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A Straightforward and Novel Synthesis of Sulfur Compounds from Aliphatic Cyclic Ketones and CS_2

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ABSTRACT: *The reaction of aliphatic cyclic ketones with carbon disulfide under basic conditions, followed by an acidic treatment, unexpectedly afforded—in a mild, one-pot reaction—sulfur compounds, such as 1,2-dithiole-3-thiones, 1,3-dithiole-4-thiones, 1,3-dithiin-4-thiones, 1,2,4-trithioles, and dixanthates, instead of the usual conjugated α-oxoketene dithiolic acids*. © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:120–128, 2000

INTRODUCTION

With the aim of preparing functionalized ligands, mostly β-positioned on α,β-unsaturated carbonylic compounds, Dieter's procedure [1] was employed in the reaction of aliphatic cyclic ketones with carbon disulfide, followed by an acidic treatment. Instead of the usual synthesis of conjugated α-oxoketene dithioic acids (Figure 1), we unexpectedly obtained the 1,2-dithiole-3-thione **1a** and 1,3-dithiin-4-thione **2a** derivatives from the reaction with cyclopentanone; 1,3-dithiole-4-thione **1b** and the 1,3-dithiin-4-thione **2b** in the case of cyclohexanone; 1,2,4-trithiole **3** and the dixanthate **4** with cyclooctanone, and finally, the 1,2,4-trithiole **5** was obtained when the starting material was the 3,4-dihydro-1(2*H*)-naphthalenone (α-tetralone) (Table 1).

Of these compounds, the 1,2-dithiole-3-thione **1a** and the 1,3-dithiole-4-thione **1b** appear to be the most important types because of their use and applications as bioactive molecules, mainly against immunodeficiency diseases [2], allergies [3], as well as antitumoral agents [4], etc. Their syntheses have

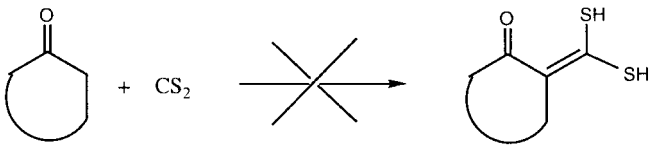

FIGURE 1 The unsuccessful synthesis of conjugated α-oxoketene dithioic acids.

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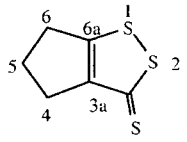
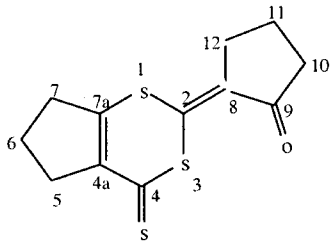
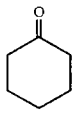
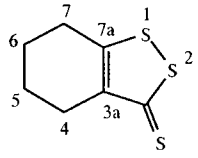
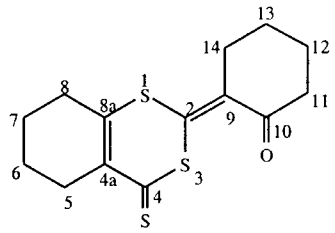
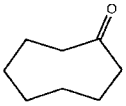
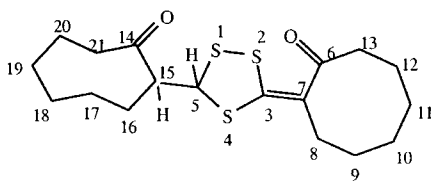
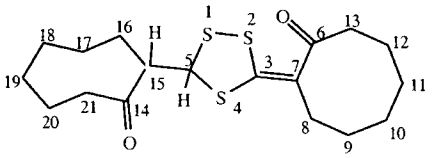
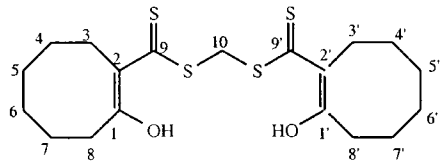
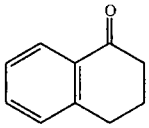
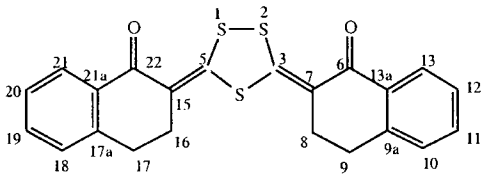
TABLE 1 Products Obtained from the Reaction of Aliphatic Cyclic Ketones and CS_2[a]

Starting material	Products
	  Compound **1a** (7.4 %) Compound **2a**(52.7%)
	  Compound **1b**(6.6%) Compound **2b**(18.9%)
	  Compound **3a** (18.7 %) Compound **3b**  Compound **4** (36.9%)
	 Compound **5** (31.2%)

[a]Yields are reported in parenthesis.

been previously described, inter alia, by the treatment of cumenes with sulfur under basic conditions [5]; by the reaction of an α-cyanodithiocarboxylate, hydrogen sulfide, and bromine water [6], and by treatment of aliphatic cyclic ketones with carbon disulfide under basic conditions yielding mainly conjugated ketene dithioacetals and further addition of P_2S_5 leading to 1,2-dithiolane-3-thiones [7]. Improvements in the synthesis of 1,2-dithiol-3-thiones have recently been communicated by Curphey et al. [8]. This author has also published on the biological activity of these compounds [9].

Herein we describe our modification of the Dieter's procedure consisting only of an acidic final treatment that affords versatile sulfur derivatives such as **1–5** whose structural novelty suggest considerable potential as substrates for sequential carbon-carbon bond-forming transformations and as interesting ligands in organometallic chemistry [10].

RESULTS AND DISCUSSION

Reaction of Cyclopentanone with CS_2

From the reaction with cyclopentanone two products were isolated, the cyclopenta[*c*]-1,2-dithiole-3-thione **1a** and the 1,3-dithiin-4-thione **2a**. The compound **1a** was identified on the basis of its spectroscopic data (IR, mass spectrometry, and ^{1}H and ^{13}C NMR spectroscopies), and its structure was confirmed by a single-crystal X-ray diffraction study (Table 2).

The X-ray data of **1a** shows that the molecule (Figure 2) is essentially planar, with maximum deviation being 0.026 Å (C6) and, although the S–S separation is so far the longest found [11], the geometric parameters (Table 2) follow the structural pattern that characterizes the 1,2-dithiole-3-thiones, *viz.* bond distances: S–S, 2.047–2.050 Å; C=S, 1.655–1.669 Å; and C–S, 1.731–1.762 Å, with the endocyclic angle subtended at S2 being larger than the one at S1. Packing appears to be governed by S . . . S interactions. The relevant nonbonding contacts involved are S1 . . . S3(0.5 + x, 0.5 − y, −0.5 + z) 3.528 and S2 . . . S3(0.5 + x, 0.5 − y, −0.5 + z) 3.442 Å.

The most abundant product was ascribed as 2-(2′-oxocyclopentyliden)-cyclopenta[*d*]-1,3-dithiin-4-thione **2a**, supported by the assignments of ^{1}H and ^{13}C NMR ($CDCl_3$, 500 MHz) spectra and confirmed by HMQC and HMBC along with HOMOCOSY experiments and by the mass spectrum (El), which exhibits the peak for the molecular ion M^+ at 268 m/z, matching the expected molecular weight for such a structure.

Reaction of Cyclohexanone with CS_2

The compounds cyclohexa[c]-1,3-dithiole-4-thione **1b** and the 2-(2′-oxocyclohexyliden)-cyclohexa[*d*]-1,3-dithiin-4-thione **2b** were isolated when cyclohexanone was used as the starting material. The structure was supported by ^{1}H and ^{13}C NMR ($CDCl_3$, 500 MHz) spectroscopies and by using HMQC and HMBC experiments. Its mass spectrum (El) displays the peak for the molecular ion M^+ at 188 *m/z*, in agreement with the expected molecular weight for the proposed compound.

Furthermore, the IR (KBr) spectrum of the compound **2b** exhibits a band at 1626 cm^{-1} for an α,β-unsaturated carbonyl group; also a band at 1542 cm^{-1} assigned to a C=C double bond and another band at 1295 cm^{-1} to a C=S double bond. The mass spectrum (El) displayed the molecular ion M^+ at 296 *m/z,* which corresponds to the expected molecular weight. Therefore, the structure **2b** is proposed (vide supra) as in the case of compound **1b.**

Reaction of Cyclooctanone with CS_2

When the reaction was carried out using cyclooctanone, the compounds 3-(2′-oxocyclooctyliden)-5-(2-oxocyclooctyl)-1,2,4-trithiole **3** and bis(2-hydroxy-1-cyclooct-1-enylxanthate)methane **4** were isolated. The first approach in the structure elucidation was by NMR spectroscopy using long-range ^{1}H-^{13}C correlations; these data suggested the presence of a mixture of two isomers **3a** and **3b** in a ratio of 8:2 respectively. The X-ray crystallographic analysis of **3** confirmed the NMR findings. In the crystal, isomers **3a** and **3b** cocrystallized in nonstoichiometric quantities (85.5:14.5% respectively) as three independent molecules in the asymmetric unit. While molecule A (Figure 3) appeared as a pure isomer **3a**, molecules B and C showed statistical disorder by site sharing of isomers **3a** and **3b.** In addition, both molecules B and C also showed conformational disorder in one of the eight-membered rings.

The conformation of the five-membered heterocyclic ring can be described as a twisted conformation, while the eight-membered rings were found in the boat-chair conformation. The S2-C3-C7-C6-O1 moiety was essentially planar (average deviation: 0.0204 Å) with an S2 . . . O1 nonbonding interaction significantly shorter than the sum of the van der Waals radii (molecule A: 2.470, molecule B: 2.524 and molecule C: 2.497 Å).

On the other hand, the less abundant product **4** has the structure depicted in Figures 4 and 5, supported by ^{1}H and ^{13}C NMR ($CDCl_3$, 500 MHz) spectroscopies and by X-ray diffraction studies.

TABLE 2 Crystal Data and Experimental Crystallographic Details for Compounds **1a, 3, 4**, and **5**[a]

Compound	**1a**	**3**	**4**	**5**
Crystal Size	0.46 × 0.44 × 0.44	0.44 × 0.38 × 0.30	0.72 × 0.40 × 0.08	0.70 × 0.24 × 0.08
Color/Shape	yellow/prism	yellow/block	yellow/plate	yellow/plate
Empirical Formula	$C_6H_6S_3$	$C_{18}H_{26}O_2S_3$	$C_{19}H_{28}O_2S_4$	$C_{22}H_{16}O_2S_3$
M	174.29	370.57	416.65	408.53
Crystal System	monoclinic	monoclinic	monoclinic	triclinic
Space Group	$P2_1/n$	$P2_1/c$	$P2_1/c$	P-1
a/Å	7.196(1)	21.198(1)	12.608(3)	7.7636(5)
b/Å	10.630(1)	11.425(1)	9.926(2)	15.410(1)
c/Å	9.617(1)	24.329(3)	17.352(3)	15.546(1)
α/°	90	90	90	96.272(9)
β/°	94.75(1)	107.73(5)	105.04	93.856(4)
γ/°	90	90	90	100.112(7)
V/Å^3	733.11(14)	5612.3(9)	2097.2(7)	1812.9(2)
Z	4	12	4	4
F(000)	360	2376	888	848
D_c/g cm^{-3}	1.579	1.316	1.320	1.497
μ/mm^{-1}	0.910	3.668	0.463	3.863
Radiation	Mo Kα	Cu Kα	Mo Kα	Cu Kα
Tmin/Tmax	—	0.2952 / 0.4058	—	0.1729 / 0.7475
θ range	1.5–30.0°	1.5–56.75°	1.5–25.0°	1.5–56.75°
Index ranges	$h = 0 \rightarrow 10$ $k = 0 \rightarrow 14$ $l = -13 \rightarrow 13$ plus Friedel pairs	$h = -1 \rightarrow 22$ $k = -1 \rightarrow 12$ $l = -26 \rightarrow 25$	$h = 0 \rightarrow 14$ $k = 0 \rightarrow 11$ $l = -20 \rightarrow 19$	$h = 0 \rightarrow 8$ $k = -16 \rightarrow 16$ $l = -16 \rightarrow 16$
Reflns. Collected	4546	9165	3689	4487
Data/Parameters	2129/107	7462/665	3689/261	498
Final *R*	0.0357	0.0723	0.0691	0.0481
Final *wR*	0.0795	0.1860	0.1599	0.1258
Goodness-of-fit	1.082	1.036	1.008	1.045
Largest Diff. Peak and Hole	0.348 and −0.286	0.482 and −0.369	0.315 and −0.279	0.305 and −0.336

[a]R indices; $R = \Sigma(F_o^2 - F_c^2)/\Sigma F_o^2$ (based on *F*), $wR = [\Sigma(w|F_o^2 - F_c^2|)^2/\Sigma(wF_o^2)^2]^{1/2}$, (based on F^2).
$wR = \Sigma[w(F_o^2 - F_c^2)^2]/\Sigma w(F_o^2)^2]\}^{1/2}$

The formation of the compound **4** can be explained as illustrated in Figure 5.

With regard to this molecule, the symmetric structure observed in solution is no longer retained in the solid state, probably due to the conformational disorder observed in both eight-membered rings which, in turn, was modeled into two contributors (70:30%). For major components, the ring conformation can be described as a boat-chair conformation for ring A (C1 to C8) and as an intermediate conformation between boat-chair and twist-boat-chair conformations for ring B (C1′ to C8′). The conjugated C=S and C=C double bonds adopt a quite closely coplanar s-cis conformation, stabilized by strong intramolecular hydrogen bonds; O1-H1 . . . S2 [O1-H1: 1.15(9), H1 . . . S2 1.75(9), O1 . . . S2: 2.844(6)Å, O1-H1 . . . S2 158(7)°], and O1′-H1′ . . . S2′ [O1′-H1′: 1.15(8), H1′ . . . S2′: 1.69(8), O1 . . . S2: 2.804(6)Å, O1′-H1′ . . . S2′: 163(6)°].

Reaction of α-Tetralone and CS_2

When the 3,4-dihydro-1(2H)-naphthalenone (α-tetralone) was used as the starting material under the aforementioned conditions, the 3,5-*bis*(2-tetralonyliden)-1,2,4-trithiole **5** was obtained. The molecular ion M^+ was observed in mass spectrometry (El) at 408 *m/z,* in agreement with the molecular weight for a dimeric derivative and, tentatively, two symmetric structures (**5a** and **5b**) may be considered (see Figure 6).

The ^1H and ^{13}C NMR ($CDCl_3$, 500 MHz) spectra, together with HMQC and HMBC experiments were in good agreement with both structures. Nevertheless, using such data, we were unable to distinguish between them. The X-ray crystallographic study of the compound (**5a** or **5b**) enabled us to make the assignment of the structure as depicted in Figure 7.

Compound **5b** crystallizes with two chemically similar, but crystallographically different, molecules A (S1 → O2) and B (S31 → O4). The spectroscopic analyses confirm the 1,2,4-trithiacyclopentane structure. Furthermore, it reveals that the molecules possess the s-syn conformation with respect to the α,β-unsaturated carbonyl moiety in all cases. Overall conformations are roughly planar in both cases, with the benzene rings slightly twisted in the same direc-

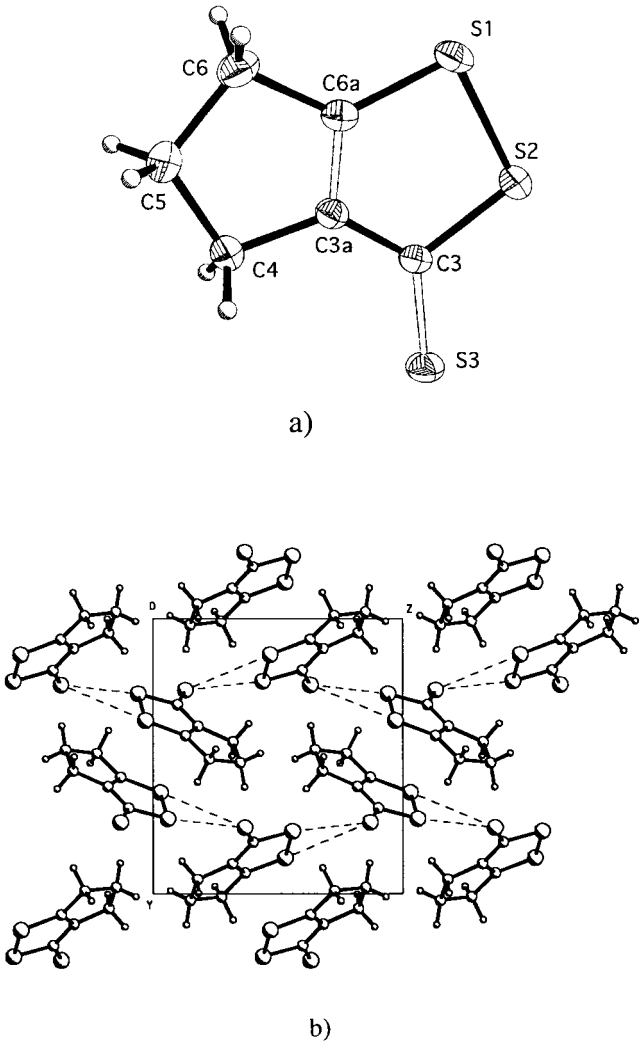


FIGURE 2 (a) ORTEP-like view of **1a.** Thermal ellipsoids at 30% probability level. (b) Unit cell of **1a** projected down the **a** axis showing the S ⅔ S interactions.

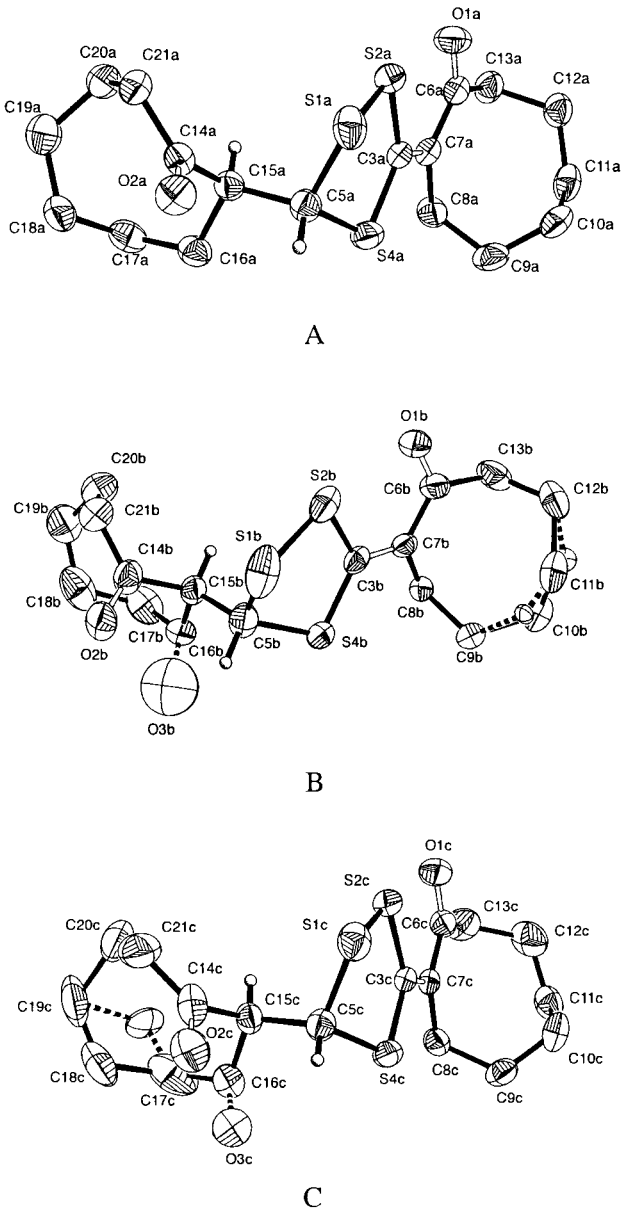


FIGURE 3 ORTEP-like view of **3,** minor components shown connected by dashed lines. Thermal ellipsoids at 30% probability level.

tion (molecule A, 14.9 and 11.5°; molecules B, 12.9 and 8.1°), apparently as result of the twist-boat conformation adopted by the cyclohexanone rings. As found in compound **3**, the coplanar system S–C = C–C = O gives rise to strong S···O intramolecular interactions (S1···O2: 2.501, S2···O1: 2.555, S31···O4: 2.525 and S32···O3: 2.472 Å). Comparison of the bond lengths (Table 2) shows that, although not required by the crystal, the molecule (isolated) would be expected to have a mirror plane. Additional S···O intermolecular interactions (S1···O3: 2.995 and S32···O2: 3.212 Å) are responsible for the fact that, in the crystal, pseudo-centrosymmetric dimers can be observed with single molecules stacking in alternate fashion into columns parallel to the **a** direction.

A mechanism which would account for the formation of the new compounds **2** thought to be similar to that proposed by Yokoyama et al. [6] for compounds **1** and is given in Figure 8.

As can be observed in Figure 8, two dithioic derivatives react, affording an intermediate with loss of H_2S, and further rearrangement of this intermediate yields **2.** On the basis of the mechanism proposed by Tominaga [12] for 1,2,4-trithioles, a similar mechanism can be suggested for the formation of compounds **3** and **5.**

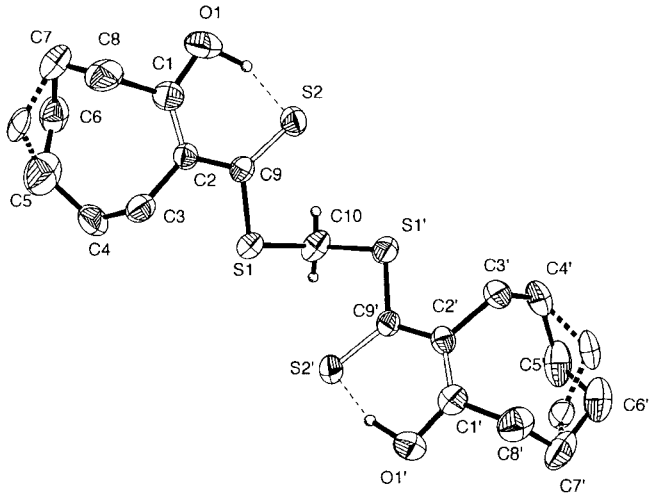


FIGURE 4 ORTEP-like view of **4,** minor components shown connected by dashed lines. Thermal ellipsoids at 30% probability level.

CONCLUSION

A simple one-pot synthesis leading to new sulfur compounds of noteworthy structural variety and novelty is reported. Work is in progress to increase the scope of our method, and attempts to increase the applications of these compounds in the syntheses of metallic complexes are also underway.

EXPERIMENTAL

General Methods

All NMR spectra were recorded on a Varian Unity 500 MHz spectometer (500 MHz for ^{1}H and 125.7 MHz for ^{13}C) at a probe temperature of 25°C. Reported peaks are referenced to internal TMS. All normal mode ^{13}C NMR spectra were acquired with composite pulse decoupling, namely wide band alternating phase lower-power technique for zero residue splitting (Waltz 16) as implemented in the spectrometer software. The sequence for the inverse mode heteronuclear multiple bond correlation (HMBC) includes a low-pass J filtered [13] to suppress one bond correlation (evolution time: 3.6 milliseconds). The polarization transfer time was set to 90 ms to optimize for long range heterodecoupling. The recycling delay was 2.5 seconds. A total of 128 2K point spectra were acquired and zero filled to 256 in t_1 window functions including a shift by $\pi/6$ in t_2 and 2 Hz Lorentzian broadening in t_1 dimensions. The IR spectra were recorded on a Perkin-Elmer 283 B or 1420 spectrometer. The electronic impact (EI) ionization mass spectra were acquired on a JEOL JMS-SX102-A Mass spectrometer operated in the positive ion mode. The acquisition conditions were ion source temperature 230°C, ionization energy 70 eV and ionization current 100 μA. High-resolution measurements were performed at 10000 resolutions using magnetic field scans and perfluorokerosene as internal reference. Melting points were measured using a Mel-Temp II apparatus and are uncorrected. Column chromatography was performed with Merck silica-gel (70-230 mesh) using hexane:ethyl acetate in a 9:1 ratio as eluent. All reagents were obtained from commercial suppliers and used as received. Reactions were performed under a nitrogen atmosphere in carefully dried glassware. Tetrahydrofuran (THF) was distilled from sodium-benzophenone under an argon atmosphere.

Reaction of the Aliphatic Cyclic Ketones with CS_2

A solution of hexamethyldisilazane (8.25 g, 51.1 mmol) in THF was kept in an ice bath under magnetic stirring and allowed to react with *n*-BuLi (51.1 mmol) for 15 minutes. The mixture was cooled at −78°C and HMPA (9g, 50 mmol) was added, the stirring being continued for 30 minutes. The aliphatic cyclic ketone (49 mmol) was then added dropwise during another 45 minutes together with CS_2 (3.9 g, 51.1 mmol), and the mixture was then warmed to room temperature. Finally, a solution of H_2SO_4 10% was added to effect neutralization. The reaction mixture was extracted with CH_2Cl_2 and dried with anhydrous Na_2SO_4. The solvent was removed under reduced pressure, and the residue was recrystallized from CH_2Cl_2 or chromatography was performed on the residue on silica-gel, eluting with hexane/AcOEt in a ratio 9/1 to obtain the corresponding products.

Compound **1a** (537 mg, 7.4%), yellow crystals, m.p. 121–122 °C; IR ν_{max}(KBr)/cm^{-1}: 1508 (C=C), 1141 (C=S); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.68 (m, 4H, CH_2-5, CH_2-4), 2.96 (t, 2H, CH_2-6) ppm.; ^{13}C NMR (50 MHz, $CDCl_3$): δ 29.0, 30.4, 34.0 (C-5, C-4, C-6), 175.1, 155.7 (C-6a, C-3a), 208.2 (C-3) ppm.; MS-EI (*m/z*): 174(M^+); 141(M^+-S); 109(M^+-2S). HRMS: Found, 173.9627. $C_6H_6S_3$ (M^+). Calcd. 173.9632.

Compound **2a** (3.83 g, 52.7%), dark orange solid, m.p. 155–157°C; IR ν_{max}(KBr)/cm^{-1}: 1674 (C=O), 1535 (C=C), 1124 (C=S); ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.98 (q, 2H, CH_2-6), 2.05 (q, 2H, CH_2-11), 2.43 (t, 2H, CH_2-10), 2.62 (t, 2H, CH_2-12), 2.83 (tt, 2H, J = 1 Hz, CH_2-7), 3.01 (tt, 2H, J = 1 Hz, CH_2-5) ppm.; ^{13}C NMR (125 MHz, $CDCl_3$); δ 203.5 (C-9), 203.2 (C-4), 148.1, 138.5 (C-7a, C-4a), 136.4, 125.8 (C-2, C-8), 39.9, 39.3, 34.4, 30.2, 20.2, 20.1 (C-7, C-

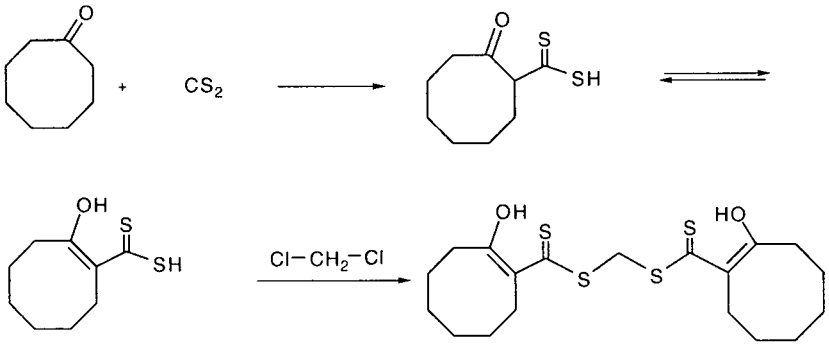


FIGURE 5 Formation of compound **4.**

TABLE 3 Selected Geometric Parameters (Å, °)

	Compound **1a**		
S1–S2	2.0580(8)	S1–C6a	1.712(2)
S2–C3	1.744(2)	S3–C3	1.662(2)
C6a–S1–S2	93.07(7)	C3–S2–S1	97.58(7)
	Compound **3**		
S1A–S2A	2.095(3)	S1A–C5A	1.816(6)
S2A–C3A	1.754(6)	C3A–S4A	1.750(6)
S4A–C5A	1.786(6)		
C6A–O1A	1.224(8)	C14A–O2A	1.208(7)
S1B–S2B	2.088(4)	S1B–C5B	1.801(9)
S2B–C3B	1.748(6)	C3B–S4B	1.753(7)
S4B–C5B	1.808(7)		
C6B–O1B	1.221(8)	C14B–O2B	1.203(9)
S1C–S2C	2.090(3)	S1C–C5C	1.814(7)
S2C–C3C	1.760(6)	C3C–S4C	1.736(6)
S4C–C5C	1.808(7)		
C6C–O1C	1.235(8)	C14C–O2C	1.268(10)
	Compound **4**		
S1–C9	1.762(6)	S1–C10	1.799(7)
S2–C9	1.661(6)	S1′–C9′	1.751(6)
S1′–C10	1.787(7)	S2′–C9′	1.681(6)
O1–C1	1.335(8)	O1′–C1′	1.329(8)
C1–C2	1.371(9)	C1′–C2′	1.364(9)
	Compound **5**		
S1–C5	1.736(3)	S1–S2	2.1137(13)
S2–C3	1.741(3)	C3–C7	1.360(5)
C3–S4	1.745(3)	S4–C5	1.733(3)
C5–C15	1.369(5)	C6–C7	1.456(5)
C6–O1	1.243(4)	C14–C15	1.447(5)
C14–O2	1.243(5)	S31–C35	1.738(3)
S31–S32	2.1125(13)	S32–C33	1.733(3)
C33–C37	1.371(6)	C33–S34	1.736(3)
S34–C35	1.753(4)	C35–C45	1.356(5)
C36–C37	1.449(5)	C36–O3	1.236(5)
C44–C45	1.447(6)	C44–O4	1.244(4)

10, C-5, C-12, C-6, C-11) ppm.; MS-EI (*m/z*): 268 (M^+); 235(M^+-S); 142(M^+-$C_6H_6S_2$). HRMS: Found, 268.0049. $C_{12}H_{12}OS_3$ (M^+). Calcd. 268.0050.

Compound **1b** (580 mg, 6.6%), yellow crystals, m.p. 118–120°C; IR ν_{max}(KBr)/cm^{-1}: 1528 (C=C), 1146 (C=S); ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.82 (t, 2H, CH_2-7), 2.59 (t, 2H, CH_2-4), 1.82 (m, 4H, CH_2-5, CH_2-6) ppm.; ^{13}C NMR (50 MHz $CDCl_3$): δ 20.8, 21.3 (C-5, C-6), 27.4, 29.5 (C-7, C-4), 143.4, 169.0 (C-3a, C-7a), 215.5 (C-3) ppm.; MS-EI (*m/z*): 188(M^+), 155(M^+-S), 123(M^+-2S). HRMS: Found, 187.9783. $C_7H_8S_3$ (M^+). Calcd. 187.9788

Compound **2b** (1.63 g, 18.9%), orange solid, m.p. 149–151°C; IR ν_{max}(KBr)/cm^{-1}: 1626 (C=O), 1542 (C=C), 1295 (C=S).; ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.72 (m, 4H, CH_2-12, CH_2-13), 1.80 (m, 4H, CH_2-6, CH_2-7), 2.45 (m, 2H, CH_2-11), 2.50 (m, 2H, CH_2-14), 2.78 (tt, 2H, CH_2-5), 2.44 (tt, 2H, CH_2-8) ppm.; ^{13}C NMR (125 MHz, $CDCl_3$): δ 208.7 (C-4), 196.7 (C-10), 147.9 (C-8a), 134.3 (C-4a), 134.2 (C-2), 123.4 (C-9), 39.6 (C-11), 32.6 (C-8), 28.4 (C-14), 28.0 (C-5), 23.3 (C-12), 22.8 (C-13), 22.4 (C-6), 22.0 (C-7); MS-EI (m/z): 296(M^+); 263(M^+-S); 156(M^+-$C_7H_8S_2$). HRMS: Found, 296.0354. $C_{14}H_{16}OS_3$ (M^+). Calcd. 296.0363.

Compound **3a** (0.77 g, 18.7%), light yellow crystals, m.p. 125–127°C; IR ν_{max}(KBr)/cm^{-1}: 1697 (C=O); 1246 (C=S); ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.86 (d, 1H, CH-5), 3.45 (dt, 1H, J = 10, 10, 3.5 Hz, CH-15), 2.76–2.8 (m, 2H, CH_2-12), 2.90 (m, 2H, CH_2-8) ppm.; ^{13}C NMR (125 MHz, $CDCl_3$): δ 217.1 (C-14), 199 (C-6), 161.8, 127.3 (C-3, C-7), 59.0 (C-5), 51.3 (C-15), 45.7 (C-21), 28.3 (C-20), 24.7 (C-19), 26.1 (C-18), 21.8 (C-17), 34.8 (C-16), 37.9 (C-13), 28.6 (C-12), 28.9 (C-11), 28.3 (C-10), 24.3 (C-9), 33.2 (C-8) ppm.; MS-EI (*m/z*): 370. (M^+). HRMS: Found, 370.1105. $C_{18}H_{26}O_2S_3$ (M^+). Calcd. 370.1095.

Compound **3b:** ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.88 (d, 1H, J = 10 Hz, CH-5), 3.96 (dt, 1H, J = 10, 10, 3.5 HZ CH-15), 2.76–2.80 (m, 2H, CH_2-13), 2.81

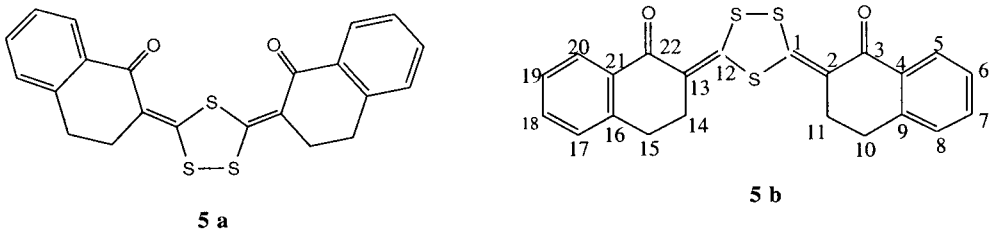


FIGURE 6 The two isomers of compound **5.**

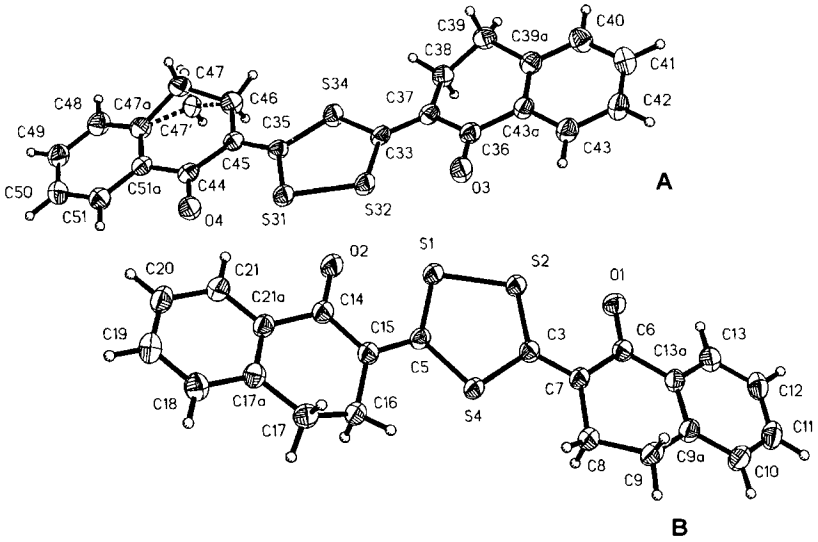


FIGURE 7 ORTEP-like view of **5b,** minor components shown connected by dashed lines. Thermal ellipsoids at 30% probability level.

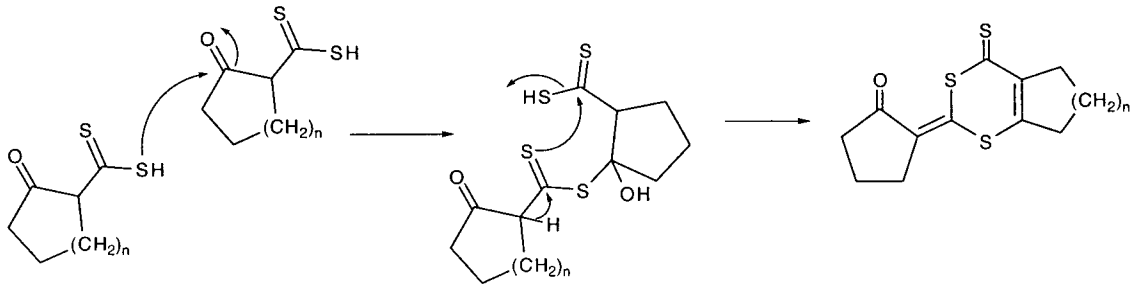


FIGURE 8 Proposed mechanism for the formation of compounds **2.**

(m, 2H, CH_2-8) ppm.; ^{13}C NMR (125 MHz, $CDCl_3$): δ 217.2 (C-14), 199.4 (C-6), 161.4, 126.8 (C-3, C-7), 59.8 (C-5), 51.7 (C-15), 35.7 (C-16), 22.0 (C-17), 26.1 (C-18), 24.7 (C-19), 28.1 (C-20), 45.5 (C-21), 32.9 (C-8), 24.2 (C-9), 28.1 (C-10), 29.0 (C-11), 28.4 (C-12), 37.8 (C-13) ppm.

Compound **4** (3.54 g, 36.9%), yellow crystals, m.p. 103–106 °C; IR ν_{max}(KBr)/cm^{-1}: 1628 (C=C); ^1H NMR (500 MHz, $CDCl_3$): δ 5.08 (s, 2H, CH_2-10), 2.82 (m, 4H, CH_2-8, CH_2-8′), 2.58 (m, 4H, CH_2-3, CH_2-3′), 1.71, 1.81, 1.48 (m, 16H, CH_2-4, CH_2-4′, CH_2-7, CH_2-7′, CH_2-5, CH_2-5′, CH_2-6, CH_2-6′), 15.81 (t, 2H, OH) ppm.; ^{13}C NMR (125 MHz, $CDCl_3$): δ 212.2 (C-9, C-9′), 180.6 (C-1, C-1′), 37.8 (C-10) ppm.; MS-EI (*m/z*):

416. (M^+). HRMS: Found, 416.0967. $C_{19}H_{28}O_2S_4$ (M^+). Calcd. 416.0972.

Compound **5** (3.11 g, 31.2%), orange crystals, m.p. 205 °C (dec.); IR ν_{max}(KBr)/cm^{-1}: 1587 (C=O); ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.05 (dd, 2H, J = 1.5, 7.5 Hz, CH-13, CH-21), 7.36 (dt, 2H, J = 1.5, 7.5, 7.5 Hz, CH-12, CH-20), 7.48 (dt, 2H, J = 1.5, 7.5, 7.5 Hz, CH-11, CH-19), 7.26 (d, 2H, CH-10, CH-18), 3.06 (s, 8H, CH_2-8, CH_2-9, CH_2-16, CH_2-17) ppm.; ^{13}C NMR (125 MHz, $CDCl_3$): δ 182.1 (C-6, C-14), 157.2 (C-3, C-5), 121.8 (C-7, C-15), 132.0 (C-13a, C-21a), 127.6 (C-13, C21), 127.1 (C-12, C-20), 132.8 (C-11, C-19), 127.9 (C-10, C-18), 141.8 (C-9a, C-17a), 30.3 (C-8, C-16), 27.8 (C-9, C-17) ppm.; MS-EI (*m/z*): 408 (M^+). HRMS: Found, 408.0320. $C_{22}H_{16}O_2S_3$ (M^+). Calcd. 408.0312.

X-ray Crystal Structure Determinations of Compounds **1a, 3-5**

Molecular structures of compounds **1a, 3–5** were analyzed by X-ray diffraction methods following very similar procedures. Crystal data for the four samples and details of the experimental results are shown in Table 1.

For each sample, crystals were mounted in air on glass fibers. Accurate cell parameters were determined by refinement from the setting of 25 reflections and diffraction intensities measured at 293 K using an ω-θ scan method on a Siemens P4/PC difractometer equipped with graphite-monochromated radiation. The intensities of three standard reflections, recorded every 100 collected reflections, showed no changes. All data sets were corrected for Lorentz-polarization effects and empirical absorption corrections based on y scans were applied to data sets of compounds **3** and **5.**

The structure of each compound was determined by direct methods (SIR92) [14] and refined by full-matrix least-squares methods using SHELXL97 [15]. Hydrogen atoms, except in compound **2,** were set to ride on the parent C atoms. The nonhydrogen atoms were refined with anisotropic thermal parameters. Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). Any request to the CCDC for this material should quote the full literature citation and the reference number CCDC 135304 to CCDC 135307.

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