Asian Journal of Chemistry Vol. 19, No. 3 (2007), 1783-1788

New Dendrimers with Multi Arm 1,2,3-Thiadiazoles as a Nucleus

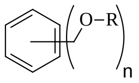
MOUSA AL-SMADI
Department of Chemistry, Jordan University of Science and Technology
P.O.Box 3030, Irbid 22110, Jordan
E-mail: mariam10@just.edu.jo

New dendrimers **1c-4c** with multi-arm 1,2,3-thiadiazole systems **1a-4a** have been prepared and characterized. Alkaline cleavage of **1a-4a** led to the corresponding alkynethiolate **1b-4b**, which were trapped by electrophiles such as Fréchet's[G-3]-Br to furnish the third-generation dendrimers. The advantage of the use of **1a-4a** as nucleophilic core reagents lies in the linear alkyne groups that emanate from the benzene nucleus, thus allowing the construction of high molecular weight dendrimers.

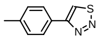
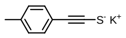
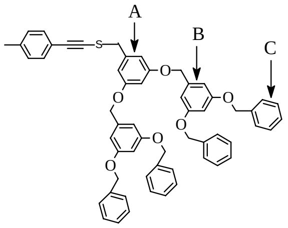
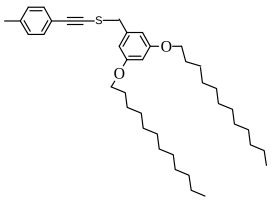
Key Words: Alkynethiolale, 1,2,3-thiadiazoles, Dendrimers.

INTRODUCTION

Dendrimers are considered to be a class between low molecular weight compounds and polymers and therefore they show a series of distinguished properties[1-6]. They consist of a central polyfunctional core from which arise successive branched layers, called generations. Each subsequent generation brings about a doubling of these end groups and a change of conformation until the dendrimer adopts a spherical shape. At this stage, the interior zone and the exterior surface region allow for unusual physical and chemical properties (endo- and exo-receptors). The volume inside this dendrimer is shielded from relatively large molecules while still remaining accessible to small ones (host-guest recognition). The chains ends at the outer surface, on the other hand, can be functionalized and used in many applications[7-9]. This globular shape of large dendrimers contrasts sharply with the heavily entangled structure of conventional high polymers and their accurate control of molecular architecture suggests many potential applications, such as synthetic models for biological structures (enzymes, globular proteins), selective catalysts and template reagents, biosensors, drug carriers and transporters, genetransfer vehicles, unimolecular micelles and reverse micelles, synthetic membranes, molecular electronic devices, *etc*. For example, dendrimer **3c** (**Scheme-I**) illustrates a third generation dendrimer with a core multiplicity $N_c = 4$, a branch multiplicity $N_b = 2$ and having a peripheral number of terminal groups Z = 32. In most reported cases, the reactive functions at the core template were amine, hydroxyl or activated carboxyl. The structure and properties of dendrimers can be altered by changing the anchoring core multiplicity N_c, the degree of branching N_b, the length of the branch segments and the surface groups. As stated by Tomalia[1], the selection of the reactive core is of great importance since it determines the size, shape, multiplicity and specific functions of the dendrimer. In this work, new multifunctional core reagents for dendrimers synthesis have been described.



1a-1c (n = 2) 1,4-
2a-2c (n = 3) 1,3,5-
3a-3c (n = 4) 1,2,4,5-
4a-4d (n = 6) 1,2,3,4,5,6-

		Yield[%]			
1-4	R	1	2	3	4
a					
b		>77	>66	>69	>71
c		48	43	36	24
& **4d**			71		

Scheme-I

Multiple [(1,2,3-thiadiazol-4-yl)phenoxymethyl]benzene derivatives **1a-4a**[10] are stable compounds that decompose above 180ºC. They are insoluble in most common solvents, but lose nitrogen at 0ºC when a suspension of them in THF, CH_3CN, DMF or DMSO is treated with a strong base (*t*-BuOK or NaH) to give the soluble thiolate intermediates in high yield. These intermediates can be used as a suitable core template for the synthesis of dendrimers following the divergent or convergent strategies[2]. Dendrones [G-3]-Br of the Fréchet-type[5] were coupled with the thiolate intermediates at room temperature to produce the third-generation dendrimers.

The advantage of the thiolate over other nucleophilic core reagents lies in the linear alkyne groups that emanate from the benzene nucleus, thus allowing the construction of high molecular weight dendrimers before the critical dense-packet stage, predicted by de Gennes[11], is reached.

EXPERIMENTAL

Diethyl ether, tetrahydrofuran (THF) and petroleum ether were dried by refluxing over sodium/benzophenone. Acetone, dichloromethane and chloroform were dried over P_2O_5. All the solvents were distilled just prior to use. The following chemicals were used as received. Potassium *t*-butoxide, potassium iodide, magnesium sulfate and aliquate 336 (Fluka), potassium carbonate (Acros). The starting compounds **1a-4a**[10,12] and 3,5-*bis*-dodecyloxybenzylbromide[13,14] were prepared according to procedures described in the literature.

IR spectra: Nicolet-Impact 410 FT-IR spectrometer; in cm^{-1}. ^1H, ^{13}C NMR spectra: Bruker AC 200 or AM 400 spectrometers; in ppm. MS: Finnigan MAT 95 (FD and FAB). Elemental analysis: Microanalytical laboratory of the Institute of Organic Chemistry of the University of Mainz, Germany. M.p. : Thomas Hoover Capillary melting point apparatus and are uncorrected.

General procedure for the preparation of the dendrimers 1c-4c: (500 mg, 0.41 mmol) of the corresponding 1,2,3-thiadiazoles **1a-4a** was suspended under nitrogen in dry THF (70 mL) and treated dropwise at -20ºC with equivalent amount of potassium *tert*-butoxide dissolved in THF (70 mL). After stirring the mixture for 6 h at this temperature, a solution of Fréchet[G-3]-Br dendrones in dry THF (70 mL) was added dropwise and stirring was continued overnight. The reaction mixture was then diluted with water (100 mL) and extracted with chloroform (3 × 150 mL). The combined extracts were washed with water (300 mL), dried with $MgSO_4$ and the solvent was evaporated. The crude product was chromatographed on a column of silica gel (60 × 2 cm) with chloroform as the eluent to afford the dendrimers **1c-4c** in good yields.

Dendrimer 1c: m.p. 167ºC. IR (KBr, cm^{-1}, ν_{max}) 2961, 2253,1575, 1473, 1430, 1235, 1120, 1008, 833. HRMS-FAB (m/z): $[M + H]^+$ calcd. for $C_{120}H_{102}O_{14}S_2$, 1832.27; found, 1832.32. Anal. Calcd. for $C_{120}H_{102}O_{14}S_2$: C

78.66, H 5.61, S 3.50. Found: C 78.70, H 5.59, S 3.89.

Dendrimer 2c: m.p. 186ºC. IR (KBr, cm^{-1}, ν_{max}) 3040, 2915, 2170,1595, 1560, 1500, 1448, 1365, 1280, 1230, 1170, 1005, 880, 832. HRMS-FAB (m/z): $[M + H]^+$ calcd. for $C_{177}H_{150}O_{21}S_3$, 2707.10; found, 2707.32. Anal. Calcd. for $C_{177}H_{150}O_{21}S_3$: C 78.16, H 5.59, S 3.55. Found: C 78.58, H 5.69, S 3.76.

Dendrimer 3c: m.p. glass. IR (KBr, cm^{-1}, ν_{max}) 3065, 2925, 2188,1587, 1564, 1503, 1445, 1375, 1286, 1231, 1008, 886, 834. HRMS-FAB (m/z): $[M + H]^+$ calcd. for $C_{234}H_{198}O_{28}S_4$, 3586.42; found, 3586.61. Anal. Calcd. for $C_{234}H_{198}O_{28}S_4$: C 78.37, H 5.56, S 3.58. Found: C 78.48, H 5.68, S 3.72.

Dendrimer 4c: m.p. glass. IR (KBr, cm^{-1}, ν_{max}) 3055, 2918, 2208,1577, 1569, 1493, 1455, 1370, 1289, 1227, 1018, 832. HRMS-FAB (m/z): $[M + H]^+$ calcd. for $C_{348}H_{294}O_{42}S_6$, 5361.67; found, 5361.81. Anal. Calcd. for $C_{348}H_{294}O_{42}S_6$: C 77.96, H 9.85, S 3.59. Found: C 78.23, H 9.61, S 3.52.

1,2,3,4,5,6-Hexakis[4-((3,5-didodecyloxy)benzylthioethynyl)-phenoxymethyl]-benzene (4d): Compound **4c** (400 mg, 0.33 mmol) was suspended under nitrogen in dry THF (70 mL) and treated dropwise at -20ºC with 6.6 equiv. of potassium *tert*-butoxide (260 mg, 2.32 mmol) dissolved in THF (70 mL). After stirring the mixture for 6 h at this temperature, a solution of 3,5-bisdodecyloxybenzylbromide (1.45 g, 2.01 mmol) in dry THF (70 mL) was added dropwise and stirring was continued overnight. The reaction mixture was then diluted with water (200 mL) and extracted with chloroform (3 × 150 mL). The combined extracts were washed with water (300 mL), dried with $MgSO_4$ and the solvent was evaporated. The crude product was separated from the excess of 3,5-*bis*-dodecyloxybenzylbromide by chromatography on a column of silica gel (8 × 20 cm) with petroleum ether/chloroform (8/2 ratio). The product was separated as the last fraction using chloroform/petroleum ether/ethyl acetate (2/1/0.1 ratio) as brown oil 460 mg (71%). IR (KBr, cm^{-1}, ν_{max}) 2915, 2240, 1585, 1495, 1458, 1430, 1230, 1110, 1003, 831. HRMS-FAB (m/z): $[M + H]^+$ calcd. for $C_{246}H_{360}O_{18}S_6$, 3797.98; found, 3798.20. Anal. Calcd. for $C_{246}H_{360}O_{18}S_6$: C 77.80, H 9.55, S 5.07. Found C 77.65, H 9.61, S 5.09.

RESULTS AND DISCUSSION

The synthesis of the compounds **1a-4a** was successfully carried out through a multistep sequence from the appropriate ketones with the help of the Hurd and Mori method[15].

The action of strong bases such as potassium *t*-butoxide results in cleavage of (4-substituted) 1,2,3-thiadiazoles. Extrusion of nitrogen and deprotonation leads to alkynethiolates **1b-4b**. Trapping of the alkynethiolates with halogenalkanes leads to the formation of a star form structures with

TABLE-1
^{1}H NMR DATA OF THE COMPOUNDS **1-,2-,3-,4-c** AND **4d** IN $CDCl_3$ [$\delta(^1H)$ VALUES WITH RESPECT TO TMS AS INTERNAL STANDARD]

Compound	Central benzene ring H(s)	Side Chains α-CH_2 H(s)	-C_6H_4- H(AA'BB')	β-CH_2 H(s)	Benzene rings						
					A H(s)	B H(s)	AA' H(s)	BB' H(s)	C H(s)	γ-CH_2 H(s)	δ-CH_2 H(s)
1c	7.49	5.13	6.80 & 7.34	3.96	6.65	6.57	7.33	7.35	7.33	4.90	4.96
2c	7.43	5.18	6.81 & 7.35	3.86	6.69	6.49	7.31	7.34	7.31	4.88	4.91
3c	7.44	5.17	6.83 & 7.37	3.91	6.63	6.52	7.37	7.42	7.37	4.85	4.93
4c	–	5.14	6.82 & 7.39	3.97	6.61	6.53	7.39	7.46	7.39	4.83	4.99
4d	–	5.15	6.86 & 7.39	3.96	6.60	6.57	–	–	–	–	–

TABLE-2
^{13}C NMR DATA OF THE COMPOUNDS **1-,2-,3-,4-c** AND **4d** IN $CDCl_3$ [$\delta(^{13}C)$ VALUES WITH RESPECT TO TMS AS INTERNAL STANDARD]

Comp.	Central benzene ring		Side chains	-C_6H_4-		C≡C		β-CH_2	Benzene rings									
	CH	Cq	α-CH_2 CH	CH	Cq	C	CS	CH	A CH	B CH	Cq	CqO	AA' CH	BB' CH	C CH	Cq	γ-CH_2 CH	δ-CH_2 CH
1c	131.70	137.20	64.60	114.79 132.40	116.40 158.50	92.70	80.10	40.60	106.80	101.60	140.30	160.20	127.60	128.50	128.10	136.70	70.10	70.20
2c	131.81	137.28	64.40	114.13 132.62	116.57 158.70	92.32	80.57	40.90	106.20	101.30	140.32	160.27	127.90	128.42	128.13	136.81	70.31	70.21
3c	131.79	137.31	64.51	114.67 132.41	116.52 158.81	92.70	80.39	40.93	106.61	101.47	140.35	160.30	127.83	128.52	128.18	136.72	70.31	70.24
4c	–	136.95	64.54	114.74 132.40	116.53 158.83	92.95	80.36	40.95	106.68	101.48	140.37	160.32	127.77	128.55	128.22	136.70	70.35	70.25
4d	–	137.11	63.68	114.53 132.37	116.56 158.88	93.01	80.36	40.93	105.99	101.52	–	–	–	–	–	–	–	–

alkinylthioether units. Fréchet type dendrones are selected in order to prepare a new dendrimers with benzene core. For comparison, two-, three-, four- and six-arm systems bearing 1,2,3-thiadiazole rings are successfully used to prepare dendrimers with core multiplicity $N_c = 2, 3, 4, 6$ and branch multiplicity $N_b = 2$ and having a peripheral number of terminal groups $Z = 8, 12, 16$ and 24, respectively.

The dendrimers are fully charachterized using IR, NMR spectroscopy and elemental analysis. The ^1H , ^{13}C NMR data are shown in Tables 1 and 2. They are mostly similar in values for different dendrimers, especially in case of the chemical shift for the OCH_2-groups (β to δ, **Scheme-I** and Tables 1 and 2). According to the δ-value, it can be observed that in the ^1H NMR-scale: $\alpha > \delta > \gamma > \beta$; while in the ^{13}C NMR-scale, the opposite is correct, such that the β-OCH_2-group has the highest value where as the α-OCH_2-group has the lowest chemical shift. The photochemical reactivity of the dendrimers **1c**-**4c** may be studied later.

ACKNOWLEDGEMENTS

The author is grateful to the Deanship of Research, Jordan University of Science & Technology and to Prof. H. Meier from the University of Mainz for contribution and support.

REFERENCES

1. D.A. Tomalia and A.M. Naylor, *Angew. Chem. Int. Ed. Engl.*, **29**, 138 (1990); H.B. Mekelburger, W. Jaworek and F. Voegtle, *Angew. Chem. Int. Ed. Engl.*, **31**, 1571 (1992); J. Lssberner, R. Moors and F. Voegtle, *Angew. Chem. Int. Ed. Engl.*, **33**, 2413 (1994).
2. G. L'abbe', B. Haelterman and W.J. Dehaen, *J. Chem. Soc. Perkin Trans. I*, 2203 (1994).
3. N.M. Bikales, *Polym. J.*, **19**, 11 (1989).
4. E. Buhleier, W. Wehner and F. Vogtle, *Synthesis*, 155 (1987).
5. B.M. Tande, N.J. Wagner, M.E. Mackay, C.J. Hawker, R. Vestberg and M. Jeong, *Macromolecules*, **34**, 8580 (2001).
6. M.E. Mackay, Y. Hong, S. Hong, T.P. Russell, C.J. Hawker, R. Vestberg and J. Douglas, *Langmuir*, **18**, 1877 (2002).
7. L.J. Twyman, A.S. King and I.K. Martin, *Chem. Soc. Rev.*, **31**, 69 (2002).
8. S. Tepavcevic, Y. Choi and L. Hanley, *J. Am. Chem. Soc.*, **125**, 2396 (2003).
9. H. Ihre, O. Padilla and J. Fréchet, *J. Am. Chem. Soc.*, **123**, 5908 (2001).
10. M. Al-Smadi, N. Hanold and H. Meier, *J. Heterocycl. Chem.*, **34**, 605 (1997).
11. P.G. De Gennes and H. Hervet, *Phys. Lett.*, **44**, 351 (1983).
12. C.D. Hurd and R.I. Mori, *J. Am. Chem. Soc.*, **77**, 5359 (1955).
13. M. Al-Smadi and H. Meier, *Liebigs Ann. Chem.*, 2357 (1997).
14. J. Crivello, M. Deptolla and H. Ringsdorf, *Liq. Cryst.*, **3**, 2, 235 (1988).
15. C.J. Hawker and J. Fréchet, *J. Am. Chem. Soc.*, **112**, 7638 (1990).

(*Received*: 16 February 2006; *Accepted*: 13 October 2006) AJC-5181