Preparation of Congested Thiophenes Carrying Bulky Substituents on the 3- and 4-Positions and Their Conversion to the Benzene Derivatives

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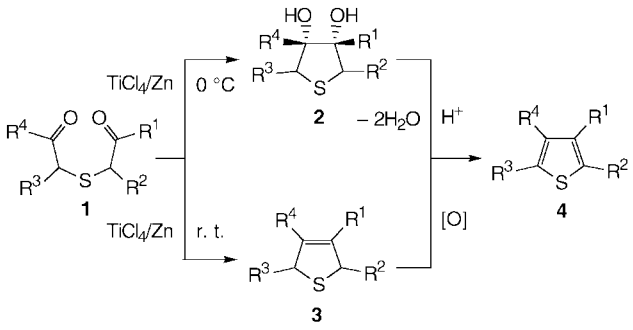
Highly congested thiophenes, 3,4-di-*tert*-butyl-, 3,4-di(1-adamantyl)-, 3,4-dineopentyl-, and 3-(1-adamantyl)-4-*tert*-butylthiophenes (**4a**−**d**), were prepared in satisfactory overall yields by intramolecular reductive coupling of 3-thiapentane-1,5-diones (**1a**−**d**) followed by acid-catalyzed dehydration of the resulting thiolane-3,4-diols (**2a**−**d**). Experimental procedures of this thiophene synthesis are fully described. Oxidation of the thiophenes **4a**−**d** with *m*-CPBA gave the corresponding thiophene 1,1-dioxides **13a**−**d** in good yields. The Diels−Alder reactions of **13a**−**d** with phenyl vinyl sulfone gave *o*-di-*tert*-butyl-, *o*-di(1-adamantyl)-, *o*-dineopentyl-, and *o*-(1-adamantyl)-*tert*-butylbenzenes (**17a**−**d**) directly in high yields with loss of benzenesulfinic acid and sulfur dioxide. The dioxides **13a**−**d** also underwent Diels−Alder reactions with alkynic dienophiles to give the corresponding benzene derivatives carrying two bulky substituents on adjacent positions. Pyridazines **25b**,**c**, carrying bulky substituents on the 4- and 5-positions, were also synthesized through Diels−Alder reaction of **13b**,**c** with PTAD. Dimethylation of the 2- and 5-positions of **13a**−**d** was attained by treatment with strong bases followed by reactions with methyl iodide. The resulting tetrasubstituted thiophene 1,1-dioxides **14a**−**d** reacted with DMAD to give highly congested hexasubstituted benzene derivatives **15a**−**d** in good yields. Finally, structural features of the congested molecules are discussed on the basis of NMR analyses. Typically, the barriers to rotation ($\Delta H^{\ddagger}$) about the benzene to the bulky substituents of **15a**,**c**,**d** were determined to be 8.59, 15.3, and 7.40 kcal/mol, respectively, by NMR total line-shape analysis.

Introduction

In the past decade, much progress has been made in the synthetic chemistry of thiophenes.[1] We have also partly contributed to the progress by developing a new thiophene synthesis, which involves intramolecular reductive coupling of 3-thiapentane-1,5-diones (**1**) leading to thiolane-3,4-diols (**2**) or 2,5-dihydrothiophenes (**3**) in good yields depending mainly on the reaction temperature.[2,3] Both **2** and **3** are converted to the corresponding thiophenes (**4**) in high yields by dehydration and dehydrogenation, respectively (Scheme 1). The new method has been proven to be very useful for the preparation of a wide variety of thiophenes such as congested thiophenes,[4] angle-strained thiophenes,[5] and some structurally interesting thiophenes.[6] These preparations were mostly reported as communications where experimental details were not included. We therefore report here the experimental details on applications to the synthesis of congested thiophenes carrying two bulky substituents on the 3- and 4-positions. Also reported is the conversion of these thiophenes to the corresponding congested benzene and pyridazine derivatives in which two bulky substituents occupy vicinal positions. This conversion was attained by oxidation of the thiophenes to the corresponding thiophene 1,1-dioxides and their Diels−Alder reactions with appropriate alkenic and alkynic dienophiles. Furthermore, dilithiation of the thiophene 1,1-dioxides followed by dimethylation produced more congested thiophene 1,1-dioxides. Conversion of these thiophene 1,1-dioxides to tetra- and hexasubstituted benzene derivatives by Diels−Alder reactions is also

Scheme 1



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(4) For preliminary reports, see: (a) Nakayama, J.; Yamaoka, S.; Hoshino, M. *Tetrahedron Lett.* **1988**, 29, 1161. (b) Nakayama, J.; Hasemi, R. *J. Am. Chem. Soc.* **1990**, *112*, 5654. (c) Nakayama, J.; Yoshimura, K. *Tetrahedron Lett.* **1994**, *35*, 2709.

(5) Nakayama, J.; Kuroda, K. *J. Am. Chem. Soc.* **1993**, *115*, 4612.

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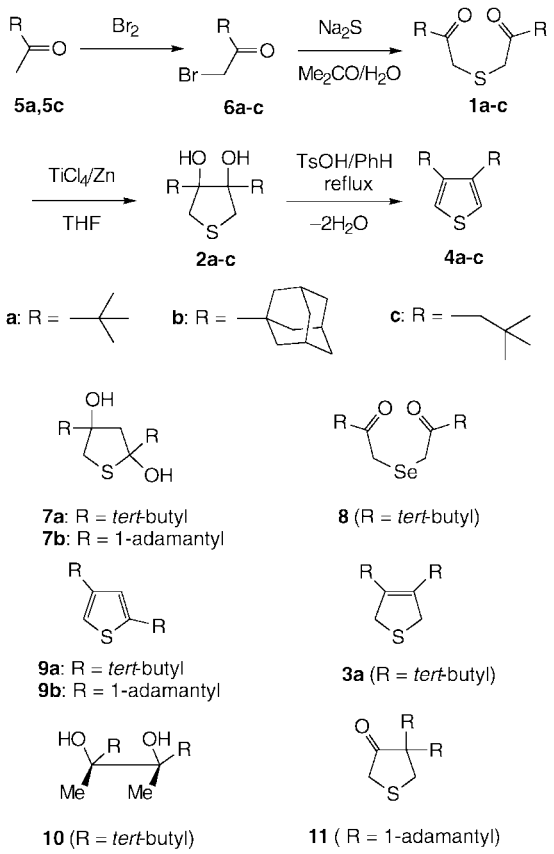
Scheme 2



described. Structural features of the congested molecules synthesized in this way are briefly discussed finally.

Results and Discussion

The present paper is composed of three parts. The first part describes preparation of congested thiophenes, the second part treats conversion of these thiophenes to the corresponding congested benzene and pyridazine derivatives, and the third part comments on structural features of the congested molecules.

1. Preparation of Congested Thiophenes

3,4-Di-*tert*-butylthiophene (4a). This congested thiophene **4a** was first synthesized in 1980 in a low overall yield after numerous unsuccessful attempts.[7] The present method provides a more convenient synthesis of **4a** (Scheme 2).[4a] 1,5-Di-*tert*-butyl-3-thiapentane-1,5-dione (**1a**)[8] was obtained in a good overall yield (~80%) by bromination of pinacolone (**5a**) with bromine followed by reaction with sodium sulfide nonahydrate. The intramolecular reductive coupling of **1a** was carried out by using a low-valent titanium reagent prepared from titanium(IV) chloride and zinc powder.[9] Thus, the reduction, carried out at −18 to −10 °C in tetrahydrofuran (THF), gave 3,4-di-*tert*-butyl-*cis*-thiolane-3,4-diol (**2a**) in 60−80% yields. Nevertheless, the reaction was not free from a side reaction. Detailed product analysis revealed the formation of the isomeric diol **7a** in a small amount. Structural proof of the diol **7a** was provided by acid-catalyzed dehydration leading to 2,4-di-*tert*-butylthiophene (**9a**)[10] nearly quantitatively. Exclusive formation of such a rearrangement product was encountered when the present reduction was applied to 1,5-di-*tert*-butyl-3-selenapentane-1,5-dione **8**.[11] The stereochemistry and the mechanism of the formation of the diol **7a** remain unclear at present. Further reduction of **2a** to 3,4-di-*tert*-butyl-2,5-dihydrothiophene (**3a**) did not take place even on prolonged reaction or reaction at higher temperatures, probably because of steric hindrance. The reduction at higher temperatures gave a complex mixture containing a decreased yield of **2a**. Treatment of **2a** with *p*-toluenesulfonic acid (TsOH) in refluxing benzene gave 3,4-di-*tert*-butylthiophene (**4a**) in 89% yield. The yield given here was based on a 1-g-scale reaction, and it may decrease in a larger scale reaction (more than 10 g) because of side reactions such as de-*tert*-butylation and migration of the *tert*-butyl group. Treatment of **4a** with aluminum chloride in carbon disulfide at room temperature resulted in quantitative rearrangement to the thiophene **9a**. 2,5-Di-*tert*-butylthiophene also rearranges to **9a** when treated with aluminum chloride.[10] The cis geometry of **2a** was determined by X-ray single-crystal structure analysis.[12,13] Furthermore, Raney nickel desulfurization of **2a** led to the formation of the diol **10** in 90% yield.[14]

3,4-Di(1-adamantyl)thiophene (4b). The 1-adamantyl group is a bulky substituent similar to *tert*-butyl but is less flexible because it is composed of a rigid cagelike framework and thus might behave as a much bulkier substituent than the *tert*-butyl group. There had been no report on the successful synthesis of five-membered aromatic compounds carrying two 1-adamantyl groups on adjacent positions until we reported the synthesis of 3,4-di(1-adamantyl)thiophene (**4b**).[4b,15] Treatment of commercially available 1-adamantyl bromomethyl ketone (**6b**) with sodium sulfide nonahydrate in aqueous acetone affords 1,5-di(1-adamantyl)-3-thiapentane-1,5-dione (**1b**) in high yield.[16] Intramolecular reductive coupling of **1b** with the foregoing low-valent titanium reagent at −18 °C for 18 h gave the expected thiolane-3,4-diol **2b** in reasonable yield. Although the yield of **2b** under the optimized conditions reached 58%, the isomeric thiolanediol **7b** was formed as a byproduct in varying amounts as was observed in the case of the

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(9) (a) Mukaiyama, T.; Sato, T.; Hanna, J. *Chem. Lett.* **1973**, 1041. For reviews on McMurry coupling, see: (b) McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513. (c) Lenoir, D. *Synthesis* **1989**, 883.
(10) Wynberg, H.; Wiersum, U. E. *J. Org. Chem.* **1965**, *30*, 1058.
(11) Nakayama, J.; Murai, F.; Hoshino, M.; Ishii, A. *Tetrahedron Lett.* **1988**, *29*, 1399.
(12) Unpublished results of the Professor F. Iwasaki group of the University of Electro-Communications.
(13) Intramolecular reductive coupling of a series of 3-thiapentane-1,5-diones produces the corresponding *cis*-thiolane-3,4-diols exclusively: Nakayama, J.; Yamaoka, S.; Hoshino, M. *Tetrahedron Lett.* **1987**, *28*, 1799.
(14) Backer, H. J.; Bos, H., *Recl. Trav. Chim. Pays-Bas* **1937**, *57*, 967.
(15) To our knowledge, even (*Z*)-1,2-di(1-adamantyl)ethenes are unknown. For preparation of 1,1-di(1-adamantyl)ethenes: (a) Olah, G. A.; Wu, A.-h.; Farooq, O. *J. Org. Chem.* **1989**, *54*, 1375. 3,4-Di(1-adamantyl)-1,2-dithiete is a compound in which two adamantyl groups are placed in vicinal positions on the double bond in cis-orientation: (b) Nakayama, J.; Choi, K. S.; Akiyama, I.; Hoshino, M. *Tetrahedron Lett.* **1993**, *34*, 115. (c) Choi, K. S.; Akiyama, I.; Hoshino, M.; Nakayama, J. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 623.
(16) Nakayama, J.; Konishi, T.; Ishii, A.; Hoshino, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2608.

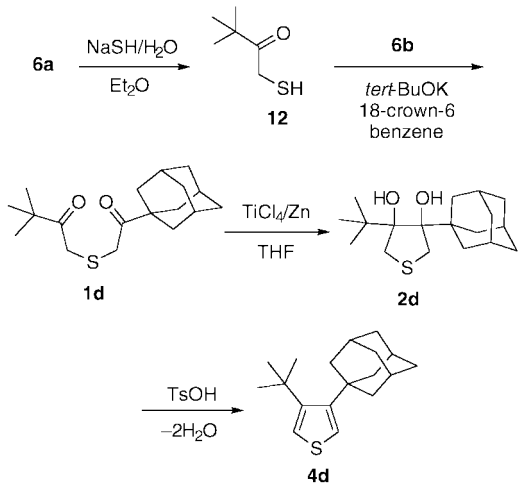
reduction of **1a**. TsOH-catalyzed dehydration of the diol **2b** in refluxing benzene gave 3,4-di(1-adamantyl)thiophene **4b** in 75% yield under the optimized conditions. Previously, it was reported that dehydration of a series of thiolane-3,4-diols gives the corresponding thiophenes in high yields and no pinacol rearrangement takes place because the formation of thiophenes, a typical heteroaromatic compound, is much more favorable.[3,17] However, in the case of **2b**, the pinacol rearrangement that gives 4,4-di(1-adamantyl)-3-thiolanone (**11**) was observed as a side reaction because dehydration leading to the thiophene **4b** causes a severe steric repulsion between adamantyl groups on an adjacent position. On the other hand, acid-catalyzed dehydration of the isomeric thiolanediol **7b**, which is free of such steric repulsion, took place smoothly to give 2,4-di(1-adamantyl)thiophene (**9b**) quantitatively. In this case, even mere heating in refluxing ethanol brought about the formation of **9b**. The thiophene **9b** was also formed in 95% yield by treatment of **4b** with aluminum chloride.

3,4-Dineopentylthiophene (4c). Neopentyl is another bulky group, and synthesis and structural chemistry of benzene derivatives carrying two neopentyl groups on adjacent positions have attracted considerable attention.[18] Application of our thiophene synthesis to 3,4-dineopentylthiophene (**4c**) is also successful.[4c] Although preparation of bromomethyl neopentyl ketone (**6c**) from methyl neopentyl ketone (**5c**) had been examined under a variety of conditions, reported yields were generally not good, mainly because of the lack of regioselectivity in bromination.[19] We have found that addition of bromine in a single stream to an ice-cooled solution of **5c** in methanol affords **6c** in 89% yield. The reaction of **6c** with sodium sulfide gave the sulfide **1c** in 87% yield, and the intramolecular reductive coupling of **1c** gave the expected thiolane-3,4-diol **2c** in 78% yield. The stereochemistry of **2c** is unknown, but cis geometry is most probable.[13] Acid-catalyzed dehydration of **2c** worked cleanly to give the expected thiophene **4c** in 90% yield.

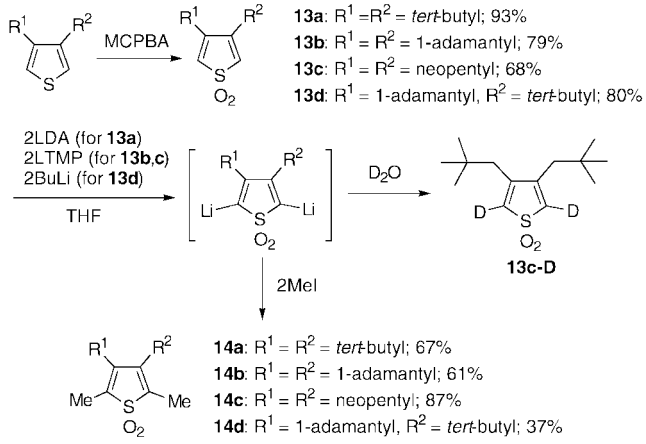
3-(1-Adamantyl)-4-*tert*-butylthiophene (4d). The unsymmetrically substituted congested thiophene **4d** could be also satisfactorily synthesized. In this case, the starting material, 1-(1-adamantyl)-5-*tert*-butyl-3-thiapentane-1,5-dione (**1d**), was prepared nearly quantitatively by reaction of the bromomethyl ketone **6b** with pivaloylmethanethiol (**12**), which was in turn prepared by reaction of bromomethyl *tert*-butyl ketone (**6a**) with sodium hydrosulfide (Scheme 3). Intramolecular reductive coupling of **1d** with the low-valent titanium reagent gave the expected thiolane-3,4-diol **2d** in 63% yield. Acid-catalyzed dehydration of **2d** worked without difficulty to give the desired thiophene **4d** in 77% yield.

Disappointingly, however, the present intramolecular reductive coupling was unsuccessful when applied to the severely sterically hindered dicarbonyl compounds **1e**−**h**. In these cases, reductive cleavage of the C−S bond

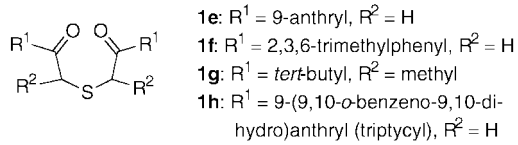
Scheme 3



Scheme 4



took place preferentially to give the corresponding methyl or ethyl ketones (RCOMe or RCOEt, R = bulky group).



2. Conversion of Thiophenes to Congested Benzene and Pyridazine Derivatives

Oxidation of congested thiophenes **4a**−**d** with 2 M amounts of *m*-chloroperoxybenzoic acid (*m*-CPBA) afforded the corresponding thiophene 1,1-dioxides **13a**−**d** in 93, 79, 68, and 80% yields, respectively (Scheme 4). Oxidation of thiophenes with a peracid generally affords the corresponding thiophene 1,1-dioxides, but the yields are not necessarily good, mainly because thiophene 1-oxide intermediates are very reactive and undergo a [2 + 4] self-dimerization.[20] The satisfactory yields of **13a**−**d** attained above should be ascribed to steric hindrance, which prevents the thiophene 1-oxides from selfdimerization.[21] Nevertheless, the thiophene 1,1-dioxides **13a**−**d** can act as 4π-components on strong

(17) 2,2,5,5-Tetramethyl-3,4-diphenylthiolane-3,4-diol affords 2,2,5,5-tetramethyl-4,4-diphenyl-3-thiolanone by pinacol rearrangement: Nakayama, J.; Hirashima, A.; Yokomori, Y. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3593.

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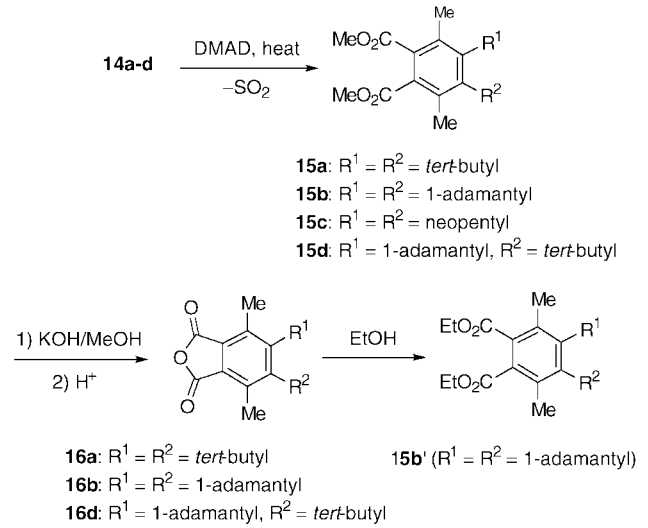
dienophiles to give Diels–Alder adducts in high yields, thus providing a convenient synthesis of highly congested benzene derivatives and other compounds as discussed below.[20,22] Lithiation of the α-positions of the thiophene **4a** does not take place even by action of strong bases such as alkyllithiums and lithium diisopropylamide (LDA) because of steric hindrance.[4a] However, conversion of thiophenes **4a**–**d** to the corresponding thiophene 1,1-dioxides **13a**–**d** makes the α-hydrogens acidic enough to be lithiated. Thus, treatment of the thiophene 1,1,-dioxide **13a** with excess LDA and then with methyl iodide gave 3,4-di-*tert*-butyl-2,5-dimethylthiophene 1,1-dioxide (**14a**) in 67% yield. However, dilithiation of the more congested **13b** with LDA was not complete and gave a complex mixture containing the expected dimethylated product **14b**, from which its isolation was difficult. Therefore, dilithiation of thiophene 1,1-dioxides **13b** and **13d** was done by use of a stronger base, lithium 2,2,6,6-tetramethylpiperidide (LTMP), which gave, after treatment with methyl iodide, dimethylated thiophene 1,1-dioxides **14b** and **14d** in 61% and 37% yields, respectively. Dilithiation of the less hindered thiophene 1,1-dioxide **13c** did not require the use of LDA or LTMP. Thus, treatment of **13c** with butyllithium and quenching of the reaction with D_2O gave 2,5-dideuterio-3,4-dineopentylthiophene 1,1-dioxide (**13c-D**) in good yield. The deuterium content of **13c-D** is nearly 100% by ^1H NMR analysis. Meanwhile, 3,4-dineopentyl-2,5-dimethylthiophene 1,1-dioxide (**14c**) was obtained in 87% yield by lithiation followed by treatment with methyl iodide. The tetrasubstituted thiophene 1,1-dioxides **14a**–**d** also undergo Diels–Alder reactions with dienophiles to give more congested tetra- and hexasubstituted benzene derivatives.

Dimethyl 4,5-Di-*tert*-butyl-2,6-dimethylphthalate (15a). We have preliminarily reported the cycloaddition of the thiophene 1,1-dioxide **13a** leading to *o*-di-*tert*-butylbenzene (**17a**) and its derivatives.[22a,23] Also reported were the cycloadditions giving cycloalkenes in which two *tert*-butyl groups are attached to the double bond in a cis orientation.[22c] We therefore report here only the new finding that even more congested **14a** is able to react with dimethyl acetylenedicarboxylate (DMAD) under forcing conditions to give the highly congested hexasubstituted *o*-di-*tert*-butylbenzene **15a** in 67% yield (Scheme 5).

Scheme 5



Alkaline hydrolysis of **15a** afforded the corresponding phthalic acid, which spontaneously eliminated water, because of relief from steric strain, to give the phthalic anhydride derivative **16a** quantitatively.

***o*-Di(1-adamantyl)benzenes and 4,5-Di(1-adamantyl)pyridazine.** Cycloadditions of the thiophene 1,1-dioxide **13b** were partly reported in a preliminary form.[4b] Thus, heating the thiophene 1,1-dioxide **13b** and phenyl vinyl sulfone in refluxing *o*-dichlorobenzene for 25 h afforded the parent *o*-di(1-adamantyl)benzene (**17b**)[24] in 93% yield (Scheme 6). Extrusion of sulfur dioxide and benzenesulfinic acid of the probable intermediate **18b** would explain the present results. Similarly, **13b** reacted with DMAD in refluxing *o*-dichlorobenzene to give dimethyl 4,5-di(1-adamantyl)phthalate (**20b**) in 87% yield by elimination of sulfur dioxide from the probable intermediate **19b**. The more congested thiophene 1,1-dioxide **14b** failed to react with phenyl vinyl sulfone even under forcing conditions, but satisfactorily reacted with DMAD to give a highly congested hexasubstituted benzene, dimethyl 4,5-di(1-adamantyl)-3,6-dimethylphthalate (**15b**), in 56% yield. Attempted application of high pressure (8 kbar, 100 °C, 20 h) to the reaction of **13b** with DMAD mainly brought about polymerization of DMAD; **15b** was formed in a trace amount with near-quantitative recovery of **14b**.[25] Alkaline hydrolysis of **15b** gave the corresponding phthalic acid, which spontaneously eliminated water to give the phthalic anhydride derivative **16b** quantitatively. Treatment of **16b** with sodium ethoxide gave the ethyl ester **15b′** quantitatively. The conversion of **15b** to **15b′** was carried out to improve the solubility of the compound for determination of NMR spectra at low temperatures.

The reaction of **13b** with 2 M amounts of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) gave the bis-adduct **22b** in 71% yield by further addition of PTAD to the initial adduct **21b** (Scheme 7). The adduct **22b** turned red when heated at 220 °C neat because of the retro-Diels–Alder

(20) For chemistry of thiophene 1,1-dioxides, see: (a) Rajappa, S. In *Comprehensive Heterocyclic Chemistry*; Bird, C. W., Cheeseman, G. W. H., Eds.; Pergamon Press: Oxford, 1984; Vol. 4, Chapter 3.14. (b) Rajappa, S.; Natekar, N. V. In *Comprehensive Heterocyclic Chemistry II*; Bird, C. W., Ed.; Pergamon Press: Oxford, 1996; Vol. 2, Chapter 2.10. (c) Raasch, M. S. In *Thiophene and Its Derivatives*; Gronowitz, S., Ed.; John Wiley: New York, 1985; p 571. (d) Simpkins, N. S. *Sulphonse in Organic Synthesis*; Pergamon Press: Oxford, 1993; p 319. (e) Nakayama, J.; Sugihara, Y. In *Organosulfur Chemistry* (*Synthetic Aspects*); Page, P. C. B., Ed.; Academic Press: New York, in press.

(21) Recently, we have succeeded in the preparation of 3,4-di-*tert*-butyl- and 3,4-di(1-adamantyl)thiophene 1-oxides, which did not show any tendency to undergo selfdimerization; Nakayama, J.; Yu, T.; Sugihara, Y.; Ishii, A. *Chem. Lett.* in press.

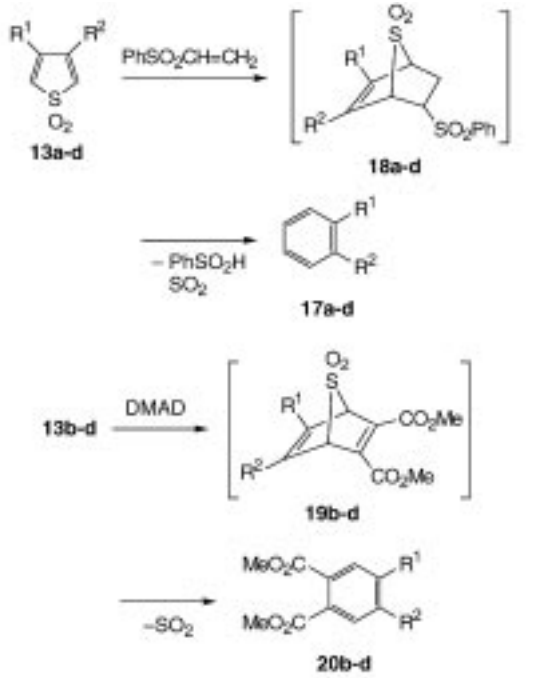
(22) For cycloadditions of **13a**, see: (a) Nakayama, J.; Yamaoka, S.; Nakanishi, T.; Hoshino, M. *J. Am. Chem. Soc.* **1988**, *110*, 6598. (b) Nakayama, J.; Hirashima, A. *Heterocycles* **1989**, *29*, 1241. (c) Nakayama, J.; Hirashima, A. *J. Am. Chem. Soc.* **1990**, *112*, 7648.

(23) For *o*-di-*tert*-butylbenzene and related compounds, see: (a) Hoogzand, C.; Hübel, W. *Angew. Chem.* **1961**, *73*, 680. (b) Arnett, E. M.; Strem, M. E. *Chem. Ind. (London)* **1961**, 2008. (c) Barclay, L. R. C.; Milligan, C. E.; Hall, N. D. *Can. J. Chem.* **1962**, *40*, 1664. (d) Burgstahler, A. W.; Abdel-Rahman, M. O. *J. Am. Chem. Soc.* **1963**, *85*, 173. (e) Viehe, H. G.; Merenyi, R.; Oth, J. F. M.; Valange, P. *Angew. Chem.* **1964**, *76*, 885. (f) Viehe, H. *Angew. Chem.* **1965**, *77*, 768. (g) Hoogzand, C.; Hübel, W. *Tetrahedron Lett.* **1961**, 637. (h) Arnett, E. M.; Strem, J. E.; Friedel, R. A. *Tetrahedron Lett.* **1961**, 658. (i) Krebs, A.; Franken, E.; Müller, S. *Tetrahedron Lett.* **1981**, *22*, 1675.

(24) 1-Adamantylbenzene was first synthesized by Friedel–Crafts reaction: Stetter, H.; Schwarz, M.; Hirschhorn, A. *Chem. Ber.* **1959**, *92*, 1629. Then, *p*-di(1-adamantyl)- and 1,3,5-tri(1-adamantyl)benzenes were obtained by Friedel–Crafts reaction of 1-adamantylbenzene: Rundel, W. *Chem. Ber.* **1966**, *99*, 2707.

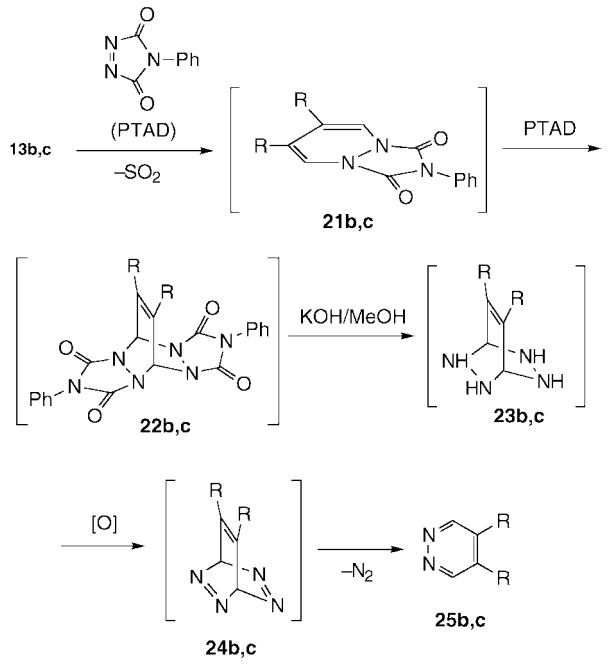
(25) We thank Dr. I. Shibuya of the National Institute of Materials and Chemical Research for his assistance with the high-pressure reaction.

Scheme 6



a: $R^1 = R^2$ = *tert*-butyl **b**: $R^1 = R^2$ = 1-adamantyl
c: $R^1 = R^2$ = neopentyl **d**: R^1 = 1-adamantyl, R^2 = *tert*-butyl

Scheme 7

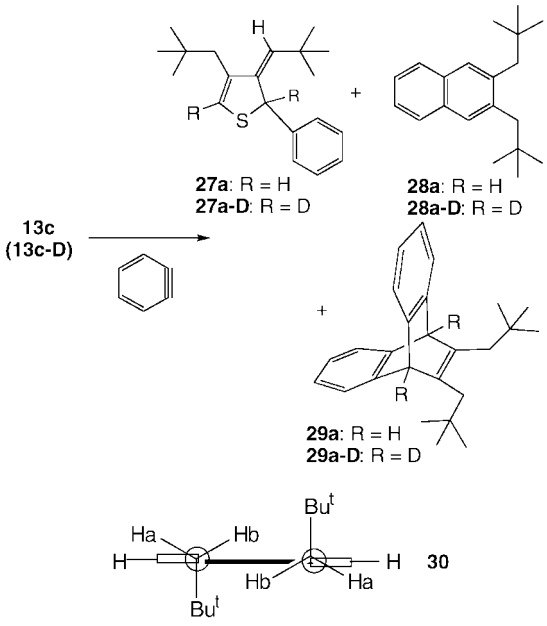


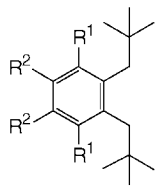
b: R = 1-adamantyl **c**: R = neopentyl

reaction leading to **21b** and PTAD. When the adduct **22b** was treated with methanolic KOH, 4,5-di(1-adamantyl)-pyridazine (**25b**) formed in 83% yield with evolution of gas. The reaction probably proceeds through air oxidation of the methanolysis product **23b** to the azo compound **24b** and extrusion of nitrogen from **24b**. This pyridazine synthesis was first reported by us in the conversion of the thiophene 1,1-dioxide **13a** to 4,5-di-*tert*-butylpyridazine.[22b,c]

***o*-Dineopentylbenzenes and 4,5-Dineopentylpyridazine.** The Diels–Alder reaction of thiophene 1,1-dioxides **13c** and **14c** provides a convenient synthesis of congested molecules that carry two neopentyl groups on adjacent positions of the six-membered aromatic compounds. 3,4,5,6-Tetramethyl-1,2-dineopentylbenzene, the first compound of this class, was synthesized in 1964.[18a] Later, the parent *o*-dineopentylbenzene (**17c**) was synthesized in 1974 starting from *o*-xylene in two ways in low overall yields (1.8 and 1.7%).[18b] Heating the thiophene 1,1-dioxide **13c** and phenyl vinyl sulfone in refluxing chlorobenzene for 15 h gave **17c** directly in 83% yield with elimination of benzenesulfinic acid and sulfur dioxide. Similarly, **13c** reacted with DMAD and cyclooctyne in refluxing *o*-chlorotoluene to give *o*-dineopentylbenzene derivatives **20c** and **26a** in 93% and 100% yields, respectively. Even diphenylacetylene reacted with **13b** under forcing conditions (neat, 230 °C) to give 4,5-diphenyl-1,2-dineopentylbenzene (**26b**) in 19% yield.

Scheme 8



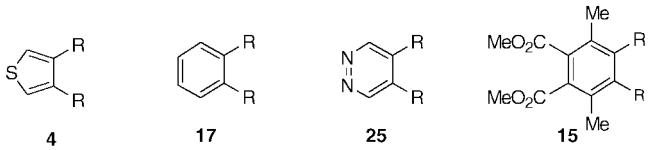


26a: R^1 = H, R^2,R^2 = –$(CH_2)_6$–
26b: R^1 = H, R^2 = phenyl
26c: R^1 = methyl, R^2 = H

The reaction of **13c** with excess benzyne, generated from 2-carboxybenzenediazonium chloride,[26] is of interest (Scheme 8). The reaction gave the expected product 2,3-dineopentylnaphthalene (**28a**)[27] only in 20% yield. The major product was the ene reaction product **27a** in 68% yield. The dibenzobarrelene **29a** was also formed in 7% yield. When the D-labeled thiophene 1,1-dioxide **13c-D** was allowed to react with benzyne in order to facilitate the structural analyses of **27a**–**29a** by NMR, the D-labeled compound **27a-D** was obtained as the major product along with **28a-D** and **29a-D**. The geometry of the exo methylene part of **27a** was determined by NOE experiments; NOE's between ═CHBu-*t* and the methine

(26) Klanderman, B. H.; Criswell, T. R. *J. Org. Chem.* **1969**, *34*, 3426.
(27) Molecular mechanics calculations of **29a**, which was a hypothetical molecule at that time, were reported.[18e]

Table 1. ^{13}C NMR Chemical Shift Values (δ) of Aromatic Carbons Carrying a Bulky Substituent in Thiophenes 4, Benzenes 17, Pyridazines 25, and Dimethyl Phthalates 15



4 17 25 15

R	25	17	4	15
neopentyl	137.9	138.6	140.1	141.3
tert-butyl	146.5	148.8	150.6	155.4
1-adamantyl	148.8	150.4	152.2	156.7

hydrogen of the five-membered ring and between = C*H*Bu-*t* and C*H*$_2$Bu-*t* are 12.4% and 22.2%, respectively, in harmony with the assigned structure. The most stable conformation of **13c** would be the one given in **30**, where two *tert*-butyl groups are placed in an anti-orientation.[18b−e] Thus, the less hindered hydrogen Ha participates in the ene reaction with benzyne, thus giving **27a** in which neopentyl and *tert*-butyl groups are placed on the opposite side. The formation of **29a** implies that electron-donating properties of the neopentyl groups, and not steric demand, control the regiochemistry in such a way that the Diels−Alder reaction with electrophilic benzyne takes place on the benzene ring carrying neopentyl groups.

The thiophene 1,1-dioxide **13c** was also satisfactorily converted to 4,5-dineopentylpyridazine (**25c**); the bis-adduct **22c**, obtained in 77% yield from **13c** and PTAD, was converted to **25c** in 76% yield by treatment with methanolic KOH. The Diels−Alder reactions of the tetrasubstituted thiophene 1,1-dioxide **14c** proceeded more easily than those of the thiophene 1,1-dioxides **14a** and **14b**. Thus, **14c** reacted with phenyl vinyl sulfone and DMAD in refluxing *o*-dichlorobenzene to give *o*-dineopentylbenzenes **26c** and **15c** in 81 and 86% yields, respectively.

The reaction of the thiophene 1,1-dioxide **13d** with phenyl vinyl sulfone produced nearly quantitatively a new congested benzene derivative **17d** carrying 1-adamantyl and *tert*-butyl groups on adjacent positions. DMAD also reacted with **14d** under forcing conditions to give the highly congested compound **15d** in 68% yield. The alkaline hydrolysis of **15d** also formed the phthalic anhydride derivative **16d** nearly quantitatively.

3. Structural Features of Congested Molecules on NMR Analysis

Summarized in Table 1 are the ^{13}C NMR data for the aromatic ipso carbons with bulky substituents in thiophenes **4**, benzenes **17**, pyridazines **25**, and dimethyl phthalates **15**. Inspection of Table 1 makes one notice that two trends without any exception may be present: first, the chemical shift increases in the order **25** < **17** < **4** < **15**; and, second, it increases in the order neopentyl < *tert*-butyl < 1-adamantyl. While the carbon signal of the 4,5-positions of the parent pyridazine appears at δ 126.7, much higher than that of its 3,6-positions (δ 151.7),[28] the carbon signal of the 3,4-positions of the parent thiophene occurs at δ 127.3, slightly lower than that of its 2,5-positions (δ 125.6).[29] Since the carbon signal of benzene appears at δ 128.5, this places the corresponding carbon signals of **17** at the highest field, though pyridazines are a π-deficient aromatic compound. As is well documented, the chemical shifts of aromatic hydrocarbons move downward as the degree of branching of the alkyl substituent increases.[30] However, it is also observed that the ipso carbon signal of *o*-dineopentylbenzene appears at a higher field (δ 138.6) than that of *o*-diethylbenzene (δ 141.0), thus indicating that branching at the β-position causes an upfield shift.[31]

On the other hand, in the present *tert*-butyl series, the ipso carbon signals appear at relatively lower field. Furthermore, the corresponding ipso carbons for the adamantyl compounds display their signals at much lower field than those for the *tert*-butyl compounds. Finally, it should be stressed that the signals of the carbons bearing a *tert*-butyl or 1-adamantyl group in dimethyl phthalates **15a** and **15b**, which are the most congested compounds in this series, appear at very low fields of δ 155.4 and 156.7, respectively. Perturbation due to steric congestion[32] and the electron-withdrawing property of the methoxycarbonyl group should be responsible for this downfield shift (the magnitude of the shift difference observed on going from *o*-di(1-adamantyl)benzene **17b** to dimethyl 4,5-di(1-adamantyl)phthalate **20b** is 2.3 ppm).

Table 2. ^{1}H NMR Chemical Shift Values (δ) of Aromatic Ring Hydrogens in Thiophenes 4 and Benzenes 17

R	4	17
neopentyl	6.88	7.10
tert-butyl	7.16	7.40 (3- and 6-positions) 7.10 (4- and 5-positions)
1-adamantyl	7.20	7.64 (3- and 6-positions) 7.13 (4- and 5-positions)

Relevant ^{1}H NMR data of thiophenes **4** and benzenes **17** are summarized in Table 2. The α-hydrogen signals of 3,4-dineopentyl-, 3,4-di-*tert*-butyl-, and 3,4-di(1-adamantyl)thiophenes (**4c**, **4a**, and **4b**) appear at δ 6.88, 7.16, and 7.20, respectively, suggesting that a downfield shift of the ring proton signal takes place with increasing bulkiness of the substituent on the thiophene ring. While *o*-dineopentylbenzene (**17c**), *o*-xylene, and *o*-diethylbenzene show their ring proton signal at δ 7.10, 7.11, and 7.17 as a singlet, respectively, *o*-di-*tert*-butyl- (**17a**) and *o*-di(1-adamatyl)benzenes (**17b**) display their aromatic protons in 3,6-positions at δ 7.40 and 7.64 as a multiplet, respectively, and those in 4,5-positions at δ 7.10 and 7.13 as a multiplet, respectively. This apparently indicates that the resonance signal due to the protons adjacent to the bulky substituents undergo a sizable low-field shift, whereas those in 4- and 5-positions remain at a chemical shift comparable to those of *o*-xylene, *o*-diethylbenzene, and *o*-dineopentylbenezene. Since electron-donating properties of these alkyl substituents are almost similar to each other, then the low-field shift observed here should be mainly ascribed to the perturbation caused by the bulky substituents.

(28) Heinisch, G.; Holzer, W. *Chem. Ber.* **1991**, *69*, 972.
(29) Gronowitz, S.; Johnson, I.; Hörnfeldt, A.-B. *Chem. Scr.* **1975**, *7*, 76.
(30) (a) Friedel, R. A.; Retcofsky, H. L. *J. Am. Chem. Soc.* **1963**, *85*, 1300. (b) Ernst, L. *Tetrahedron Lett.* **1974**, 3079. (c) Kalinowski, H.-O.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy*; translated by Becconsall, J. K.; John-Wiley: New York, 1986; p 152.
(31) An upfield shift for *o*-dineopentylbenzene and related compounds may be due to the fixed conformation of the neopentyl groups.
(32) (a) Woolfenden, W. R.; Grant, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 1496. (b) Grant, D. M.; Cheney, B. V. *J. Am. Chem. Soc.* **1967**, *89*, 5315. (c) Dalling, D. K.; Grant, D. M. *J. Am. Chem. Soc.* **1967**, *89*, 6612.

It is well-known that rotation about an sp^2-carbon-to-sp^3-carbon single bond can be frozen on an NMR time scale when the steric hindrance is seemingly moderate, whereas the barriers to rotation for compounds bearing large groups become too low to be determined by NMR techniques. Thus, ^{1}H NMR spectra of *o*-di-*tert*-butylbenzene (**17a**)[33] and 1,3,6,8-tetra-*tert*-butylnaphthalene[34] show only a singlet at room temperature for the *tert*-butyl groups in the adjacent and 1,8-positions, respectively; as for the latter compound, the signal broadening began at −80 °C and separate signals were observed at −153 °C.[35] The low barriers to rotation for those overcrowded systems are well interpreted by the idea that the ground-state energy of the molecule is raised more than the transition-state energy to result in a net decrease in the energy gap between these two states, namely, the activation energy.

On the other hand, in 3,4,5,6-tetramethyl-1,2-dineopentylbenzene, where steric congestion is seemingly moderate, the methylene protons become nonequivalent by −30 °C to give a typical AB quartet. The Arrhenius plot of the dynamic NMR data afforded the rotational barrier of 11.5 kcal/mol. The rotational barrier of the less crowded *o*-dineopentylbenzene (**17c**) was also estimated to be ca. 5.8 kcal/mol by similar treatment.[18e] Since examination of our congested molecules is expected to provide some new information in this context, their dynamic ^{1}H and ^{13}C NMR spectra were determined.

At 27 °C in CD_2Cl_2, the *tert*-butyl signal of one of the most congested molecules, dimethyl 4,5-di-*tert*-butyl-3,6-dimethylphthalate (**15a**),[36] appeared as a singlet broader than those of both the ester methyls and the methyls attached to the benzene ring (Figure 1). The signal reached maximum in width at −50 °C and then split into three separate singlets of equal intensities at −91 °C. The spectra were examined in detail in the temperature range between 27 and −76 °C at 14 different temperatures. After total line-shape analysis of these spectra obtained above, followed by least-squares fitting of the rate constant vs temperature data, the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the internal rotation of **15a** were determined to be 8.59 ± 0.3 kcal/mol and −8.8 ± 1.4 eu ($\Delta G_c^{\ddagger}$ = 10.6 kcal/mol), respectively, with a correlation coefficient of 0.9988. In a similar manner, the activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ for the internal rotation of dimethyl 4-(1-adamantyl)-5-*tert*-butyl-3,6-dimethylphthalate (**15d**) were determined to be 7.40 ± 0.6 kcal/mol and −15.5 ± 2.9 eu ($\Delta G_c^{\ddagger}$ = 10.9 kcal/mol), respectively. The difference in the enthalpy of activation ($\Delta\Delta H^{\ddagger}$) between **15a** and **15d** is ca. 1.2 kcal/mol, suggesting that structural distortion in **15d** is larger than in **15a** to cause higher ground-state energy in the former. Meanwhile, the negatively larger entropy of activation of **15d** as compared to that of **15a** is an indication of structural randomness of these two molecules both in ground and transition states and may partly come from its unsymmetrical structure and partly from its more distorted structure in the ground state than in the transition state where a highly aligned structure is required to escape various repulsive interactions.

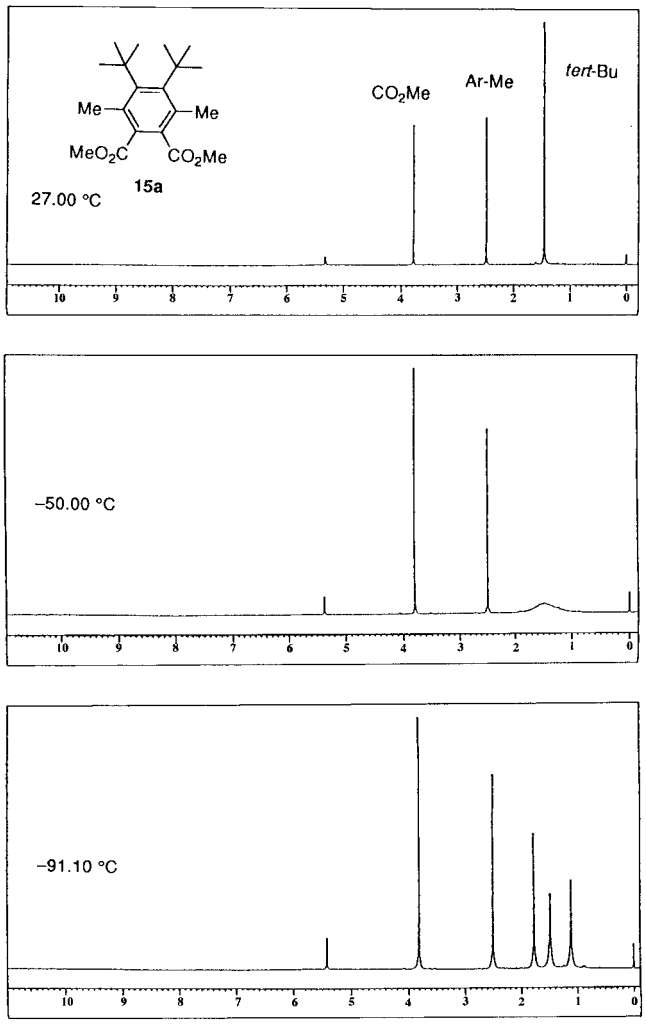


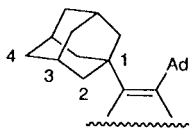
Figure 1. Temperature-dependent ^{1}H NMR spectra of **15a** with CD_2Cl_2 as the solvent.

As for *o*-di-*tert*-butylbenzene (**17a**), two adamantyl groups of 3,4-di(1-adamantyl)thiophene (**4b**) and *o*-di(1-adamantyl)benzene (**17b**) rotate freely as shown by ^{1}H NMR even at −80 °C.[36] However, in the most crowded molecules, dimethyl and diethyl 4,5-di(1-adamantyl)-3,6-dimethylphthalates (**15b** and **15b′**, respectively), only the rotational freezing in question could be observed without elucidation of the corresponding activation parameters mainly because of severe disturbance by complex coupling patterns of the adamantyl groups. To avoid this difficulty, ^{13}C NMR spectra were employed for the analysis of their dynamic behaviors.

Compound **15b′**, which is more soluble in CD_2Cl_2, gave apparently temperature-dependent spectra (Figure 2). Four carbon signals in the 1-, 2-, 4-, and 3-positions of the adamantyl groups were observed at δ 46.46, 42.60, 36.77, and 29.57, respectively, at 27 °C. On lowering the temperature, the carbon-2 signal broadened, while other signals still remained rather sharp. And finally, at −60.9 °C, the signal position of the carbon-2 could not be recognized due to maximum broadening, and two peaks due to the carbons-3 and -4 also began to broaden, but the signal of the carbon-1 remained still sharp.

Carbon-13 NMR spectra of **15b** were also determined in CD_2Cl_2 at temperatures down to −84 °C. In this case, the single signal as observed at an ambient temperature due to the carbon-2 of the adamantyl group split into

(33) Gibbons, W. A.; Gil, V. M. S. *Mol. Phys.* **1965**, *9*, 163.
(34) Franck, R. W.; Leser, E. J. *J. Am. Chem. Soc.* **1969**, *91*, 1577.
(35) Anderson, J. E.; Franck, R. W.; Mandella, W. L. *J. Am. Chem. Soc.* **1972**, *94*, 4608.
(36) The torsion angle between *tert*-butyl groups of **15a** is as large as 50.3°, making the benzene ring nonplanar, while those between adamantyl groups of **4b** and **17b** are 12.6 and 16.6°, respectively.[12]



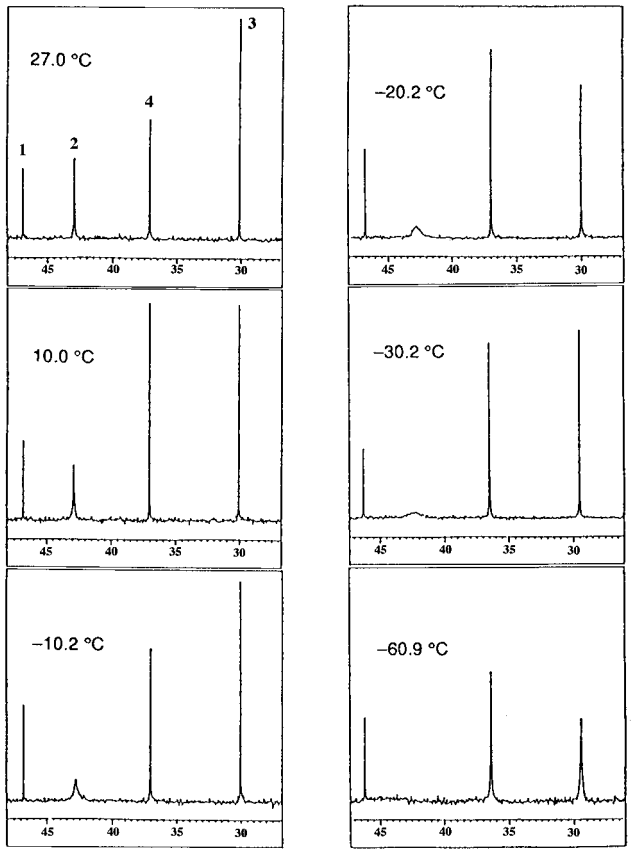


Figure 2. Adamantyl part of the temperature-dependent ^{13}C NMR spectra of **15b** with CD_2Cl_2 as the solvent.

three singlets at δ 29.30, 29.60, and 29.83 at −84 °C, and these signals coalesced into a single broad peak at ca. −72.5 °C.

The rotational behavior of the neopentyl groups of dimethyl 3,6-dimethyl-4,5-dineopentylphthalate (**15c**) and 1,4-dimethyl-2,3-dineopentylbenzene (**32**) was frozen out in an NMR time scale even at room temperature, and thus, the methylene protons of **15c**, for example, appeared as two distinct doublets at δ 2.68 and 2.99 with a geminal coupling constant of 14.3 Hz at 22 °C in toluene-d_8. Variable-temperature NMR studies on **15c** were performed in a temperature range between 52 and 102 °C, and the data so obtained at 21 independent temperatures afforded the coalescence temperature of 72 °C and the enthalpy of activation of 15.3 ± 2.3 kcal/mol after total line-shape analyses. This $\Delta H^{\ddagger}$ value is considerably larger than that for 3,4,5,6-tetramethyl-1,2-dineopentylbenzene (11.5 kcal/mol in CCl_4),[18b] indicating that the methoxycarbonyl group is a better substituent than the methyl group from the viewpoint of the so-called buttressing effect, by which the transition state of the system experiences more energy increase than the ground state.

Experimental Section

General Methods. Melting points are uncorrected. Elemental analyses were performed by the Chemical Analysis Center of Saitama University. Column chromatography was performed with Merck Kieselgel 60 (70−230 mesh). Intramolecular reductive coupling reaction of **1a**−**h** and preparation of **14a**−**d** were carried out under an atmosphere of argon or nitrogen. Unless otherwise noted, ^1H and ^{13}C NMR spectra were determined in $CDCl_3$ as the solvent and with tetramethylsilane as the internal standard.

3,4-Di-*tert*-butyl-*cis*-thiolane-3,4-diol (2a). Titanium(IV) chloride (49.3 mL, 0.45 mol) was added dropwise over a period of 3−4 h to a stirred mixture of 34.5 g (0.15 mol) of 1,5-di-*tert*-butyl-3-thiapentane-1,5-dione (**1a**)[8] and 59 g (0.9 mol) of zinc powder in 800 mL of THF at −18 °C under argon. After the addition, the mixture was stirred at −10 °C for 5 h. The reaction was quenched by addition of about 500 g of crushed ice, and then the pH of the mixture was adjusted to about 8 by addition of aqueous Na_2CO_3. After 1000 mL of hexane was added, the whole mixture was stirred for 1 h and then filtered by use of a large Büchner funnel (diameter, about 25 cm) on which a 3-cm-thick pad of Celite was placed. The Celite and the solid material on the Büchner funnel were washed with 500 mL of hexane. The organic layer of the filtrate was concentrated to about 500 mL, washed with 100 mL of water 10 times, dried over anhydrous $MgSO_4$, and evaporated. The resulting residue was recrystallized from pentane to give 21.0−27.8 g (60−80%) of **2a**: mp 108.5−110 °C; colorless needles; IR (KBr) 3408, 3398 (OH), (CCl_4) 3532 cm^{-1}; ^1H NMR (400 MHz) δ 1.24 (s, 18H), 2.81 (d, J = 12.2 Hz, 2H), 3.27 (d, J = 12.2 Hz, 2H), 3.41 (s, 2H); ^{13}C NMR (100.6 MHz) δ 28.3 (very broad s), 37.4 (t), 38.2 (s), 91.0 (s). Anal. Calcd for $C_{12}H_{24}O_2S$: C, 62.02; H, 10.41; S, 13.80. Found: C, 61.83; H, 10.41; S, 13.95. Purification of the mother liquor of the recrystallization by silica gel column chromatography gave 2,4-di-*tert*-butylthiolane-2,4-diol (**7a**) in a small amount: mp 87−87.5 °C; colorless needles (from pentane); ^1H NMR (90 MHz) δ 1.03 (s, 9H), 1.11 (s, 9H), 1.93 (dd, J = 13.4, 1.5 Hz, 1H), 2.27 (d, J = 13.4 Hz, 1H), 2.94 (dd, J = 11.6, 1.5 Hz, 1H), 3.14 (s, 1H), 3.26 (d, J = 11.6 Hz, 1H), 3.99 (s, 1H); ^{13}C NMR (22.5 MHz) δ 25.9, 26.0, 26.5, 26.6, 37.3, 39.4, 40.8, 43.7, 90.5, 104.0. Heating a mixture of 338 mg (1.45 mmol) of **7a** and 30 mg of *p*-toluenesulfonic acid (TsOH) in 30 mL of refluxing benzene for 1 h and chromatographic purification gave 283 mg (99%) of 2,4-di-*tert*-butylthiophene (**9a**):[11] colorless oil; ^1H NMR (90 MHz) δ 1.27 (s, 9H), 1.37 (s, 9H), 6.69 (d, J = 1.6 Hz, 1H), 6.75 (d, J = 1.6 Hz, 1H); ^{13}C NMR (22.5 MHz) δ 31.3 (q), 32.6 (q), 33.5 (s), 34.5 (s), 114.4 (d), 120.6 (d), 152.4 (s), 157.1 (s).

3,4-Di-*tert*-butylthiophene (4a). A mixture of 1.07 g (4.6 mmol) of the thiolanediol **2a** and 100 mg of TsOH in 60 mL of benzene was heated under reflux for 1 h. The mixture was washed with aqueous sodium bicarbonate, dried over Na_2SO_4, and evaporated. The resulting residue was chromatographed on a column of silica gel with hexane as the eluent to give 803 mg (89%) of **4a**: bp 75 °C/4 mmHg (bulb-to-bulb distillation); mp 43.0−43.5 °C (lit.[7] mp 42 °C); ^1H NMR (90 MHz) δ 1.47 (s, 18H), 7.16 (s, 2H); ^{13}C NMR (22.5 MHz) δ 33.5 (q), 35.3 (s), 122.3 (d), 150.6 (s). For a larger scale synthesis of **4a**, dehydration was carried out by use of a Dean−Stark apparatus.

Stirring a mixture of 98 mg (0.5 mmol) of the thiophene **4a** and 70 mg of aluminum chloride in 5 mL of carbon disulfide for 44 h at room temperature, quenching of the reaction by addition of water, and chromatographic purification gave 98 mg (100%) of 2,4-di-*tert*-butylthiophene (**9a**).[11]

2,2,3,4,5,5-Hexamethylhexane-3,4-diol (10). A mixture of 1.39 g (6 mmol) of the thiolanediol **2a** and a large excess of Raney nickel in 200 mL of ethanol was heated under reflux for 1.5 h. The Raney nickel was removed by filtration, and the filtrate was evaporated. The residue was chromatographed on a column of silica gel with CH_2Cl_2 as the eluent to give 1.09 g (90%) of the diol **10**:[14] bp 80 °C/2 mmHg (bulb-to-bulb distillation); mp 70−71 °C (from pentane); ^1H NMR (90 MHz) δ 1.15 (s, 18H), 1.36 (s, 6H), 2.03 (s, 2H); ^{13}C NMR (22.5 MHz) δ 23.4 (q), 28.7 (q), 40.5 (s), 84.0 (s).

1,5-Di(1-adamantyl)-3-thiapentane-1,5-dione (1b). A solution of 5.61 g (23.4 mmol) of sodium sulfide nonahydrate in 40 mL of water was added over a period of 1 h to an ice-

cooled solution of 12.00 g (46.7 mmol) of 1-adamantyl bromomethyl ketone (**6b**) (purchased from Aldrich) in 125 mL of acetone. The mixture was warmed to room temperature and stirred for 3 h. The mixture was diluted with 100 mL of water, and the resulting precipitate was collected by filtration. Recrystallization of the crude product from about 100 mL of MeOH gave 8.44 g (100%) of **1b**: mp 79.5−81 °C (lit.[16] mp 81−82 °C).

3,4-Di(1-adamantyl)thiolane-3,4-diol (2b). Titanium(IV) chloride (4.0 mL, 36.5 mmol) was added to a well-stirred mixture of 4.71 g (72.1 mmol) of zinc powder in 50 mL of THF cooled at −18 °C. The mixture was warmed slowly, heated under reflux for 1 h, and cooled to −78 °C. A solution of 4.64 g (12.9 mmol) of the sulfide **1b** in 40 mL of THF was added over a period of 1 h to the above mixture. The mixture was warmed to −18 °C and stirred at that temperature for 18 h. The reaction was quenched by addition of crushed ice, the pH of the mixture was adjusted to 8 by addition of aqueous Na_2CO_3, and then CH_2Cl_2 (200 mL) was added. The whole mixture was stirred for 2 h and filtered by use of a Büchner funnel on which a pad of Celite was placed. The Celite was washed with CH_2Cl_2 (200 mL). The organic layer of the filtrate and the washings were combined, washed with water 10 times, dried over Na_2SO_4, and evaporated. The resulting white solid was triturated with ether (20 mL), collected by filtration, washed with a small amount of ether, and dried to give 2.72 g (58%) of **2b**. Evaporation of the filtrate and recrystallization of the residue from EtOH will give some 2,4-di-1-adamantylthiolane-2,4-diol (**7b**). Since both **2b** and **7b** partly decompose on purification by silica gel column chromatography and as **7b** is more soluble in ether than **2b**, the method described above is the best way to separate these compounds. **2b**: mp 205−220 °C dec; colorless crystalline powder (from 1,2-dichloroethane); IR (KBr) 3500, 3360 cm^{-1} (OH); ^1H NMR (400 MHz) δ 1.70 (s, 12H), 2.04 (s, 6H), 2.14 (broad s, 12H), 2.72 (d, J = 11.7 Hz, 2H), 3.34 (s, 2H), 3.35 (d, J = 11.7 Hz, 2H); ^{13}C NMR (100.6 MHz) δ 28.9 (d), 36.0 (t), 37.0 (t), 37.9 (broad s), 41.2 (s), 92.4 (s); EIMS m/z 352 ($M^+ - 2H_2O$), 135 (100). Anal. Calcd for $C_{24}H_{36}O_2S$; C, 74.18; H, 9.34. Found: C, 74.09; H, 9.10. **7b**: mp 191−197 °C dec; colorless crystals (from ethanol); IR (KBr) 3438 cm^{-1} (OH); ^1H NMR (60 MHz) δ 1.50−2.15 (m, 32H), 2.80 (d, J = 10.8 Hz, 1H), 3.15 (d, J = 10.8 Hz, 1H), 3.30 (s, 1H), 3.90 (s, 1H). Anal. Calcd for $C_{24}H_{36}O_2S$; C, 74.18; H, 9.34. Found: C, 74.11; H, 9.24. A mixture of 37.1 mg (0.1 mmol) of **7b** and 5.2 mg of TsOH in 6 mL of benzene was heated under reflux for 5 h. Purification of the mixture by silica gel column chromatography gave 33.7 mg (100%) of 2,4-di-1-adamantylthiophene (**9b**): mp 180−181.5 °C; colorless crystals (from MeOH); IR (KBr) 2900, 2846, 1450, 1351, 1341, 1315, 1251, 1209, 1100, 976, 809, 730, 656 cm^{-1}; ^1H NMR (90 MHz) δ 1.60−2.20 (m, 30H), 6.70 (d, J = 1.5 Hz, 1H), 6.79 (d, J = 1.5 Hz, 1H); ^{13}C NMR (22.5 MHz) δ 28.8 (d), 28.9 (d), 35.2 (s), 36.2 (s), 36.7 (t), 36.9 (t), 43.4 (t), 44.9 (t), 113.7 (d), 118.5 (d), 152.6 (s), 157.3 (s). Anal. Calcd for $C_{24}H_{32}S$: C, 81.76; H, 9.15. Found: C, 81.63; H, 9.08.

3,4-Di(1-adamantyl)thiophene (4b). A mixture of 78 mg (0.2 mmol) of the thiolanediol **2b** and 17 mg of TsOH in 12 mL of benzene was heated under reflux for 25 min. The mixture was washed with aqueous $NaHCO_3$ and then with water, dried over $MgSO_4$, and evaporated. The resulting white solid was purified by silica gel column chromatography with hexane as the eluent to give 53 mg (75%) of **4b**. Further elution of the column with benzene gave 4,4-di(1-adamantyl)-3-thiolanone (**11**) in a small amount. **4b**: mp 197−198 °C; colorless needles (from hexane); IR (KBr) 2990, 2908, 2844, 1451, 1365, 1340, 1307, 1242, 1192, 1175, 1097, 990, 977, 924, 784, 539 cm^{-1}; ^1H NMR (400 MHz) δ 1.76 (broad s, 12H), 2.10 (broad s, 6H), 2.18 (d, J = 3.1 Hz, 12H), 7.20 (s, 2H); ^{13}C NMR (100.6 MHz) δ 29.3 (d), 36.8 (t), 38.2 (s), 44.1 (t), 122.2 (d), 152.2 (s); UV λ_{max} (ϵ) 237 (5350), 242 nm (5350); EIMS m/z 352 (M^+, 100), 217 ($M^+ - 135$, 12), 135 (Ad^+, 57). Anal. Calcd for $C_{24}H_{32}S$: C, 81.76; H, 9.15. Found: C, 81.75; H, 8.93. **11**: mp 222−225 °C; yellow prisms (from hexane); IR (KBr) 1708 cm^{-1} (C=O); ^1H NMR (90 MHz) δ 1.50−2.24 (m, 30H), 3.30 (s, 2H), 3.31 (s, 2H); ^{13}C NMR (22.5 MHz) δ 29.0 (d), 32.8 (t), 36.7 (t), 39.5 (t), 42.3 (t), 44.5 (s), 63.1 (s), 216.9 (s); EIMS m/z 370 (M^+, 12), 135 (Ad^+, 100). Anal. Calcd for $C_{24}H_{34}OS$; C, 77.78; H, 9.25. Found: C, 77.68; H, 9.04. Standing a mixture of 70 mg (0.2 mmol) of the thiophene **4b** and 35 mg of $AlCl_3$ in 3 mL of carbon disulfide for 1 week at room temperature and purification of the mixture by column chromatography gave 67 mg (96%) of the rearranged product, 2,4-di(1-adamantyl)-thiophene (**9b**), whose properties agreed with those of **9b** obtained by dehydration of the diol **7b**.

1,5-Dineopentyl-3-thiapentane-1,5-dione (1c). Bromine (64.8 g, 0.41 mol) was added in a single stream to an ice-cooled solution of 46.3 g (0.41 mol) of methyl neopentyl ketone (**5c**) in 50 mL of methanol. The mixture was warmed slowly and stirred at 10 °C for 0.5 h and at room temperature for 15 min. The mixture was diluted with 300 mL of water and extracted with ether (400 mL × 4). The extracts were washed with aqueous Na_2CO_3 and then with water, dried over $CaCl_2$, and evaporated to give 69.5 g (89%) of bromomethyl neopentyl ketone (**6c**),[19] which was practically pure and used for the preparation of **1c** without further purification. A solution of 42.8 g (178 mmol) of sodium sulfide nonahydrate in 120 mL of water was added to an ice-cooled solution of 68.6 g (355 mmol) of **6c** in 1000 mL of acetone over a period of 1.3 h. After the addition, the mixture was warmed to room temperature, stirred at room temperature for 1 h, diluted with water (1000 mL), and extracted with ether (500 mL × 3). The extracts were washed with water, dried over Na_2SO_4, and evaporated. The resulting yellow oil was distilled to give 40.0 g (87%) of **1c**: bp 106 °C/0.25 mmHg (mp 22.5−23.0 °C); IR (neat) 1708 cm^{-1} (C=O); ^1H NMR (200 MHz) δ 1.02 (s, 18H), 2.45 (s, 4H), 3.27 (s, 4H); ^{13}C NMR (50 MHz) δ 29.6 (q), 31.1 (s), 42.5 (t), 53.2 (t), 204.3 (s); EIMS m/z 258 (M^+), 159, 103. Anal. Calcd for $C_{14}H_{26}O_2S$; C, 65.07; H, 10.14. Found: C, 64.98; H, 10.01.

3,4-Dineopentylthiolane-3,4-diol (2c). Titanium(IV) chloride (18.7 mL, 174 mmol) was added over a period of 75 min to a well-stirred mixture of 7.40 g (113 mmol) of zinc powder and 15.0 g (58 mmol) of **1c** in 600 mL of THF cooled at −18 °C. The mixture was warmed slowly to 0 °C and stirred for 3.5 h at 0−15 °C. The reaction was quenched by addition of crushed ice (500 g), and the pH of the mixture was adjusted to 9 by addition of aqueous Na_2CO_3. CH_2Cl_2 (1000 mL) was added to the mixture, and the whole mixture was stirred for 90 min and filtered by a large Büchner funnel on which a pad of Celite was placed. The organic layer of the filtrate was washed with water 10 times, dried over Na_2CO_3, and evaporated. The resulting crude product was recrystallized from hexane to give 8.25 g of **2c**. Evaporation of the mother liquor of the recrystallization and purification of the residue by silica gel column chromatography gave another crop of **2c** (3.60 g). Total yield, 78%. **2c**: mp 118−119 °C; colorless plates (from hexane); IR (KBr) 3546, 3448 cm^{-1} (OH); ^1H NMR (400 MHz) δ 1.07 (s, 18H), 1.42 (d, J = 14.6 Hz, 2H), 1.52 (d, J = 14.6 Hz, 2H), 2.37 (s, 2H), 2.90 (d, J = 11.2 Hz, 2H), 2.97 (d, J = 11.2 Hz, 2H); ^{13}C NMR (100.6 MHz) δ 31.4 (s), 31.5 (q), 36.7 (t), 44.2 (t), 85.7 (s). Anal. Calcd for $C_{14}H_{28}O_2S$: C, 64.57; H, 10.84. Found: C, 64.65; H, 10.69.

3,4-Dineopentylthiophene (4c). A mixture of 7.43 g (28.7 mmol) of **2c** and 1.53 g of TsOH in 200 mL of benzene was refluxed for 4.5 h. The mixture was washed with aqueous $NaHCO_3$ and then with water, dried over Na_2SO_4, and evaporated. The resulting oil was distilled to give 5.74 g (90%) of **4c** as a colorless oil: bp 65 °C/0.3 mmHg; IR (neat) 2952, 2906, 2866, 1474, 1466, 1389, 1361, 1236, 886, 876, 793 cm^{-1}; ^1H NMR (200 MHz) δ 0.90 (s, 18H), 2.50 (s, 4H), 6.88 (s, 2H); ^{13}C NMR (50 MHz) δ 29.6 (q), 32.4 (s), 42.0 (t), 121.4 (d), 140.1 (s); EIMS m/z 224 (M^+), 167 (M^+ − *tert*-butyl), 149, 102. Anal. Calcd for $C_{14}H_{24}S$: C, 74.93; H, 10.78. Found: C, 74.81; H, 10.66.

1-(1-Adamantyl)-5-*tert*-butyl-3-thiapentane-1,5-dione (1d). To an ice-cooled solution of 33.7 g (0.42 mol as 70% purity) of sodium hydrosulfide hydrate in 150 mL of water was added slowly 60 mL (0.12 mol) of 2 M hydrochloric acid. After the addition, a solution of 53.4 g (0.30 mol) of bromomethyl *tert*-butyl ketone in 30 mL of ether was added over a period of 1 h. The mixture was stirred for 1 h at 0 °C, 200 mL of ether

was added to it, and the whole mixture was extracted with 160 mL of 2 M NaOH. The extract was acidified by 2 M hydrochloric acid and re-extracted with 200 mL of ether. The ether extract was washed with 100 mL of water, dried over Na_2SO_4, and evaporated. The resulting oil was distilled to give 9.93 g (25%) of pivaloylmethanethiol (**12**) as a colorless oil: bp 38 °C/1.2 mmHg; ^{1}H NMR (60 MHz) δ 1.16 (s, 9H), 2.03 (t, J = 7.0 Hz, 1H), 3.56 (d, J = 7.0 Hz, 2H). Since **12** is thermally labile and has a stench, it was immediately used for the preparation of **1d**. To a solution of 4.98 g (19.3 mmol) of 1-adamantyl bromomethyl ketone (**6b**) and 2.56 g (19.3 mmol) of the thiol **12** in 55 mL of benzene were added 22 mg of 18-crown-6-ether and 2.17 g (19.3 mmol) of *t*-BuOK. The mixture was stirred for 2 h at room temperature and diluted with water. The organic layer was washed with water, dried over $MgSO_4$, and evaporated. The resulting oil was purified by silica gel column chromatography to give 5.97 g (100%) of **1d**: viscous oil; ^{1}H NMR (300 MHz) δ 1.19 (s, 9H), 1.64−1.79 (m, 6H), 1.82−1.95 (m, 6H), 2.01−2.12 (m, 3H), 3.50 (d, J = 6.8 Hz, 2H), 3.54 (d, J = 6.8 Hz, 2H) (every hydrogen of two methylenes appeared as doublets because of the geminal coupling, but chemical shift values accidentally overlapped); ^{13}C NMR (50 MHz) δ 26.6, 27.8, 35.6, 35.8, 36.3, 38.4, 44.1, 46.4, 209.5, 210.2.

3-(1-Adamantyl)-4-*tert*-butylthiolane-3,4-diol (2d). Titanium(IV) chloride (0.66 mL, 6.0 mmol) was added to a mixture of 792 mg (12.0 mmol) of zinc powder in 10 mL of THF cooled at −18 °C. After the addition, the mixture was stirred for 10 min, and then a solution of 617 mg (2.0 mmol) of **1d** in 3 mL of THF was added slowly. The mixture was stirred for 24 h at −18 °C, and the reaction was quenched by addition of crushed ice. The pH of the mixture was adjusted to 9 by addition of aqueous Na_2CO_3, and the mixture was stirred for 1 h after 100 mL of CH_2Cl_2 was added. The whole mixture was filtered with a Büchner funnel on which a pad of Celite was placed. The organic layer of the filtrate was washed with water 10 times, dried over $MgSO_4$, and evaporated. The resulting white solid was recrystallized from hexane to give 392 mg (63%) of **2d**: mp 154.0−154.5 °C; colorless needles; IR (KBr) 3412, 3372 cm^{-1} (OH); ^{1}H NMR (400 MHz) δ 1.27 (s, 9H), 1.69 (broad s, 6H), 1.89−2.18 (m, 9H), 2.78 (d, J = 12.2 Hz, 2H), 3.27 (s, 1H), 3.27 (d, J = 12.2 Hz, 1H), 3.32 (d, J = 12.2 Hz, 1H), 3.37 (s, 1H); ^{13}C NMR (100.6 MHz) δ 28.9 (d), 35.9 (t), 37.0 (t), 37.6 (t), 37.8 (broad signal), 38.5 (s), 41.0 (s), 91.2 (s), 92.1 (s). Anal. Calcd for $C_{18}H_{30}O_2S$: C, 69.63; H, 9.74. Found: C, 69.41; H, 9.59.

3-(1-Adamantyl)-4-*tert*-butylthiophene (4d). A mixture of 1.55 g (5 mmol) of **2d** and 0.43 g (2.5 mmol) of TsOH in 200 mL of benzene was heated under reflux for 50 min. The mixture was washed with aqueous $NaHCO_3$ and then with water, dried over $MgSO_4$, and evaporated. The resulting viscous oil was chromatographed on a column of silica gel with hexane as the eluent to give 1.06 g (77%) of **4d**: mp 97.5−80 °C; colorless plates (from ethanol); IR (KBr) 3000, 2958, 2918, 2904, 1466, 1454, 1361, 1342, 1311, 1233, 1207, 1176, 1102, 995, 969, 923, 789, 548 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.50 (s, 9H), 1.76 (broad s, 6H), 2.09 (broad s, 3H), 2.14 (s, 6H), 7.17 (s, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 29.2 (d), 33.7 (q), 35.6 (s), 36.7 (t), 37.9 (s), 43.7 (t), 122.2 (d), 122.3 (d), 150.6 (s), 152.0 (s). Anal. Calcd for $C_{18}H_{26}S$: C, 78.77; H, 9.55. Found: C, 78.78; H, 9.45.

Thiophene 1,1-Dioxides 13a−d. A solution of 5.03 g (29.2 mmol) of *m*-chloroperbenzoic acid (*m*-CPBA) in 60 mL of CH_2Cl_2 was added over a period of 1 h to a stirred and ice-cooled solution of 3.00 g (8.5 mmol) of the thiophene **4b** in 60 mL of CH_2Cl_2. After the addition, the mixture was stirred at room temperature for 24 h, washed with aqueous $NaHSO_3$, $NaHCO_3$, and water, dried over Na_2SO_4, and evaporated. The resulting yellow solid residue was recrystallized from cyclohexane to give 1.88 g of 3,4-di(1-adamantyl)thiophene 1,1-dioxide (**13b**). Purification of the mother liquor of the recrystallization by silica gel column chromatography (CH_2Cl_2 as the eluent) gave a further amount (0.71 g) of **13b**. Total yield, 79%. In a similar way, 3,4-di-*tert*-butyl-, 3,4-dineopentyl-, and 3-(1-adamantyl)-4-*tert*-butylthiophene 1,1-dioxides (**13a**, **13c**, and **13d**) were prepared in 93%, 68%, and 80% yields, respectively. **13a**: mp 132.5−133 °C; colorless needles (from hexane); IR (KBr) 1284, 1134 cm^{-1} (SO_2); ^{1}H NMR (400 MHz) δ 1.39 (s, 18H), 6.44 (s, 2H); ^{13}C NMR (100.6 MHz) δ 31.5, 35.7, 127.5, 156.8. Anal. Calcd for $C_{12}H_{20}O_2S$; C, 63.12; H, 8.83; S, 14.04. Found: C, 62.93; H, 8.78; S, 14.21. **13b**: mp 279−282 °C; coloress crystals (from CH_2Cl_2/cyclohexane); IR (KBr) 1284, 1237, 1115, 1102 cm^{-1} (SO_2); ^{1}H NMR (400 MHz) δ 1.71 (d, J = 12.3 Hz, 6H), 1.77 (d, J = 12.3 Hz, 6H), 2.03 (broad s, 12H), 2.13 (broad s, 6H), 6.41 (s, 2H); ^{13}C NMR (100.6 MHz) δ 28.5 (d), 36.1 (t), 38.7 (s), 41.9 (t), 128.5 (d), 158.3 (s); EIMS m/z 384 (M^+, 2), 352 ($M^+ - 2O$, 4), 320 ($M^+ - SO_2$, 3), 135 (Ad^+, 100). Anal. Calcd for $C_{24}H_{32}O_2S$: C, 74.96; H, 8.39. Found: C, 74.68; H, 8.24. **13c**: 141.5−142.0 °C; colorless needles (from hexane); IR (KBr) 1282, 1181, 1084 cm^{-1} (SO_2); ^{1}H NMR (200 MHz) δ 0.98 (s, 18H), 2.29 (s, 4H), 6.26 (s, 2H); ^{13}C NMR (50 MHz) δ 29.6 (q), 32.5 (s), 40.6 (t), 126.9 (d), 144.8 (s). Anal. Calcd for $C_{14}H_{24}O_2S$: C, 65.58; H, 9.43. Found: C, 65.63; H, 9.23. **13d**: mp 149.5−150.0 °C; colorless crystals (from hexane); IR (KBr) 1286, 1129 cm^{-1} (SO_2); ^{1}H NMR (400 MHz) δ 1.42 (s, 9H), 1.71 (d, J = 12.3 Hz, 3H), 1.76 (d, J = 12.3 Hz, 3H), 1.97 (d, J = 2.6 Hz, 6H), 2.12 (broad s, 3H), 6.43 (s, 1H), 6.44 (s, 1H); ^{13}C NMR (100.6 MHz) δ 28.4 (d), 31.7 (q), 36.01 (s), 36.01 (t), 38.4 (s), 41.6 (t), 127.4 (d), 127.6 (d), 157.1 (s), 157.8 (s). Anal. Calcd for $C_{18}H_{26}O_2S$: C, 70.54; H, 8.55. Found: C, 70.33; H, 8.54.

Thiophene 1,1-Dioxides 14a−d. Lithium diisopropylamide (LDA) was prepared from 927 mg (9.0 mmol) of diisopropylamine and 5.9 mL (9.2 mmol) of 1.55 M butyllithium in hexane in 8 mL of THF at −18 °C and was added over a period of 1 h to a solution of 836 mg (3.7 mmol) of the thiophene 1,1-dioxide **13a** in 30 mL of THF cooled at −78 °C under argon. The mixture was stirred for 3 h at that temperature, and then a solution of 1.1 mL (18 mmol) of methyl iodide in 3 mL of THF was added. The mixture was warmed slowly to room temperature and stirred for 15 h. The reaction was quenched by adding crushed ice and CH_2Cl_2. The organic layer was washed with 1 M hydrochloric acid and then with water, dried over Na_2SO_4, and evaporated. The residue was chromatographed on a column of silica gel to give 629 mg (67%) of **14a**: mp 161−162 °C; colorless needles (from hexane); IR (KBr) 1280, 1165, 1116 cm^{-1} (SO_2); ^{1}H NMR (400 MHz) δ 1.43 (s, 18H), 2.21 (s, 6H); ^{13}C NMR (100.6 MHz) δ 11.2 (q), 31.8 (q), 36.6 (s), 133.8 (s), 150.1 (s); MS m/z 256 (M^+, 36), 57 (t-Bu^+, 100). Anal. Calcd for $C_{14}H_{24}O_2S$: C, 65.58; H, 9.43. Found: 65.47; H, 9.26.

Lithium 2,2,6,6-tetramethylpiperidide (LTMP) was prepared from 1.27 g (9.0 mmol) of 2,2,6,6-tetramethylpiperidine and 5.8 mL (9.0 mmol) of 1.55 M butyllithium in hexane in 5 mL of THF at −78 °C and was added over a period of 20 min to a solution of 1.15 g (3.0 mmol) of the thiophene 1,1-dioxide **13b** in 90 mL of THF cooled at −78 °C under argon. The mixture was stirred for 4 h at that temperature, and then a solution of 1.32 g (9.3 mmol) of methyl iodide in 5 mL of THF was added at −78 °C over a period of 15 min. The mixture was stirred for 2.5 h at that temperature and warmed slowly to room temperature. The reaction was quenched by adding crushed ice and then CH_2Cl_2 (100 mL). The organic layer was washed with 1 M hydrochloric acid, water, aqueous $NaHCO_3$, and water, dried over Na_2SO_4, and evaporated. The resulting solid was chromatographed on a column of silica gel with CH_2Cl_2 as the eluent to give 0.75 g (61%) of 3,4-di(1-adamantyl)-2,5-dimethylthiophene 1,1-dioxide (**14b**). In a similar way, 3-(1-adamantyl)-4-*tert*-butyl-2,5-dimethylthiophene 1,1-dioxide (**14d**) was prepared in 37% yield. **14b**: mp 296−297 °C; colorless crystals (from cyclohexane); IR (KBr) 1275, 1140 cm^{-1} (SO_2); ^{1}H NMR (400 MHz) δ 1.73 (broad s, 12H), 2.08 (broad s, 6H), 2.15 (broad s, 12H), 2.25 (s, 6H); ^{13}C NMR (100.6 MHz) δ 11.9 (q), 28.9 (d), 36.3 (t), 40.7 (s), 41.1 (t), 134.0 (s), 151.6 (s); MS m/z 412 (M^+, 8), 135 (100, Ad^+). Anal. Calcd for $C_{26}H_{36}O_2S$: C, 75.68; H, 8.79. Found: 75.42; H, 8.79. **14d**: mp 178−180 °C; colorless crystals (from cyclohexane); IR (KBr) 1272, 1180, 1130, 1109, 1092 cm^{-1} (SO_2); ^{1}H NMR (90 MHz) δ 1.44 (s, 9H), 1.73 (broad s, 6H), 2.11 (broad s, 9H), 2.19 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (22.5 MHz) δ 11.2 (q), 11.9 (q), 28.8 (d), 31.9

(q), 36.2 (t), 37.0 (s), 40.1 (s), 40.7 (t), 133.8 (s,), 134.1 (s), 150.6 (s), 150.7 (s). Anal. Calcd for $C_{20}H_{30}O_2S$: C, 71.81; H, 9.04. Found: C, 71.78; H, 8.90.

To a solution of 513 mg (2 mmol) of the thiophene 1,1-dioxide **13c** in 14 mL of THF cooled at −94 °C was added slowly 2.72 mL of 1.62 M butyllithium in hexane. The mixture was stirred for 1 h at that temperature. Quenching of the reaction at this stage with D_2O afforded 2,5-didueterio-3,4-dineopentylthiophene 1,1-dioxide (**13c-D**). The deuterium content of the 2,5-positions was revealed to be near 100% by ^{1}H NMR analysis. For the preparation of 2,5-dimethyl-3,4-dineopentylthiophene 1,1-dioxide (**14c**), 1.25 mL (20 mmol) of methyl iodide was added slowly to the above mixture and the mixture warmed slowly to room temperature and quenched by addition of water. The mixture was extracted with CH_2Cl_2, and the extracts were washed with water, dried over Na_2SO_4, and evaporated. The resulting pale yellow solid was recrystallized from hexane to give 263 mg of the thiophene 1,1-dioxide (**14c**). Purification of the mother liquor of the recrystallization by silica gel column chromatography with CH_2Cl_2 as the eluent gave another crop (234 mg) of **14c**. Total yield 87%. **14c**: mp 152.5−153.0 °C; colorless crystals (from hexane); IR (KBr) 1277, 1167, 1145, 1089 cm^{-1} (SO_2); ^{1}H NMR (200 MHz) δ 0.94 (s, 18H), 2.08 (s, 6H), 2.35 (s, 4H); ^{13}C NMR (50 MHz) δ 9.0 (q), 30.2 (q), 35.2 (s), 38.5 (t), 133.7 (s), 137.7 (s). Anal. Calcd for $C_{16}H_{28}O_2S$: C, 67.56; H, 9.92. Found: 67.50; H, 9.82.

Dimethyl 4,5-Di-*tert*-butyl-3,6-dimethylphthalate (15a) and 4,5-Di-*tert*-butyl-3,6-dimethylphthalic Anhydride (16a). A solution of 256 mg (1 mmol) of the thiophene 1,1-dioxide **14a** in 20 mL of *o*-dichlorobenzene was heated at reflux. To this refluxing solution was added 284 mg (2 mmol) of neat DMAD, and the mixture was heated at reflux for 5 h. Addition of the same quantity of DMAD was continued at 1.5-h intervals nine times. In this way, 2.84 g of DMAD was added in total, and the mixture was heated at reflux for about 20 h. The resulting mixture was evaporated under reduced pressure, and the residue was chromatographed on a column of silica gel with CH_2Cl_2 as the eluent to give 224 mg (67%) of **15a**: mp 102 °C (from hexane); ^{1}H NMR (270 MHz) δ 1.43 (s, 18H), 2.45 (s, 6H), 3.77 (s, 6H); ^{13}C NMR (67 MHz) δ 20.0, 34.2, 40.9, 52.3, 128.7, 133.0, 155.4, 167.8. Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 72.02; H, 8.88.

A solution of 68 mg (0.2 mmol) of **15a** in 1 mL of ethanol and a solution of 400 mg of KOH in 2 mL of water were mixed and heated at reflux for 1 h. The mixture was diluted with water, extracted with ether, washed with water, dried over Na_2SO_4, and evaporated to leave 58 mg (99%) of **16a**: mp 181.0−181.5 °C; colorless plates (from hexane); ^{1}H NMR (60 MHz) δ 1.67 (s, 18H), 2.76 (s, 6H); EIMS *m*/*z* 288 (M^+, 7), 58 (*t*-Bu^+ + 1, 100); HRMS $C_{18}H_{24}O_3$ calcd 288.1726, found 288.1726.

***o*-Di(1-adamantyl)benzene (17b).** A mixture of 381 mg (1.0 mmol) of the thiophene 1,1-dioxide (**13b**) and 460 mg (2.7 mmol) of phenyl vinyl sulfone in 10 mL of *o*-dichlorobenzene was heated under reflux for 25 h. The mixture was evaporated under reduced pressure, and the residue was chromatographed on a column of silica gel. Elution with hexane gave 320 mg (93%) of **17b**: mp 184.5−185.0 °C; colorless prisms (from hexane); IR (KBr) 3044, 2894, 2652, 1586, 1572, 1447, 1434, 1370, 1339, 1304, 1237, 1183, 1089, 1015, 961, 811, 739, 525 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.74 (d, J = 12.1 Hz, 6H), 1.80 (d, J = 12.1 Hz, 6H), 2.13 (broad s, 6H), 2.29 (broad s, 12H), 7.13 (A_2B_2m, 2H), 7.64 (A_2B_2m, 2H); ^{13}C NMR (100.6 MHz) δ 29.7 (d), 36.8 (t), 41.0 (s), 44.6 (t), 125.5 (d), 128.7 (d), 150.4 (s); UV (hexane) λ_{max} (ϵ) 264 nm (145); EIMS *m*/*z* 346 (M^+, 16), 135 (Ad^+, 100). Anal. Calcd for $C_{26}H_{34}$: C, 90.11; H, 9.89. Found: C, 90.04; H, 9.82.

Dimethyl 4,5-Di(1-adamantyl)phthalate (20b). A mixture of 154 mg (0.4 mmol) of the dioxide **13b** and 173 mg (1.2 mmol) of dimethyl acetylenedicarboxylate (DMAD) in 12 mL of *o*-dichlorobenzene was heated under reflux for 7 h. The mixture was evaporated under reduced pressure, and the residue was chromatographed on a column of silica gel with benzene as the eluent to give 161 mg (87%) of **20b**: mp 192−193 °C; colorless needles (from hexane); IR (KBr) 1721 cm^{-1} (C═O); ^{1}H NMR (400 MHz) δ 1.75 (d, J = 12.8 Hz, 6H), 1.80 (d, J = 12.8 Hz, 6H), 2.15 (broad s, 6H), 2.26 (broad s, 12H), 3.89 (s, 6H), 7.99 (s, 2H); ^{13}C NMR (100.6 MHz) δ 29.4 (d), 36.5 (t), 41.4 (s), 44.2 (t), 52.5 (q), 128.0 (s), 129.7 (d), 154.5 (s), 168.5 (s); EIMS *m*/*z* 462 (M^+, 4), 431 (M^+ − MeO, 3), 135 (Ad^+, 100). Anal. Calcd for $C_{30}H_{38}O_4$: C, 77.89; H, 8.28. Found: C, 77.85; H, 8.22.

Dimethyl 4,5-Di(1-adamantyl)-3,6-dimethylphthalate (15b). A solution of 206 mg (0.5 mmol) of the thiophene 1,1-dioxide **14b** in 20 mL of *o*-dichlorobenzene was heated at reflux. To this refluxing solution was added 213 mg (1.5 mmol) of neat DMAD, and the mixture was heated at reflux. Addition of the same quantity of DMAD was continued at intervals of 1.5 h 14 times. In this way, 3.13 g of DMAD was added in total and the mixture was heated under reflux for 35 h. The resulting mixture was evaporated under reduced pressure, and the residue was chromatographed on a column of silica gel with CH_2Cl_2 as the eluent to give faint pale yellow crystals, which was further purified by recrystallization from cyclohexane to give 138 mg (56%) of analytically pure **15b**: mp 261−262 °C; colorless needles; IR (KBr) 1729 cm^{-1} (C═O); ^{1}H NMR (400 MHz) δ 1.68 (d, J = 12.5 Hz, 6H), 1.71 (d, J = 12.5 Hz, 6H), 2.02 (broad s, 6H), 2.16 (broad s, 12H), 2.57 (s, 6H), 3.80 (s, 6H); ^{13}C NMR (100.6 MHz) δ 19.8 (q), 29.6 (d), 36.8 (t), 42.6 (t), 46.6 (s), 52.0 (q), 127.8 (s), 132.6 (s), 156.7 (s), 169.7 (s). Anal. Calcd for $C_{32}H_{42}O_4$: C, 78.33; H, 8.63. Found: C, 78.32; H, 8.68. Treatment of 123 mg (0.25 mmol) of **15b** in the same manner as described for **15a** gave 110 mg (99%) of 4,5-di(1-adamantyl)-3,6-dimethylphthalic anhydride (**16b**): mp 373−375 °C dec (from 1,2-dichloroethane); IR (KBr) 1823, 1762 cm^{-1} (C═O); ^{1}H NMR (60 MHz) δ 1.57−2.28 (m, 30H), 2.92 (s, 6H); EIMS *m*/*z* 444 (M^+); HRMS $C_{30}H_{36}O_3$ calcd 444.2664, found 444.2669. Heating a mixture of 77 mg (0.17 mmol) of **16b** and sodium ethoxide (prepared from 40 mg of sodium) in 15 mL of ethanol under reflux for 11 h gave 88 mg (98%) of diethyl 4,5-di(1-adamantyl)-3,6-dimethylphthalate (**15b′**): mp 168.5−169 °C (from hexane); ^{1}H NMR (400 MHz) δ 1.33 (t, J = 7.2 Hz, 6H), 1.64−1.73 (m, 12H), 2.02 (broad s, 6H), 2.17 (broad s, 12H), 2.57 (s, 6H), 4.268 (q, J = 7.2 Hz, 2H), 4.273 (q, J = 7.2 Hz, 2H); ^{13}C NMR (100.6 MHz) δ 14.1, 19.8, 29.6, 36.8, 42.6, 46.5, 61.0, 128.0, 132.3, 156.3, 169.4.

4,5-Di(1-adamantyl)pyridazine (25b). A mixture of 77 mg (0.2 mmol) of the thiophene 1,1-dioxide **13b** and 78 mg (0.44 mmol) of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) in 5 mL of toluene was heated at reflux for 1.5 h. A further amount of PTAD (200 mg) was added to the refluxing mixture in four portions at 1-h intervals. In this way, the mixture was refluxed for 6 h and then evaporated under reduced pressure. The residue was purified by silica gel column chromatography to give 96 mg (71%) of the bis-adduct **22b**: mp 220 °C dec; colorless crystals (from cyclohexane/$CHCl_3$); ^{1}H NMR (400 MHz) δ 1.73 (d, J = 14.4 Hz, 6H), 1.77 (d, J = 14.4 Hz, 6H), 2.13 (broad s, 6H), 2.15 (broad s, 12H), 7.01 (s, 2H), 7.39−7.44 (m, 6H), 7.46−7.52 (m, 4H); ^{13}C NMR (100.6 MHz) δ 28.6 (d), 36.1 (t), 38.3 (s), 42.3 (t), 64.6 (d), 125.6 (d), 129.0 (d), 129.4 (d), 130.6 (s), 142.8 (s), 154.1 (s); HRMS $C_{40}H_{42}N_6O_4$ calcd 670.3286, found 670.3271.

A solution of 322 mg of KOH in 2 mL of methanol was added to a well-stirred and ice-cooled suspension of 100 mg (0.15 mmol) of the adduct **22b** in 3 mL of methanol. The mixture was warmed to room temperature, stirred for 4 h, diluted with water, and extracted with ether. The ether extracts were washed with water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on a column of silica gel. The column was first eluted with CH_2Cl_2 to remove byproducts and then with ether to give 43 mg (83%) of the pyridazine **25b**: mp 256.5−257 °C; colorless needles (from cyclohexane/$CHCl_3$); IR (KBr) 3008, 2914, 2846, 1556, 1490, 1452, 1341, 1278, 1101, 977, 817, 702, 662 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.75 (broad s, 12H), 2.13 (broad s, 6H), 2.21 (broad s, 12H), 9.15 (s, 2H); ^{13}C NMR (100.6 MHz) δ 29.0 (d), 36.3 (t), 39.8 (s), 43.3 (t), 147.8 (s), 150.3 (d); HRMS $C_{24}H_{32}N_2$ calcd 348.2523, found 348.2545.

***o*-Dineopentylbenzene (17c).** A solution of 257 mg (1 mmol) of the thiophene 1,1-dioxide **13c** and 370 mg (2.2 mmol)

of phenyl vinyl sulfone in 4 mL of chlorobenzene was heated at reflux for 16 h. The mixture was evaporated and the residue was chromatographed on a column of silica gel. Elution with hexane gave 182 mg (83%) of **17c**: bp 89 °C/22 mmHg (bulb-to-bulb distillation) (lit.[18d] bp 135−137 °C/24 mmHg); ^{1}H NMR (200 MHz) δ 0.89 (s, 18H), 2.63 (s, 4H), 7.10 (s, 4H); ^{13}C NMR (50 MHz) δ 29.8 (q), 33.0 (s), 45.8 (t), 124.9 (d), 131.5 (d), 138.6 (s).

Dimethyl 4,5-Dineopentylphthalate (20c). A solution of 128 mg (0.5 mmol) of **13c** and 142 mg (1 mmol) of DMAD in 15 mL of *o*-chlorotoluene was heated at reflux for 34 h. Chromatographic purification of the mixture (silica gel, CH_2Cl_2 as the eluent) gave 156 mg (93%) of **20c**: mp 36−37 °C; IR (neat) 1728 cm^{-1} (C=O); ^{1}H NMR (200 MHz) δ 0.90 (s, 18H), 2.69 (s, 4H), 3.89 (s, 6H), 7.48 (s, 2H); ^{13}C NMR (50 MHz) δ 29.6 (q), 33.1 (s), 45.6 (t), 52.4 (q), 128.5 (s), 131.8 (d), 142.4 (s), 168.4 (s); EIMS *m*/*z* 334 (M^+), 319 (M^+ − Me), 57 (100%); HRMS $C_{20}H_{30}O_4$ calcd 334.2142, found 334.2152.

8,9-Dineopentylbenzocyclooctene (26a). A solution of 259 mg (1 mmol) of **13c** and 328 mg (3 mmol) of cyclooctyne[37] in 6 mL of *o*-chlorotoluene was heated at reflux for 2 h. Chromatographic purification of the mixture (silica gel, hexane as the eluent) gave 305 mg (100%) of **26a**: mp 60.0−60.5 °C (after sublimed at 55 °C/0.15 mmHg); ^{1}H NMR (200 MHz) δ 0.87 (s, 18H), 1.25−1.40 (m, 4H), 1.54−1.71 (m, 4H), 2.56 (s, 4H), 2.60−2.77 (m, 4H), 6.80 (s, 2H); ^{13}C NMR (50 MHz) δ 26.0 (t), 29.8 (q), 31.9 (t), 32.5 (t), 32.8 (s), 45.5 (t), 132.0 (d), 136.2 (s), 137.5 (s). Anal. Calcd for $C_{22}H_{36}$: C, 87.93; H, 12.07. Found: C, 88.03; H, 12.31.

1,2-Dineopentyl-4,5-diphenylbenzene (26b). A mixture of 128 mg (0.5 mmol) of **13c** and 178 mg (1 mmol) of diphenylacetylene was heated at 220−235 °C for 1 h, and the mixture was chromatographed on a column of silica gel with hexane as the eluent to give 35 mg (19%) of **26b**: mp 108−110 °C (from MeOH); ^{1}H NMR (200 MHz) δ 0.98 (s, 18H), 2.69 (s, 4H), 7.10−7.22 (m, 12H); ^{13}C NMR (50 MHz) δ 29.9 (q), 33.1 (s), 45.6 (t), 126.1 (d), 127.7 (d), 129.9 (d), 133.7 (d), 136.9 (s), 137.8 (s), 141.8 (s); EIMS *m*/*z* 370 (M^+), 355 (M^+ − Me), 257 (100). Anal. Calcd for $C_{28}H_{34}$: C, 90.75; H, 9.25. Found: C, 90.32; H, 9.27.

Reaction of 13c with Benzyne. A mixture of 256 mg (1 mmol) of **13c**, 790 mg (4.3 mmol) of 2-carboxybenzenediazonium chloride,[26] and 1 mL of propylene oxide in 100 mL of 1,2-dichloroethane was heated under reflux for 35 min. The mixture was evaporated, and the residue was chromatographed on a column of silica gel with hexane as the eluent to give 54 mg (20%) of 3,4-dineopentylnaphthalene (**28a**) and 24 mg (7%) of 9,10-dihydro-9,10-(11,12-dineopentyletheno)anthracene (**29a**). Further elution of the column with CH_2Cl_2 gave 226 mg (68%) of 3-(3,3-dimethylbutylidene)-4-neopentyl-2-phenyl-2,3-dihydrothiophene 1,1-dioxide (**27a**). The reaction of **13c**-**D** with benzyne was carried out in the same manner. **27a**: mp 115.5−116.0 °C (from hexane); IR (KBr) 1629, 1600 (C=C), 1286, 1194 cm^{-1} (SO_2); ^{1}H NMR (200 MHz) δ 0.95 (s, 9H), 1.07 (s, 9H), 2.42 (d, J = 13.8 Hz, 1H), 2.53 (d, J = 13.8 Hz, 1H), 5.23 (s, no signal for **27a**-**D**, 12.4% NOE on irradiation of δ = 0.95, 1H), 6.13 (s, 22.2% NOE on irradiation of δ = 2.48, 1H), 6.28 (s, no signal for **27a**-**D**, 17.2% and 13.3% NOE on irradiation of δ = 1.07 and 2.48, respectively, 1H), 7.19 (m, 2H), 7.36 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.6 (q), 30.4 (q), 32.0 (s), 34.6 (s), 40.8 (t), 66.6 (d), 125.7 (d), 128.7 (d), 128.87 (d), 128.92 (d), 131.3 (s), 134.4 (s), 144.0 (d), 151.8 (s). Anal. Calcd for $C_{20}H_{28}O_2S$: C, 72.25; H, 8.49. Found: C, 72.22; H, 8.52. **28a**: mp 120 °C (from methanol); ^{1}H NMR (200 MHz) δ 0.92 (s, 18H), 2.81 (s, 4H), 7.32−7.43 (m, 2H), 7.57 (s, no signal for **28a**-**D**, 2H), 7.69−7.79 (m, 2H); ^{13}C NMR (50 MHz) δ 29.8 (q), 33.2 (s), 46.0 (t), 124.9 (d), 127.1 (d), 129.5 (d), 131.8 (s), 135.6 (s); EIMS *m*/*z* 268 (M^+), 253 (M^+ − Me), 155 (100). Anal. Calcd for $C_{20}H_{28}$: C, 89.49; H, 10.51. Found: C, 89.57; H, 10.68. **29a**: mp 126−127 °C (from methanol); ^{1}H NMR (200 MHz) δ 0.86 (s, 18H), 2.18 (s, 4H), 4.89 (s, no signal for **29a**-**D**, 2H), 6.86−6.94 (m, 4H), 7.16−7.24 (m, 4H); ^{13}C NMR (50 MHz) δ 30.4 (q), 33.2 (s), 44.6 (t), 57.1 (d), 122.6 (d), 124.0 (d), 144.4 (s), 146.4 (s); MS *m*/*z* 344 (M^+), 329 (M^+ − Me), 231 (100). HRMS $C_{26}H_{32}$ calcd 344.2504, found 344.2532.

4,5-Dineopentylpyridazine (25c). A mixture of 257 mg (1 mmol) of **13c** and 367 mg (2.1 mmol) of PTAD in 7 mL of benzene was heated under reflux for 6 h. The mixture was evaporated, and the residue was recrystallized from cyclohexane to give 418 mg (77%) of the bis-adduct **22c**: mp > 175 °C dec; ^{1}H NMR (200 MHz) δ 1.09 (s, 18H), 2.38 (s, 4H), 6.54 (s, 2H), 7.43 (m, 10H); ^{13}C NMR (50 MHz) δ 30.3 (q), 33.2 (s), 43.2 (t), 67.0 (d), 125.4 (d), 128.9 (d), 129.3 (d), 130.6 (s), 134.5 (s), 154.0 (s); IR (KBr) 1732 cm^{-1} (C=O); EIMS *m*/*z* 542 (M^+), 527 (M^+ − Me), 367 (100). A solution of 419 mg of KOH in 10 mL of methanol was added to an ice-cooled suspension of 101 mg (0.19 mmol) of **22c** in 3 mL of methanol, and the mixture was stirred for 50 h at room temperature and evaporated. The residue was stirred with ether (30 mL) and the insoluble material removed by filtration. The filtrate was washed with water, dried over Na_2SO_4, evaporated, and chromatographed on a column of silica gel with ether as the eluent to give 31 mg (76%) of **25c**: mp 66.5−67.0 °C (after sublimation at 35 °C/0.2 mmHg); ^{1}H NMR (200 MHz) δ 0.93 (s, 18H), 2.63 (s, 4H), 8.87 (s, 2H); ^{13}C NMR (50 MHz) δ 29.5 (q), 33.2 (s), 42.6 (t), 137.9 (s), 153.8 (d); IR (KBr) 2954, 2868, 1562, 1477, 1363, 1231, 1040, 994, 799 cm^{-1}. Anal. Calcd for $C_{14}H_{24}N_2$; C, 76.31; H, 10.98; N, 12.71. Found: 76.36; H, 11.12; N, 12.68.

1,4-Dimethyl-2,3-dineopentylbenzene (26c). A solution of 51 mg (0.18 mmol) of **14c** and 88 mg (0.45 mmol) of phenyl vinyl sulfone in 1 mL of *o*-chlorotoluene was heated under reflux for 83 h. The mixture was evaporated under reduced pressure and chromatographed on a column of silica gel with hexane as the eluent to give 36 mg (81%) of **26c**: bp 100 °C/0.1 mmHg (bulb-to-bulb distillation); mp 23.0−23.5 °C; ^{1}H NMR (200 MHz) δ 0.85 (s, 18H), 2.31 (s, 6H), 2.65 (d, J = 13.3 Hz, 2H), 2.97 (d, J = 13.3 Hz, 2H), 6.88 (s, 2H); ^{13}C NMR (50 MHz) δ 22.1 (q), 30.2 (q), 34.5 (s), 41.1 (t), 127.4 (d), 134.6 (s), 138.0 (s); EIMS *m*/*z* 246 (M^+), 231 (M^+ − Me), 133 (100); HRMS $C_{18}H_{30}$ calcd 246.2348, found 246.2368.

Dimethyl 3,6-Dimethyl-4,5-dineopentylphthalate (15c). A solution of 50 mg (0.18 mmol) of **14c** and 100 mg (0.70 mmol) of DMAD in 8 mL of *o*-dichlorobenzene was heated under reflux. The mixture was heated for 40 h, during which time 2.37 g of DMAD was added further in small portions at intervals of about 2.5 h. The mixture was evaporated under reduced pressure and chromatographed on a column of silica gel with CH_2Cl_2 as the eluent to give 55 mg (86%) of **15c**: mp 81.0−82.5 °C; IR (KBr) 1728 cm^{-1} (CO); ^{1}H NMR (200 MHz) δ 0.84 (s, 18H), 2.34 (s, 6H), 2.78 (d, J = 14.2 Hz, 2H), 3.04 (d, J = 14.2 Hz, 2H), 3.85 (s, 6H); ^{13}C NMR (50 MHz) δ 19.1 (q), 30.0 (q), 34.6 (s), 41.2 (t), 52.1 (q), 130.3 (s), 132.5 (s), 141.3 (s), 169.9 (s); EIMS *m*/*z* 362 (M^+), 347 (M^+ − Me), 218 (100); HRMS $C_{22}H_{34}O_4$ calcd 364.2455, found 362.2396.

1-(1-Adamantyl)-2-*tert*-butylbenzene (17d). A solution of 154 mg (0.5 mmol) of the thiophene 1,1-dioxide **13d** and 210 mg (1.25 mmol) of phenyl vinyl sulfone in 5 mL of *o*-dichlorobenzene was heated at reflux for 23 h. An additional amount (41 mg) of phenyl vinyl sulfone was added, and the mixture was refluxed again for additional 4.5 h. The mixture was evaporated under reduced pressure to leave a dark solid, which was chromatographed on a column of silica gel. Elution with hexane gave 134 mg (99%) of **17d**: mp 77 °C; colorless needles (from MeOH); IR (KBr) 3118, 3050, 2914, 2890, 2852, 1594, 1453, 1432, 1413, 1342, 745, 537 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.59 (s, 9H), 1.74 (d, J = 12.0 Hz, 3H), 1.81 (d, J = 12.0 Hz, 3H), 2.12 (broad s, 3H), 2.23 (d-like, 6H), 7.08−7.18 (m, 2H), 7.58−7.65 (m, 2H); ^{13}C NMR (100.6 MHz) δ 29.6 (d), 35.4 (q), 36.8 (t), 38.4 (s), 40.3 (s), 43.9 (t), 125.4 (d), 125.6 (d), 128.6 (d), 129.8 (d), 149.2 (s), 149.9 (s). Anal. Calcd for $C_{20}H_{28}$; C, 89.49; H, 10.51. Found: C, 89.67; H, 10.48.

Dimethyl 4-(1-Adamantyl)-5-*tert*-butyl-3,6-dimethylphthalate (15d). A mixture of 338 mg (1 mmol) of the thiophene 1,1-dioxide **14d** and 284 mg (2 mmol) of DMAD in 50 mL of *o*-dichlorobenzene was heated at reflux for 4 h. After

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that, 4.03 g (28 mmol) of DMAD was added in 142-mg portions at intervals of about 3.5 h. In this way, the mixture was refluxed for 5 days and evaporated under reduced pressure. The resulting dark oil was chromatographed on a column of silica gel to give 285 mg (68%) of **15d**: mp 91−92 °C (from MeOH); ^{1}H NMR (90 MHz) 1.46 (s, 9H), 1.70 (broad s, 6H), 2.02 (broad s, 3H), 2.15 (broad s, 6H), 2.51 (s, 3H), 2.58 (s, 3H), 3.81 (s, 6H); ^{13}C NMR (22.5 MHz) δ 19.6 (q), 19.8 (q), 29.5 (d), 34.3 (q), 36.7 (t), 41.2 (s), 42.2 (t), 45.7 (s), 51.8 (q, overlapping of two CO_2*Me* signals), 127.6 (s), 128.4 (s), 132.4 (s), 132.7 (s), 155.4 (s), 156.0 (s), 169.5 (s), 169.6 (s). Anal. Calcd for $C_{26}H_{36}O_4$: C, 75.69; H, 8.80. Found: C, 75.56; H, 8.80. This compound was converted to the corresponding acid anhydride **16d** quantitatively by alkaline hydrolysis followed by acidification: mp 181.0−182 °C; ^{1}H NMR (60 MHz) 1.48 (s, 9H), 1.55−2.27 (m, 15H), 2.77 (s, 3H), 2.85 (s, 3H); EIMS *m*/*z* 366 (M^+, 0.5), 135 (Ad^+, 100); HRMS $C_{24}H_{30}O_3$ calcd 366.2195, found 366.2209.

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