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for the Preparation
of Organic Compounds

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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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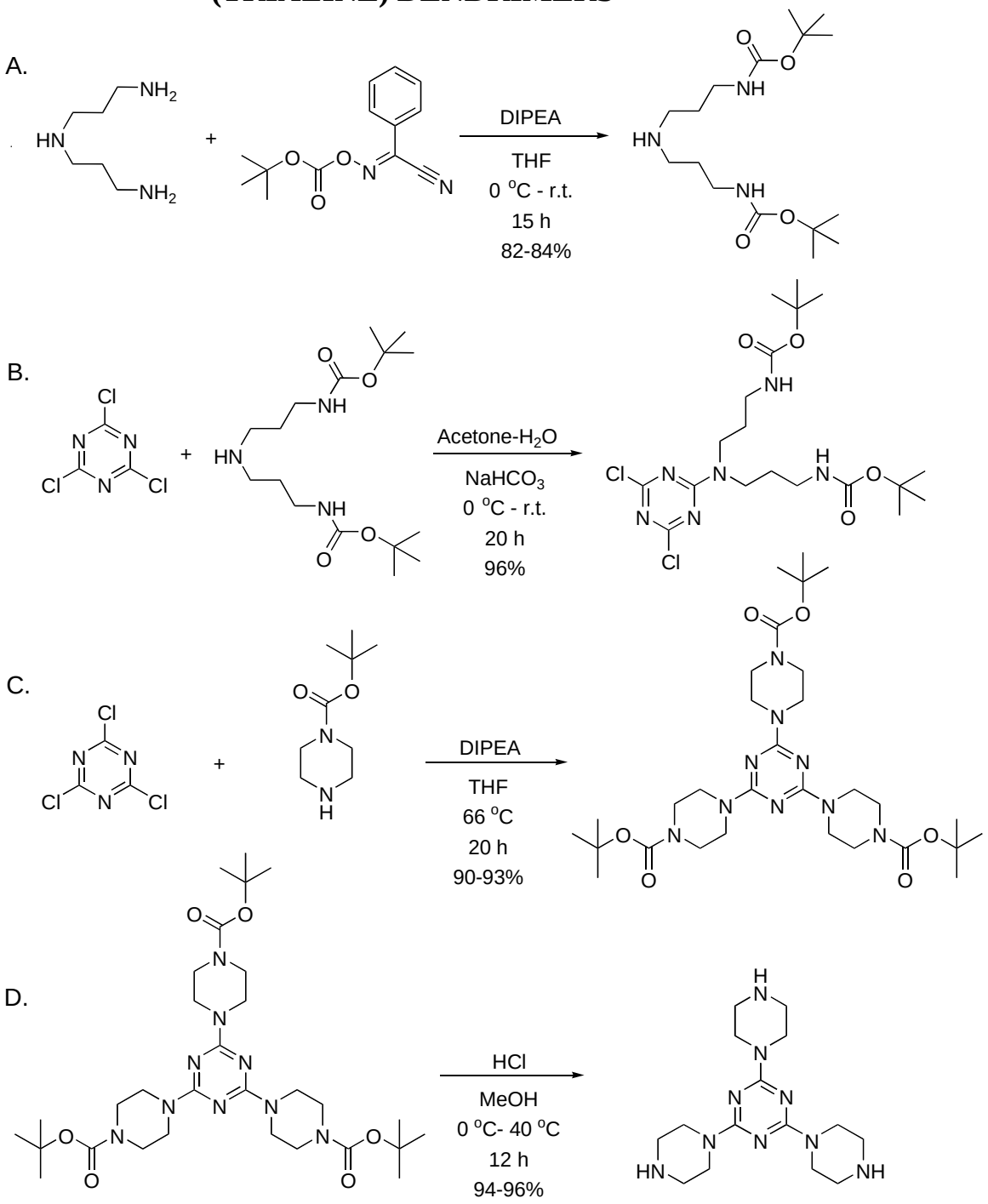
SYNTHESIS OF 2-[3,3'-DI-(*TERT*-BUTOXYCARBONYL)-AMINODIPROPYLAMINE]-4,6,-DICHLORO-1,3,5-TRIAZINE AS A MONOMER AND 1,3,5-[*TRIS*-PIPERAZINE]-TRIAZINE AS A CORE FOR THE LARGE SCALE SYNTHESIS OF MELAMINE (TRIAZINE) DENDRIMERS



Submitted by Abdellatif Chouai, Vincent J. Venditto, and Eric E. Simanek.[1]
Checked by Ruth E. McDermott and John A. Ragan.

1. Procedure

Caution! Cyanuric chloride is a lachrymator and causes burns on contact with the skin. All operations with this reagent should be carried out in a well-ventilated hood.

A. 3,3'-Di-(tert-butoxycarbonyl)-aminodipropylamine. A 1-L, three-necked, round-bottomed flask equipped with a magnetic stirrer, a 500-mL addition funnel, a temperature probe and a static nitrogen inlet is charged with 3,3'-diaminodipropylamine (28.2 mL, 0.20 mol, 1.0 equiv) (Note 1), 300 mL of tetrahydrofuran (Note 1), and *N*,*N*-diisopropylethylamine (100 mL, 0.57 mol, 2.8 equiv) (Note 1). A 500-mL Erlenmeyer flask is charged with 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile (BOC-ON) (100 g, 0.41 mol, 2.0 equiv) (Note 1) and 300 mL of tetrahydrofuran. The resulting solutions are separately stirred at 0 °C for 30 min (Note 2). The BOC-ON solution is then transferred to the addition funnel and added dropwise to the solution of 3,3'-diaminodipropylamine over a 90-100 min period. After addition is complete, the solution is left to stir at 0 °C for 3 h, warmed to ambient temperature, and left to stir for an additional 20 h. The solvent is removed using a rotary evaporator at 39 °C (Note 3) and the residue is dissolved in 400 mL of dichloromethane (Note 1). The organic solution is washed with 10% NaOH (3 x 200 mL) (Notes 1 and 4), a saturated, aqueous solution of sodium chloride (1 x 300 mL) (Note 1), and dried over sodium sulfate (Note 1). Following filtration, the solvent is removed using a rotary evaporator at 32–39°C (Note 3) to afford the product as an oily material which is precipitated as an off-white solid by addition of hexane (500 mL) (Note 1) and traces of MeOH (3 mL) (Note 1). After standing in the freezer for 24 h, the solids are filtered, washed with hexane, and dried under vacuum overnight to provide the product as an off-white solid (54.2–55.9 g, 82–84 %), mp 68.1–70.0 °C (Notes 5 and 6).

B. 2-[3,3'-Di-(tert-Butoxycarbonyl)-aminodipropylamine]-4,6-dichloro-1,3,5-triazine. A 3-L, three-necked, round-bottomed flask equipped with a mechanical stirrer, static nitrogen inlet and 1-L addition funnel is charged with cyanuric chloride (30.5 g, 0.165 mol, 1.00 equiv) (Note 1) and 300 mL of acetone (Note 1). The resulting solution is left to stir at 0 ºC for 1 h (Note 7). A cooled solution of 3,3'-di-(*tert*-butoxycarbonyl)-aminodipropylamine (54.9 g, 0.166 mol, 1.01 equivalent) in acetone (686

mL) is then added dropwise to the cyanuric chloride solution over a period of 3 h (the internal temperature remained at or below 2 ºC during this addition). A white suspension forms during the course of addition. Sodium bicarbonate (13.9 g, 0.166 mol, 1.00 equiv) (Note 1) in water (195 mL) is added dropwise over a period of 1 h. A yellow mixture is obtained after complete addition. The resulting solution is left to stir at 0 ºC for 3 h, which resulted in the formation of a white suspension. The mixture is allowed to warm to ambient temperature and stirred for an additional 15 h. The reaction mixture is concentrated without filtration (to approximately 200 mL) on a rotary evaporator at 31–40 °C (Note 3). The resulting aqueous suspension is filtered. The solids are dissolved in 600 mL of dichloromethane (Note 1). The organic phase is washed with water (3 x 250 mL), and a saturated, aqueous solution of sodium chloride (300 mL) (Note 1). The organic layer is dried with sodium sulfate (Note 1), filtered, and the solvent is concentrated using a rotary evaporator at 40 °C (Note 3). The resulting solids are dried under vacuum (Note 5) to provide the product as an off-white solid (76.5 g, 0.160 mol, 96 %), mp 122.4-125.7 °C (Notes 8, 9 and 10).

C. 1,3,5-[Tris-N-(*tert*-butoxycarbonyl)-*piperazine]-triazine***.** A 2-L, three-necked, round-bottomed flask equipped with a magnetic stirrer**,** reflux condenser, temperature probe, glass stopper and static nitrogen inlet is charged with cyanuric chloride (10.0 g, 54.2 mmol, 1.00 equiv) (Note 1) and tetrahydrofuran (1 L) (Note 1?). *N*-(*tert*-Butoxycarbonyl)-piperazine (34.0 g, 183 mmol, 3.38 equiv) (Note 1) is added in ~10 g portions over 17 min (during the addition, the temperature rose from 20 to 28 °C; an ambient temperature water bath was used to moderate the exotherm). White solids are formed in the reaction mixture during the addition of the piperazine. *N*,*N*-Diisopropylethylamine (96.2 mL, 552 mmol, 10.2 equiv) (Note 1) is added, and the reaction mixture is stirred at ambient temperature for 1 h, then heated to an internal temperature of 66 °C for 20 h at which point the reaction was judged to be complete by HPLC (Note 11). Upon cooling to ambient temperature, a white precipitate forms (Note 12). The solvent is removed using a rotary evaporator at 31 °C (Note 3). The white residue is taken up in dichloromethane (300 mL) (Note 1) and washed with water (2 x 150 mL), 10% $NaHSO_4$ (2 x 150 mL) and a saturated, aqueous solution of sodium chloride (2 x 100 mL) (Note 1). The organic layer is dried over anhydrous sodium sulfate (Note 1), filtered, and the solvent is removed using a rotary evaporator at 35–41 °C (Note 3). The resulting white solids

are granulated in EtOAc (35 mL, ca. 1 mL/g) (Note 1) to yield a white crystalline material (31.0–32.0 g, 90–93 %), mp 223.4–226.1 °C (Note 13).

*D. 1,3,5-[Tris-piperazine]-triazine***.** A 1-L, three-necked, round-bottomed flask, fitted with a magnetic stirrer, condenser, nitrogen inlet, and 250 mL addition funnel is charged with 1,3,5-[*N*-(*tert*-butoxycarbonyl)-piperazine]-triazine (27.9 g, 44.1 mmol, 1.00 equiv) and 286 mL of methanol (Note 1). The solution is left to stir at 0 °C for 30 min. A solution of 153 mL (0.918 mol, 21 equiv) of 6N hydrochloric acid (Note 1) is then added over 70 min keeping the temperature at ~ 1 °C and the resulting light yellow slurry is left to stir at 0 °C for 2 h (Note 2). The reaction slurry is then allowed to warm to ambient temperature over 3 h and then slowly heated to an internal temperature of 40 °C for 12 h (the slurry became homogeneous at 27 °C). Off-gassing was observed as the temperature increased. The volatile organic components are removed using a rotary evaporator 34–40 °C (Note 3) until only ca. 100 mL of water remains. The resulting aqueous solution is cooled to 0 °C and made alkaline (pH = 14) by addition of 237 mL (657 mmol, 15 equiv) of a 10% NaOH solution (Note 1). The resulting alkaline solution is extracted with chloroform (3 x 250 mL) (Note 1), and the organic phases are combined and dried over sodium sulfate (Note 1). The solvent is filtered and evaporated at 34 °C (Note 3) to afford the product as a white solid (14.1 g, 96 %), mp 200–208 °C (Notes 14 and 15).

2. Notes

1. All solvents and reagents were purchased from commercial suppliers and used as received. Acetone (99.5%), 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile (BOC-ON), chloroform (99.8%), 3,3'-diaminodipropylamine (98%), dichloromethane (99.6%), *N*,*N*-diisopropylethylamine (99%), methanol (99.8%), sodium chloride, sodium sulfate (anhydrous) and tetrahydrofuran (99.9%, anhydrous) were purchased from Sigma-Aldrich. Cyanuric chloride was purchased from Alfa Aesar. *N*-Boc-piperazine was purchased from AK Scientific. Hydrochloric acid and sodium bicarbonate were purchased from J. T. Baker. Sodium hydroxide was purchased from Fisher Scientific. Hexanes (98.5%) were purchased from Mallinckrodt.

2. All reactions were performed in an ambient-temperature lab (ca. 23 °C). The submitters performed all experiments in a walk-in cold room (0 °C).

3. All solvent evaporations were performed using a rotary evaporator using appropriate temperature and pressure to afford efficient concentration (THF: 75-150 mmHg; CH_2Cl_2: 200-300 mmHg; acetone: 200-300 mmHg; $CHCl_3$ and methanol: 15-75 mmHg).

4. The first and second extractions resulted in a yellow aqueous solution (color of the byproduct of BOC-ON), while the third extraction gave a clear aqueous solution.

5. All products were dried using a Büchi vacuum pump with a vacuum pressure of 76 mmHg.

6. The product has the following spectral characteristics: TLC R_f = 0.0 (silica gel 60 $F_{254,}$ EMD Chemicals, Inc. in 5:95 methanol:dichloromethane); IR (neat) cm^{-1}: 3342, 2975, 2931, 1686, 1518, 1365, 1273, 1250, 1168; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.41 (s, 18 H), 1.60–1.66 (m, 4 H), 2.63 (t, 4 H, *J* = 6.6), 3.15–3.20 (br, 4 H), 5.2 (br, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.4(s), 29.7 (s), 38.9 (s), 47.4 (s), 78.9 (s), 156.1 (s); MS (CI), *m/z* 332.2 (M+H). Anal. Calcd for $C_{16}H_{33}N_3O_4$: C, 57.98; H, 10.04; N, 12.68. Found: C, 57.86; H, 9.84; N, 12.51.

7. The submitters noted that after 1 h at 0 °C, undissolved cyanuric chloride remained visible in the reaction flask (estimated at 10–20% of the initial charge). The presence of this material does not adversely affect the reaction. The checkers observed a homogeneous solution at this stage.

8. During melting point determination, some bubbling was observed above 125 °C.

9. The product has the following characteristics: TLC R_f = 0.3 (silica gel 60 $F_{254,}$ EMD Chemicals, Inc. in 5% methanol:dichloromethane); IR (neat) cm^{-1}: 3349, 2976, 1691, 1573, 1475, 1233, 1160, 847, 733; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.41 (s, 18 H), 1.77 (tt, apparent quintet, 4 H, *J* = 6.6), 3.07-3.12 (br/quartet-depending on sample concentration, 4 H), 3.60 (t, 4 H, *J* = 7.1), 5.05 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 27.7 (s), 28.3 (s), 37.3 (s), 44.9 (s), 79.3 (s), 156.0 (s), 164.7 (s), 170.1 (s); MS (CI): *m/z* 479, 379. Anal. Calcd for $C_{19}H_{32}Cl_2N_6O_4$: C, 47.60; H, 6.73; N, 17.54; Cl, 14.79. Found: C, 47.87; H, 6.82; N, 17.48; Cl, 14.47.

10. In a second run using 53.2 g of the starting di-(BOC)-dipropylamine, 71.5 g of product was obtained (93%).

11. The reaction was monitored by HPLC on a 4.6 x 50 Zorbax C-8 column at 30 °C with a flow rate 0.7 mL per min of eluent composed of 95% of 0.5% $HClO_4$ and 5% ACN. RT cyanuric chloride = 6.68 min, RT product =11.54 min. Also TLC (silica gel, 5% methanol:dichloromethane), R_f (product) = 0.35, Silica Gel 60 $F_{254,}$ EMD Chemicals, Inc.

12. The precipitate corresponds to the formation of the hydrochloride salt of *N*,*N*-diisopropyl ethylamine.

13. The product has the following characteristics: TLC, R_f 0.35 (silica gel 60 $F_{254,}$ EMD Chemicals, Inc. in 5% methanol:dichloromethane); IR (neat) cm^{-1}: 1679, 1535, 1419, 1227, 998, 725; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.46 (s, 27 H), 3.42 (m, 12 H), 3.72 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 28.4, 43.0, 79.9, 154.8, 165.2; MS (CI) *m/z* 634.3; Anal. Calcd for $C_{30}H_{51}N_9O_6$: C, 56.85; H, 8.11; N, 19.89. Found: C, 56.69; H, 8.26; N, 19.82.

14. In a second run, 29.2 g of starting triazine provided 14.5 g of product (94%).

15. The product has the following characteristics: TLC R_f = 0.0 (silica gel 60 $F_{254,}$ EMD Chemicals, Inc. in 10% methanol:dichloromethane); IR (neat) cm^{-1}: 3278, 2846, 1523, 1433, 1242, 1007, 806, 728; ^1H NMR (400 MHz, $CDCl_3$) δ: 1.62 (s, 3 H), 2.81 (t, 12 H, *J* = 5.0), 3.68 (t, 12 H, *J* = 5.0); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 44.3, 46.0, 165.2; MS (CI) *m/z* 334.4 Anal. Calcd for $C_{15}H_{27}N_9$: C, 54.03; H, 8.16; N, 37.81. Found: C, 53.72; H, 8.32; N, 37.48.

Safety and Waste Disposal Information

All hazardous materials should be handled and disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

3. Discussion

s-Triazines have seen applications as precursors for polymers,[2] as scavenging resins in organic manipulations,[3] as components of host–guest assemblies,[4] as ligand scaffolds for catalysis,[5] and in medicinal chemistry.[6] The appeal of the *s*-triazine core is largely due to the ease of systematic substitution of the chlorine atoms with amine nucleophiles to generate a variety of structures. Consecutive substitution reactions with amine

nucleophiles can proceed in a one-pot procedure: the first substitution on cyanuric chloride occurs in minutes at 0 °C; the second substitution occurs in 12–24 hours at ambient temperature; the third substitution typically occurs in 12–24 hours and requires temperatures above 80 °C.[7]

Our interest in *s*-triazines derives from their use in dendrimer synthesis.[8] Triazine dendrimers offer distinct advantages including tractable syntheses and reactivity that can be efficiently manipulated in a stepwise manner to construct pure monodisperse products with unique compositional diversity.[9] This paper describes the use of 1,3,5-triazine in the synthesis of 2-[3,3'-di-(tert-butoxycarbonyl)-aminodipropylamine]-4,6,-dichloro-1,3,5-triazine as a building block and 1,3,5-[*tris*-piperazine]-triazine as a core.

The building block, a dichloro-1,3,5-triazine substituted with a branching group presenting two Boc-protected amines, is available in 96% overall yield from the reaction of cyanuric chloride with 3,3'-di-(*tert*-butoxycarbonyl)-aminodipropylamine in acetone-water, without chromatographic purification. The latter is prepared from the reaction of 3,3'-diaminodipropylamine with BOC-ON in THF under simple experimental conditions. This building block can be regarded as AB_2B' (where A is the first chloride displaced via nucleophilic aromatic substitution, B' is the second chloride to be displaced, and B represents the BOC-protected amines). It undergoes clean, stepwise nucleophilic aromatic substitution (S_NAr) reactions to afford intermediate monochlorotriazine bearing macromolecules.

The synthesis of the core proceeds by the reaction of cyanuric chloride with *N*-(*tert*-butoxycarbonyl)-piperazine in THF at 66 °C in the presence of *N*,*N*-diisopropyl ethylamine at moderate reaction times (16 h) (Step C). Cleavage of the BOC-group using 6N hydrochloric acid in methanol at 0 °C for 3 h and at room temperature for 12 h followed by neutralization affords the desired product in high yield (Step D). The synthesis of higher generation dendrimers relies on iterative addition of the AB_2B' building block to core structure followed by capping and deprotection steps.[10]

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2. (a) Hirschberg, J. H. K. K.; Ramzi, A.; Sijbesma, R. P.; Meijer, E. W.; *Macromolecules* **2003**, *36*, 1429-1432. (b) Berl, V.; Schmutz, M.; Krische, M. J.; Khoury, R. G.; Lehn, J. -M. *Chem. Eur. J.* **2002**, *8*,

1227-1244. (c) Choi, I. S.; Li, X.; Simanek, E. E.; Akaba, R.; Whitesides, G. W. *Chem. Mater*. **1999**, *11*, 684-690.

3. Marsh, A., Carlisle, S. J.; Smith, S.C . *Tetrahedron Lett.* **2001**, *42*, 493-496.

4. (a) Linton, B.; Hamilton, A. D. *Curr. Opin. Chem. Biol.* **1999**, *3***,** 307-312. (c) Simanek, E. E.; Isaacs, L.; Li, X.; Wang, C. C. C.; Whitesides, G. W. *J. Org. Chem.* **1997**, *62*, 8994-9000.

5. (a) Gamez, P.; de Hoog, P.; Lutz, M.; Spek, A. L.; Reedijk, J. *Inorg. Chim. Acta* **2003**, *351*, 319-325. (b) Britovsek, G. J. P.; Gibson, V. C.; Hoarau, O. D.; Spitzmesser, S. K.; White, A. J. P.; Williams, .; D. J. *Inorg. Chem.* **2003**, *42*, 3454-3465.

6. (a) Pattarawarapan, M.; Reyes, S.; Xia, Z.; Zaccaro, M. C.; Saragovi, H. U.; Burgess, K. *J. Med. Chem.* **2003**, *46*, 3565-3567. (b) Pitts, W. J.; Guo, J.; Dhar, T. G. M.; Shen, Z.; Gu, H. H.; Watterson, S. H.; Bednarz, M. S.; Chen, B. –C.; Barrish, J. C.; Bassolino, D.; Cheney, D.; Fleener, C. A.; Rouleau, K. A.; Hollenbaugh, D. L.; Iwanowicz, E. J. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 2137-2140.

7. (a) Blotny, G. *Tetrahedron* **2006**, *62*, 9507-9522 and references therein. (b) Steffensen, M. B.; Hollink, E.; Kuschel, F.; Bauer, M.; Simanek, E. E. *J. Polym. Sci., Part A: Polym. Chem*. **2006**, *44*, 3411-3433. (c) Steffensen, M. B.; Simanek, E. E. *Org. Lett.* **2003**, *5*, 2359-2361. (d) Chen, H. –T.; Neerman, M. F.; Parrish, A. R.; Simanek, E. E. *J. Am. Chem. Soc.* **2004**, *126*, 10044-10048. (e) Umali, A. P.; Simanek, E. E. *Org. Lett*. **2003**, *5*, 1245-1247. (f) Cuthbertson, W. W.; Moffatt, J. S. *J. Chem. Soc.* **1948**, 561-564.

8. (a) Hollink, E.; Simanek, E. E. *Org. Lett.* **2006**, *8*, 2293-2295. (b) Chouai, A.; Simanek, E.E.; *J. Org. Chem.* **2008**, *73*, 2357-2366.

9. (a) Lim, J.; Simanek, E.E. *Org. Lett.* **2008**, *10*, 201-204. (b) Steffensen, M.B.; Simanek, E.E. *Angew. Chem. Int. Ed.* **2004**, *43*, 5178-5180.

10. Crampton, H.; Hollink, E.; Perez, L. M.; Simanek, E. E. *New J. Chem.***2007**, *31*, 1283-1290.

Appendix
Chemical Abstracts Nomenclature; (Registry Number)

3,3’-Diaminodipropylamine; (56-18-8)

2-(*tert*-Butoxycarbonyloxyimino)-2-phenylacetonitrile; (58632-95-4)

Cyanuric chloride; (108-77-0)

N-(*tert*-Butoxycarbonyl)-piperazine; (57260-71-6)

N,*N*-Diisopropyl ethylamine; (7087-68-5)

2-[3,3'-Di-(*tert*-butoxycarbonyl)-aminodipropylamine]-4,6-dichloro-1,3,5-triazine; 12-Oxa-2,6,10-triazatetradecanoic acid, 6-(4,6-dichloro-1,3,5-triazin-2-yl)-13,13-dimethyl-11-oxo-, 1,1-dimethylethyl ester; (947602-03-1)

1,3,5-[Tris-piperazine]-triazine: 1,3,5-Triazine, 2,4,6-tri-1-piperazinyl-; (19142-26-8)

Eric E. Simanek was born in 1969 in Tuscola, IL. He obtained a B.S. in Chemistry in 1991 from the University of Illinois at Urbana-Champaign while working in the laboratories of the late Dr. Kenneth L. Rinehart, Jr. After completing doctoral studies with Dr. George M. Whitesides at Harvard University in 1997, he joined Dr. Chi-Huey Wong's laboratory at The Scripps Research Institute. Since joining Texas A&M University in 1998, he has risen through the ranks to Professor of Chemistry. His interests lie in drug delivery and K-20 education.

Abdellatif Chouai was born in 1971 in Morocco. He earned a B.S. in Chemistry in 1995 from the University of Sidi Mohamed Ben Abdellah, Morocco, and a Ph.D. in Organic Chemistry from University of Houston in 2003 under Dr. Randolph P. Thummel. He joined Dr. Kim R. Dunbar's group at Texas A&M University as a postdoctoral research associate where he worked on reversible DNA biosensors complexes and bimetallic complexes as photodynamic therapy agents. He then moved to a research scientist position in 2006 in Dr. Simanek's laboratory. His research focused on an industrial scale production of triazine-based dendrimers and application in drug delivery. Currently, Dr. Chouai holds a professional development chemist position with BASF Corporation.

Vincent J. Venditto was born in 1981 in Philadelphia, PA. He earned a B.S. in Chemistry from Gettysburg College in 2003 and began working in the laboratory of Dr. Martin W. Brechbiel in the Radioimmune and Inorganic Chemistry Section of the National Cancer Institute within the NIH. After two years at the NIH, Vincent joined of Dr.Simanek's laboratory at Texas A&M University to pursue a graduate degree in chemistry. His graduate work focuses on the synthesis of triazine-based dendrimers as drug carriers for a range of therapeutic applications.

Ruth McDermott was born in Boston, MA and received a B.S. in Chemistry from the University of Massachusetts at Boston. She completed her undergraduate research under the direction of J.-P. Anselme. She is currently part of the Chemical Research and Development group at Pfizer in Groton, CT where she has been employed for 20 years. She enjoys photography and participating in short-term mission trips in the US and abroad.

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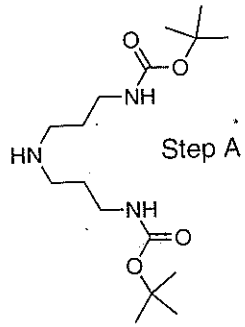

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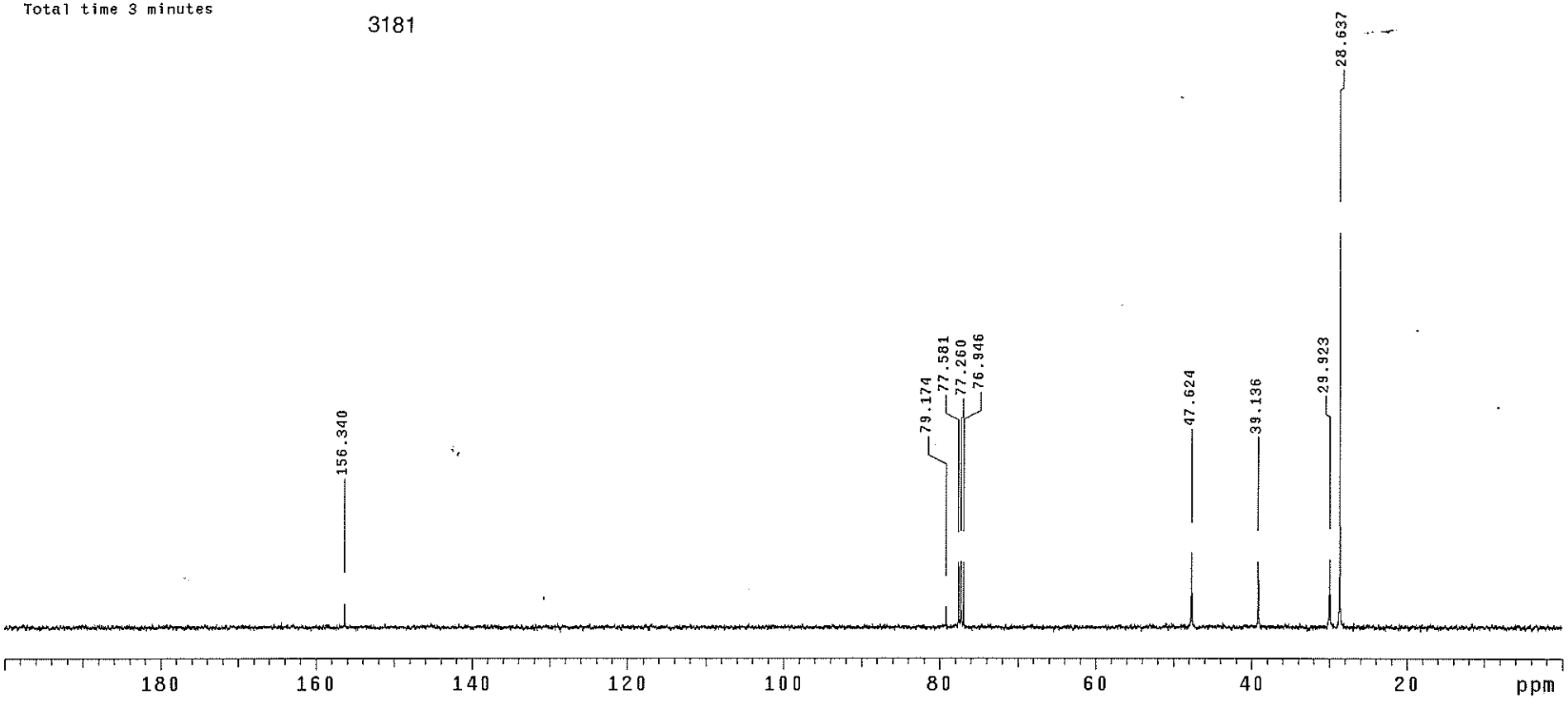

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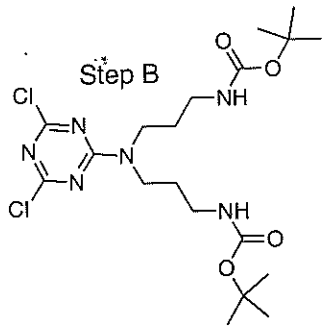

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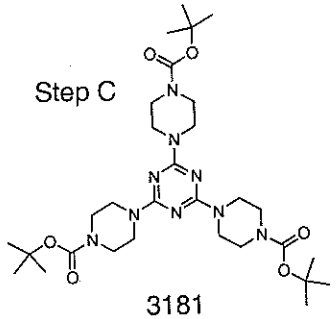
Total time 6 minutes

Step C



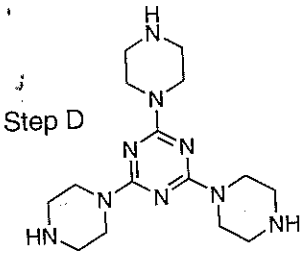
3181

GAINS_SAMPLE_REFERENCE: 116349-110-c
GAINS_USER_ID: mcdermottre
GAINS_INSTRUMENT: unityc
GAINS_EXPERIMENT_TIME: 02/27/2008 08:36:33
GAINS_END_TIME: 02/27/2008 08:37:36

116349-110
isol sol in CDCl3

Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
UNITYplus-400
PULSE SEQUENCE
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 0.664 sec
Width 24668.5 Hz
256 repetitions
OBSERVE C13, 100.6736235 MHz
DECOUPLE H1, 400.3741134 MHz
Power 37 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 2.0 Hz
FT size 65536
Total time 3 minutes

Step D



3181

Filename: 116349-110-c_c13.fid

unityc: 080227

GAINS_SAMPLE_REFERENCE: 116349-104-1
GAINS_USER_ID: mcdermottre
GAINS_INSTRUMENT: unityb
GAINS_EXPERIMENT_TIME: 02/20/2008 11:26:44
GAINS_END_TIME: 02/20/2008 11:27:38

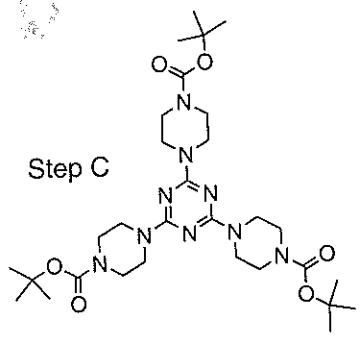
116349-104-1

Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
UNITYplus-400
PULSE SEQUENCE
Pulse 45.0 degrees
Acq. time 2.410 sec
Width 6799.3 Hz
16 repetitions
OBSERVE H1, 399.9506330 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 minute

Filename: 116349-104-1_H1.fid

unityb: 080220

Step C



3181

GAINS_SAMPLE_REFERENCE= 116349-104-1

Filename: 116349-104-1_H1.fid

unityb: 080220

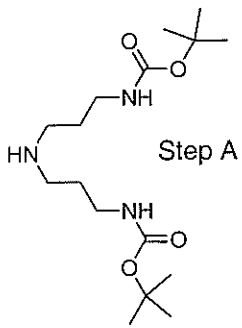
INDEX	FREQUENCY	PPM	HEIGHT
1	2897.509	7.245	158.5
2	2112.709	5.282	14.6
3	1491.426	3.729	105.3
4	1486.860	3.718	151.2
5	1481.880	3.705	117.4
6	1373.145	3.433	117.3
7	1368.580	3.422	149.5
8	796.684	1.992	14.8
9	646.032	1.615	7.7
10	629.847	1.575	13.4
11	604.116	1.510	4.1
12	583.365	1.459	1843.1
13	575.894	1.440	40.6
14	563.029	1.408	25.1
15	543.108	1.358	6.8
16	519.452	1.299	7.4
17	492.891	1.232	2.7
18	19.769	0.049	4.0

3181 C

GAINS_SAMPLE_REFERENCE: 116349-113-1
GAINS_USER_ID: mcdermottre
GAINS_INSTRUMENT: unityc
GAINS_EXPERIMENT_TIME: 03/10/2008 09:38:17
GAINS_END_TIME: 03/10/2008 09:39:12

116349-113-1

Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
UNITYplus-400
PULSE SEQUENCE
Pulse 45.0 degrees
Acq. time 2.407 sec
Width 6806.2 Hz
16 repetitions
OBSERVE H1, 400.3721116 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 minute



Step A

3181

Filename: 116349-113-1_h1.fid

unityc: 080310

GAINS_SAMPLE_REFERENCE= 116349-113-1

Filename: 116349-113-1_h1.fid

unityc: 080310

INDEX	FREQUENCY	PPM	HEIGHT
1	2900.084	7.243	17.3
2	2107.835	5.265	3.1
3	2089.971	5.220	22.3
4	1277.781	3.191	23.9
5	1271.965	3.177	57.6
6	1265.733	3.161	60.5
7	1259.917	3.147	29.4
8	1050.949	2.625	75.1
9	1044.718	2.609	151.2
10	1038.071	2.593	79.7
11	854.445	2.134	13.7
12	655.864	1.638	18.7
13	649.632	1.623	60.4
14	642.985	1.606	84.1
15	636.753	1.590	57.1
16	630.522	1.575	17.1
17	622.628	1.555	6.6
18	601.025	1.501	2.8
19	572.775	1.431	39.0
20	559.896	1.398	908.2
21	537.462	1.342	4.1
22	495.918	1.239	7.0
23	488.440	1.220	4.5
24	475.146	1.187	5.7
25	336.388	0.840	2.1

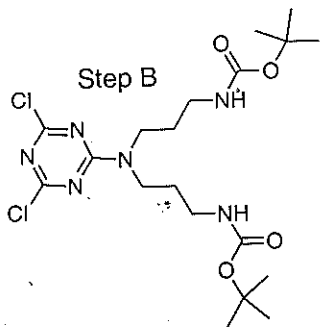
3181

A

GAINS_SAMPLE_REFERENCE: 116349-119
GAINS_USER_ID: mcdermottre
GAINS_INSTRUMENT: unityc
GAINS_EXPERIMENT_TIME: 03/12/2008 08:09:00
GAINS_END_TIME: 03/12/2008 08:09:54

116349-119
isol prod

Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
UNITYplus-400
PULSE SEQUENCE
Pulse 45.0 degrees
Acq. time 2.407 sec
Width 6806.2 Hz
16 repetitions
OBSERVE H1, 400.3721116 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 minute



3181

Filename: 116349-119_h1.fid

unityc: 080312

GAINS_SAMPLE_REFERENCE= 116349-119

Filename: 116349-119_h1.fid

unityc: 080312

INDEX	FREQUENCY	PPM	HEIGHT
1	2900.084	7.243	38.0
2	2110.328	5.271	5.4
3	2022.669	5.052	33.0
4	1446.866	3.614	75.0
5	1439.803	3.596	151.2
6	1432.741	3.579	78.7
7	1248.700	3.119	33.9
8	1242.468	3.103	85.3
9	1236.652	3.089	89.5
10	1230.420	3.073	42.0
11	722.334	1.804	23.7
12	715.687	1.788	83.4
13	709.040	1.771	112.9
14	702.393	1.754	75.9
15	695.746	1.738	22.2
16	627.613	1.568	7.1
17	575.268	1.437	55.1
18	564.882	1.411	1480.6
19	500.904	1.251	7.7

3181 B

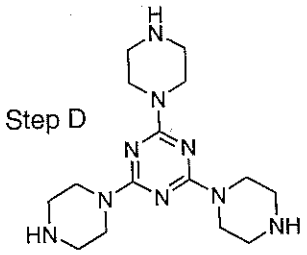
GAINS_SAMPLE_REFERENCE: 116349-110-c
GAINS_USER_ID: mcdermottre
GAINS_INSTRUMENT: unityc
GAINS_EXPERIMENT_TIME: 02/27/2008 08:34:25
GAINS_END_TIME: 02/27/2008 08:35:21

116349-110
isol sol in CDCl3

Pulse Sequence: s2pul
Solvent: cdcl3
Ambient temperature
UNITYplus-400

PULSE SEQUENCE
Pulse 45.0 degrees
Acq. time 2.407 sec
Width 6806.2 Hz
16 repetitions
OBSERVE H1, 400.3721116 MHz
DATA PROCESSING
Line broadening 0.1 Hz
FT size 32768
Total time 1 minute

Step D



3181

Filename: 116349-110-c_h1.fid

unityc: 080227

GAINS_SAMPLE_REFERENCE= 116349-110-c

3181 D

Filename: 116349-110-c_h1.fid

unityc: 080227

INDEX	FREQUENCY	PPM	HEIGHT
1	2900.499	7.245	15.6
2	1479.686	3.696	113.8
3	1474.701	3.683	147.8
4	1469.715	3.671	117.7
5	1132.376	2.828	122.9
6	1127.391	2.816	151.2
7	1122.405	2.803	116.8
8	668.742	1.670	77.6