Tetraoxaspiroalkanes for Polymerization Stress Reduction of Silorane Resins

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ABSTRACT: This study involved the synthesis and characterization of tetraoxaspiroalkane monomers and evaluated their potential to reduce polymerization stress when formulated in a Silorane resin system. The tetraoxaspiroalkane monomers had two main structural features (a) two different types of core ring structures (a 1,5,7,11-tetraoxaspirocyclic ring or a 2,4,8,10-tetraoxaspirocyclic ring) and (b) four different types of ring substituents (normal alkyl, allyloxyalkyl, trimethylsilylalkyl, or oxabicycloalkyl). The resin formulations contained (a) 20 mol % of a 1,5,7,11- or 2,4,8,10-tetraoxaspiroalkyl monomer; (b) a phenylmethylsilane containing two oxabicycloheptyl groups; (c) a cyclotetrasiloxane containing four oxabicycloheptyl groups; and (d) a photocationic initiator system. Three main aspects were studied (a) the photoreactivity of the formulations using PDSC, (b) photopolymerization stress, and (c) mechanical properties (flexural elastic modulus, ultimate strength, and work of fracture) which were measured using an electromagnetic mechanical testing machine. The main findings were (a) formulations containing 2,4,8,10-tetraoxaspiroalkane monomers had measured net enthalpies greater than those containing 1,5,7,11-tetraoxaspiroalkane monomers, and above those calculated for addition of an inert diluent; (b) all formulations containing tetraoxaspiroalkane monomers exhibited photopolymerization stress values that were 40–99% less than the nonaddition control; (c) the formulation containing a 1,5,7,11-tetraoxaspiroalkane monomer with an oxirane functionality had mechanical properties that were not significantly different from the nonaddition control. J Appl Polym Sci 108: 3738–3747, 2008

Key words: cationic polymerization; dental polymers; stress; mechanical properties; synthesis

INTRODUCTION

The development of stress is inherent in most polymerization reactions because of volume contraction. Stress is found within the hardened (cured) product as well as externally between bonded surfaces.[1] For dental materials, this results in decreased longevity of the composite restorative as well as marginal discontinuity.[2] Strategies that have been explored to reduce polymerization shrinkage and stress in dental restoratives include the use of inert fillers, compliant fillers and nano particles, elastic linings between the tooth and composite, incremental resin introduction, liquid crystals, plasticizers, and the addition of nonshrinking monomers.[3,4]

Polymeric restorative dentistry has been dominated by free radical methacrylate-based chemistry for over 50 years. Bowen, who introduced bis(glycidyl methacrylate), BISGMA, systems had previously researched epoxides (oxiranes) as possible matrix resin candidates.[5] Concerns about water stability, biocompatibility, and initiator systems prevented further development of oxiranes as restoratives until the 1990s.

A variety of organosilicon compounds with oxirane functionality were first synthesized and polymerized by Sato et al.[6] Similar compounds were studied by Crivello and coworkers in the early 1990s.[7–11] 3M-ESPE adapted and innovated this technology for applications in dentistry, and coined the term ''Silorane'' to refer to monomers containing both oxirane and siloxane moieties.[12] The Silorane-based composite system exhibits greater hydrophobicity[13] and significantly reduced polymerization stress and shrinkage compared to methacrylates, with average mechanical properties and good biocompatibility.[14–16]

The development of tetraoxaspiroalkane monomers that have the potential to reduce polymerization shrinkage and stress in photocationic dental resins has been a major focus of our research for more than a decade.[17–22] We have recently synthesized and evaluated a new tetraoxaspiroalkane monomer

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containing silicon in Silorane-based systems. The monomer[23] was found to significantly reduce polymerization stress.[24] This article will focus on the synthesis and characterization of five additional tetraoxaspiroalkane monomers, and evaluation of the reactivity and physicomehanical properties of Silorane-based resins containing them. The literature on tetraoxaspiroalkane monomers with potential for expansion on polymerization has been extensively reviewed.[25,26] These monomers polymerize cationically and are generally compatible with oxirane-based systems. Cationically-initiated reactions at the spiro center commence with an essentially irreversible protonation of one of the spiro oxygens to form a carbocation that becomes the polymerizing species. Theoretical calculations (enthalpy, activation energy) and modeling of transition states and reaction pathways for both homopolymerization and copolymerization of 1,5,7,11-tetraoxaspiroalkanes have been conducted.[27–29]

EXPERIMENTAL

Materials

The two-component Silorane-based resin (Sil-Mix), composed of a 1 : 1 w/w (2 : 1 mol/mol) ratio of methylbis[2-(7-oxabicyclo[4.1.0]hept-3-yl)ethyl]phenylsilane **I** and 2,4,6,8-tetramethyl-2,4,6,8-tetrakis-[2-(7-oxabicyclo[4.1.0]hept-3-yl)ethyl]-1,3,5,7-tetraoxa-2,4,6,8-tetrasilacyclooxetane **II** (Fig. 1), and a conventional methacrylate-based dental matrix resin formulation (BT) containing 2,2-bis[4-(2-hydroxy-3-methacryloyloxypropoxy)phenyl]propane (BIS-GMA) and triethylene glycol dimethacrylate (TEGDMA) were supplied by 3M-ESPE, St. Paul, MN and Seefeld, Germany. Tetraoxaspirocyclic monomers **1–5** (Fig. 2) were synthesized at Midwest Research Institute, Kansas City, MO as described later. Photoinitiator system components: phenyl[*p*-(2-hydroxytetradecyloxy)phenyl] iodoniumhexafluoroantimonate, PI (OMAN072, Gelest; Morrisville, PA); camphorquinone, CQ (Aldrich; Milwaukee, WI); ethyl 4-dimethylaminobenzoate, ED (Fisher/ACROS, Pittsburg, PA). Synthesis reagents: trimethylolpropane allyl ether, allyl alcohol, bromoacetaldehyde, 2,2-diethyl-1,3-propanediol, thiophosgene, 3-cyclohexene-1,1-dimethanol, dibutyltin oxide,

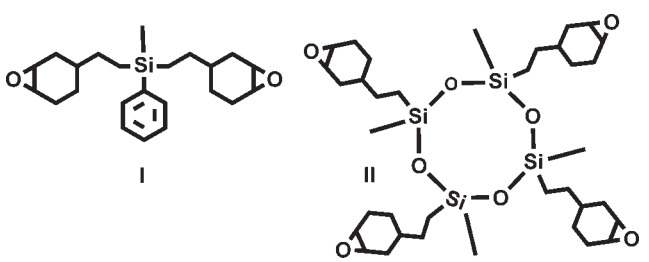

Figure 1 Structures of Sil-Mix components **I, II**.

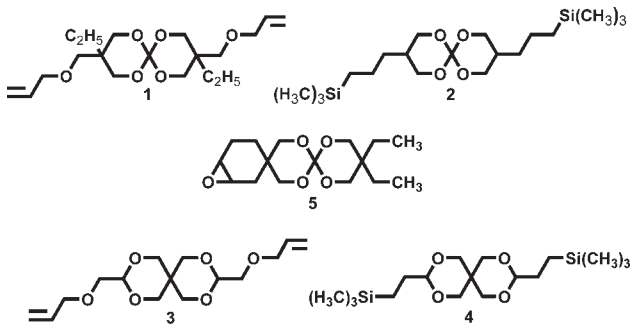

Figure 2 Structures of oxaspirocyclic monomers **1–5**.

m-chloroperbenzoic acid (*m*CPBA), lithium aluminum hydride (LAH), and sodium metal (Aldrich; Milwaukee, WI); 4-(dimethylamino)pyridine DMAP (Fisher/ACROS; Pittsburg, PA); pentaerythritol (Avocado/Alfa Aesar; Ward Hill, MA); acrolein (AlfaAesar; Ward Hill, MA); anhydrous *p*-toluene sulfonic acid (*p*TSA) was prepared by drying the monohydrate (Aldrich; Milwaukee, WI) at 100°C in vacuo for 6 h[30]; tetraethylorthocarbonate $C(OEt)_4$, was synthesized at Midwest Research Institute, Kansas City, MO according to a reported procedure[31]; Wilkinson's catalyst, tris (triphenylphosphine)rhodium chloride $RhCl(Ph_3P)_3$ (Strem; Newburyport, MA); trimethylsilane $(CH_3)_3$ SiH (Gelest; Morrisville, PA); hexanes, anhydrous ether Et_2O, toluene, methylene chloride CH_2Cl_2, triethylamine Et_3N, acetic acid, sodium bicarbonate $NaHCO_3$, anhydrous magnesium sulfate $MgSO_4$, anhydrous sodium sulfate Na_2SO_4, potassium sodium tartrate tetrahydrate (Rochelle's salt), sodium hydroxide NaOH, hydroquinone HQ, and silica gel (Fisher; Pittsburg, PA).

Synthesis and characterization

The synthesis and characterization of tetraoxaspiroalkane monomers **1–5** (Fig. 2) is detailed below.

3,9-Diethyl-3,9-bis(allyloxymethyl)-1,5,7,11-tetraoxaspiro[5.5]undecane [DEBAOM-1,5,7,11-TOSU] **1**

The synthesis scheme is shown in Figure 3. The transesterification procedure was similar to that of Endo et al.[30] To a three-neck 1-L round-bottom flask equipped with magnetic stir bar, Dean-Stark trap with reflux condenser, and a thermometer, was placed a mixture of toluene (500 mL) and the starting trimethylolpropane allyl ether (**1a**; 8.89 g, 50 mmol). The solution was refluxed for 2 h to azeotropically remove water. Twenty-five milliliter of azeotrope was collected. The mixture was allowed to cool to below 70°C. Anhydrous *p*TSA (0.09 g) was added and the mixture was allowed to cool to room temperature (RT). $C(OEt)_4$ (**1b**; 5.39 mL, 25 mmol)

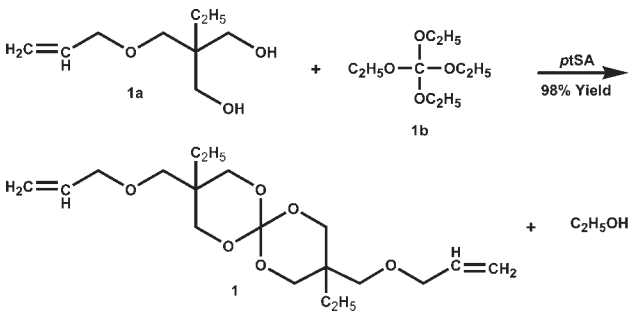

Figure 3 Synthesis of 3,9-Diethyl-3,9-bis(allyloxymethyl)-1,5,7,11-tetraoxaspiro[5.5]-undecane [DEBAOM-TOSU] **1**.

was added slowly. The resulting mixture was refluxed to azeotropically remove the by-product C_2H_5OH. The azeotropic mixture (160 mL) was shaken with brine to determine the amount of ethanol collected. The reaction mixture was allowed to reflux for an additional hour and then allowed to cool to RT. Et_3N (2 mL) was added and the resulting mixture was stirred at room temperature for 1.5 h and concentrated under reduced pressure to obtain a light yellow liquid (14.84 g). This crude material was purified by flash chromatography (silica gel, 10–20% Et_2O/hexanes) and the desired product **1** was obtained as colorless liquid in 98% yield (8.92 g). Purity (GC): ~ 96%; DSC exotherm peak: 184.48°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.93–5.81 (m, 2H), 5.29–5.21 (dd, 2H, J = 12.9, 1.2 Hz), 5.17–5.12 (dd, 2H, J = 7.8, 0.9 Hz), 3.99–3.95 (d, 4H, J = 3.9 Hz), 3.85–3.66 (m, 12H), 3.47 (s, 4H), 1.42–1.35 (q, 4H, J = 5.7 Hz), 0.85–0.79 (t, 6H, J = 5.7 Hz); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 134.74, 116.36, 114.75, 72.13, 69.25, 67.39, 66.97, 36.16, 23.42, 7.11; FTIR (cm^{-1}) 3081, 2966, 2882, 1646, 1456, 1364,1261, 1228, 1189, 1112, 1071, 1014, 927.

3,9-Bis(3-trimethylsilylpropyl)-1,5,7,11-tetraoxaspiro-[5.5]undecane [BTMSP-1,5,7,11-TOSU] **2**

The three-step synthesis scheme is presented in Figure 4.

*Step 1: 2-Allylpropane-1,3-diol **2a**.* To a four-neck, 1-L round-bottom flask under argon, with dropping funnel, reflux condenser, thermometer, and sparkless mechanical stirrer was charged 560 mL anhydrous Et_2O. The system was stirred and cooled to 5°C and LAH (18.40 g, 0.4606 mol) was added to the flask followed by diethyl allylmalonate (**2b**; 42.19 g, 0.2044 mol) in 15 mL Et_2O over a period of 0.5 h. Upon completion of addition, the reaction mixture is refluxed (34–35°C) for ~ 6 h, allowed to cool to RT, and stirred slowly overnight. The reaction mixture was then cooled to ~ 5°C and quenched with MeOH (51 mL) and slowly poured into 700 mL of cold saturated Rochelle's salt solution. The heterogeneous mixture was stirred until whitish and then extracted with 600 mL Et_2O. Both the aqueous and organic phases were neutralized to pH 7 by slowly adding small pieces of dry ice under vigorous stirring. The aqueous phase was back extracted with Et_2O two more times (2 × 600 mL). All the organic phases were combined, dried over Na_2SO_4, filtered, and stripped of volatiles yielding 35.1 g of crude product which was purified by distillation at 0.14–0.16 mmHg through a 8″ Vigreaux column to give 20.2 g (85% yield) of colorless diol **2a**. bp: 70–72°C/0.14–0.16 mmHg; Purity (GC): 97%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.82–5.72 (m, 1H), 5.07–5.00 (m, 2H), 3.78–3.74 (d,d, 2H, J = 4 Hz), 3.64–3.60 (d,d, 2H, J = 7.2 Hz), 3.16 (s, 2H), 2.05–2.01 (m, 2H), 1.86–1.80 (m, 1H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 136.15, 116.53, 65.34, 41.72, 32.45; FTIR (cm^{-1}) 3338, 3077, 2927, 2980, 1641, 1470, 1442, 1092, 1035, 995, 970, 915.

*Step 2: 3,9-Bis(allyl)-1,5,7,11-tetraoxaspiro[5.5]undecane **2c**.* Into a flame-dried three-neck 250-mL round-bottom flask under argon, with Dean-Stark trap, reflux condenser, stir bar, and a thermometer were charged the diol **2a** from Step 1 (35.52 g, 0.28 mol), $C(OEt)_4$ (27.75 g, 0.140 mol), and dry *p*TSA (0.50 g). The heterogeneous mixture was stirred and slowly heated to 111°C over a period of 2 h to azeotropically remove the ethanol byproduct (24 mL; 92% of theory). The reaction mixture was then neutralized (1.5 mL Et_3N) to pH ~ 9, and stripped under reduced pressure to give 33.68 g of crude product as a yellowish oil which was subjected to vacuum distillation at 0.23 mmHg to give 22.96 g (85% yield) of the colorless product **2c** which solidified easily at RT. bp: 111–112°C/0.23 mmHg; mp (DSC): 42.13°C; Purity (GC) 99%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.74–5.64 (m, 2H), 5.06–5.00 (m, 4H), 4.01–3.91 (m, 4H), 3.79–3.74 (m, 2H), 3.68–3.63 (m, 2H), 2.03–1.94 (m, 6H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 134.82, 117.05, 114.36, 66.51, 66.07, 32.61, 32.36; FTIR (cm^{-1}) 3084, 2995, 2976, 2893, 1640, 1457, 1378, 1354, 1238, 1202, 1158, 1099, 1022, 998, 984, 935.

*Step 3: 3,9-Bis(3-trimethylsilylpropyl)-1,5,7,11-tetraoxaspiro[5.5]undecane [BTMSP-1,5,7,11-TOSU] **2**.* The gen-

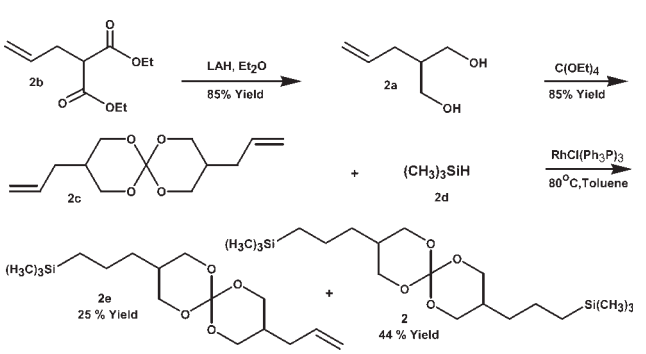

Figure 4 Synthesis of 3,9-Bis(3-trimethylsilylpropyl)-1,5,7,11-tetraoxaspiro[5.5]-undecane [BTMSP-1,5,7,11-TOSU] **2**.

eral hydrosilylation procedure was similar to that reported by Crivello and Bi.[32] To a flame-dried three-neck 250-mL round-bottom flask with magnetic stir bar, thermometer, dry ice-acetone cold finger, and addition port were placed the diallyl spirocyclic product from Step 2 (**2c**; 6.07 g, 25 mmol), toluene (100 mL), and Wilkinson's catalyst [$RhCl(Ph_3P)_3$, 2.5 mg]. $(CH_3)_3SiH$ (**2d**; 5.62 g, 75 mmol] was bubbled very slowly through the mixture at room temperature with stirring over a period of 3 h. The resulting mixture was slowly heated to 80°C, held 4.5 h, cooled to RT, and stirred overnight. The mixture was filtered and concentrated under reduced pressure to obtain a yellowish liquid (11.96 g). The crude material was purified by column chromatography (silica gel, 10% Et_2O/hexanes). The desired hydrosilylation product **2**, a white crystalline solid (4.31 g), was obtained in 44.3% yield. mp (DSC): 69.41°C; ^1H NMR ($CDCl_3$, 400 MHz) δ 3.98–3.84 (m, 4H), 3.79–3.72 (dd, 2H, J = 8.1, 7.2 Hz), 3.65–3.52 (dd, 2H, J = 8.1, 7.2 Hz), 2.01–1.89 (m, 2H), 1.31–1.15 (m, 8H), 0.49–0.40 (m, 4H), −0.06 (s, 18H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 114.44, 67.12, 66.54, 32.57, 31.84, 21.05, 16.74, −1.73; FTIR (cm^{-1}) 2953, 2923, 1460, 1374, 1248, 1210, 1169, 1117, 1015, 860, 838. In addition, some monohydrosilylated byproduct 3-allyl-9-(3-trimethylsilylpropyl)-1,5,7,11-tetraoxaspiro[5.5]undecane (**2e**; 2.0 g, 25% yield) was obtained as a colorless liquid. ^1H NMR ($CDCl_3$, 400 MHz) δ 5.50–5.47 (m, 1H), 5.11–4.93 (m, 1H), 3.87–3.52 (m, 8H), 1.86 (s, 1H), 1.54 (s, 2H), 1.15 (s, 5H), 0.37 (s, 2H), 0.11–0.14 (m, 9H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 128.58, 125.81 124.38, 114.13, 113.82, 66.80, 66.71, 66.21, 66.16, 65.73, 65.23, 36.46, 32.27, 31.54, 29.90, 20.76, 19.50, 17.82, 16.42, 13.81, 12.87, −2.01; FTIR (cm^{-1}) 2954, 2922, 2884, 1456, 1373, 1246, 1210, 1114, 1006, 860, 838.

3,9-Bis(allyloxymethyl)-2,4,8,10-tetraoxaspiro[5.5]-undecane [BAOM-2,4,8,10-TOSU] **3**

The two-step synthetic sequence is shown in Figure 5.

*Step 1: 2-Allyloxyacetaldehyde dimethyl acetal **3a**.* In a flame-dried three-neck 1-L round-bottom flask under argon, with dropping funnel, reflux condenser, thermometer, and a stir bar, was placed allyl alcohol (345 mL, 5.02 mol). Sodium (1.14 mol) was added slowly in small pieces with vigorous stirring and gradual heating to ~ 90°C. HQ (0.2 g) was then added. The sodium alcoholate **3b** was heated to 93–100°C while bromoacetaldehyde (**3c**; 193.32 g, 1.14 mol) was added at the rate of 1.5–2 mL/min. Half way through the addition, white precipitates were formed. The reaction mixture was allowed to cool to RT, stirred overnight, reheated to 99–100°C for 8 h, again allowed to cool to RT, and was filtered under aspiration and argon. Into the filtrate (pH 9–10) ~ 5 mL acetic acid was added over a period of 45 min. The neutralized filtrate was concentrated to ~ 70 mL (120 mmHg, ~ 53°C to 60 mmHg, 50–67°C) and allowed to stand overnight. This residue was filtered under argon and the filtrate was stripped under reduced pressure to obtain 66.04 g crude product which was then distilled using a 11-plate Oldershaw at 25 mmHg, 73°C (reflux ratio 1.0–1.2) to obtain 51.95 g (yield 31%) of the dimethyl acetal **3a** as a colorless liquid. Purity (GC): 99%; ^1H NMR ($CDCl_3$, 400 MHz) δ 5.93–5.83 (m, 1H), 5.28–5.22 (qq, J = 10.8 Hz, 1H), 5.18–5.15 (dd, J = 5.8 Hz, 1H), 4.51–4.48 (t, J = 5.2 Hz, 1H), 4.02–4.00 (J = 4.0 Hz, 2H), 3.47, 3.45 (s,s, 2H), 3.37 (s, 6H); ^{13}C NMR ($CDCl_3$, 400 MHz,) δ 134.43, 117.45, 102.76, 72.45, 69.62, 53.89; FTIR (cm^{-1}) 3082, 2988, 2912, 2833, 1648, 1448, 1194, 1114, 1080, 1067, 993, 926.

*Step 2: 3,9-Bisallyloxymethyl-2,4,8,10-tetraoxaspiro[5.5]-undecane [BAOM-2,4,8,10-TOSU] **3**.* To a three-neck 100-mL round-bottom flask with Dean-Stark trap, reflux condenser, thermometer, and stir bar were charged 2-allyloxyacetaldehyde, the dimethyl acetal from Step 1 (**3a**; 29.50 g, 201.80 mmol), pentaerythritol (**3d;** 14.00 g, 100.9 mmol), and *p*TSA (0.45 g). The heterogeneous mixture was heated to 110–150°C for ~ 7 h and ~ 3.4 mL MeOH were collected. Upon cooling to RT, Et_3N (5 mL) was added, the mixture was stirred for 0.5 h at 45°C (pH 8–9). The crude product was purified by flash chromatography with a deactivated (2% Et_3N) column (silica gel, hexanes/Et_2O 1/1, v/v) to obtain the desired product (**3**;

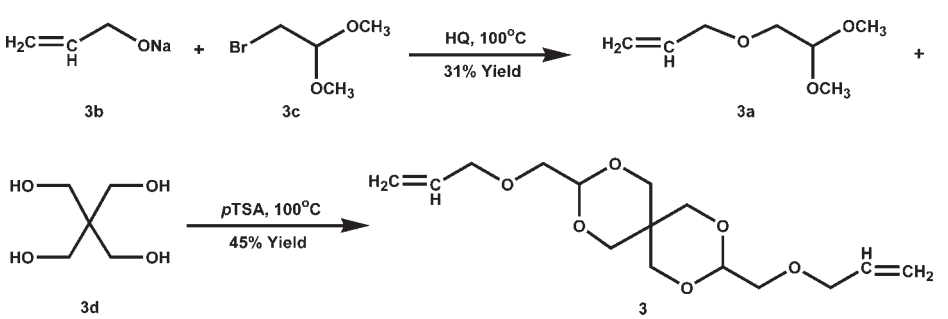

Figure 5 Synthesis of 3,9-Bis(allyloxymethyl)-2,4,8,10-tetraoxaspiro[5.5]undecane [BAOM-TOSU] **3**.

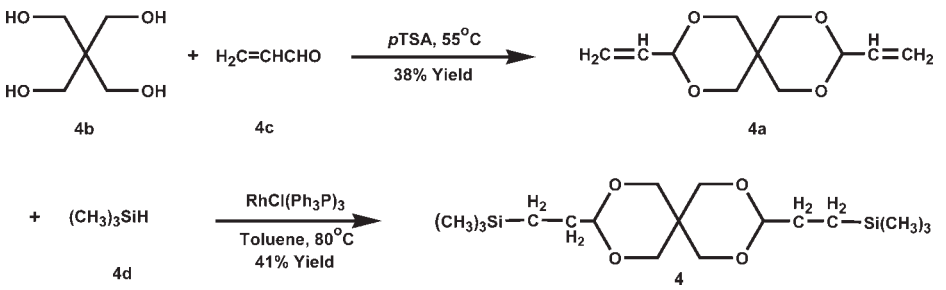

Figure 6 Synthesis of 3,9-Bis(2-trimethylsilylethyl)-2,3,8,10-tetraoxaspiro[5.5]undecane [BTMSE-2,4,8,10-TOSU] **4**.

13.55 g, 45% yield) as a colorless liquid. Purity (GC): ~ 95%; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.91–5.81 (m, 2H), 5.26–5.14 (qqqq, J = 24.2 Hz, 4H), 4.63–4.60 (m, 2H), 4.56–4.53 (m, 2H), 4.01–3.96 (m, 4H), 3.61–3.52 (m, 4H), 3.49–3.36 (m, 4H), 3.38–3.08 (m, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz,) δ 134.14, 117.70, 100.59, 72.62, 70.93, 70.35, 69.87, 32.74; FTIR (cm^{-1}) 3080, 2981, 2910, 2855, 1647, 1464, 1204, 1170, 1119, 1067, 927, 858.

3,9-Bis(2-trimethylsilylethyl)-2,3,8,10-tetraoxaspiro-[5.5]undecane [BTMSE-2,4,8,10-TOSU] **4**

The two-step synthesis scheme is shown in Figure 6.

Step 1: 3,9-Divinyl-2,4,8,10-tetraoxaspiro[5.5]undecane ***4a***. To a flame-dried three-neck 1-L round-bottom flask, with stir bar, thermometer, reflux condenser, and addition funnel was charged pentaerythritol (**4b**; 65.30 g, 0.47 mol). Acrolein (**4c**; 82.65 g, 1.43 mol) was added via a dropping funnel with stirring followed by addition of 0.5 g of dry *p*TSA. The mixture was slowly heated to ~ 55°C, stirred for 4 h, and allowed to cool to RT. After standing overnight, 100 mL 5% $NaHCO_3$ was added and the mixture stirred for 0.5 h. After extracting with 300 mL Et_2O, the organic phase was separated and washed with 100 mL portions of 5% $NaHCO_3$ and brine successively (pH 7), dried over $Na_2SO_4/MgSO_4$, and stripped under reduced pressure to obtain 93.54 g of crude product. The crude product was distilled and the distillate was recrystallized from hexanes/ether 1/3 v/v to obtain 38.31 g (yield 38%) of the white crystalline product **4a**. bp: 90–92°C/0.5–0.65 mmHg; Purity (GC): ~ 97%; mp (DSC): 42.06°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.87–5.79 (m, 1H), 5.47–5.42 (tt, J = 1.2, 1.2 Hz, 1H), 5.31–5.28 (m, 1H), 4.86–4.85 (d, J = 2.2 Hz, 1H), 4.62–4.57 (m, 1H), 3.65–3.39 (m, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 134.19, 119.00, 101.27, 70.53, 70.07, 32.33; FTIR (cm^{-1}) 2986, 2955, 2851, 1437, 1422, 1204, 1166, 1078, 978, 940.

Step 2: 3,9-Bis(2-trimethylsilylethyl)-2,4,8,10-tetraoxaspiro[5.5]undecane [BTMSE-2,4,8,10-TOSU] ***4***. The general hydrosilylation procedure was similar to that reported by Crivello and Bi.[32] To a flame-dried three-neck 250-mL round-bottom flask with a magnetic stir bar, thermometer, dry ice-acetone cold finger, and addition port were placed the divinyl spirocyclic intermediate from Step 1 (**4a**; 7.14 g, 32.98 mmol), toluene (120 mL), and Wilkinson's catalyst [$RhCl(Ph_3P)_3$, 3.3 mg]. $(CH_3)_3SiH$ (**4d**; 7.42 g, 98.94 mmol) was bubbled very slowly through the mixture at RT with stirring over a period of 4 h. The resulting mixture was slowly heated to 80°C, held 4.5 h, and cooled to room temperature. The mixture was filtered and concentrated under reduced pressure to give a yellowish liquid (13.73 g). This crude product was purified by column chromatography (silica gel, deactivated with 1% Et_3N; 3–5% Et_2O/hexanes). The desired hydrosilylation product (**4**), a white crystalline solid (4.82 g), was obtained in 40.5% yield. Purity (GC): 93%; mp (capillary): 63–66°C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.55–4.50 (dd, 2H, J = 8.7, 1.8 Hz), 4.36–4.32 (t, 2H, J = 3.9 Hz), 3.57–3.52 (dd, 2H, J = 8.7, 1.8 Hz), 3.52–3.48 (d, 2H, J = 8.7 Hz), 3.34–3.30 (d, 2H, J = 8.7 Hz), 1.60–1.52 (m, 4H), 0.56–0.50 (m, 4H), −0.05 (s, 18H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 104.42, 70.61, 70.19, 32.41, 29.18, 10.12, −1.88; FTIR (cm^{-1}) 2953, 2853, 1457, 1380, 1250, 1208, 1170, 1122, 1050, 859, 837, 774.

3,3-Diethyl-11,12-epoxy-1,5,7,16-tetraoxadispiro-[5.2.5.2]hexadecane [DECHE-1,5,7,11-TOSU] **5**

The four-step reaction sequence is shown in Figure 7.

Step 1: 5,5-Diethyl-1,3-dioxane-2-thione ***5a***. This thiocarbonate was prepared by a variation of the thiocarbonylation procedure developed by Correy and Hopkins.[33] To a three-neck round-bottom flask under nitrogen, with mechanical stirrer and an additional funnel, was placed 2,2-diethyl-1,3-propanediol (**5b**; 15.86 g, 120 mmol), DMAP (29.32 g, 240 mmol), and 120 mL toluene. The mixture was allowed to stir at RT until a homogeneous solution was obtained. The mixture was cooled to 0–5°C and a solution of thiophosgene (**5c**; 9.43 mL, 120 mmol) in 90 mL toluene was added dropwise over a period of 90 min. This resulted in the formation of a bright orange DMAP-thiophosgene complex. The reaction mixture was allowed to stir for 1 h at 0–5°C, slowly warmed to

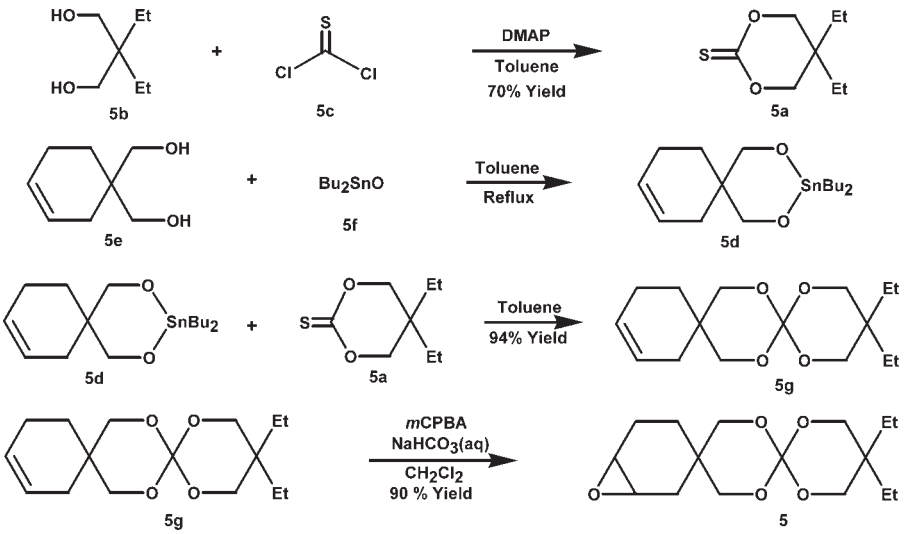

Figure 7 Synthesis of 3,3-Diethyl-11,12-epoxy-1,5,7,16-tetraoxadispiro [5.2.5.2]-hexadecane [DECHE-1,5,7,11-TOSU] **5**.

RT, stirred for an additional hour before the precipitated DMAP-HCl salt was removed by filtration. The filtrate was concentrated under reduced pressure and the crude material was purified by recrystallization (dissolved in refluxing ether, allowed to cool to room temperature, and ether slowly evaporated) or by column chromatography (silica gel, 2/1 v/v CH_2Cl_2/hexanes). The desired thiocarbonate **5a** was obtained as white crystalline solid in 70% yield. mp (DSC): 64.4°C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.17 (s, 4H), 1.51–1.43 (q, 4H, J = 7.5 Hz), 0.92–0.87 (t, 6H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 189.53, 76.08, 33.67, 23.09, 6.97; FTIR (cm^{-1}) 2960, 2920, 1455, 1395, 1380, 1290, 1240, 1200, 1180, 1060, 990, 930, 720.

*Step 2: 3,3-Dibutyl-2,4-dioxa-3-stannaspiro[5.5]undec-8-ene **5d**.* This tin adduct and the unsaturated intermediate (**5g**; Step 3) were prepared employing procedures similar to those reported by Stansbury and Bailey.[34] To a three-neck round-bottom flask with thermometer, reflux condenser, and a Dean-Stark trap with extension condenser, was placed a heterogeneous mixture of 3-cyclohexene-1,1-dimethanol (**5e**; 8.48 g, 59.6 mmol, purified by recrystallization from Et_2O), and dibutyltin oxide (**5f**; 15.14 g, 59.6 mmol) in 250 mL of toluene. The reaction mixture was refluxed for 3 h and the liberated water/toluene azeotrope was collected (5 × 20 mL). The Dean-Stark trap was removed and the reaction mixture was then refluxed for additional 2 h and slowly cooled to RT under nitrogen. The dibutyltin adduct product **5d** generated *in situ* was carried on to the subsequent reaction without further purification.

*Step 3: 3,3-Diethyl-1,5,7,16-tetraoxadispiro[5.2.5.2]hexadec-11-ene **5g**.* To the solution of **5d** from Step 2 was added the thione product from Step 1 (**5a**; 10.39 g, 59.6 mmol) in several small portions at RT over a period of 20 min and stirred for 24 h. The reaction mixture was then concentrated under reduced pressure and the residue taken up in Et_2O (white suspension formed upon standing). The ether solution was filtered and concentrated under reduced pressure to give light yellowish oil. The crude product was purified by column chromatography (silica gel, 10–15% Et_2O/hexanes). The desired unsaturated spirocyclic product **5g** was obtained as colorless oil in 94% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.68–5.58 (m, 2H), 3.74–3.68 (4s, 8H), 2.08–1.94 (m, 4H), 1.63–1.56 (t, 2H, J = 6.6 Hz), 1.46–1.37 (q, 4H, J = 7.5 Hz), 0.84–0.76 (t, 6H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 126.03, 124.16, 114.68, 70.03, 69.32, 34.27, 30.50, 26.44, 23.14, 21.30, 13.92, 7.01; FTIR (cm^{-1}) 3020, 2960, 2880, 1640, 1450, 1360, 1250, 1220, 1200, 1185, 1160, 1105, 1020, 995, 920, 730, 655; Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28; Found: C, 68.20; H, 9.59.

*Step 4: 3,3-Diethyl-11,12-epoxy-1,5,7,16-tetraoxadispiro-[5.2.5.2]hexadecane [DECHE-1,5,7,11-TOSU] **5**.* This tetraoxabispirocyclic oxirane was prepared employing the biphasic epoxidation procedure described by Anderson and Veysoglu[35] because of the acid sensitive nature of this class of compounds. In a round-bottomed flask was placed the unsaturated intermediate **5g** from Step 3 (10.02 g, 35.4 mmol) and 350 mL CH_2Cl_2. To this was added 0.5*M* aqueous $NaHCO_3$ (110 mL, pH ~ 8). The resulting biphasic mixture was allowed to stir vigorously at room temperature and then *m*CPBA (9.00 g, ~ 35.77 mmol) was slowly added in several portions over a period of 30 min. The resulting mixture was stirred for 5 h at RT. The two phases were separated and the organic phase was washed successively with 1*N* aqueous NaOH (2 × 100 mL) and water (2 × 100 mL), dried over anhydrous Na_2SO_4, and concentrated

TABLE I
Photopolymerization Enthalpies and Exotherm Peak Maximum Times

Formulation	Net enthalpy ΔH (J/g)	ΔH (Exptl)/ΔH (Calcd) (%)	Exotherm peak maximum (s)
Sil-Mix	−181[a]	–	14
1 DEBAOM-1,5,7,11[b]	−116[a]	80	14
2 BTMSP-1,5,7,11[b]	−78[a]	54	14
3 BAOM-2,4,8,10[b]	−170[a]	117	15
4 BTMSE-2,4,8,10[b]	−170[a]	117	17
5 DECHE-1,5,7,11[b]	−82[a]	57	16
INERT[b]	−145[c]	–	–

[a] Experimental value.
[b] 20 mol % in Sil-Mix (DEBAOM = 14.70 wt %; BTMSP = 15.81 wt %; BAOM = 12.69 wt %; BTMSE = 14.77 wt %; DECHE = 12.60 wt %).
[c] Calculated value; assumes no enthalpy contribution from an inert diluent and 20% less oxirane groups available to react.

under reduced pressure to give an off-white solid. The crude product was washed with 5 mL of cold Et_2O (precooled at 0°C) and purified by flash chromatography (silica gel, 15% ethyl ether/hexanes) or by two recrystallizations from Et_2O/hexanes (the crude material was dissolved in refluxing ether, allowed to cool to room temperature and then hexanes was slowly added). The desired oxiranyl spirocyclic product **5** was obtained as a white crystalline solid in 90% yield. mp (DSC): 67.4°C; ^{1}H NMR ($CDCl_3$, 300 MHz, mixture of diastereomers) δ 3.70–3.50 (m, 8H), 3.16–3.04 (m, 2H), 2.08–1.92 (m, 2H), 1.80–1.60 (m, 2H), 1.44–1.18 (m, 6H), 0.86–0.70 (m, 6H); ^{13}C NMR ($CDCl_3$, 300 MHz, mixture of diastereomers) δ 114.53, 71.56, 69.45, 69.33, 68.98, 51.57, 50.07, 34.30, 31.43, 29.41, 29.29, 23.21, 23.09, 22.79, 19.86, 13.95, 7.07, 7.00; FTIR (KBr pellet) (cm^{-1}) 2970, 1455, 1365, 1255, 1225, 1205, 1180, 1110, 1060, 1020, 1000, 920, 810, 795, 780, 730; Anal. Calcd for $C_{16}H_{26}O_5$: C, 64.41; H, 8.78; Found: C, 64.86; H, 8.93.

Formulation of test and control mixtures

Test mixtures (0 or 20 mol % tetraoxaspiroalkane monomer in Sil-Mix) were formulated with 4.1 wt % photoinitiator system (3 wt % PI; 1 wt % CQ; 0.1 wt % ED). The Sil-Mix control formulation (no tetraoxaspiroalkane monomer) contained 95.9 wt % Sil-Mix and 4.1 wt % photoinitiator system. The BisGMA/TEGDMA control formulation was received already formulated from 3M-ESPE and contained a proprietary photoinitiator system. Test mixture formulations were prepared by weighing a predetermined amount of Sil-Mix into a glass scintillation vial, and then adding one of the tetraoxaspiroalkane monomers so that the mol ratio of Sil-Mix to tetraoxaspiroalkane monomer was 80 : 20. Based on the total mixture weight, the photoinitiator system was added so that it comprised 4.1 wt % of the total mix. Weight percents for tetraoxaspiroalkane monomers are listed in footnote ''a'' of Tables I and II. Formulated test mixtures and the Sil-Mix control formulation were heated for 5 min on an oil bath at 60°C and stirred magnetically to aid dissolution of the photoinitiator system and monomer. Formulations were prepared and stored away from ambient light. Mixtures were tested for photoreactivity the same day as prepared.

Photoreactivity assessment

Photoreactivity assessments (n = 1) were made using an EXFO Novacure light curing unit interfaced with a Perkin-Elmer Diamond DSC. The experimental conditions were as follows: 25°C; N_2 atmosphere; 400–500 nm light; 3 mm quartz light quides; output: 500 mW/cm measured 15 mm from sample surface. The sample weights were 15–18 mg. Standard Al pans were used. An empty pan was placed in the reference position. Irradiation time was for 10 min following a 1 min equilibration. After the initial run, the sample was reirradiated for an additional 10 min. This second curve was subtracted from the initial exotherm curve to zero out artifacts because of beginning and ending of irradiation, and to compensate for the heat capacity differences between the sample pan and empty reference pan. Integrations were from time t = 1.1 min (lamp shutter opened) to 11.1 min (lamp shutter closed). Enthalpies of mixtures containing oxaspirocyclic monomers were measured and compared to the enthalpy calculated for a comparable formulation containing an inert diluent at the same addition level.

Photopolymerization stress measurement

Stress generated during photopolymerization was measured (n = 3) using an electromagnetic mechanical testing machine (Enduratec Model 3200, Bose Corp., Minnetonka, MN) adapted to be a tensilometer.[36,37] Briefly, two identical glass rods, 5 mm in di-

TABLE II
Polymerization Stress and 24-h Mechanical Properties [Mean (SD)] for Sil-Mix Formulations as Compared to a Conventional Methacrylate-Based Resin Control (BT)

Formulation	Polymerization stress (N/mm^2)	Ultimate strength (MPa)	Flexural elastic modulus (GPa)	Work of fracture (kJ/m^2)
BT	13.37 (0.76)	106.3 (8.8)	2.71 (0.19)	7.58 (2.05)
Sil-Mix	11.50 (1.32)	100.4 (10.7)	2.70 (0.24)	7.60 (3.74)
1 DEBAOM-1,5,7,11[a]	0.17 (0.06)[b]	84.6 (8.4)[b]	2.20 (0.21)[b]	5.82 (2.02)
2 BTMSP-1,5,7,11[a]	0.23 (0.06)[b]	42.4 (8.5)[b]	1.90 (0.14)[b]	1.12 (0.42)[b]
3 BAOM-2,4,8,10[a]	1.20 (0.17)[b]	87.8 (6.7)[b]	2.13 (0.21)[b]	7.17 (1.58)
4 BTMSE-2,4,8,10[a]	6.90 (1.76)[b]	92.2 (13.5)	2.36 (0.30)[b]	5.63 (1.82)
5 DECHE-1,5,7,11[a]	0.33 (0.15)[b]	96.0 (8.6)	2.58 (0.18)	5.33 (1.09)

[a] 20 mol % in Sil-Mix (DEBAOM = 14.70 wt %; BTMSP = 15.81 wt %; BAOM = 12.69 wt %; BTMSE = 14.77 wt %; DECHE = 12.60 wt %).
[b] Indicates significant difference from the methacrylate resin control (BT).

ameter, were placed opposing one another and separated by 1 mm (C-factor = 2.5). A displacement transducer (LVDT, Enduratec, 0.1 μm resolution, range ± 1 mm) was mounted on one glass rod and was touching a plate attached to the opposing glass rod. The distance between the mounts on the opposing glass rods was ~ 9 mm (including the 1 mm separation between the rods). Samples placed between the glass rods were cured by irradiation (500 mW/cm^2), while under LVDT displacement control. Load–displacement data were collected at 200 Hz for 30 min. Loads were measured using an 1125 N load cell (0.03 N resolution). Measured displacements varied by ± 1.0 μm during measurements. From the load–displacement data, peak loads were obtained and normalized by the original area to obtain the polymerization stresses.

Mechanical properties measurement

Elastic modulus, ultimate strength, and work of fracture were determined (sample size: $n = 6$ per group) using three-point bend tests to failure as per ADA 27 and ISO 4049 standards.[38,39] Briefly, specimens were manufactured in polyvinylsiloxane molds with dimensions of 2 × 2 × 25 mm^3. The resin was injected into the mold and cured by irradiation (500 mW/cm^2) followed by storage in the dark for 4 and 24 h before mechanical tests were conducted. Three-point bending tests were conducted using an electromagnetic mechanical testing machine (Enduratec Model 3200) with a 20-mm span and at a crosshead displacement rate of 0.5 mm/min at room temperature (25°C). Load–displacement data were collected at 100 Hz. Loads were measured using a 225 N load cell with a resolution of 0.01 N (1500ASK, Enduratec) and displacement was measured at a resolution of 1 μm. Flexural modulus was determined using the initial slope of the load–displacement curves (from 10 to 25% of ultimate load values). Flexural ultimate strength was determined from the peak loads and work of fracture was determined from the area under the stress–strain curve.

Statistical methods

For photopolymerization stress and mechanical properties results, an analysis of variance (ANOVA, one way) was carried out to assess the impact of formulations on dependent measures. Results for Silorane-based test formulations were analyzed for significant differences as compared to a standard methacrylate control using Dunnett's *post hoc* test (two-sided; $P = 0.05$).

RESULTS AND DISCUSSION

Photoreactivity parameters

Enthalpies and exotherm peak maximum times ($n = 1$) are given in Table I. Formulations containing 1,5,7,11-tetraoxaspiroalkane monomers (**1, 2,** and **5,** Fig. 2) had measured enthalpies 20–43% less than those calculated for a comparable mixture containing an inert diluent. We have learned from our modeling and computational studies of 1,5,7,11-tetraoxaspiroalkane monomers that ring protonation and ring opening proceed via both exothermic and endothermic processes.[7] The reduced enthalpies of mixtures containing these monomers may be a direct effect of TOSU ring opening polymerization that is necessary for possible volume expansion and stress reduction to take place. By contrast, formulations containing 2,4,8,10-tetraoxaspiroalkane monomers (**3** and **4,** Fig. 2) had enthalpies 17% above those calculated for a Sil-Mix reaction mixture assuming the addition of an inert diluent. Computational studies of the polymerization reactions for these cyclic acetals have not been conducted. The coefficient of variation for repli-

cate ($n = 3$) enthalpy determinations (same mix; same day) in our laboratories is 1.8%.

Photopolymerization stress

Photopolymerization stress results ($n = 3$) are given in Table II. An asterisk indicates significant difference from the methacrylate control (BT). ANOVA: $F(6,14) = 123.56$; $P < 0.01$; adjusted $R^2 = 0.974$. Photopolymerization stress was reduced >90% for TOSU-containing formulations, except **4** (40%); 2,4,8,10-isomers (**3** and **4,** Fig. 2) were somewhat less effective stress reducers than their 1,5,7,11-counterparts. We have previously reported the polymerization stress-reducing effects of the 1,5,7,11-oxirane functional monomer **5** in nonsilicon-containing dioxirane/polyol resin systems.[40] The mechanism responsible for the stress-reducing properties of the tetraoxaspirocyclic monomers is not known. Our studies with a trimethylsilyl-substituted 1,5,7,11-TOSU in Sil-Mix indicated that there was a significant reduction in polymerization stress with no improvement in polymerization volume change (shrinkage).[41] This suggests that the photopolymerization stress-reducing effects of the tetraoxaspiroalkanes in Sil-Mix may not be related to mechanisms postulated for shrinkage reduction (double ring-opening leading to expansion during polymerization). Factors such as lower elastic modulus, higher gel point (slower polymerization rate), lower glass transition temperatures, and even plasticization effects may be responsible. The nature of the interaction of these tetraoxaspiroalkanes with Sil-Mix components during light curing at room temperature has not been determined, and may or may not involve some degree of copolymerization. We have reported the copolymerization of a tetraoxaspiroalkane with a conventional oxirane during light curing at elevated temperatures.[42]

Mechanical properties

Results for mechanical properties testing ($n = 6$) are given in Table II. An asterisk indicates significant difference from the methacrylate control (BT). Ultimate strength—ANOVA: $F(6,35) = 29.10$; $P < 0.01$; adjusted $R^2 = 0.804$. Flexural Modulus—ANOVA: $F(6,35) = 12.34$; $P < 0.01$; adjusted $R^2 = 0.624$. Work of Fracture—$F(6,35) = 7.20$; $P < 0.01$; adjusted $R^2 = 0.477$. Measured values (all mechanical properties) for Sil-Mix and Sil-Mix/DECHE (**5**) were not significantly different than those for the methacrylate control (BT). Sil-Mix/**2** had the lowest mechanical property values. Sil-Mix formulations containing tetraoxaspiroalkane monomers **1**, **2**, or **3** had significantly lower ultimate strength values than the methacrylate control (BT). Sil-Mix formulations containing tetraoxaspiroalkane monomers **1**, **2**, **3,** or **4** had significantly lower elastic modulus values than the methacrylate control (BT). The Sil-Mix formulation containing tetraoxaspiroalkane monomer **2** was the only one with significantly lower work of fracture values than the methacrylate control (BT). The test results suggest that incorporating oxirane functionality in the stress-reducing monomer can help maintain the mechanical properties of the cured resin system. In general, the tetraoxaspiroalkane monomers showed the ability to greatly reduce the polymerization stress of Silorane-based matrix resins without a proportional reduction in 24 h mechanical properties.

Oxaspirocyclic monomers with various substituents have been used in several types of filled and unfilled resin systems in an attempt to mitigate polymerization shrinkage and stress. The resin systems included methacrylates, epoxides, and urethanes. Results were mixed with respect to effects on properties, and depended primarily on the initiator system used, amount of oxaspirocyclic monomer added, and curing temperature.[25] It was often difficult to relate the structure of the oxaspirocyclic monomers to the observed effects, and sometimes physical rather than chemical mechanisms were postulated. In our studies to date, it has also been difficult to relate monomer structure to observed effects on mechanical properties in Silorane resin systems. There were no clear trends for a given measured property that could be directly related to tetraoxaspiroalkane structural variants (e.g., 1,5,7,11- vs. 2,4,8,10-core; saturated vs. unsaturated substituents).

Alternatives for managing polymerization stress development in photocured resin systems continue to be discussed.[43] There is a concern that observed stress reduction in some systems may be caused by or accompanied by a lower degree of conversion. Recently, a method has been devised to simultaneously measure the real-time development of photopolymerization stress and degree of double bond conversion in methacrylate resin systems.[44] Degree of conversion can be an issue, especially for biomedical resin systems, because of the potential for residual monomers or low molecular weight oligomers to leach from the matrix into the surrounding tissue. Having established that tetraoxaspiroalkanes have the potential to reduce photopolymerization stress in Silorane-based resin systems, further developmental work should include studies relating, monomer structure, degree of conversion, and stress reduction to other physicochemical and mechanical properties.

CONCLUSIONS

The isomeric tetraoxaspiroundecane (TOSU) monomers investigated in this study contained a variety

of different hydrocarbon substituents and exhibited similar capabilities to greatly reduce the polymerization stress of Siloxane-based experimental resin formulations without a proportional reduction in 24 h mechanical properties. The results of these studies provide the basis for the development of new and novel polymerization stress reducing monomers for the formulation of Silorane-based composites useful in a wide spectrum of dental and biomaterial applications.

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