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Synthesis of Bis-Ketene *N,S*-Acetals with a Polymethylene Linkage

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ABSTRACT

α-Aroyl substituted bis-ketene N,S-acetals **3–6** *with a polymethylene linkage, N,N'-bis(1-methylthio-2-aroyl)vinyl polymethylene diamines, were synthesized by reactions between α-aroyl ketene dithioacetals* **1** *and polymethylene diamines* **2** *in moderate yields. © 1996 John Wiley & Sons, Inc.*

INTRODUCTION

Ketene dithioacetals [1–6] carrying one or two electron-withdrawing groups at the α-carbon atom, generally known as either polarized [7,8], push-pull [7,8], or donor-acceptor [8] ethylenes, are versatile intermediates in many synthetic transformations. The alkylthio groups at the β carbon in these intermediates are activated by the presence of the electron-withdrawing group(s) at the α position and can therefore be displaced sequentially by various carbon, nitrogen, and oxygen nucleophiles, creating a variety of applications in C–C, C–N, and C–O bond formation [5,6]. Since the electron-withdrawing groups at the α position can also be involved in reactions with nucleophiles under some conditions, α-substituted ketene dithioacetals may also be viewed as ambident electrophiles.

In our previous work, ketene dithioacetals have been used for the preparation of heterocyclic ketene *N,N*-[9], *N,O*-[11], and *N,S*-acetals [10], which are important synthons, especially in heterocyclic synthesis [9]. Herein, we wish to report the reaction of α-aroyl ketene dithioacetals with polymethylene diamines, in anticipation of formation of ketene *N,N*- or *N,S*-acetals with a polymethylene linkage.

RESULTS AND DISCUSSION

α-Aroyl ketene dithioacetals **1**, prepared from acetophenones by successive treatment with sodium hydride, carbon disulfide, and methyl iodide in one-pot reactions [12], have been reacted with polymethylene diamines **2** in boiling toluene for a suitable period of time. After work-up and purification, bis-ketene *N,S*-acetals **3–6**, *N,N'*-bis(1-methylthio-2-aroyl)vinyl polymethylene diamines, were produced in moderate yields (Table 1). The reaction took place smoothly and was easily monitored by following the evolution of methanethiol (Scheme 1).

In addition to the main products **3–6**, a mixture of complicated polymers also resulted from the above reactions. It seems that the ratio of the reactants largely affected the final results of the reactions, and the best yields for the desired products were obtained when reacting **1** with **2** in a 5:3 molar ratio. It was also noteworthy that prolonged refluxing of the starting materials **1** and **2** in toluene led to the formation of polymers. Thus, each reaction was monitored by TLC and stopped as soon as the reacting ketene dithioacetal **1** had disappeared.

The structures of the reaction products **3–6** were confirmed by elemental analyses and spectroscopic data, and it became apparent that compounds **3–6** were formed by condensation reactions of **1** with **2**

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in a 2:1 molar ratio, with the loss of two moles of methanethiol. An intensive aroyl ion peak in the mass spectra and a carbonyl carbon resonance at δ 183.1–185.0 in the ^{13}C-NMR spectra of the products excluded from consideration reactions at the α-aroyl group. Therefore, each reaction evidently occurred at the β carbon, with one of the methylthio groups in each ketene dithioacetal being displaced by an amino group to produce a ketene *N,S*-acetal. Other spectroscopic data also substantiated the bis-ketene *N,S*-acetal structure. The intramolecular hydrogen bond of each product (*E*-configuration) is indicated by the down-field shift of the amino proton signal in the ^{1}H-NMR spectrum and the bathochromic shift of absorption of the ketonic carbonyl in the IR spectrum.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 782 spectrometer for KBr tablets. UV spectra were measured by a Hitachi 340 spectrometer in methanol solution. ^{1}H- and ^{13}C-NMR spectra were recorded in CDCl$_3$ using TMS as an internal standard on Varian Unity 200 and Geminal 300 instruments. Mass spectra were obtained on an AEI MS-50 instrument. Microanalyses were carried out by the Analytical Laboratory of the Institute.

General Procedure for the Synthesis of N,N′-Bis(1-Methylthio-2-Aroyl)Vinyl Polymethylene Diamines 3–6

To a boiling solution of 5 mmol of each α-aroyl ketene dithioacetal **1** in 90 mL of toluene was added dropwise a solution of 3 mmol of either 1,6-hexamethylenediamine or 1,8-octamethylenediamine. Since 1,10-decamethylenediamine and 1,12-dodecamethylenediamine are poorly soluble in toluene, these diamines were added portionwise to the refluxing solution of **1** in toluene. The reaction mixture was stirred continuously under refluxing and monitored by TLC. On disappearance of **1**, the solvent was evaporated under vacuum. The resultant yellow oil was redissolved in chloroform and chromatographed on a silica gel column to give pure **3–6** as solids.

N,N′-Bis(1-methylthio-2-benzoyl)vinyl-1,6-hexamethylenediamine

3a: White solid (ethyl acetate-petroleum ether, 1:7, v/v). IR: ν = 3444 (NH), 1580 (CO), 1554, 1532 cm^{-1}. UV: λ_{max} = 346 (log ε = 4.46), 248 nm (4.28). ^{1}H NMR: δ = 11.92 (t, 2H, N*H*), 7.90–7.34 (m, 10H, Ar*H*), 5.65 (s, 2H, >C=C*H*–), 3.42 (q, 4H, –NH–C*H*$_2$–), 2.47 (s, 6H, SC*H*$_3$), 1.76 (quin, 4H), 1.50 ppm (quin, 4H). ^{13}C NMR: δ = 185.0, 169.5, 140.7, 130.3, 128.1, 126.8, 86.1, 43.8, 29.3, 26.4, 14.2. MS: *m/z* = 468 (M$^+$, 6), 453 (15), 421 (44), 373 (41), 276 (25), 146 (42), 105 (100). Anal calcd for $C_{26}H_{32}N_2O_2S_2$: C, 66.63; H, 6.88; N, 5.98. Found: C, 66.77; H, 7.03; N, 5.97.

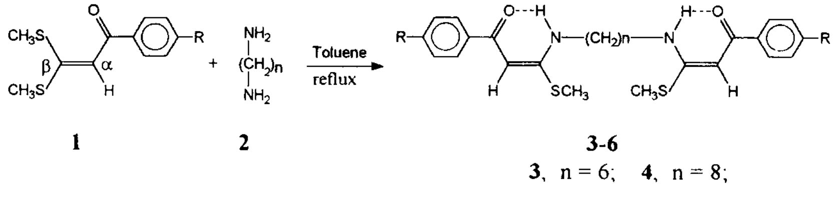
N,N′-Bis[1-methylthio-2-(4-methylbenzoyl)vinyl]-1,6-hexamethylenediamine

3b: Pale yellow solid (ethyl acetate-petroleum ether, 1:7, v/v). IR: ν = 3453 (NH), 1582 (CO), 1551, 1532 cm^{-1}. UV: λ_{max} = 347 (log ε = 4.55), 260 nm (4.67). ^{1}H NMR: δ = 11.85 (t, 2H, N*H*), 7.75 (d, 4H, Ar*H*), 7.20 (d, 4H, Ar*H*), 5.62 (s, 2H, >C=C*H*–), 3.37 (q, 4H, –NH-C*H*$_2$–), 2.44 (s, 6H, SC*H*$_3$), 2.37 (s, 6H, C*H*$_3$), 1.70 (quin, 4H), 1.47 (quin, 4H). ^{13}C NMR: δ = 184.7, 169.0, 140.4, 137.7, 128.7, 126.6, 85.8, 43.8, 29.4, 26.4, 21.4, 14.2. MS: *m/z* = 496 (M$^+$, 1), 481 (2), 449 (3), 401 (5), 119 (100). Anal calcd for $C_{28}H_{36}N_2O_2S_2$: C, 67.70; H, 7.31; N, 5.64. Found: C, 67.72; H, 7.45; N, 5.98.

N,N′-Bis[1-methylthio-2-(4-chlorobenzoyl)vinyl]-1,6-hexamethylenediamine

3d: Yellow solid (ethyl acetate-petroleum ether, 1:7, v/v). IR: ν = 3444 (NH), 1581 (CO), 1551, 1529 cm^{-1}.

SCHEME 1



1 2 3-6

3, n = 6; 4, n = 8;

5, n = 10; 6, n = 12

3–6	a	b	c	d
R	H	CH$_3$	OCH$_3$	Cl

TABLE 1 The Reaction Time, Yield, and Melting Point of Compounds **3–6**

Compound	*Time (h)*	*Yield*^{a} *(%)*	*Mp (°C)*
3a	12	49	143–145
3b	12	46	140–142
3d	12	48	158–160
4a	14	58	127–128
4c	14	65	134–136
4d	14	60	155–157
5a	18	50	112–114
5b	18	52	116–118
5d	18	56	124–126
6b	24	49	106–108
6c	24	50	144–146
6d	24	57	104–106

^{a}Isolated yield.

UV: λ_{max} = 351 (log ε = 4.58), 258 nm (4.49). ^{1}H NMR: δ = 11.87 (t, 2H, N*H*), 7.76 (d, 4H, Ar*H*), 7.35 (d, 4H, Ar*H*), 5.57 (s, 2H, >C=C*H*−), 3.37 (q, 4H, −NH-C*H*$_2$−), 2.45 (s, 6H, SC*H*$_3$), 1.71 (quin, 4H), 1.46 (quin, 4H). ^{13}C NMR: δ = 183.2, 169.7, 138.9, 136.1, 128.2, 128.0, 85.7, 43.8, 29.3, 26.4, 14.2. MS: *m*/*z* = 538 (1.8), 536 (M$^+$, 2.4), 521 (6), 489 (15), 441 (17), 301 (18), 180 (23), 139 (100). Anal calcd for $C_{26}H_{30}Cl_2N_2O_2S_2$: C, 58.09; H, 5.63; N, 5.21. Found: C, 58.03; H, 5.86; N, 4.99.

N,N'-Bis(1-methylthio-2-benzoyl)vinyl-1,8-octamethylenediamine

4a: White solid (ethyl acetate-petroleum ether, 1:7, v/v). IR: ν = 3438 (NH), 1578 (CO), 1552, 1532 cm^{-1}. UV: λ_{max} = 349 (log ε = 4.65), 265 nm (4.68). ^{1}H NMR: δ = 11.90 (t, 2H, N*H*), 7.88–7.28 (m, 10H, Ar*H*), 5.64 (s, 2H, >C=C*H*−), 3.38 (q, 4H, −NH-C*H*$_2$−), 2.47 (s, 6H, SC*H*$_3$), 1.69 (quin, 4H), 1.58–1.40 (m, 8H). ^{13}C NMR: δ = 185.0, 169.5, 140.7, 130.3, 128.1, 126.8, 86.0, 43.9, 29.4, 28.9, 26.7, 14.2. MS: *m*/*z* = 496 (M$^+$, 3), 481 (7), 449 (14), 401 (8), 377 (9), 146 (21), 105 (100). Anal calcd for $C_{28}H_{36}N_2O_2S_2$: C, 67.70; H, 7.31; N, 5.64. Found: C, 67.71; H, 7.41; N, 5.91.

N,N'-Bis[1-methylthio-2-(4-methoxybenzoyl) vinyl]-1,8-octamethylenediamine

4c: White crystals (ethyl acetate-petroleum ether, 1:7, v/v). IR: ν = 3434 (NH), 1582 (CO), 1550, 1532 cm^{-1}. UV: λ_{max} = 348 (log ε = 4.73), 280 nm (4.21). ^{1}H NMR: δ = 11.77 (t, 2H, N*H*), 7.81 (d, 4H, Ar*H*), 6.69 (d, 4H, Ar*H*), 5.59 (s, 2H, >C=C*H*−), 3.81 (s, 6H, OC*H*$_3$), 3.34 (q, 4H, −NH-C*H*$_2$−), 2.43 (s, 6H, SC*H*$_3$), 1.67 (quin, 4H), 1.50–1.28 (m, 8H). ^{13}C NMR: δ = 184.0, 168.6, 161.2, 133.0, 128.4, 113.2, 85.3, 55.2, 43.9, 29.5, 29.0, 26.7, 14.2. MS: *m*/*z* = 556 (M$^+$, 1), 541 (3), 509 (4), 460 (8), 325 (6), 176 (9), 152 (14), 135 (100). Anal calcd for $C_{30}H_{40}N_2O_4S_2$: C, 64.71; H, 7.24; N, 5.03. Found: C, 64.79; H, 7.27; N, 5.11.

N,N'-Bis[1-methylthio-2-(4-chlorobenzoyl)vinyl]-1,8-octamethylenediamine

4d: Yellow crystals (ethyl acetate-petroleum ether, 1:9, v/v). IR: ν = 3434 (NH), 1569 (CO), 1534, 1489 cm^{-1}. UV: λ_{max} = 349 (log ε = 4.71), 248 nm (4.62). ^{1}H NMR: δ = 11.85 (t, 2H, N*H*), 7.76 (d, 4H, Ar*H*), 7.35 (d, 4H, Ar*H*), 5.57 (s, 2H, >C=C*H*−), 3.36 (q, 4H, −NH-C*H*$_2$−), 2.45 (s, 6H, SC*H*$_3$), 1.68 (quin, 4H), 1.50–1.30 (m, 8H). ^{13}C NMR: δ = 183.1, 169.7, 138.9, 136.1, 128.1, 128.0, 85.6, 44.0, 29.3, 28.9, 26.7, 14.3. MS: *m*/*z* = 566 (2), 564 (M$^+$, 2), 549 (8), 517 (11), 469 (13), 445 (11), 180 (20), 156 (19), 139 (100). Anal calcd for $C_{28}H_{34}Cl_2N_2O_2S_2$: C, 59.47; H, 6.06; N, 4.95. Found: C, 59.47; H, 6.12; N, 4.93.

N,N'-Bis(1-methylthio-2-benzoyl)vinyl-1,10-decamethylenediamine

5a: White crystals (chloroform-methanol, 20:1, v/v). IR: ν = 3434 (NH), 1579 (CO), 1552, 1532 cm^{-1}. UV: λ_{max} = 348 (log ε = 4.57), 247 nm (4.32). ^{1}H NMR: δ = 11.90 (t, 2H, N*H*), 7.90–7.30 (m, 10H, Ar*H*), 5.60 (s, 2H, >C=C*H*−), 3.35 (q, 4H, −NH-C*H*$_2$−), 2.48 (s, 6H, SC*H*$_3$), 1.70 (quin, 4H), 1.52–1.20 (m, 12H). ^{13}C NMR: δ = 185.0, 169.5, 140.7, 130.3, 128.1, 126.8, 86.0, 44.0, 29.5, 29.4, 29.2, 26.8, 14.2. MS: *m*/*z* = 524 (M$^+$, 2), 509 (7), 477 (9), 105 (100). Anal calcd for $C_{30}H_{40}N_2O_2S_2$: C, 68.66; H, 7.68; N, 5.34. Found: C, 68.58; H, 7.83; N, 5.56.

N,N'-Bis[1-methylthio-2-(methylbenzoyl)vinyl]-1,10-decamethylenediamine

5b: Pale yellow crystals (chloroform-methanol, 20:1, v/v). IR: ν = 3430 (NH), 1580 (CO), 1558, 1530 cm^{-1}. UV: λ_{max} = 349 (log ε = 4.80), 255 nm (4.61). ^{1}H NMR: δ = 11.82 (t, 2H, N*H*), 7.76 (d, 4H, Ar*H*), 7.20 (d, 4H, Ar*H*), 5.62 (s, 2H, >C=C*H*−), 3.36 (q, 4H, −NH-C*H*$_2$−), 2.46 (s, 6H, SC*H*$_3$), 2.38 (s, 6H, C*H*$_3$), 1.70 (quin, 4H), 1.60–1.15 (m, 12H). ^{13}C NMR: δ = 184.7, 169.0, 140.4, 137.8, 128.7, 126.7, 85.7, 43.9, 29.4, 29.2, 29.0, 26.7, 21.3, 14.1. MS: *m*/*z* = 552 (M$^+$, 3), 537 (13), 505 (19), 457 (22), 433 (11), 160 (26), 119 (100). Anal calcd for $C_{32}H_{44}N_2O_2S_2$: C, 69.52; H, 8.02; N, 5.07. Found: C, 69.64; H, 8.12; N, 5.44.

N,N'-Bis[1-methylthio-2-(chlorobenzoyl)vinyl]-1,10-decamethylenediamine

5d: Yellow crystals (chloroform-methanol, 20:1, v/v). IR: ν = 3438 (NH), 1580 (CO), 1563, 1532 cm^{-1}. UV:

λ_{max} = 352 (log ε = 4.69), 253 nm (4.50). ^{1}H NMR: δ = 11.84 (t, 2H, N*H*), 7.76 (d, 4H, Ar*H*), 7.34 (d, 4H, Ar*H*), 5.56 (s, 2H, >C=C*H*$-$), 3.34 (q, 4H, $-$NH-C$H_2$$-$), 2.44 (s, 6H, SC$H_3$), 1.65 (quin, 4H), 1.48–1.20 (m, 12H). ^{13}C NMR: δ = 183.1, 169.7, 138.9, 136.1, 128.1, 128.0, 85.6, 44.0, 29.4, 29.3, 29.1, 26.8, 14.2. MS: *m/z* = 594 (6), 592 (M^+, 6), 577 (33), 545 (43), 497 (33), 446 (23), 366 (25), 180 (49), 139 (100). Anal calcd for $C_{30}H_{38}Cl_2N_2O_2S_2$: C, 60.69; H, 6.45; N, 4.72. Found: C, 60.62; H, 6.76; N, 4.56.

N,N'-Bis[1-methylthio-2-(methylbenzoyl)vinyl]-1,12-dodecamethylenediamine

6b: Pale yellow crystals (chloroform-methanol, 20:1, v/v). IR: ν = 3434 (NH), 1585 (CO), 1558, 1530 cm^{-1}. UV: λ_{max} = 348 (log ε = 4.75), 255 nm (4.59). ^{1}H NMR: δ = 11.83 (t, 2H, N*H*), 7.76 (d, 4H, Ar*H*), 7.20 (d, 4H, Ar*H*), 5.62 (s, 2H, >C=C*H*$-$), 3.36 (q, 4H, $-$NH-C$H_2$$-$), 2.45 (s, 6H, SC$H_3$), 2.38 (s, 6H, C$H_3$), 1.68 (quin, 4H), 1.48–1.20 (m, 16H). ^{13}C NMR: δ = 184.6, 168.9, 140.4, 137.8, 128.7, 126.7, 85.7, 44.0, 29.5, 29.4, 29.3, 29.2, 26.8, 21.4, 14.3. MS: *m/z* = 580 (M^+, 1), 565 (12), 533 (34), 483 (41), 365 (20), 223 (62), 119 (100). Anal calcd for $C_{34}H_{48}N_2O_2S_2$: C, 70.30; H, 8.33; N, 4.82. Found: C, 70.00; H, 8.42; N, 4.76.

N,N'-Bis [1-methylthio-2-(methoxybenzoyl) vinyl]-1,12-dodecamethylenediamine

6c: White crystals (chloroform-methanol, 20:1, v/v). IR: ν = 3434 (NH), 1584 (CO), 1550, 1470 cm^{-1}. UV: λ_{max} = 342 (log ε = 4.92), 271 nm (4.34). ^{1}H NMR: δ = 11.77 (t, 2H, N*H*), 7.82 (d, 4H, Ar*H*), 6.90 (d, 4H, Ar*H*), 5.60 (s, 2H, >C=C*H*$-$), 3.83 (s, 6H, OCH_3), 3.36 (q, 4H, $-$NH-C$H_2$$-$), 2.46 (s, 6H, SC$H_3$), 1.68 (quin, 4H), 1.52–1.21 (m, 16H). ^{13}C NMR: δ = 184.1, 168.7, 161.3, 133.2, 128.5, 113.3, 85.4, 55.3, 44.0, 29.6, 29.5, 29.4, 29.2, 26.9, 14.3. MS: *m/z* = 612 (M^+, 1), 597 (18), 565 (29), 517 (27), 135 (69), 43 (100). Anal calcd for $C_{34}H_{48}N_2O_4S_2$: C, 66.63; H, 7.89; N, 4.57. Found: C, 66.61; H, 7.91; N, 4.30.

N,N'-Bis[1-methylthio-2-(chlorobenzoyl)vinyl]-1,12-dodecamethylenediamine

6d: Yellow crystals (chloroform-methanol, 20:1, v/v). IR: ν = 3429 (NH), 1582 (CO), 1552, 1530 cm^{-1}. UV: λ_{max} = 349 (log ε = 4.68), 252 nm (4.55). ^{1}H NMR: δ = 11.84 (t, 2H, N*H*), 7.76 (d, 4H, Ar*H*), 7.35 (d, 4H, Ar*H*), 5.56 (s, 2H, >C=C*H*$-$), 3.35 (q, 4H, $-$NH-C$H_2$$-$), 2.44 (s, 6H, SC$H_3$), 1.67 (quin, 4H), 1.48–1.19 (m, 16H). ^{13}C NMR: δ = 183.1, 169.6, 138.9, 136.1, 128.1, 128.0, 85.6, 44.1, 29.4, 29.3, 29.2, 29.1, 26.8, 14.2. MS: *m/z* = 622 (1), 620 (M^+, 3), 605 (3), 573 (3), 523 (10), 501 (5), 139 (100). Anal calcd for $C_{32}H_{42}Cl_2N_2O_2S_2$: C, 61.82; H, 6.81; N, 4.51. Found: C, 61.93; H, 6.87; N, 4.51.

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