Chain Transfer Kinetics of Acid/Base Switchable *N*-Aryl-*N*-Pyridyl Dithiocarbamate RAFT Agents in Methyl Acrylate, *N*-Vinylcarbazole and Vinyl Acetate Polymerization

Daniel J. Keddie, Carlos Guerrero-Sanchez, Graeme Moad,* Roger J. Mulder, Ezio Rizzardo and San H. Thang*

CSIRO Materials Science and Engineering, Bag 10, Clayton South VIC 3169, Australia

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*Corresponding authors Email: daniel.keddie@csiro.au (D.J.K.), graeme.moad@csiro.au (G.M.).

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Abstract

The structures of the ‘Z’ and ‘R’ substituents of a RAFT agent (Z-SCS₂-R) determine a RAFT agent’s ability to control radical polymerization. In this paper we report new acid/base switchable *N*-aryl-*N*-pyridyl dithiocarbamates (R= -CH₂CN, Z = -N(Py)(Ar)) which vary in substituent at the 4-position of the aryl ring and the use of these to control molecular weight and dispersity. In their protonated form, the new RAFT agents are more effective in controlling polymerization of the more activated monomer, methyl acrylate (MA), whereas in their neutral form they provide more effective control of the polymerization of less activated monomers, *N*-vinyl carbazole (NVC) and vinyl acetate (VAc). For each polymerization, the apparent chain transfer coefficient (C_{tr}^{app}) shows a good correlation with Hammett parameters. Dithiocarbamates with more electron-withdrawing aryl ring substituents have the higher C_{tr}^{app} . This demonstrates the influence of polar effects on C_{tr}^{app} and supports the hypothesis that the

activity of these RAFT agents is determined by the availability of the lone pair of the dithiocarbamate nitrogen.

Introduction

The level of control over polymer molar mass and dispersity achievable using the reversible addition-fragmentation chain transfer (RAFT) process is dependent on the intrinsic structure of the monomer and RAFT agent (**1**) employed.¹⁻⁵

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Monomers can be broadly divided into two classes based on their reactivity. RAFT polymerization of “more-activated monomers” (MAMs, e.g. (meth)acrylates, (meth)acrylamides and styrenics) are best controlled by RAFT agents that possess high transfer constants, such as dithioesters (**1**, Z=alkyl or aryl) or trithiocarbonates (Z=SR’).¹⁻⁴ However, these same RAFT agents give inhibition or retardation in the polymerization of “less-activated monomers” (LAMs; such as vinyl esters, vinyl amides). Alternately, RAFT agents where the thiocarbonyl group is comparatively electron rich, such as xanthates (**1**, Z=OR’) and dithiocarbamates (**1**, Z=NR’₂), due to donation of the heteroatom lone-pair into the thiocarbonyl (see Scheme 1), have lower transfer constants and give good control over the polymerization of LAMs but poor to no control over MAMs.¹⁻⁴ Their ability to control MAM polymerization can be improved via the incorporation of substituents such as electron-withdrawing groups strategically placed on the heteroatom of the ‘Z’-group that reduce the contribution of the zwitterionic canonical form **3** (see Scheme 1).⁶⁻⁸ For instance, *N,N*-diaryl dithiocarbamates have been shown to give some (but less than ideal) control over the polymerization of both MAMs and LAMs.^{9, 10} Further reports on use of *N,N*-diaryl dithiocarbamates for the control of the polymerization of either MAMs^{11, 12} or LAMs¹³ demonstrate the potential utility in these types of RAFT agent.

Scheme 1: Canonical Structures of dithiocarbamates

Recently, we have reported acid/base switchable RAFT agents (**4**, $R' = \text{CH}_3$) which possess a pyridyl moiety capable of moderating the electron density, and hence reactivity, of the thiocarbonyl group (see Scheme 2).¹⁴⁻¹⁶ The pyridinium species **5** allows for control over the polymerization of MAMs, whilst the neutral species **4** controls the polymerization of LAMs. Factors that affect the acid/base equilibria and hence the extent of protonation of the RAFT agent in solution have a marked effect on the dispersity of the polymers obtained during MAM polymerization.¹⁶ Importantly, the switchable RAFT protocol also allows for the preparation of block copolymers incorporating both MAM and LAM monomer units (i.e. poly(MAM)-*block*-poly(LAM))¹⁴⁻¹⁶ which are generally unobtainable using the conventional RAFT methodology.

Scheme 2: Acid/base switchable RAFT agents

Herein, we show that new acid/base “switchable” *N*-aryl-*N*-pyridyl dithiocarbamates of structure **4**, where R' is aryl or pyridyl, possess enhanced activity in both the acidified and neutral forms when compared to that of the parent class ($R' = \text{CH}_3$). These specific RAFT agents (**4**) were synthesized as the incorporation of aryl substituents as R' , due to their electron withdrawing character, should enhance their activity and improve control over molar mass (M_n) and dispersity ($\mathcal{D}$). We also demonstrate how manipulation of the RAFT agent structure influences chain transfer kinetics during homopolymerization of methyl acrylate

(MA), *N*-vinylcarbazole (NVC) and vinyl acetate (VAc) and how this in turn affects the properties of the polymers obtained.

Experimental Section

Materials. All solvents were of analytical reagent grade unless otherwise stated. 4-Aminobenzonitrile, 4-aminopyridine, aniline, *p*-anisidine, bromoacetonitrile, carbon disulfide (CS₂), 4-chloropyridine hydrochloride, 1,4-dioxane (anhydrous), dodecylbenzenesulfonic acid (DDBSA), 4-fluoroaniline, MA, potassium *tert*-butoxide (KO^tBu), pyridine, VAc, NVC were purchased from Sigma-Aldrich and used as received unless otherwise stated. 2,2'-Azobis[2-methyl propionitrile] (AIBN) was purchased from Acros and purified by recrystallization twice from methanol prior to use. All deuterated solvents were obtained from Cambridge Isotope Laboratories. MA was filtered through neutral alumina activity I (70-230 mesh) and fractionally distilled under reduced pressure immediately before use. 4-Chloropyridine was prepared by neutralization of 4-chloropyridine hydrochloride with aqueous sodium hydroxide (25 % w/v), extracted with diethyl ether (Et₂O) and dried (Na₂SO₄) and the solvent removed immediately prior to use. Cyanomethyl methyl(pyridin-4-yl)carbamodithioate (**21**),¹⁴ 4,4'-dipyridylamine (**15**),¹⁷ tris(benzylideneacetone) dipalladium(0) (Pd₂(dba)₃),¹⁸ 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride (IPr·HCl)¹⁹ were prepared by the reported literature procedures. Analytical thin layer chromatography (TLC) was performed on Merck Aluminium oxide F₂₅₄ neutral TLC plates. Preparative column chromatography was performed using Merck Aluminium oxide 90 neutral (mesh 70-230) Brockmann activity III (prepared from activity I by addition of 6 % w/w of H₂O).

Characterization. Nuclear magnetic resonance (NMR) spectra for structural assignments were obtained with a Bruker Avance 200 or 400 MHz spectrometer (¹H 200 or 400 MHz, ¹³C 50 or 100 MHz). Where required, carbon spectra were assigned by use of HSQC and HMBC experiments. High resolution electron impact (HR-EI) mass spectra recorded using a ThermoQuest MAT95XP operating at 70 eV using perfluorokerosene (PFK) as a reference. Gel permeation chromatography (GPC) for poly(methyl acrylate) and poly(vinyl acetate) samples was performed on Waters Alliance e2695 liquid chromatograph equipped

with a Waters 2414 differential refractometer and 3 × mixed C and 1 mixed E PLgel columns (each 300 mm × 7.5 mm) from Polymer Laboratories. The eluent was tetrahydrofuran (THF) at 30 °C (flow rate: 1 mL min⁻¹). Number (M_n) and weight-average (M_w) molar masses were evaluated using Waters Empower Pro software. The GPC columns were calibrated with low dispersity polystyrene standards (Polymer Laboratories) and molecular weights are reported as polystyrene (PS) equivalents. A third order polynomial was used to fit the log M_p vs. time calibration curve, which was linear across the molecular weight range $2 \times 10^2 - 2 \times 10^6$ g mol⁻¹. GPC measurements for poly(*N*-vinylcarbazole) samples was performed on a Shimadzu system equipped with a CMB-20A controller system, a SIL-20A HT autosampler, a LC-20AT tandem pump system, a DGU-20A degasser unit, a CTO-20AC column oven, a RDI-10A refractive index detector, and 3 × Waters Styragel columns (HT2, HT3, HT4, each 300 mm × 7.8 mm providing an effective molecular weight range of 100-600000). *N,N*-dimethylformamide (DMF) (containing 0.45% w/v lithium bromide (LiBr)) at 80 °C (flow rate: 1 mL min⁻¹. Number (M_n) and weight-average (M_w) molar masses were evaluated using Shimadzu LC Solution software. The GPC columns were calibrated with low dispersity PS standards (Polymer Laboratories) ranging from 3100 to 650000 g mol⁻¹ and molar masses are reported as polystyrene equivalents. A 3rd order polynomial was used to fit the log M_p vs. time calibration curve, which was linear across the molecular weight ranges.

Synthesis of *N*-Aryl-*N*-Pyridyl Amines **11-14**

The *N*-aryl-*N*-pyridyl amines **11-14** were prepared by Pd-catalyzed amination of 4-chloropyridine with substituted anilines, employing a method adapted from that reported by Nolan and co-workers.²⁰ The synthesis of *N*-(4-methoxyphenyl)pyridin-4-amine (**11**) is shown as an example, below. Modifications in the amine used, yield and characterization data for the additional examples can be found below.

N-(4-Methoxyphenyl)pyridin-4-amine (**11**)

KO^tBu (4.9 g, 43.5 mmol, 1.5 equiv.), Pd₂(dba)₃ (316 mg, 0.58 mmol, 2 mol %), 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride (232 mg, 0.58 mmol, 2 mol %), 4-chloropyridine (3.3 g, 29 mmol) and *p*-anisidine **7** (3.92 g, 32 mmol, 1.1 equiv.) were dissolved in 1,4-dioxane (90 mL) and

degassed by sparging nitrogen (30 mins), sealed under nitrogen and heated at 100 °C for 20 h. The reaction was diluted with HCl (200 mL, 1 M), washed with Et₂O (2 × 100 mL) and basified (pH ~14) with NaOH (6.25 M). The resulting solution was extracted with CHCl₃ (3 × 100 mL), washed with brine, dried (Na₂SO₄) and solvent removed under reduced pressure. The crude product was recrystallised from acetonitrile (MeCN) to give *N*-(4-methoxyphenyl)pyridin-4-amine (**11**) as yellowish-brown crystals (3.99 g, 20.0 mmol, 69 %); ¹H NMR (400 MHz, CDCl₃) δ 3.82 (s, 3H, OCH₃), 5.96 (br s, 1H, NH), 6.65 (d, *J* = 6.0 Hz, 2H, pyridyl ArH), 6.91 (d, *J* = 8.8 Hz, 2H, ArH), 7.13 (d, *J* = 8.8 Hz, 2H, ArH), 8.22 (d, *J* = 6.0 Hz, 2H, pyridyl ArH); ¹³C NMR (50 MHz, CDCl₃) δ 55.5 (OCH₃), 108.6 (PyC-3), 114.8 (ArC-3), 125.2 (ArC-2), 132.1 (ArC-1), 150.3 (PyC-2), 151.9 (ArC-4), 157.1 (PyC-4). LR-EI-MS *m/z* 200 (M⁺, 85 %), 185 (100). HR-EI-MS *m/z* = found 200.0941 M⁺ (calcd 200.0944 for C₁₂H₁₂ON₂).

***N*-Phenylpyridin-4-amine (12)**

Coupling of aniline (**8**) (2.9 mL, 2.97 g, 32 mmol, 1.1 equiv.) with 4-chloropyridine, following the above procedure, gave *N*-phenylpyridin-4-amine (**12**) as colourless off white crystals (3.93 g, 22.9 mmol, 79 %); ¹H NMR (400 MHz, CDCl₃) δ 6.19 (br s, 1H, NH), 6.81 (d, *J* = 5.8 Hz, 2H, pyridyl ArH), 7.13 (t, *J* = 7.7 Hz, 1H, ArH), 7.19 (d, *J* = 7.7 Hz, 2H, ArH), 7.36 (t, *J* = 7.7 Hz, 2H, ArH), 8.28 (d, *J* = 5.8 Hz, 2H, pyridyl ArH); ¹³C NMR (50 MHz, CDCl₃) δ 109.5 (PyC-3), 121.6 (ArC-2), 124.1 (ArC-4), 129.5 (ArC-3), 139.6 (ArC-1), 150.4 (PyC-2), 150.5 (PyC-4). LR-EI-MS *m/z* 170 (M⁺, 100 %), 169 (50). HR-EI-MS *m/z* = found 170.0840 M⁺ (calcd 170.0838 for C₁₁H₁₀N₂).

***N*-(4-Fluorophenyl)pyridin-4-amine (13)**

Coupling of 4-fluoroaniline (**9**) (3.56 g, 3.03 mL, 32 mmol, 1.1 equiv.) with 4-chloropyridine, following the above procedure, gave *N*-(4-fluorophenyl)pyridin-4-amine (**13**) as off white crystals (4.35 g, 23.1 mmol, 80 %); ¹H NMR (400 MHz, DMSO-*d*₆) δ 6.79 (m, 2H, pyridyl ArH), 7.12-7.22 (m, 4H, ArH), 8.14 (m, 2H, pyridyl ArH), 8.71 (br s, 1H, NH); ¹³C NMR (50 MHz, DMSO-*d*₆) δ 109.0 (PyC-3), 116.2 (ArC-3, *J*_(C-F) = 22.4 Hz), 122.8 (ArC-2, *J*_(C-F) = 8.1 Hz), 136.9 (ArC-1, *J*_(C-F) = 2.5 Hz), 150.3 (PyC-2), 150.7

(PyC-4), 158.2 (ArC-4, $J_{(C-F)} = 239.3$ Hz). LR-EI-MS m/z 188 (M^+ , 100 %), 187 (35). HR-EI-MS m/z = found 188.0744 M^+ (calcd 188.0744 for $C_{11}H_9N_2F$).

4-(Pyridin-4-ylamino)benzonitrile (**14**)

Coupling of 4-aminobenzonitrile (**10**) (3.78 g, 32 mmol, 1.1 equiv.) with 4-chloropyridine, following the above procedure, gave 4-(pyridin-4-ylamino)benzonitrile (**14**) as yellowish-brown crystals (3.00 g, 15.4 mmol, 53 %); 1H NMR (400 MHz, $DMSO-d_6$) δ 7.05 (m, 2H, pyridyl ArH), 7.28 (m, 2H, ArH), 7.71 (m, 2H, ArH), 8.30 (m, 2H, pyridyl ArH), 9.35 (br s, 1H, NH); ^{13}C NMR (50 MHz, $DMSO-d_6$) δ 102.8 (ArC-4), 111.7 (PyC-3), 118.2 (ArC-2), 119.8 (CN), 134.2 (ArC-3), 145.9 (ArC-1), 148.4 (PyC-4), 150.9 (PyC-2); LR-EI-MS m/z 195 (M^+ , 100 %), 194 (36). HR-EI-MS m/z = found 195.0791 M^+ (calcd 195.0791 for $C_{12}H_9N_3$).

RAFT agent synthesis

The cyanomethyl *N*-aryl-*N*-pyridyl dithiocarbamate RAFT agents **16-20** were prepared by modification of the previously reported procedure.^{14, 16} The synthesis of cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamdithioate (**16**) provided is typical. The pyridylaniline used, the yield and characterization data are listed below for **17-20**.

Cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamdithioate (**16**)

KO^tBu (1.54 g, 13.8 mmol, 1.03 equiv) was added to a solution of *N*-(4-methoxyphenyl)pyridin-4-amine (**11**) (2.68 g, 13.4 mmol) in dry tetrahydrofuran (THF, 90 mL) and the resultant mixture stirred for 1 h at room temperature (RT). Subsequently, CS₂ (2.4 mL, 3.1 g, 40.1 mmol, 3 equiv.) was added dropwise and the reaction mixture stirred for a further 16 h at RT, after which bromoacetonitrile (1.1 mL, 1.58 g, 13.4 mmol, 1 equiv.) was added and the mixture stirred for a further 24 h. The mixture was diluted with H₂O and subsequently extracted with CHCl₃, the combined organics washed with H₂O, dried (Na₂SO₄) and the solvent removed under reduced pressure. The residue was dissolved in a minimal volume of CHCl₃ and purified by column chromatography (neutral Al₂O₃ activity III, 50 % EtOAc/50 % *n*-hexane) to give

cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamodithioate (**16**) as a orange gum that solidified upon standing (3.52 g, 11.2 mmol, 83 %). ^1H NMR (400 MHz, CDCl_3) δ 3.85 (s, 3H, OCH_3), 4.06 (s, 2H, CH_2CN), 6.98 (m, 2H, ArH), 7.30 (m, 2H, ArH), 7.35 (m, 2H, pyridyl ArH), 8.65 (m, 2H, pyridyl ArH); ^{13}C NMR (50 MHz, CDCl_3) δ 23.3 (CH_2CN), 55.6 (OCH_3), 115.3 (ArC-3), 115.5 (CH_2CN), 121.6 (PyC-3), 129.8 (ArC-2), 134.5 (ArC-1), 151.1 (PyC-2), 152.5 (PyC-4), 160.6 (ArC-4), 196.9 (C=S); LR-EI-MS m/z 315 (M^+ , 24 %), 275 (11), 243 (21), 211 (62), 176 (100). HR-EI-MS m/z = found 315.0497 M^+ (calcd 315.0495 for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{OS}_2$).

Cyanomethyl phenyl(pyridin-4-yl)carbamodithioate (**17**)

Reaction of *N*-phenylpyridin-4-amine (**12**) (2.28 g, 13.4 mmol) with KO^tBu , CS_2 and bromoacetonitrile in dry THF gave cyanomethyl phenyl(pyridin-4-yl)carbamodithioate (**17**) as an orange solid (3.14 g, 11.0 mmol, 82 %). ^1H NMR (400 MHz, CDCl_3) δ 4.07 (s, 2H, CH_2CN), 7.35 (m, 2H, pyridyl ArH), 7.38 (m, 3H, ArH), 7.41 (m, 2H, ArH), 8.67 (m, 2H, pyridyl ArH); ^{13}C NMR (50 MHz, CDCl_3) δ 23.3 (CH_2CN), 115.5 (CN), 121.8 (PyC-3), 128.5 (ArC-3), 130.1 (ArC-4), 130.2 (ArC-2), 142.2 (ArC-1), 151.4 (PyC-2), 152.1 (PyC-4), 196.3 (C=S); LR-EI-MS m/z 285 (M^+ , 42 %), 245 (79), 213 (99), 211 (62), 176 (100). HR-EI-MS m/z = found 285.0385 M^+ (calcd 285.0389 for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{S}_2$).

Cyanomethyl (4-fluorophenyl)(pyridin-4-yl)carbamodithioate (**18**)

Reaction of *N*-(4-fluorophenyl)pyridin-4-amine (**13**) (2.52 g, 13.4 mmol), with KO^tBu , CS_2 and bromoacetonitrile in dry THF gave cyanomethyl (4-fluorophenyl)(pyridin-4-yl)carbamodithioate (**18**) as an orange solid (2.48 g, 8.2 mmol, 61 %); ^1H NMR (400 MHz, CDCl_3) δ 4.07 (CH_2CN), 7.18 (m, 2H, ArH), 7.34 (m, 2H, pyridyl ArH), 7.39 (m, 2H, ArH), 8.69 (m, 2H, pyridyl ArH); ^{13}C NMR (50 MHz, CDCl_3) δ 23.4 (CH_2CN), 115.4 (CN), 117.4 (ArC-3 , $J_{(\text{C-F})} = 23.2$ Hz), 121.8 (PyC-3), 130.5 (ArC-2 , $J_{(\text{C-F})} = 9.2$ Hz), 138.2 (ArC-1 , $J_{(\text{C-F})} = 3.4$ Hz), 151.5 (PyC-2), 151.9 (PyC-4), 162.9 (ArC-4 , $J_{(\text{C-F})} = 252.3$ Hz), 196.5 (C=S). LR-EI-MS m/z 303 (M^+ , 24 %), 263 (34), 231 (61), 176 (100). HR-EI-MS m/z = found 303.0287 M^+ (calcd 303.0295 for $\text{C}_{14}\text{H}_{10}\text{FN}_3\text{S}_2$).

Cyanomethyl di(pyridin-4-yl)carbamodithioate (**19**)

Reaction of 4,4'-dipyridylamine (**15**) (2.29 g, 13.4 mmol) with KO^tBu, CS₂ and bromoacetonitrile in dry THF gave cyanomethyl di(pyridin-4-yl)carbamodithioate (**19**) as an orange solid (1.85 g, 6.0 mmol, 45 %). ¹H NMR (400 MHz, DMSO-*d*₆) δ 4.32 (s, 2H, CH₂CN), 7.71 (m, 2H, pyridyl ArH), 8.73 (m, 2H, pyridyl ArH); ¹³C NMR (50 MHz, DMSO-*d*₆) δ 23.5 (CH₂CN), 117.2 (CH₂CN), 123.5 (PyC-3), 150.9 (PyC-4), 152.3 (PyC-2), 196.9 (C=S); MS (HR-EI) 286.0340 m/z [M]⁺ (C₁₃H₁₀N₄S₂ requires 286.0347).

Cyanomethyl (4-cyanophenyl)(pyridin-4-yl)carbamodithioate (**20**)

Reaction of *N*-(4-cyanophenyl)pyridin-4-amine (**14**) (2.62 g, 13.4 mmol) with KO^tBu, CS₂ and bromoacetonitrile in dry THF gave cyanomethyl 4-(cyanophenyl)(pyridin-4-yl)carbamodithioate (**20**) as an orange solid (1.85 g, 6.0 mmol, 45 %). ¹H NMR (400 MHz, CDCl₃) δ 4.09 (s, 2H, CH₂CN), 7.32 (m, 2H, pyridyl ArH), 7.52 (m, 2H, ArH), 7.78 (m, 2H, ArH), 8.74 (m, 2H, pyridyl ArH); ¹³C NMR (50 MHz, CDCl₃) δ 23.4 (CH₂CN), 113.4 (ArCN), 115.0 (CH₂CN), 117.4 (ArC-4), 122.2 (PyC-3), 129.2 (ArC-2), 133.9 (ArC-3), 146.7 (ArC-1), 150.6 (PyC-4), 151.9 (PyC-2), 195.3 (C=S); MS (HR-EI) 310.0338 m/z [M]⁺ (C₁₅H₁₀N₄S₂ requires 310.0341).

RAFT polymerization

Polymerization of Methyl Acrylate (MA)

The procedure for polymerization of MA in the presence of RAFT agent **16** is shown below, that using RAFT agents **17-21** can be found in the Supporting Information.

Preparation of poly(methyl acrylate) using cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamodithioate (**16**) at 70 °C – with and without acid

Stock solution I of AIBN (17.5 mg) in MeCN was prepared in a 50 mL volumetric flask. Stock solution II of dodecylbenzenesulfonic acid (DDBSA) (220.5 mg) in MeCN was prepared in a 5 mL volumetric flask. Reaction mixture A (with acid) was prepared by addition of cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamodithioate (**16**) (21.3 mg), stock solution I (1 mL), stock solution II

(0.5 mL), MA (1.20 g) and MeCN to a volume of 5 mL was prepared in a volumetric flask. Reaction mixture B (without acid) was prepared by addition of cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamodithioate (**16**) (21.3 mg), stock solution I (1 mL), MA (1.20 g) and MeCN to a volume of 5 mL was prepared in a volumetric flask. Each reaction mixture was divided in two and transferred to ampules which were degassed by three repeated freeze-evacuate-thaw cycles and sealed. The ampules were heated at 70 °C for either 2 or 6 h.

Polymerization of *N*-Vinyl Carbazole (NVC)

The polymerization of NVC was performed by preparing stock solutions of known concentration which were placed in ampules, degassed via three freeze-evacuate-thaw cycles, flame sealed and heated for the designated time period. An example, using RAFT agent **16** is shown below (further examples using RAFT agents **17-21** can be found in the supporting information).

Preparation of poly(*N*-vinylcarbazole) using cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamodithioate (16**) at 60 °C**

A stock solution containing cyanomethyl (4-methoxyphenyl)(pyridin-4-yl)carbamodithioate (**16**) (24.3 mg), NVC (2.12 g), AIBN (8.3 mg) and 1,4-dioxane to a volume of 5 mL was prepared in a volumetric flask. The reaction mixture was divided in three and transferred to ampules which were degassed by three repeated freeze-evacuate-thaw cycles and sealed. The ampules were heated at 60 °C for 2, 6 or 20 h (see supporting information for details of additional polymerizations).

Polymerization of Vinyl Acetate (VAc)

The procedure for polymerization of VAc with dithiocarbamate RAFT agents **16-21** was adapted from previously reported method.¹⁵ Syntheses were performed using a Chemspeed Swing-SLT automated synthesizer.^{16, 21, 22} Stock solutions of VAc, RAFT agents **16-21** and AIBN in MeCN were prepared (see Supporting Information for more details), degassed by sparging with nitrogen for 5 min, and placed inside

the automated synthesizer, directly into the reactor vessels. The reaction solutions were further degassed through three freeze-evacuate-thaw cycles, the reaction vessels backfilled with nitrogen and heated at 70 °C with vortex stirring (150 rpm); the temperature of the reflux condensers on top of the reactors was set to 7 °C. Time zero (t_0) for kinetic data was taken to be the moment the reactors reached 70 °C. At pre-established times, monomer conversions and molecular weights of the formed polymers were followed by sampling 75 μ L from the reaction mixtures with the automated liquid handling system into NMR tubes and GPC vials. GPC and NMR samples for analysis were prepared with the automated liquid handling system of the synthesizer at the end of the experiment by adding the corresponding GPC (THF) and NMR (deuterated chloroform, CDCl_3) solvents.

Calculation of Apparent Transfer Coefficients (C_{tr}^{app}) of RAFT agents

Transfer coefficients of the RAFT agents **16-21** in polymerization of MA, NVC and VAc and **16-H⁺-21-H⁺** in the polymerization of MA were calculated numerically from the slope of a plot of $\ln[\text{Monomer}]$ versus $\ln[\text{RAFT}]$ using the method of Walling.^{7, 23, 24} The concentrations of monomer and RAFT agent were obtained via *in situ* ^1H NMR. Prior to polymerization each reaction mixture was degassed via 3 freeze/pump/thaw cycles and sealed in an NMR tube equipped with a PTFE screw cap. Reaction conditions and reagent concentrations were the same as those used in the preparative experiments, but used the deuterated analogue of the reaction solvent (see Supporting Information for plots).

Results and Discussion

Previous work has shown that *N,N*-diaryl dithiocarbamates offer some utility in controlling the polymerization of both MAMs^{11, 12} and LAMs.^{9, 10, 13} For example, diethylmalon-2-yl *N,N*-diphenyl dithiocarbamate **6** gave the targeted molar mass in the polymerization in both ethyl acrylate (EA) and VAc polymerization but delivered polymers of only slightly lowered dispersity ($\bar{D}$ = ca. 1.40).⁹ The result for polymerization of VAc may be considered typical for the conversion and polymerization conditions and reflects the high reactivity of the propagating radical ($\text{PVAc}^\bullet$). However the control over acrylate

polymerization is poor with respect to that provided by more suitable RAFT agents, such as dithioesters²⁵,²⁶ and trithiocarbonates,²⁷⁻³⁰ which give much lower dispersity (i.e. $\bar{D}$ = ca. 1.1). In this work, we sought to prepare an acid/base “switchable” *N*-aryl-*N*-pyridyl dithiocarbamates of structure **4** (R' = aryl or pyridyl) which could give improved control of acrylates by use of the pyridinium species **5**, whilst inspecting how these changes in structure affected the ability for the same RAFT agents, in their neutral form to control the polymerization of LAMs, in particular, NVC and VAc. The cyanomethyl R-group was selected as it has been shown to be a relatively good homolytic leaving group that is effective in reinitiating polymerization of both MAMs and LAMs.¹⁴

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RAFT Agent Synthesis

The RAFT agents precursors, *N*-aryl-*N*-pyridyl amine **11-14**, were synthesized by the Pd-catalyzed Buchwald-Hartwig amination³¹ of 4-chloropyridine (see Scheme 3 below).²⁰ The products were obtained in high purity and in moderate to high yields without need for chromatographic separation. Higher yields of the desired products were obtained using the freshly neutralized free base of 4-chloropyridine than were obtained with the HCl salt as reported by Nolan and co-workers.²⁰ The reduced yield observed for the synthesis of the nitrile derivative **14** is attributed to lower reactivity of the aniline starting material **10** due to it being more electron deficient.^{32, 33} *N,N*-Dipyridylamine (**15**) was prepared by reaction of 4-aminopyridine with pyridine in PCl₃ at 140 °C according to the literature procedure.¹⁷

Scheme 3: The synthesis of *N*-aryl-*N*-pyridyl Amines **11-14** and the structure of **15**

Transformation of the *N*-aryl-*N*-pyridyl amines to their corresponding cyanomethyl dithiocarbamates was achieved by adapting the standard method used for alkylation of carbodithioate salts.^{14, 34} Best yields were obtained using the non-nucleophilic base KO^tBu to deprotonate the amines, which were reacted with CS_2 to give the carbodithioate salt. Subsequent alkylation by addition of bromoacetonitrile to the reaction mixture gave the cyanomethyl RAFT agents **16-20** in moderate to high yields (see Scheme 4). The lower yields obtained for the *N*-(4-cyanophenyl)-*N*-pyridyl **20** and the *N,N*-dipyridyl **19** are attributed to decreased nucleophilicity of the amide anions of **14** and **15** towards CS_2 due to the strongly electron-withdrawing substituents on the aryl ring. Low solubility of **14** and **15** in THF also reduces the rate of reaction and hence the yield of the desired RAFT agents (**19** and **20**). The use of *n*-BuLi as the base, as previously employed in the synthesis of *N*-methyl-*N*-pyridyl dithiocarbamates such as **21**,¹⁴ gave very poor or no yield (ca. 0-5 %) and the crude reaction products contained significant amounts of dark coloured highly-polar components. This was circumvented by using KO^tBu under otherwise identical reaction conditions.

Scheme 4: The synthesis of RAFT agents **16-19** and the structure of RAFT agent **21**

Apparent Transfer Coefficient (C_{tr}^{app})

Determination of the apparent transfer coefficient (C_{tr}^{app})²⁶ allows for the direct comparison of RAFT agent activity. This was achieved using the method of Walling²³ by plotting the natural log of monomer concentration against the natural log of RAFT agent concentration ($\ln[M]$ vs $\ln[RAFT]$) which gives a straight line with gradient C_{tr}^{app} .²⁶ The derivation of the Walling method includes an assumption that chain transfer is irreversible. For application of this method in a RAFT context, where chain transfer is reversible, it should be noted that only those processes that lead to consumption of the initial RAFT agent will be observed. Whilst the actual transfer constant may be higher by several orders of magnitude in the case of more active RAFT agents, we have demonstrated that the values of C_{tr}^{app} obtained provide a good guide to relative reactivities of RAFT agents.^{7, 26, 35} The transfer coefficients are, therefore, called apparent transfer coefficients (C_{tr}^{app}). The polymerizations were monitored by *in situ* NMR, with the concentration of monomer and RAFT agent determined by the disappearance of the vinylic (MA: 5.7-6.5 ppm in MeCN-d₃, NVC: 4.8-5.5 ppm in 1,4-dioxane-d₈, VAc: 4.1-5.0 ppm in MeCN-d₃) and cyanomethyl protons (~4.0-4.1 ppm in MeCN-d₃, ~3.9 ppm in 1,4-dioxane-d₈) respectively (see Supporting Information for $\ln[M]$ vs $\ln[RAFT]$ plots, Figures S1-S4).

Polymerization of Methyl Acrylate

In our previous work, we showed that in the presence of a stoichiometric amount of strong acid (i.e. *p*-toluenesulfonic acid)¹⁴⁻¹⁶ *N*-4-pyridyl-substituted dithiocarbamates (**4**, R'=CH₃) have increased activity,

due to a decrease in the electron density of the thiocarbonyl group. This provides improved control during the polymerization of MAMs.

To ascertain the effect of this on the polymerization of MA, controlled with *N*-aryl-*N*-pyridyl RAFT agents **16-20**, we performed experiments both with and without acid (see Scheme 5 and Table 1). Experiments were also performed using *N*-methyl-*N*-pyridyl analogue¹⁴ **21** to aid in a direct comparison with our previous work. In the absence of acid, the *N*-aryl-*N*-pyridyl compounds give reasonable control over MA polymerization (see Entries 2A-6A, Table 1), with a linear increase in M_n with conversion observed (see Figure 1 (a)) and dispersities in line with results previously reported for other *N,N*-diaryl dithiocarbamates.¹⁰⁻¹² In comparison, the polymerization of MA with *N*-methyl-*N*-pyridyl RAFT agent **21** gives polymers of relatively high dispersity and a non-linear increase of M_n with conversion. In this case the C_{tr}^{app} is less than one, indicating the addition of more than one monomer unit per active cycle and relatively poor control over the polymerization (see Entry 1A, Table 1 and Figure 1 (a)). The C_{tr}^{app} values for the RAFT agents were found to increase as the electron density on the dithiocarbamate nitrogen decreased as a consequence of stronger electron withdrawing substituents at the 4-position of the aryl ring. The effect that the C_{tr}^{app} has upon the evolution of the molar mass with monomer conversion, from *in situ* NMR (calculated as $M_n(NMR) = ([M]_0 - [M]_t) / ([RAFT]_0 - [RAFT]_t) \times MW_M$), can be appreciated from Figure 1 (b), with RAFT agents with highest C_{tr}^{app} more closely resembling the theoretical molecular weight evolution (dashed line, Figure 1 (b)). As anticipated, the RAFT agents with higher activity provided polymers of lower dispersity.

For protonation of the pyridyl moiety of the RAFT agents **16-21**, DDBSA which contains a long C12 aliphatic chain, was used to improve solubility of the charged species (**16-H⁺**-**21-H⁺**). TsOH, used as a “switching” acid in previous work,¹⁴⁻¹⁶ did not allow for complete dissolution of some of the more polar protonated RAFT agents, such as **19-H⁺**. Polymerization of MA in the presence of the acid “switched” RAFT agents **16-H⁺**-**21-H⁺** furnished PMA of significantly lower dispersity (ca. 1.1) than did the neutral

RAFT agents (see Table 1, Entries 1B-6B and Figure 2 (a)), approaching that of PMA produced using dithioester²⁶ or trithiocarbonate²⁸³⁶ RAFT agents. The reactions displayed a linear increase in M_n with conversion (Figure 2 (a)) and the C_{tr}^{app} were again found to increase for the RAFT agents possessing stronger electron withdrawing substituents in the 4-position of the aryl ring. The significant decrease in dispersity is attributed to a significant increase in C_{tr}^{app} of the protonated RAFT agents with respect to the neutral analogues, allowing for enhanced equilibration between the growing chains during polymerization. This can be seen by comparison of the evolution of molar mass in the presence of acid (Figure 2 (b), calculated from *in situ* NMR)) to that in the absence of acid (Figure 1 (b)) where the results compare much more closely to the theoretical (dotted line in both Figure 1(b) and Figure 2 (b)). This shows an increase in the rate of the RAFT pre-equilibrium process in the presence of acid, which culminates in lower dispersity polymers.

Overall, the polymerization of MA is well controlled by switchable cyanomethyl *N*-aryl-*N*-pyridyl dithiocarbamates **16-20** in the presence of one equivalent of DDBSA, giving polymers with lower dispersity than those achieved using the protonated *N*-methyl-*N*-pyridyl dithiocarbamate **21**.

Scheme 5: Polymerization of MA with RAFT agents **16-21**, **16-H⁺-21-H⁺** and **19-2H⁺**

Table 1: Details of MA Polymerization Using Standard Experimental Methods^a

Entry	RAFT agent	R'	time (h)	M_n^b	M_n (calc) ^c	$\bar{D}^b$	conv. (%)	$C_{tr}^{app\ d}$
1A	21	Me	2	22900	11200	1.66	63	0.9

Entry	RAFT agent	R'	time (h)	M_n^b	M_n (calc) ^c	$\bar{D}^b$	conv. (%)	$C_{tr}^{app\ d}$
			6	22900	15000	1.69	85	
2A	16	4-MeOPh	2	12600	11000	1.47	62	1.9
			6	16700	15100	1.52	86	
3A	17	Ph	2	11700	11500	1.42	65	2.9
			6	15000	14800	1.33	84	
4A	18	4-FPh	2	12300	11700	1.46	66	3.0
			6	16000	15000	1.35	85	
5A	19	4-Pyridyl	2	8320	7100	1.35	40	5.0
			6	15000	13800	1.20	78	
6A	20	4-NCPh	2	8740	7300	1.33	41	5.2
			6	10800	10900	1.33	62	
1B	21-H⁺	Me	2	8620	10100	1.30	57	6.9
			6	14400	14400	1.19	82	
2B	16-H⁺	4-MeOPh	2	8990	10300	1.16	58	10.1
			6	14700	14600	1.19	83	
3B	17-H⁺	Ph	2	6790	8700	1.16	49	12.5
			6	13400	13500	1.10	77	
4B	18-H⁺	4-FPh	2	7560	8700	1.13	49	17.0
			6	14400	14100	1.10	80	
5B	19-H⁺	4-Pyridyl	2	5990	5300	1.14	30	34.0
			6	14700	12700	1.09	72	
6B	20-H⁺	4-NCPh	2	2340	4100	1.32	23	26.0
			6	10500	10600	1.11	60	

Entry	RAFT agent	R'	time (h)	M_n^b	M_n (calc) ^c	$\bar{D}^b$	conv. (%)	$C_{tr}^{app\ d}$
5C	19-2H⁺	4-Pyridyl	2	5650	6730	1.09	38	— ^e
			6	13200	11100	1.10	63	

^a[MA] = 2.79 M, [RAFT] = 1.35×10^{-2} M, [AIBN] = 4.0×10^{-4} M in MeCN, T = 70 °C, M_n (theory) = 17800 at 100 % conv. ^bGPC THF eluent, PS equivalents ^c M_n (calc) = $([M]_0 - [M]_t)/([RAFT]_0 + df([I]_0(1 - e^{-k_d t})) \times MW_{monomer}$, (where d is number of chains formed by radical-radical termination (= 1), ³⁷ f is the initiator efficiency (= 0.7)³⁸ and $k_d = 3.77 \times 10^{-5} s^{-1}$, calculated from Arrhenius parameters)³⁷ ^dCalculated from plot of $\ln [MA]$ vs $\ln [RAFT]$ from *in situ* NMR polymerization experiments ^e C_{tr}^{app} was unable to be measured accurately due to low solubility of RAFT agent at t_0

Figure 1: Evolution of (a) number-average molar mass and dispersity from GPC with conversion of MA using neutral RAFT agents **16** (◆, blue diamonds), **17** (▼, dark red triangles), **18** (▲, green triangles), **19** (◆, purple hexagons), **20** (+, gray crosses), **21** (●, red circles), theoretical M_n excluding initiator derived chains (---), theoretical M_n including initiator derived chains (···) and (b) evolution of molar mass from *in situ* NMR calculated from RAFT agent and MA conversion ($M_n = \{([MA]_0 - [MA]_t)/([RAFT]_0 - [RAFT]_t)\} \times MW_{MA}$).

Figure 2: Evolution of (a) number-average molar mass and dispersity from GPC with conversion of MA using protonated RAFT agents **16- H^+** (◆, blue diamonds), **17- H^+** (▼, dark red triangles), **18- H^+** (▲, green triangles), **19- H^+** (◆, purple hexagons), **20- H^+** (+, gray crosses), **21- H^+** (●, red circles), theoretical M_n excluding initiator derived chains (---), theoretical M_n including initiator derived chains (···) and (b) evolution of molar mass from *in situ* NMR calculated from RAFT agent and MA conversion ($M_n = \{([MA]_0 - [MA]_t) / ([RAFT]_0 - [RAFT]_t)\} \times MW_{MA}$).

Polymerization of *N*-Vinyl Carbazole

Polymerization of NVC has been previously reported to be most suitably controlled using xanthates³⁹⁻⁴¹ and has therefore been classified among the LAM class of monomers.^{3, 14} As such, it might be expected that some inhibition/retardation would be observed with increase in C_{tr}^{app} , towards that of the more active RAFT agents (e.g. dithiobenzoates or pyrrolocarbodithioates).³⁹ For polymerization of NVC in the presence of the dithiocarbamates **16-21** dispersities decrease as RAFT agent activity increases (see Scheme 6 and Table 2) with no significant change in the rate of polymerization (i.e. no inhibition or

retardation). As was observed in MA polymerization, the *N*-aryl-*N*-pyridyl compounds **16-20** delivered lower dispersity than the *N*-methyl-*N*-pyridyl analogue **21**. The lowest dispersities and the molar mass evolution from NMR closest to theoretical were obtained from the polymerizations controlled with the RAFT agents with the highest C_{tr}^{app} (see Figure 3 (a) and (b)). These results suggest that RAFT agents with higher activity may provide better control over NVC polymerization. Unfortunately, NVC is incompatible with protonated form of switchable RAFT agents,^{14, 16} as acid, in the presence of trace amounts of water, promotes hydrolysis of the monomer to carbazole and acetaldehyde.⁴² For this reason, polymerization of NVC could only be performed in the presence of the RAFT agents in their neutral form. Upon inspection of the evolution of M_n with conversion it can be seen that at high conversion the dispersity increases (see Figure 3 (a)) and the M_n deviates significantly from the theoretical, when initiator derived chains are not taken into account (dashed line, Figure 3 (a)). Due to the high initiator to RAFT agent ratio (1:1.5) used to obtain polymer at high conversion, there is a large proportion of initiator derived chains. When this factor is included in calculation of the theoretical M_n value (dotted line, Figure 3 (a)) the evolution of the experimental M_n for each of the polymerizations is matched more closely, with the remaining discrepancy is most likely attributable to the difference between PNVC and the PS GPC standards. Despite this, NVC polymerization in the presence of RAFT agents **16-20** are well controlled at lower conversion ($t \leq 6$ h), providing PNVC of low dispersity (ca. 1.1-1.15). RAFT agent **21** was found to give comparatively higher dispersity (cf. 1.25) in all cases.

Scheme 6: Polymerization of NVC with RAFT agents **16-21**

Table 2: Details of NVC Polymerization Using Standard Experimental Methods^a

Entry	RAFT agent	R'	time (h)	M_n^b	M_n (calc) ^c	$\bar{D}^b$	conv. (%)	$C_{tr}^{app\ d}$
1	21	Me	2	3460	1330	1.27	5	23.3
			6	12500	16400	1.24	65	
			20	16400	21500	1.23	96	
2	16	4-MeOPh	2	2310	1330	1.18	5	47.6
			6	10900	12400	1.15	49	
			20	17200	21500	1.19	96	
3	17	Ph	2	2390	1330	1.16	5	56.0
			6	11000	12400	1.14	49	
			20	16900	21200	1.19	95	
4	18	4-FPh	2	2490	1330	1.14	5	68.5
			6	12500	13900	1.13	55	
			20	17800	21900	1.18	98	
5	19	4-Pyridyl	2	2340	1870	1.10	7	111
			6	11000	10900	1.12	43	
			20	17400	21000	1.22	94	
6	20	4-NCPh	2	1470	530	1.11	2	117
			6	8690	7840	1.10	31	
			20	17900	20300	1.20	91	

^a[NVC] = 2.19 M, [RAFT] = 1.54×10^{-2} M, [AIBN] = 1.01×10^{-2} M in 1,4-dioxane, T = 60 °C, M_n (theory) = 27500 at 100 % conv. ^bGPC DMF eluent ^c M_n (calc) = $([M]_0 - [M]_t)/([RAFT]_0 + df([I]_0(1 - e^{-k_d t}))) \times MW_{monomer}$, (where d is number of chains formed by radical-radical termination (= 1),³⁷ f is the initiator efficiency (= 0.7)³⁸ and $k_d = 9.6 \times 10^6 \text{ s}^{-1}$)³⁷ ^dCalculated from plot of ln [NVC] vs ln [RAFT] from *in situ* NMR polymerization experiments

Figure 3: Evolution of (a) number-average molar mass and dispersity from GPC with conversion of NVC using neutral RAFT agents **16** (◆, blue diamonds), **17** (▼, dark red triangles), **18** (▲, green triangles), **19** (◆, purple hexagons), **20** (+, gray crosses), **21** (●, red circles), M_n (theory) excluding initiator derived chains (---), M_n (theory) including initiator derived chains (···) and (b) evolution of molar mass from *in situ* NMR calculated from RAFT agent and NVC conversion ($M_n = \{([NVC]_0 - [NVC]_t)/([RAFT]_0 - [RAFT]_t)\} \times MW_{NVC}$)

Polymerization of Vinyl Acetate

For polymerization of VAc in the presence of the RAFT agents **16-21** (Scheme 7) very good control was observed for lower monomer conversions as evidenced by low dispersities (see Table 3 and Figure 4 (a)) and close correlation of the experimental molar masses with the theoretical values calculated from NMR (Figure 4 (b)). However, for higher conversion dispersities increase significantly which is attributed to the occurrence of the usual side reactions associated with radical polymerization VAc, such as chain transfer to monomer,⁴³ and polymer^{44, 45} and head-to-head propagation.^{46, 47} Slight retardation is observed in rate of polymerization the presence of *N*-aryl-*N*-pyridyl RAFT agents **16-18** (conversion ~65 % at 14 h) with respect that with the *N*-methyl-*N*-pyridyl dithiocarbamate **21** (conversion 87 % at 14 h)

(see Figure 5). More substantial retardation is observed with the more active *N*-aryl-*N*-pyridyl RAFT agents **19** and **20** (conversion ~20 % at 14 h). The retardation is most likely due fragmentation of the RAFT intermediate being slow with respect to propagation of VAc. Intermediate radical stability is expected to increase with increasing RAFT agent activity.

Scheme 7: Polymerization of VAc with RAFT agents **16-21**

Table 3: Details of VAc Polymerization Using High-Throughput Experimental Methods^a

Entry	RAFT agent	R'	time (h)	M_n^b	M_n (calc) ^c	$\bar{D}^b$	conv. (%)	$C_{tr}^{app\ d}$
1	21	Me	3	7900	7420	1.39	50	41.7
			10	11000	12300	1.60	85	
			14	10800	12500	1.66	87	
2	16	4-MeOPh	3	2240	1930	1.31	13	92.9
			10	9880	8810	1.37	61	
			14	8860	9750	1.67	68	
3	17	Ph	3	3850	3120	1.19	21	124
			10	9850	8370	1.36	58	
			14	10400	9460	1.51	66	
4	18	4-FPh	3	3930	2970	1.18	20	153
			10	8750	8230	1.44	57	
			14	9770	9320	1.48	65	

Entry	RAFT agent	R'	time (h)	M_n^b	M_n (calc) ^c	$\bar{D}^b$	conv. (%)	$C_{tr}^{app\ d}$
5	19	4-Pyridyl	3	710	450	1.19	3	320
			10	3170	2600	1.19	18	
			14	4150	3440	1.22	24	
6	20	4-NCPh	3	630	220	1.15	1.5	>320 ^e
			10	2870	1880	1.19	13	
			14	4350	2870	1.22	20	

^a[VAc] = 6.35 M, [RAFT] = 3.6×10^{-2} M, [AIBN] = 3.6×10^{-3} M in MeCN, T = 70 °C, M_n (theory) = 15200 at 100 % conv. ^bGPC THF eluent ^c M_n (calc) = $([M]_0 - [M]_t)/([RAFT]_0 + df([I]_0(1 - e^{-k_d t})) \times MW_{monomer}$, (where d is number of chains formed by radical-radical termination (= 1),³⁷ f is the initiator efficiency (= 0.7)³⁸ and $k_d = 3.77 \times 10^{-5} s^{-1}$, calculated from Arrhenius parameters)³⁷ ^dCalculated from an plot of $\ln [VAc]$ vs $\ln [RAFT]$ from *in situ* NMR polymerization experiments ^eAn exact value of C_{tr}^{app} was unable to be calculated as data could not be accurately fitted

Figure 4: Evolution of (a) number-average molar mass and dispersity from GPC with conversion of VAc using neutral RAFT agents **16** (◆, blue diamonds), **17** (▼, dark red triangles), **18** (▲, green triangles), **19**

(**15**, purple hexagons), **20** (+, gray crosses), **21** (●, red circles), theoretical M_n excluding initiator derived chains (---), theoretical M_n including initiator derived chains (···) and (b) evolution of effective molar mass from *in situ* NMR calculated from RAFT agent and VAc conversion ($M_n = \{([VAc]_0 - [VAc]_t)/([RAFT]_0 - [RAFT]_t)\} \times MW_{VAc}$).

Figure 5: VAc conversion at 14 h for RAFT agents **16-21**, illustrating increased retardation with increasing C_{tr}^{app}

Correlation between Hammett coefficients and apparent transfer coefficients (C_{tr}^{app})

For the *N*-aryl-*N*-pyridyl RAFT agents **16-20** the value of C_{tr}^{app} and the control over molecular weight increase and the breadth of the molecular weight distribution decreases as the electron withdrawing character of the 4-substituent increases. A trend for increase in RAFT agent activity with the electron withdrawing character of Z has also been observed for other classes of RAFT agent.⁴⁸ These observations are consistent with the activity of the *N*-aryl-*N*-pyridyl RAFT agents **16-20** being dictated by the availability of the lone pair of the dithiocarbamate nitrogen. We note that there is also an excellent correlation of the Hammett coefficient⁴⁹⁻⁵¹ with the ¹H NMR chemical shift of the N-H of the precursor anilines (see Figure 6).

Figure 6: Correlation plot of the Hammett coefficient of the 4-aryl substituent of the amines **11** (◆, blue diamonds), **12** (▼, dark red triangles), **13** (▲, green triangles), **15** (●, purple hexagons), **14** (+, gray crosses) and their NH chemical shift in DMSO- d_6

In order to gain further mechanistic understanding, we examined the relationship between the electronic demand of the 4-aryl substituent and C_{tr}^{app} through construction of a series of Hammett plots⁴⁹ (Figure 7) for each set of polymerization experiments. For the polymerization of the MAM, MA, the measured C_{tr}^{app} of the *N*-aryl-*N*-pyridyl RAFT agents **16-20** correlates well with the Hammett coefficients of the 4-aryl substituents,⁴⁹⁻⁵¹ whether in both neutral (dotted line, Figure 7 (a)) and protonated (solid line, Figure 7 (a)) forms. We postulate that the measured C_{tr}^{app} for **19-H⁺** in MA polymerization is elevated from its true value due to the presence of a small amount of the dipyridium species **19-2H⁺**. RAFT agent **19-2H⁺** would be expected to have a higher C_{tr}^{app} . Attempts to measure the C_{tr}^{app} of **19-2H⁺** in MA polymerization directly were unsuccessful as the doubly protonated RAFT agent was not completely soluble in the reaction mixture. For the polymerization of the LAMs, NVC (Figure 7 (b)) and VAc (Figure 7 (c)), the C_{tr}^{app} values of the RAFT agents were also found to correlate well with Hammett coefficients for the 4-aryl substituent.⁴⁹⁻⁵¹ Note that the transfer coefficient of **20** in VAc polymerization (see Entry 6, Table 3) could not be determined accurately as excessive instrument noise frustrated attempts to fit the experimental data. However, the monomer conversion and the dispersity of the polymer formed suggest that C_{tr}^{app} for **20** is greater than C_{tr}^{app} for **19**, as would be expected based on the Hammett correlation (Entries 5 and 6, Table 3, a graphical comparison of the NMR integration data can be found in the Supporting Information, Figure S4).

Figure 7: Correlation plots between the Hammett coefficient of the 4-aryl substituent of RAFT agents **16** (◆, blue diamonds), **17** (▼, dark red triangles), **18** (▲, green triangles), **19** (●, purple hexagons), **20** (+, gray crosses) and their apparent transfer coefficients in (a) MA polymerization with neutral (**16-20** (---)) or protonated (**16-H⁺-20-H⁺** (—)) RAFT agents, (b) in NVC polymerization (**16-20** (—)) and (c) in VAc polymerization (**16-19** (—), **20** omitted as C_{tr}^{app} was unable to be calculated accurately)

From these Hammett correlation plots (Figure 7) a predictable relationship between RAFT structure and activity can be observed, where the activity of dithiocarbamates in RAFT polymerization can be correlated to the availability of the nitrogen lone pair.

Conclusion

In this contribution, we have shown how alterations to RAFT agent structure can lead to appreciable (and, in hindsight, predictable) changes in reactivity. This was facilitated by use of *N*-aryl-*N*-pyridyl dithiocarbamates that contain strategically placed substituents with differing electronic demand.

Synthesis of a series of *N*-aryl-*N*-pyridyl dithiocarbamates differing in substituent on the 4-position of the aryl ring was achieved in two steps. The functional *N*-aryl-*N*-pyridyl amines were prepared by Pd-catalyzed amination of 4-chloropyridine with the appropriate 4-substituted aniline in moderate to high yield. These were converted to the dithiocarbamate RAFT agents **16-21** by alkylation of the carbodithioate salts formed by reaction of the aniline with CS₂ in the presence of KO^tBu.

The apparent chain transfer coefficients of dithiocarbamates **16-21** (C_{tr}^{app}) in MA, NVC and VAc polymerizations were found to increase with decreasing thiocarbonyl electron density. The magnitude of

C_{tr}^{app} of the *N*-aryl-*N*-pyridyl RAFT agents **16-20** in MA (in the presence or absence of acid), NVC and VAc polymerization correlated well with Hammett coefficients, indicating a predictable relationship between RAFT agent structure and activity. As expected, the protonated RAFT agents **16-H⁺**-**21-H⁺** offered significantly improved control with respect to the neutral **16-21**, in polymerization of the MAM MA. Best control was obtained with cyano-functional **20-H⁺** or pyridyl-functional **19-H⁺**. For NVC polymerization, the RAFT agent of choice was that with the highest activity, namely **19** or **20**. Whilst these same RAFT agents delivered PVAc of low dispersity, these RAFT agent were found to strongly retard polymerization. Thus, the best performing RAFT agents for VAc polymerization were **16-18** which provide the best balance between dispersity and extent of retardation. The side reactions inherent in VAc polymerization (transfer to monomer, polymer, head addition) dictate that conversion should be $\leq 50\%$ to ensure the lowest dispersity. The fact that no inhibition/retardation is observed during NVC polymerization, even with the more active RAFT agents (**19** or **20**), indicates that the PNVC propagating radical is much better homolytic leaving group than the PVAc propagating radical. This also suggests that NVC may be “more-activated” than LAMs such as VAc and *N*-vinylpyrrolidone. The status of NVC as a LAM is the subject of current investigation.

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Chain Transfer Kinetics of Acid/Base Switchable *N*-Aryl-*N*-Pyridyl Dithiocarbamate
RAFT Agents in Methyl Acrylate, *N*-Vinylcarbazole and Vinyl Acetate Polymerization

Daniel J. Keddie, Carlos Guerrero-Sanchez, Graeme Moad, Roger J. Mulder, Ezio Rizzardo and San H. Thang