Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Continuous-flow chemistry for the determination of comonomer reactivity ratios

Marcus H. Reis, Cullen L. G. Davidson IV, and Frank A. Leibfarth*

Department of Chemistry, The University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, United States

*frankl@email.unc.edu

Table of Contents

General methods and materials **S2**

Flow equipment **S3**

Sample calculation for determining F_A and f_A from ^{1}H NMR spectrum **S5**

Specific procedures for lignin based monomer reactivity ratios **S8**

Comments about internal standards **S8**

Importance of mixing **S8**

Copolymerization data

- methyl methacrylate — styrene (1 of 3) **S9**
- methyl methacrylate — styrene (2 of 3) **S10**
- methyl methacrylate — styrene (3 of 3) **S11**
- *tert*-Butyl acrylate — vinyl pyrrolidone **S12**
- methyl methacrylate — methacrylate **S13**
- styrene — *n*-butyl acrylate **S14**
- methyl methacrylate — *n*-butyl acrylate **S15**
- guaiacol methacrylate — methyl methacrylate **S16**
- 4-ethyl guaiacol methacrylate — methyl methacrylate **S17**
- 4-ethyl guaiacol methacrylate — *tert*-butyl acrylate **S18**

References **S19**

General Methods and Materials

Reagents, unless otherwise specified, were purchased and used without further purification. Methacrylated lignin monomers were synthesized according to literature procedures and purified by column chromatography using a 92:8 hexanes:ethyl acetate mobile phase.[1]

Analysis

Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker 500 MHz or Bruker AVANCE III 600 MHz CryoProve spectrometer with a solvent resonance as the internal standard (^{1}H NMR: $CDCl_3$ at 7.26 ppm). ***Acquisition parameters***: relaxation delay (D1 time) of 5 seconds, acquisition time of 6 seconds, spectral width was set to 11ppm, and O1p was set to 4 ppm. ***Additional notes***: high quality shimming was necessary to fully resolve integrated peaks from ^{13}C satellites. Proper baseline corrections and manual phase correction are recommended to ensure accurate integrations.

Flow Equipment

Flow tubing and connections were purchased from Upchurch Scientific (IDEX Health and Science). Syringe pumps and syringes were purchased from Harvard Apparatus.

Figure S1. A. PEEK super-flangeless nut **B.** Yellow super-flangeless ferrule with corresponding stainless steel ferrule ring -- sold separately. **C.** 0.02 ID PFA tubing **D.** Standard union, Tefzel **E.** 4-way "L" switch valve **F.** back pressure regulator, 40 PSI (part number P-785) **G.** Static mixing Tee **H.** 20 mL stainless steel syringe **I.** Ph.D Ultra syringe pump

Additional components: Chemraz O-rings were purchased for the 20 mL syringes in order to prevent swelling due to exposure to Toluene (Harvard Apparatus). Luer-lock adapters were purchased to allow withdrawing reaction solution using standard needles (Idex Health and Science).

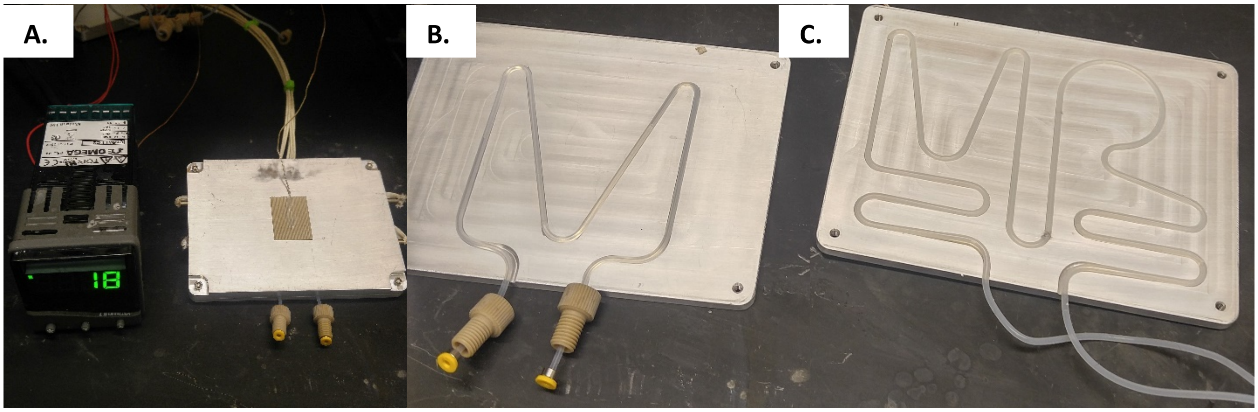
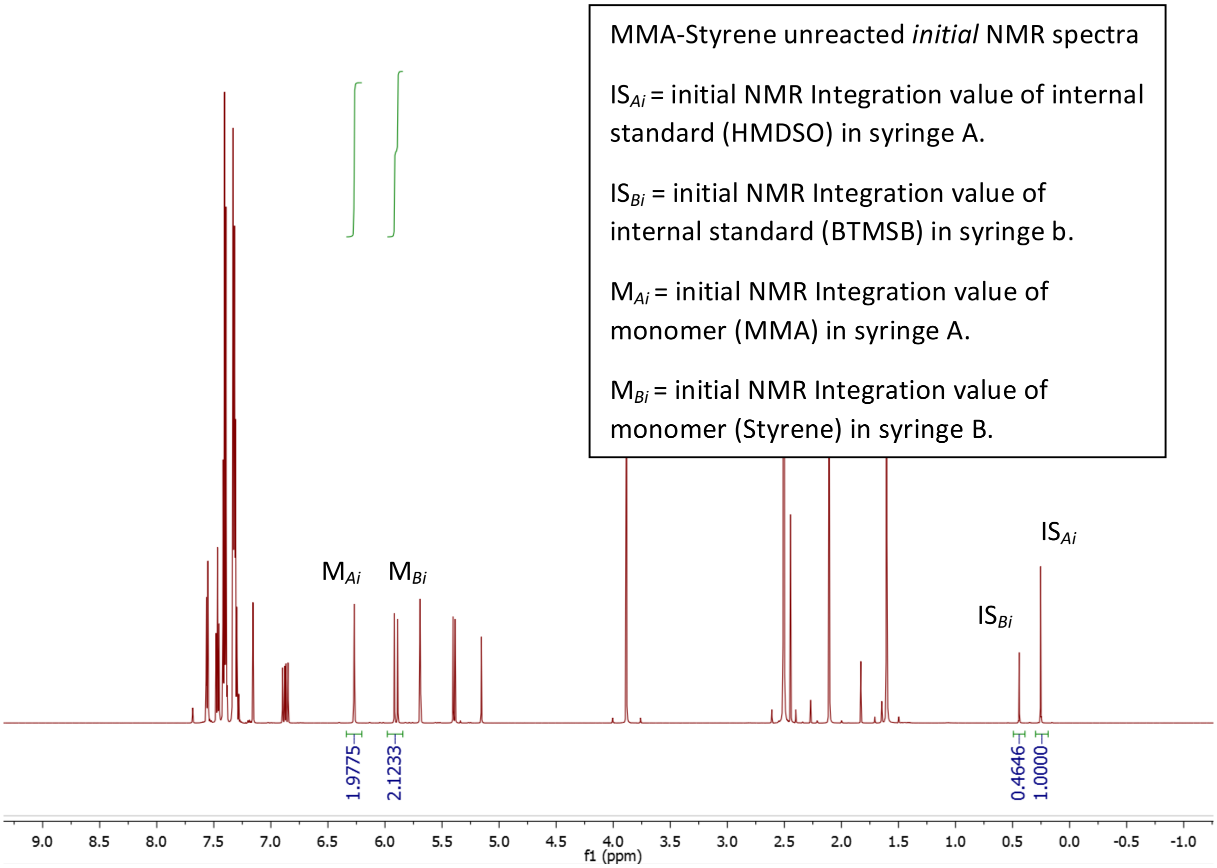


Figure S2: A. Custom aluminum heating block with a digital temperature controller, imbedded tubular heating elements, and a thermal couple for temperature detection was used to achieve accurate and reproducible heating. Different reactor volumes were used to help control reaction time. **B.** Cross section of 11in “M” reactor geometry. **C.** Cross section of 22in “MR” reactor geometry.

Sample calculation for determining F_A and f_A from ^{1}H NMR spectrum

Calculation of a monomer pair's reactivity ratio requires the experimental determination of f_A and F_A for multiple different monomer compositions. The various linear and non-linear methods match those values of f_A and F_A to a pair of reactivity ratios based on the copolymer equation. Here is a short discussion on how to calculate f_A and F_A using this continuous flow methodology. A discussion on how to implement the various linear and non-linear methods can be found elsewhere.[2,3,4,5]

The first value we will calculate is f_A which describes the initial mole fraction of unreacted monomer before any polymerization has occurred. Rather than determining f_A by taking an initial NMR spectra for each sample, this method uses two internal standards whose NMR integrations directly correspond to initial monomer concentrations. This initial monomer-to-internal standard ratio is calculated from one initial NMR. Initial NMR spectra is for MMA-Styrene trial 1 is shown below.



MMA-Styrene unreacted *initial* NMR spectra

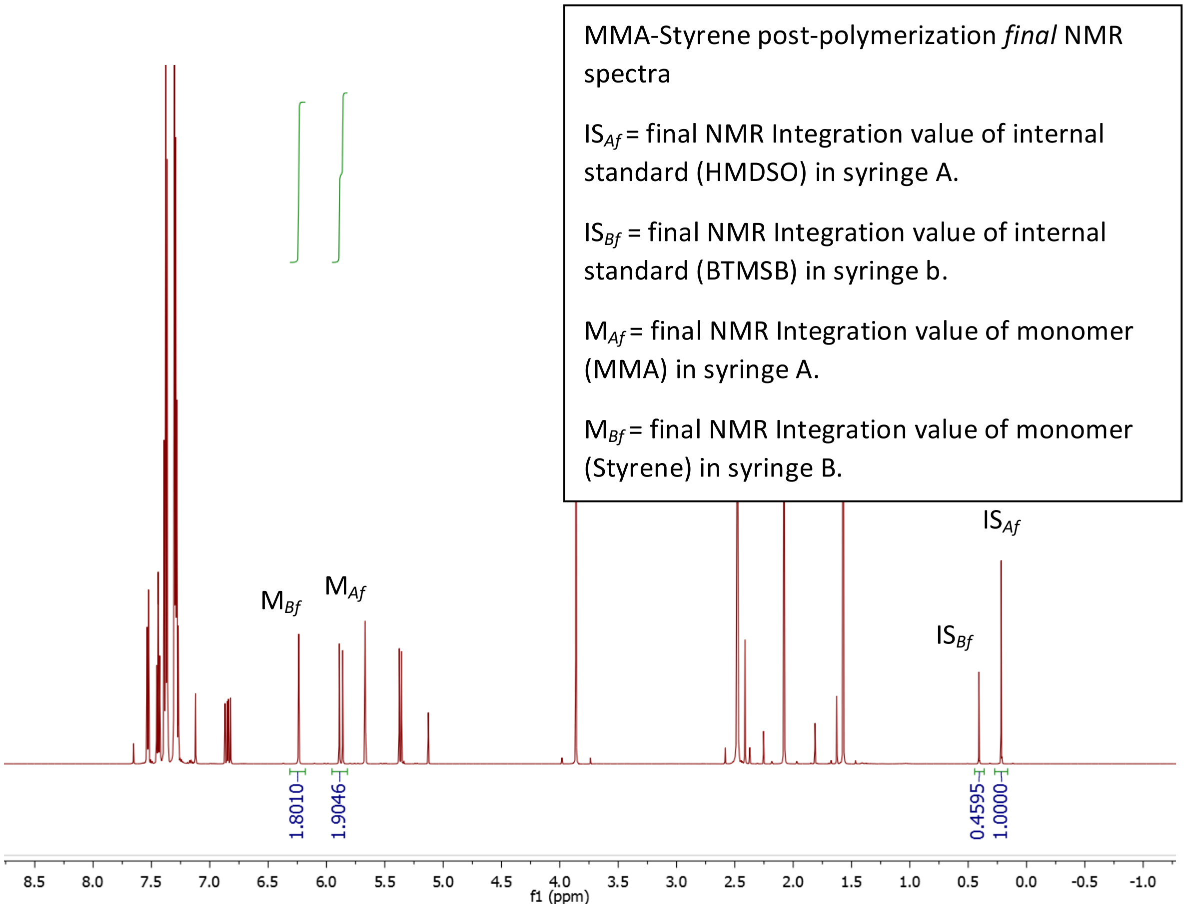
IS_{Ai} = initial NMR Integration value of internal standard (HMDSO) in syringe A.

IS_{Bi} = initial NMR Integration value of internal standard (BTMSB) in syringe b.

M_{Ai} = initial NMR Integration value of monomer (MMA) in syringe A.

M_{Bi} = initial NMR Integration value of monomer (Styrene) in syringe B.

Analysis of the initial, unreacted solution (MMA-Styrene trial 1 shown above) determines the ratio of unreacted monomer to internal standard. Since we assume the concentrations of unreacted monomer and internal standard inside the syringes remain homogeneously mixed and unchanged during the reaction, analysis of internal standard peaks is used as an indirect measurement of initial monomer concentrations for all final, post-polymerization samples.



MMA-Styrene post-polymerization *final* NMR spectra

IS_{Af} = final NMR Integration value of internal standard (HMDSO) in syringe A.

IS_{Bf} = final NMR Integration value of internal standard (BTMSB) in syringe b.

M_{Af} = final NMR Integration value of monomer (MMA) in syringe A.

M_{Bf} = final NMR Integration value of monomer (Styrene) in syringe B.

The above sample, taken post polymerization, shows a decrease in monomer concentration corresponding to polymerization. Internal standard peaks determine initial monomer concentration. Combination of the integral values of these two spectra allow the calculation of f_A.

$$f_A = \frac{\text{Initial concentration of monomer A}}{\text{Initial concentration of monomer A} + \text{Initial concentration of monomer B}}$$

$$f_A = \frac{\frac{\mathrm{M}_{Ai}}{\mathrm{IS}_{Ai}}\ x\ \mathrm{IS}_{AF}}{\left(\frac{\mathrm{M}_{Ai}}{\mathrm{IS}_{Ai}}\ x\ \mathrm{IS}_{AF}\right) + \left(\frac{\mathrm{M}_{Bi}}{\mathrm{IS}_{Bi}}\ x\ \mathrm{IS}_{BF}\right)}$$

Next, we will calculate F_A which corresponds to the mole fraction of monomer A incorporated into the final polymer. Rather than directly measuring the composition of the resulting polymer, this method measures the change in monomer concentration. This makes the assumption that any decrease in monomer NMR peaks corresponds to polymerization.

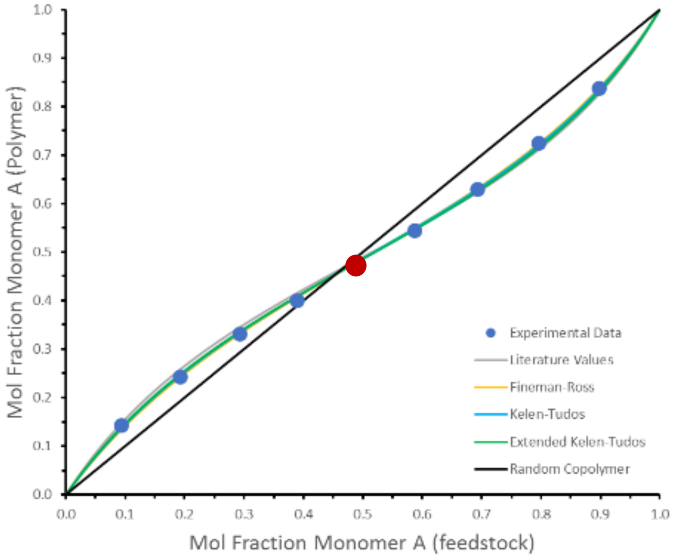
$$F_A = \text{Mol ratio of monomer A incorporated into polymer}$$

$$F_A = \frac{\text{Amount of monomer A in polymer}}{\text{Amount of monomer A in polymer} + \text{Amount of monomer B in polymer}}$$

$$F_A = \frac{\Delta\text{Monomer A concentration}}{\Delta\text{Monomer A concentration} + \Delta\text{Monomer B concentration}}$$

$$F_A = \frac{(\frac{\mathrm{M}_{Ai}}{\mathrm{IS}_{Ai}}\ x\ \mathrm{IS}_{Af}) - \mathrm{M}_{Af}}{(\frac{\mathrm{M}_{Ai}}{\mathrm{IS}_{Ai}}\ x\ \mathrm{IS}_{Af}) - \mathrm{M}_{Af} + (\frac{\mathrm{M}_{Bi}}{\mathrm{IS}_{Bi}}\ x\ \mathrm{IS}_{Bf}) - \mathrm{M}_{Bf}}$$

Calculating f_A and F_A for this sample allows us to plot one point (red) on the Mayo-Lewis plot shown below. Repeat calculations for the other eight points using the same initial spectra allows further calculation of reactivity ratio using linear or non-linear methods.



Specific procedures for lignin based monomer reactivity ratios

A slightly modified procedure was used to calculate the reactivity ratios of the lignin based monomers. These monomers had higher molecular weights compared to the other monomers studied. This made it impractical to create solutions using the typical (2.8M) concentrations. Instead, lower monomer concentrations and higher initiator concentrations were used for these copolymerizations. These changes did not influence the quality of the data for calculating reactivity ratios. Sample stoichiometry is shown below.

Syringe 1: 6 mL (34 mmol) of guaiacol methacrylate (GM) + 200 mg (0.9 mmol) 1,4-bis(trimethylsilyl)benzene +10mL of toluene.

Syringe 2: 3.6 mL (34 mmol) of MMA + 0.4 mL (2 mmol) hexamethyldisiloxane + 12.4 mL toluene

Syringe 3: 395 mg (2.4 mmol) of AIBN + 16mL toluene

Comments about internal standards

Proper selection of ^{1}H NMR internal standards is crucial for accurate determination of reactivity ratios via this method. General guidelines for picking internal standards are as follows:

- Each internal standard needs to be resolved from any other peaks (including formed copolymer peaks)
- They should be non-volatile
- They should have a large number of equivalent hydrogens to increase signal to noise without requiring high concentrations
- They should be inert to the reaction conditions

With these requirements in mind, we propose the use of hexamethyldisiloxane (HMDSO) and 1,4-bis(trimethysilyl)benzene (BTMSB) as a general set of internal standards, however these compounds are not universally applicable. For example, HMDSO was found to react with monomers containing free alcohols such as hydroxy ethylacrylate. HMDSO also showed slight reactivity with styrene. As a result, styrene and HMDSO were combined in separate syringes for all copolymerizations.

Importance of mixing

Proper mixing is crucial in calculating accurate reactivity ratios. Poorly mixed regions can lead to increased homopropogation and skewing of reactivity ratio values. We found that flow rates below 0.3 mL/min produced less reproducible data which could be attributed to poor mixing. To keep flow rates above this threshold larger reactors were used for slow polymerizations. In addition, two feet of tubing was used to separate the reactor and the point where the three solutions were combined at a T-mixer. This extra length before the reactor was used to increase mixing via diffusion before the solution was reacted.

methyl methacrylate – styrene copolymerization (1 of 3)

Figure S3. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

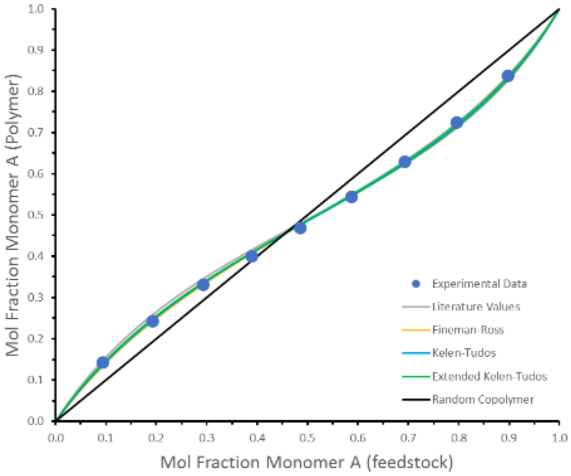
A.

	rMMA	rStyrene
Literature Values[6] @ 60°C	0.46	0.52
Fineman-Ross	0.52	0.60
Kelen-Tudos	0.50	0.58
Extended Kelen-Tudos	0.48	0.57
NLLS	0.47±0.04	0.56±0.02

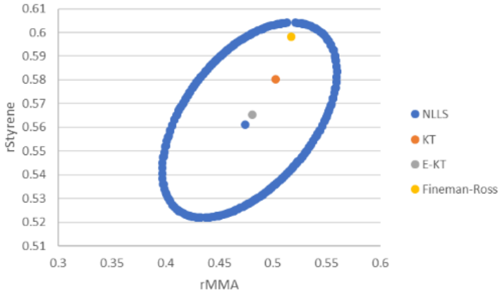
B.

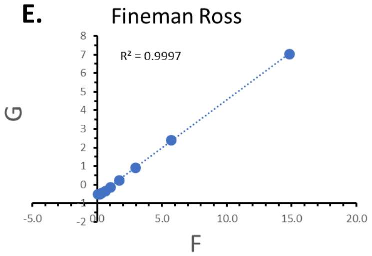
Reaction Time = 30s		
Mol Fraction MMA	Conversion MMA	Conversion Styrene
0.09	11.6%	7.0%
0.19	9.9%	7.4%
0.29	9.7%	8.1%
0.39	9.6%	9.1%
0.48	9.0%	9.6%
0.59	9.4%	11.1%
0.69	10.0%	13.2%
0.79	11.6%	17.0%
0.90	13.5%	22.9%

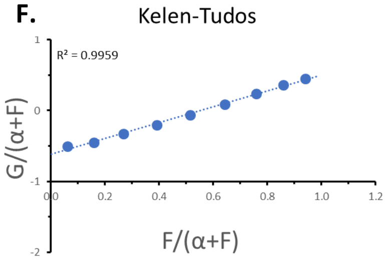
C.

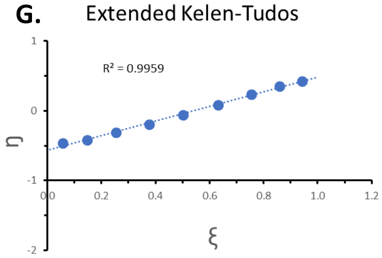


D.

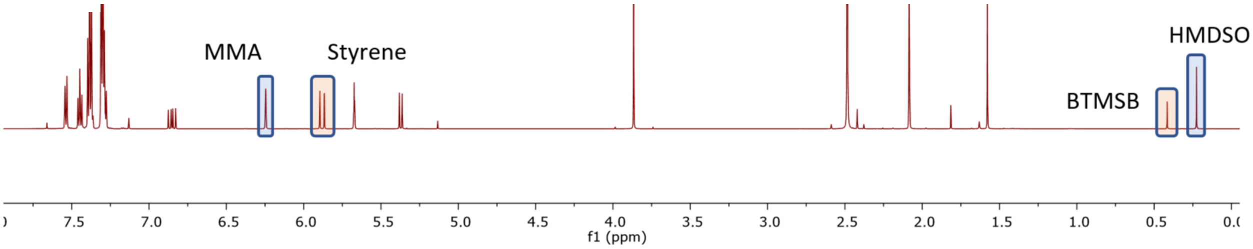








H.



methyl methacrylate – styrene copolymerization (2 of 3)

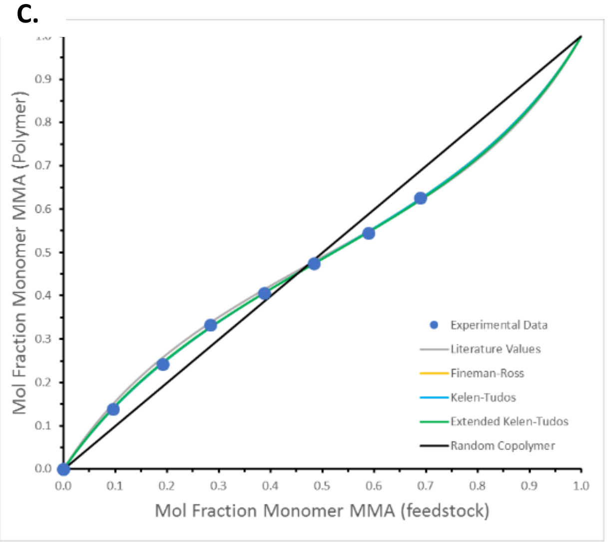
Figure S4. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. Two points missing due to pump malfunction. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

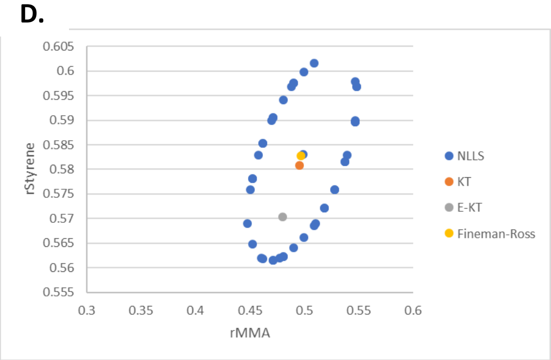
A.

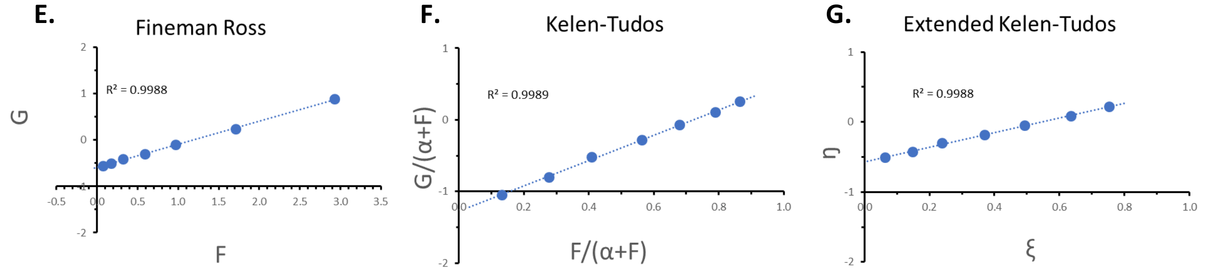
	rMMA	rStyrene
Lit Values[6] @ 60°C	0.46	0.52
Fineman-Ross	0.50	0.58
Kelen-Tudos	0.50	0.58
Extended Kelen-Tudos	0.48	0.57
NLLS	0.50±0.02	0.58±0.01

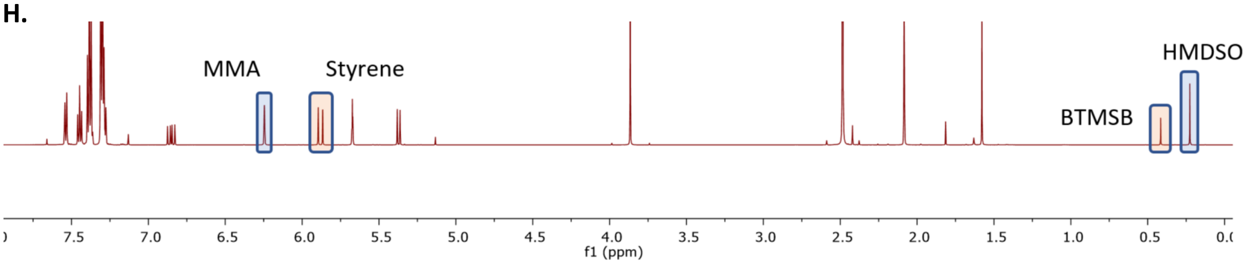
B.

Reaction Time = 30s		
Mol Fraction MMA	Conversion MMA	Conversion Styrene
0.10	7.6%	5.0%
0.19	6.9%	5.1%
0.28	6.8%	5.4%
0.39	6.5%	6.1%
0.48	8.5%	8.8%
0.59	6.8%	8.1%
0.69	11.0%	14.6%









methyl methacrylate – styrene copolymerization (3 of 3)

Figure S5. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

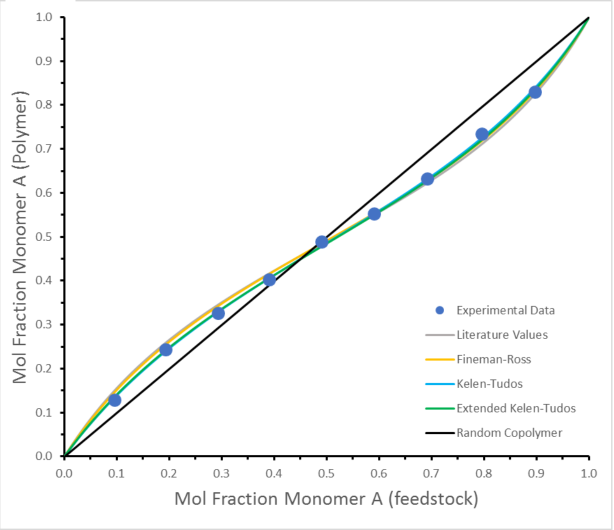
A.

	rMMA	rStyrene
Lit Values[6] @ 60°C	0.46	0.52
Fineman-Ross	0.49	0.54
Kelen-Tudos	0.53	0.62
Extended Kelen-Tudos	0.51	0.60
NLLS	0.55±0.03	0.63±0.02

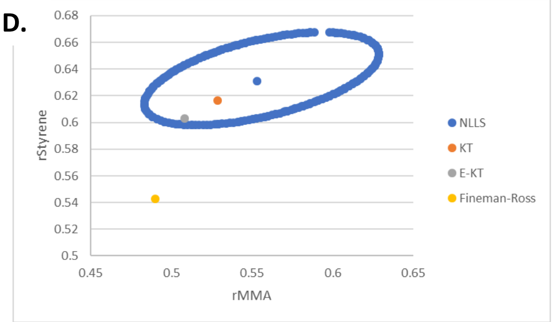
B.

Reaction Time = 30s		
Mol Fraction MMA	Conversion MMA	Conversion Styrene
0.10	9.4%	6.7%
0.19	9.0%	6.7%
0.29	7.5%	6.4%
0.39	7.5%	7.1%
0.49	8.9%	9.0%
0.59	8.8%	10.2%
0.69	9.0%	11.8%
0.80	10.5%	14.7%
0.90	12.1%	21.5%

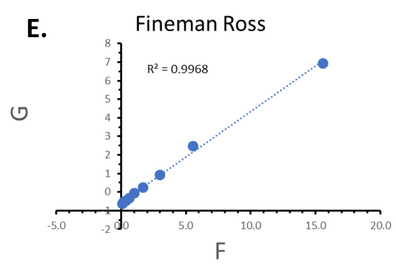
C.



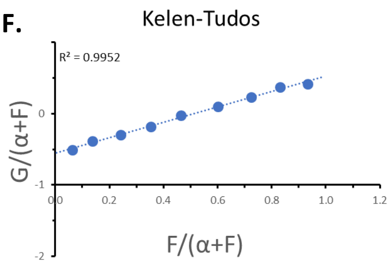
D.



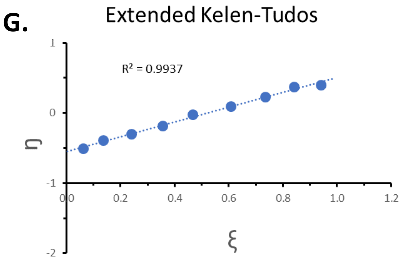
E.



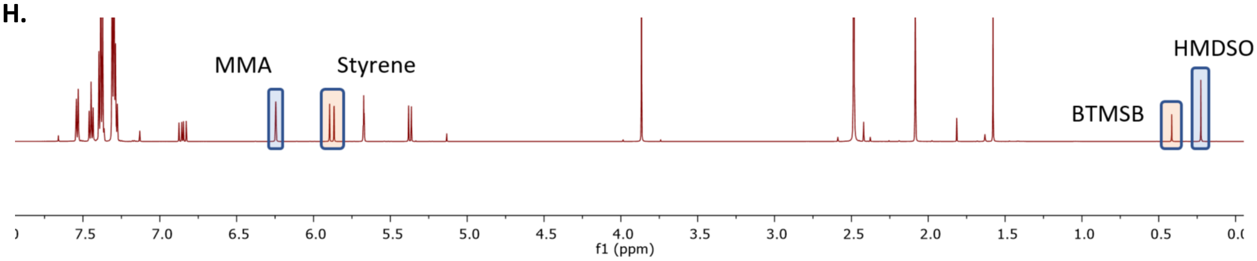
F.



G.



H.



tert-butyl acrylate – vinyl pyrrolidone copolymerization

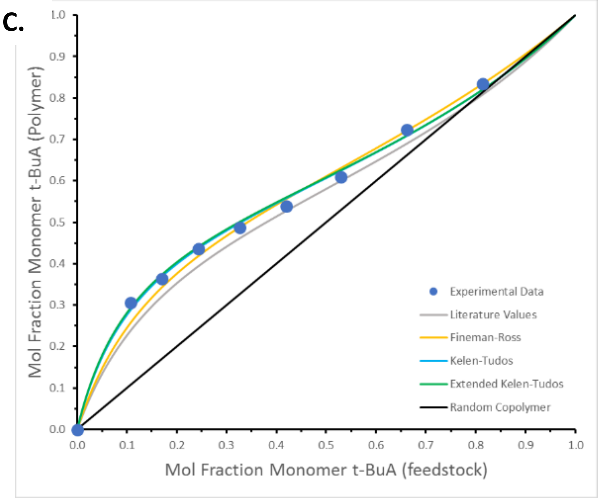
Figure S6. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

A.

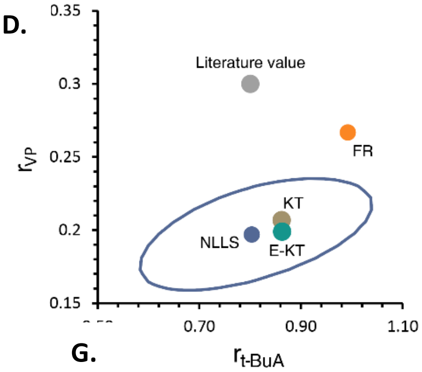
	r*t*BuA	rVP
Lit Values[7] @ 50°C	0.80	0.30
Fineman-Ross	0.99	0.27
Kelen-Tudos	0.86	0.21
Extended Kelen-Tudos	0.86	0.20
NLLS	0.8±0.1	0.20±0.02

Reaction Time = 5s		
Mol Fraction *t*BuA	Conversion *t*BuA	Conversion VP
0.11	10.0%	2.7%
0.17	9.0%	3.2%
0.24	8.5%	3.5%
0.33	7.2%	3.7%
0.42	6.7%	4.1%
0.53	5.7%	4.1%
0.66	5.1%	3.8%
0.81	4.5%	3.9%

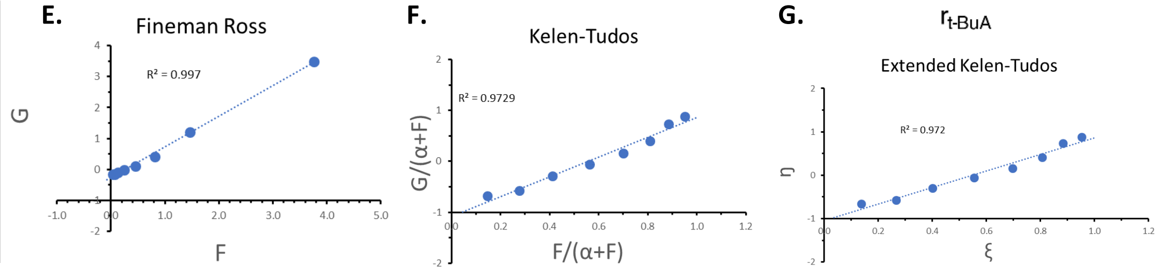
C.



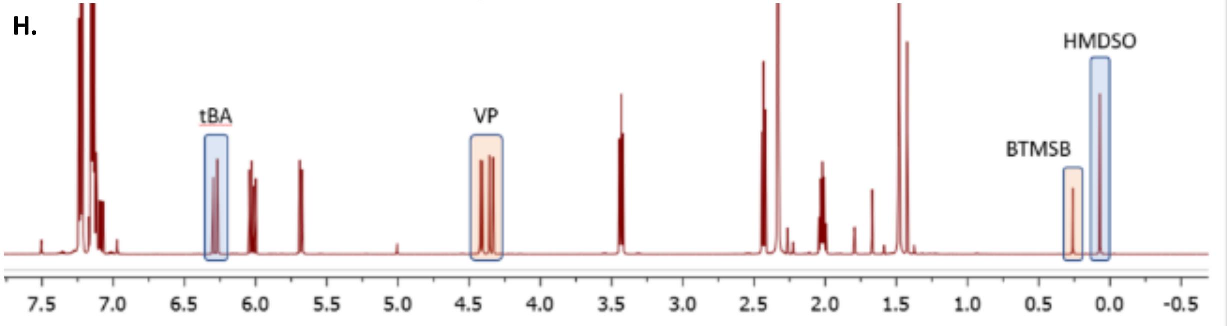
D.



E. **F.** **G.**



H.



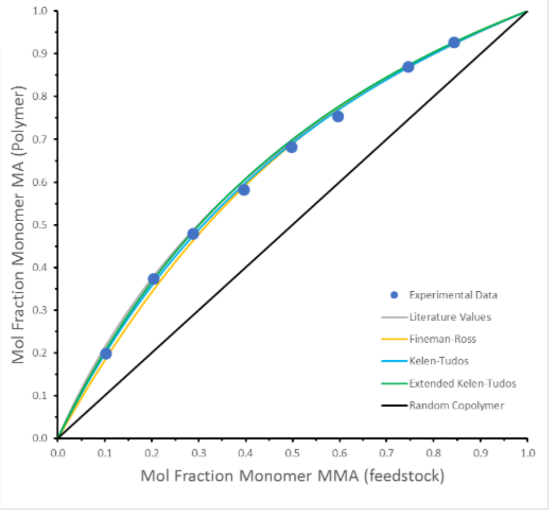
methyl methacrylate - methacrylate copolymerization

Figure S7. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

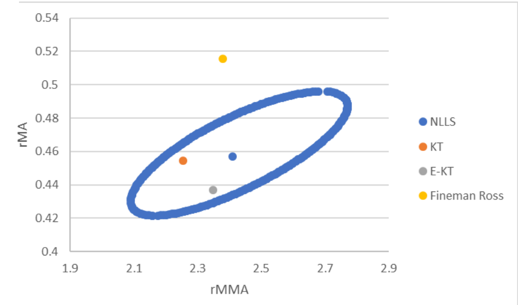
A.	rMMA	rMA
Lit Values[6] @ 50°C	2.20	0.40
Fineman-Ross	2.37	0.46
Kelen-Tudos	2.35	0.45
Extended Kelen-Tudos	2.44	0.43
NLLS	2.4±0.2	0.46±0.02

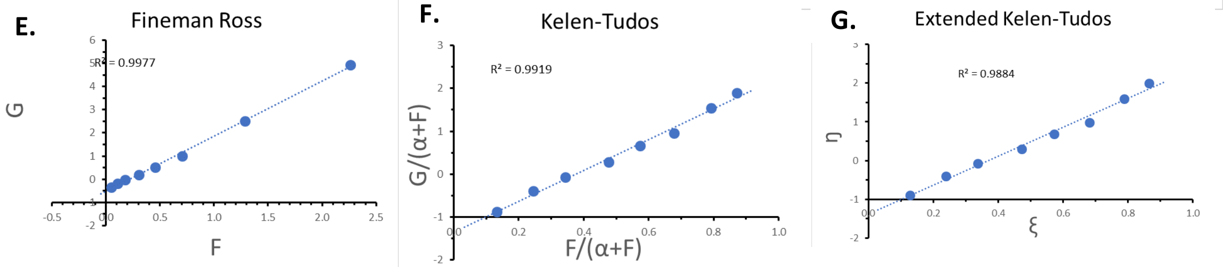
Reaction Time = varies			
Mol Fraction MMA	Conversion MMA	Conversion MA	Reaction Time (s)
0.10	14.5%	6.6%	90
0.20	14.0%	6.0%	60
0.40	13.5%	6.3%	30
0.50	11.2%	5.2%	30
0.60	8.3%	4.0%	30
0.29	13.8%	6.0%	25
0.75	13.2%	5.8%	20
0.84	17.2%	7.2%	15

C.

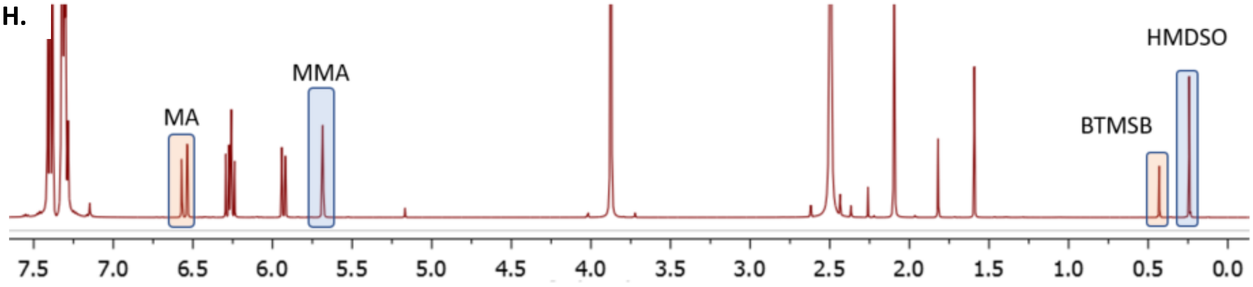


D.





H.



styrene – n-butyl acrylate copolymerization

Figure S8. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

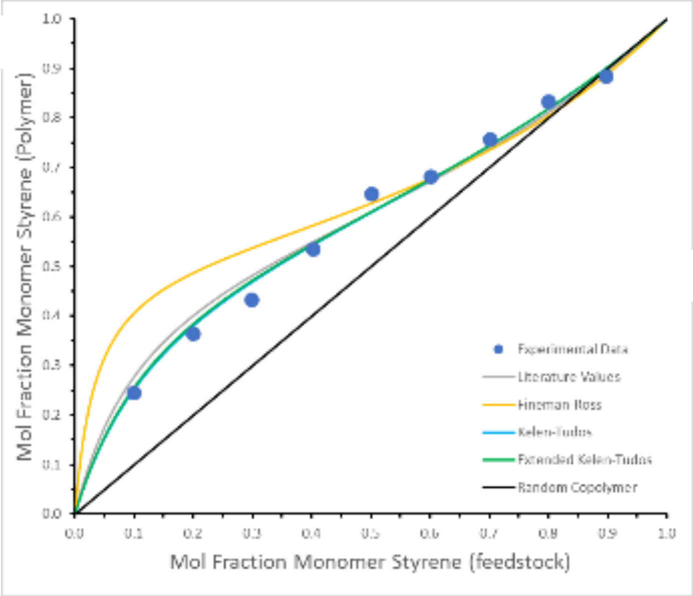
A.

	rStyrene	r*n*BuA
Lit Values[8] @ 80°C	0.88	0.21
Fineman-Ross	0.79	0.07
Kelen-Tudos	0.95	0.25
Extended Kelen-Tudos	0.95	0.25
NLLS	1.0±0.2	0.29±0.03

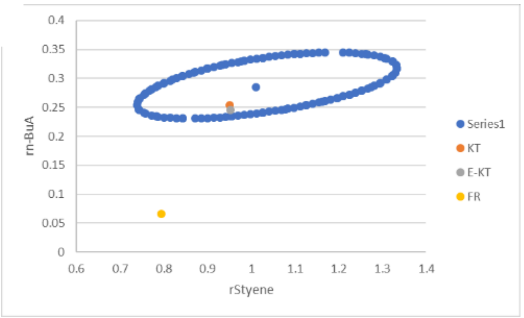
B.

Mol Fraction Styrene	Conversion Styrene	Conversion *n*BuA
0.10	4.0%	3.5%
0.20	3.2%	4.0%
0.30	4.1%	5.4%
0.40	4.2%	6.0%
0.50	3.2%	5.8%
0.60	5.1%	8.8%
0.70	2.2%	3.9%
0.80	2.6%	6.0%
0.90	4.4%	12.9%

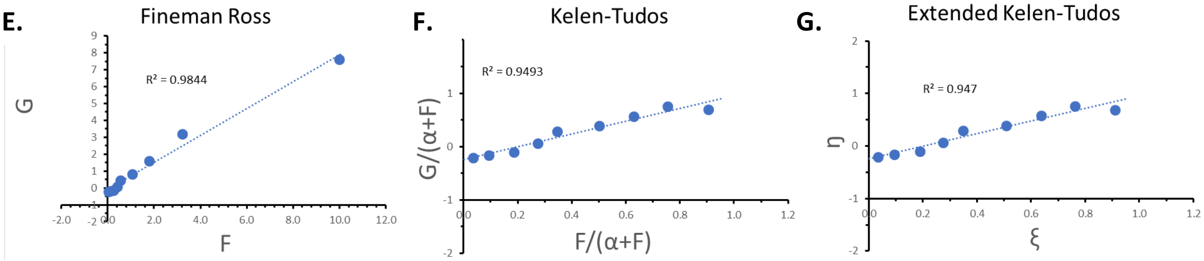
C.



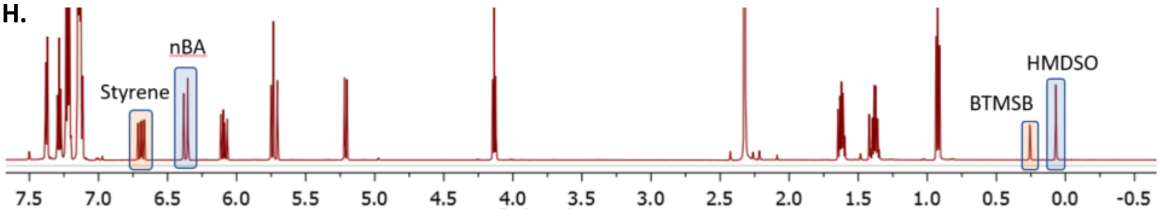
D.



E. **F.** **G.**



H.



methyl methacrylate – n-butyl acrylate copolymerization

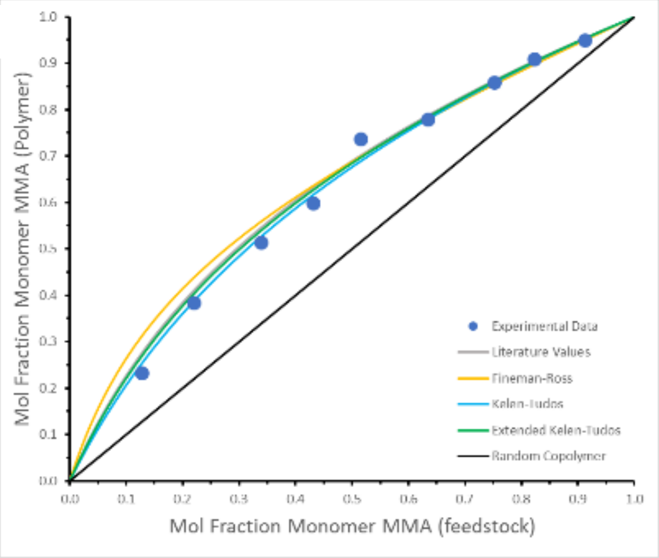
Figure S9. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

A.	rMMA	r*n*BuA
Lit Values[9] @ 90°C	2	0.35
Fineman-Ross	1.78	0.26
Kelen-Tudos	1.95	0.41
Extended Kelen-Tudos	1.97	0.37
NLLS	2.2±0.3	0.48±0.05

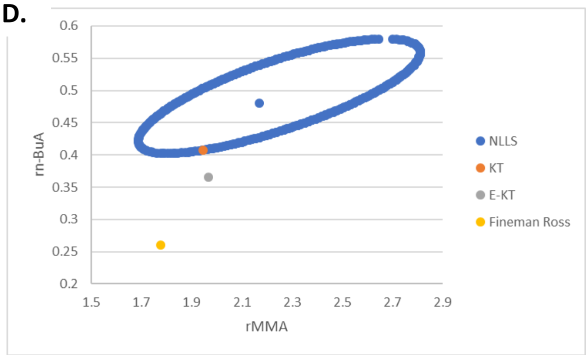
B.

Reaction Time = 60s		
Mol Fraction MMA	Conversion MMA	Conversion *n*BuA
0.91	7.7%	4.3%
0.82	7.5%	3.5%
0.75	8.1%	4.1%
0.63	9.8%	4.8%
0.43	13.9%	7.1%
0.34	18.0%	8.7%
0.22	26.7%	12.0%
0.13	38.9%	18.8%

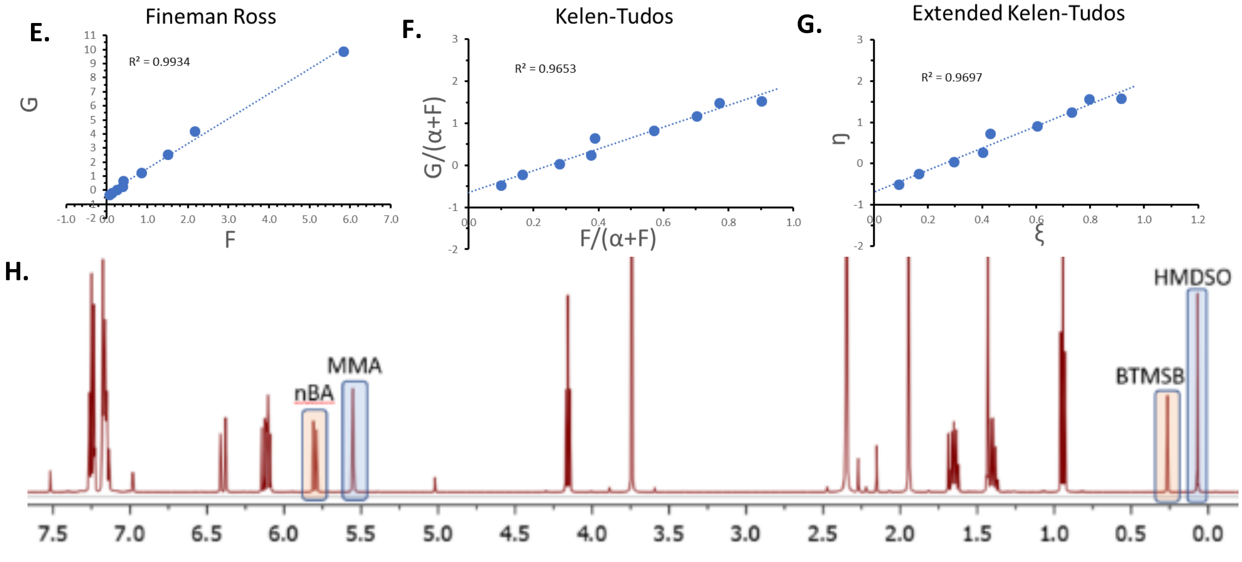
C.



D.



E. **F.** **G.** **H.**



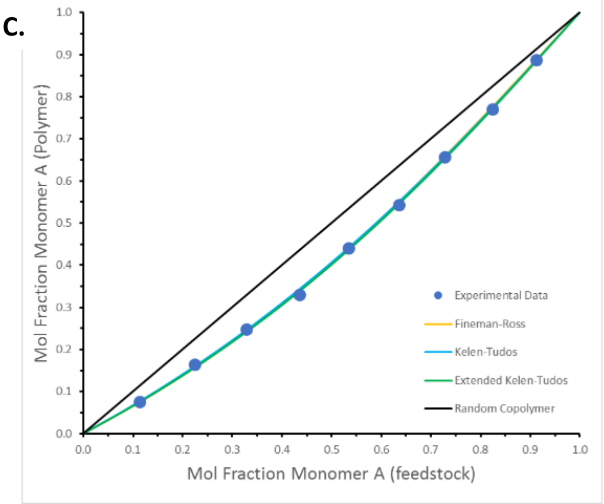
guaiacol methacrylate – methyl methacrylate copolymerization

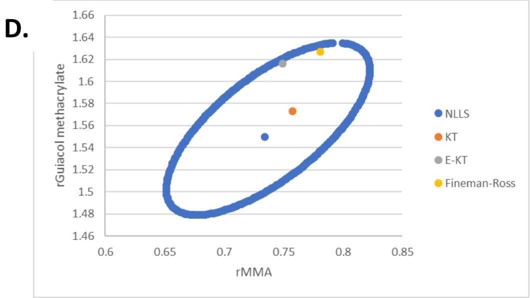
Figure S10. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

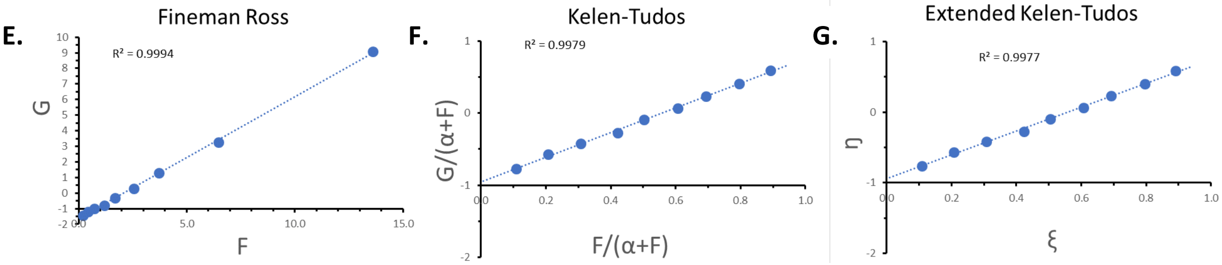
A.

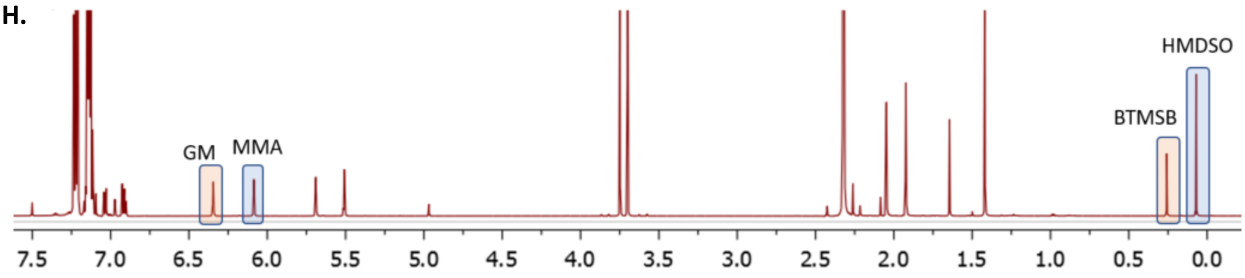
	rMMA	rGM
Lit Values	n/a	n/a
Fineman-Ross	0.78	1.63
Kelen-Tudos	0.76	1.57
Extended Kelen-Tudos	0.75	1.62
NLLS	0.73±0.04	1.55±0.04

Mol Fraction MMA	Conversion MMA	Conversion GM
0.11	8.6%	13.4%
0.22	8.9%	13.2%
0.33	7.9%	11.7%
0.43	7.7%	11.9%
0.53	8.2%	11.9%
0.63	7.5%	10.9%
0.73	7.4%	10.3%
0.82	7.8%	10.8%
0.91	7.3%	9.6%









4-ethyl guaiacol methacrylate – methyl methacrylate copolymerization

Figure S11. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with other methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

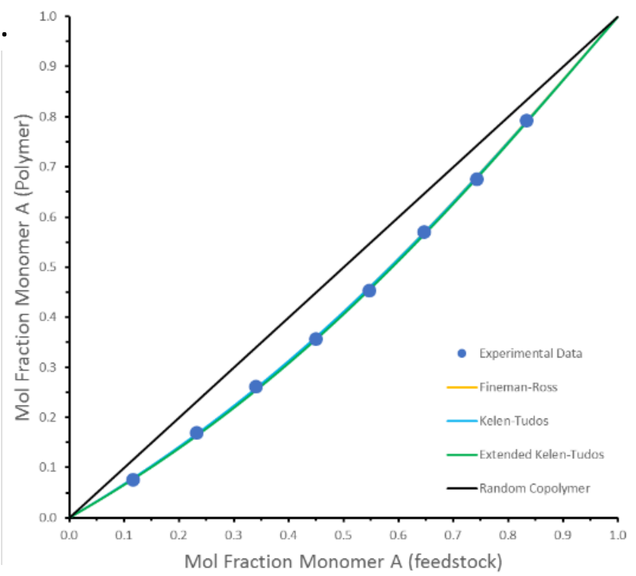
A.

	rMMA	rEGM
Lit Values	n/a	n/a
Fineman-Ross	0.80	1.58
Kelen-Tudos	0.79	1.57
Extended Kelen-Tudos	0.79	1.61
NLLS	0.8±0.05	1.57±0.04

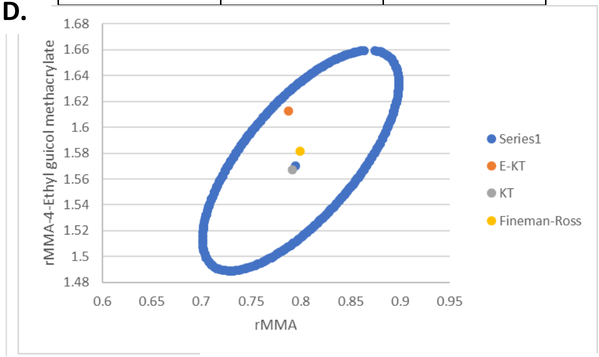
B.

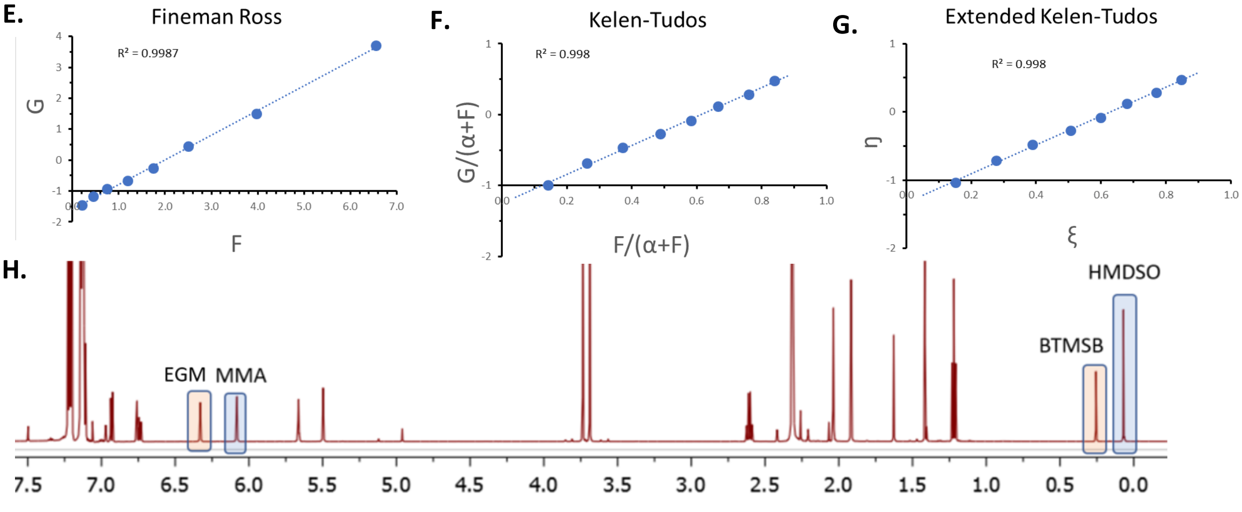
Reaction Time = 30s		
Mol Fraction MMA	Conversion MMA	Conversion EGM
0.12	8.6%	13.6%
0.23	9.4%	13.8%
0.34	8.3%	12.0%
0.45	7.7%	11.3%
0.55	6.9%	10.0%
0.65	7.5%	10.3%
0.74	6.5%	9.0%
0.83	7.8%	10.2%

C.



D.





4-ethyl guaiacol methacrylate – *tert*-butyl acrylate copolymerization

Figure S12. A. Comparison of literature values with our experimental data (100 °C) calculated using four different methods. **B.** Individual monomer conversion at different comonomer ratios. **C.** Mayo-lewis plot of data points overlaid with literature and calculated reactivity ratios. **D.** NLLS 95% joint confidence region with Dother methods for comparison. **E.** Fineman Ross plot. **F.** Kelen-Tudos plot **G.** Extended Kelen-Tudos plot. **H.** representative NMR spectra highlighting what peaks were used for calculation and what internal standard was used for each monomer.

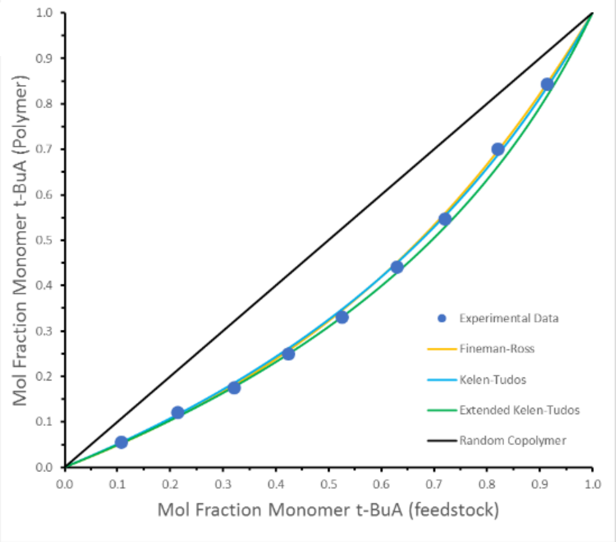
A.

	r*t*BuA	rEGM
Lit Values	n/a	n/a
Fineman-Ross	0.53	2.22
Kelen-Tudos	0.48	2.08
Extended Kelen-Tudos	0.41	2.16
NLLS	0.43±0.07	2.0±0.1

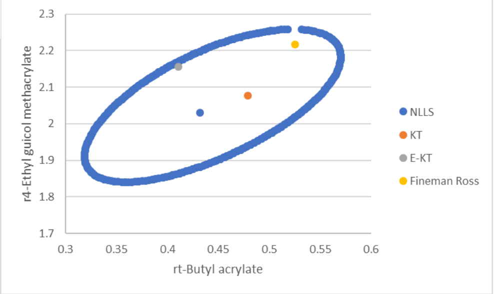
B.

Reaction Time = 30s		
Mol Fraction *t*BuA	Conversion *t*BuA	Conversion EGM
0.11	8.5%	16.9%
0.21	8.9%	17.5%
0.32	8.7%	19.4%
0.42	9.8%	21.5%
0.53	10.2%	22.6%
0.63	11.6%	25.0%
0.72	13.7%	29.2%
0.82	19.1%	36.9%
0.91	22.9%	44.7%

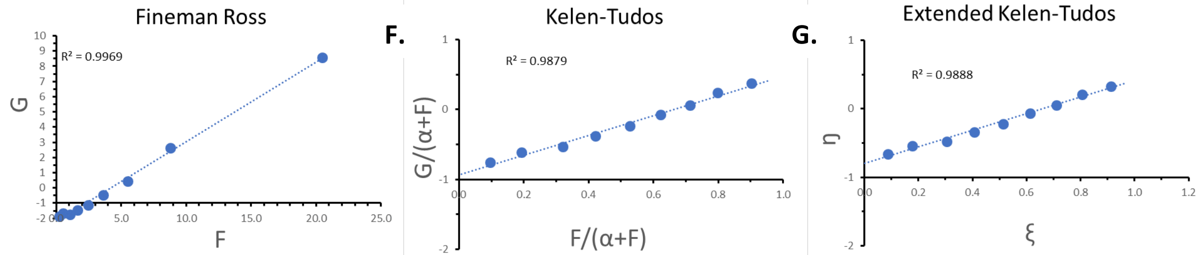
C.



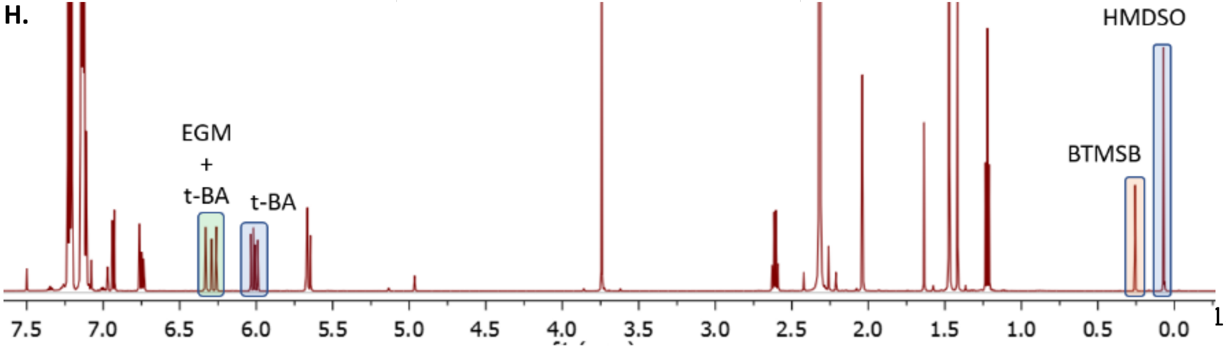
D.



E. **F.** **G.**



H.



References

(1) Stanzione, J. F.; Sadler, J. M.; La Scala, J. J.; Wool, R. P. *ChemSusChem* **2012**, *5* (7), 1291.

(2) Tgdos, F.; Kelen, T.; Foldes-Berezsnich, T.; Turcsanyi, B. **1976**, *10* (8), 1513.

(3) Kelen, T.; TÜd[Otilde]s, F. *J. Macromol. Sci. Part A - Chem.* **1975**, *9* (1), 1.

(4) Fineman, M.; Ross, S. D. *J. Polym. Sci.* **1950**, *5* (2), 259.

(5) Van Herk, A. M.; Dröge, T. *Macromol. Theory Simulations* **1997**, *6* (6), 1263.

(6) Odian, G. *Principles of Polymerization*, 4th ed.; Wiley-Interscience, 2004.

(7) Gatica, N.; Fernández, N.; Opazo, A.; Alegría, S.; Gargallo, L.; Radic, D. *Polym. Int.* **2003**, *52* (8), 1280.

(8) Ziaee, F.; Nekoomanesh, M. *Polymer (Guildf).* **1998**, *39* (1), 203.

(9) Sebastian G. Roos; Axel H. E. Müller*, †; Matyjaszewski, K. *Macromolecules* **1999**, *32* (25), 8331.