised successfully and were used to synthesise microcapsules containing active IPDI using an interfacial polymerisation technique. The release of active isocyanate crosslinkers was achieved upon exposing the microcapsules to a heat stimulus. The mechanical strength of the microcapsules was dependent on the structure of the thermally-reversible groups, the non-linear and high steric structure of the Diels-Alder adduct prevented the formation of mechanically robust microcapsules. Microcapsules containing a thermally-reversible oxime-urethane demonstrated excellent mechanical strength and stability in PU formulations. Release studies of the microcapsules have demonstrated the potential of this technology for use in the controlled polymerisation of polymer systems.

Acknowledgements

The authors would like to acknowledge BAE Systems for funding a PhD studentship (MEB) and also the University of Reading for access to analytical instrumentation in the Chemical Analysis Facility.

Data Availability

The raw/processed data required to reproduce these findings cannot be shared at this time due to technical or time limitations. Processed data can be found in the associated Supporting Information file.

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Figures and schemes captions

Figure 1. ^{1}H NMR spectra of maleimide-furan adduct **6** before and after exposure to heat, regenerating the maleimide and furan components.

Figure 2a. Variable-temperature IR spectra of oxime-urethane **8** at 10 °C increments between 20 and 140 °C, highlighting the appearance of an absorbance corresponding to the isocyanate moiety. **Figure 2b.** An increase in intensity in the IR absorption at 2263 cm^{-1} corresponding to the NCO stretching vibration and a slight decrease in the IR absorbtion at 3408 cm^{-1} corresponding to the N-H moiety is observed upon an increase in temperature.

Figure 3. a) Interfacial polymerisation technique used for the synthesis of microcapsules containing IPDI. b) Optical microscopic image of microcapsules **M1** synthesised using a prepolymer containing a thermally-reversible Diels-Alder adduct c) Optical microscopic image of microcapsules synthesised using a prepolymer containing a thermally-reversible oxime urethane **M2**.

Figure 4. Optical microscopic images of microcapsules **M1** a) at 25 °C and b) 140 °C. c) SEM image of microcapsules **M1** after heating to 140 °C. Optical microscopic images of microcapsules **M2** d) at 25 °C and e) 150 °C. f) SEM image of microcapsules **M2** after heating to 150 °C. Optical microscopic images of 'control microcapsules' g) at 25 °C and h) 140 °C.

Figure 5. Stress-strain curves of **PUM2** mixture and **PU** mixture after 24 hours at 60 °C.

Figure 6. Stress-strain curves of **PUM2** before and after exposure to heat stimulus.

Scheme 1. Release of core from microcapsules achieved by depolymerisation of the microcapsule shell wall.

Scheme 2. Synthesis of isocyanate terminated Diels-Alder prepolymer **7** i) furan, toluene ii) 3-amino-1-propanol, MeOH iii) toluene reflux iv) furfuryl alchol, toluene v) TDI, THF.

Scheme 3. i) TBDMSCl, Et_3N, CH_2Cl_2 ii) HO-NH_3Cl, Et_3N, EtOH iii) TMXDI, THF iv) TBAF, THF v) TDI, THF.

Figures and Schemes

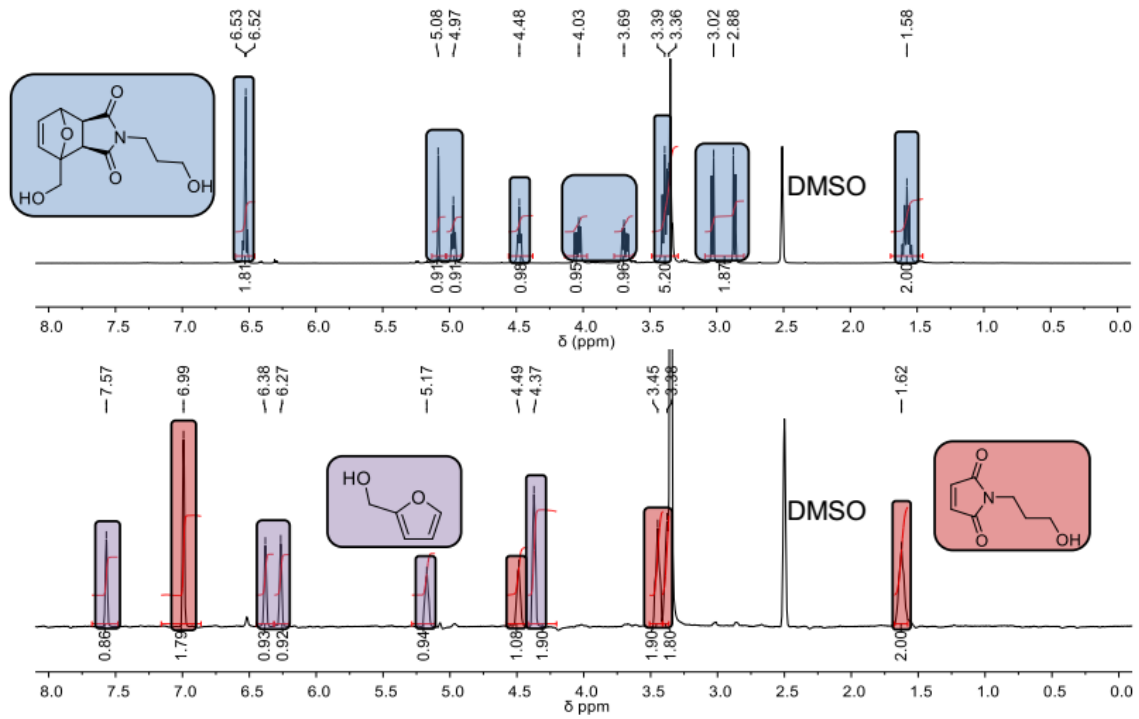


Figure 1

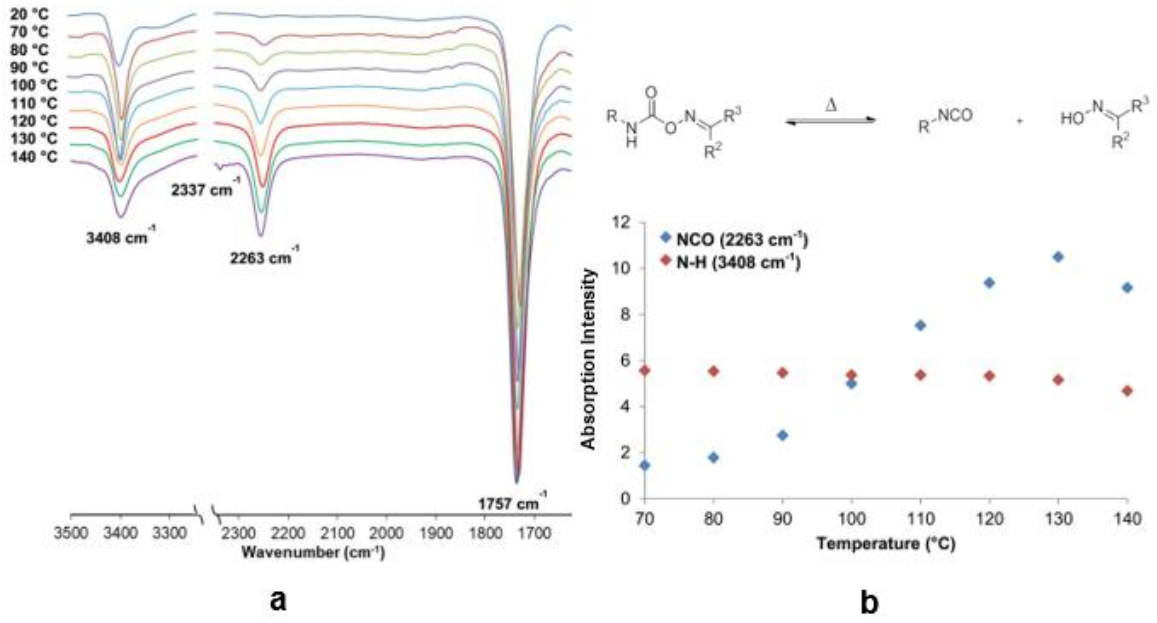


Figure 2

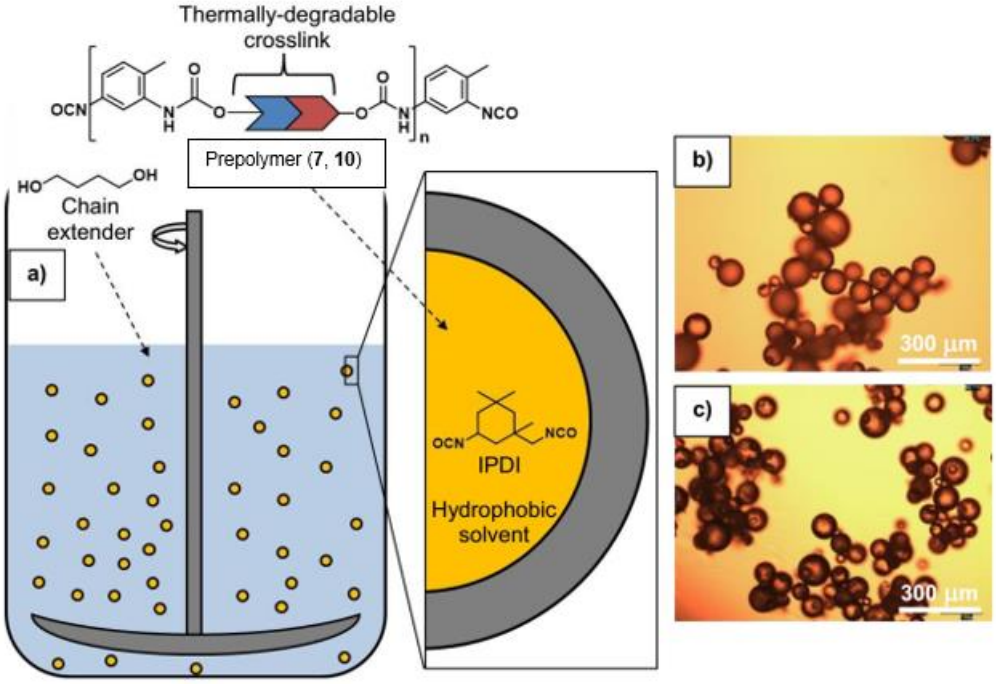


Figure 3

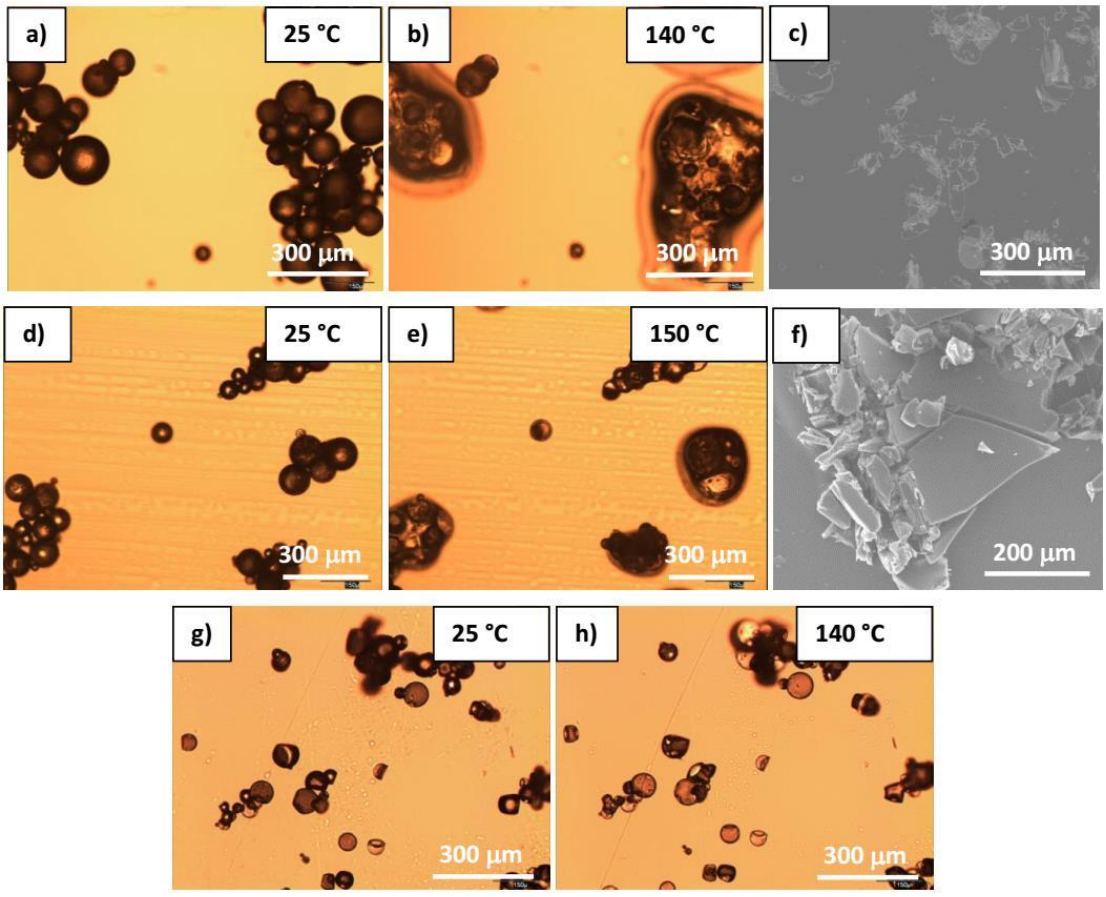


Figure 4

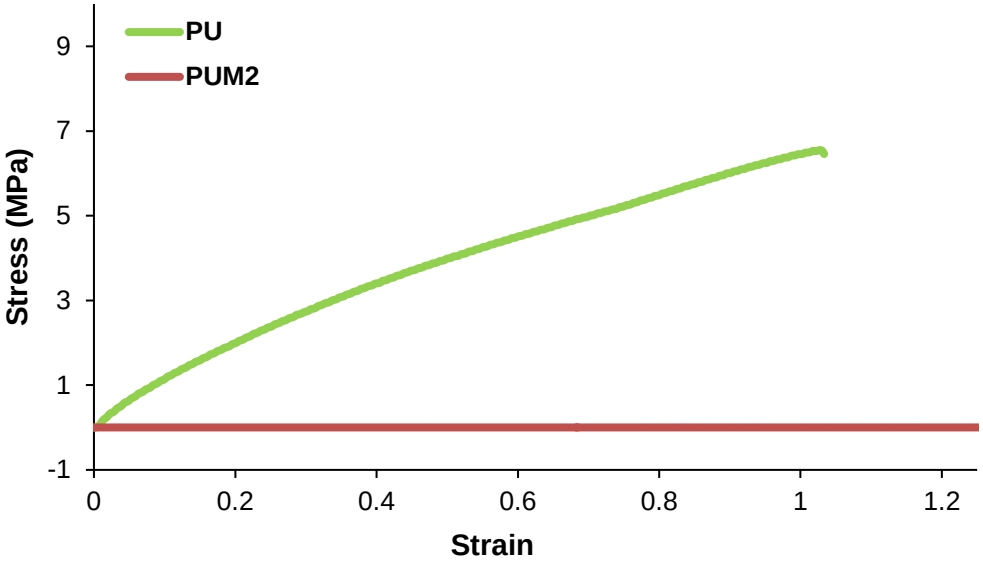
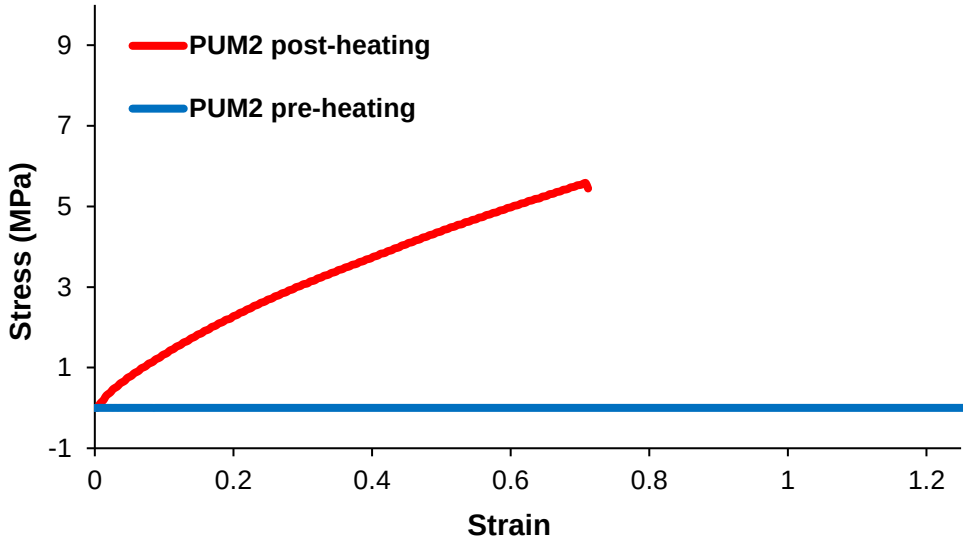


Figure 5



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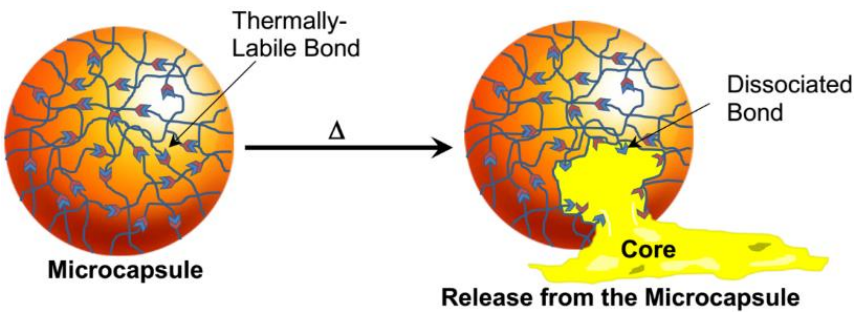
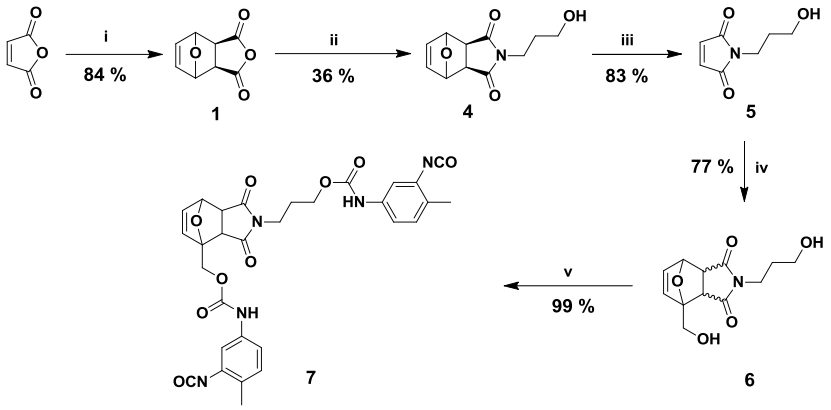
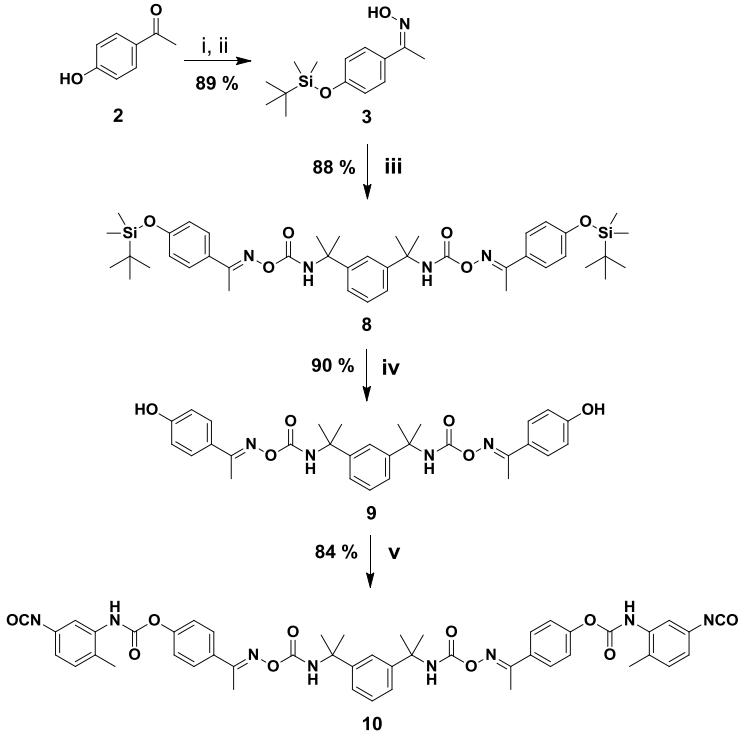


Scheme 1



Scheme 2



Scheme 3