

Dendro-shaped blocks with arylsulfanyl fragments based on *p*-toluic acid

Victoria N. Berezhnaya,^{a,b} Alexander M. Maksimov,^{*a}
Vyacheslav E. Platonov^a and Vladimir V. Shelkovnikov^{a,c}

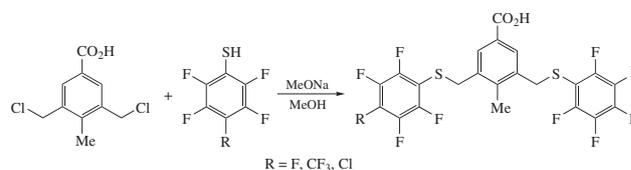
^a N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation. E-mail: maksimov@nioch.nsc.ru

^b Novosibirsk State University, 630090 Novosibirsk, Russian Federation

^c Novosibirsk State Technical University, 630073 Novosibirsk, Russian Federation

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Chloromethylation of *p*-toluic acid affords 3,5-bis(chloromethyl)-4-methylbenzoic acid whose subsequent treatment with arenethiols brings about spacer dendrimeric blocks containing polyfluoroarylsulfanyl fragments in a total yield of 60–75%.



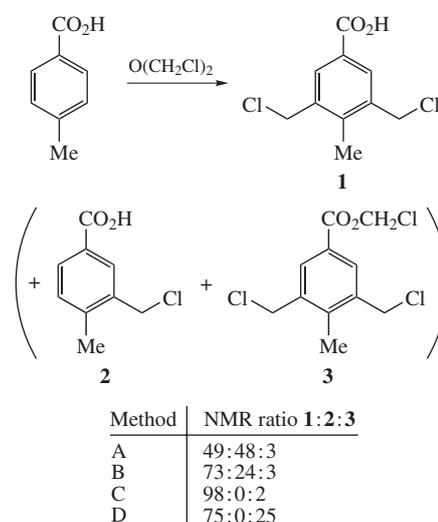
Spacer blocks of the dendron structure with aromatic rings, *e.g.*, benzoyloxy and polyfluorobenzoyloxy fragments, serve as a separator of chromophores and decrease their intermolecular aggregation in the materials possessing nonlinear optical (NLO) properties.^{1,2} Special attention is paid to dendrons containing polyfluorinated aromatic rings, which are used in electro-optical materials as functional blocks separating nonlinear optical chromophores to increase the NLO coefficient.^{3–5} The oxygen-containing polyfluorinated dendrons based on pentafluorobenzoyloxy fragments were described as electro-optical materials.⁶ Compounds containing tetrafluorophenylene(bis)phenoxy fragments were used for the synthesis of polymers with high thermal stability and good optical characteristics.⁷ The positive factor for NLO compounds is the enhanced polarizability of the molecule as a whole. Atomic refraction and, consequently, the polarizability of the sulfur atom or the C–S bond are greater than those for the oxygen atom or the C–O bond.⁸ Therefore, one can expect that the introduction of a sulfur atom instead of an oxygen one into the dendro-shaped separating fragment of a NLO chromophore will increase its polarizability. In this connection, the synthesis of dendrons containing, for example, aryl- and polyfluoroarylsulfanyl structural fragments is an actual task. Dendritic structures of palladium catalysts incorporating phenylsulfanyl fragments are known.^{9,10} However, no description has been found for the synthesis of the corresponding sulfur-containing polyfluoroaryl dendrons.

In this work, to create the nucleus of the dendrone, the following functional moieties seemed necessary: group (*e.g.*, carboxyl one) that assures the attachment of the spacer block to the NLO chromophore molecule, as well as groups suitable for obtaining the branches of the dendrone and located in a *meta*-orientation relative to each other and to the group joining the chromophore. For the starting core of the spacer block, a toluic acid derivative bearing two 3,5-positioned chloromethyl groups is generally selected.

Since arenethiols are strong nucleophiles, it seems expedient to introduce functional substituents into a dendrimer, which are capable of reacting with nucleophiles. For this purpose, active chloromethyl group of benzylic type was that of choice. In the

thus obtained aryl benzyl sulfides, the CH₂ group interrupts the conjugation between their aromatic moieties. We used the chloromethylation reaction¹¹ to synthesize the nucleus of the dendron. The introduction of two chloromethyl groups into the benzene ring requires relatively harsh reaction conditions, and the presence of a donor substituent (*e.g.*, methyl group) in the aromatic ring is necessary to facilitate the process.

It is known¹² that chloromethylation of *p*-toluic acid gives 3,5-bis(chloromethyl) derivative **1**. In our hands, chloromethylation of *p*-toluic acid with bis(chloromethyl) ether in commercially available 93% H₂SO₄ at 5–10 °C led to the mixture containing, according to the NMR data, acid **1** and 3-(chloromethyl)-4-methylbenzoic acid¹³ **2** in an equal ratio and small amount (~3%) of chloromethyl ester **3** (Scheme 1, method A). Raising the concentration of H₂SO₄ to 100% (12–15 °C) increased the yield of acid **1** and decreased the yield of the 3-monochloromethyl derivative **2** (method B). When the reaction was carried out in



Scheme 1 Reagents and conditions: method A: 93% H₂SO₄, 12–15 °C; method B: 100% H₂SO₄, 12–15 °C; method C: 100% H₂SO₄, 30 °C; method D: 30% oleum, 12–15 °C.

30% oleum, a mixture of acid **1** and its chloromethyl ester **3** in a ratio of ~3:1 was formed (method D). Chloromethylation of *p*-toluic acid with 100% H₂SO₄ at ~30 °C proceeded fully to afford the target acid **1** with ~2% of chloromethyl ester **3** (method C). The obtained product has a melting point of 170–180 °C and also contains 5–10% of by-products, probably formaldehyde oligomers.¹¹ For the further purification it was treated with water at room temperature and sublimated, which provided pure acid **1** in 87% yield. Ester **3** was hydrolyzed 93% H₂SO₄ to the desired acid **1**.

Reactions of compound **1** with substituted arenethiols resulted in 3,5-bis(arylsulfanylmethyl) derivatives being the target dendron compounds **4a–f** (Scheme 2). For this transformation, various conditions were tested. Reaction in dioxane at room temperature in the presence of K₂CO₃, took 7–9 days, while carrying out this process at 85–90 °C took 7–11 h. The processing in methanol in the presence of sodium methoxide at room temperature requires 2 h, followed by keeping the mass overnight, the yields of the target products being 84–95%.[†]

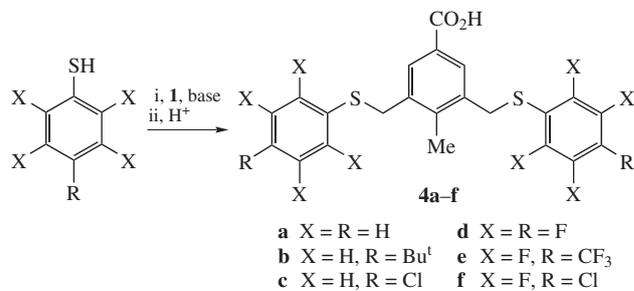
[†] Reactions of 3,5-bis(chloromethyl)-4-methylbenzoic acid **1** with arenethiols.

Procedures A and B: A solution of the corresponding arenethiol (4.2 mmol) in dioxane (5 ml) was immediately added to a suspension of dichloro acid **1** (2 mmol) and anhydrous K₂CO₃ (8 mmol) in dioxane (5 ml) with stirring. The mixture was stirred at room temperature for 7–9 days (Procedure A) or at 85–90 °C for 7–11 h (Procedure B) until the initial acid disappeared (¹H NMR monitoring). To isolate the product, the reaction mass was poured into water (250 ml), acidified with 5% hydrochloric acid and filtered. The precipitate formed was washed with water to pH 6 and dried at 50 °C. The yield of product **4** was close to quantitative.

Procedure C: A solution of MeONa in MeOH (1 equiv.) was added to a solution of 3,5-bis(chloromethyl)-4-methylbenzoic acid **1** (1 equiv.) in MeOH. Separately, solution of MeONa in MeOH (2 equiv.) was added to a solution of arenethiol (2 equiv.) in methanol. The second solution was added dropwise with stirring to the first solution of Na salt of acid **1** at room temperature. Then the reaction mixture was stirred for more 2 h and left overnight. An aliquot was sampled, acidified and analyzed by GC-MS which indicated that the reaction mixture contained the target dendron **4** in an amount of 96 to 98% and all the reactants were consumed. The solvent was removed, the residue was treated with stirring with 5% H₂SO₄ and hexane. The resulting slurry was filtered, the solid was washed with water until neutral and dried at 110–120 °C to constant weight. Practically pure dendrons **4** were thus obtained.

4-Methyl-3,5-bis(phenylsulfanylmethyl)benzoic acid 4a. Yield 98% (procedure A), 97% (procedure B), 93% (procedure C). Mp 165 °C (decomp.). IR (C₆H₆, ν/cm⁻¹): 3425, 3054, 2924, 2856, 2705, 2600, 2540, 1689, 1608, 1579, 1479, 1421, 1311, 1248, 1088, 943, 917, 758, 737, 690, 574, 471. ¹H NMR (400 MHz, CDCl₃) δ: 2.45 (s, 3H, Me), 4.14 (s, 4H, SCH₂), 7.18–7.35 (m, 10H, SPh), 7.72 (s, 2H, H-2,6). ¹³C NMR (75 MHz, DMSO-*d*₆) δ: 14.8, 35.9, 126.3, 127.9, 129.0, 129.2, 129.9, 135.7, 136.3, 141.2, 166.9. MS (EI), *m/z*: 380.0905 [M]⁺ (calc. for C₂₂H₂₀O₂S₂, *m/z*: 380.0099). Found (%): C, 69.86; H, 5.19; S, 16.52. Calc. for C₂₂H₂₀O₂S₂ (%): C, 69.47; H, 5.15; S, 16.84.

For characteristics of compounds **4b–f**, see Online Supplementary Materials.



Scheme 2

In summary, new spacer dendritic blocks for NLO dyes containing arylsulfanyl structural fragments including polyfluorinated ones, were obtained.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2018.07.035.

References

- H. Ma, S. Liu, J. Luo, S. Suresh, L. Liu, S. H. Kang, M. Haller, T. Sassa, L. R. Dalton and A. K.-Y. Jen, *Adv. Funct. Mater.*, 2002, **12**, 565.
- S. H. Kang, J. Luo, H. Ma, R. R. Barto, C. W. Frank, L. R. Dalton and A. K.-Y. Jen, *Macromolecules*, 2003, **36**, 4355.
- W. Wu, Q. Huang, G. Qui, C. Ye, J. Qin and Z. Li, *J. Mater. Chem.*, 2012, **22**, 18486.
- S. R. Hammond, J. Sinness, S. Dubbury, K. A. Firestone, J. B. Benedict, Z. Wawrzak, O. Clot, P. J. Reid and L. R. Dalton, *J. Mater. Chem.*, 2012, **22**, 6752.
- M. Faccini, M. Balakrishnan, M. B. J. Diemeer, Z.-P. Hu, K. Clays, I. Asselberghs, A. Leinse, A. Driessen, D. N. Reinhoudt and W. Verboom, *J. Mater. Chem.*, 2008, **18**, 2141.
- J. Luo, M. Haller, H. Ma, S. Liu, T.-D. Kim, Y. Tian, B. Chen, S.-H. Jang, L. R. Dalton and A. K.-Y. Jen, *J. Phys. Chem. B*, 2004, **108**, 8523.
- I. M. Tkachenko, O. G. Purikova, O. V. Shekera and V. V. Shevchenko, *Mendeleev Commun.*, 2016, **26**, 77.
- B. V. Ioffe, *Refraktometricheskie Metody v Khimii (Refractometric Methods in Chemistry)*, Khimia, Leningrad, 1974 (in Russian).
- M. D. Meijer, B. Mulder, G. P. M. van Klink and G. van Koten, *Inorg. Chim. Acta*, 2003, **352**, 247.
- N. J. M. Pijnenburg, M. Lutz, M. A. Siegler, A. Spek, G. van Koten and R. J. M. Klein Gebbink, *New J. Chem.*, 2011, **35**, 2356.
- L. I. Belen'kii, Yu. B. Vol'kenshtein and I. B. Karmanova, *Russ. Chem. Rev.*, 1977, **46**, 891 (*Usp. Khim.*, 1977, **46**, 1698).
- M. M. Dashevskii and Yu. F. Bartkovskaya, *Zh. Prikl. Khim.*, 1972, **45**, 1087 (in Russian).
- M. M. Dashevskii and Yu. F. Bartkovskaya, *Zh. Prikl. Khim.*, 1968, **41**, 2794 (in Russian).

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