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A New General Route to Thiophenophanes: Synthesis and Properties of [*n*](2,5)Thiophenophane-1,*n*-diones

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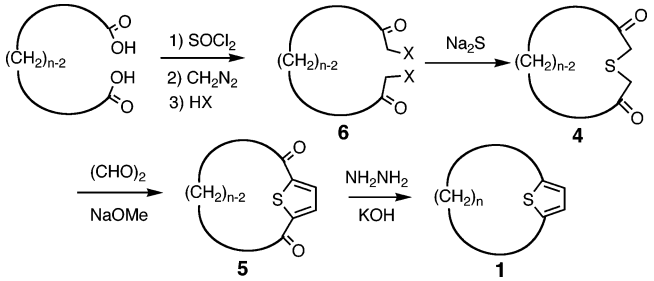
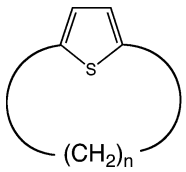


A series of [*n*](2,5)thiophenophane-1,*n*-diones (**5**) ($n = 9$, 10, 12, 14, 16, and 20) were synthesized in a simple four-step route starting from the appropriate 1,ω-oligomethylenedicarboxylic acids. The bis(halomethylketones) (**6**), which were obtained by successive treatment of the diacids with $SOCl_2$, diazomethane, and HBr or HCl, were cyclized by Na_2S under high dilution conditions. The obtained monomeric cyclic diketosulfides (**4**) were condensed with glyoxal in MeOH by slowly adding dilute NaOMe affording **5**. The thiophene-2,5-dicarbonyl moiety of **5** ($n = 9$) is significantly deformed as shown by X-ray crystallography, and the effect of the strain is reflected in the C=O stretching frequencies and the $\pi-\pi^*$ and the $n-\pi^*$ absorptions.

Introduction

Since a thiophene ring is readily manipulated synthetically, it has been used as a latent functionality in organic synthesis.[1] However, thiophene-containing macrocycles, thiophenophanes, have received only limited attention mainly because of the lack of a general and mild synthetic method.

The most common [*n*](2,5)thiophenophanes (**1**) and their derivatives have been synthesized by methods that can be classified into two types: (I) cyclization of suitably substituted thiophene derivatives and (II) construction of a thiophene ring in a macrocycle. The first type includes intramolecular acylation of ω-(2-thienyl)alkanoic acid chloride in chloroform in the presence of partially hydrolyzed $AlCl_3$ affording [*n*](2,5)-thiophenophan-1-one (**2**) ($n = 9-12$) in 8−64% yield[2] or intramolecular acylation of ω-(2-thienyl)alkanoic acid in acetonitrile in the presence of excess $(CF_3CO)_2O$ and a catalytic amount of H_3PO_4 giving **2** ($n = 9$, 10, 12, 14, and 18) in 9−66% yield.[3]



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Cyclization of thiophene derivatives also has been accomplished by intramolecular alkylation of ω-iodo-β-ketoesters (**3**) in methyl ethyl ketone (MEK) in the presence of K_2CO_3 followed by hydrolysis with decarboxylation that provided **2** ($n = 11$ and 13).[4] This method was simplified later to use a thienylacetate moiety instead of a β-ketoester group as the

(1) Meyers, A. I. *Heterocycles in Organic Synthesis*, John Wiley & Sons: New York, 1974.

(2) Gol'dfarb, Ya. L.; Taits, S. Z.; Belen'kii, L. I. *Tetrahedron* **1963**, *19*, 1851−1866.

(3) (a) Galli, C.; Illiminati, G.; Mandolini, L. *J. Org. Chem.* **1980**, *45*, 311−316. (b) Catoni, G.; Galli, C.; Mandolini, L. *J. Org. Chem.* **1980**, *45*, 1906−1908.

(4) Gol'dfarb, Ya. L.; Taits, S. Z.; Bulgakova, V. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1963**, 1299−307.

10.1021/jo060889n CCC: $33.50
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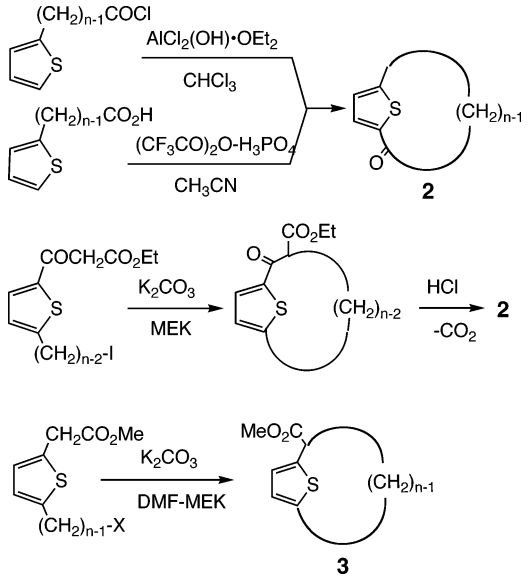
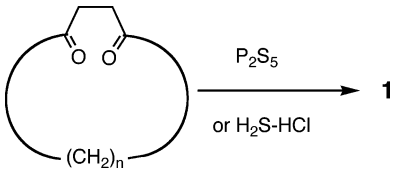
SCHEME 1. Cyclization of Thiophene-Containing Precursors



SCHEME 2. Construction of a Thiophene Ring on a Macrocycle

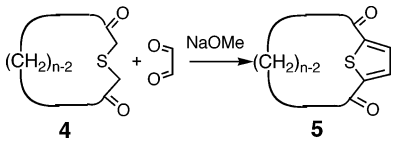


precursor of an anion for cyclization to thiophenophanes **3** ($n = 10$ and 12).[5] These methods have wide applicability but suffer from the accessibility of the appropriate thiophene-containing precursors (Scheme 1).[6]

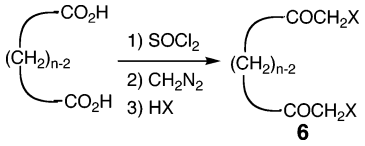
The only reported method of the second type is the application of the Paal−Knorr reaction on macrocyclic 1,4-dicarbonyl compounds to produce **1** (Scheme 2). The drawbacks of this method are limited availability of the diketones, and the conversion to the thiophenophane is not always successful even though several sulfurization reagents and conditions may be applied: 80% yield for $n = 8$,[7−8] but 37% yield for $n = 11$,[9] and only a trace in the case of $n = 10$.[10]

Here, we describe a new general synthetic method for **1**, which belongs to the second type. The method is an extension of our thiophenophane synthesis[11] and includes condensation

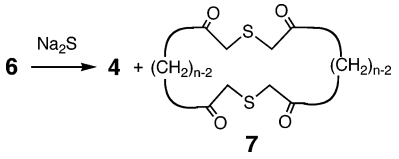
SCHEME 3. Condensation of Cyclic Diketosulfides 4 with Glyoxal to Form Thiophenophanediones 5



SCHEME 4. Preparation of Bis(halomethylketones) 6



SCHEME 5. Cyclization of Bis(halomethylketones) 6



of cyclic oligomethylene diketosulofides (**4**) with glyoxal to give [*n*](2,5)thiophenophane-1,*n*-diones (**5**) as the key step (Scheme 3).

Results and Discussion

Commercially available 1,ω-oligomethylenedicarboxylic acids were converted to the corresponding 1,ω-dihalooligomethylene-2,(ω-1)-dione (**6**) (Scheme 4) by successive treatments with thionyl chloride, diazomethane, and hydrochloric or hydrobromic acid in excellent yields.[12−15] As reported already,[11] the more reactive bromides are preferred over the chlorides for the subsequent cyclization reaction with Na_2S, but because the preparation of the bis(bromoacetyl) compounds requires a large excess of diazomethane to make pure bis(diazoketones)[12] we utilized bromides only for short chain compounds.

Cyclization of 6 with Na_2S. Cyclization of the bis(haloacetyl) compounds **6** (Scheme 5) was conducted under our standard high dilution conditions in which a solution of a bis(haloacetyl) compound in benzene or other suitable solvents and a solution of sodium sulfide in aqueous EtOH were added simultaneously to refluxing EtOH over a period of 8−12 h. Chromatographic separation (silica gel) of the crude products gave the monomeric cyclic diketosulfide **4** and the corresponding dimer **7** as listed in Table 1.

Most of the cyclic diketosulfides **4** ($n = 9$, 10, 12−16, and 19) already have been prepared by Baccetti and co-workers using **6** (X = Cl).[16] However, they obtained **4** ($n = 9$) only as an impure solid in yield of 5% as estimated from its bis(2,4-dinitrophenylhydrazone). By using bromide **6** ($n = 9$, X = Br), we could obtain pure **4** ($n = 9$) in 20% yield.

(5) Taits, S. Z.; Bulgakova, V. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1984**, 218−225 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1984**, 105−201).

(6) For the synthesis of 3,4-dibromo derivatives of **1**, a general method applicable for $n = 8$, 10−12, and 14 has been developed utilizing pyrolysis of the appropriate disulfones of dithiathiophenophanes. See: Li, Y.-Q.; Thiemann, T.; Mimura, K.; Sawada, T.; Mataka, S.; Tashiro, M. *Eur. J. Org. Chem.* **1998**, 1841−1850. Unfortunately, the method does not appear to be examined for its applicability to unsubstituted **1**, which requires a method for selective oxidation of sulfide groups in the presence of electron-rich thiophene.

(7) (a) Nozaki, H.; Koyama, T.; Mori, T.; Noyori, R. *Tetrahedron Lett.* **1968,** 2181−2182. (b) Nozaki, H.; Koyama, T.; Mori, T. *Tetrahedron* **1969**, *25*, 5357−5364.

(8) Helder, R.; Wynberg, H. *Tetrahedron* **1975,** *31*, 2551−2557.

(9) Gronowitz, S.; Frejd, T. *Acta Chem. Scand.* **1976**, *B30*, 341−344.

(10) Hadj-Abo, F.; Bienz, S.; Hesse, M. *Tetrahedron* **1994**, *50*, 8665−8672

(11) (a) Miyahara, Y.; Inazu, T.; Yoshino, T. *Chem. Lett.* **1978**, 563−566. (b) Miyahara, Y.; Inazu, T.; Yoshino, T. *J. Org. Chem.* **1984**, *49*, 1177−1182.

(12) Fahr, E. *Liebigs Ann. Chem.* **1960**, *638*, 1−32. If the bis(diazoketones) were not isolated, even when an excess of diazomethane was used, the bromides were contaminated with a small amount (ca. 5%) of the chloride.

(13) Work, T. S. *J. Chem. Soc.* **1940**, 1315−1320.

(14) Canonica, L.; Bacchetti, T. *Atti. Accad. Naz. Lincei, Rend., Cl. Sci. Fis., Mat. Nat.* **1951**, *10*, 479−484.

(15) Canonica, L.; Bacchetti, T. *Atti. Accad. Naz. Lincei, Rend., Cl. Sci. Fis., Mat. Nat.* **1953**, *15*, 278−285.

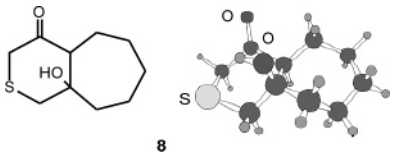
(16) (a) Baccetti, T.; Canonica, L. *Gazz. Chim. Ital.* **1952**, *82*, 243−251 (*Chem. Abstr.* **1953**, *47*, 8718c). (b) Baccetti, T.; Canonica, L. *Gazz. Chim. Ital.* **1953**, *83*, 832 (*Chem. Abstr.* **1954**, *49*, 4679h).

TABLE 1. Cyclization of 6 with Na_2S

halide **6**		monomer **4**		dimer **7**	
N	X	yield, %	mp (lit mp) °C	yield, %	mp °C
8	Br[12]	12.3	52−53	27.4	119−120
9	Br[12]	19.5	73−74 (solid)[16a]	11.6	114.5−115
10	Cl[12]	30.2	75.5−76.5 (75)[16a]	2.9	132−133
12	Cl[13]	46.1	73−74 (74)[16a]	3.1	139−140
14	Cl[14]	47.0	64−65 (67)[16a]	6.6	136.5−137.5
16	Cl[15]	53.5	46−47 (44)[16b]		
20	Cl	33.3	42−42.5		

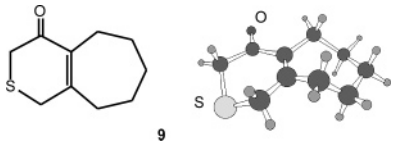
Even smaller **4** ($n = 8$) also could be prepared in 12% yield by using the bromide along with the dimer **7** ($n = 8$) in 27% yield. This reaction was extremely sensitive to the presence of an excess of Na_2S. Although we were aware that the addition of excess Na_2S should be avoided throughout the cyclization reaction to prevent aldol-type condensation of the products,[11] this reaction was far more sensitive to the excess of Na_2S than in the previous cases where intermolecular condensation occurred between the carbonyl group and the methylene group, which was doubly activated by a carbonyl group and a thioether group. Without rigorous control of the addition of the solutions keeping the bromide solution in slight excess, the yield of **4** ($n = 8$) dropped seriously and provided an oily mixture of products instead. On the other hand, the yield of the dimer was barely affected by the presence of excess Na_2S.

Separation of the oil by preparative TLC furnished colorless plates with low R_f and an oil with high R_f. The former compound showed a very complex ^{1}H NMR spectrum, but its molecular mass (M^+ *m/z* 200) in the mass spectra and molecular composition by elemental analysis are the same as **4** ($n = 8$). Since this compound contains a hydroxyl group as suggested by the presence of a sharp absorption at 3478 cm^{-1} in the IR spectrum together with a carbonyl group ($\nu_{C=O}$ 1697 cm^{-1}), it is assigned as **8**, which is formed by an intramolecular addition reaction.[18] The participation of the less acidic methylene group activated by one carbonyl group rather than the methylene activated by a carbonyl group and a sulfide group was unexpected, but the close proximity of the reacting groups and the thermodynamic stability of the bicyclic structure **8** appears to make this transformation feasible.



8

The latter compound, an olefin **9**,[14] resulted from the dehydration of **8**, which was suggested from the presence of olefinic carbon signals in its ^{13}C NMR spectrum. The detrimental effect of a base was demonstrated by immediate changes in the ^{1}H NMR spectrum of pure **4** ($n = 8$) in $CDCl_3$ when a catalytic amount of NaOMe in CD_3OD was added: the singlet peak for the $COCH_2S$ moiety of **4** ($n = 8$) was completely replaced by the peaks for **8** and **9**.



9

Conversion of 4 to [*n*](2,5)Thiophenophane-1,*n*-diones 5. As reported, the cyclic aromatic diketosulfides could be converted to the corresponding thiophenediones by condensation with glyoxal in high yields for larger cyclic compounds.[11] Although we have succeeded in extending the reaction to include [3.3](2,5)furanothiophenophane and [3.3]metathiophenophane and its derivatives from the corresponding alkyl chain-substituted diketosulfides,[17] the yields tend to be lower because the acidity of the methylene attached to an alkyloyl group is lower than the acidity of the methylene next to an aroyl group in the thiophene-forming condensation, and the aldol-type side reactions of the product diones are possible. Our original intention of the present study was to examine the scope of this thiophenophane synthesis to [*n*](2,5)thiophenophanediones whose ring sizes can be changed at will.

As compared with the corresponding open chain compounds, the reactions of the conformationally restricted cyclic diketosulfides are disfavored, since the thiophene-forming condensation of a diketosulfide with glyoxal involves two addition−elimination sequences. Therefore, slow addition of a dilute NaOMe solution to the mixture of **4** and glyoxal by a syringe pump over 10−12 h was essential.[11] Otherwise, the reaction conditions are very simple and mild. After a workup including filtration chromatography, the desired thiophenophanediones **5** were obtained in yields as shown in Table 2, except for **4** ($n = 8$), which has a high tendency for self-addition under the basic conditions as noted above.

Note that **5** ($n = 12$) has been isolated in 14% yield from the cyclization of **10**, and the formation of **10** was assumed to occur via oxidative decarboxylation of the intermediate **11**[5] (Scheme 6).

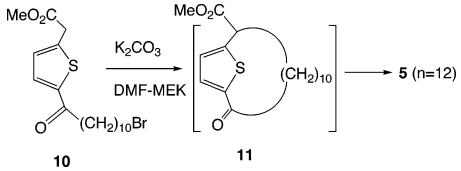
The dimer **7** ($n = 8$), which was obtained as a major product, can be converted to the corresponding thiophenophane **12** in 55% yield even though two thiophene rings have to be constructed (Scheme 7).

Conversion of 5 ($n = 10$) to 1 ($n = 10$). As an example for the reduction of thiophenophanedione **5** to the corresponding **1**, the Wolff−Kishner reaction was carried out for $n = 10$. By

TABLE 2. Conversion to Thiophenophanes

	5 (from **4**)		**12** (from **7**)	
n	yield, %	mp (lit. mp) °C	yield, %	mp °C
8			54.7	225−226
9	29.9	138−139		
10	22.1	76.5−77.5		
12	50.7	80.5−81 (77.5−78.5)		
14	54.1	98−98.5		
16	47.8	121.5−122		
20	40.4	115.5−116		

SCHEME 6



10 **11**

(17) (a) Miyahara, Y.; Inazu, T.; Yoshino, T. *Chem. Lett.* **1980**, 397−400. (b) Miyahara, Y.; Inazu, T.; Yoshino, T. *Tetrahedron Lett.* **1984**, *25*, 415−418.

(18) The presumed structure depicted is the most stable structure obtained by Monte Carlo conformational searches using MMFF94 force field as implemented in Spartan and confirmed as the lowest energy structure by DFT calculations at the B3LYP/6-31G(d) level (Gaussian03).

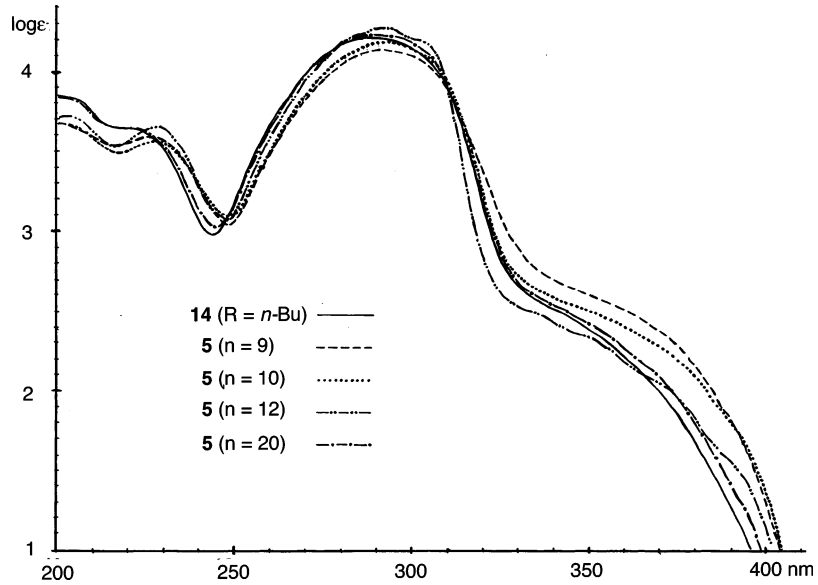
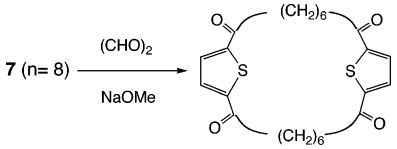
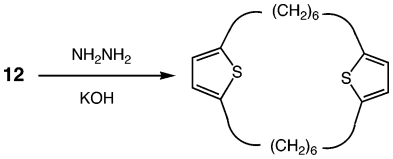


FIGURE 1. The electronic spectra of **5** (n = 9, 10, 12, and 20) and **14** (R = n-Bu) in cyclohexane.

SCHEME 7. Conversion of the Dimer 7 (n = 8) to Thiophenophane 12



SCHEME 8. The Wolff−Kishner Reduction of the Tetraketone 12 to Thiophenophane 13

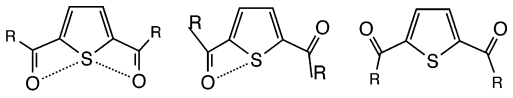


use of the usual Kindler modification, **1** (n = 10) was readily obtained in 87% yield.

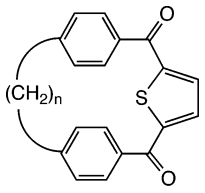
Reduction of the Tetraone 12 to [8.8](2,5)Thiophenophane 13. The Wolff−Kishner reduction of the tetraone **12** (n = 6), which is sparingly soluble in most solvents, was not as straightforward as for **5** (n = 10); the usual procedure led to immediate precipitation of insoluble, possibly polymeric, orange azines, and the yield of the reduction product was negligible. This problem could be solved by reversing the order of addition. Thus, when a hot solution of **12** (n = 6) in diethylene glycol was added to refluxing hydrazine hydrate in diethylene glycol containing hydrazine dihydrochloride as a catalyst, a clear yellow solution resulted without any sign of formation of azines. After the addition of KOH, the solution was heated at 200 °C for 15 h, and pure thiophenophane **13** was obtained in 70% yield (Scheme 8).

The Structural Features of [n](2,5)Thiophenophane-1,n-diones 5. As summarized in several review articles, the thiophene-2-carbonyl compounds have a tendency to take the S,O-cis conformation.[19]

In the case of open chain 2,5-diacylthiophenes **14**, the planar O,S,O-cis,cis conformation is the most stable conformation, which is revealed by their NMR and IR spectra.[11b,20] The preference for cis,cis over trans,cis or trans,trans could be reasonably predicted by DFT calculations (Gaussian03) (trans,trans and trans,cis forms are less stable than cis,cis by 1.34 and 0.20 kcal/mol, respectively, for **14** (R = Me) and 1.12 and 0.09 kcal/mol, respectively, for **14** (R = n-Bu) at the B3LYP/6−31(G) level).



However, when the thiophene-2,5-dicarbonyl moiety is incorporated in macrocyclic systems, it no longer can be planar, but it may be deformed depending on the ring size. In our previous paper,[11b] we disclosed that the effect of the ring size is clearly reflected in the chemical shift of the thiophene proton and the carbonyl stretching frequency of macrocyclic [n.1.1]-paracyclo(2,5)thiophenoparacyclophane-(n + 7),(n + 13)-diones (n = 3−8, 10) **15**.



Although the ^{1}H NMR signals for the thiophene protons in the present [n](2,5)thiophenophane-1,n-dione **5** system (δ 7.72,

(19) (a) Sheinker, V. N.; Garnovskii, A. D.; Osipov, O. A. *Usp. Khim.* **1981**, *50*, 632−664 *(Russ. Chem. Rev.* **1981**, *50*, 336−352). (b) Kucsman, A.; Kapovits, I.. In *Organic Sulfur Chemistry;* Bernadi, F., Czimadia, I. G., Mangini, A., Eds.; Elsevier: New York, 1985; pp 191−245. (c) Benassi, R.; Folli, U.; Schenetti, L.; Taddei, F. *Adv. Heterocycl. Chem.* **1987**, *41*, 75−186.

(20) Miyahara, Y. *J. Heterocycl. Chem.* **1979**, *16*, 1147−1151.

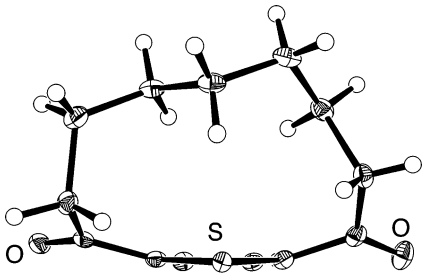


FIGURE 2. The ORTEP drawing of **5** ($n = 9$) at the 50% probability level.

7.75, 7.78, 7.82, 7.69, and 7.55 for $n = 20$, 16, 14, 12, 10, and 9, respectively, compared to δ 7.70 and 7.68 for **14** ($R =$ Me) and **14** ($R = n$-Bu), respectively) appear to reflect the changes around the thiophene−diacarbonyl moiety, the chemical shift changes observed are very small compared to the NMR spectral changes observed for **15**. Because of the absence of the large and far-reaching anisotropic shielding effect of the benzene rings in **15**, meaningful discussion of the whole series is not possible at this stage. However, the gradual upfield shifts as the ring size n decreases from 12 to 9 suggest the strain is in the smallest **5**.

The uniqueness of **5** ($n = 9$) also is apparent from its carbonyl frequencies ($\nu_{C=O}$) in the IR spectra in solution ($CDCl_3$): $\nu_{C=O}$1667, 1667, 1668, 1669, 1665, and 1674 cm^{-1} for $n = 20$, 16, 14, 12, 10, and 9, respectively.

The electronic spectra of **5** ($n = 9$) in cyclohexane also are different from the larger thiophenophanes as shown in Figure 1. Although the λ_{max} of thiophene $\pi-\pi^*$ absorption at ca. 290 nm does not change appreciably, the intensity reduces with decreasing ring size, while the $n-\pi^*$ band appears as a shoulder at ca 350 nm and increases its intensity with ca. 10 nm red shift for **5** ($n = 9$): $\lambda_{max}(\epsilon)$ 290 (16800), 291 (16500), 292 (17200), 292 (18400), 293 (15200), 292 (13500) for $n = 20$, 16, 14, 12, 10, and 9, respectively, as compared with **14** (R = n-Bu) [289 (16200)].

Since all the data indicate the strained nature of **5** ($n = 9$), the X-ray crystal structure was determined. As shown in Figure 2, the thiophene-2,5-dicarbonyl moiety is in an O,S,O-trans,trans conformation and is deformed significantly out of planarity. While the thiophene ring itself is almost planar, the $C_{thiophene}-C_{carbonyl}$ bonds are significantly bent from the thiophene plane (18.6° and 14.6°).

The detailed conformational analysis of **5** in solution, which must take the large flexibility of the oligomethylene chain and possibilities of the cis,cis, cis,trans, and trans,trans forms for the thiophenedicarbonyl moiety into account, is in progress and will be reported elsewhere.

Conclusions

We disclosed that a suitable diacid can be converted through diacid chloride, bis(diazoketone), and cyclic ketosulfide to the corresponding thiophenophanediones under mild reaction conditions. This method fails for $n = 8$ because the intramolecular self-addition of the monomeric diketosulfide readily occurs, but both of the diketosulfide moieties of the dimer **9** ($n = 8$) obtained as the major product can be transformed to thiophene rings, which opens a new route to thiophenophanes with two thiophene rings.

In the present investigation, the carbonyl groups simply were reduced to give [n](2,5)thiophenophanes so they may be fully or partially protected as ketals for later use. Although in this investigation only simple thiophenophanes were synthesized, the mild reaction conditions throughout the synthetic route would be beneficial for synthesis of functionalized compounds.

Experimental Section

Cyclization of 1,ω-Bis(haloacetyl)alkane 6. Cyclization of 1,10-Dibromodecane-2,8-dione 6 ($n = 8$, X = Br). TSolutions of the dibromide (13.1 g) in 500 mL of benzene, sodium sulfide (9.6 g of decahydrate) in 150 mL of water, and 350 mL of ethanol were added separately under high dilution conditions to refluxing ethanol (1.0 L) over 9 h. After an additional hour of refluxing, the colorless solution was evaporated and dissolved in 150 mL of chloroform. Column chromatography (silica gel 37 × 250, 1:1 chloroform−benzene) gave 987 mg (12.3%) of the monomer **4** ($n = 8$) and 2.19 g (27.4%) of the dimer **7** ($n = 8$).

Thiacycloundecane-3,10-dione 4 ($n = 8$). Colorless plates (hexane), mp 54−54.5 °C. Anal. Calcd for $C_{10}H_{16}O_2S$: C, 59.97; H, 8.05. Found: C, 59.83; H, 8.13. MS m/z 200 (M^+). IR (KBr) ν: 1705, 1692 (equal intensity, C=O), 2922, 2860, 1459, 1402, 1208, 1103, 943 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33 (s, 4H), 2.60 (t, $J = 6.4$ Hz, 4H), 1.70 (quint, $J = 6.4$ Hz, 4H), 1.38 (quint, $J = 6.4$ Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.1, 41.6, 39.0, 25.2, 22.4.

1,12-Dithiadocosane-3,10,14,21-tetraone 7 ($n = 8$). Colorless plates (PhH), mp 119−120 °C. Anal. Calcd for $C_{20}H_{32}O_4S_2$: C, 59.97; H, 8.05. Found: C, 59.92; H, 8.06. IR (KBr) ν: 1708 (C=O), 2928, 2856, 1462, 1405, 1372, 1223, 1184, 1104, 713, 579 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.30 (s, 8H), 2.55 (t, $J = 7.3$ Hz, 8H), 1.58 (quint, $J = 7.3$ Hz, 8H), 1.30 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.3, 41.4, 40.7, 28.6, 23.4.

When Na_2S was added in excess in the reaction even if temporarily, the monomer fractions in chromatographic separation contained unstable side products, ketoalcohol **10** and ketoolefin **11** in varying amounts and ratios. Preparative TLC (silica gel, chloroform−hexane 1:1) gave two products along with **4** ($n = 8$) (TLC (silica gel, chloroform): **9** R_f 0.70, **4** R_f 0.54, **8** R_f 0.30).

Ketoalcohol 8. Colorless needles (hexane), mp 53−54 °C. Anal. Calcd. for $C_{10}H_{16}O_2S$: C, 59.97; H, 8.05. Found: C, 59.89; H, 8.00. MS m/z 200 (M^+). IR (KBr) ν: 3478 (sp, OH), 1697 (C=O), 2926, 2856, 1457, 1327, 1223, 1066 cm^{-1}. ^{1}H NMR (400 MHz, C_6D_6): δ 2.65 (s, 1H, OH), 2.64 (d, $J = 12.2$ Hz, 1H), 2.55 (dd, $J = 12.2$, 2.0 Hz, 1H), 2.48 (d, $J = 13.7$ Hz, 1H), 2.06 (ddd, $J = 14.7$, 5.9, 2.4 Hz, 1H), 1.92 (dd, $J = 13.7$, 2.4 Hz, 1H), 1.78 (td, $J = 12.2$, 2.4 Hz, 1H), 1.67 (m, 1H), 1.61 (ddd, $J = 14.7$, 9.3, 1.5 Hz, 1H), 1.35 (ddd, $J = 14.7$, 10.3, 1.5 Hz, 1H), 1.43 (m, 1H), 1.29 (m, 1H), 1.09 (m, 1H), 0.94 (m, 1H). ^{13}C NMR (100 MHz, C_6D_6): δ 203.2, 81.0, 61.8, 42.5, 42.1, 37.7, 28.6, 27.2, 21.7, 21.5.

Ketoolefin 9. Light yellow oil, bp 109−110 °C/0.2 mmHg, decomposed on standing. Anal. Calcd for $C_{10}H_{14}OS$: C, 65.89; H, 7.74. Found: C, 65.23; H, 7.68 (attempts at further purification resulted in loss of the material and in decomposition). IR (neat) ν: 1655 (C=O), 1624 (C=C), 2923, 2851, 1451, 1270, 1215, 1070, 963, 754 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.36 (s, 2H), 3.21 (s, 2H), 2.55 (t, $J = 5.0$ Hz, 2H), 2.37 (t, $J = 5.0$ Hz, 2H), 1.77 (quint, $J = 6.0$ Hz, 2H), 1.58 (quint, $J = 5.5$ Hz, 2H), 1.44 (quint, $J = 5.5$ Hz, 2H). ^{13}C NMR (100 NHz, $CDCl_3$): δ 191.7, 157.8, 138.2, 36.9, 33.5, 32.0, 31.8, 25.9, 25.2, 25.0.

The larger cyclic diketosulfides **4** and the corresponding dimers **7** were prepared in a similar fashon except that the solvent for the halides was changed according to its solubility: PhH, PhH, THF, PhH−dioxane (7:1), THF, and PhH−dioxane (1:1) for $n = 9$, 10, 12, 14, 16, and 20, respectively (see Supporting Information).

Conversion of 4 to [n](2,5)Thiophenophane-1,n-dione 5. Attempts at obtaining **12** ($n = 8$) gave brown oils, which decomposed upon standing.

[9](2,5)Thiophenophane-1,9-dione 5 (*n* = 9). To a mixture of **4** (*n* = 9) (860 mg, 4.0 mmol) in 160 mL of MeOH and 40 mL of a solution of glyoxal (8.40 g of glyoxal trimer dihydrate dissolved in 500 mL of MeOH), 20 mL of a solution of NaOMe (0.55 g of Na dissolved in 100 mL of MeOH) was injected over 10 h via a syringe pump, and the solution was stirred overnight at room temperature. The resulting solution was evaporated, and the residue was treated with 100 mL of water, acidified with dil HCl, and extracted with chloroform. The extract was dried ($MgSO_4$) and filtered through a column of silica gel and evaporated. The residue was sublimed (140 °C/0.1 mmHg) to give pale yellow crystals, 284 mg (29.9%). Recrystallization from acetone gave colorless prisms, mp 138−139 °C. Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 65.84; H, 6.87. IR (KBr) *ν*: 1689 (m), 1671 (s) (C═O, 1674 in $CDCl_3$), 2935, 1503, 1253, 1230, 1112, 841, 804 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.55 (s, 2H), 2.81 (t, *J* = 6.8 Hz), 1.68 (quint, *J* = 7.3 Hz, 4H), 1.60 (br quint, *J* = 5.9 Hz, 4H), 1.03 (br quint, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 194.2, 147.2, 130.9, 25.7, 24.7, 24.4.

The larger thiophenophanediones **5** were prepared similarly and described in the Supporting Information.

[8.8](2,5)Thiophenophane-1,8,14,21-tetraone 12. To a solution of **7** (*n* = 6) (801.2 mg, 4.0 mmol) in 100 mL of CH_2Cl_2, 40 mL of the glyoxal solution mentioned above was added and 20 mL of the NaOMe solution was injected over 12 h at room temperature. The mixture was diluted with water and was acidified with HCl. After the organic layer was separated, the aqueous phase was extracted twice with CH_2Cl_2 (50 mL × 2). The solution was washed with water and brine, dried over $MgSO_4$, and passed through a short column of silica gel eluted with CH_2Cl_2. Evaporation of the eluate gave 486.3 mg (54.7%) of a pale tan granular powder. Recrystallization from *N*,*N*-dimethylformamide gave pale yellow crystalline powder, mp 225−226 °C. Anal. Calcd for $C_{24}H_{28}O_4S_2$: C, 64.83; H, 6.35. Found: C, 64.58; H, 6.32. IR (KBr) *ν*: 1668, 1649 (C═O, equal intensity), 2945, 2924, 2902, 1457, 1325, 1259, 1214, 1185 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): *δ* 7.61 (s, 2H), 2.83 (t, *J* = 7.0 Hz), 1.79 (quint, *J* = 6.5 Hz, 2H), 1.37 (quint, *J* = 3.3 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 194.1, 148.9, 131.7, 38.4, 27.0, 24.1.

The Wolff-Kishner Reduction to Thiophenophanes. [10](2,5)-Thiophenophane 1 (*n* = 10). The diketone **5** (*n* = 10) (98.0 mg, 0.40 mmol) was dissolved in 10 mL of diethylene glycol by heating briefly at 100 °C and by adding 5 mL of 100% hydrazine hydrate. After the addition of 20 mg of hydrazine dihydrochloride, the mixture was refluxed for 30 min then 1.0 g of KOH was added and the mixture was refluxed for an additional 30 min. The mixture was heated to 200 °C while distilling off the hydrazine for 1 h. After the reaction, the reaction mixture and the distillate were combined, diluted with water, and extracted with hexane (2 × 10 mL). The combined extract was washed with dil HCl and then with water, dried over $MgSO_4$, passed through a short column of silica gel, and evaporated to give 75.8 mg (86.5%) of a colorless liquid, which was almost pure by ^1H NMR. Further purification was carried out by distillation in a sublimator at ca 100 °C/20 mmHg. Anal. Calcd for $C_{14}H_{22}S$: C, 75.61; H, 9.97. Found: C, 75.45; H, 9.85. ^1H NMR (400 MHz, $CDCl_3$): *δ* 6.62 (s, 2H), 2.75 (t, *J* = 6.0 Hz, 4H), 1.60 (m, 4H), 1.34 (m, 4H), 1.07 (m, 4H), 0.81 (quint, *J* = 7.5 Hz, 4H). ^{13}C NMR (400 MHz, $CDCl_3$): *δ* 143.4, 124.9, 30.7, 30.5, 28.4, 27.2, 27.1.

[8.8](2,5)Thiophenophane 13. The tetraketone **12** (200 mg, 0.45 mmol) was dissolved in 20 mL of diethylene glycol by heating at 140 °C, and the solution was added gradually to a refluxing solution of hydrazine hydrate (100%, 10 mL) in 10 mL of diethylene glycol-containing 60 mg of hydrazine dihydrochloride with a Pasteur pipet over 5 min. The clear yellow solution was refluxed for 1 h then 2.0 g of KOH was added and refluxing was continued for 1 h. The excess of hydrazine was distilled out using a Dean−Stark trap and the bath temperature was raised to 200 °C. After the mixture was heated at 200 °C for 15 h, the resultant colorless solution was cooled and diluted with water. The mixture was extracted (2 × 30 mL hexane) and the combined extract was washed with dil HCl and then with water. After drying ($MgSO_4$), the solution was filtered through a short column of silica gel. Evaporation of the solvent left a colorless oil (122 mg, 69.9%), which crystallized immediately (mp 52−53 °C). Anal. Calcd. for $C_{24}H_{36}S_2$: C, 74.16; H, 9.34. Found: C, 74.07; H, 9.32. ^1H NMR (400 MHz, $CDCl_3$): *δ* 6.53 (s, 4H), 2.74 (t, *J* = 7.0 Hz, 8H), 1.62 (quint, *J* = 7.0 Hz, 8H), 1.29 (s, 16H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 143.3, 123.5, 31.0, 29.6, 28.2, 27.4.

The X-ray Crystal Structure Determination of 5 (*n* = 9). A colorless prismatic crystal grown from acetone was cut into 0.4 × 0.4 × 0.4 mm, suspended in liquid paraffin, and taken up with a sampling loop. The X-ray reflection data were collected at −180 °C and treated with teXan. Crystal data belongs to monoclinic space group $P2_1/n$ (No. 14) with $a = 7.0433(3)$ Å, $b = 11.6066(4)$ Å, $c = 14.5664(8)$ Å, $\beta = 101.330(2)°$, $V = 1167.57(9)$ Å^3, $D_{calc} = 1.344$ g cm^{-3}, and $Z = 4$. The structure was solved by the direct methods (SIR92) and refined to $R_1 = 0.0339$, $R_w = 0.1169$, GOF = 1.056 for 2423 reflections with $F^2 > 2.0\sigma(F^2)$. The details are in the Supporting Information.

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Supporting Information Available: The experimental procedures for the preparation of 1,*ω*-(bishaloacetyl)alkanes **6**, the properties of **4**, **5**, and **7**, the ^1H and ^{13}C spectra of **1** (*n* =10), **4** (*n* = 8, 9, 10, 12, 14, 16, and 20), **5** (*n* = 9, 10, 12, 14, 16, and 20), **7** (*n* = 8, 9, 10, 12, and 14), **8**, **9**, **12**, and **14** (*R* = *n*-Bu) and the CH correlation spectra for **8** and **9**, the molecular calculation results for **8**, **9**, and **14** (*R* = Me, *n*-Bu), and the details of the X-ray structural analysis of **5** (*n* = 9). These materials are available free of charge via the Internet at http://pubs.acs.org.

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