A Model for Late-Stage Modification of Polyurethane Dendrimers Using Thiol-Ene Click Chemistry

Dhruba Poudel, Richard Taylor

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Protecting group free, one-pot multicomponent Curtius reaction was utilized to afford diurethane G-1 dendron. In our synthetic approach, G-1 dendron can undergo late-stage modification using thiol-ene click reaction, which was then attached to the core to furnish a dendrimer. In another approach, the G-1 dendron was attached to the core and so formed dendrimer was surface functionalized using thiol-ene click chemistry. Either way, we can synthesize the dendrimer.

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A Model for Late-Stage Modification of Polyurethane Dendrimers Using Thiol-Ene Click Chemistry

Dhruba P. Poudel and Richard T. Taylor*

Department of Chemistry and Biochemistry, Miami University, 501 E High Street, Oxford, Ohio 45056

ABSTRACT: Protecting group free one-pot multicomponent Curtius reaction affords a robust and versatile AB₂ type diurethane dendron, which ensures late-stage modification of both dendron and dendritic macromolecule yielding a surface functionalized polyurethane dendrimer. This strategy is highly useful in the synthesis of unsymmetrical or Janus dendrimers.

Since the first successful synthesis of poly(amideamine) dendrimers by Tomalia et al. in 1985,¹ development of dendritic macromolecules, including dendrimers and hyperbranched polymers has developed rapidly in the field of macromolecular chemistry² because of their extensive applications in the chemical³ and biomedical fields.⁴,⁵ Dendritic macromers have been reported for a wide variety of compounds like polyethers, polyamines, polyamides, polyylenes, polycarbonates, and polycarbonates. Though a few such structures are reported in the field of polyurethanes, construction of a well-defined architecture of polyurethane dendrimers (PUDs)⁶ is challenging owing to high reactivity of externally added or in-situ formed isocyanates towards nucleophiles, which could lead to significant amounts of side products. Pleasingly, two seminal works published simultaneously in 1993 by two research groups founded synthetic routes to PUDs, which are valid to date. The first route described by Spindler and Fréchet⁷ using isocyanate chemistry assured the synthesis of dendritic structures via growth of two generations in a single synthetic operation. The second route described by Kumar and Ramakrishnan⁸ using Curtius rearrangement as an isocyanate free approach trapped in-situ formed isocyanate by an alcohol affirming a urethane.

PUDs have been synthesized employing both divergent⁹–¹² and convergent¹³–¹⁶ methods in the last two and half decades after the aforementioned pioneering works. First reported by Hawker and Fréchet,¹³ the convergent synthesis involves a small number reactions per molecule during the coupling of dendron and activation of functional group at focal point. This ensures greater structural control than in divergent synthesis approach.¹⁷ Moreover, the functional groups can be precisely placed throughout the dendritic structure, an attribute required to construct functional macromolecules. Nevertheless, fewer reports have been reported on PUDs employing the convergent method. Previously, our group reported convergent synthesis of PUDs containing dodecyl as end groups using a protection/deprotection strategy.¹⁸,¹⁹ This work reports on a fast, efficient, and protecting group free approach to the synthesis of PUDs where terminal pentene functionalized dendron can further undergo pre- or post-modification via thiol-ene click chemistry. This enables easy modification of the dendritic periphery, which could be of particular interest because these peripheral groups are the moieties to come in frequent contact with the external environment.

As a proof of concept, herein we report the synthesis of the first-generation dendritic wedge, its attachment to a core structure, and pre- and post-modification using thiol-ene reaction. The versatility of this approach is depicted by an AB₂ type dendritic monomer that can undergo either a thiol-ene click reaction²⁰ or attachment to the core. As shown in Scheme 1 'hydroxy’ and ‘ene’ functionalized dendrons can be utilized in either of the two ways- click and attach to the core or attach to the core and click- to synthesize a polyurethane dendrimer.
To build AB₂ type dendron or branching monomer, we selected three molecules, 5-hydroxyisophthalic acid, 4-penten-1-ol, and 11-bromoundecanol as branching unit, peripheral group, and spacer group respectively. Accordingly, the branching monomer was prepared in a two-step sequence of reactions. We exploited the Curtius reaction to synthesize the phenolic diurethane 1. The formation of 1 involved one-pot multicomponent Curtius reaction in which 5-hydroxyisophthalic acid (1 eq) 1a was converted to an isocyanate analogue 1b through an acyl azide intermediate under mild condition using diphenyl phosphoryl azide (DPPA, 2.1 eq) and triethylamine (2 eq) (Scheme S2). Organic isocyanates are electrophilic reactive intermediates, which can be trapped easily by nucleophiles in situ thereby forming the urethane linkage. The hydroxy disiocyanate 1b was trapped by 4-penten-1-ol to afford the phenolic diurethane 1, which in turn furnished branching monomer 2 with an excellent yield when refluxed with 11-bromoundecanol. Unlike previously reported synthetic protocol, this strategy is concise and does not require any protection-deprotection of functional groups.

Protecting group-free Curtius reaction is a key step to from the urethane linkage in this approach and we spent some time investigating the efficacy of this reaction. This reduces an extra step required to activate the dendron at its focal point. Since the reaction intermediate 1b (Scheme 2) has nucleophilic phenolic group, it could potentially compete with 4-penten-1-ol to react with its own isocyanate leading to the formation of polymeric side products. This directed us to optimize the reaction conditions. Unprotected phenolic hydroxy group in 1b resulted in two noticeable side products – diurethane phosphate 1c and dimer of monourethane 1d. Taking advantage of difference between pKa values of aromatic hydroxy (~10) and carboxylic groups (~3-5), we anticipated that a base with pKa less than that of phenolic -OH (~10) could prevent the potential formation of urethane phosphate. Surprisingly, the bases with low pKa

| Entry | Base     | pKa   | Yield (%) |
|-------|----------|-------|-----------|
| 1     | Pyridine | 5.2   | 19        | 11       | 2         |
| 2     | PVP      | 5.6   | 5         | 11       | 36        |
| 3     | DMAP     | 9.6   | 20        | 12       | 5         |
| 4     | Et₃N    | 10.8  | 39        | 10       | 4         |
| 5     | No base  | -     | 1         | 24       | 1         |

*a Conditions: 1a (1.0 eq), DPPA (2.1 eq), triethylamine (2.0 eq), 4-penten-1-ol (1.5 eq). Crude was purified by flash chromatography using ethyl acetate/hexane as eluting solvent.*
values did not increase the yield of 1 (Table 1; entry 1, 2, and 3) and the base with larger pKa (triethylamine) gave better yields (Table 1; entry 4). This reaction did require a base as depicted by entry 5 in Table 1, where the yield of 1 is negligible in absence of a base. In addition, while good yields were obtained at temperature 85 – 95 °C, side products were formed in higher amounts at higher temperature. It is noteworthy that one of the side products 1c can be recycled back to branching monomer 1.

Being a green reaction, thiol-ene click chemistry has been widely used in the efficient growth of dendrimers. We utilized thiol-ene click here as a tool to ascertain the robustness of monomer 1 towards synthesis of PUDs by functionalizing the dendritic surface via different methods. Accordingly, 4 was synthesized via two different routes as shown in Scheme 4. To accomplish this, 1-octanethiol and 1,3,5-trisocyanatobenzene 3b (preparation in Scheme S3) were selected as thiol-ene click partner and a simple trifunctional core respectively. In its click and attach approach, the wedge 2 was irradiated with 1-octanethiol under UV light in presence of free radical initiator 2,2′-azobis (2-methyl propionitrile) (AIBN) to obtain thioether functionalized dendron 3 in high yield (82%). The convergent synthesis of 4 was accomplished when dendron 3 was attached to the core 3b in presence of Lewis acid BF₃·OEt₂. In the attach and click approach, dendron 2 was attached to the core 3b under identical conditions to furnish a dendrimer 5 with pentene peripheral groups, which underwent subsequent thiol-ene click with 1-octanethiol under identical reaction conditions to produce dendrimer 4. Its noticeable that the overall yield of post-modification route is lower because of larger number of reactions required to undergo completion at periphery.

The most powerful feature of convergent synthesis lies on its ability to selectively modify both focal point and chain ends. This strategy allows one to vary the number and type of functional moieties in the resultant dendrimers. In this study, we modified the chain ends without changing its focal point, which in turn resulted in surface modified dendrimer 4. There are two possible approaches for the installation of functionality at the core – introduction of end groups prior to and after the dendritic growth. The structural features of dendron 2 guarantee both pre- and post-modification routes.
All novel compounds including dendritic wedges and dendrimers were characterized by $^1$H, $^{13}$C NMR, and mass spectrometry (HRESI-MS or MALDI-TOF) (details in SI). Figure 1 shows solution state $^1$H NMR of branching monomers (2 and 3) and dendrimers (4 and 5) in deuterated acetone as a solvent before and after thiol-ene functionalization. Disappearance of peaks with chemical shifts at 5.0 and 5.9 ppm (-CH=CH$_2$) (Figure 1a and 1d) and appearance of new peaks at 2.6 ppm (-SCH$_2$-), 0.9 ppm (-CH$_3$) (Figure 1b and 1c) provided a clear evidence that thiol-ene click preceded successfully. Moreover, a new peak assigned at 7.5 ppm (aromatic H) (Figure 1c and 1d) furnished further evidence of successful attachment of dendron 2 or 3 to the trifunctional core.

In summary, we presented thiol-ene click inspired protecting group free approach to the convergent synthesis of polyurethane dendrimers. As a representative of proposed approach, generation one dendrimers were synthesized via click and attach, and attach and click methods under mild conditions. An efficient and robust bifunctional dendron synthesized from a one-pot multicomponent Curtius reaction enabled late stage modification of itself and accompanying dendrimers. Additionally, functionalization of a bifunctional core with two different dendrons furnished a mixture of three dendrimers including a Janus dendrimer. Access to this type of investigation will contribute to concise and versatile synthesis of dendritic macromolecules.

ASSOCIATED CONTENT

Supporting Information
The Supporting Information is available free of charge.
Experimental procedures, $^1$H NMR, $^{13}$C NMR and IR spectra as well as mass spectrometric data of the novel compounds described (PDF)

AUTHOR INFORMATION

Corresponding Author
Richard T. Taylor – Department of Chemistry and Biochemistry, Miami University, 501 E High St, Oxford, OH 45056, USA
Email: taylorrt@miamioh.edu

Author
Dhruba P. Poudel – Department of Chemistry and Biochemistry, Miami University, Oxford, OH 45056, USA;

Notes
The authors declare no competing financial interest.

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REFERENCES

(1) Tomalia, D. A.; Baker, H.; Hall, M.; Kallos, G.; Martin, S.; Ryder, J.; Smith, P. Dendritic Macromolecules: I. Synthesis of Starburst Dendrimers. Macromolecules 1986, 19 (9), 2466–2468. https://doi.org/10.1021/ma00163a029.

(2) Sowinska, M.; Urbanczyk-Lipkowska, Z. Advances in the Chemistry of Dendrimers. New J. Chem. 2014, 38 (6), 2168–2203. https://doi.org/10.1039/c3nj01239e.

(3) Astruc, D.; Chardac, F. Dendritic Catalysts and Dendrimers in Catalysis. Chem. Rev. 2001, 101 (9), 2991–3023. https://doi.org/10.1021/cr010325t.

(4) Majoral, J. P.; Mignani, S. M.; Shi, X.; Rodrigues, J. M.; Muñoz-Fernández, M. A.; Ceña, V.; Roy, R. Dendrimers towards Translational Nanotherapeutics: Concise Key Step Analysis. Bioconjug. Chem. 2020. https://doi.org/10.1021/acs.bioconjchem.0c00395.

(5) Jezek, J.; Reimis M., Sebestik. Biomedical Applications of Peptide-, Glyco-, and Glycopeptide Dendrimers and Analogous Dendrimeric Structures. Springer: Wien, 2012; ISBN: 978-37091-1205-2.

(6) Bruchmann, B. Dendritic Polymers Based on Urethane Chemistry - Syntheses and Applications. Macromol. Mater. Eng. 2007, 292 (9), 981–992. https://doi.org/10.1002/mame.200700119.

(7) Spindler, R.; Fréchet, J. M. J. Two-Step Approach towards the Accelerated Synthesis of Dendritic Macromolecules. J. Chem. Soc. Perkin Trans 1 1993, No. 8, 913–918. https://doi.org/10.1039/p19930000913.

(8) Reimers, S.; Mouroum, A.; Keul, H.; Möller, M. Novel Route to Dendritic Structures and Their Application for Surface Modification. J. Polym. Sci. Part A Polym. Chem. 2006, 44 (4), 1372–1386. https://doi.org/10.1002/pola.21251.

(9) Ali, B. M.; Kumar, K. A.; Nasar, A. S. Fifth-Generation Polyurethane Dendrimers Decorated with Amine, Free Amine, and Block Isocyanate End Groups: Synthesis and Electrolytic Performance to Increase the Efficiency of Dye-Sensitized Solar Cell. ChemistrySelect 2014, 5, 12983–12991.

(10) Veerapandian, S.; Nasar, A. S. Amine- and blocked isocyanate-terminated polyurethane dendrimers: integrated synthesis, photophysical properties, and applications in heat curable systems. RSC Adv. 2015, 5, 3800–3806.

(11) Peerlings, H. W. I.; Van Benthem, R. A. T. M.; Meijer, E. W. Fast and Convenient Construction of Carbamate/Urea-Based Dendrimers with a Disocyanate Building Block. J. Polym. Sci. Part A Polym. Chem. 2001, 39 (18), 3112–3120. https://doi.org/10.1002/pola.1292.

(12) Mohamad Ali, B.; Velavan, B.; Sudhandiran, G.; Sridivi, J.; Sultan Nasar, A. Dendrimers: Synthesis, Anti-Tumor Activity and Enhanced Cytoprotective Performance of TEMPO Free Radical Functionalized Polyurethane Dendrimers. Eur. Polym. J. 2020, 122 (August 2019), 109354. https://doi.org/10.1016/j.eurpolymj.2019.109354.

(13) Hawker, C. J.; Fréchet, J. M. J. Preparation of Polymers with Controlled Molecular Architecture: A New Convergent Approach to Dendritic Macromolecules. J. Am. Chem. Soc. 1990, 112 (21), 7638–7647. https://doi.org/10.1021/ja00177a027.

(14) Goodwin, A. P.; Lam, S. S.; Fréchet, J. M. J. Rapid, Efficient Synthesis of Heterofunctional Biodegradable Dendrimers. J. Am. Chem. Soc. 2007, 129, 6994-6995.

(15) Clark, A. M.; Echenique, J.; Huddleton, D. M.; Straw, T. A.; Taylor, P. C. A Nonisocyanate Route to Monodisperse Branched Polyurethanes. J. Org. Chem. 2001, 66, 8687-8689.

(16) Feast, W. J.; rannard, S. P.; Stoddart, A. Selective Convergent Synthesis of Aliphatic Polyurethane Dendrimers. Macromolecules, 2003, 36, 9704–9706.

(17) Grayson, J.; Fréchet, J. M. J. Convergent Dendrons and Dendrimers. Chem. Rev. 2001, 101, 3819-3867.

(18) Puapaiboon, U.; Taylor, R. T.; Jai-Nukun, J. Structural Confirmation of Polyurethane Dendritic Wedges and Dendrimers Using Post Source Decay Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry. Rapid Commun. Mass Spectrom. 1999, 13 (6), 516–520. https://doi.org/10.1002/(SICI)1097-2613(19990630)13:6<516::AID-RCM518>3.0.CO;2-P.

(19) Taylor, R. T.; Puapaiboon, U. Polyurethane Dendrimers via Curtius Reaction. Tetrahedron Lett. 1998, 39 (44), 8005–8008. https://doi.org/10.1016/S0040-4039(98)01787-0.

(20) Hoyle, C. E.; Bowman, C. N. Thiol-Ene Click Chemistry. Angew. Chemie - Int. Ed. 2010, 49 (9), 1540–1573. https://doi.org/10.1002/anie.200903924.

(21) Ghosh, K. K.; Shaik, A.; Brückl, M. The Curtius Rearrangement: Mechanistic Insight and Recent Applications in Natural Product Syntheses. Org. Biomol. Chem. 2018, 16 (12), 2006–2027. https://doi.org/10.1039/c8ob00138c.

(22) Phosphorazidate, D.; More, D.; Three, T.; Later, D.; Shioiri, T. Contribution. 1972, No. 134, 2–19.

(23) Sharma, A.; Sharma, R.; Zhang, Z.; Liaw, K.; Kambhampati, S. P.; Porterfield, J. E.; Liu, M. C.; DeRidder, L. B.; Kannan, S.; Kannan, R. M. Dense Hydroxy Polyethylene Glycol Dendrimer Targets Activated Glia in Multiple CNS Disorders. Sci. Adv. 2020, 6 (4), 1–15. https://doi.org/10.1126/sciadv.aay8514.

(24) García-Gallego, S.; Andrade, O. C. J.; Malkoch, M. Accelerated Chemoselective Reactions to Sequence-Controlled Heterolayered Dendrimers. J. Am. Chem. Soc. 2020, 142 (3), 1501–1509. https://doi.org/10.1021/jacs.9b11726.

(25) Killops, K. L.; Campos, L. M.; Hawker, C. Robust, Efficient, and Orthogonal Synthesis of Dendrimers via Thiol-ene "Click" Chemistry. J. Am. Chem. Soc. 2008, 130, 5062-5064.

(26) Montaney, M. I.; Campos, L. M.; Anton, P.; Heed, Y.; Walte, M. V.; Krull, B. T.; Khan, A.; Hult, A.; Hawker, C. J.; Malkoch, M. Accelerated Growth of Dendrimers via Thiol-ene and Esterification Reactions. Macromolecules 2010, 43, 6004-6013.

(27) Hoff, E. A.; De Hoe, G. X.; Mulvancy, C. M.; Hillmayer, M. A.; Alabi, C. A. Thiol-Ene Networks from Sequence-Defined Polyurethane Macromers. J. Am. Chem. Soc. 2020, 43, 6004-6013.

(28) Caminade, A. M.; Laurent, R.; Delavaux-Nicot, B.; Majoral, J. P. “Janus” Dendrimers: Syntheses and Properties. New J. Chem. 2012, 36 (2), 217–226. https://doi.org/10.1039/c1nj20458k.

(29) Sikwal, D. R.; Kalhapure, R. S.; Govender, T. An Emerging Class of Amphiphilic Dendrimers for Pharmaceutical and Biomedical Applications: Janus Amphiphilic Dendrimers. Eur. J. Pharm. Sci. 2017, 97, 113–134. https://doi.org/10.1016/j.ejps.2016.11.013.
SUPPORTING INFORMATION

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Dhruba P. Poudel and Richard T. Taylor*

Faculty of Department of Chemistry and Biochemistry, Miami University, 501 E High Street, Oxford, Ohio 45056, USA
E-mail: taylorrt@miamioh.edu
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1. General information

Starting materials were used as obtained from commercial sources: Sigma Aldrich (NaN₃, AIBN, 1-octadecanethiol, triethylamine), TCI (4-penten-1-ol, 1-bromoundecanol, benzene-1,3,5-tricarbonyltrichloride, 1-octanethiol, BF₃.OEt₂), and Alfa Aesar (5-hydroxyisophthalic acid, DPPA). Whereas anhydrous solvents were used in the dendrimer synthesis, DMF (Acros Organics), DCM (Fischer Scientific), and acetone (Acros Organics) were used as received, reagent toluene was used without distillation. Curtius reaction was set in a Carousel reactor and all other reactions were performed using classical batch process using oil bath (if heat needed). A UV lamp from American Ultraviolet Company (model: PC-100S; 120 V, 60 Hz, 5 Amp; S/N: 9902L3669) was used to carry out thiol-ene click reaction. Melting points were determined using Thermo Scientific MelTemp 3.0 instrument.

¹H, ¹³C, and 2D NMR spectra were recorded with a Bruker Advance 500 MHz NMR instrument at 298K. NMR spectra were recorded using either acetone-d₆ or CDCl₃ as deuterated solvent and accordingly the solvent residual peaks were obtained at δ 2.05 ppm (qn) and δ 7.26 ppm (s) respectively in ¹H NMR. In ¹³C NMR, solvent residual peaks were recorded at δ 206.68 ppm (s) and δ 29.92 ppm (septet) for acetone-d₆ and δ 77.23 ppm (s) for CDCl₃. Coupling constants (J) are given in hertz (Hz) whereas chemical shifts are given in δ scale (ppm). Moreover, the multiplicities are indicated as - s (singlet), d (doublet), t (triplet), q (quartet), qn (quintet), or m (multiplet). IR spectra were obtained from PerkinElmer Spectrum One FT-IR Spectrometer.

HRMS spectra of small molecules including dendrons were obtained from FTMS plus CESI mass spectrometer using DCM as solvent. MALDI of larger molecules were recorded with a Bruker 15 FT-ICR instrument using HCCA as matrix in positive ion mode.

Purification of compounds were carried out using flash chromatography with irregular silica of 40-60 µm, 60 Å. Small scale purification was achieved using auto-column flash cartridges packed with 12g or 40g silica of 40-75 µm, 60 Å (obtained from Sorbtech and Supelco Technologies). Flow rate was 10 mL/min - 30 mL/min. Mobile phase used in these separations was ethyl acetate, hexane, DCM or mixture of these solvents.
2. Experimental: synthesis of dendrons and dendrimers

2.1. One-pot multicomponent Curtius reaction affording phenolic diurethane, 1

5-Hydroxyisophthalic acid (5.0 g, 27.45 mmol, 1.0 eq) was dissolved in anhydrous DMF (20 mL) under nitrogen in an oven-dried Carousel flask provided with a magnetic stir bar. After complete dissolution, Et$_3$N (12.4 mL, 54.90 mmol, 2.0 eq) was added slowly followed by dropwise addition of DPPA (18.9 mL, 54.90 mmol, 2.0 eq) at rt. This reaction is exothermic and turns the solution yellow. Stirring was continued for 15 min at rt before adding 4-penten-1-ol (5.1 mL, 49.41 mmol, 1.8 eq) at rt. The solution was heated to 95 °C for 20 h, then diluted 20 times with water, and extracted with EtOAc (4x150 mL). The combined organic layers were washed multiple times with water to remove DMF, washed with brine, dried with anhydrous MgSO$_4$, concentrated, and purified by flash chromatography using 7:3 hexane/EtOAc as mobile phase to give 1 as slightly purple solid (3.39 g, 39% yield). The diurethane phosphate 10% (slightly yellow solid) and the dimer of monourethane 4% (white solid) were also isolated as side products. This reaction can be monitored by FTIR. (Caution: During Curtius rearrangement (CON$_3$ $\rightarrow$ NCO) the reaction proceeds violently releasing N$_2$ gas. The reaction vessel should not be sealed completely in this step to avoid possible explosion.)

Phenolic diurethane 1

**m.p.** 86-89 °C

**TLC (30% EtOAc in hexane):** R$_f$ 0.34

$^1$H NMR (500 MHz, CD$_3$COCD$_3$): δ 8.54 (s, 2H, aromatic -NH-), 8.29 (s, 1H, -OH), 7.20 (t, $J = 1.8$ Hz, 1H), 6.91 (d, $J = 1.6$ Hz, 2H), 5.82 – 5.90 (m, 2H), 4.96 – 5.08 (m, 4H), 4.12 (t, $J = 6.6$ Hz, 3H), 2.14 - 2.18 (m, 4H), 1.72 - 1.77 (m, 4H)

$^{13}$C NMR (500 MHz, CD$_3$COCD$_3$): δ 158.1, 153.6, 140.6, 137.8, 114.6, 100.2, 63.7, 29.8, 28.1, 28.0
**HRMS (ESI-MS):** Calculated [M+Na] 371.1577, Measured [M+Na] 371.1573

Diurethane phosphate

**TLC (30% EtOAc in hexane):** R<sub>f</sub> 0.40

**<sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>COCD<sub>3</sub>):** δ 8.89 (s, 2H, OH), 7.66 (s, 1H), 7.45 (t, J = 7.5 Hz, 4H), 7.40 (s, 2H), 7.36 (dd, J = 8.6, 1.0 Hz, 4H), 7.29 (dt, J = 6.9, 1.1 Hz, 4H), 5.90 – 5.83 (m, 2H), 5.08 – 4.97 (m, 4H), 4.15 (t, J = 6.6 Hz, 4H), 2.19. – 2.15 (m, 4H), 1.79 – 1.74 (m, 4H).

**<sup>13</sup>C NMR (500 MHz, CD<sub>3</sub>COCD<sub>3</sub>):** δ 157.9, 157.8, 153.6, 153.5, 151.1, 151.1, 150.7, 150.6, 141.1, 137.8, 130.1, 130.0, 125.7, 120.2, 114.8, 114.0, 105.0, 104.2, 104.1, 64.6, 64.4, 64.1, 64.0, 29.8, 28.0

**ESI-MS:** Calculated [M+Na] 603.2 measured [M+Na] 603.3

Dimer of monourethane

**TLC (30% EtOAc in hexane):** R<sub>f</sub> 0.29

**<sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>COCD<sub>3</sub>):** δ 8.75 (s, 2H, -NH-), 7.75 (t, J = 3.2, 2H), 7.48 (s, 2H), 7.21 (q, 2H, J = 0.9 Hz), 5.90 – 5.85 (m, 2H), 5.09 – 4.97 (m, 4H), 4.15 (t, J = 6.6 Hz, 4H), 2.20 – 2.15 (qn, J = 6.8Hz, 4H), 1.80 – 1.74 (qn, J = 8.1 Hz, 4H).

**<sup>13</sup>C NMR (500 MHz, CD<sub>3</sub>COCD<sub>3</sub>):** δ 166.6, 157.8, 153.5, 140.8, 137.8, 132.1, 114.6, 110.9, 110.6, 109.6, 63.9, 59.6, 19.9, 13.6

**ESI-MS:** Calculated monomer [M-H] 264.0 calculated monomer [M-H] 263.9

Formation urethane bond via one pot multicomponent reaction is the key step of whole process, which proceeds via three subsequent intermediate steps as demonstrated below.
Supplementary Scheme S1. Sequential transformation during Curtius reaction

**Supplementary Figure S1.** FT-IR spectra of Curtius reaction in DMF as a function of time and temperature.
Purification by silica gel column chromatography

**Supplementary Figure S2.** TLC of crude products obtained after Curtius reaction (above) and structure of two major side products (below).

**Table S1. Effect of base on Curtius reaction**

| Entry | Base                     | pKa | Yield % | Compound 1 | Phosphate | Dimer |
|-------|--------------------------|-----|---------|------------|-----------|-------|
| 1     | Pyridine                 | 5.2 | 19      | 11         | 2         |
| 2     | Polyvinylpyridine (PVP)  | 5.6 | 5       | 11         | 36        |
| 3     | DMAP                     | 9.6 | 20      | 12         | 5         |
| 4     | Et$_3$N                  | 10.8| 39      | 10         | 4         |
| 5     | Without a base           | -   | 1       | 24         | 1         |

This shows that bases with lower pKa than that of phenolic OH (pKa~10) do not increase the yield of 1. Also, this reaction requires a base as depicted by entry 5 where yield of 1 is negligible in absence of a base. Moreover, the good yields are obtained at temperature between 90-97 °C. Higher temperature tends to decompose DMF into dimethyleamine leading to formation of side products in higher amount.
Supplementary Scheme S2: Recycling 1 from side products

Phosphate compound (1.97 g, 3.40 mmol) was dissolved in 1,4-dioxane/water (2:1) in a carousel flask charged with a magnetic stir bar. HCl (37.4%, 2 mL) was added to the flask, which was then set to 99 °C in carousel reactor. After 26h, reaction mixture was extracted with EtOAc, washed with water and brine, dried with anhydrous MgSO₄, concentrated, and purified by silica gel chromatography using 7:3 hexane/EtOAc as mobile phase. Slightly pink solid was obtained as product (980 mg, 82% yield).

2.2. Attaching undecyl tail to phenolic diurethane: formation of dendron, 2
An oven-dried 100 mL RB flask was charged with 11-bromoundecanol (1.5 g, 5.9 mmol, 1.2 eq), K₂CO₃ (3.3 g, 22.5 mmol, 5.0 eq), KI (166 mg, 0.2 mmol, 0.2 eq), and a magnetic stir bar. The flask was placed under nitrogen and compound 1 (1.7 g, 4.9 mmol, 1.0 eq) dissolved in acetone (20 mL) was transferred into it via syringe. The reaction mixture was set to reflux for 18 h. The progress of reaction was checked with TLC (7:3 hexane/EtOAc). After complete reaction, acetone was evaporated and residue was extracted with EtOAc, washed with brine, dried with anhydrous MgSO₄, and concentrated. The crude was purified by flash chromatography gradient elution using silica gel as stationary phase and 10% -30% EtOAc in hexane as mobile phase to give transparent viscous oil as product (2.32 g, 91% yield).

**TLC (1:1 hexane/EtOAc):** Rₜ 0.55

**¹H NMR (500 MHz, CD₃COCD₃):** δ 8.60 (s, 2H), 7.29 (t, J = 1.8 Hz, 1H), 6.98 (d, J = 1.4 Hz 2H), 5.83 – 5.91 (m, 2H), 4.97 – 5.08 (m, 4H), 4.13 (t, J = 6.6 Hz, 3H), 3.95 (t, J = 6.5 Hz, 2H), 3.54 (q, J = 5.4 Hz, 2H), 3.41 (t, J = 5.2 Hz, 1H), 2.15 – 2.19 (m, 4H), 1.73 – 1.79 (m, 6H), 1.47 – 1.54 (m, 4H), 1.36 – 1.42 (m, 14H)

**¹³C NMR (500 MHz, CD₃COCD₃):** δ 160.1, 153.5, 140.6, 137.9, 114.5, 99.2, 67.6, 63.7, 61.6, 32.9, 29.9, 29.8, 29.5, 29.4, 29.2, 28.1, 25.9, 25.8

**HRMS (ESI-MS):** Calculated [M+H] 519.3429 measured [M+H] 519.3421

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**Click and attach approach**

### 2.3. General procedure of thiol-ene click reaction represented by reaction of dendron 1 with 1-octanethiol, 3

Dendron 2 (285.5 mg, 0.55 mmol, 1.0 eq) was dissolved in dry DCM (1.5 mL) in a regular vial charged with a magnetic stirrer. 1-Octanethiol (382 µL, 2.2 mmol, 4.0 eq) and azobisisobutyronitrile, AIBN (18 mg, 0.11 mmol, 0.2 eq) were added and vial was placed under
UV light at rt for 20 h. Solvent was evaporated and crude was purified by silica gel chromatography using 7:3 hexane/EtOAc as mobile phase to get white solid (364.5 mg, 82% yield).

m.p.: 46 °C
TLC (30% EtOAc in hexane): Rf 0.26

$^1$H NMR (500 MHz, CD$_3$COCD$_3$): δ 8.58 (s, 2H, -NH-), 7.29 (s, 1H), 6.99 (s, 2H), 4.13 (t, $J = 6.6$, 4H), 3.96 (t, $J = 6.5$, 2H), 3.54 (q, $J = 18.4$, 5.5, 2H), 3.39 (t, $J = 5.3$, 1H, -OH), 2.54 (q, $J = 8.6$, 8H), 1.79 (m, 2H), 1.72 – 1.46 (m, 22H), 1.43 – 1.26 (m, 34H), 0.89 (t, $J = 6.8$, 6H).

$^{13}$C NMR (500 MHz, CD$_3$COCD$_3$): δ 160.1, 153.5, 153.4, 140.7, 140.6, 140.5, 100.7, 99.1, 6.5, 64.2, 61.6, 61.5, 32.9, 31.6, 31.5, 31.4, 29.6, 25.8, 25.0, 22.2, 13.5.

HRMS (ESI-MS): Calculated [M+H] 811.5687 measured [M+H] 811.5675.

**Supplementary Scheme S3: Synthesis of 1,3,5-triisocyanatobenzene.**

1,35-Triisocyanatobenzene was prepared by modifying procedure reported by M.C. Davis. Briefly, at 0 °C, sodium azide (4.30g, 66 mmol, 3.3 eq) was dissolved in water (8 mL) and 1,3,5-benzenetricarbonyl chloride (5.31g, 20 mmol, 1.0 eq) in DCM (60 mL) was added slowly over 30 min. After addition, ice-bath was removed and the solution was stirred at room temperature for 2.5h. DCM was evaporated under reduced pressure and the solid residue was dissolved in toluene (60 mL) and refluxed for 3h. Removing toluene under reduced pressure gave fine, needle-shaped crystals as product (3.27g, 87% yield). M.p. 83-85 °C (lit. 84-85 °C). NMR and IR were similar to that previously reported. The product was satisfactory for the next step.
2.4. General procedure of attaching a dendron to the core represented by attachment of 3 to the core

An oven-dried 10 mL RB flask was charged with 1,3,5-triisocyanatobenzene (30.4 mg, 0.15 mmol, 1.0 eq) and a magnetic stirrer. Under nitrogen and at 0 °C (ice bath), anhydrous methylene chloride (0.5 mL) was added to dissolve the compound. BF$_3$OEt$_2$ (23 µL, 0.09 mmol, 0.6 eq) was added dropwise under stirring at 0 °C. The solution was stirred for 5 min and dendritic wedge 3 (405.3 mg, 0.500 mmol, 3.3 eq) in 1 mL anhydrous methylene chloride was added dropwise. After stirring for 5 min, the solution was allowed to warm to room temperature and stirring was continued for 22 h at rt. Progress of reaction was monitored by FTIR; when isocyanate peak was gone, reaction was stopped. Without any work-up, crude was purified by flash chromatography using 10% EtOAc - 30% EtOAc in hexane (gradient elution) to give highly viscous colorless oil 4 as product (183.2 mg, 46% yield).
**TLC (20% EtOAc in hexane):** R<sub>f</sub> 0.46

**<sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>COCD<sub>3</sub>):** δ 8.59 (s, 9H, -NH-), 7.49 (s, 3H), 7.29 (s, 3H), 6.99 (s, 6H), 4.12 (t, J = 6.4 Hz, 18H), 3.95 (t, J = 6.4 Hz, 6H), 2.53 (q, J = 7.5 Hz, 24H), 1.80 – 1.74 (m, 6H), 1.72 – 1.45 (m, 64H), 1.43 – 1.24 (m, 110H), 0.89 (t, J = 6.8 Hz, 18H).

**<sup>13</sup>C NMR (500 MHz, CD<sub>3</sub>COCD<sub>3</sub>):** δ 160.1, 153.6, 153.5, 140.6, 140.5, 140.1, 103.0, 100.7, 99.2, 67.5, 64.3, 64.2, 31.7, 31.6, 31.5, 29.6, 25.9, 25.7, 25.0, 22.4, 13.5.

**MALDI-TOF:** Calculated [M+H] 2633.70901 calculated [M+H] 2633.69930.

**Attach and click approach**

### 2.5. Attaching dendron 2 to the core 3b

![Diagram showing the attachment of dendron 2 to core 3b](image)

**General procedure of attaching dendron to the core using 1,3,5-triisocyanatobenzene (45.0 mg, 0.244 mmol, 1.0 eq), BF<sub>3</sub>.OEt<sub>2</sub> (35 µL, 0.13 mmol, 0.6 eq), dry DCM 0.5 m, and dendritic wedge 2 (383.0 mg, 0.740 mmol, 3.3 eq) in 1 mL dry DCM afforded highly viscous colorless oil 5 as product.**
(203.4 mg, 52% yield after flash chromatography using 10% EtOAc-40% EtOAc in hexane (gradient elution). No workup was performed.

**TLC (40% EtOAc in hexane):** \( R_f \) 0.58

**\(^1\)H NMR (500 MHz, CD\(_3\)COCD\(_3\)):** \( \delta \) 8.60 (s, 9H, -NH-), 7.50 (s, 3H), 7.29 (t, 3H), 6.99 (d, 6H), 5.89 – 5.83 (m, \( J = 10.3, 10.2 \) Hz, 6H), 5.08 – 4.97 (m, \( J = 17.1, 10.2, 1.4 \) Hz, 12H), 4.12 (t, \( J = 6.6 \) Hz, 18H, overlapped), 3.95 (t, \( J = 6.5 \) Hz, 6H), 2.19 – 2.14 (m, \( J = 7.2 \) Hz, 12H), 1.70 – 1.63 (m, 6H), 1.79 – 1.73 (m, 18H), 1.51 – 1.44 (m, 6H), 1.43 – 1.30 (m, 40H).

**\(^{13}\)C NMR (500 MHz, CD\(_3\)COCD\(_3\)):** \( \delta \) 160.1, 153.6, 153.5, 153.4, 140.6, 140.2, 137.9, 137.8, 114.6, 114.5, 103.1, 100.7, 99.2, 67.6, 64.2, 63.7, 29.8, 28.1, 25.9, 25.7.

**MALDI-TOF:** Calculated. [M+H] 1757.03148 calculated [M+H] 1757.03092.

2.6. Thiol-ene click reaction of dendrimer 5 with 1-octanethiol to form surface functionalized PUD 4

General procedure of thiol-ene click reaction using dendrimer 5 (117.6 mg, 0.067 mmol, 1.0 eq), 1-Octanethiol (139 µL, 0.803 mmol, 12.0 eq), AIBN (13.2 mg, 0.080 mmol, 1.2 eq), and dry DCM (0.6 mL) in a vial were placed under UV light at rt for 22h to afford highly viscous transparent oil as product (87.5 mg, 50% yield) on flash chromatography (10% EtOAc – 30% EtOAc/hexane).
2.7. Synthesis of dendron 6 via thiol-ene click reaction between 2 and 1-octadecanethiol

Generation-one wedge 2 (195.5 mg, 0.375 mmol, 1.0 eq) was dissolved in dry DCM (2 mL) in a regular vial charged with a magnetic stirrer. 1-Octadecanethiol (322.4 mg, 1.125 mmol, 3.0 eq) and AIBN (12.3 mg, 0.075 mmol, 0.2 eq) were added and vial was placed under UV light at rt for 20 h. Solvent was evaporated and crude was purified by silica gel chromatography using 4:1 hexane/EtOAc as mobile phase to get white waxy solid (350.0 mg, 85% yield).

m.p.: 69 °C
TLC (30% EtOAc in hexane): Rf 0.42
$^1$H NMR (500 MHz, CD$_3$COCD$_3$): δ 7.03 (s, 1H), 6.79 (s, 2H), 6.73 (s, 2H), 4.16 (t, $J = 6.6$ Hz, 4H), 3.94 (t, $J = 6.5$ Hz, 2H)), 3.66 (t, $J = 6.6$ Hz, 3H), 2.52 (t$_{overlapped}$, $J = 14.8$, 11.0 Hz, 8H), 1.77 – 1.27 (m, 102H), 0.90 (t, $J = 6.9$ Hz, 3H).
$^{13}$C NMR (500 MHz, CD$_3$COCD$_3$): δ 160.4, 153.5, 139.5, 100.8, 99.9, 68.1, 65.2, 63.1, 32.8, 32.2, 32.0, 31.9, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.2, 28.9, 28.6, 25.9, 25.7, 25.2, 22.7, 14.1
HRMS (ESI-MS): Calculated [M+H] 1091.8817 measured [M+H] 1091.8810
2.8. Attaching two different dendrons 3 and 6 to a core

Hexamethylene diisocyanate (34.2 µL, 0.214 mmol, 1.0 eq) was dissolved in anhydrous dichloromethane (0.5 mL) in an oven-dried 10 mL RB flask at 0 °C (ice bath) under nitrogen to which BF₃·OEt₂ (11 µL, 0.0428 mmol, 0.2 eq) was added and stirred the solution for 5 min at rt. Dendritic wedge 3 (208.3 mg, 0.257 mmol, 1.2 eq) and wedge 6 (280.4 mg, 0.257 mmol, 1.2 eq) in anhydrous dichloromethane (2.5 mL) was added dropwise to the stirring solution at 0 °C and stirring was continued for 5 min. The solution was warmed up to room temperature and stirred for 15 h. Progress of reaction was monitored using FTIR checking for disappearance of the NCO peak. Stirring was stopped, the solvent was evaporated, and the crude was purified by flash chromatography (5% EtOAc – 30% EtOAc in hexane, gradient elution). Three fractions were obtained as white solid product (198.0 mg, 72% yield) in the ratio of 1:2:1 by mass (45.0 mg, 99.1 mg, 53.9 mg) of dendrimers 7, 8, and 9 respectively.

Dendrimer 7

**m.p.:** 64-66 °C  
**TLC (30% EtOAc in hexane):** 7 (Rf = 0.20)
\( ^1\text{H NMR} (500 \text{ MHz, CD}_3\text{COCD}_3): \delta 8.58 (s, 4H, aromatic -NH-), 6.99 (s, 4H), 7.29 (s, 2H), 6.12 (s, 2H, aliphatic -NH-), 4.13 (t, \text{J} = 6.5 \text{ Hz, 8H}), 3.96 (t, \text{J} = 6.5 \text{ Hz, 8H}), 2.54 (t_{\text{overlapped}}, \text{J} = 8.8, 6.2 \text{ Hz, 16H}), 1.81 - 1.75 (m, 4H), 1.72 - 1.46 (m, 50H), 1.43 - 1.25 (m, 100H), 0.90 (t, \text{J} = 6.9 \text{ Hz, 12H}). \)

\( ^{13}\text{C NMR} (500 \text{ MHz, CD}_3\text{COCD}_3): \delta 160.1, 156.6, 153.6, 140.7, 100.8, 99.2, 66.6, 64.2, 63.8, 40.4, 31.8, 31.7, 31.6, 31.5, 29.86, 26.2, 25.9, 25.8, 25.0, 22.4, 13.5 \)

MALDI-TOF: Measured [M+H+K] 1829.18427 calculated [M+H+K] 1829.17646

Dendrimer 8
m.p.: 71-73 °C

TLC (30% EtOAc in hexane): 8 (R\(_f\) = 0.31)

\( ^1\text{H NMR} (500 \text{ MHz, CDCl}_3): \delta 7.04 (s, 2H), 6.79 (s, 4H), 6.71 (s, 4H, aromatic -NH-), 4.71 (s, 2H, aliphatic -NH-), 4.16 (t, \text{J} = 6.6 \text{ Hz, 8H}), 4.06 (t, \text{J} = 6.4 \text{ Hz, 4H}), 3.94 (t, \text{J} = 6.5 \text{ Hz, 4H}), 3.17 (q, \text{J} = 6.4 \text{ Hz, 4H}), 2.54 (dt, \text{J} = 14.8, 10.9 \text{ Hz, 16H}), 1.80 - 1.25 (m, 196H), 0.90 (t, \text{J} = 6.9 \text{ Hz, 12H}). \)

\( ^{13}\text{C NMR} (500 \text{ MHz, CDCl}_3): \delta 160.4, 156.9, 153.5, 139.5, 100.8, 99.9, 68.1, 65.1, 64.9, 40.8, 32.2, 32.0, 31.9, 31.8, 29.9, 29.7, 28.6, 29.5, 29.5, 29.3, 29.2, 29.1, 29.0, 28.9, 28.6, 26.3, 26.0, 25.9, 25.2, 22.7, 22.6, 14.1 \)

MALDI – TOF: Calculated [M+H] 2070.53302 measured [M+H] 2070.53209

Dendrimer 9
m.p.: 78-80 °C

TLC (30% EtOAc in hexane): 9 (R\(_f\) = 0.42)

\( ^1\text{H NMR} (500 \text{ MHz, CDCl}_3): \delta 7.04 (s, 2H), 6.79 (s, 4H), 6.71 (s, 4H, aromatic -NH-), 4.71 (s, 2H, aliphatic -NH-), 4.16 (t, \text{J} = 6.6 \text{ Hz, 8H}), 4.06 (t, \text{J} = 6.4 \text{ Hz, 4H}), 3.94 (t, \text{J} = 6.5 \text{ Hz, 4H}), 3.17 (q, \text{J} = 6.4 \text{ Hz, 4H}), 2.54 (dt, \text{J} = 14.8, 10.9 \text{ Hz, 16H}), 1.80 - 1.25 (m, 196H), 0.90 (t, \text{J} = 6.9 \text{ Hz, 12H}). \)

\( ^{13}\text{C NMR} (500 \text{ MHz, CDCl}_3): \delta 160.4, 156.9, 153.4, 139.5, 100.7, 99.8, 68.1, 65.1, 64.9, 40.8, 32.2, 32.0, 31.9, 31.8, 29.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.9, 28.6, 26.3, 26.0, 25.9, 25.2, 22.7, 22.6, 14.1 \)

MALDI – TOF: Calculated [M+H+Na] 2373.83633 measured [M+H+Na] 2373.82192

3. Copy of NMR spectra of synthesized compounds
Supplementary Figure S3. $^1$H NMR of phenolic diurethane 1 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S4. $^{13}$C NMR of phenolic diurethane 1 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S5. $^1$H NMR of diurethane phosphate (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S6. $^{13}$C NMR of diurethane phosphate (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S7. $^1$H COSY of phosphate compound (500MHz, CD$_3$COCD$_3$).
Supplementary Figure S8. $^1$H NMR of dimer of monourethane (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S9. $^{13}$C NMR of dimer of monourethane (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S10. $^1$H COSY of dimer of monourethane (500 MHz, CD$_3$COCD$_3$).
**Supplementary Figure S11.** $^{13}$C HSQC of dimer of monourethane (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S12. $^1$H NMR of dendron 2 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S13. $^{13}$C NMR of dendron 2 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S14. $^1$H NMR of thiol-ene clicked dendron 3 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S15. $^{13}$C NMR of thiol-ene clicked G-1 dendritic wedge, 3 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S16. $^1$H COSY of thiol-ene clicked dendron 3 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S17. $^{13}$C HSQC of thiol-ene clicked dendron 3 (500 MHz, CD$_3$COCD$_3$).
**Supplementary Figure S18.** $^1$H NMR of post-modified G-1 polyurethane dendrimer 4 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S19. $^{13}$C NMR of thiol-ene designed G-1 polyurethane dendrimer, 4 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S20. $^1$H COSY of thiol-ene designed G-1 polyurethane dendrimer, 4 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S21. $^{13}$C HSQC of thiol-ene designed G-1 polyurethane dendrimer, 4 (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S22. $^1$H NMR of G1 polyurethane dendrimer 5 with pentene periphery (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S23. $^{13}$C NMR of G-1 polyurethane dendrimer 5 with pentene periphery (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S24. $^1$H COSY of G-1 polyurethane dendrimer 5 with pentene periphery (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S25. $^{13}$C HSQC of G-1 polyurethane dendrimer 5 with pentene periphery (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S26. $^1$H NMR of pre-modified dendron 6 (500 MHz, CDCl$_3$).
Supplementary Figure S27. $^{13}$C NMR of pre-modified dendron 6 (500 MHz, CDCl$_3$).
Supplementary Figure S28. $^1$H NMR of thiol-ene designed G-1 polyurethane dendrimer 7 prepared from hexamethylene diisocyanate core (500 MHz, CD$_3$COCD$_3$).
**Supplementary Figure S29.** $^{13}$C NMR of thiol-ene designed G-1 polyurethane dendrimer 7 prepared from hexamethylene diisocyanate core (500 MHz, CD$_3$COCD$_3$).
Supplementary Figure S30. $^1$H NMR of thiol-ene designed G-1 polyurethane Janus dendrimer 8 prepared from hexamethylene diisocyanate core (500 MHz, CDCl$_3$).
Supplementary Figure S31. $^{13}$C NMR of thiol-ene designed G-1 polyurethane Janus dendrimer 8 prepared from hexamethylene diisocyanate core (500 MHz, CDCl$_3$).
Supplementary Figure S32. $^1$H NMR of thiol-ene designed G-1 polyurethane dendrimer 9 prepared from hexamethylene diisocyanate core (500 MHz, CDCl$_3$).
Supplementary Figure S33. $^{13}$C NMR of thiol-ene designed G-1 polyurethane dendrimer 9 prepared from hexamethylene diisocyanate core (500 MHz, CDCl$_3$).

4. Copy of mass spectra of synthesized compounds
**Supplementary Figure S34.** HRMS spectra of phenolic diurethane, 1.

Calculated M+Na 371.1577  
Measured M+Na 371.1573  
1.1ppm

![HRMS spectra of phenolic diurethane, 1.](image1)

**Supplementary Figure S35.** HRMS spectra of dendron, 2.

Calculated M+H 519.3429  
Measured M+H 519.3421  
1.5ppm

![HRMS spectra of dendron, 2.](image2)
**Supplementary Figure S36.** HRMS spectra of thiol-ene clicked dendron, 3.

Calculated M+H 811.5687
Measured M+H 811.5675
1.5ppm

**Supplementary Figure S37.** HRMS spectra of thiol-ene clicked dendron, 6.

Calculated M+H 1091.8817
Measured M+H 1091.8810
0.6ppm
Supplementary Figure S38. MALDI spectra of dendrimer 5.

Supplementary Figure S39. MALDI spectra of dendrimer 4.
Supplementary Figure S40. MALDI spectra of dendrimer 7.
Supplementary Figure S41. MALDI spectra of Janus dendrimer 8.
Supplementary Figure S42. MALDI spectra of Janus dendrimer 9.

5. References

1. Davis, M. C. Safer Conditions for the Curtius Rearrangement of 1,3,5-Benzene-tricarboxylic Acid, *Synth Commun.* 2007, 37, 3519-3528.
