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Synthesis of multifunctional hydroxyethyl tetrazoles

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Abstract

A series of di-, tri-, and tetra-tetrazoloalkanes were synthesized from the corresponding nitrile and sodium azide. These were alkylated to give hydroxy terminated chains for possible use as high energy oligomers.
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1. Introduction

Tetrazoles are used as bioequivalent for carboxylic acids[1] and as energetic materials. High nitrogen heterocycles are currently being evaluated as gas generators and/or burn rate modifiers for the next generation of propellant systems.[2] Tetrazoles have a special place due to their nitrogen content and high heats of formation. Approximately 10–20% of the weight of a propellant is binder used to provide mechanical integrity and act as a fuel.[3] Most commercially useful propellant binder systems are based on polybutadiene. Several energetic polymers have been developed that typically have nitrate ester or azide pendent groups.[4] Though, none of the available high energy binders systems have the optimal combination of good mechanical properties over a wide temperature range and long-term chemical stability. This has lead to our research into more stable energetic binders. The candidate binder must add to the energy of the system and also have the proper mechanical properties. In addition, it must have long-term stability in the presence of the other ingredients. In this Letter, we will report on the synthesis of oligomeric hydroxyethyl tetrazoles for use as energetic binders.

Tetrazoles can be synthesized by a number of methods including the addition of azide salts to nitriles.[5,6] The tetrazoles presented were synthesized using the method of Sharpless et al., due to the reported high yields and the use of water as the primary solvent (Fig. 1). Similar materials have been made via trialkyltin azides which were subsequently alkylated through the bound trialkyltin for their interesting structural chemistry.[7–9] The multifunctional tetrazoles were then alkylated in high yields with 2-chloroethanol to give a mixture of the 1- and 2-alkylated products which were not separated.[10] Since the ultimate use of these materials is for binders and the dissymmetry of the monomers will lead to polymers with lower glass transition temperatures (T_g), the mixture of isomers is a benefit. The isomers and their approximate ratios have been identified by ^{1}H NMR.

The starting nitriles were chosen with the eventual binder properties in mind. The difunctional monomers (**1-6**; see Table 1) will be used for chain extension with the ether functionalized monomers (**4** and **6**) to decrease crystallinity. The tri-functional monomer (**8**) will be used as a

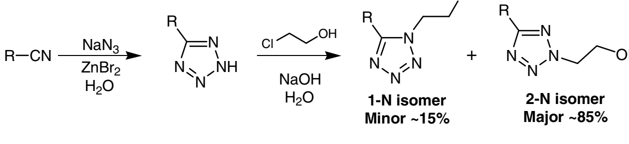

Fig. 1. General reaction scheme for the synthesis of N-alkylated tetrazole monomers.

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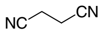
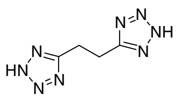
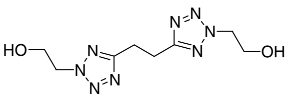
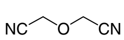
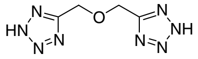
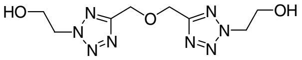
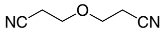
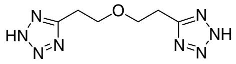
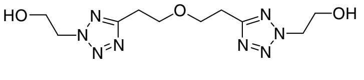
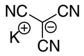
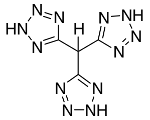
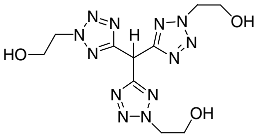
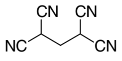
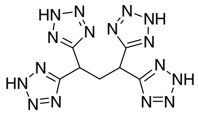
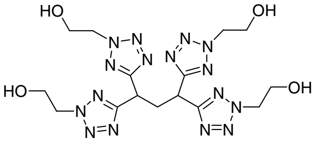
Table 1
Structures and yields of tetrazoles and tetrazole alcohols

Substrate	Structure of major isomer	Yield (%)	Structure of major isomer	Yield[a] (%)	Physical state of alcohols
	 **1**	73	 **2**	90	Oil
	 **3**	68	 **4**	70	Oil
	 **5**	30	 **6**	97	Oil
	 **7**	38	 **8**	70	Glass
	 **9**	59	 **10**	85	Oil

[a] Yield includes all isomers; isomers were not separated.

cross-linking material. The last material (tetra-functional **10**) was chosen as cross-linking agent with a higher nitrogen content.

The difunctional tetrazoles were produced in good yields and were purified by recrystallization or used as such. The alkylation with chloroethanol produced a mixture of the 1-*N*- and 2-*N*-product in the ratios of ~15:85 per tetrazole (as determined by NMR). This leads to three possible isomers with two symmetrically identical tetrazoles (1,1′; 1,2′; 2,1′, and 2,2′ where 1,2′ = 2,1′), four isomers with tris-tetrazoles and six with tetrakis-tetrazoles.

The tri-functional and tetra-functional tetrazoles were also produced in good yields and were purified by recrystallization or used as such. The ratio of 1-N- and 2-N-alkylation remained the same.

The alkylations were run in water as the solvent which was removed during workup. This gave a mixture of the product hydroxyethyl tetrazoles and sodium chloride. Most of the sodium chloride could be removed by dissolution in ethanol then filtering and concentrating the filtrate or by chromatography on silica gel. The hydroxyethyl tetrazoles are quite polar and tend to stick to the column with normal solvents but we found that a mixture of methanol and acetone or ethyl acetate will elute them. Both the ethanol dissolution and the chromatography tended to leave a small amount of salt in the product. In the end we found that *n*-propanol will dissolve the product and leave all of the salts behind. This followed by chromatography led to analytically pure hydroxyethyl tetrazoles.

We attempted to form the tris-tetrazole of 2,4,6-tricyano-1,3,5-triazine using the above procedure but was unsuccessful, being unable to isolate anything from the dark reaction mixture. Additional attempts using trimethylsilyl azide and tributyltin azide in acetonitrile were similarly unsuccessful.

2. Experimental

2.1. 1,2-Bis(5-tetrazolo)ethane (**1**)

To a stirred mixture of 100 g succinonitrile (1.25 mol) and 563 g zinc bromide (2.5 mol) in 1 L water was added 179 g sodium azide (2.75 mol) and the solution was heated to reflux and stirred for 18 h. The mixture was cooled and placed in an ice bath. Concd HCl (200 mL) was added. The solids all dissolved and the solution was stirred for 2 h. The solids were then filtered off and washed with water to give 152.44 g product (73%). Mp 228–232 °C (dec). ^{1}H NMR (DMSO-d_6): (δ) 3.38 (s). Calcd for $C_4H_6N_8$: C, 28.92; H, 3.64; N, 67.44. Found: C, 29.03; H, 3.69; N, 67.66.

2.2. 1,2-Bis(hydroxyethyl-5-tetrazolo)ethane (**2**)

To a suspension of 20 g 1,2-bis(5-tetrazolo)ethane (120 mmol) in 150 mL water was added 10.6 g NaOH (226 mmol) followed by 17.8 mL 2-chloroethanol (266 mmol). The solution was heated to reflux and stirred for 18 h then cooled and concentrated in vacuum. The residue was taken up in 500 mL hot ethanol. The sodium chloride was filtered off and the filtrate concentrated in vacuum to give 36.78 g of a thick oil. This was chromatographed on silica gel using 20% MeOH/acetone to give 27.32 g of a thick oil (90%). ^{1}H NMR (DMSO-d_6): (δ) 4.64 (m, 2.2H), 4.43 (m, 1.8H), 3.88 (m, 2.2H), 3.75 (m, 1.8H), 3.43 (s, 0.9H), 3.69 (m, 2.2H), 3.31 (d, 1.6H); ^{13}C NMR (DMSO-d_6): (δ) 164.59, 164.38, 155.58, 154.99, 154.82, 62.84, 59.72, 59.08, 55.44, 55.38, 49.41, 23.21, 23.09, 22.60, 21.67, 20.84, 20.31; Calcd for $C_8H_{14}N_8O_2$: C, 37.79; H, 5.55; N, 44.07. Found: C, 36.77; H, 5.68; N, 44.07.

2.3. 1,3-Bis(5-tetrazolo)-2-oxapropane (**3**)

To a stirred mixture of 14.09 g bis-cyanomethyl ether (147 mmol) and 33 g zinc bromide (147 mmol) in 150 mL water was added 19.07 g sodium azide (293 mmol). The solution was heated to reflux and stirred overnight. The mixture was cooled and 35 mL concd HCl was added. The solids all dissolved and the solution was stirred for 2 h while a new solid precipitated. The solids were filtered off and washed with water to give 22.88 g product (85%). This was recrystallized from 250 mL ethanol to give 18.28 g 1,3-bis(5-tetrazolo)-2-oxapropane (68%) as a white crystalline solid. Calcd for $C_4H_6N_8O$: C, 26.38; H, 3.32; N, 61.52. Found: C, 26.62; H, 3.34; N, 61.38.

2.4. 1,3-Bis(hydroxyethyl-5-tetrazolo)-2-oxapropane (**4**)

To a suspension of 15.63 g 1,3-bis(5-tetrazolo)-2-oxapropane (86 mmol) in 100 mL water was added 6.87 g NaOH (174 mmol) followed by 13 mL 2-chloroethanol (194 mmol). The solution was heated to reflux and stirred for 18 h then cooled and concentrated in vacuum. The residue was taken up in 75 mL *n*-propanol. The sodium chloride was filtered off and the filtrate concentrated in vacuum to give 32.42 g of a thick oil. This was taken up in 250 mL *n*-propanol and allowed to stand for about 4 h. The solids were filtered off and the filtrate concentrated in vacuum to give 23.88 g of a thick clear oil (100%). The crude product was then chromatographed on silica gel eluting with 10% methanol/ethyl acetate to give 16.17 g of a clear thick oil (70%). An analytical sample was obtained after a second chromatography of ~2 g on silica gel using 10% MeOH/EtOAc to give 1.28 g of a clear oil. ^{1}H NMR (DMSO-d_6): (δ) 5.03 (d, 1.5H), 4.88 (d, 2.9H), 4.72 (t, 2.9H), 4.52 (t, 1.0H), 3.95 (t, 2.8H), 3.80 (t, 1.0H); ^{13}C NMR (DMSO-d_6): (δ) 162.52, 162.31, 153.83, 152.48, 63.02, 62.88, 62.80, 62.50, 61.39, 60.31, 59.71, 59.25, 55.83, 50.08; Calcd for $C_8H_{14}N_8O_3$: C, 35.56; H, 5.22; N, 41.46. Found: C, 35.47; H, 5.36; N, 41.28; Cl, 0.0.

2.5. 1,5-Bis(5-tetrazolo)-3-oxapentane (**5**)

To a stirred mixture of 12.41 g 2-cyanoethyl ether (100 mmol) and 45 g zinc bromide (200 mmol) in 150 mL water was added 15 g sodium azide (230 mmol) and the solution was heated to reflux and stirred overnight. The mixture was cooled and 75 mL of 4 N HCl was added. The solids all dissolved and the solution was stirred for 2 h. The solids were then filtered off and washed with water to give 9.46 g product (45%). This was recrystallized from acetonitrile to give 6.29 g 1,5-bis(5-tetrazolo)-3-oxapentane (30%) as a white crystalline solid. Mp 193–195 °C. ^{1}H NMR (DMSO-d_6): (δ) 3.84 (t, 4H), 3.16 (t, 4H). Calcd for $C_6H_{10}N_8O$: C, 34.28; H, 4.80; N, 53.31. Found: C, 34.39; H, 4.88; N, 53.39.

2.6. 1,5-Bis(hydroxyethyl-5-tetrazolo)-3-oxapentane (**6**)

To a suspension of 40.00 g 1,5-bis(5-tetrazolo)-3-oxapentane (0.19 mol) in 300 mL water was added 15.2 g NaOH (0.38 mol) followed by 27 mL 2-chloroethanol (0.41 mol). The solution was heated to reflux and stirred for 18 h then cooled and concentrated in vacuum. The residue was taken up in 250 mL *n*-propanol. The sodium chloride was filtered off and the filtrate concentrated in vacuum to give 54.98 g of a thick oil (97%). ^{1}H NMR (DMSO-d_6): (δ) 4.63 (t, 2.5H), 4.37 (m, 1.5H), 3.89 (t, 2.7H), 3.79 (bm, 6.5H), 3.13 (t, 1.7H), 3.04 (t, 3.1H); ^{13}C NMR (DMSO-d_6): (δ) 163.44, 154.60, 153.93, 153.85, 67.90, 67.75, 67.59, 67.41, 67.34, 59.65, 59.03, 55.31, 49.25, 25.70, 24.41, 24.33, 23.38. Calcd for $C_{10}H_{18}N_8O_3$: C, 40.26; H, 6.08; N, 37.56. Found: C, 40.00; H, 6.18; N, 37.00.

2.7. Tris(5-tetrazolo)methane (**7**)

To a solution of 3.88 g potassium tricyanomethide (30 mmol), 7.81 g sodium azide (120 mmol), and 20.27 g zinc bromide (90 mmol) in 150 mL H_2O was added 8 mL 4 N HCl and refluxed overnight. The mixture was then cooled and filtered. The solids were washed with water and then dissolved in 200 mL 1 M NaOH. After stirring at rt for 6 h the solution was filtered and the filtrate was neutralized with 75 mL 4 N HCl. The solids were filtered off and washed with water then dried to give 2.52 g of an off white solid (38%). ^{13}C NMR (DMSO-d_6): 154.46, 29.37.

2.8. Tris(hydroxyethyl-5-tetrazoyl)methane (**8**)

To a suspension of 2.52 g tris-5-tetrazoylmethane (11.4 mmol) in 25 mL water was added 1.51 g NaOH (38 mmol). This was heated to just below reflux at which time 2.6 mL 2-chloroethanol (38 mmol) was added. The solution was refluxed overnight then cooled and concentrated in vacuum. The residue was taken up in 100 mL hot ethanol. The solids were filtered off and the filtrate again concentrated in vacuum to give 4.47 g of a golden oil. A second dissolution, filtration, and concentration, this time from 75 mL hot acetone produced 4.08 g crude product. This was chromatographed on silica gel using 8% MeOH in acetone to yield 2.80 g of a thick colorless oil (70%). ^{1}H NMR (DMSO-d_6): (δ) 7.55 (s), 7.28 (s), 6.95 (s), 4.79 (q), 4.50 (br m), 4.09 (t), 3.96 (t).

2.9. *1,1,3,3-Tetrakis(5-tetrazolo)propane* (**9**)

To a mixture of 25.0 g 1,1,3,3-tetrakis-cyanopropane (0.173 mol) and 78.1 g zinc bromide (0.347 mol) in 500 mL water was added 56.3 g sodium azide (0.866 mol) and the solution heated to reflux. After stirring overnight the mixture was cooled and 80 mL concentrated HCl was added. The solids initially dissolved and a new solid precipitated after about 10 min. The mixture was stirred for an additional 50 min then the solids were filtered off and washed with water to give 45.26 g of an orange solid (83%). This could be recrystallized from 3 L water (decolorizing carbon) to give 32.43 g of white crystals (59%). Mp 266 °C (dec). Calcd for $C_7H_8N_{16}$: C, 26.59; H, 2.55; N, 70.86. Found: C, 26.64; H, 2.54; N, 70.78.

2.10. *1,1,3,3-Tetrakis(hydroxyethyl-5-tetrazolyl)propane* (**10**)

To a suspension of 9.96 g 1,1,3,3-tetrakis(5-tetrazolo)propane (0.0315 mol) in 100 mL water was added 5.5 g sodium hydroxide (0.138 mol) followed by 13 mL 2-chloroethanol (0.194 mol). The solution was heated to reflux and stirred overnight. The solution was then cooled and concentrated in vacuum. The residue was taken up in 150 mL hot *n*-propanol. This was filtered hot and the filtrate concentrated in vacuum to give 19.52 g of a clear oil. This was chromatographed on silica gel using 15% MeOH/EtOAc to give 13.22 g of a clear oil (85%). Calcd for $C_{15}H_{24}N_{16}O_4$: C, 36.58; H, 4.91; N, 45.51. Found: C, 36.56; H, 5.04; N, 45.71.

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References and notes

1. Herr, R. J. *Bioorg. Med. Chem.* **2002**, *10*, 3379.
2. Chavez, D. E.; Hiskey, M. A. *J. Energ. Mater.* **1999**, *17*, 357.
3. Sutton, G. P.; Biblarz, O. *Solid Rocket Propulsion*, 7th ed.; John Wiley and Sons: New York, 2001; Chapter 12.
4. Judge, M. D.; Lessard, P. *Propell. Explos. Pyrot.* **2007**, *32*, 175.
5. Finnegan, W. G.; Henry, R. A.; Lofquist, R. *J. Am. Chem. Soc.* **1958**, *80*, 3908.
6. Demko, Z. P.; Sharpless, K. B. *J. Org. Chem.* **2001**, *66*, 7945.
7. Bethel, P. A.; Hill, M.; Mahon, M. F.; Molloy, K. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3507.
8. Goodger, A.; Hill, M.; Mahon, M. F.; McGinley, J.; Molloy, K. C. *J. Chem. Soc., Dalton Trans.* **1996**, 847.
9. Hill, M.; Mahon, M. F.; Molloy, K. C. *J. Chem. Soc., Dalton Trans.* **1996**, 1857.
10. Finnegan, W. G.; Henry, R. A. US Patent 3,055,911, September 25, 1962.