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RAFT Polymerization of Bio-Based 1-Vinyl-4-dianhydrohexitol-1,2,3-triazole Stereoisomers Obtained via Click Chemistry

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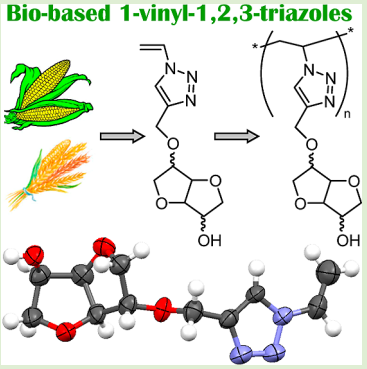
Supporting Information

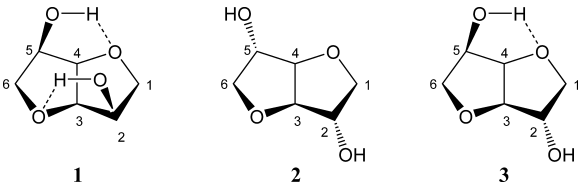
ABSTRACT: Four 1-vinyl-4-dianhydrohexitol-1,2,3-triazole stereoisomers are prepared from isomannide, isoidide, and isosorbide using an alkylation/CuAAC-ligation/elimination three-step strategy. After characterization of the monomers by NMR, differential scanning calorimetry (DSC), and high-resolution mass spectrometry (HRMS), the corresponding stereocontrolled poly(1-vinyl-4-dianhydrohexitol-1,2,3-triazole)s are obtained by RAFT polymerization using a xanthate chain transfer agent. A systematic investigation of the structure-properties relationship of both the monomers and polymers highlights the significant impact of the dianhydrohexitols stereochemistry on their physical properties (^{1}H and ^{13}C NMR chemical shifts, physical state, T_g, thermal stability and solubility). A particularly original and unexpected behavior is highlighted since the two different isosorbide-based poly(1-vinyl-4-dianhydrohexitol-1,2,3-triazole) stereoisomers exhibit contrasting solubility in water.



INTRODUCTION

Among the immense library of biosourced chemicals suitable for the generation of sustainable polymer materials,[1−15] 1,4:3,6-dianhydrohexitols (DAHs), i.e., isomannide (**1**), isoidide (**2**), and isosorbide (**3**), have recently raised particular attention.[16] DAHs are chiral, rigid, and nontoxic heterocyclic diols composed of two cis-fused V-shaped tetrahydrofuran rings that can be generated from cereal-based polysaccharides (Scheme 1). These stereoisomers differ from the absolute configuration of the C2 and C5 carbon atoms, and several functionalized derivatives have been widely used as biobased comonomers for step growth polymerization methods to generate a wide range of amorphous and semicrystalline polymers such as polyesters, polyurethanes, polyamides, polycarbonates, polyethers, poly(ester-imide)s, poly(ester-amide)s, poly(ether-urethane)s, or polytriazoles.[16−19] Owing to their particularly strained structure, incorporation of a small fraction (typically 2−10 mol %) of DAH comonomer generally affords a significant increase in the glass transition temperature (T_g).[20,21] In parallel, fully biosourced materials have also been generated from the polyaddition of DAH-based monomers by either AA+BB or AB+AB approaches.[22−27] Surprisingly, whereas the preparation of DAH-based polymers by step growth polymerization has been extensively investigated, the synthesis of DAH-containing materials using a chain growth polymerization process has attracted very little attention so far.[28,29]

Scheme 1. Isomannide (1), Isoidide (2), and Isosorbide (3) DAHs



1 **2** **3**

Although known for decades, the potential of 1-vinyl-, 4-vinyl- and 5-vinyl-1,2,3-triazole regioisomers has been highlighted recently.[30,31] The spectacular development of copper(I)-catalyzed azide−alkyne cycloaddition (CuAAC)[32−36] has contributed to the development of a broad library of 1-vinyl- and 4-vinyl-1,2,3-triazole regioisomers and polymer analogues with a large variety of functional groups and physical properties.[30,37−40] Thanks to the versatile character and the functional tolerance of CuAAC, these original materials gather the large structural diversity of vinylic polymers and the peculiar properties of the 1,2,3-triazole ring (e.g., aromaticity, polarity, metal complexation, adhesion properties, and *H*-

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bonding capacities). The present study intends to combine the inherent properties of the 1,2,3-triazole and DAH groups by developing a series of stereocontrolled biobased 1-vinyl-1,2,3-triazole monomers and their polymer analogues using reversible addition−fragmentation chain transfer (RAFT) polymerization. The structure-properties relationship of these original materials are investigated by carefully examining the impact of the DAHs stereochemistry on the physical properties (M_n, T_g, T_m, thermal stability, and solubility) of both the monomers and polymers.

EXPERIMENTAL SECTION

Materials. Sodium hydroxide (NaOH, Aldrich, 98%), propargyl bromide (Aldrich, 80 wt % in toluene), 2-chloroethanol (Aldrich, 99%), sodium azide (NaN_3, Alfa Aesar, 99%), copper iodide triethylphosphite ($CuIP(OEt)_3$, Aldrich, 97%), pyridine (Aldrich, anhydrous, 99.8%), mesyl chloride (Aldrich, 99%), sodium iodide (NaI, Aldrich, 99.5%), 1,8-diazabicycloundec-7-ene (DBU, Aldrich, 98%), 1,2-dimethoxyethane (glyme, Aldrich, anhydrous, 99.5%), diisopropylethylamine (DIPEA, Aldrich, 99%), isosorbide (1,4:3,6-dianhydro-D-glucitol, Aldrich, 98%), isomannide (1,4:3,6-dianhydro-D-mannitol, Aldrich, 95%) and isoidide (1,4:3,6-dianhydro-L-iditol, Roquette Frères, 99%) were used as received. Azobisisobutyronitrile (AIBN) was crystallized twice from methanol and stored at −20 °C. *O*-ethyl-*S*-(1-phenylethyl) dithiocarbonate (**17**) was synthesized as previously described.[41] All other reagents were purchased from Aldrich and used as received.

Characterization Methods. NMR spectra were recorded on a Bruker AC spectrometer at 400 MHz for ^{1}H and 100 MHz for ^{13}C. High-resolution mass spectrometry (HRMS) was performed on a MicroTOFQ-II (Bruker Daltonics, Bremen) equipped with an electrospray ionization (ESI) ion source in positive mode. The sample was infused at 150 μL/h in a mixture of water, methanol and dichloromethane with 0.1% of formic acid. The gas flow of the sprayer was 0.6 bar, the spray voltage was 3.5 kV, and the capillary temperature was 200 °C. The mass range of the time-of-flight mass spectrometer (TOF) was 50−1000 *m*/*z*. For calibration, a solution of formiate was used. X-ray diffraction experiments were performed on a suitable crystal using a Gemini kappa-geometry diffractometer (Agilent Technologies UK Ltd.) equipped with an Atlas CCD detector and using Mo radiation (λ = 0.71073 Å). Size exclusion chromatography (SEC) analyses were performed on an EcoSEC semimicro GPC system from Tosoh equipped with a dual flow refractive index (RI) detector and a UV detector. The samples were analyzed in DMF (with LiBr at 0.01 mol/L) at 50 °C using a flow rate of 1 mL/min. All polymers were filtrated through a 0.45 μm pore-size membrane before injection. Separation was performed with a guard column and two PSS GRAM columns (7 μm, 300 × 7.5 mm). The average molar masses (number-average molar mass M_n and weight-average molar mass M_w) and the molar mass dispersities ($Đ = M_w/M_n$) were derived from the RI signal by a calibration curve based on polystyrene standards with molar masses ranging from 580 Da to 3053 kDa. A third-degree polynomial regression was applied. WinGPC Unity software was used for data collection and calculation. Differential scanning calorimetry (DSC) measurements were performed under nitrogen using a DSC 2920 (TA Instruments) at a heating rate of 20 °C/min. T_g values were measured during the second heating cycle. Thermal gravimetry analysis (TGA) was performed under nitrogen using a TGA 2950 (TA Instruments) at a heating rate of 10 °C/min.

General Procedure for Alkylation. *Synthesis of 1,4:3,6-Dianhydro-2-O-propargyl-D-mannitol (**4**).* NaOH (2.8 g, 68 mmol) was added to a solution of isomannide (**1**, 10 g, 68 mmol) in H_2O (65 mL) maintained at 0 °C. Propargyl bromide (7.7 mL, 68 mmol) was added dropwise at 0 °C, and the solution was stirred for 2 additional hours at room temperature. The crude mixture was extracted with ethyl acetate (2 × 100 mL). The organic layer was dried with $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with a 4:6 mixture of petroleum ether and ethyl acetate giving after evaporation of the solvents **4** (4.82 g, 38.0%) and the corresponding dialkyne (1.45 g, 9.60%) as colorless viscous oils. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.72 (d, *J* = 7.2 Hz, O**H**, 1H), 4.49 (dd, *J* = 4.8, 4.8 Hz, **H**4, 1H), 4.30 (dd, *J* = 4.8, 4.8 Hz, **H**3, 1H), 4.20 (oct, *J* = 23.2, 15.6, 2.4 Hz, **H**a, 2H), 4.17−4.06 (m, **H**2, **H**5, 2H), 3.91 (dd, *J* = 8.4, 6.8 Hz, **H**6a, 1H), 3.79 (dd, *J* = 8.0, 6.8 Hz, **H**1a, 1H), 3.47 (dd, *J* = 8.4, 8.4 Hz, **H**6b, 1H), 3.38−3.31 (m, **H**1b, **H**c, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 81.65 (**C**4), 80.21 (**C**b), 79.54 (**C**3), 78.88 (**C**2), 77.21 (**C**c), 72.26 (**C**5), 72.00 (**C**6), 70.17 (**C**1), 57.52 (**C**a). HRMS (*m*/*z*): calcd for $C_9H_{12}NaO_4$, 207.0628; found, 207.0634 $[M + Na]^+$.

*Synthesis of 1,4:3,6-Dianhydro-2-O-propargyl-L-iditol (**5**).* The general procedure for alkylation was applied to isoidide (**2**, 10 g, 68 mmol), NaOH (2.8 g, 68 mmol), and propargyl bromide (7.7 mL, 68 mmol) to obtain **5** (5.75 g, 46.0%) and the corresponding dialkyne (1.84 g, 12.0%) as colorless viscous oils. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 5.13 (d, *J* = 3.6 Hz, O**H**, 1H), 4.53 (d, *J* = 4.0 Hz, **H**4, 1H), 4.29 (d, *J* = 4.0 Hz, **H**3, 1H), 4.20 (dd, *J* = 2.6, 0.8 Hz, **H**a, 2H), 4.07−4.02 (m, **H**2, **H**5, 2H), 3.76 (d, *J* = 10.4 Hz, **H**6a, 1H), 3.70−3.64 (m, **H**1a, **H**1b, 2H), 3.62 (d, *J* = 9.2 Hz, **H**6b, 1H), 3.36 (t, *J* = 2.4 Hz, **H**c, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 87.46 (**C**3), 84.34 (**C**4), 82.24 (**C**5), 80.16 (**C**b), 77.18 (**C**c), 74.80 (**C**2), 74.12 (**C**1), 71.13 (**C**6), 56.18 (**C**a). HRMS (*m*/*z*): calcd for $C_9H_{12}NaO_4$, 207.0628; found, 207.0637 $[M + Na]^+$.

*Synthesis of 1,4:3,6-Dianhydro-2-O-propargyl-D-sorbitol (**6**) and 1,4:3,6-Dianhydro-5-propargyl-D-sorbitol (**7**).* The general procedure for alkylation was applied to isosorbide (**3**, 20.0 g, 137 mmol), NaOH (5.50 g, 137 mmol), and propargyl bromide (20.4 mL, 137 mmol). The crude mixture was separated by column chromatography eluting with a 1:1 mixture of petroleum ether and ethyl acetate. After evaporation of the solvents, **6** (2.44 g, 10.0%), **7** (6.06 g, 24.0%), **6**+**7**, (2.25 g, 8.90%), and di-*O*-propargyl-isosorbide (3.21 g, 11.0%) were recovered as colorless viscous oils. **Analysis of 6**: ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 4.74 (s, O**H**, 1H), 4.43 (d, *J* = 4.4 Hz, **H**3, 1H), 4.34 (dd, *J* = 4.4, 4.8 Hz, **H**4, 1H), 4.20 (d, *J* = 2.0 Hz, **H**a, 2H), 4.14−4.03 (m, **H**2, **H**5, 2H), 3.86 (d, *J* = 10.0 Hz, **H**1a, 1H), 3.77 (dd, *J* = 10.2, 3.8 Hz, **H**1b, 1H), 3.71 (dd, *J* = 8.2, 6.6 Hz, **H**6a, 1H), 3.41−3.35 (m, **H**c, 1H), 3.31 (dd, *J* = 8.0, 8.0 Hz, **H**6b, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 84.88 (**C**3), 83.04 (**C**2), 81.50 (**C**4), 80.11 (**C**b), 77.21 (**C**c), 72.27 (**C**1), 72.06 (**C**5), 71.18 (**C**6), 56.05 (**C**a). HRMS (*m*/*z*): calcd for $C_9H_{12}NaO_4$, 207.0628; found, 207.0628 $[M + Na]^+$. **Analysis of 7**: ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 5.15 (s, O**H**, 1H), 4.57 (dd, *J* = 5.8, 5.8 Hz, **H**4, 1H), 4.27 (d, *J* = 5.6 Hz, **H**3, 1H), 4.21 (oct, *J* = 21.2, 17.6, 3.2 Hz, **H**a, 2H), 4.16−4.08 (m, **H**5, 1H), 4.06−4.01 (m, **H**2, 1H), 3.80 (dd, *J* = 11.6, 8.8 Hz, **H**6a, 1H), 3.75−3.66 (m, **H**1, 2H), 3.46 (t, *J* = 3.2 Hz, **H**c, 1H), 3.38 (dd, *J* = 10.8, 10.8 Hz, **H**6b, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 88.10 (**C**3), 80.16 (**C**b), 79.41 (**C**4), 78.65 (**C**5), 77.09 (**C**c), 75.33 (**C**1), 75.28 (**C**2), 69.13 (**C**6), 56.73 (**C**a). HRMS (*m*/*z*): calcd for $C_9H_{12}NaO_4$, 207.0628; found, 207.0635 $[M + Na]^+$.

*Synthesis of 1-Mesyl-2-azidoethanol (**8**).* A solution of 2-chloroethanol (20.0 g, 248 mmol) and NaN_3 (48.3 g, 744 mmol) in water (200 mL) was stirred at 60 °C for 48 h. After cooling the solution at room temperature, the crude product was extracted with diethyl ether (3 × 300 mL) to afford, after evaporation of the solvent under reduced pressure and at room temperature, 2-azidoethanol as a colorless liquid (19.8 g, 91.9%). *Caution: Handling of this low molar mass azide is hazardous as* $[n_C+n_O]/n_N = 1$.[42] *Therefore it should be manipulated with extreme caution, and the crude product was thus directly involved in the next step without further purification, handling, or storage.* 2-Azidoethanol (19.8 g, 228 mmol) was dissolved in anhydrous pyridine (250 mL) and stirred at 0 °C under argon. Mesyl chloride (39.2 g, 342 mmol) was then added dropwise, and the mixture was further stirred for 24 h at room temperature under argon. The pyridinium salt was filtered, distilled water (150 mL) was added, and the crude product was extracted with diethyl ether (3 × 300 mL). The organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography eluting with a 6:4 mixture of petroleum ether and ethyl acetate, giving after evaporation of the solvent **8** as a colorless oil (14.9 g, 39.6%). As a consequence of the presence of the mesyl group ($[n_C + n_O + n_S]/n_N = 2.33$), **8** is much more stable than the

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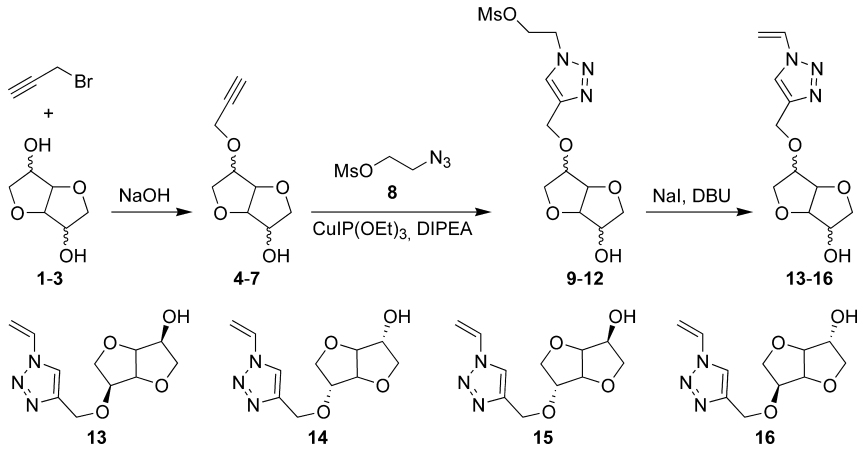
Scheme 2. Three-Step Synthesis of VDT Stereoisomers 13−16



corresponding alcohol. However, it is still suggested to handle this compound with extreme caution and to protect it from light, high temperature, acids, and metals. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 4.33 (t, J = 3.9 Hz, C**H**$_2$N$_3$, 2H), 3.6 (t, J = 3.6 Hz, OC**H**$_2$, 2H), 3.09 (s, C**H**$_3$, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm) 67.4 (**C**H$_2$N$_3$), 49.9 (O**C**H$_2$), 37.8 (**C**H$_3$).

General Procedure for the Two-Step Synthesis of 1-Vinyl-4-dianhydrohexitol-1,2,3-triazoles (VDTs) by a CuAAC-Ligation/Elimination Strategy. *Synthesis of* ***13****.* A solution of **4** (2.02 g, 11.0 mmol) in tetrahydrofuran (THF; 10 mL) was added dropwise to a solution of **8** (1.82 g, 11.0 mmol), DIPEA (1.42 g, 11.0 mmol) and CuIP(OEt)$_3$ (196 mg, 0.55 mmol) in THF (10 mL) maintained at 0 °C. The solution was then stirred for 24 h at 45 °C. After evaporation of the solvent and DIPEA under reduced pressure, the crude mesyl derivative **9** was recovered as a yellow oil and involved in the elimination reaction without further purification. Crude **9** was thus dissolved in anhydrous glyme (100 mL) before sequential addition of NaI (4.95 g, 33.0 mmol) and DBU (3.35 g, 22.0 mmol). The solution was then stirred under argon for 5 h at 70 °C. The solvent was then evaporated under reduced pressure, water (20 mL) was added, and the residue was extracted with dichloromethane (3 × 100 mL). The organic layers were dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography eluting with a 96:4 mixture of ethyl acetate and methanol giving after evaporation of the solvents **13** as a slightly yellow viscous oil (1.58 g, 56.5%). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 8.56 (s, **H**c, 1H), 7.52 (dd, J = 15.9, 9.0 Hz, **H**d, 1H), 5.90 (dd, J = 15.9, 1.5 Hz, **H**e-*trans*, 1H), 5.22 (dd, J = 9.0, 1.5 Hz, **H**e-*cis*, 1H), 4.81 (d, J = 6.8 Hz, O**H**, 1H), 4.75−4.50 (m, **H**a, **H**3, 3H), 4.30 (t, J = 4.7 Hz, **H**4, 1H), 4.19−4.04 (m, **H**2, **H**5, 2H), 3.95−3.76 (m, **H**1a, **H**6a, 2H), 3.51−3.29 (m, **H**1b, **H**6b, 2H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 144.36 (**C**b), 130.31 (**C**d), 121.32 (**C**c), 105.26 (**C**e), 81.55 (**C**4), 79.40 (**C**3), 79.23 (**C**2), 72.16 (**C**5), 71.87 (**C**6), 70.09 (**C**1), 62.33 (**C**a). HRMS (m/z): calcd for $C_{11}H_{16}N_3O_4$, 254.1135; found, 254.1137 [M + H]$^+$.

Synthesis of ***14****.* The general procedure for the two-step synthesis of VDTs was applied to **5** (2.02 g, 11.0 mmol), **8** (1.82 g, 11.0 mmol), DIPEA (1.42 g, 11.0 mmol), and CuIP(OEt)$_3$ (196 mg, 0.55 mmol) to obtain after evaporation of the solvents crude **10** as a slightly yellow viscous oil. Then the general procedure for elimination was applied to crude **10** using NaI (4.95 g, 33.0 mmol) and DBU (3.35 g, 22.0 mmol) in anhydrous glyme (100 mL) to obtain, after purification by column chromatography on silica gel eluting with a 99:1 mixture of ethyl acetate and methanol, **14** as a slightly yellow viscous oil (1.45 g, 51.8%). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 8.55 (s, **H**c, 1H), 7.52 (dd, J = 15.9, 9.0 Hz, **H**d, 1H), 5.90 (dd, J = 15.9, 1.5 Hz, **H**e-*trans*, 1H), 5.22 (dd, 1H, J = 9.0, 1.5 Hz, **H**e-*cis*, 1H), 5.18 (d, J = 3.6 Hz, O**H**, 1H), 4.63 (s, **H**a, 2H), 4.54 (d, J = 3.8 Hz, **H**3, 1H), 4.30 (d, J = 3.8 Hz, **H**4, 1H), 4.06−3.96 (m, **H**2, **H**5, 2H), 3.81−3.60 (m, **H**1, **H**6, 4H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 144.32 (**C**b), 130.30 (**C**d), 121.29 (**C**c), 105.27 (**C**e), 87.33 (**C**4), 84.40 (**C**3), 82.48 (**C**2), 74.61 (**C**5), 73.96 (**C**6), 71.15 (**C**1), 61.67 (**C**a). HRMS (m/z): calcd for $C_{11}H_{16}N_3O_4$, 254.1135; found, 254.1134 [M + H]$^+$.

Synthesis of ***15****.* The general procedure for the two-step synthesis of VDTs was applied to **6** (2.02 g, 11.0 mmol), **8** (1.82 g, 11.0 mmol), DIPEA (1.42 g, 11.0 mmol), and CuIP(OEt)$_3$ (196 mg, 0.55 mmol) to obtain, after evaporation of the solvents, crude **11** as a slightly yellow viscous oil. Then the general procedure for elimination was applied to crude **11** using NaI (4.95 g, 33.0 mmol) and DBU (3.35 g, 22.0 mmol) in anhydrous glyme (100 mL) to obtain after purification by column chromatography on silica gel eluting with a 99:1 mixture of ethyl acetate and methanol **15** as a slightly yellow viscous oil (1.65 g, 59.1%). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 8.51 (s, **H**c, 1H), 7.50 (dd, J = 16.0, 9.0 Hz, **H**d, 1H), 5.88 (dd, J = 16.0, 1.2 Hz, **H**e-*trans*, 1H), 5.22 (dd, 1H, J = 9.0, 1.2 Hz, **H**e-*cis*, 1H), 4.78 (d, J = 5.8 Hz, O**H**, 1H), 4.62 (s, **H**a, 2H), 4.45 (d, J = 4.3 Hz, **H**3, 1H), 4.36 (t, J = 4.5 Hz, **H**4, 1H), 4.16−4.04 (m, **H**2, **H**5, 2H), 3.91−3.67 (m, **H**1, **H**6a, 3H), 3.40−3.25 (m, **H**6b, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 144.34 (**C**b), 130.29 (**C**d), 121.32 (**C**c), 105.29 (**C**e), 85.02 (**C**4), 83.47 (**C**3), 81.42 (**C**2), 72.35 (**C**6), 71.96 (**C**5), 71.03 (**C**1), 61.62 (**C**a). HRMS (m/z): calcd for $C_{11}H_{16}N_3O_4$, 254.1135; found, 254.1139 [M + H]$^+$. Single crystals of **15** suitable for X-ray diffraction experiments were grown from a mixture of methanol and ethyl acetate.

Synthesis of ***16****.* The general procedure for the two-step synthesis of VDTs was applied to **7** (2.02 g, 11.0 mmol), **8** (1.82 g, 11.0 mmol), DIPEA (1.42 g, 11.0 mmol), and CuIP(OEt)$_3$ (196 mg, 0.55 mmol) to obtain after evaporation of the solvents crude **12** as a slightly yellow viscous oil. Then the general procedure for elimination was applied to crude **12** using NaI (4.95 g, 33.0 mmol) and DBU (3.35 g, 22.0 mmol) in anhydrous glyme (100 mL) to obtain after purification by column chromatography on silica gel eluting with a 99:1 mixture of ethyl acetate and methanol **16** as a slightly yellow viscous oil (1.60 g, 57.4%). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 8.51 (s, **H**c, 1H), 7.50 (dd, J = 15.8, 9.0 Hz, **H**d, 1H), 5.90 (dd, J = 15.8, 1.2 Hz, **H**e-*trans*, 1H), 5.22 (dd, J = 9.0, 1.5 Hz, **H**e-*cis*, 1H), 5.14 (d, J = 3.8 Hz, O**H**, 1H), 4.79−4.57 (m, **H**a, **H**4, 3H), 4.29 (t, J = 4.0 Hz, **H**3, 1H), 4.15−3.97 (m, **H**2, **H**5, 2H), 3.81−3.65 (m, **H**1, **H**6a, 3H), 3.39 (t, J = 8.0 Hz, **H**6b, 1H). ^{13}C NMR (100 MHz, DMSO-d_6, δ, ppm): 144.42 (**C**b), 130.23 (**C**d), 121.29 (**C**c), 105.20 (**C**e), 88.11 (**C**3), 79.39 (**C**4), 79.10 (**C**5), 75.29 (**C**1, **C**2), 69.15 (**C**6), 62.35 (**C**a). HRMS (m/z): calcd for $C_{11}H_{16}N_3O_4$, 254.1135; found, 254.1137 [M + H]$^+$.

General Procedure for the RAFT Polymerization of VDTs in Dimethyl Sulfoxide (DMSO). *Synthesis of* ***19****.* A solution of VDT (**14**, 100 mg, 0.395 mmol), xanthate (**17**, 0.9 mg, 0.004 mmol), and AIBN (0.32 mg, 0.002 mmol) in DMSO-d_6 (0.654 g) was degassed by three freeze−pump−thaw cycles before being sealed off under vacuum. After 48 h at 80 °C, the polymerization medium was precipitated in dichloromethane and dried under vacuum to recover **19** as a white powder (60 mg, Y = 68%, M_n = 19.5 kDa, $Đ$ = 1.70, T_g = 52 °C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.70−7.27 (m, **H**c, 1H), 5.19

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Table 1. Properties of VDT Stereoisomers 13−16 and Polymer Analogues 18−21 Obtained by RAFT Polymerization

monomer	m/z (Da)[a]	T_g or T_m (°C)[b]	polymer	T_g (°C)[b]	M_n (kDa)[c]	$Đ$[c]	T_{d10} (°C)[d]
13	254.1137	−22	**18**	49	18.2	1.65	310
14	254.1134	−28	**19**	52	19.5	1.70	318
15	254.1139	139[e]	**20**	118	15.0	1.56	313
16	254.1137	−14	**21**	71	20.2	1.60	312

[a]Obtained by HRMS. [b]Obtained by DSC. [c]Obtained by SEC in DMF (RI detection and PS calibration). [d]Temperature at 10 wt % loss obtained by TGA. [e]C_p = 195 J/g.

(s, O**H**, 1H), 4.64−4.24 (m, **Ha**, **H2**, **H3**, 4H), 4.10−3.86 (m, **H4**, **H5**, 2H), 3.80−3.58 (m, **H1**, **H6**, 4H), 2.44−1.88 (m, **Hd**, **He**, 3H). The same procedure was applied to the synthesis of poly(1-vinyl-4-dianhydrohexitol-1,2,3-triazole)s (PVDTs) **18**, **20**, and **21**.

Synthesis of ***18***. (M_n = 18.2 kDa, $Đ$ = 1.65, T_g = 49 °C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.70−7.27 (m, **Hc**, 1H), 5.19 (s, O**H**, 1H), 4.64−4.24 (m, **Ha**, **H2**, **H3**, 4H), 4.10−3.86 (m, **H4**, **H5**, 2H), 3.80−3.58 (m, **H1**, **H6**, 4H), 2.44−1.88 (m, **Hd**, **He**, 3H).

Synthesis of ***20***. (M_n = 15.0 kDa, $Đ$ = 1.56, T_g = 118 °C). ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 7.79−7.22 (m, **Hc**, 1H), 4.82 (s, O**H**, 1H), 4.65−4.20 (m, **Ha**, **H2**, **H3**, 4H), 4.21−3.90 (m, **H4**, **H5**, 2H), 3.90−3.63 (m, **H1**, **H6**, 4H), 2.54−1.78 (m, **Hd**, **He**, 3H).

Synthesis of ***21***. (M_n = 20.2 kDa, $Đ$ = 1.60, T_g = 71 °C). 1H NMR (400 MHz, DMSO-d6, δ, ppm): 7.88−7.29 (m, **Hc**, 1H), 5.17 (s, O**H**, 1H), 4.73−4.17 (m, **Ha**, **H4**, **H5**, 4H), 4.17−3.88 (m, **H2**, **H3**, 2H), 3.73−3.59 (m, **H1**, **H6**, 4H), 2.56−1.72 (m, **Hd**, **He**, 3H).

RESULTS AND DISCUSSION

Synthesis of VDT Stereoisomers 13−16. VDT stereoisomers **13**−**16** were synthesized from DAHs **1**−**3** using a modified procedure adapted from the pioneering work of Hawker and co-workers (Scheme 2).[40] Indeed, no protection of the DAH remaining alcohol groups was required, reducing the previously reported approach from five to three synthetic steps and only two purifications by column chromatography. Initially, straightforward alkylation between diols **1**−**3** and one equivalent of propagyl bromide afforded mixtures of alkynes **4**−**7** and the corresponding dialkyne side-products. Although not used in the frame of this contribution, those biobased dialkynes could be advantageously valued as A_2 monomers in, e.g., CuAAC step growth polymerization processes.[24] Alkynes **4**−**7** were separated from the corresponding dialkynes by column chromatography. As expected in the case of isosorbide **3** that displays two spatially nonequivalent hydroxyl groups, regioisomers **6** and **7** respectively bearing the *O*-propargyl group in the C2 (exo) and C5 (endo) positions could be isolated. Pure alkyne-functionalized DAH stereoisomers **4**−**7** were thus obtained as colorless viscous oils in 38, 46 and 43% yields (for **4**, **5**, and **6**+**7**, respectively). The preparation of pure stereoisomers only differing in their spatial arrangement was first confirmed by HRMS, as a unique molecular ion was observed whatever the nature of the initial DAH (Table 1). ^{1}H and ^{13}C NMR spectra of alkynes **4**−**7** (Figure 1 and Figure S1 in the Supporting Information) undoubtedly probed the dissimilarities of alkyne functionalized DAH in terms of stereochemistry. Except for the alkyne group, strong disparities in terms of chemical shift were indeed observed for all other protons and carbons.

The second step relies on the CuAAC coupling between a stoichiometric mixture of alkyne-functionalized DAHs **4**−**7** and 1-mesyl-2-azidoethanol **8** to afford 1-(2-mesyl-ethanol)-4-dianhydrohexitol-1,2,3-triazole stereoisomers **9**−**12**. After evaporation of the volatiles, the crude mesylated 1,2,3-triazole intermediates **9**−**12** were finally engaged in the elimination reaction to yield the targeted VDT stereoisomers **13**−**16** after purification by column chromatography (Scheme 1).

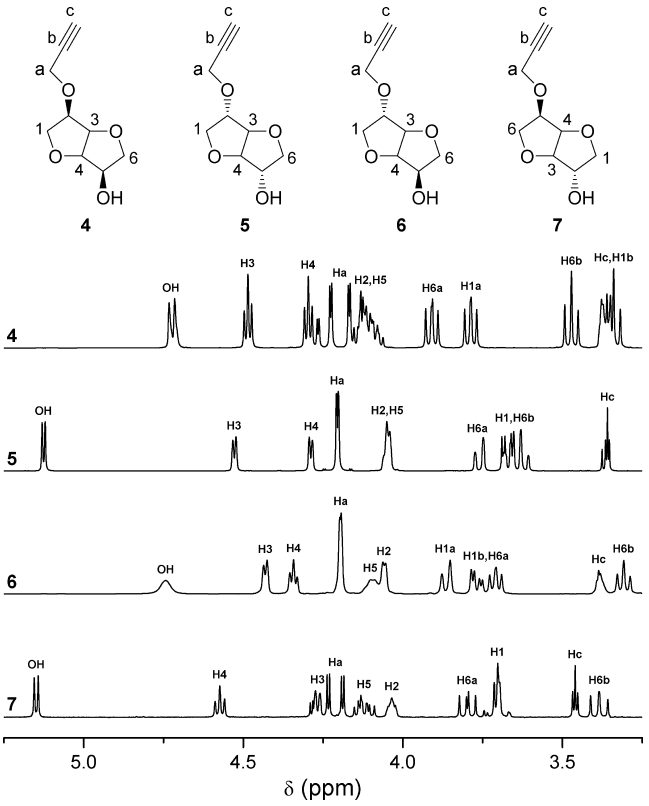

Figure 1. ^{1}H NMR (DMSO-d_6) of alkyne-functionalized DAHs **4**−**7**.

As a direct consequence of their distinct stereochemistry, monomers **13**, **14**, and **16** were recovered as viscous oils, whereas **15** was a crystalline solid. This was further corroborated by DSC as stereoisomers **13**, **14**, and **16** exhibited T_g values of −22, −28, and −14 °C, respectively, whereas a T_m value of 139 °C was observed for **15** (Table 1).

Examination of single crystals of **15** by X-ray diffraction experiments (Figure 2 and Supporting Information) confirmed the stereochemistry of the DAH moiety as well as the presence of a relatively strong hydrogen bonding between the hydroxyl group on the C2 carbon atom of the DAH ring and the N3 nitrogen atom of the triazole ring from an adjacent monomer in the crystal lattice. The geometry of this hydrogen bond ($d_{(O-N)}$ = 2.88 Å and $\theta_{(OHN)}$ = 176°) is fully consistent with the *H*-bonding nature of the 1,2,3-triazole ring.[39,40,43] The purity of the obtained monomers was confirmed by NMR spectroscopy and HRMS measurements. Again, HRMS spectra of VDT stereoisomers **13**−**16** exhibited a single molecular ion perfectly matching the expected theoretical value (Table 1). In analogy with DAH-based alkynes **4**−**7**, the chemical shifts, multiplicity and splitting constants of the proton signals, and the chemical

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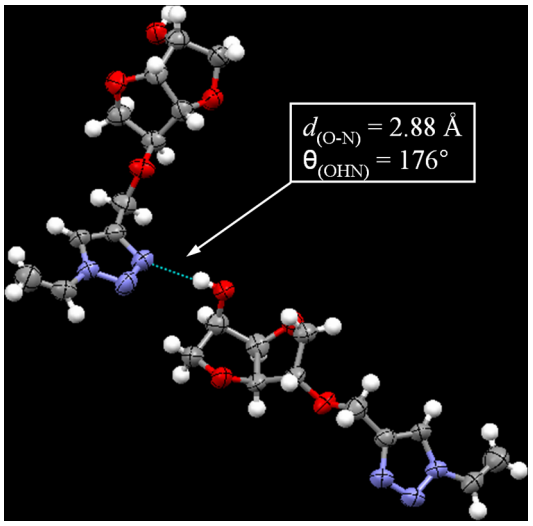

Figure 2. X-ray structure of VDT stereoisomer **15** (C: gray, O: red, N: blue, H: white).

shifts of carbon signals corresponding to the DAH moieties and the methylene group adjacent to the triazole ring were significantly impacted by the DAHs stereochemistry (Figure 3

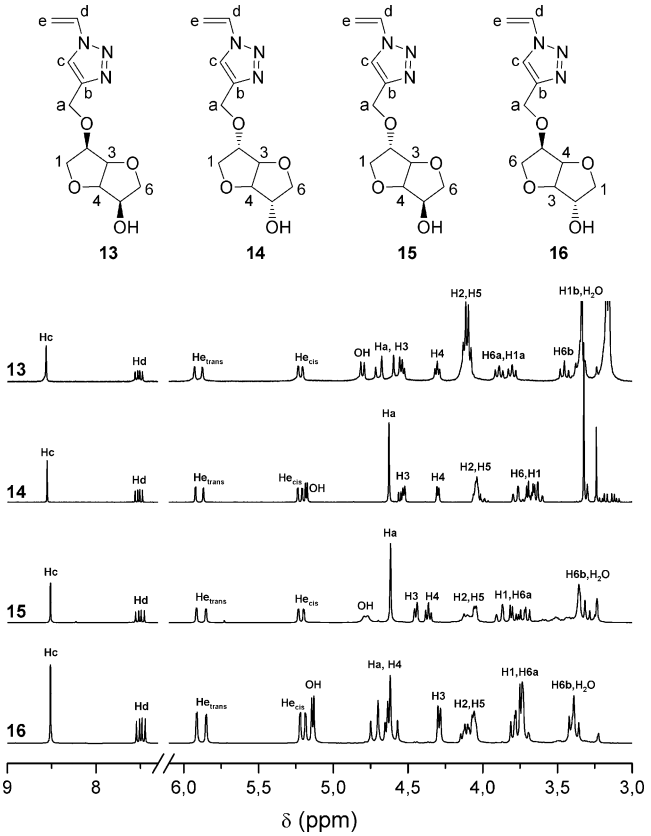

Figure 3. ^{1}H NMR (DMSO-d_6) of VDT stereoisomers **13**−**16**.

and Figure S2 in the Supporting Information). In particular, the signal of the methylene group adjacent to the triazole ring was a singlet for **14** and **15** (OCH_2 in exo position) and a pseudoquadruplet for **13** and **16** (OCH_2 in endo position), again confirming the importance of spatial arrangement on the properties of the resulting stereoisomers. Conversely, both ^{1}H and ^{13}C NMR spectra revealed almost identical resonances for the vinyl and 1,2,3-triazole protons and carbons, indicating that the electronic density of these fragments is not impacted by the stereochemistry of the DAH moieties. Finally, the solubility of monomers **13**−**16** was only slightly impacted by the stereochemistry of the DAH moieties (Table 2). All stereoisomers are

Table 2. Solubility of VDT Stereoisomers 13−16 and Polymer Analogues 18−21[a]

	monomers				polymers			
	13	**14**	**15**	**16**	**18**	**19**	**20**	**21**
H_2O	−	−	−	−	−	−	−	+
MeOH	+	+	+	+	−	−	−	−
AcOEt	+	+	−	+	−	−	−	−
Acetone	+	+	+	+	−	−	−	−
THF	+	+	+	+	−	−	−	−
CH_2Cl_2	+	+	+	+	−	−	−	−
$CHCl_3$	+	−	+	+	−	−	−	−
DMF	+	+	+	+	+	+	+	+
DMSO	+	+	+	+	+	+	+	+

[a]"+" indicates solubility of about 10 mg/mL, while "−" indicates no detectable solubility even at 0.1 mg/mL.

soluble in methanol (MeOH), acetone, dichloromethane (CH_2Cl_2), dimethylformamide (DMF), and DMSO and insoluble in water (H_2O). It is, however, worth mentioning that, contrary to the other stereoisomers, **14** and **15** are not soluble in chloroform ($CHCl_3$) and ethyl acetate (AcOEt), respectively.

RAFT Polymerization of VDT Stereoisomers 13−16. As xanthates have been previously proven to be suitable chain transfer agents (CTAs) for the controlled polymerization of nonactivated *N*-vinyl monomers such as *N*-vinylcarbazole,[41] *N*-vinylindole,[44] *N*-vinylphtalimide,[45] *N*-vinylpyrrolidone,[46] *N*-vinylimidazolium salts,[47] *N*-vinyl-1,2,3-triazoles,[40] and *N*-vinyl-1,2,4-triazoles,[48] VDT stereoisomers **13**−**16** were polymerized by RAFT polymerization in DMSO-d_6 at 80 °C using *O*-ethyl-*S*-(1-phenylethyl) dithiocarbonate **17** as CTA and AIBN as thermal initiator (Scheme 3). For each stereoisomer, the following ratios were maintained constant, i.e., 13 wt % of monomers **13**−**16** in DMSO.

For all stereoisomers, monomer conversion was monitored by ^{1}H NMR by following the progressive decrease of the characteristic signals of the vinyl group at 7.5, 5.9, and 5.2 ppm as well as the concomitant appearance of the signals of the polymer backbone at 2.5−1.8 ppm. Another significant change in the ^{1}H NMR spectra was the upfield shift of the triazole proton signal. Indeed, the well-defined singlet at about 8.5 ppm for the monomer progressively disappears in favor of a broad multimodal signal at about 7.8−7.3 ppm for the polymer. In contrast with the contribution of Hawker and co-workers,[40] which underlined relatively fast kinetics for the polymerization of 4-octyl-vinyl-1,2,3-triazole (respectively about 30 and 80% of conversion for xanthate and dithiocarbamate mediated polymerization during 6 h at 60 °C, [M]/[CTA]/[AIBN] = 200:1:0.25, 10 wt % of monomer in DMF), stereoisomers **13**−**16** displayed surprisingly slow polymerization kinetics in the presence of **17** (i.e., about 50−70% of conversion after 48 h of reaction at 80 °C). Similar results were obtained using a dithiocarbamate CTA.[48] As observed earlier,[49] the combined steric hindrance of the 1,2,3-triazole and DAH moieties might hamper the polymerization kinetics of such monomers

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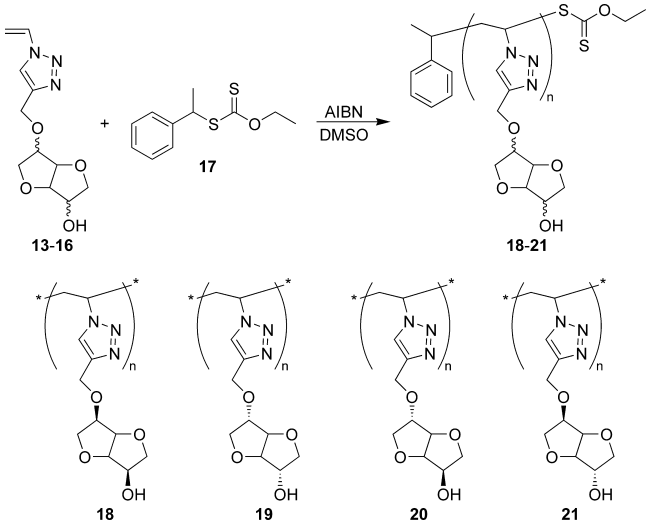
Scheme 3. Synthesis of Polymers 18−21 by RAFT Polymerization of Monomers 13−16



compared to previously studied 1-vinyl-1,2,3-triazoles.[40] As the main purpose of this preliminary report is to evaluate the properties of PVDT stereoisomers, the origin of the slow polymerization kinetics was not investigated in the details herein. Nevertheless, each polymerization medium remained homogeneous throughout the polymerization process. Polytriazoles **18−21** were precipitated in CH_2Cl_2 and dried under vacuum before characterization by SEC, ^{1}H NMR, DSC, and TGA.

As for alkynes **4−7** and 1-vinyl-1,2,3-triazole monomers **13−16**, the stereochemistry of the DAH moieties strongly impacts the ^{1}H NMR chemical shifts of polymers **18−21** (Figure 4). Whereas similar signals are observed for the vinylic backbones and the triazole rings, strong disparities appear for the DAH units and the adjacent methylene segments.

The polymerizations resulted in symmetrical and monomodal SEC traces. PVDTs **18−21** display M_n values ranging from 15 to 20 kDa with relatively high $Đ$ (ranging from 1.56 to 1.70) in regards to a controlled radical polymerization (CRP) process (Table 1). However, these surprisingly high $Đ$ values may not reflect a poor control of the polymerization, as polystyrene (PS) calibration can lead to a substantial overestimation of $Đ$.[50]

Similarly to the parent monomers **13−16** and corroborating ^{1}H NMR data, the influence of the pendent DAH stereochemistry was clearly illustrated by DSC experiments that underlined the amorphous character of all polymers with T_g values of 49, 52, 118, and 71 °C for PVDTs **18−21**, respectively (Table 1). Compared to previously reported DAH-based polytriazoles,[23,24] these T_g values are unexpectedly low considering the combination of relatively rigid, polar and *H*-bonding DAH and 1,2,3-triazole groups as well as hydroxyl functionalities. However, this probably stems from the presence of a methylene segment between the triazole and the DAH moieties, which provides significant mobility to the pendent DAH moieties. Thermal stability and solubility behavior of polymers **18−21** were then investigated. Stereochemistry of the DAH moieties has no significant impact on the resistance to thermal degradation since T_{d10} values ranging from 310 to 318 °C were observed. PVDTs **18−21** are rather stable toward degradation under nonoxidative atmosphere since these T_{d10} values are comparable to stereocontrolled DAH-based polytriazoles obtained earlier by step growth polymerization (T_{d10} = 314−347 °C depending on the stereochemistry of the DAH unit). The impact of the DAH stereochemistry was further observed on the solubility of the polymers (Table 2). Although PVDTs exhibit some common features of being soluble in DMF and DMSO and insoluble in CH_2Cl_2, $CHCl_3$, MeOH, acetone, AcOEt, and THF, the solubility behavior of PVDTs **18−21** in water was quite unexpected. Indeed, whereas PVDTs **18−20** swell in water without dissolution of the hygroscopic polymer chains, PVDT **21** is water-soluble. This original behavior potentially allows the formation of amphiphilic diblock copolymers where the two blocks are stereoisomers of each other.

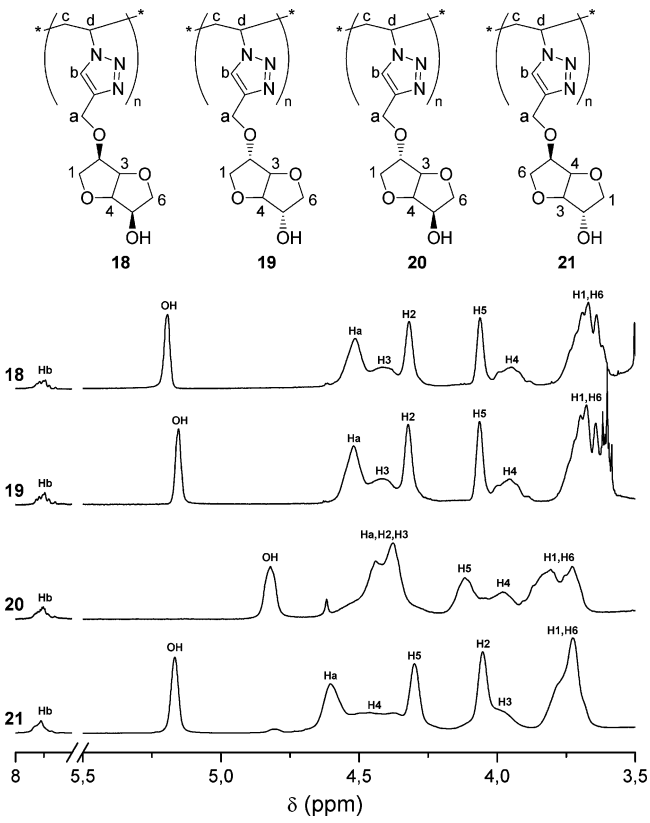


Figure 4. ^{1}H NMR (DMSO-d_6) of polymers **18−21**.

CONCLUSION

A series of biosourced VDT stereoisomers has been synthesized by an efficient three-step chemical pathway starting from isomannide, isoidide, and isosorbide. The RAFT polymerization of the different stereoisomers afforded a library of four PVDTs with controlled stereochemistry and relatively well-defined structures (M_n = 15−20 kDa and $Đ$ ∼ 1.5−1.7). A thorough investigation of the structure-properties relationship of these novel biobased monomers and polymers highlighted a significant influence of the DAH moieties on their physicochemical properties. Interestingly, isosorbide-based PVDT stereoisomers **20** and **21** exhibit relatively high glass transition temperatures (T_g = 71 and 118 °C) and contrasting solubility in water. This unique behavior together with the strong complexation properties resulting from the combination of triazole and dianhydrohexitol moieties, make these materials promising candidates for the development of renewable

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chelating polymers and self-assembled nanostructures. The study in aqueous media of random or diblock copolymers comprising isosorbide-based stereoisomers **20** and **21** having distinct solubility in water is currently under investigation.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{13}C NMR of **4**-**7**,**13**-**16**, SEC (DMF) of **18**-**21**, and crystallographic data of **15**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

This work is dedicated to Professor Jean-Pierre Pascault on occasion of his 68th anniversary.

■ REFERENCES

(1) Meier, M. A. R.; Metzger, J. O.; Schubert, U. S. *Chem. Soc. Rev.* **2007**, *36*, 1788−1802.
(2) Williams, C. K.; Hillmeyer, M. A. *J. Macromol. Sci., Polym. Rev.* **2008**, *48*, 1−10.
(3) Raquez, J.-M.; Deléglise, M.; Lacrampe, M.-F.; Krawczak, P. *Prog. Polym. Sci.* **2010**, *35*, 487−509.
(4) Hong, J.; Luo, Q.; Shah, B. K. *Biomacromolecules* **2010**, *11*, 2960−2965.
(5) Palaskar, D. V.; Boyer, A.; Cloutet, E.; Alfos, C.; Cramail, H. *Biomacromolecules* **2010**, *11*, 1202−1211.
(6) Lligadas, G.; Ronda, J. C.; Galia, M.; Cadiz, V. *Biomacromolecules* **2010**, *11*, 2825−2835.
(7) Hojabri, L.; Kong, X.; Narine, S. S. *Biomacromolecules* **2010**, *11*, 911−918.
(8) Stemmelen, M.; Pessel, F.; Lapinte, V.; Caillol, S.; Habas, J.-P.; Robin, J.-J. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 2434−2444.
(9) Gandini, A. *Green Chem.* **2011**, *13*, 1061−1083.
(10) Brocas, A.-L.; Cendejas, G.; Caillol, S.; Deffieux, A.; Carlotti, S. *J. Polym. Sci., Part A: Polym. Chem.* **2011**, *49*, 2677−2684.
(11) Rose, M.; Palkovits, R. *Macromol. Rapid Commun.* **2011**, *32*, 1299−1311.
(12) Barker, I. A.; Hall, D. J.; Hansell, C. F.; Du Prez, F. E.; O'Reilly, R. K.; Dove, A. P. *Macromol. Rapid Commun.* **2011**, *32*, 1362−1366.
(13) Besset, C. J.; Lonnecker, A. T.; Streff, J. M.; Wooley, K. L. *Biomacromolecules* **2011**, *12*, 2512−2517.
(14) Firdaus, M.; Montero de Espinosa, L.; Meier, M. A. R. *Macromolecules* **2011**, *44*, 7253−7262.
(15) Mathers, R. T. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 1−15.
(16) Fenouillot, F.; Rousseau, A.; Colomines, G.; Saint-Loup, R.; Pascault, J.-P. *Prog. Polym. Sci.* **2010**, *35*, 578−622.
(17) Besset, C.; Bernard, J.; Fleury, E.; Pascault, J.-P.; Cassagnau, P.; Drockenmuller, E.; Williams, R. J. J. *Macromolecules* **2010**, *43*, 5672−5678.
(18) Bersot, J. C.; Jacquel, N.; Saint-Loup, R.; Fuertes, P.; Rousseau, A.; Pascault, J.-P.; Spitz, R.; Fenouillot, F.; Monteil, V. *Macromol. Chem. Phys.* **2011**, *212*, 2114−2120.
(19) Ben Abderrazak, H.; Fildier, A.; Marque, S.; Prim, D.; Ben Romdhane, H.; Kricheldorf, H. R.; Chatti, S. *Eur. Polym. J.* **2011**, *47*, 2097−2110.
(20) Kricheldorf, H. R.; Behnken, G.; Sell, M. *J. Macromol. Sci., Part A: Pure Appl.Chem.* **2007**, *44*, 679−684.
(21) Inkinen, S.; Stolt, M.; Sodergard, A. *Biomacromolecules* **2010**, *11*, 1196−1201.
(22) Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thiem, J. *Macromol. Rapid Commun.* **1998**, *19*, 21−26.
(23) Bachmann, F.; Reimer, J.; Ruppenstein, M.; Thiem, J. *Macromol. Chem. Phys.* **2001**, *202*, 3410−3419.
(24) Chatti, S.; Schwarz, G.; Kricheldorf, H. R. *Macromolecules* **2006**, *39*, 9064−9070.
(25) Besset, C.; Binauld, S.; Ibert, M.; Fuertes, P.; Pascault, J.-P.; Fleury, E.; Bernard, J.; Drockenmuller, E. *Macromolecules* **2010**, *43*, 17−19.
(26) Besset, C.; Pascault, J.-P.; Fleury, E.; Drockenmuller, E.; Bernard, J. *Biomacromolecules* **2010**, *11*, 2797−2803.
(27) Noordover, B. A. J.; Haveman, D.; Duchateau, R.; van Benthem, R. A. T. M.; Koning, C. E. *J. App. Polym. Sci.* **2011**, *121*, 1450−1463.
(28) Sato, K.; Kodama, K. (Fuji Photo Film Co.). WO Patent 341062, December 02, 2004.
(29) Koyama, H.; Tsutsumi, K. (Daicel Chemical Industries). WO Patent 113404, December 29, 2004.
(30) Beghdadi, S.; Abdelhedi Miladi, I.; Addis, D.; Ben Romdhane, H.; Bernard, J.; Drockenmuller, E. *Polym. Chem.* **2012**, *3*, 1680−1692.
(31) Danilovtseva, E. N.; Chafeev, M. A.; Annenkov, V. V. *J. Polym. Sci., Part A: Polym. Chem.* **2012**, *50*, 1539−1546.
(32) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596−2599.
(33) Meldal, M.; Tornoe, C. W. *Chem. Rev.* **2008**, *108*, 2952−3015.
(34) Iha, R. K.; Wooley, K. L.; Nystrom, A. M.; Burke, D. J.; Kade, M. J.; Hawker, C. J. *Chem. Rev.* **2009**, *109*, 5620−5686.
(35) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302−1315.
(36) Sumerlin, B. S.; Vogt, A. P. *Macromolecules* **2010**, *43*, 1−13.
(37) Thibault, R. J.; Takizawa, K.; Lowenheilm, P.; Helms, B.; Mynar, J. L.; Frechet, J. M. J.; Hawker, C. J. *J. Am. Chem. Soc.* **2006**, *128*, 12084−12085.
(38) Takizawa, K.; Nulwala, H.; Thibault, R. J.; Lowenheilm, P.; Yoshinaga, K.; Wooley, K. L.; Hawker, C. J. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 2897−2912.
(39) Nulwala, H.; Takizawa, K.; Odukale, A.; Khan, A.; Thibault, R. J.; Taft, B. R.; Lipshutz, B. H.; Hawker, C. J. *Macromolecules* **2009**, *42*, 6068−6074.
(40) Nulwala, H.; Burke, D. J.; Khan, A.; Serrano, A.; Hawker, C. J. *Macromolecules* **2010**, *43*, 5474−5477.
(41) Mori, H.; Ookuma, H.; Nakano, S.; Endo, T. *Macromol. Chem. Phys.* **2006**, *207*, 1005−1017.
(42) Brase, S.; Gil, C.; Knepper, K.; Zimmermann, V. *Angew. Chem., Int. Ed.* **2005**, *44*, 5188−5240.
(43) Steiner, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 48−76.
(44) Maki, Y.; Mori, H.; Endo, T. *Macromolecules* **2007**, *40*, 6119−6130.
(45) Maki, Y.; Mori, H.; Endo, T. *Macromol. Chem. Phys.* **2007**, *208*, 2589−2599.
(46) Guinaudeau, A.; Mazieres, S.; Wilson, D. J.; Destarac, M. *Polym. Chem.* **2012**, *3*, 81−84.

(47) Mori, H.; Yahagi, M.; Endo, T. *Macromolecules* **2009**, *42*, 8082−8092.
(48) Mori, H.; Ishikawa, K.; Abiko, Y.; Maki, Y.; Onuma, A.; Morishima, M. *Macromol. Chem. Phys.* **2012**, *213*, 1803−1814.
(49) Bertrand, A.; Stenzel, M.; Fleury, E.; Bernard, J. *Polym. Chem.* **2012**, *3*, 377−383.
(50) Guillaneuf, Y.; Castignolles, P. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 897−911.