

Communication

1-(4-{[3,5-bis([3,5-Dimethyl-4-(4-methyl-3,5-dioxo-1,2,4-triazolidin-1-yl)-phenoxy]methyl))phenyl]methoxy}-2,6-dimethyl-phenyl)-4-methyl-1,2,4-triazolidine-3,5-dione

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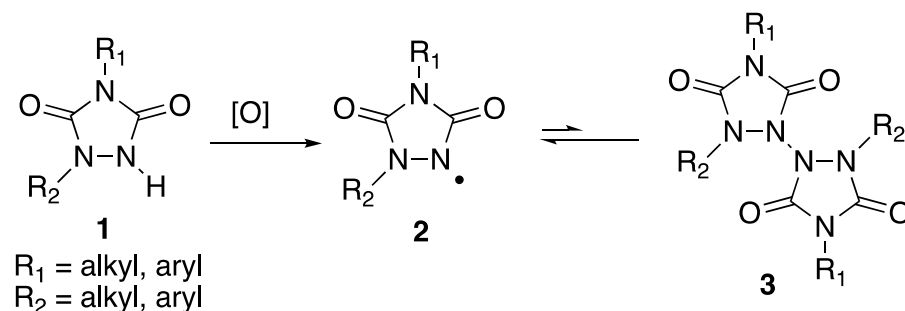
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Abstract: Appropriately substituted N-centered urazoly radicals are capable of generating interesting cage-like structures upon forming N-N bonds. The radicals are generated by the oxidation of the corresponding NH urazole precursors. We synthesized a triurazole precursor that we hoped would dimerize through the formation of three N-N bonds to afford a large molecular cage. Unfortunately, the attempts at the oxidation of the urazoles to form urazoly radicals instead only lead to random oligomerization, forming plastic-like materials rather than the desired cages.

Keywords: urazole; radicals; molecular cages

1. Introduction

1-Substituted urazole radicals are a class of deeply colored persistent nitrogen-centered radicals, **2**, that exist in equilibrium with the N-N dimers, **3**, in solution [1,2]. The urazoly radicals are generated from the oxidation of precursor N-H urazoles, **1**, via various oxidants, including *tert*-butyl hypochlorite and Ni₂O₃ (Scheme 1) [1–3]. With simple alkyl or aryl substituents at the N1 and N4 positions of the urazole ring, the radical form seen in **2** remains heavily populated in the solution [1–3]. We have reported that for 1-aryl urazoly radicals in which there is present a bis-ortho substitution relative to the urazole radical ring (i.e., **4**) that the N-N dimer form seen in **5** predominates instead (Scheme 2) [3,4]. By leveraging this behavior, we were able to synthesize the cage compound shown by **7** via the dimerization of the triurazoly radical seen in **6** via the formation of three N-N bonds (Scheme 3) [4]. In an attempt to form even larger cage structures in an analogous manner, we were interested in the synthesis and oxidation of a triurazole compound, as shown in **8** (Figure 1). Herein we report our synthesis, the characterization of this compound, and its attempted oxidation.



Scheme 1. Oxidation of urazoles, **1**, to form N-centered urazoly radicals, **2**, that exist in equilibrium with N-N dimers, **3**, in solution.



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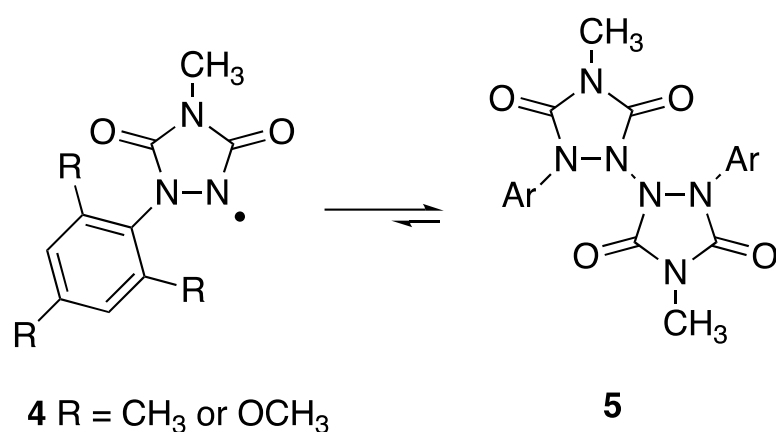
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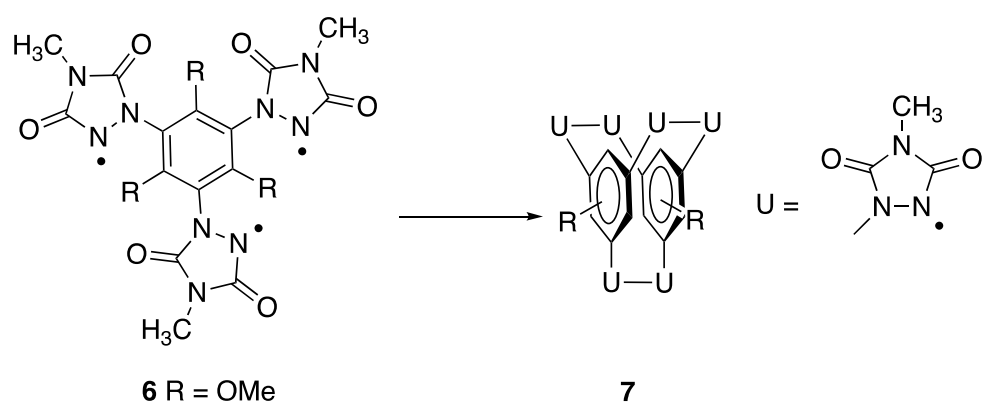
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Scheme 2. Bis-ortho-substituted 1-aryl urazoly radicals, **4**, exist predominantly in the N-N dimer form, **5**, in solution.



Scheme 3. Formation of cage compound shown in **7** via the formation of three N-N bonds from the radical sites of precursor triradical, **6**.

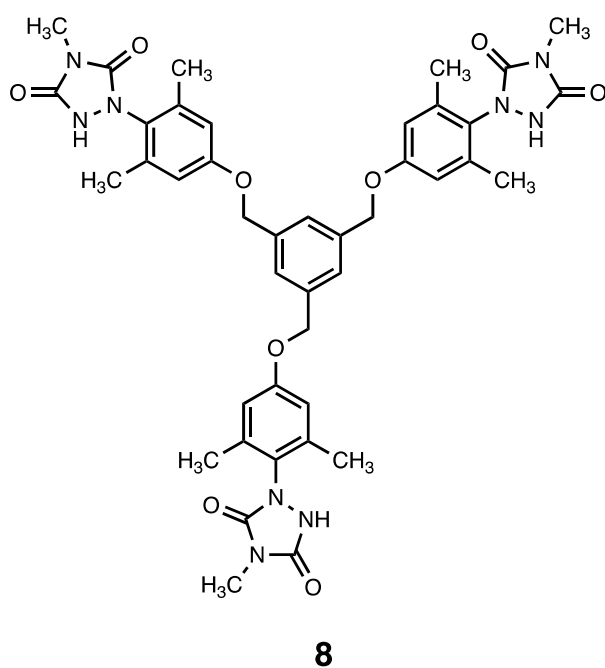
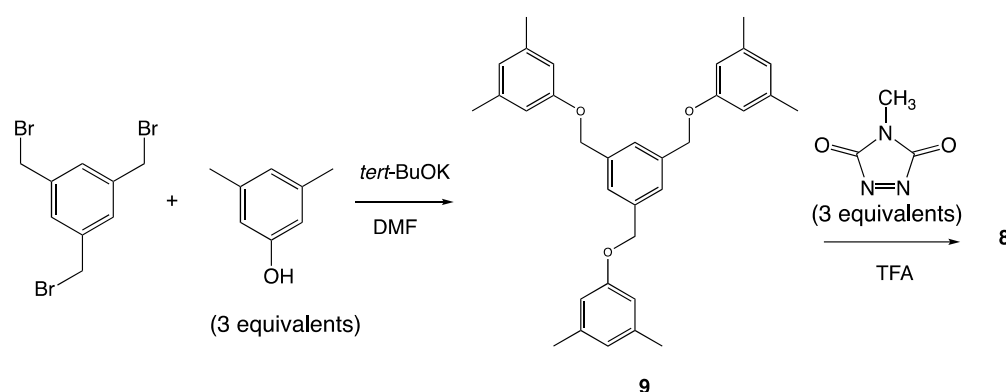


Figure 1. Structure of target triurazole, **8**.

2. Results and Discussion

Scheme 4 outlines the synthetic route utilized for the synthesis of the target molecule, triurazole, as shown in **8**. The treatment of commercially available 1,3,5-tris(bromomethyl)benzene with three equivalents of the 3,5-dimethylphenoxide generated via the deprotonation of the phenol using potassium *tert*-butoxide afforded the known compound tris(phenoxymethyl)benzene, shown in **9**, at a 96% yield [5]. Compound **9** was analyzed using ^1H and ^{13}C NMR, IR, and HRMS analyses. The NMR spectra were deceptively simple for its molecular size due to the symmetry of the structure and, in the ^1H NMR spectrum, the lack of H-H coupling that meant all signals were simple singlets (see the spectra provided in the Supplementary Materials). The treatment of **9** with three equivalents of MeTAD in the presence of trifluoroacetic acid as a catalyst led to the formation of target triurazole **8** at a 98% yield. Compound **8** was characterized using ^1H and ^{13}C NMR, DEPT, IR, and HRMS analyses. As with **9**, the symmetry and lack of H-H coupling rendered the ^1H NMR spectrum as a simple series of singlets but with proper integrations. The *N*-methyl signals of the urazole rings are readily identified as a singlet at 2.99 ppm in the ^1H NMR spectrum (relative integration of 6H), and the carbonyl groups of the ring appear at 153.6 and 152.5 ppm in the ^{13}C NMR spectrum. Triurazole **8** exhibited extremely low solubility in chlorinated solvents (CHCl_3 , CH_2Cl_2) and acetonitrile but was fairly soluble in the highly polar solvents DMSO and DMF.



Scheme 4. Synthesis of triurazole **8**.

The oxidation of urazoles to form the corresponding urazolyl radicals can be effected by using the heterogeneous oxidant Ni_2O_3 in CHCl_3 or CH_2Cl_2 [3,4]. However, attempts at oxidation in these solvents (even in boiling CHCl_3) were unsuccessful, apparently due to the poor solubility of the starting triurazole. Unfortunately, DMSO and DMF, solvents that are better able to dissolve **8**, were incompatible with the oxidizing agent.

The NHs of urazoles are fairly acidic, with pK_a 's close to 5 [6]. Therefore, the reaction of **8** with three equivalents of NaOH in water resulted in the slow dissolution of the starting material due to the deprotonation of the urazole NHs by the hydroxide. The treatment of the resulting trianion with the oxidizing agent $(\text{NH}_4)_2\text{S}_2\text{O}_8$ resulted in the formation of a plastic-like material that separated from the aqueous layer. This material was also not particularly soluble in CDCl_3 , but from the amount that we were able to dissolve, a very complex ^1H NMR spectrum that lacked the NH's of the starting urazole **8** but included very broad signals at the remaining chemical shifts analogous to those of **8** were observed. This observation suggested that instead of forming the desired cage compound via a "dimerization" of two tri-radical units, the tri-radicals prefer to engage in oligomerization via random N-N bond formation to form the observed plastic-like material, as represented in Figure 2.

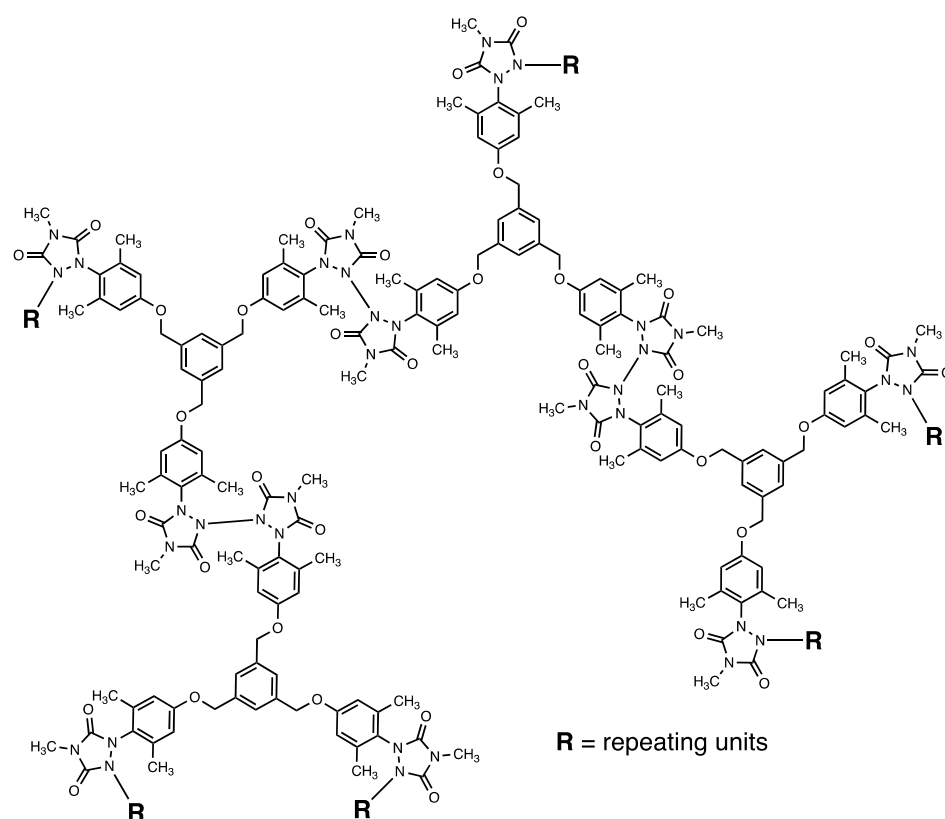


Figure 2. Representation of plastic-like material resulting from random oligomerization of radical sites via N-N bond formation.

3. Materials and Methods

3.1. General Methods

The ^1H and ^{13}C NMR spectra were obtained using a 400 MHz NMR spectrometer. The chemical shifts were reported in units of parts per million downfield from TMS. High-resolution mass spectra (HRMS) were acquired via electron spray ionization on an LTQ-FTMS hybrid mass spectrometer. N-Methyl-1,3,5-triazoline-3,5-dione (MeTAD) was synthesized via the oxidation of N-methylurazole with DABCO- Br_2 , as described in the literature [7,8]. All of the other compounds were commercially available and used as received.

3.2. 1,3,5-Tris[(3,5-dimethylphenoxy)methyl]benzene (9) [5]

To a stirring solution of 2 g (0.016 mole, 4 eq) of 3,5-dimethylphenol in 50 mL dry DMF, 1.8 g (0.016 mole) of potassium tert-butoxide was added as a solid. The tert-butoxide dissolved, and the reaction mixture was stirred at room temperature for 45 min. To the resulting clear pale brown solution, solid 1,3,5-tris(bromomethyl)benzene was added at once. This mixture was stirred for 48 hours and then poured into 100 mL of ether. The organic layer was washed 3×50 mL 1M aq. NaOH, 1×50 mL sat. aq. NaCl, dried over Na_2SO_4 , filtered, and concentrated to afford a white solid. The solid was dissolved in 80 mL of acetone, and 100 mL of methanol was then added while swirling. Crystallization began to take place almost immediately. The mixture was cooled in a freezer for 1 h, and the crystalline product was isolated via vacuum filtration to afford 1.50 g (96% yield) of **9** as colorless crystals, m.p. 129–130 °C. IR (ATR) cm^{-1} 2916, 2862, 1617, 1596, 1325, 1298, 1174, 1160, 1084, 845, 824; ^1H NMR (400 MHz, CDCl_3) δ 7.46 (s, 3H), 6.62 (s, 9H), 5.05 (s, 6H), 2.29 (s, 18H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 158.9, 139.4, 138.2, 126.0, 123.0, 112.7, 69.7, 21.6; HRMS (electron spray ionization) m/z $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{33}\text{H}_{37}\text{O}_3$ 481.2737; Found 481.2745. The NMR data were consistent with the data provided in the literature [5].

3.3. 1-(4-([3,5-bis((3,5-Dimethyl-4-(4-methyl-3,5-dioxo-1,2,4-triazolidin-1-yl)-phenoxy)methyl))phenyl]methoxy)-2,6-dimethylphenyl)-4-methyl-1,2,4-triazolidine-3,5-dione (**8**)

To a stirring solution of 0.5 g of **9** (1.18 mmol) in 20 mL of CH₂Cl₂, 0.4 g (3.54 mmol, 3.1 eq) of MeTAD was added as a solid. To the resulting deep red solution, 0.27 mL (3.1 equiv) of CF₃CO₂H was added via a syringe. After stirring overnight, the resulting pale pink solution was concentrated and subjected to column chromatography (SiO₂, 90:10 ethyl acetate/methanol) to afford 0.904 g (98% yield) of triurazole **9** as a white solid, m.p. 266–268 °C (decomp): IR (ATR) cm^{−1} 1697, 1483, 1164, 857. ¹H NMR (400 MHz, DMSO-d₆) δ 10.8 (s, 3H), 7.51 (s, 3H), 6.87 (s, 6H), 5.16 (s, 6H), 2.99 (s, 9H), 2.13 (s, 18H); ¹³C{¹H} NMR (100 MHz, DMSO-d₆) 158.7, 153.6, 151.5, 139.7, 137.5, 126.4, 125.8, 114.4, 69.1, 24.9, 17.6; HRMS (electron spray ionization) m/z [M+H]⁺ Calcd for C₄₂H₄₆N₉O₉ 820.3413; Found 820.3390.

Supplementary Materials: The following supporting information can be downloaded: For compound **8**: ¹H NMR spectrum, ¹³C NMR spectrum, DEPT spectrum, IR spectrum, HRMS spectra. For compound **9**: ¹H NMR spectrum, ¹³C NMR spectrum, IR spectrum, HRMS spectra.

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Data Availability Statement: Copies of spectral data for novel compounds **8** and **9** are available in the Supplementary Materials.

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Conflicts of Interest: The authors declare no conflict of interest.

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