Synthesis of *N*-Aryl Azetidine-2,4-diones and Polymalonamides Prepared from Selective Ring-Opening Reactions

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ABSTRACT: Improved high-yield synthesis of *N*-aryl azetidine-2,4-dione has been achieved. The azetidine-2,4-dione undergoes ring-opening reactions with aliphatic primary amines to form malonamide linkages. More importantly, this compound exhibits a high reactivity toward primary aliphatic amine group over alcohols or secondary amines. This selective end-group functionalization is useful for preparing useful polymer intermediates. In this study polymalonamides were synthesized by fast addition reaction of aliphatic diamine and azetidine-2,4-dione. In the meantime, further application for structure-controlled reaction also has been demonstrated. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 103: 3591–3599, 2007

Key words: polyamide; polyurethane; polymalonamide; selective; ring opening

INTRODUCTION

Synthesis of complex structures without resorting to protection/deprotection strategies are valued in biology and nanoscale chemistry.[1–4] For example, the preparation of elaborate dendritic species is also inevitably associated with a need for a selective functionalization.[5,6] Nevertheless, there is still a strong demand for improved procedures which could lead to the formation of a complex structure without need for protection/deprotection strategies. Therefore, choosing an efficient and selective-addition-type methodology to serve this purpose would be a favorable approach. Via this selective-addition reaction, rapid entry into a complex structure can be achieved via a convenient route with the processing advantages of easy purification, high yield, and rapid synthesis. One approach to pursue this efficient and selective addition-type methodology is to attempt the following selective ring-opening addition reaction.

Facile ring-opening reactions of azetidine-2,4-diones with amines in formation of malonamides have been known for many years.[7] Except for an earlier polyamide synthesis by Imai and Hirukawa,[8] useful applications of azetidine-2,4-diones for synthesis of malonamides and other derivatives have remained unexplored to this date. Lack of an efficient synthesis to produce them in sufficient quantities may be the primary reason.

The first synthesis of azetidine-2,4-diones were reported by Staudingers in 1914, based on the cycloaddition reaction of ketenes with isocyanates.[7] The instability and highly reactive nature of ketenes, however, make this approach impractical. Herein we report an efficient preparation of *N*-aryl-azetidine-2,4-diones by a modified Poshkus's method under an ''*in situ*'' ketene generating method.[9,10] The ketene concentration was purposefully limited throughout the course of the reaction, while maintaining the concentration of aromatic isocyanate in excess. With this new approach, the yield of azetidine-2,4-dione can be achieved at a level greater than 80%. Moreover, the scope and utility of our methodology have also been examined thoroughly, including the selective-reactivity nature of azetidine-2,4-dione, the ring-opening polymerization of aliphatic diamine/azetidine-2,4-dione, and the example of preparing the structure-controlled compounds without protection/deprotection steps.[11–13]

EXPERIMENTAL

Materials and methods

All chemicals were purchased from Aldrich and were used as received. All reactions were carried out under nitrogen. ^{1}H NMR spectra were taken on a Varian Gemini-200 FT-NMR spectrometer using $CDCl_3$,

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acetone-d_6, and DMSO-d_6. IR measurements were performed on a Perkin-Elmer Spectrum One FT-IR spectrometer. Thermal analysis was performed in N_2 on a TA Instruments DSC2010 at a heating rate of 10°C/min. Thermogravimetric analysis (TGA) was performed using a Seiko SSC-5200 Thermogravimetric Analyzer at a heating rate of 10°C/min under nitrogen. Thermal degradation temperature (T_d) was taken at the temperature with 5% weight loss. Electro spray ionization (ESI) mass spectra were recorded on a Finnigan/Thermo Quest MAT 95XL mass spectrometer. Gel permeation chromatography (GPC) was performed in THF using a Waters Apparatus equipped with Waters Styragel columns with a refractive index detector and polystyrene calibration. Elemental analysis was performed on a Heraeus CHN-OS Rapid Analyzer.

Synthesis of *N*-aryl azetidine-2,4-dione (1a–1c)

The general procedure for preparing the *N*-phenyl-3,3-dimethyl-azetidine-2,4-dione (**1a**) is described below. A solution of triethylamine (12.6 g, 0.12 mol) in dry xylene 15 ml was added to a solution of phenyl isocyanate (23 g, 0.19 mol) and isobutyryl chloride (10.6 g, 0.1 mol) in dry xylene 150 ml. Reaction mixture was refluxed for 7 h and then cooled to room temperature. The resulting solution was filtered to remove the salt, and then concentrated to about 50 ml. The product was crystallized from cyclohexane, yielding the compound as a white powder (50%) (mp. 36°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.41 (s, 6H, —CH_3), 7.25 (m, 2H, ArH), 7.34 (d, 1H, ArH), 7.78 (d, 2H, ArH). Moreover, the syntheses and analysis of compound **1b** (*N*-phenyl-3,3-diethyl-azetidine-2,4-dione) and compound **1c** (*N*-phenyl-3,3-ethylbutyl-azetidine-2,4-dione) were also performed in the same manner as compound **1a**. Compound **1b**: white powder (85%) (mp. 86–87°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.08 (t, 6H, —CH_3), 1.85 (s, 4H, —CH_2—), 7.30 (m, 2H, ArH), 7.43 (m, 1H, ArH), 7.82 (d, 2H, ArH); compound **1c**: white powder (91%) (mp. 103–104°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 0.95 (m, 3H, —CH_3), 1.10 (t, 3H, —CH_3), 1.45 (m, 4H, —CH_2—), 1.90 (q, 4H, —CH_2), 7.34 (m, 2H, ArH), 7.39 (m, 1H, ArH), 7.86 (d, 2H, ArH).

Synthesis of bisazetidine-2,4-diones (BAZs; 2a–2c)

The general procedure for preparing 4,4-bis(3,3-dimethyl-2,4-dioxo-azetidino)-diphenyl-methane (**2a**) is described below. A solution of triethylamine (121.2 g, 1.2 mol) in dry xylene 200 ml was added to a solution of methylenedi-*p*-phenyl diisocyanate (50 g, 0.2 mol) and isobutyryl chloride (123.5 g, 1.16 mol) in dry xylene 250 ml. The reaction mixture was refluxed for 7 h and then cooled to room temperature. The resulting solution was filtered to remove the salt, and then concentrated to about 50 ml. The product was crystallized from cyclohexane, yielding the compound as a white powder (42%) (mp. 170–171°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.41 (s, 6H, —CH_3), 3.98 (s, 2H, Ar—CH_2—Ar), 7.34 (d, 4H, ArH), 7.7 (d, 4H, ArH). Moreover, the syntheses and analysis of compound **2b** (4,4-bis(3,3-diethyl-2,4-dioxo-azetidino)-diphenyl-methane) and compound **2c** (4,4-bis(3,3-ethylbutyl-2,4-dioxo-azetidino)-diphenyl-methane) were also performed in the same manner as compound **2a**. Compound **2b**: white powder (84%) (mp. 102–103°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.01 (t, 6H, —CH_3), 1.80 (m, 4H, —CH_2), 4.04 (s, 2H, Ar—CH_2—Ar), 7.38 (d, 4H, ArH), 7.71 (d, 4H, ArH); Compound **2c**: white powder (84%) (mp. 41–42°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 0.88 (t, 3H, —CH_3), 1.02 (t, 3H, —CH_3), 4.02 (s, 2H, Ar—CH_2—Ar), 7.37 (d, 4H, ArH), 7.76 (d, 2H, ArH).

Synthesis of 4-isocyanato-4′ (3,3-dimethyl-2, 4-dioxo-acetidino)-diphenylmethane (3a)

A solution of triethylamine (45 g, 0.44 mol) in dry xylene 100 ml was added to a solution of methylenedi-*p*-phenyl diisocyanate (125 g, 0.5 mol) and isobutyryl chloride (38.6 g, 0.36 mol) in dry xylene 250 ml. Reaction mixture was refluxed for 7 h and then cooled to room temperature. The resulting solution was filtered to remove the salt, and then concentrated to about 50 ml. The product was crystallized from cyclohexane, yielding the compound as a white powder (33%) (mp. 100–101°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.40 (s, 6H, —CH_3), 3.87 (s, 2H, Ar—CH_2—Ar), 6.90 (d, 2H, ArH), 7.00 (d, 2H, ArH), 7.10 (d, 2H, ArH), 7.66 (d, 2H, ArH).

Synthesis of *N*-phenyl-*N*′-ethanol dimethyl malonamide (4a) and *N*-phenyl-*N*′-ethanol diethyl malonamide (4b)

The general procedure for preparing the *N*-phenyl-*N*′-ethanol dimethyl malonamide (**4a**) is as follows: a solution of *N*-phenyl-3,3-dimethyl-azetidine-2,4-dione (**1a**) (9.45 g, 0.05 mol) in dry toluene (20 ml) was added to a solution of aminoethanol (3.05 g, 0.05 mol) in the same solvent (10 ml). The mixture was stirred for 6 h at 60°C. The resulting mixture was collected and purified by recrystallization from toluene. The yield of compound **4a** was 84% (mp.125–126°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.56 (s, 6H, —CH_3), 3.42 (t, 2H, —CH_2NHCO), 3.72 (t, 2H —CH_2OH), 7.11 (t, 1H, ArH), 7.32 (t, 2H, ArH), 7.56 (d, 2H, ArH). Elem. Anal. Calcd. for $C_{13}H_{18}N_2O_3$: C, 62.40%; H, 7.20%; *N*, 11.20%. Found: C, 62.03%; H, 6.93%; *N*, 10.66%. Moreover, the syntheses and analysis of compound **4b** was also performed in the same manner as compound **4a**. The yield of compound **4b** was 91%

(mp.106–107°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 0.92 (t, 6H, —CH_3), 2.05 (t, 4H, —CH_2), 3.52 (t, 2H, —CH_2NH), 3.77 (t, 2H, —CH_2OH), 7.12 (d, 2H, ArH), 7.32 (d, 2H, ArH), 7.55 (d, H, ArH). Elem. Anal. Calcd. for $C_{15}H_{22}N_2O_3$: C, 64.75%; H, 7.90%; *N*, 10.07%. Found: C, 64.39%; H, 8.05%; *N*, 10.73%.

Synthesis of *N*-phenyl-*N*′-(ethylene-*N*-phenyl-carbamate) dimethyl malonamide (5a) and *N*-phenyl-*N*′-(ethylene-*N*-phenyl-carbamate) diethyl malonamide (5b)

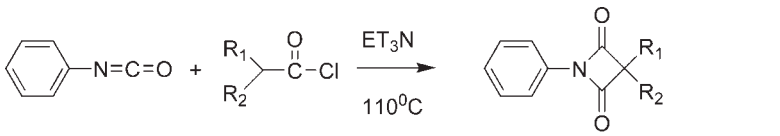
The general procedure for preparing the *N*-phenyl-*N*′-(ethylene-*N*-phenyl-carbamate) dimethyl malonamide (**5a**) is described below. A solution of **4a** (5 g, 0.02 mol) in dry toluene (20 ml) was added to a solution of phenyl isocyanate (2.38 g, 0.02 mol) in the same solvent (10 ml). The mixture was stirred for 2 h at 60°C. The resulting mixture was collected and purified by recrystallization from toluene. The yield of compound **5a** was 87% (mp. 134–135°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 1.56 (s, 6H, —CH_3), 3.59 (t, 2H, —CH_2NHCO), 4.30 (t, 2H, —CH_2OCONH), 7.11 (t, 2H, ArH), 7.27 (m, 6H, ArH), 7.54 (d, 2H, ArH). Elem. Anal. Calcd. for $C_{20}H_{23}N_3O_4$: C, 65.04%; H, 6.23%; *N*, 11.38%. Found: C, 65.02%; H, 6.39%; N, 11.27%. Moreover, the syntheses and analysis of **5b** (*N*-phenyl-*N*′-(ethylene-*N*-phenyl-carbamate) diethyl malonamide) was also performed in the same manner as compound **5a**. The yield of compound **5b** was 90% (mp. 145–146.1°C). ^{1}H NMR ($CDCl_3$) δ (ppm): 0.90 (t, 6H, —CH_3), 2.05 (t, 4H, —CH_2), 3.60 (t, 2H, —CH_2NH), 4.38 (t, 2H, —CH_2OCONH), 7.12 (d, 2H, ArH), 7.34 (d, 2H, ArH), 7.61 (d, H, ArH). Elem. Anal. Calcd. for $C_{22}H_{27}N_3O_4$: C, 66.50%; H, 6.80%; *N*, 10.58%. Found: C, 66.31%; H, 6.82%; *N*, 10.30%.

Synthesis of polymalonamides (6a–6e)

The general procedure for preparing the polymalonamide (**6e**) is described below. Bisazetidine-2,4-dione (8.92 g, 20 mmol; **2b**) was added to a 100 ml three-necked, round-bottomed flask equipped with a mechanical stirrer, nitrogen inlet-outlet lines, and a thermometer, while temperature was maintained at 130°C (mp. of **2b**). The designated amount of aliphatic diamines [2.32 g, 20 mmol; (H_2N-$(CH_2)_6$-NH_2)] was then added to the reactor. During the addition, the mixtures were stirred vigorously by a melt process at 130°C. In general, the mixture was stirred for only 2 min or less and the corresponding polymalonamide was obtained. The progress was monitored by the disappearance of azetidine-2,4-dione C=O stretching (1740 cm^{-1} and 1856 cm^{-1}) and emergence of malonamide C=O stretching (1670 cm^{-1}). The compound **6e** were in the form of a deep brown, hard solid. ^{1}H NMR (DMSO-d_6) δ (ppm): 0.66 (t, 12H, —CH_3), 1.23 (m, 8H, —CH_2—), 1.88 (s, 8H, —CH_2—), 3.10 (s, 4H, —CH_2—), 3.80 (s, 2H, —CH_2—), 7.08 (d, 4H, ArH), 7.46 (d, 4H, ArH), 8.09 (s, 2H, —NH), 10.57 (s, 2H, —NH). Moreover, the syntheses and analysis of polymalonamides (**6a–6d**) were also performed in the same manner as polymalonamide **6e**.

Synthesis of compound 9

3a (3 g, 9.38 mmol) was added to disperse red 1 (DR1) (2.95 g 9.38 mmol) in dry 1,4-dioxane (20 ml). The mixture was stirred for 6 h at 100°C. The resulting mixture was collected and purified by recrystallization from 1,4-dioxane and cyclohexane mixture (1 : 5). The yield of compound **7** was 95%. ^{1}H NMR (Acetone-d_6) δ (ppm): 1.24 (t, 3H, —CH_3), 1.44 (s, 6H, —CH_3), 3.61 (m, 2H, —CH_2N), 3.81 (t, 2H, —CH_2N), 3.94 (s, 2H, —CH_2Ar), 4.37 (t, 2H, —CH_2OCO), 6.95 (d, 2H, ArH), 7.12 (d, 2H, ArH), 7.23 (d, 2H, ArH), 7.43 (d, 2H, ArH), 7.65 (d, 2H, ArH), 7.86(d, 2H, ArH), 7.95 (d, 2H, ArH), 8.34 (d, 2H, ArH). ELEM. ANAL. Calcd. for $C_{35}H_{34}N_6O_6$: C, 66.23%; H, 5.40%; *N*, 13.24%. Found: C, 66.02%; H, 5.29%; *N*, 14.02%. A mixture of **7** (5 g, 7.87 mmol) and 1,3-diamino-2-propanol DAPO (0.41 g, 3.94 mmol) in dry 1,4-dioxane (30 ml) was prepared. The mixture was stirred for 2.5 h at 60°C. The resulting mixture was collected and purified by recrystallization from 1,4-dioxane and cyclohexane mixture (1 : 2). The yield of compound **8** was 90%. ^{1}H NMR (Acetone-d_6) δ (ppm): 1.23 (t, 6H , —CH_3), 1.48 (s, 12H —CH_3), 3.33 (t, 4H —CH_2N), 3.60 (m, 4H, —CH_2N), 3.79 (m, 1H —OCH), 3.79 (m, 4H —CH_2N), 3.85 (s, 4H, CH_2Ar), 4.36 (t, 4H, —CH_2OCO), 6.99 (d, 4H, ArH), 7.14 (d, 8H, ArH), 7.46 (d, 4H, ArH), 7.58 (d, 4H, ArH), 7.90 (d, 4H, ArH), 7.99 (d, 4H, ArH), 8.38 (d, 4H, ArH). ELEM. ANAL. Calcd. for $C_{73}H_{78}N_{14}O_{13}$: C, 64.49%; H, 5.78%; *N*, 14.42%. Found : C, 63.79%; H, 5.63%; *N*, 14.70%. A mixture of **8** (3 g, 2.20 mmol) and 4,4′-methylene-bis(phenyl isocyanate) (MDI) (0.275 g, 1.1 mmol) in dry 1,4-dioxane (20 ml) was prepared. The mixture was stirred for 6 h at 100°C. The crude product was obtained by pouring the reaction solution into hexane, and the precipitate was collected. The crude product was purified by washing with acetone and collected to afford compound **9** as a red powder. The yield of compound **9** was 89%. ^{1}H NMR (DMSO-d_6) δ (ppm): 1.14 (s, 12H, —CH_3), 1.37 (s, 24H, —CH_3), 3.08 (s, 8H, —CH_2N), 3.55 (m, 8H, —CH_2N), 3.73 (m, 2H, —OCH), 3.73 (m, 8H, —CH_2N), 3.85 (s, 10H, —CH_2Ar), 4.26 (t, 8H, —CH_2OCO), 6.91 (d, 8H, ArH), 7.05 (d, 16H, ArH), 7.20 (d, 4H, ArH), 7.32 (d, 8H, ArH), 7.47 (d, 8H, ArH), 7.62 (d, 4H, ArH), 7.81 (d, 8H, ArH), 7.93 (d, 8H, ArH), 8.35 (d, 8H, ArH). MS (MALDI-TOF): m/z = 2970 (M^+). ELEM.



1a: R_1=R_2=Me (50%; mp=36 °C)
1b: R_1=R_2=Et (85%; mp=87 °C)
1c: R_1=Et , R_2=nBu(91%; bp=103 °C)

Scheme 1 Synthesis of *N*-Aryl-Azetidine-2,4-diones.

ANAL. Calcd. for $C_{161}H_{166}N_{30}O_{28}$: C, 65.13%; H, 5.64%; *N*, 14.15%. Found: C, 64.79%; H, 5.54%; *N*, 14.47%. $M_w/M_n = 1.02$, $T_g = 124°C$.

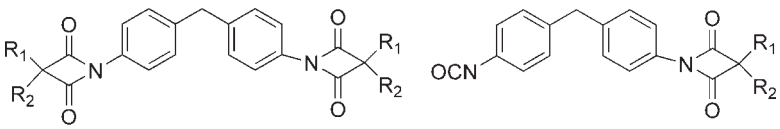
Synthesis of compound 11

3a (6 g, 18.75 mmol) was added to trimethylol propane (TMPO) (0.839 g, 6.26 mmol) in dry 1,4-dioxane (20 ml). The mixture was stirred for 6 h at 100°C. The reaction solution was poured into methanol and the precipitate was collected to give white powder. The yield of compound **10** was 90%. ^{1}H NMR (Acetone-d_6) δ (ppm): 0.93 (t, 3H , —CH_3), 1.42 (s, 18H, —CH_3), 1.49(m, 2H, —CH_2—), 3.92(s, 6H, —CH_2Ar), 4.11 (s, 6H, —CH_2OCO), 7.09 (d, 6H, ArH), 7.28 (d, 6H, ArH), 7.40 (d, 6H, ArH), 7.64 (d, 6H, ArH). Elem. Anal. Calcd. for $C_{63}H_{62}N_6O_{12}$: C, 69.09%; H, 5.71%; *N*, 7.67%. Found: C, 68.30%; H, 5.93%; *N*, 8.31%. A mixture of compound **10** (3 g, 2.74 mmol) and *N*-(3-aminopropyl)diethanolamine (1.333 g, 8.22 mmol) in 1,4-dioxane (20 ml) was prepared. The mixture was stirred for 2.5 h at 60°C. The crude product was obtained by pouring the reaction solution into hexane, and the precipitate was collected. The crude product was purified by washing with cyclohexane and collected to afford compound **11** as a white powder. The yield of compound **11** was 86%. ^{1}H NMR (Acetone-d_6) δ (ppm): 0.92 (t, 3H, —CH_3), 1.46 (s, 18H, —CH_3), 1.49 (m, 2H, —CH_2—), 1.69 (m, 6H, —CH_2—), 2.62 (m, 18H, —CH_2N), 3.25 (d, 6H, —CH_2N), 3.54 (m, 12H, —CH_2O), 3.78 (s, 6H, —CH_2Ar), 4.14 (s, 6H, —CH_2OCO), 6.98 (d, 6H, ArH), 7.02 (t, 6H, ArH), 7.30 (d, 6H, ArH), 7.437 (d, 6H, ArH). MS (ESI): $m/z = 1581$ (M^+). ELEM. ANAL. Calcd. for $C_{84}H_{116}N_{12}O_{18}$: C, 63.78%; H, 7.39%; *N*, 10.63%. Found: C, 63.42%; H,7.99%; *N*, 10.41%. $M_w/M_n = 1.06$, $T_g = 29°C$.

RESULTS AND DISCUSSION

In order to enhance the yield of azetidine-2,4-diones, Poshkus's original procedure[9] was modified in this work. The dialkyl acid chlorides, such as 2-ethylbutyroyl chloride and 2-ethylhexanyol chloride, were used instead of cyclohexane-carboxylic acid as the ketene precursors. These two acid chlorides can produce more stable dialkyl keto-ketenes, respectively, upon addition of triethylamine. In order to enhance the cycloaddition reaction (Scheme 1), the reaction temperature was also raised to 110°C from 45°C. Moreover, the addition of triethylamine to the mixed solution of isocyanate and acid chloride was performed dropwise over a period of 3 to 6 h so that in-situ ketene concentration could be maintained at minimum in the solution throughout the reaction. By these alterations, the yields of azetidine-2,4-diones, **1b** and **1c**, were enhanced to 85% and 91%, respectively (Scheme 1). Low yield of **1a** (Scheme 1), however, was observed in a reaction involving isobutyryl chloride and isocyanates. This result is possibly attributed to the volatility and highly reactive nature of dimethyl ketenes.[14]

Based on the new procedure, high-yield syntheses of the BAZs from acid chlorides and MDI have been achieved (**2b**, **2c** of Figure 1). These cycloadducts are white crystalline solids at room temperature. IR absorptions for carbonyl groups were found at around 1850 and 1740 cm^{-1}. By adjusting to lower relative molar ratios of acid chlorides to MDI, mono-isocyanato-azetidine-2,4-diones (MAZs) were synthesized as the major products. For instance, compound **3a**

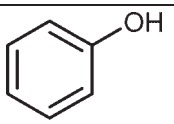
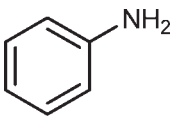
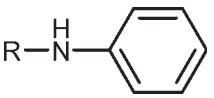
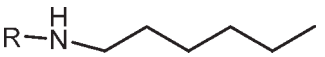
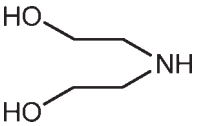
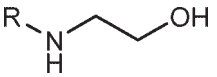
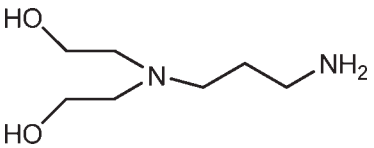
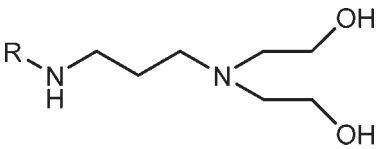


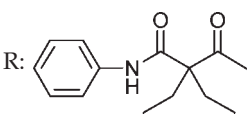
2a:R_1=R_2=Me (42%; mp=170 °C)
2b:R_1=R_2=Et (84%; mp=102 °C)
2c:R_1=Et, R_2=nBu (84%; mp=41°C)

3a:R_1=R_2=Me (33%; mp=100 °C)
3b:R_1=R_2=Et (crude yield=60%)

Figure 1 Chemical structures of BAZs and MAZs.

TABLE I
Reaction of 1b with Various Compounds Possessing Different Active Hydrogens

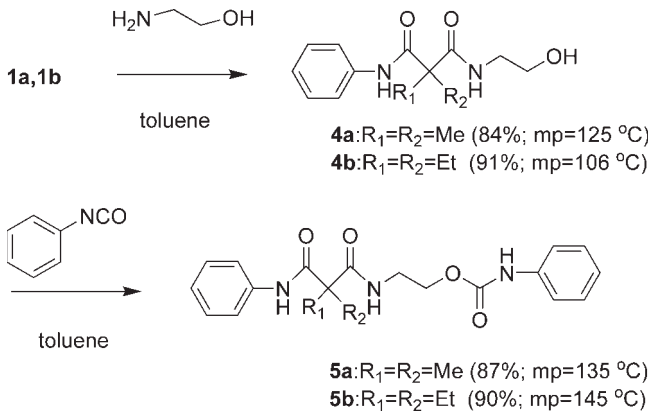
Starting compounds	Product and Isolated Yield (%)
	no reaction
CH_3-OH	no reaction
	no reaction
	 26%[a]
	 97%
	no reaction
	 91%
	 96%



[a] Reaction temperature is 110°C.

(Fig. 1) was synthesized with a yield of 33% in the 1/0.72/0.89 molar ratio of p-MDI/isobutyryl chloride/triethylamine. Higher yield of **3b** (60%) was obtained via a similar molar ratio.

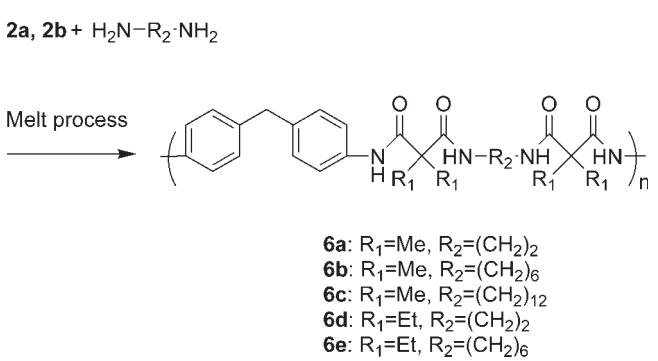
To demonstrate the highly selective nature of the azetidine-2,4-dione, **1b** was used as a model to react with compounds possessing different active hydrogens such as aliphatic amine, aromatic amine, aliphatic alcohol, and phenol (Table I). The reaction was proceeded in 20 wt % toluene solution at 60°C with a 1/1 molar ratio of **1b**/active hydrogen containing compound. The reactivity of these compounds was found to differ tremendously. For instance, when **1b** was independently treated with aniline, 1-hexylamine, phenol, and methanol, only 1-hexylamine, a primary aliphatic amine, reacted with **1b** rapidly at room temperature in the absence of a catalyst to afford product in essentially quantitative yield. On the other hand, a low yield (26%) of malonamide was found from reaction of **1b** with aniline, an aromatic amine, even at elevated temperatures (~ 110°C). No addition reaction took place between



Scheme 2 Reactivity of Azetidine-2,4-dione toward aminoethanol.

compound **1b** with either phenol or methanol when no catalyst was used. Based on these observations, we could conclude that the ring-opening reaction of compound **1b** appears to be more selective and faster toward relatively basic compounds such as primary aliphatic amines.

To further demonstrate the selective nature of azetidine-2,4-dione ring-opening reactions, compounds **1a** and **1b** were reacted with 2-aminoethanol, *N*-(3-aminopropyl)diethanolamine, and diethanolamine independently. In the first case, the malonamide formation occurred rapidly at the primary aliphatic amine end of aminoethanol predominantly (Scheme 2). When monitored by FT-IR analysis, disappearance of the 1855 and 1740 cm^{-1} peaks was accompanied concurrently by the emergence of a new absorption peak at 1650 cm^{-1} corresponding to the carbonyl group of the malonamide linkage. In the ^1H NMR spectrum ($CDCl_3$) of the starting compound **1a**, a chemical shift at 1.41 ppm corresponding to methyl group of azetidine-2,4-dione was shifted to 1.56 ppm, indicating the formation of malonamide. On the other hand, when compound **1a** and **1b** were treated with diethanolamine, under a similar condition, unreacted compounds **1a** and **1b** were recovered with few detectable malonamide linkages. These results further indicate that azetidine-2,4-dione strongly favors reaction with primary aliphatic amines, but not with alcohols or secondary aliphatic amines. Moreover, the selective reactivity of compounds **1a** and **1b** was driven not only by basicity, but by less steric hindrance as well. As expected, hydroxyl groups of compounds **4a** and **4b** reacted with phenyl isocyanate to form **5a** and **5b** in high yields (Scheme 2).



Scheme 3 Synthesis of polymalonamides from BAZs and aliphatic diamines.

TABLE II
Properties of Polymalonamides from BAZs and Aliphatic Diamines

No.	T_d (°C)[a]	T_g (°C)	η[b]
6a	313	115	0.47
6b	346	97	0.49
6c	344	75	0.48
6d	369	136	0.45
6e	341	104	0.78

[a] 5% weight loss.
[b] Measured at a concentration of 0.5 dL/g in sulfuric acid at 25°C.

Fast reaction of aliphatic diamine and azetidine-2,4-dione could be applied to polymalonamide syntheses (Scheme 3).[15,16] In this work, the polymerization was conveniently carried out by a melt process in a stirred resin flask at the melting point of azetidine-2,4-dione. In general, the mixture was stirred for only 2 min or less, but high-molecular-weight products have been obtained in all cases. The structures of polymalonamide (**6a–6e**) were further confirmed by ^1H-NMR analysis.[17] Selected properties of these polymers are given in Table II. The inherent viscosities obtained in this work range from 0.45 to 0.78 dL/g. These values are comparable to those (0.43–0.67 dL/g; $M_\eta = 6.0 \times 10^3 - 1.4 \times 10^4$) of polyamides reported by D. Yan et al.[18] This ensures the formation of synthesized polymaloamides with a certain degree of polymerization. Thermal stability

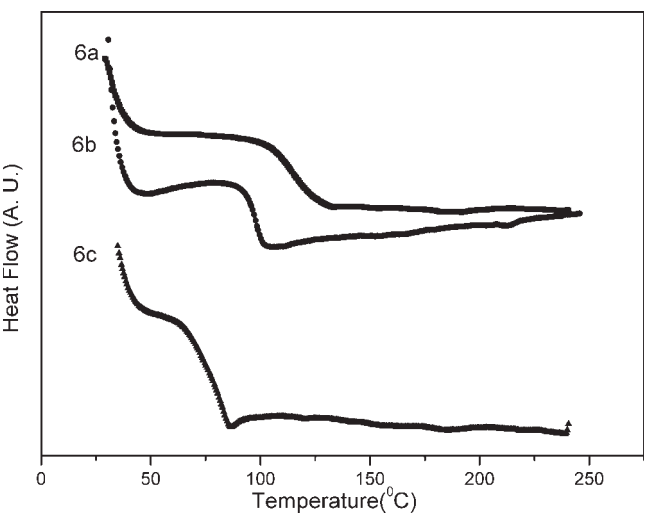
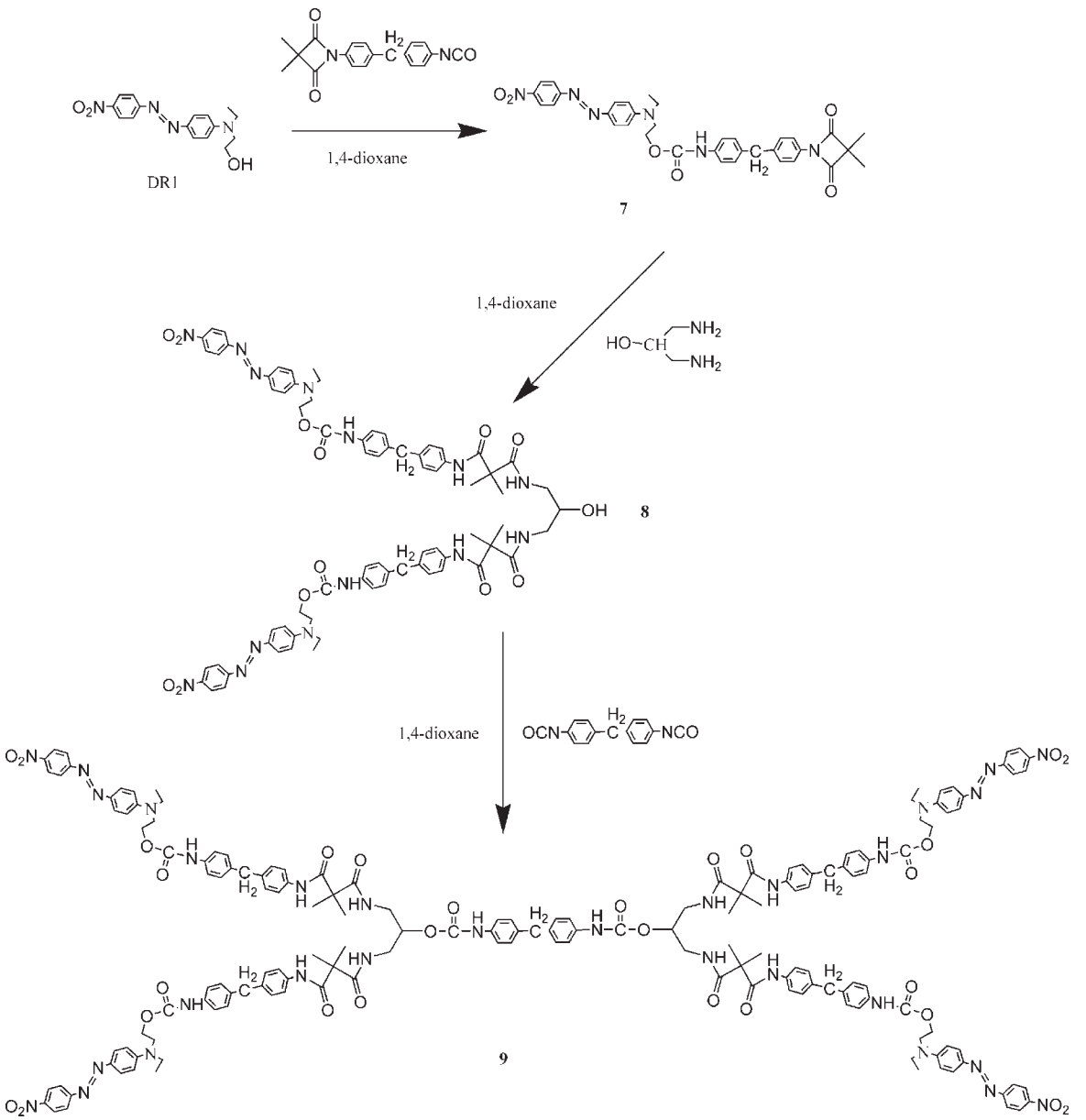
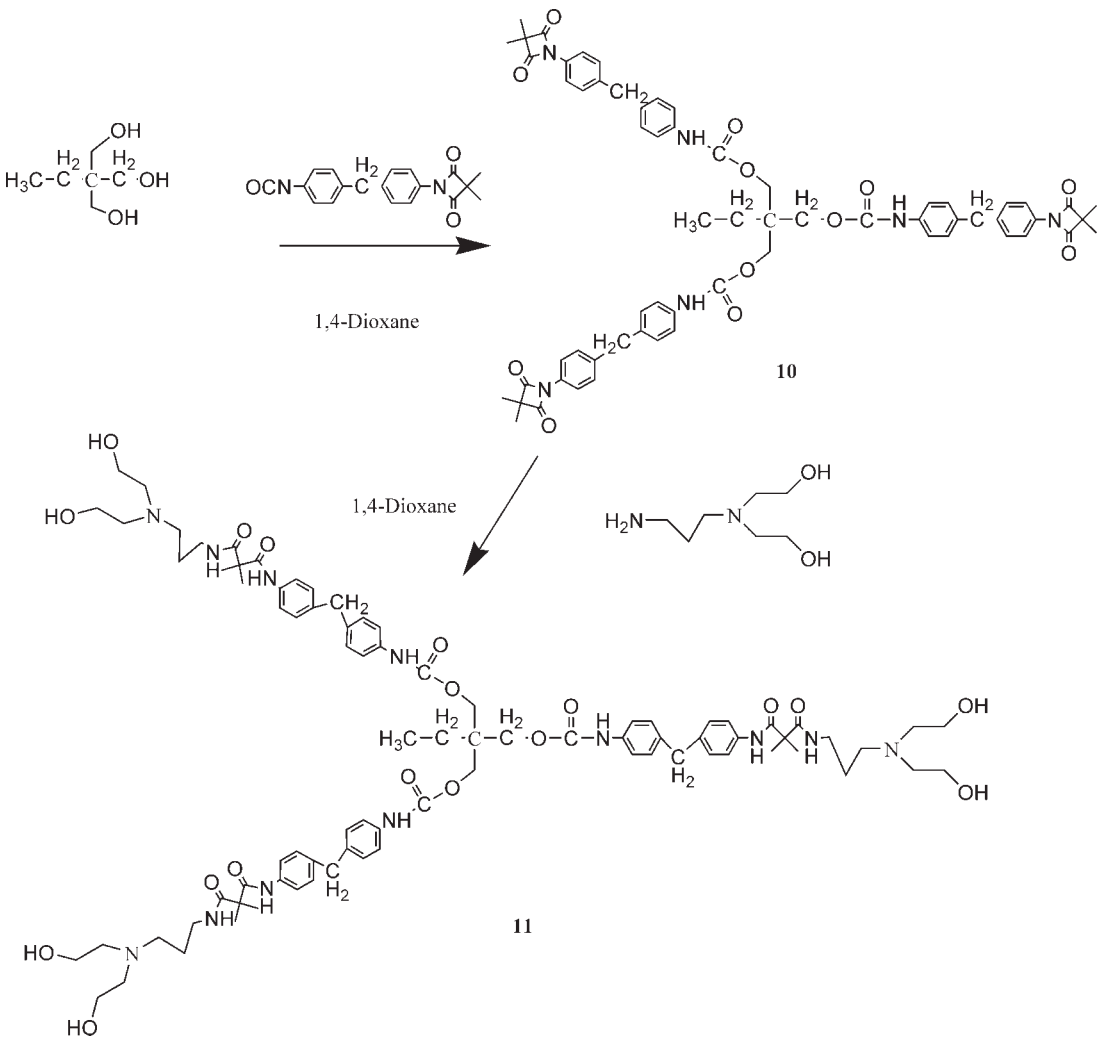


Figure 2 DSC thermograms of compounds **6a**, **6b**, and **6c**.



Scheme 4 Synthesis of structure-controlled compound **9**.

of polymalonamides was investigated by TGA analysis. All the polymers exhibited T_d values higher than 310°C. No weight loss was observed for these polymers within the temperature range of 30 to 250°C. Differential scanning calorimetry (DSC) was utilized to understand the thermal properties of polymalonamide. The same thermal treatment was used in our DSC study. The samples were heated at 200° C for 10 min in order to erase all previous thermal histories. The transition temperatures were then determined from the first heating runs, after the cooling rate of 30°C/min from 200 to 30°C. Figure 2 shows the DSC thermograms of **6a**, **6b**, and **6c** samples. The T_m values of the polymalonamides were not observed at all between 30 and 250°C. We have concluded that these polymers are amorphous in nature and exhibit glass transition temperatures only. We can find some tendency of T_g values for polymalonamide use the different aliphatic diamines. The T_g value decreases with increasing chain length of diamine. This suggests that the free volume of polymer is increased when the chain length of diamine is increased. The conditions of polymerization have also been optimized to achieve the highest molecular weight. However, the polymalonamides were found to be insoluble in the common organic solvents we tried. Therefore, we have no other alternatives but to investigate the molecular weights of the polymalonamides by viscosity determination alone instead of GPC analysis. In brief, this polymerization does not generate any by-product and requires no catalysts. Moreover, the high molecular weights can



Scheme 5 Synthesis of structure-controlled compound **11**.

be achieved through a low-reaction-temperature process in a short period of time. Therefore, the two-component system in this work offers tremendous simplicity and advantages over the conventional nylon syntheses.[19,20]

Controlled reactions of mono-isocyanato-azetidine-2,4-diones, **3a**, have also been performed in this work. The isocyanate group of **3a** is more reactive of the two functional groups, and can react readily with compounds possessing either amino, hydroxyl, or other active hydrogens. As mentioned above, the azetidine-2,4-dione, though less reactive, is more selective and can only react with aliphatic primary amines to form malonamide linkages under mild conditions. This selective reactivity seems ideal for the synthesis of complex compounds such as dendrimers without protection/deprotection steps.[21,22]

To exemplify the robustness of compound **3a**, two structure-controlled urethane/malonamide compounds were synthesized (Schemes 4 and 5). For synthesizing compound **9** (Scheme 4), compound **3a** was reacted with disperse red 1 (DR1) with a 1 to 1 molar ratio. The urethane linkage was formed by the reaction between the hydroxyl and isocyanate groups. Then the intermediate (compound **7**) was reacted with 1,3-diamino-2-propanol to give the precursor (compound **8**) of compound **9**. The core molecule was MDI. By coupling of MDI with the precursor, compound **9** was obtained in red powder form with four chromophores in periphery. Through the choice of periphery group, this approach may provide a convenient way to prepare novel nonlinear optical (NLO) materials. The incorporation of dendritic structures into NLO materials can efficiently reduce the aggregation behavior of the chromophores in the polymer matrices and subsequently enhance optical nonlinearity to a greater extent.[23] Moreover, different hydroxyl-containing periphery moieties can be incorporated in this system to derive compounds with different functionalities and properties.

In an alternative route to the structure-controlled urethane/malonamide compound, trimethylol pro-

pane (TMPO) was used as the core molecule initially (Scheme 5). Compound **10** was prepared by reacting compound **3a** with TMPO (molar ratio: 3 to 1). This led to an intermediate with azetidine-2,4-dione as the terminal groups. Compound **11** was obtained by the ring-opening addition reaction of the azetidine-2,4-dione toward the amino-containing compound, *N*-(3-aminopropyl)diethanolamine. As a result, compound **11** with six hydroxyl terminal groups was obtained in white powder form. A compound such as compound **11**, consisting of characteristics of multifunctionalities and ease of synthesis is of interest as a reactive component in thermoset or UV curable coating.[24] The structures of **9** and **11** were confirmed by ^{1}H NMR, MS and elemental analysis. The M_w/M_n value was measured by GPC using THF as eluent. The GPC traces show a single and sharp peak for compounds **9** and **11**. Moreover, their polydispersities are essentially close to unity. This indicates these molecules are in the same molecular size. Based on DSC study, compound **9** and **11** exhibited T_g values at 29 and 124°C, respectively.

CONCLUSION

In this work, improved syntheses of azetidine-2,4-diones have been achieved. The ring-opening polymerization with aliphatic amines, which is extremely rapid, has been applied to prepare polymalonamides of high molecular weight by a melt condition in absence of catalyst. The compound **3a** possessing both isocyanate and the azetidine-2,4-dione groups has also been found to provide selective chemistry that allows the rapid synthesis of controlled structures. By alternative synthesis, the controlled structures can be prepared without diverting to traditional protection and activation chemistry. The high yield, versatility, and rapid reaction of isocyanate chemistry can be widely applied to synthesis of various structures, including polyureas and polyimides.

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