

Towards biodegradable chain-growth polymers and polymer particles

Re-evaluation of reactivity ratios in copolymerization of vinyl monomers with cyclic ketene acetal using non-linear regression with proper error analysis

Supporting Information

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Measurements of the absolute error in the copolymer composition:

The residual standard deviation (*RSD*) were calculated with Equations 9 and 10. The signals and the noise were measured manually from the spectra available in the article (both noise and signal were measured with a ruler). This gives only a rough estimation of the *SNR*. When the full set of ¹H NMR spectra were not available, we considered that the *SNR* is proportional to the integral of the signal.

System MDPL/MMA¹:

Table S1: error on NMR analyses and on the fraction of MDPL in the copolymer MMA/MDPL

f_{MDPL}	F_{MDPL}	SNR_{MDPL}	SNR_{MMA}	RSD_{MDPL}	RSD_{MMA}	$RSD (F_{\text{MDPL}})$	ΔAbs
0.1	0.03	4	42	40.4 %	1.99 %	42.2 %	0.01266
0.2	0.06	6	50	24 %	1.59 %	25.6 %	0.01536
0.4	0.14	24	46	4.07 %	1.77 %	5.84 %	0.008716
0.7	0.29	32	42	2.82 %	1.99 %	4.81 %	0.013949

System MDPL/NEtMI²:

Table S2: error on NMR analyses and on the fraction of NEtMI in the copolymer NEtMI/MDPL

f_{NEtMI}	F_{NEtMI}	SNR_{NEtMI}	SNR_{MDPL}	RSD_{NEtMI}	RSD_{MDPL}	$RSD (F_{\text{NEtMI}})$	ΔAbs
0.2	0.5	19.4	28.4	5.35 %	3.28 %	8.63 %	0.04315
0.3	0.5	19.4	28.4	5.35 %	3.28 %	8.63 %	0.04315
0.4	0.53	20.6	26.7	4.95 %	3.55 %	8.5 %	0.04506
0.5	0.49	19	29	5.49 %	3.20 %	8.79 %	0.043071
0.6	0.54	20.9	26.2	4.86 %	3.64 %	8.5 %	0.0459
0.7	0.55	21.3	25.6	4.75 %	3.75 %	8.5 %	0.04675
0.8	0.7	27.1	17.1	3.49 %	6.28 %	9.77 %	0.06839

Hill *et al.* did not provide the values of f_{NEtMI} and F_{NEtMI} . The values in table S2 were estimated from the Mayo-Lewis plot.

System MDO/GMA³:

Table S3: error on NMR analyses and on the fraction of MDO in the copolymer GMA/MDO

f_{MDO}	F_{MDO}	SNR_{MDO}	SNR_{GMA}	RSD_{MDO}	RSD_{GMA}	$\text{RSD}(F_{\text{MDO}})$	ΔAbs
0.9	0.61	54	12	1.44 %	9.89 %	11.3 %	0.07
0.8	0.47	30	10	3.06 %	12.5 %	18.6 %	0.09
0.75	0.41	20	7	5.14 %	19.7 %	24.8 %	0.102
0.70	0.31	12	12	9.89 %	9.89 %	19.8 %	0.06
0.65	0.28	14	16	8.12 %	6.84 %	15 %	0.042
0.60	0.24	8	10	16.6 %	12.5 %	29.1 %	0.07

System MDO/VAc⁴:

Table S4: error on NMR analyses and on the fraction of MDO in the copolymer VAc/MDO

f_{MDO}	F_{MDO}	SNR_{MDO}	SNR_{VAc}	RSD_{MDO}	RSD_{VAc}	$\text{RSD}(F_{\text{MDO}})$	ΔAbs
0.01	0.005	3	33	58.3 %	2.71 %	61.0 %	0.0305
0.05	0.03	6	27	24 %	3.50 %	27.5 %	0.00825
0.1	0.06	9	30	14.3 %	3.06 %	17.3 %	0.01038
0.3	0.23	24	18	4.07 %	5.89 %	9.96 %	0.022908
0.5	0.42	27	9	3.50 %	14.3 %	12.5 %	0.0525
0.7	0.60	51	9	1.55 %	14.3 %	15.8 %	0.0948

System BMDO/HEMA-TMS⁵

Table S5: error on NMR analyses and on the fraction of BMDO in the copolymer BMDO/HEMA-TMS

f_{BMDO}	F_{BMDO}	SNR_{BMDO}	$\text{SNR}_{\text{HEMA-TMS}}$	RSD_{BMDO}	$\text{RSD}_{\text{HEMA-TMS}}$	$\text{RSD}(F_{\text{BMDO}})$	ΔAbs
0.25	0.06	2.18*	21	87.7 %	4.8 %	92.5 %	0.0555
0.5	0.15	5.45	19	27.1 %	5.4 %	32.5 %	0.04875
0.6	0.20	7.27	17.9	18.8 %	5.9 %	24.7 %	0.0494
0.7	0.26	9.45	16.6	13.4 %	6.5 %	19.9 %	0.05174
0.8	0.33	12	15	9.9 %	7.4 %	17.3 %	0.05709

*A $\text{SNR}=3$ usually corresponds to the limit of detection (LOD). When A $\text{SNR}<3$ is observed, it is not possible to confirm the presence of the signal. Only a maximum of F_{BMDO} can be estimated.

However, as the SNR is only roughly estimated in this work, the presence of this signal was assumed and Equation 9 was still used to determine the *RSD*.

System BMDO/MMA⁶:

Table S6: error on NMR analyses and on the fraction of BMDO in the copolymer BMDO/MMA

f_{BMDO}	F_{BMDO}	SNR_{BMDO}	SNR_{MMA}	RSD_{BMDO}	RSD_{MMA}	$RSD (F_{\text{BMDO}})$	ΔAbs
0.8	0.7	213.9	69.5	0.2%	1.0%	1.2%	0.0084
0.7	0.53	161.9	108.9	0.4%	0.6%	1.0%	0.0053
0.5	0.34	103.9	152.9	0.6%	0.4%	1.0%	0.0034
0.3	0.18	55	190	1.4%	0.3%	1.7%	0.00306

Reactivity between the different monomers present in this work:

The reactivity of each vinyl monomers with other vinyl monomers and with CKA were compared. Results are presents in Table S7.

*Reevaluated values from this study ; NA: not available in the literature.

St, styrene; MMA, methyl methacrylate; OEGMA, oligo(ethylene glycol) methacrylate; NEtMI, N-ethyl melamide; MA, methyl acrylate; NVP, N-vinylpyrrolidone; VAc, vinyl acetate; PFS, 2,3,4,4,6-pentafluorostyrene; DMAEMA, N,N-dimethylaminoethyl methacrylate; HEMA-TMS, trimethylsilyl hydroxyethyl methacrylate; nBA, n-butyl acrylate; NIPAAm, N-isopropylacrylamide.

References:

1. Tran, J.; Guegain, E.; Ibrahim, N.; Harrisson, S.; Nicolas, J., Efficient synthesis of 2-methylene-4-phenyl-1,3-dioxolane, a cyclic ketene acetal for controlling the NMP of methyl methacrylate and conferring tunable degradability. *Polymer Chemistry* **2016**, *7* (26), 4427-4435.
2. Hill, M. R.; Guegain, E.; Tran, J.; Figg, C. A.; Turner, A. C.; Nicolas, J.; Sumerlin, B. S., Radical Ring-Opening Copolymerization of Cyclic Ketene Acetals and Maleimides Affords Homogeneous Incorporation of Degradable Units. *Acs Macro Letters* **2017**, *6* (10), 1071-1077.
3. Undin, J.; Finne-Wistrand, A.; Albertsson, A. C., Copolymerization of 2-Methylene-1,3-dioxepane and Glycidyl Methacrylate, a Well-Defined and Efficient Process for Achieving Functionalized Polyesters for Covalent Binding of Bioactive Molecules. *Biomacromolecules* **2013**, *14* (6), 2095-2102.
4. Undin, J.; Illanes, T.; Finne-Wistrand, A.; Albertsson, A. C., Random introduction of degradable linkages into functional vinyl polymers by radical ring-opening polymerization, tailored for soft tissue engineering. *Polymer Chemistry* **2012**, *3* (5), 1260-1266.
5. Zhang, Y.; Chu, D. F.; Zheng, M. Y.; Kissel, T.; Agarwal, S., Biocompatible and degradable poly(2-hydroxyethyl methacrylate) based polymers for biomedical applications. *Polymer Chemistry* **2012**, *3* (10), 2752-2759.
6. Wickel, H.; Agarwal, S.; Greiner, A., Homopolymers and random copolymers of 5,6-benzo-2-methylene-1,3-dioxepane and methyl methacrylate: Structural characterization using 1D and 2D NMR. *Macromolecules* **2003**, *36* (7), 2397-2403.
7. Simionescu, C. I.; Simionescu, B. C.; Ioan, S., Plasma-induced living radical copolymerization. *Journal of Macromolecular Science-Chemistry* **1985**, *A22* (5-7), 765-778.
8. Zubov, V. P.; Valuev, L. I.; Kabanov, V. A.; Kargin, V. A., Effects of complexing agents in radical copolymerization. *Journal of Polymer Science Part a-1-Polymer Chemistry* **1971**, *9* (4), 833-&.
9. Iwakura, Y.; Kurosaki, T.; Ariga, N.; Ito, T., Copolymerization of methyl methacrylate with glycidyl methacrylate and reaction of copolymer with amines. *Makromolekulare Chemie* **1966**, *97* (SEP), 128-&.
10. Czerwinski, W. K., Solvent effect on free-radical chain polymerization .7. kinetic-analysis of the binary-system methyl methacrylate/N-vinyl pyrrolidone in bulk and in model solvents in term of the reactant-solvent complex model. *Macromolecules* **1995**, *28* (16), 5411-5418.
11. Bevington, J. C.; Johnson, M., Radical polymerizations involving esters of vinyl alcohol .2. Copolymerizations. *European Polymer Journal* **1968**, *4* (6), 669-+.
12. Orbay, M.; Laible, R.; Dulog, L., Preparation of amide and amine groups containing copolymers of methyl-methacrylate and their performance in solid polymer composites. *Makromolekulare Chemie-Macromolecular Chemistry and Physics* **1982**, *183* (1), 47-63.
13. Brosse, J. C.; Gauthier, J. M.; Lenain, J. C., Synthesis of polymers with hydroxyl end groups by radical reactions.11. Study of the co-polymerization of methyl-methacrylate with various acrylates and methacrylates - determination of reactivity ratios. *Makromolekulare Chemie-Macromolecular Chemistry and Physics* **1983**, *184* (3), 505-517.

14. Agarwal, S., Microstructural characterisation and properties evaluation of poly (methyl methacrylate-co-ester)s. *Polymer Journal* **2007**, *39* (2), 163-174.
15. Delplace, V.; Guegain, E.; Harrison, S.; Gimes, D.; Guillaneuf, Y.; Nicolas, J., A ring to rule them all: a cyclic ketene acetal comonomer controls the nitroxide-mediated polymerization of methacrylates and confers tunable degradability. *Chemical Communications* **2015**, *51* (64), 12847-12850.
16. Burlant, W. J.; Green, D. H., Some gamma-ray initiated polymerizations. *Journal of Polymer Science* **1958**, *31* (122), 227-230.
17. Iwakura, Y.; Kurosaki, T.; Nakabayashi, N., Reactive fiber .1. Copolymerization and copolymer of acrylonitrile with glycidyl methacrylate and with glycidyl acrylate. *Makromolekulare Chemie* **1961**, *44-6*, 570-590.
18. Bork, J. F.; Coleman, L. E., Nitrogen-containing monomers .2. Reactivity ratios of N-Vinylazolidone and N-vinylpyrrolidone with vinyl monomers. *Journal of Polymer Science* **1960**, *43* (142), 413-421.
19. Semchikov, Y. D.; Smirnova, L. A.; Knyazeva, T. Y.; Bulgakova, S. A.; Voskoboinik, G. A.; Sherstyanykh, V. I., General character of the effect of influence of molecular mass on the composition of copolymer during homogeneous radical copolymerization. *Vysokomolekulyarnye Soedineniya Seriya A* **1984**, *26* (4), 704-710.
20. Okano, T.; Aoyagi, J.; Shinohara, I., Wettability and composition of 2-hydroxyethyl methacrylate copolymers. *Nippon Kagaku Kaishi* **1976**, (1), 161-165.
21. Kostanski, L. K.; Hamielec, A. E., Influence of temperature on butyl acrylate styrene copolymerization parameters. *Polymer* **1992**, *33* (17), 3706-3710.
22. Bailey, W. J.; Endo, T.; Gapud, B.; Lin, Y. N.; Ni, Z.; Pan, C. Y.; Shaffer, S. E.; Wu, S. R.; Yamazaki, N.; Yonezawa, K., Synthesis of functionally-terminated oligomers by free-radical ring-opening polymerization. *Journal of Macromolecular Science-Chemistry* **1984**, *A21* (8-9), 979-995.
23. Wickel, H.; Agarwal, S., Synthesis and characterization of copolymers of 5,6-benzo-2-methylene-1,3-dioxepane and styrene. *Macromolecules* **2003**, *36* (16), 6152-6159.
24. Mayo, F. R.; Walling, C.; Lewis, F. M.; Hulse, W. F., Copolymerization .5. Some copolymerizations of vinyl acetate. *Journal of the American Chemical Society* **1948**, *70* (4), 1523-1525.
25. Varma, I. K.; Patnaik, S., Copolymerization of 2-hydroxyethyl methacrylate with alkyl acrylates. *European Polymer Journal* **1976**, *12* (4), 259-261.
26. Sun, L. F.; Zhou, R. X.; Liu, Z. L., Synthesis and enzymatic degradation of 2-methylene-1,3-dioxepane and methyl acrylate copolymers. *Journal of Polymer Science Part a-Polymer Chemistry* **2003**, *41* (18), 2898-2904.
27. Soundararajan, S.; Reddy, B. S. R., Glycidyl methacrylate and N-vinyl-2-pyrrolidone copolymers - synthesis, characterization, and reactivity ratios. *Journal of Applied Polymer Science* **1991**, *43* (2), 251-258.
28. Dhal, P. K.; Ramakrishna, M. S.; Babu, G. N., Copolymerization of glycidyl methacrylate with alkyl acrylate monomers. *Journal of Polymer Science Part a-Polymer Chemistry* **1982**, *20* (6), 1581-1585.
29. Choi, S.; Lee, K.; Kwon, S.; Kim, H., Preparation of fine particles of poly(N-vinyl-2-pyrrolidone-co-2-methylene-1,3-dioxepane) using supercritical antisolvent. *Journal of Supercritical Fluids* **2006**, *37* (3), 287-291.
30. Nikolaev, A. F.; Vishneva, L. P.; Gromova, O. A.; Grigorev, M. M.; Kleshche, M. S., Peculiarities of copolymerization of vinyl acetate with butyl acrylate. *Vysokomolekulyarnye Soedineniya Section A* **1969**, *11* (11), 2418-2421.
31. Agarwal, S., Radical ring opening and vinyl copolymerization of 2,3,4,5,6-pentafluorostyrene with 5,6-benzo-2-methylene-1,3-dioxepane: Synthesis and structural characterization using 1D and 2D NMR techniques. *Journal of Polymer Research* **2006**, *13* (5), 403-412.

32. Agarwal, S.; Ren, L. Q.; Kissel, T.; Bege, N., Synthetic Route and Characterization of Main Chain Ester-Containing Hydrolytically Degradable Poly(N,N-dimethylaminoethyl methacrylate)-Based Polycations. *Macromolecular Chemistry and Physics* **2010**, *211* (8), 905-915.
33. Huang, J. Y.; Gil, R.; Matyjaszewski, K., Synthesis and characterization of copolymers of 5,6-benzo-2-methylene-1, 3-dioxepane and n-butyl acrylate. *Polymer* **2005**, *46* (25), 11698-11706.
34. Ren, L. Q.; Agarwal, S., Synthesis, characterization, and properties evaluation of poly (N-isopropylacrylamide)-co-ester s. *Macromolecular Chemistry and Physics* **2007**, *208* (3), 245-253.