Russian Journal of Organic Chemistry, Vol. 40, No. 9, 2004, pp. 1318–1321. Translated from Zhurnal Organicheskoi Khimii, Vol. 40, No. 9, 2004, pp. 1366–1368.

Tetrazoles: XLVII.* A Route to Tetrazole-Containing Dendrimers

T. V. Artamonova, M. V. Zatsepina, and G. I. Koldobskii

St. Petersburg State Institute of Technology, Moskovskii pr. 26, St. Petersburg, 190013 Russia
e-mail: koldobsk@tu.spb.ru

Received February 12, 2004

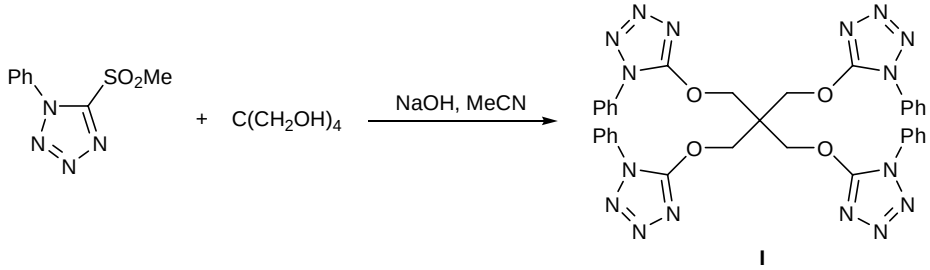
Abstract—The reaction of 5-methylsulfonyl-1-phenyltetrazole with pentaerythritol in acetonitrile in the presence of sodium hydroxide gave tetrakis(1-phenyltetrazol-5-yloxymethyl)methane. Sulfur-containing analog of the latter was obtained by alkylation of 1-phenyl-4,5-dihydrotetrazole-5-thione with 1,3-dibromo-2,2-bis(bromomethyl)propane. Nitration of the resulting polytetrazoles afforded the corresponding tetrakis(*p*-nitrophenyl) derivatives which can be used in the synthesis of tetrazole-containing dendrimers according to the divergent scheme.

Obviously increasing interest in dendrimers originates from the possibility of their use as new polymeric materials, highly efficient catalysts, and medicines [2–4]. Important factors stimulating development of the chemistry of dendrimers are beauty and structural complexity of these compounds. The number of various dendrimers continuously grows. Numerous nitrogen-, silicon-, and sulfur-containing dendrimers and those incorporating aromatic and heterocyclic fragments have been reported. However, no published data on tetrazole-containing dendrimers are available, though there are grounds to believe [5] that such compounds may be useful for the development of membranes for ultrafiltration, new sorbents, and medicines with a broad spectrum of activity.

Two possible ways of building up dendrimer structures are known. Among these, we selected an approach which is referred to as the divergent scheme. It implies stepwise synthesis of the central part (framework) of a dendrimer, followed by successive addition of new structural fragments. In terms of the selected scheme, we developed procedures for the preparation of previously unknown heterocyclic systems including more than two tetrazole rings. The resulting structures can be used as frameworks in the synthesis of tetrazole-containing dendrimers.

Heterocyclic systems including more than two tetrazole rings can be obtained by several methods some of which were widely used in the recent years. Examples are 1,3-dipolar cycloaddition of hydrazoic acid salts to polynitriles [6–8] and reaction of 1-aryl-5-methylsulfonyltetrazoles with polyfunctional O-nucleophiles [9–11]. The latter procedure was applied in the present work. By reaction of 5-methylsulfonyl-1-phenyltetrazole with pentaerythritol in acetonitrile in the presence of sodium hydroxide at 18–20°C we obtained 84% of tetrakis(1-phenyltetrazol-5-yloxymethyl)methane (**I**) (Scheme 1). Sulfur-containing

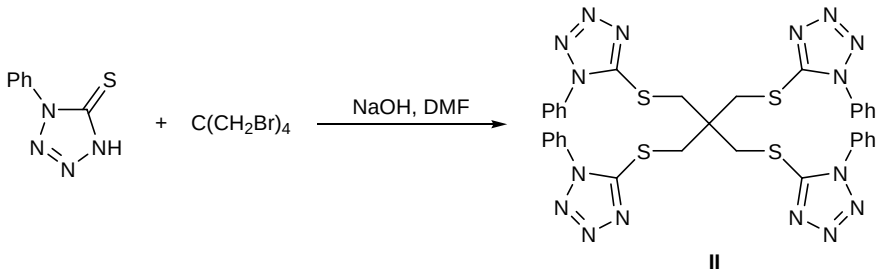
Scheme 1.



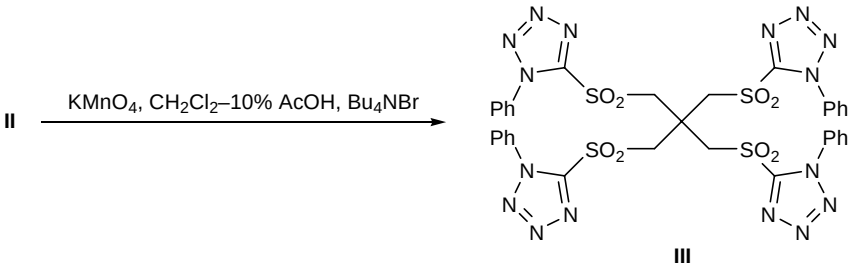
I

* For communication XLVI, see [1].

Scheme 2.



Scheme 3.

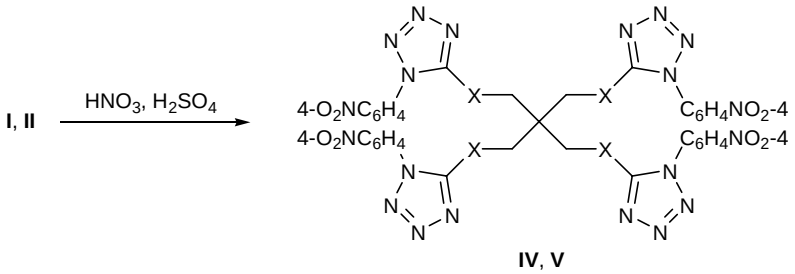


analog of **I**, which can also be used as framework for the synthesis of tetrazole-containing dendrimers, was prepared by alkylation of 1-phenyl-4,5-dihydrotetrazole-5-thione with 1,3-dibromo-2,2-bis(bromomethyl)propane in DMF at 110°C (Scheme 2). It should be noted that our numerous attempts to perform this reaction under milder conditions using such solvents as alcohol and acetonitrile, as well as in the two-phase system chloroform–aqueous sodium hydroxide in the presence of tetrabutylammonium bromide, were unsuccessful. Obviously, the reason is the specific steric structure of the alkylating agent. This is consistent with the available data on the alkylation of 1-phenyl-4,5-dihydrotetrazole-5-thione with sterically unhindered reagents [9, 12].

Like other 1-aryl-5-alkylsulfanyltetrazoles [9, 12], tetrazole **II** was smoothly oxidized with potassium permanganate under conditions of phase-transfer catalysis. The oxidation product was tetrasulfone **III** which was isolated in 51% yield (Scheme 3).

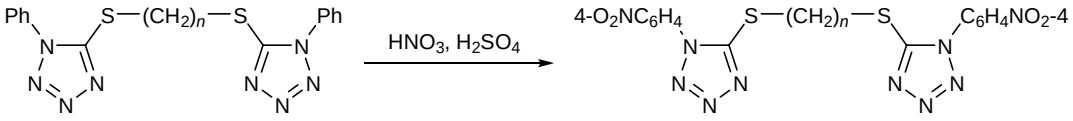
The next step toward tetrazole-containing dendrimers according to the divergent scheme was nitration of tetrazoles **I** and **II**. Treatment of these compounds with a mixture of sulfuric and nitric acids gave the corresponding tetranitro derivatives **IV** and **V** (Scheme 4). As follows from the NMR spectra, the nitration occurs at the *para* position of the phenyl substituent. Nucleophilic replacement of the nitro group in tetrazoles **IV** and **V** by the action of various alkoxide ions can be regarded as the most evident route to tetrazole-containing dendrimers in terms of the divergent scheme. It should be noted that nitrotetrazoles **VI** and **VII** obtained by nitration of the corresponding ditetrazoles (Scheme 5) can be used as dendrons for building up dendrimers according to the convergent scheme.

Scheme 4.



IV, X = O; **V**, X = S.

Scheme 5.



VI, **VII**

VI, $n = 1$; **VII**, $n = 2$.

EXPERIMENTAL

The IR spectra were recorded in KBr on a UR-20 spectrometer. The NMR spectra were obtained on a Bruker AC-200 spectrometer from solutions in DMSO-d_6.

Bis(1-phenyltetrazol-5-ylsulfanyl)methane and 1,2-bis(1-phenyltetrazol-5-ylsulfanyl)ethane were synthesized by the procedure reported in [9].

Tetrakis(1-phenyltetrazol-5-yloxymethyl)-methane (I). A mixture of 4 mmol of 5-methylsulfonyl-1-phenyltetrazole, 1 mmol of pentaerythritol, 4 mmol of NaOH, and 10 ml of acetonitrile was stirred for 5 h at 20°C. The mixture was diluted with 50 ml of water, and the precipitate was filtered off, washed with 20 ml of water, and dried in air. Yield 0.8 g (84%), mp 199°C (from aqueous DMF, 1:1). IR spectrum, ν, cm^{-1}: 900, 960, 1019, 1050, 1070, 1100, 1130, 1294, 1360, 1389, 1457, 1505, 1560, 1596, 2370, 2380, 2900, 2980, 3100. ^{1}H NMR spectrum, δ, ppm: 5.20 s (8H, CH_2), 7.50–7.70 m (20H, H_{arom}). Found, %: C 55.72; H 4.11; N 31.63. $C_{33}H_{28}N_{16}O_4$. Calculated, %: C 55.62; H 3.94; N 31.46.

Tetrakis(1-phenyltetrazol-5-ylsulfanylmethyl)-methane (II). A mixture of 3 mmol of 1-phenyl-4,5-dihydrotetrazole-5-thione, 0.7 mmol of 1,3-dibromo-2,2-bis(bromomethyl)propane, 3 mmol of NaOH, and 5 ml of DMF was stirred for 5 h at 110°C. The mixture was cooled to 18°C, 50 ml of a 5% aqueous solution of sodium hydroxide was added, and the precipitate was filtered off, washed with 20 ml of water, and dried in air. Yield 0.35 g (66%), mp 158°C (from 2-propanol). IR spectrum, ν, cm^{-1}: 900, 990, 1014, 1050, 1080, 1089, 1180, 1190, 1240, 1279, 1387, 1420, 1458, 1498, 1595, 2350, 2360, 2970, 3000, 3100. ^{1}H NMR spectrum, δ, ppm: 4.00 s (8H, CH_2), 7.70 s (20H, H_{arom}). Found, %: C 51.04; H 3.61; N 28.77. $C_{33}H_{28}N_{16}S_4$. Calculated, %: C 51.03; H 3.61; N 28.86.

Tetrakis(1-phenyltetrazol-5-ylsulfonylmethyl)-methane (III). Potassium permanganate, 6 mmol, was added to a mixture of 1.3 mmol of compound **II**, 0.13 mmol of tetrabutylammonium bromide, 1 ml of acetic acid, 5 ml of methylene chloride, and 5 ml of water. The mixture was stirred for 20 h at 35°C, 5 ml of ethanol was added, the precipitate of manganese dioxide was filtered off and washed with 10 ml of methylene chloride, and the organic phase was separated, washed with 10 ml of water, dried over magnesium sulfate, and evaporated under reduced pressure. Yield 0.54 g (51%), mp 169–171°C (from methanol). IR spectrum, ν, cm^{-1}: 920, 1020, 1080, 1160, 1250, 1350, 1400, 1470, 1510, 1600, 2940, 3080. ^{1}H NMR spectrum, δ, ppm: 4.20 s (8H, CH_2), 7.70 s (20H, H_{arom}). Found, %: C 43.79; H 2.96; N 24.63. $C_{33}H_{28}N_{16}O_8S_4$. Calculated, %: C 43.81; H 3.01; N 24.78.

Tetrakis[1-(4-nitrophenyl)tetrazol-5-yloxy-methyl]methane (IV). Compound **II**, 0.66 mmol, was dissolved in 3 ml of 94% sulfuric acid, the solution was cooled to 5°C, and 1.8 ml of 98% nitric acid was added dropwise with stirring. The mixture was stirred for 30 min at 5°C and for 1 h at 18–20°C and was poured onto 50 g of finely crushed ice. The precipitate was filtered off, washed with 20 ml of water, and dried in air. Yield 0.8 g (70%), mp 245–246°C (from DMSO). IR spectrum, ν, cm^{-1}: 920, 1012, 1040, 1059, 1112, 1189, 1308, 1354, 1420, 1468, 1504, 1529, 1567, 1614, 2361, 3140, 3150. ^{1}H NMR spectrum, δ, ppm: 5.10 s (8H, CH_2), 7.90 d (8H, H_{arom}), 8.30 d (8H, H_{arom}). Found, %: C 44.30; H 2.83; N 31.37. $C_{33}H_{24}N_{20}O_{12}$. Calculated, %: C 44.39; H 2.69; N 31.39.

Tetrazoles **V**–**VII** were synthesized in a similar way.

Tetrakis[1-(4-nitrophenyl)tetrazol-5-ylsulfanyl-methyl]methane (V). Yield 72%, mp 154–155°C (from acetonitrile). IR spectrum, ν, cm^{-1}: 980, 1006, 1028, 1055, 1080, 1114, 1176, 1215, 1244, 1279, 1313, 1344, 1385, 1398, 1433, 1494, 1533, 1595, 1610, 3080. ^{1}H NMR spectrum, δ, ppm: 3.90 s (8H, CH_2), 8.00 d (8H, H_{arom}), 8.50 d (8H, H_{arom}). Found, %: C 41.39; H 2.79; N 29.37. $C_{33}H_{24}N_{20}O_8S_4$. Calculated, %: C 41.42; H 2.51; N 29.29.

Bis[1-(4-nitrophenyl)tetrazol-5-ylsulfanyl]-methane (VI). Yield 74%, mp 195–198°C (from

acetonitrile). IR spectrum, ν, cm^{-1}: 990, 1020, 1040, 1090, 1180, 1230, 1260, 1280, 1350, 1390, 1440, 1500, 1540, 1600, 1620, 1680, 2870, 2940, 2970, 3030, 3100, 3130. ^1H NMR spectrum, δ, ppm: 5.31 s (2H, CH_2), 7.90 d (4H, H_{arom}), 8.50 d (4H, H_{arom}). Found, %: C 39.41; H 2.25; N 39.30. $C_{15}H_{10}N_{10}O_4S_2$. Calculated, %: C 39.30; H 2.18; N 30.52.

1,2-Bis[1-(4-nitrophenyl)tetrazol-5-ylsulfanyl]-ethane (VII). Yield 97%, mp 189–190°C (from DMF). IR spectrum, ν, cm^{-1}: 990, 1020, 1040, 1070, 1090, 1120, 1150, 1200, 1250, 1290, 1350, 1390, 1410, 1440, 1500, 1540, 1600, 1620, 2880, 2940, 2970, 3020, 3100, 3140. ^1H NMR spectrum, δ, ppm: 3.82 s (4H, CH_2), 7.90 d (4H, H_{arom}), 8.50 d (4H, H_{arom}). Found, %: C 40.56; H 2.31; N 29.51. $C_{16}H_{12}N_{10}O_4S_2$. Calculated, %: C 40.68; H 2.54; N 29.66.

REFERENCES

1. Myznikov, L.V., Artamonova, T.V., Koldobskii, G.I., and Hrabalek, A., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 551.
2. Beletskaya, I.P. and Chuchuryukin, A.V., *Usp. Khim.*, 2000, vol. 69, p. 699.
3. Newkome, G.R., Moorefield, C.N., and Vogtle, F., *Dendrimers and Dendrons: Concepts, Synthesis, Application*, Weinheim: Wiley, 2001.
4. Moorefield, C.N. and Newkome, G.R., *C.R. Acad. Sci.*, 2003, vol. 6, p. 715.
5. Kizhnyaev, V.N. and Vereshchagin, L.I., *Usp. Khim.* 2003, vol. 72, p. 159.
6. Zubarev, V.Yu., Gurskaya, G.V., Zavodnik, V.E., and Ostrovskii, V.A., *Khim. Geterotsikl. Soedin.*, 1997, p. 1494.
7. Zubarev, V.Yu. and Ostrovskii, V.A., *Khim. Geterotsikl. Soedin.*, 2000, p. 867.
8. Zubarev, V.Yu., Bezklubnaya, E.V., Pyartman, A.K., Trifonov, R.E., and Ostrovskii, V.A., *Khim. Geterotsikl. Soedin.*, 2003, p. 1496.
9. Gol'tsberg, M.A. and Koldobskii, G.I., *Russ. J. Org. Chem.*, 1996, vol. 32, p. 1194.
10. Gol'tsberg, M.A. and Koldobskii, G.I., *Khim. Geterotsikl. Soedin.*, 1996, p. 1515.
11. Kharbash, R.V., Gol'tsberg, M.A., Artamonova, T.V., Nordlander, E., and Koldobskii, G.I., *Russ. J. Org. Chem.*, 2002, vol. 38, p. 1356.
12. Koldobskii, G.I., Hrabalek, A., and Esikov, K.A., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 447.