† Electronic Supplementary Information (ESI)

# Development of prediction model for cloud point of thermo-responsive polymers by experiment-oriented materials informatics

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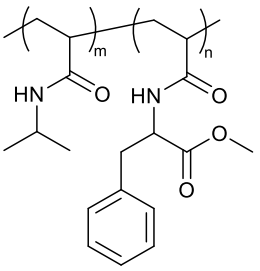
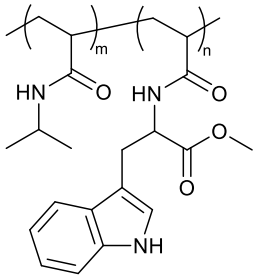
Table S1 Dataset with training data.[1–5]

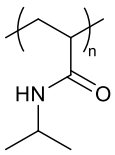
| No. | $x_1$ [g mol$^{-1}$] | $x_2$ [-] | $x_3$ [mg mL$^{-1}$] | $x_4$ [-] | $x_5$ [-] | $x_6$ [-] | $x_7$ [g mol$^{-1}$] | $x_8$[K] | $x_9$ [cm$^3$ mol$^{-1}$] | $x_{10}$ [-] | $x_{11}$ [-] | $x_{12}$ [-] | y [°C] | Ref. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 6500 | 2.1 | 5 | 16.97 | 10.795 | 7.21 | 119.1655 | 470.283 | 35.6725 | 30.415 | 0.30676 | 3.57339 | 23.3 | 1 |
| 2 | 6400 | 2.1 | 5 | 17.04 | 10.69 | 7.22 | 125.171 | 482.536 | 37.215 | 31.73 | 0.35852 | 3.73158 | 14.8 | 1 |
| 3 | 5900 | 1.8 | 5 | 17.015 | 10.875 | 7.255 | 121.117 | 435.1285 | 36.2365 | 31.0165 | 0.30626 | 3.624765 | 21.7 | 1 |
| 4 | 20100 | 1.9 | 5 | 16.9 | 10.9 | 7.2 | 113.16 | 458.03 | 34.13 | 29.1 | 0.255 | 3.4152 | 32.1 | 2 |
| 5 | 17200 | 2.9 | 5 | 16.984 | 10.825 | 7.197 | 118.2651 | 468.8462 | 35.5706 | 29.889 | 0.321276 | 3.560754 | 25.8 | 2 |
| 6 | 6300 | 1.25 | 1 | 17.4 | 6.6 | 5.7 | 125.17 | 447.71 | 35.67 | 20.31 | 0.927 | 3.6256 | 64 | 3 |
| 7 | 29000 | 1.54 | 1 | 17.2 | 5.4 | 4.7 | 139.2 | 470.83 | 40.22 | 20.31 | 1.446 | 4.0894 | 41 | 3 |
| 8 | 6700 | 1.75 | 1 | 17.2 | 5.8 | 5.1 | 139.2 | 470.59 | 40.27 | 20.31 | 1.456 | 4.0894 | 25 | 3 |
| 9 | 15000 | 2.43 | 1 | 17.3 | 6.4 | 5.4 | 169.22 | 515.89 | 46.4 | 29.54 | 0.773 | 4.7063 | 64 | 3 |
| 10 | 6100 | 2.66 | 1 | 17.1 | 6 | 5 | 183.25 | 538.77 | 51.2 | 29.54 | 1.162 | 5.1701 | 36 | 3 |
| 11 | 11000 | 1.99 | 1 | 17.7 | 6.7 | 5.9 | 211.26 | 608.41 | 55.29 | 38.77 | 0.654 | 5.6096 | 47.5 | 3 |
| 12 | 11000 | 1.53 | 1 | 17.375 | 6.55 | 5.625 | 146.705 | 481.915 | 41.8025 | 22.6175 | 1.28525 | 4.243625 | 34.5 | 3 |
| 13 | 16000 | 1.69 | 1 | 17.35 | 6.5 | 5.55 | 154.21 | 493.24 | 43.335 | 24.925 | 1.1145 | 4.39785 | 41.3 | 3 |
| 14 | 13000 | 1.35 | 1 | 17.325 | 6.45 | 5.475 | 161.715 | 504.565 | 44.8675 | 27.2325 | 0.94375 | 4.552075 | 51 | 3 |
| 15 | 15000 | 1.9 | 1 | 17.415 | 6.605 | 5.71 | 142.803 | 477.481 | 41.021 | 21.233 | 1.4159 | 4.16541 | 27.7 | 3 |
| 16 | 16000 | 1.89 | 1 | 17.475 | 6.625 | 5.75 | 157.215 | 505.045 | 44.025 | 24.925 | 1.2555 | 4.46945 | 30.5 | 3 |
| 17 | 16000 | 2.07 | 1 | 17.55 | 6.65 | 5.8 | 175.23 | 539.5 | 47.78 | 29.54 | 1.055 | 4.8495 | 32.4 | 3 |
| 18 | 12000 | 1.7 | 1 | 17.45 | 6.69 | 5.73 | 142.001 | 476.247 | 40.684 | 21.563 | 1.344 | 4.13335 | 32 | 3 |
| 19 | 14000 | 1.77 | 1 | 17.525 | 6.825 | 5.775 | 146.2025 | 484.7325 | 41.305 | 23.4425 | 1.176 | 4.199275 | 39.7 | 3 |
| 20 | 15000 | 1.7 | 1 | 17.65 | 7.05 | 5.85 | 153.205 | 498.875 | 42.34 | 26.575 | 0.896 | 4.30915 | 60.6 | 3 |
| 21 | 7100 | 2.5 | 5 | 16.9 | 10.9 | 7.2 | 113.16 | 458.03 | 34.13 | 29.1 | 0.255 | 3.4152 | 32 | 4 |
| 22 | 17500 | 2.6 | 5 | 16.873 | 10.684 | 7.131 | 114.0312 | 457.4117 | 34.3274 | 29.016 | 0.32814 | 3.43656 | 26.9 | 4 |
| 23 | 8200 | 1.89 | 5 | 16.898 | 10.864 | 7.188 | 114.302 | 459.658 | 34.4742 | 29.1648 | 0.26 | 3.450402 | 37.3 | 4 |
| 24 | 5500 | 1.15 | 1 | 16.6 | 9.6 | 6.2 | 183.21 | 537.74 | 48.21 | 46.61 | 0.622 | 4.818 | 15 | 5 |
| 25 | 8300 | 1.25 | 1 | 16.625 | 9.64 | 6.27 | 179.006 | 529.7025 | 47.28 | 45.295 | 0.58255 | 4.72467 | 24.5 | 5 |
| 26 | 6800 | 1.22 | 1 | 16.65 | 9.68 | 6.34 | 174.802 | 521.665 | 46.35 | 43.98 | 0.5431 | 4.63134 | 30.5 | 5 |
| 27 | 6200 | 1.25 | 1 | 16.7 | 9.76 | 6.48 | 166.394 | 505.59 | 44.49 | 41.35 | 0.4642 | 4.44468 | 34.5 | 5 |
| 28 | 7000 | 1.28 | 1 | 16.75 | 9.84 | 6.62 | 157.986 | 489.515 | 42.63 | 38.72 | 0.3853 | 4.25802 | 43.5 | 5 |



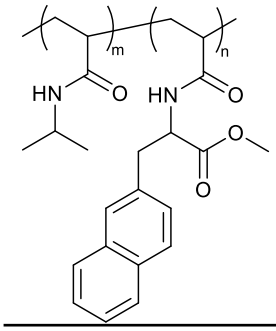
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 1 | 95 : 5 | 23.3 |
| 2 | 90 : 10 | 14.8 |



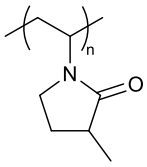
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 3 | 95 : 5 | 21.7 |



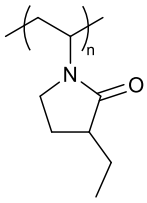
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 4 | 0 : 100 | 32.1 |



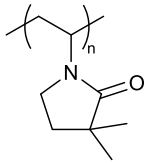
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 5 | 97 : 3 | 25.8 |



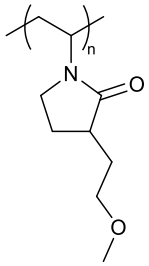
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 6 | 0 : 100 | 64 |



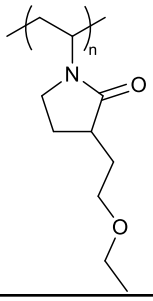
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 7 | 0 : 100 | 41 |



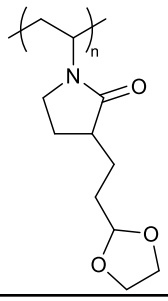
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 8 | 0 : 100 | 25 |



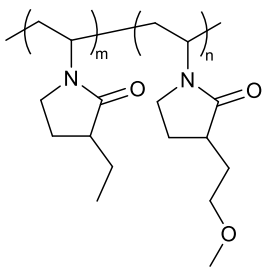
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 9 | 0 : 100 | 64 |



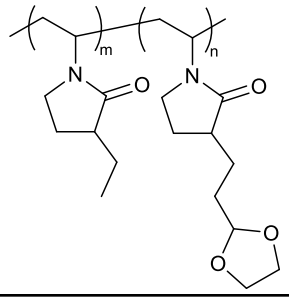
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 10 | 0 : 100 | 36 |



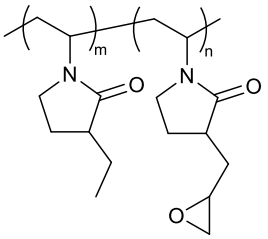
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 11 | 0 : 100 | 47.5 |



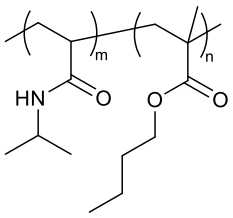
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 12 | 75 : 25 | 34.5 |
| 13 | 50 : 50 | 41.3 |
| 14 | 25 : 75 | 51 |



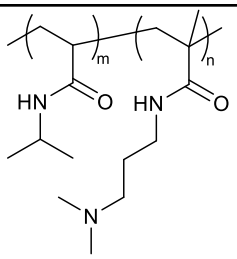
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 15 | 95 : 5 | 27.7 |
| 16 | 75 : 25 | 30.5 |
| 17 | 50 : 50 | 32.4 |



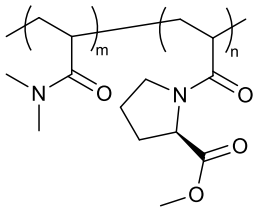
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 18 | 90 : 10 | 32.0 |
| 19 | 75 : 25 | 39.7 |
| 20 | 50 : 50 | 60.6 |



| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 21 | 100 : 0 | 32 |
| 22 | 97 : 3 | 26.9 |



| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 23 | 98 : 2 | 37.3 |



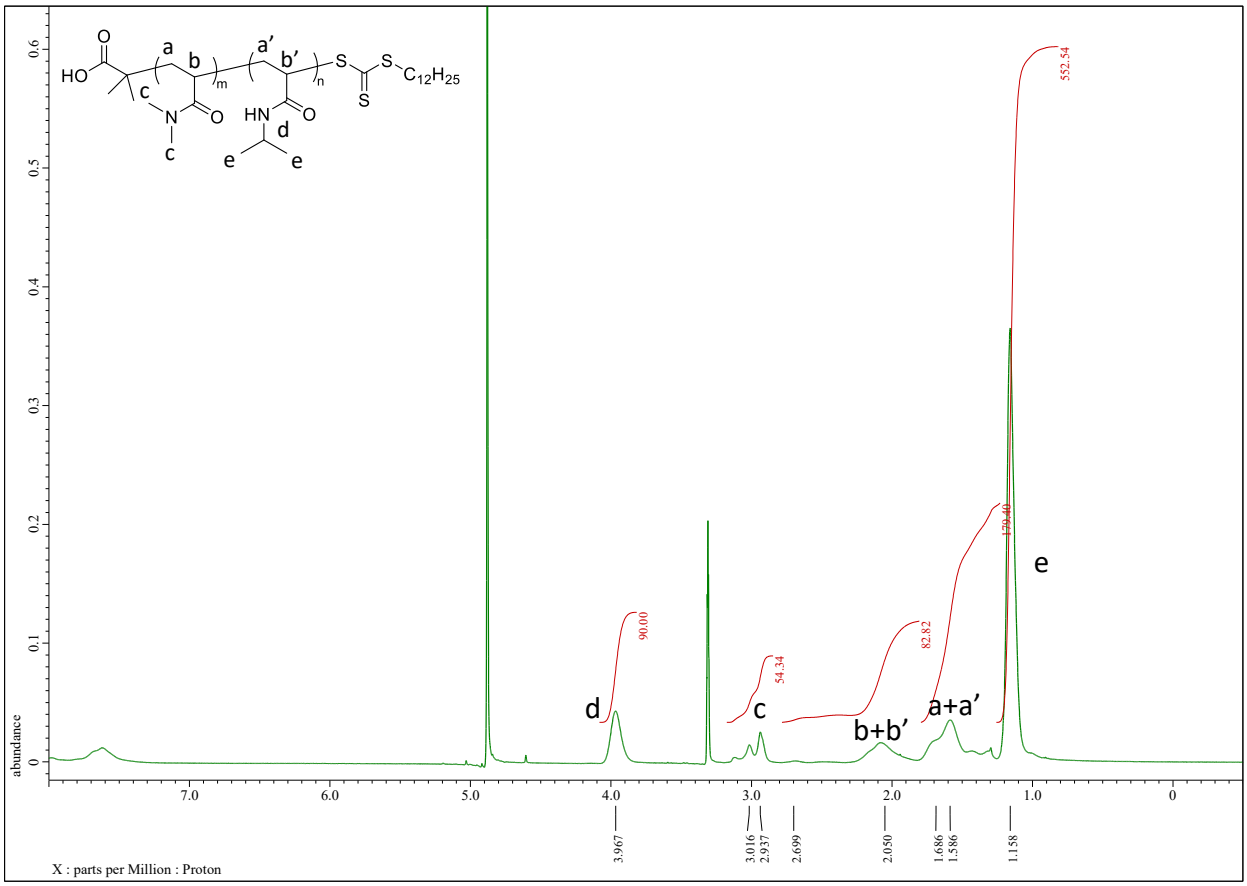
| No. | m : n | $T_{CP}$ [°C] |
|---|---|---|
| 24 | 0 : 100 | 15 |
| 25 | 5 : 95 | 24.5 |
| 26 | 10 : 90 | 30.5 |
| 27 | 20 : 80 | 34.5 |
| 28 | 30 : 70 | 43.5 |

Fig. S1 The chemical structures and cloud points of polymers included in dataset.[1–5]

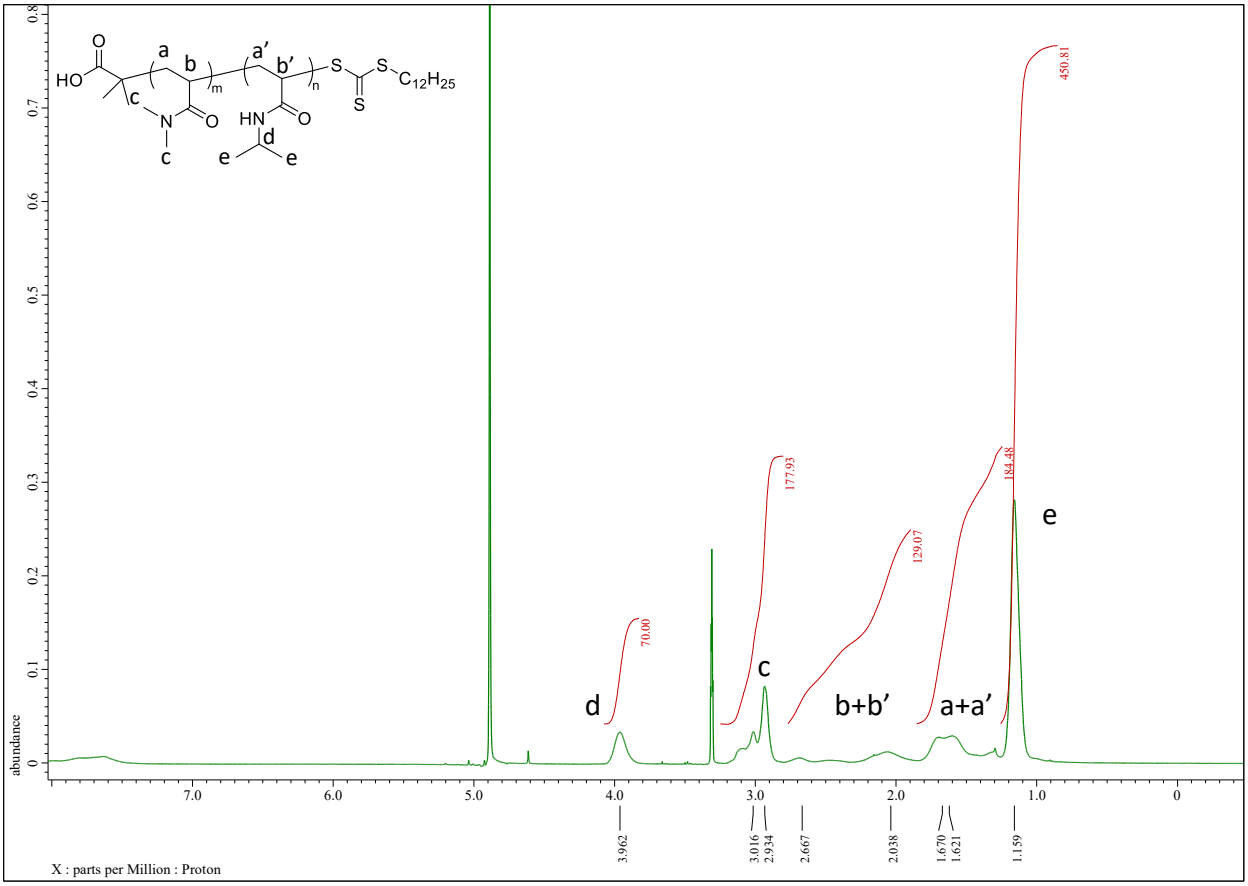
Table S2 The composition ratio of monomers from literature references used for training data. Monomers (compounds) are shown in Scheme 1.

| No. | Monomers (Compounds) | | Composition ratio [mol %] | Ref. |
|---|---|---|---|---|
| 1 | 1 | 2 | 95 : 5 | 1 |
| 2 | 1 | 2 | 90 : 10 | 1 |
| 3 | 1 | 3 | 95 : 5 | 1 |
| 4 | 1 | - | 100 : 0 | 2 |
| 5 | 1 | 4 | 97 : 3 | 2 |
| 6 | 5 | - | 100 : 0 | 3 |
| 7 | 6 | - | 100 : 0 | 3 |
| 8 | 7 | - | 100 : 0 | 3 |
| 9 | 8 | - | 100 : 0 | 3 |
| 10 | 9 | - | 100 : 0 | 3 |
| 11 | 10 | - | 100 : 0 | 3 |
| 12 | 7 | 8 | 75 : 25 | 3 |
| 13 | 7 | 8 | 50 : 50 | 3 |
| 14 | 7 | 8 | 25 : 75 | 3 |
| 15 | 7 | 10 | 95 : 5 | 3 |
| 16 | 7 | 10 | 75 : 25 | 3 |
| 17 | 7 | 10 | 50 : 50 | 3 |
| 18 | 7 | 11 | 90 : 10 | 3 |
| 19 | 7 | 11 | 75 : 25 | 3 |
| 20 | 7 | 11 | 50 : 50 | 3 |
| 21 | 1 | - | 100 : 0 | 4 |
| 22 | 1 | 12 | 97 : 3 | 4 |
| 23 | 1 | 13 | 98 : 2 | 4 |
| 24 | 14 | 15 | 0 : 100 | 5 |
| 25 | 14 | 15 | 5 : 95 | 5 |
| 26 | 14 | 15 | 10 : 90 | 5 |
| 27 | 14 | 15 | 20 : 80 | 5 |
| 28 | 14 | 15 | 30 : 70 | 5 |

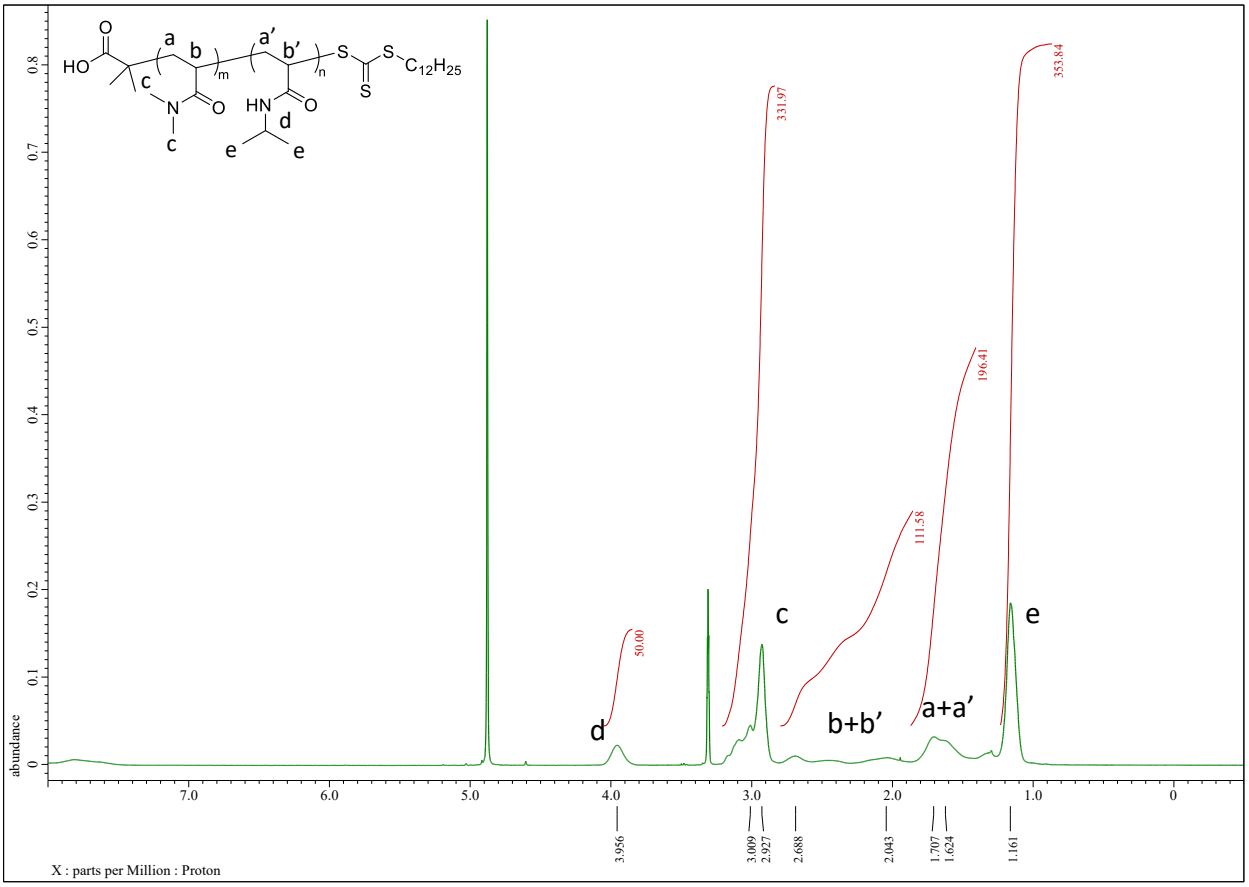
$^1$H NMR spectrum of P(NIPAAm$_{90}$-*co*-DMAAm$_{10}$) in $CD_3OD$



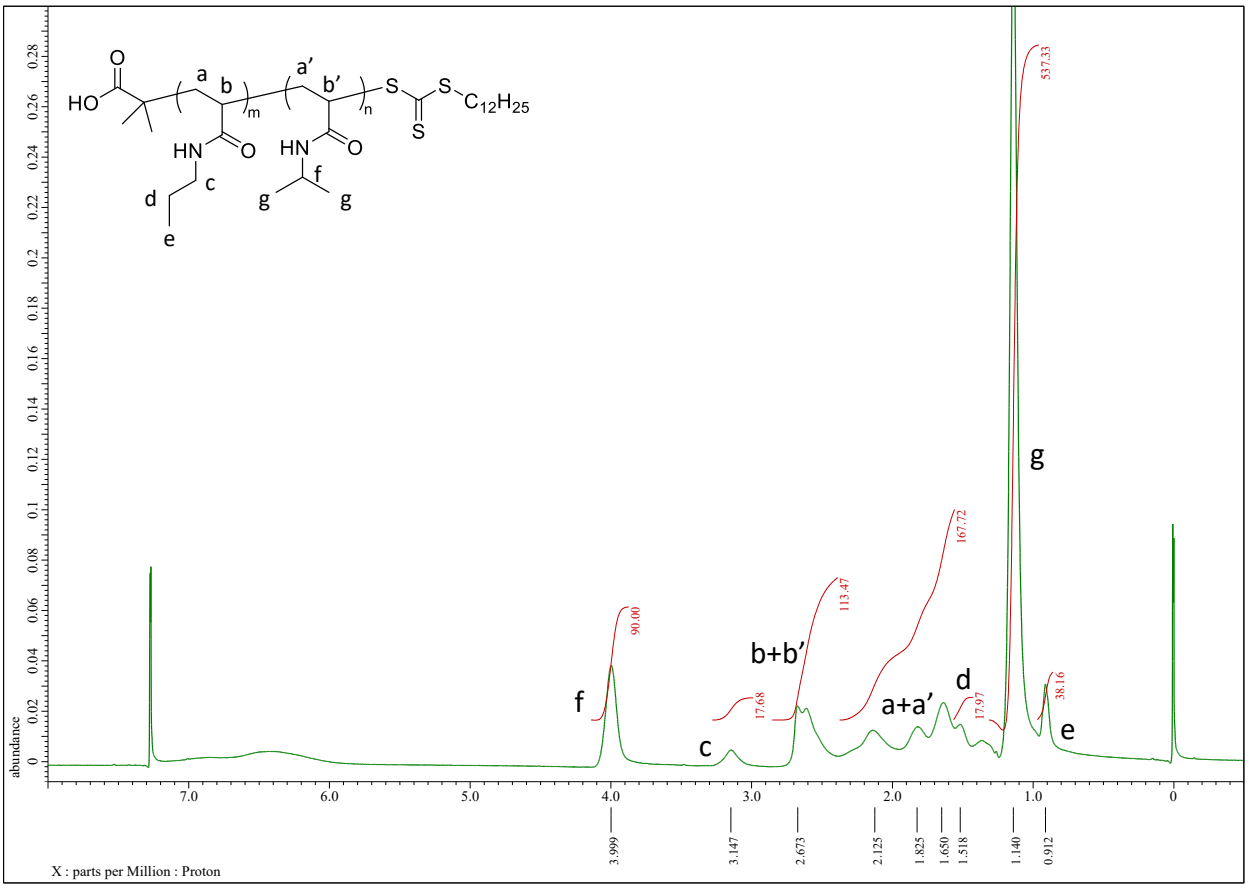

$^1$H NMR spectrum of P(NIPAAm$_{70}$-*co*-DMAA$_{30}$) in $CD_3OD$



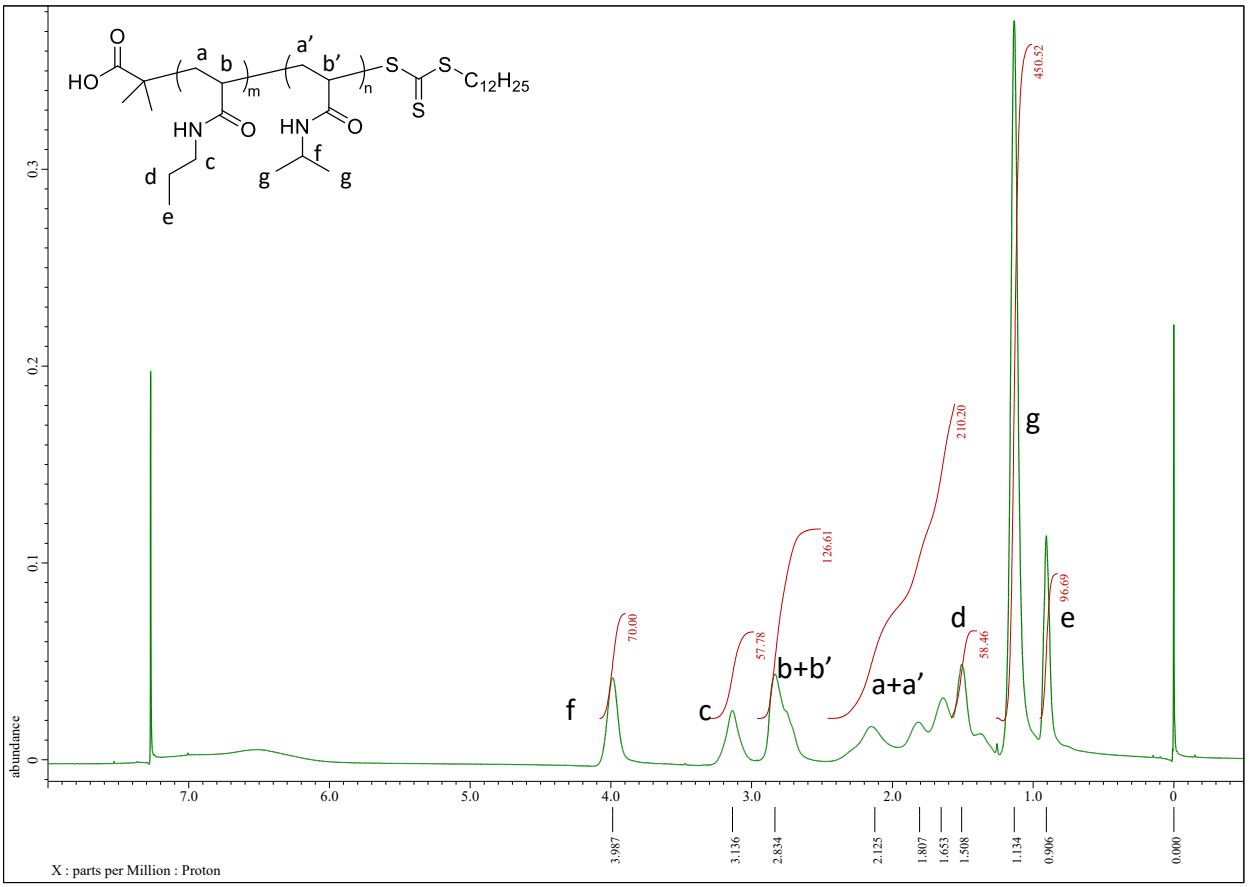
$^1$H NMR spectrum of P(NIPAAm$_{50}$-*co*-DMAAm$_{50}$) in $CD_3OD$



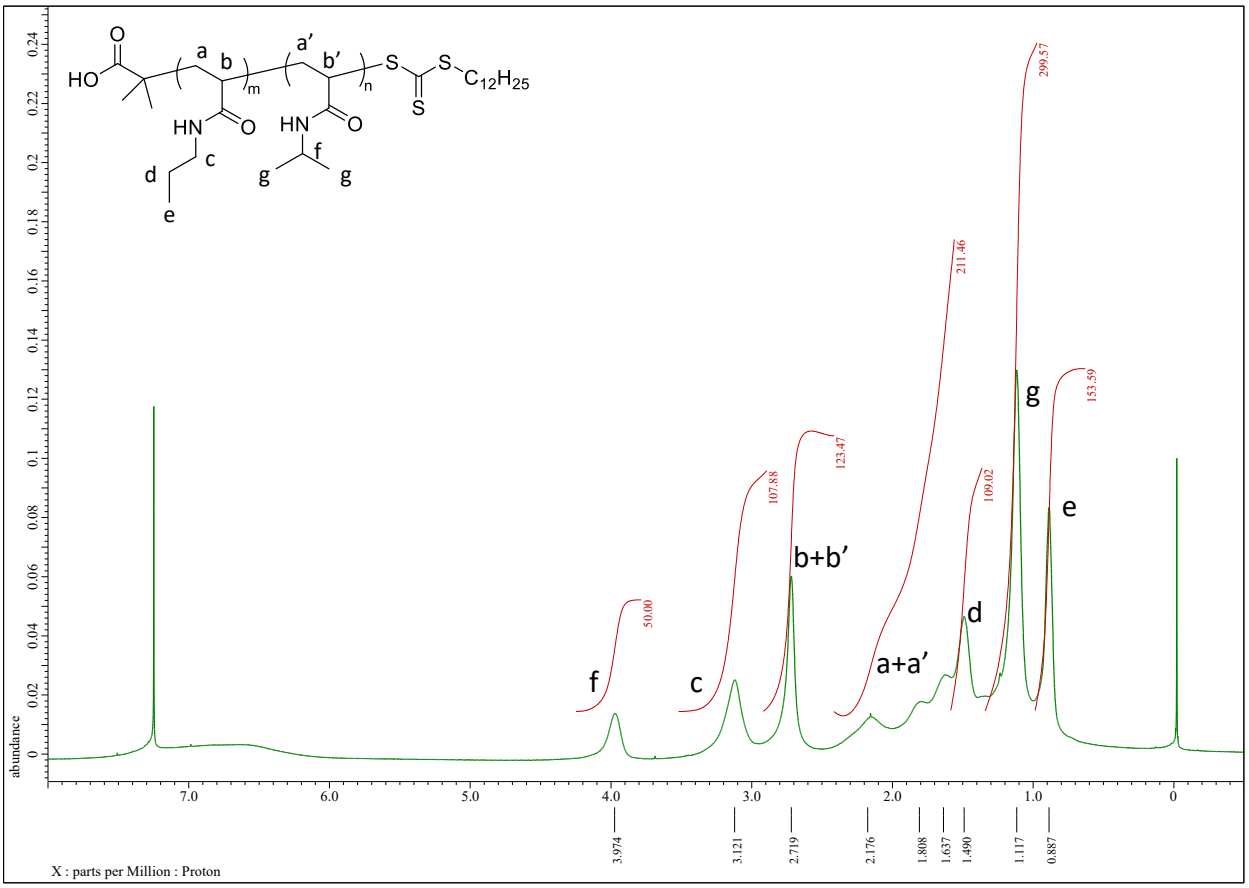

$^1$H NMR spectrum of P(NIPAAm$_{90}$-*co*-NNPAAm$_{10}$) in $CDCl_3$



$^1$H NMR spectrum of P(NIPAAm$_{70}$-*co*-NNPAAm$_{30}$) in $CDCl_3$




$^1$H NMR spectrum of P(NIPAAm$_{50}$-*co*-NNPAAm$_{50}$) in $CDCl_3$



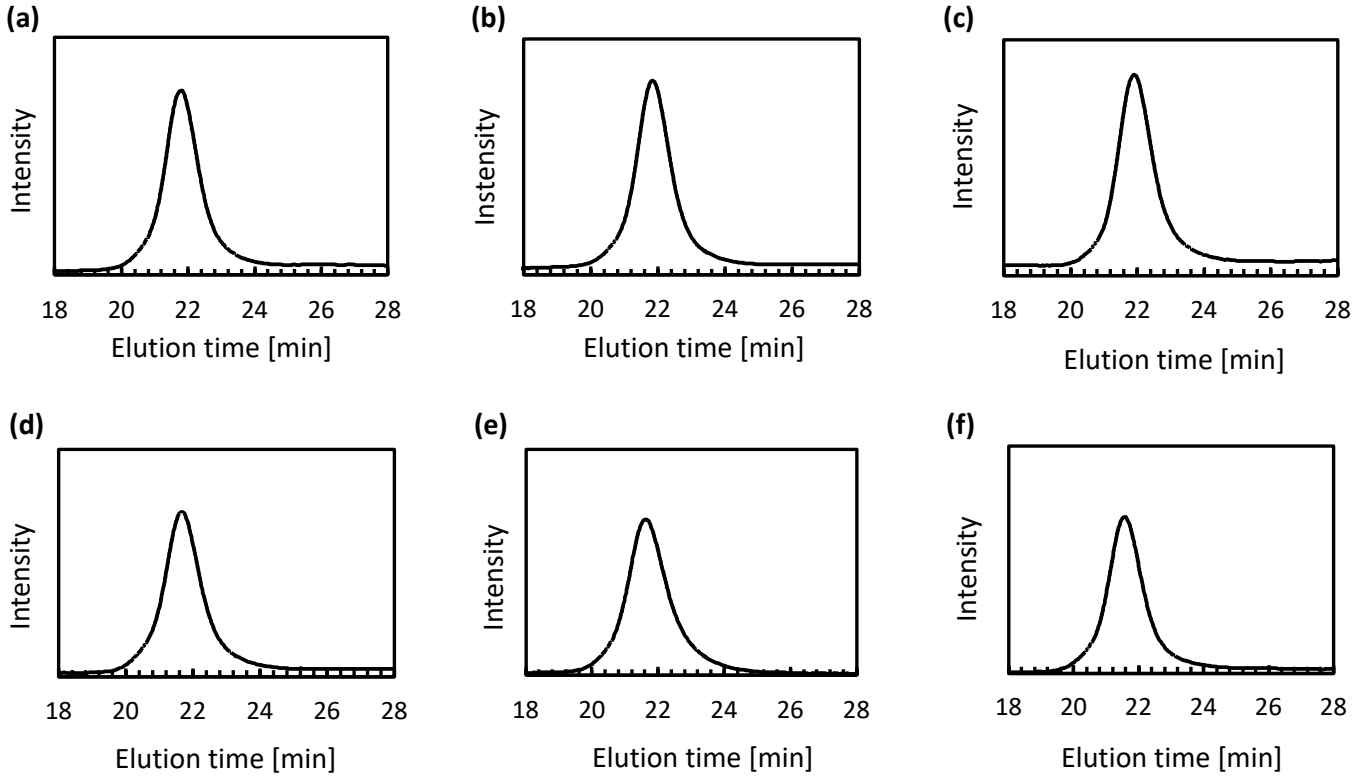



Fig. S2 GPC elution curves for (a) P(NIPAAm$_{90}$-*co*-DMAAm$_{10}$), (b) P(NIPAAm$_{70}$-*co*-DMAAm$_{30}$), (c) P(NIPAAm$_{50}$-*co*-DMAAm$_{50}$), (d) P(NIPAAm$_{90}$-*co*-NNPAAm$_{10}$), (e) P(NIPAAm$_{70}$-*co*-NNPAAm$_{30}$), (f) P(NIPAAm$_{50}$-*co*-NNPAAm$_{50}$)

Table S3 Dataset with test data from literature references.[4,6]

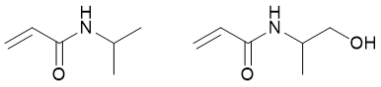
| No. | $x_3$ [mg mL$^{-1}$] | $x_5$ [-] | $x_{11}$ [-] | y [°C] | Ref. |
|---|---|---|---|---|---|
| 29 | 5 | 10.828 | 0.27938 | 31 | 4 |
| 30 | 5 | 10.756 | 0.30376 | 30.2 | 4 |
| 31 | 5 | 10.882 | 0.2575 | 34.8 | 4 |
| 32 | 5 | 10.846 | 0.2625 | 41.4 | 4 |
| 33 | 5 | 10.828 | 0.265 | 43.8 | 4 |
| 34 | 5 | 9.6 | 0.622 | 20.7 | 6 |
| 35 | 5 | 10.25 | 0.4385 | 24 | 6 |

Table S4 The composition of test data from articles. Monomers (compounds) are shown in Scheme 1.

| No. | Monomers (Compounds) | | Composition ratio [mol %] | Ref. |
|---|---|---|---|---|
| 29 | 1 | 12 | 99 : 1 | 4 |
| 30 | 1 | 12 | 98 : 2 | 4 |
| 31 | 1 | 13 | 99 : 1 | 4 |
| 32 | 1 | 13 | 97 : 3 | 4 |
| 33 | 1 | 13 | 96 : 4 | 4 |
| 34 | 15 | - | 100 : 0 | 6 |
| 35 | 1 | 15 | 50 : 50 | 6 |

Table S5 Test dataset of synthesized polymers

| Polymer | $x_3$ [mg $mL^{-1}$] | $x_5$ [-] | $x_{11}$ [-] | y [°C] |
|---|---|---|---|---|
| P(NIPAAm$_{90}$-*co*-DMAAm$_{10}$) | 5 | 10.85 | 0.2128 | 35.4 |
| P(NIPAAm$_{70}$-*co*-DMAAm$_{30}$) | 5 | 10.75 | 0.1284 | 44.7 |
| P(NIPAAm$_{50}$-*co*-DMAAm$_{50}$) | 5 | 10.65 | 0.044 | 64.0 |
| P(NIPAAm$_{90}$-*co*-NNPAAm$_{10}$) | 5 | 10.91 | 0.277 | 31.7 |
| P(NIPAAm$_{70}$-*co*-NNPAAm$_{30}$) | 5 | 10.93 | 0.321 | 29.2 |
| P(NIPAAm$_{50}$-*co*-NNPAAm$_{50}$) | 5 | 10.95 | 0.365 | 27.1 |




1 16

Fig. S3 The structure of monomers from literature references for correcting coefficients of the prediction model.[7]

Table S6 Dataset for correcting coefficients of the prediction model, containing additional data from references (No. 36-40).

| No. | $x_3$ [mg $mL^{-1}$] | $x_5$ [-] | $x_{11}$ [-] | y [°C] | Ref. |
|---|---|---|---|---|---|
| 1 | 5 | 10.795 | 0.30676 | 23.3 | 1 |
| 2 | 5 | 10.69 | 0.35852 | 14.8 | 1 |
| 3 | 5 | 10.875 | 0.30626 | 21.7 | 1 |
| 4 | 5 | 10.9 | 0.255 | 32.1 | 2 |
| 5 | 5 | 10.825 | 0.321276 | 25.8 | 2 |
| 6 | 1 | 6.6 | 0.927 | 64 | 3 |
| 7 | 1 | 5.4 | 1.446 | 41 | 3 |
| 8 | 1 | 5.8 | 1.456 | 25 | 3 |
| 9 | 1 | 6.4 | 0.773 | 64 | 3 |
| 10 | 1 | 6 | 1.162 | 36 | 3 |
| 11 | 1 | 6.7 | 0.654 | 47.5 | 3 |
| 12 | 1 | 6.55 | 1.28525 | 34.5 | 3 |
| 13 | 1 | 6.5 | 1.1145 | 41.3 | 3 |
| 14 | 1 | 6.45 | 0.94375 | 51 | 3 |
| 15 | 1 | 6.605 | 1.4159 | 32 | 3 |
| 16 | 1 | 6.625 | 1.2555 | 39.7 | 3 |
| 17 | 1 | 6.65 | 1.055 | 60.6 | 3 |
| 18 | 1 | 6.69 | 1.344 | 32 | 3 |
| 19 | 1 | 6.825 | 1.176 | 39.7 | 3 |
| 20 | 1 | 7.05 | 0.896 | 60.6 | 3 |
| 21 | 5 | 10.9 | 0.255 | 32 | 4 |
| 22 | 5 | 10.684 | 0.32814 | 26.9 | 4 |
| 23 | 5 | 10.864 | 0.26 | 37.3 | 4 |
| 24 | 1 | 9.6 | 0.622 | 15 | 5 |
| 25 | 1 | 9.64 | 0.58255 | 24.5 | 5 |
| 26 | 1 | 9.68 | 0.5431 | 30.5 | 5 |
| 27 | 1 | 9.76 | 0.4642 | 34.5 | 5 |
| 28 | 1 | 9.84 | 0.3853 | 43.5 | 5 |
| 36 | 5 | 10.9 | 0.255 | 31.6 | 7 |
| 37 | 5 | 11.15 | 0.1577 | 36.7 | 7 |
| 38 | 5 | 11.65 | -0.0369 | 41.8 | 7 |
| 39 | 5 | 12.15 | -0.2315 | 55 | 7 |
| 40 | 5 | 12.9 | -0.5234 | 80 | 7 |

Table S7 The composition of additional test data from literature references. Monomers (compounds) are shown in Fig. S2.

| No. | Monomers (Compounds) | | Composition ratio [mol %] | Ref. |
|---|---|---|---|---|
| 36 | 1 | 16 | 100 : 0 | 7 |
| 37 | 1 | 16 | 90 : 10 | 7 |
| 38 | 1 | 16 | 70 : 30 | 7 |
| 39 | 1 | 16 | 50 : 50 | 7 |
| 40 | 1 | 16 | 20 : 80 | 7 |

**References**


1 Y. Hiruta, R. Kanazashi, E. Ayano, T. Okano and H. Kanazawa, *The Analyst*, 2016, **141**, 910–917.
2 T. Nishio, R. Kanazashi, A. Nojima, H. Kanazawa and T. Okano, *J. Chromatogr. A.*, 2012, **1228**, 148–154.
3 G.-T. Chen, C.-H. Wang, J.-G. Zhang, Y. Wang, R. Zhang, F.-S. Du, N. Yan, Y. Kou and Z.-C. Li, *Macromolecules*, 2010, **43**, 9972–9981.
4 Y. Hiruta, M. Shimamura, M. Matsuura, Y. Maekawa, T. Funatsu, Y. Suzuki, E. Ayano, T. Okano and H. Kanazawa, *ACS Macro Lett.*, 2014, **3**, 281–285.
5 H. Mori, H. Iwaya, A. Nagai and T. Endo, *Chem. Commun.*, 2005, 4872.
6 H. Kanazawa, E. Ayano, C. Sakamoto, R. Yoda, A. Kikuchi and T. Okano, *J. Chromatogr. A*, 2006, **1106**, 152–158.
7 T. Maeda, K. Yamamoto and T. Aoyagi, *J. Colloid Interface Sci.*, 2006, **302**, 467–474.