SYNTHESIS OF [2.*n*]THIOPHENOPHANES BY INTRAMOLECULAR [2 + 2] PHOTOCYCLOADDITION

Yosuke Nakamura,[a] Masayoshi Kaneko,[a] Teruo Shinmyozu,[a] and Jun Nishimura*[b]

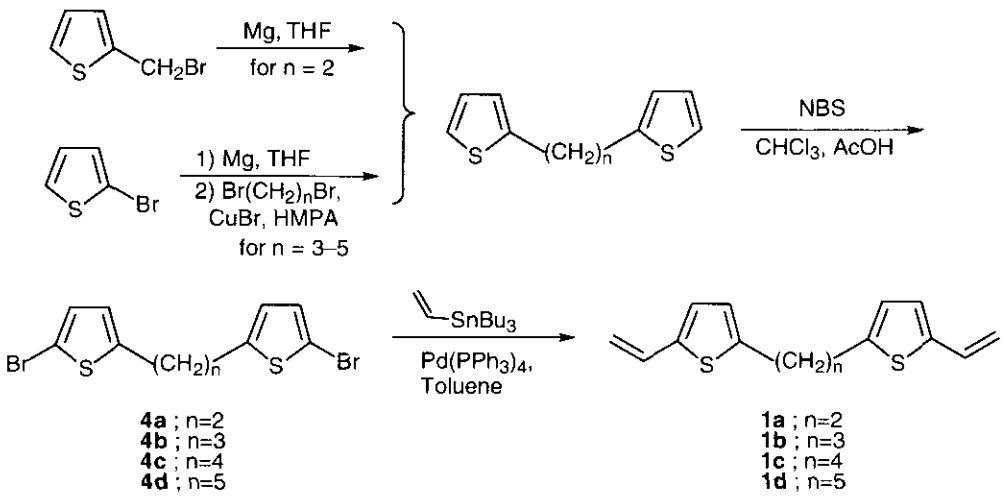
Institute for Fundamental Research of Organic Chemistry, Kyushu University, Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan[a] and Department of Chemistry, Gunma University, Tenjin-cho, Kiryu, Gunma 376-8515, Japan[b]

Abstract- [2.*n*](2,5)Thiophenophanes (*n* = 3–5) having a cyclobutane ring were successfully synthesized by the intramolecular [2 + 2] photocycloaddition of α,ω-bis(5-vinyl-2-thienyl)alkanes. The yields, conformation, and dynamic behavior of the thiophenophanes were significantly dependent on the oligomethylene chain length, *n*.

We have reported that the intramolecular [2 + 2] photocycloaddition of α,ω-bis(vinylphenyl)alkanes readily afforded [2.*n*]para- and metacyclophanes having a cyclobutane ring.[1] By this method, cyclophanes possessing various aromatic rings such as biphenyl, naphthalene, and phenanthrene have been also obtained efficiently.[1,2] However, it has not been examined whether this reaction is applicable to the synthesis of heterophanes, which are of interest from viewpoints of functional materials.[3] The synthesis, structure, and properties of [2.2]- and [3.3]heterophanes such as thiophenophanes and pyridinophanes have so far been investigated,[4,5] whereas those of [2.*n*]heterophanes (*n* ≥ 3) with different bridging length are hardly disclosed to the best of our knowledge. Thus, we were prompted to examine the photoreactions which are expected to afford [2.*n*]heterophanes. In fact, we have succeeded in the systematic synthesis of [2.*n*](2,5)thiophenophanes (*n* = 3–5) by the [2 + 2] photocycloaddition of α,ω-bis(5-vinyl-2-thienyl)alkanes. In this paper, we describe the characterization of thiophenophanes obtained and the bridging length dependence on their conformation.

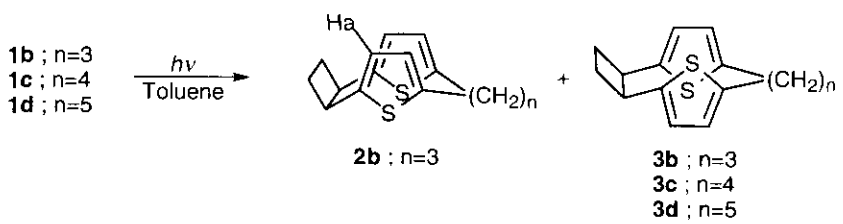
Scheme 1 depicts the synthetic sequence of α,ω-bis(5-vinyl-2-thienyl)alkanes (**1a–d**), which are the precursors of [2.*n*](2,5)thiophenophanes. 1,2-Di(2-thienyl)ethane was prepared from the homo-coupling reaction of thienylmethylmagnesium bromide by modifying the method in the literature.[6] The other α,ω-di(2-thienyl)alkanes (*n* = 3–5) were obtained from thienylmagnesium bromide and α,ω-dibromoalkane in the presence of CuBr and HMPA. The bromination of α,ω-di(2-thienyl)alkanes by NBS in chloroform and acetic acid[7] afforded the desired bromides (**4a–d**) without the substitution at other positions. Bromides

(**4a–d**) were allowed to react with tributylvinyltin in the presence of palladium catalysis,[8] readily giving vinylthiophene derivatives (**1a–d**). Since **1a–d** were rather unstable compounds, they were immediately used for the photoreaction.



Scheme 1.

The intramolecular [2 + 2] photocycloaddition of **1a–d** was carried out in toluene (*ca.* 2 mM) with a 400-W high-pressure mercury lamp through a Pyrex filter in a manner similar to that reported previously.[1,2] The reaction mixture was purified by column chromatography on silica gel and/or HPLC. The results of the photoreactions are summarized in Table 1 and Scheme 2.



Scheme 2.

Table 1. Results of Photoreactions of **1a–d**

Olefin	Irradiation time (h)	Conversion (%)	Product	Isolated yield (%)
1a	20	90	–[a]	–[a]
1b	5	78	**2b+3b**	2.5+1.5
1c	5	92	**3c**	30
1d	2	100	**3d**	34

a. No thiophenophanes were obtained.

The photoreaction of **1a** gave no thiophenophane in spite of the prolonged irradiation, only resulting in the formation of polymeric products. This result probably arises from the high strain of the cycloaddition product due to the short bridging length. On the other hand, the desired thiophenophanes were obtained

from **1b**–**d**, and the efficiency of photoreaction apparently increased with an increase in n, though the cases of $n > 5$ have not been investigated. Two rather unstable products (**2b**) and (**3b**) were obtained from **1b**, although the yields were extremely low (total 4%). The trimethylene linkage may not be long enough to bring the two vinyl groups closely in this case. Interestingly, each of **1c** and **1d** afforded a single product (**3c**) and (**3d**), respectively, in relatively high yields. No products with other conformation were detected at all in these cases.

The structures of thiophenophanes obtained were determined mainly by ^{1}H NMR spectroscopy. The ^{1}H NMR spectra of two thiophenophanes (**2b**) and (**3b**) obtained from **1b** were entirely different from each other. In **2b**, only two sets of aromatic proton peaks were observed, which were extremely high-field shifted compared to those of **1b** ($\Delta\delta$ = 0.6–0.8 ppm), and the two methine protons of the cyclobutane ring appeared as an equivalent peak. On the other hand, **3b** gave four nonequivalent aromatic protons, whose chemical shifts were quite similar to those of **1b**. The methine protons of the cyclobutane ring were observed as two nonequivalent peaks in contrast with **2b**. These results apparently indicate that **2b** and **3b** adopt *syn*- and *anti*-conformation, respectively, and both possess a *cis*-substituted cyclobutane ring, as illustrated in Scheme 2. The direction of the cyclobutane ring in **2b** was determined on the basis of NOESY experiment; NOE interaction was detected between the cyclobutane methylene protons and Ha protons of the thiophene rings.

Thiophenophane (**3c**) derived from **1c** gave a ^{1}H NMR spectrum quite similar to that of **3b**, obviously suggesting an *anti*-conformation. In the ^{1}H NMR spectrum of **3d** at room temperature, two sets of aromatic peaks and one methine peak were observed as in the case of **2b**. However, since the chemical shifts of these protons were almost comparable to those of precursor (**1d**), it is unlikely that **3d** adopts *syn*-conformation. The features in the NMR of **3d** may be associated with the flipping of the thiophene rings. Thus, the dynamic process of **3c** and **3d** was examined by variable-temperature ^{1}H NMR technique. Figure 1 illustrates the ^{1}H NMR spectra of **3d** in CD_2Cl_2 and **3c** in DMSO-d_6. As the temperature was lowered, the spectrum of **3d** exhibited broadening and, at -90 °C, became quite similar to those of **3b** and **3c** at room temperature; the aromatic proton peaks and the cyclobutane methine peak were split into four and two, respectively. These observations can be interpreted as follows. At room temperature, **3d** undergoes rapid conformational interconversion by the flipping of the thiophene rings. At -90 °C, the interconversion was highly depressed, and **3d** was frozen to the most stable *anti*-conformation where the two thiophene rings and two methine protons became nonequivalent. At room temperature, **3c** adopts an *anti*-geometry. As the temperature was raised, the two cyclobutane methine peaks and the four nonequivalent aromatic peaks were broadened and coalesced into one and two peaks, respectively, around 130 °C due to the rapid flipping of the thiophene rings, as in **3d** at room temperature. MM3 calculations supported these experimental results. In both [2.4]- and [2.5](2,5)thiophenophanes, the *anti*-isomer is predicted to be more stable than the *syn*-isomer by 3.8 and 1.4 kcal/mol, respectively, whereas both conformers are expected to have similar stabilities in [2.3]homologue.[9] On the basis of the coalescence temperatures (Tc) for the methine protons, the activation free energy ($\Delta G^{\ddagger}$) of the interconversion at Tc was calculated by the conventional method.[10] The $\Delta G^{\ddagger}$ values for **3c** and **3d** were determined as 19 and 10 kcal/mol, respectively,

at each Tc (130 °C for **3c** and -60 °C for **3d**). This remarkable difference is apparently ascribable to the difference in the oligomethylene chain length.

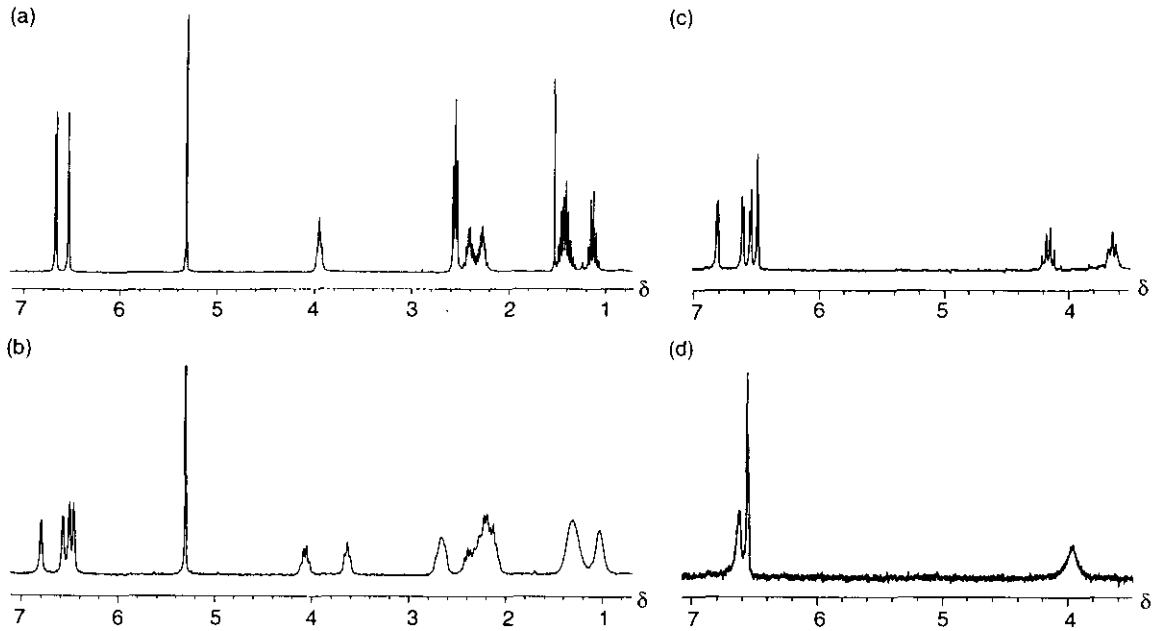


Figure 1. ^{1}H NMR spectra of **3d** in CD_2Cl_2 at (a) 25 °C and (b) –90 °C and **3c** in DMSO-d_6 at (c) 25 °C and (d) 160 °C.

In summary, a series of [2.*n*](2,5)thiophenophanes (*n* = 3–5) were successfully synthesized by the intramolecular [2 + 2] photocycloaddition of the corresponding vinylthiophene derivatives; both *syn*- and *anti*-isomers were obtained from **1b** (*n* = 3) and only *anti*-isomer from **1c** and **1d** (*n* = 4 and 5). The dynamic behavior of thiophenophanes (**3c**) and (**3d**) was remarkably dependent on the length of oligomethylene linkage. This reaction seems to be widely applicable to the synthesis of other heterophanes which are of interest from the viewpoints of photophysical properties and molecular recognition.

ACKNOWLEDGMENT

This work was financially supported by the Grant-in-Aid for Encouragement of Young Scientists from the Ministry of Education, Science, Sports, and Culture, Japan.

EXPERIMENTAL

NMR spectra were recorded on a Jeol EX-270 FT NMR spectrometer in $CDCl_3$ with TMS as an internal standard. FAB MS spectra were measured on a JEOL JMS-HX110A mass spectrometer. Melting points are not corrected. Toluene was distilled over sodium under a nitrogen atmosphere.

General procedure for the preparation of bromides (4a–d): A mixture of 1,3-di(2-thienyl)propane (2.43 g, 11.7 mmol) and *N*-bromosuccinimide (4.58 g, 25.7 mmol) in 40 mL of a 50:50 (v/v) mixture of

chloroform–acetic acid was stirred at 60 °C for 5 min. The reaction mixture was diluted with water and extracted with chloroform. The chloroform layer was washed once with 5% aqueous KOH aqueous solution and twice with water, dried over anhydrous magnesium sulfate, and evaporated. The residue was purified by column chromatography (SiO_2, hexane) to afford **4b** as a colorless oil (3.79 g, 89%).

4a: yield 36%; colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.85 (d, J= 3.5 Hz, 2H), 6.55 (d, J= 3.5 Hz, 2H), 3.07 (s, 4H).

4b: colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.85 (d, J = 3.8 Hz, 2H), 6.54 (d, J = 3.8 Hz, 2H), 2.79 (m, 4H), 1.97 (m, 2H).

4c: yield 70%; colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.84 (d, J= 3.6 Hz, 2H), 6.53 (d, J= 3.6 Hz, 2H), 2.76 (m, 4H), 1.69 (m, 4H).

4d: yield 70%; colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.85 (d, J = 3.6 Hz, 2H), 6.53 (d, J = 3.6 Hz, 2H), 2.75 (m, 4H), 1.67 (m, 4H), 1.42 (m, 2H).

General procedure for the preparation of vinyl compounds (1a–d): To a solution of bromide (**4b**) (3.79 g, 10.4 mmol) in toluene (208 mL) were added tributylvinyltin (9.89 g, 31.2 mmol), prepared from vinylmagnesium bromide and tributyltin chloride, tetrakis(triphenylphosphine)palladium (0) (1.20 g, 1.04 mmol), and a few crystals of 4-*t*-butylcatechol as a polymerization inhibitor. The resulting suspension was heated to reflux for 1 h, and cooled to rt. The toluene solution was treated with large excess of 20% aqueous potassium fluoride solution and stirred vigorously for 2 h, and filtrated. The aqueous phase was extracted with toluene three times, and the combined extracts were washed with water, dried over anhydrous magnesium sulfate, and evaporated. The residue was purified by column chromatography (SiO_2, hexane) to afford **1b** as a colorless oil (1.85 g, 68%).

1a: yield 48%; colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.76 (d, J = 3.3 Hz, 2H), 6.70 (dd, J = 11 and 18 Hz, 2H), 6.64 (d, J = 3.3 Hz, 2H), 5.45 (d, J = 18 Hz, 2H), 5.06 (d, J = 11 Hz, 2H), 3.12 (s, 4H); HRMS (FAB): calcd for $C_{14}H_{14}S_2$ (M^+) 246.0537; found 246.0530.

1b: colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.77 (d, J = 3.6 Hz, 2H), 6.73 (dd, J = 11 and 18 Hz, 2H), 6.64 (d, J = 3.6 Hz, 2H), 5.45 (d, J = 18 Hz, 2H), 5.05 (d, J = 11 Hz, 2H), 2.83 (m, 4H), 2.02 (m, 2H); HRMS (FAB): calcd for $C_{15}H_{16}S_2$ (M^+) 260.0694; found 260.0697.

1c: yield 61%; colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.74 (d, J = 3.3 Hz, 2H), 6.71 (dd, J = 11 and 17 Hz, 2H), 6.61 (d, J = 3.3 Hz, 2H), 5.42 (d, J = 17 Hz, 2H), 5.03 (d, J = 11 Hz, 2H), 2.78 (m, 4H), 1.72 (m, 4H); HRMS (FAB): calcd for $C_{16}H_{18}S_2$ (M^+) 274.0850; found 274.0860.

1d: yield 60%; colorless oil; ^{1}H NMR ($CDCl_3$): δ 6.76 (d, J = 3.5 Hz, 2H), 6.73 (dd, J = 11 and 17 Hz, 2H), 6.62 (d, J = 3.5 Hz, 2H), 5.44 (d, J = 17 Hz, 2H), 5.05 (d, J = 11 Hz, 2H), 2.77 (m, 4H), 1.70 (m, 4H), 1.45 (m, 2H); HRMS (FAB): calcd for $C_{17}H_{20}S_2$ (M^+) 288.1007; found 288.1006.

General procedure for the photoreactions of 1a–d: Photoirradiation of **1b** (260 mg, 1.0 mmol)

was carried out with a 400-W high-pressure mercury lamp through a Pyrex-filter in toluene (500 mL) under a nitrogen atmosphere for 5 h. Insoluble substance was filtered off and the filtrate was concentrated under reduced pressure. The resulting residue was purified by column chromatography (SiO_2, hexane) to give **2b** (6.5 mg, 2.5%) and **3b** (4.0 mg, 1.5%) as white solid.

2b: white solid; mp 83–84 °C (from hexane); ^{1}H NMR ($CDCl_3$): δ 6.16 (d, J = 3.4 Hz, 2H), 5.81 (d, J = 3.4 Hz, 2H), 4.47 (m, 2H, methine), 3.16 (m, 2H), 3.11 (m, 2H), 2.72 (m, 2H), 2.49 (m, 2H), 2.31 (m, 2H); HRMS (FAB): calcd for $C_{15}H_{16}S_2$ (M^+) 260.0694; found 260.0721.

3b: white solid; mp 112–113 °C (from hexane); ^{1}H NMR ($CDCl_3$): δ 6.78 (d, J = 3.3 Hz, 1H), 6.66 (d, J = 3.3 Hz, 1H), 6.58 (d, J = 3.3 Hz, 1H), 6.48 (d, J = 3.3 Hz, 1H), 4.24 (m, 1H, methine), 3.61 (m, 1H, methine), 3.02 (m, 2H), 2.68 (m, 2H), 2.56 (m, 1H), 2.20 (m, 5H); HRMS (FAB): calcd for $C_{15}H_{16}S_2$ (M^+) 260.0694; found 260.0717.

3c: yield 30%; white solid; mp 85–86 °C (from hexane); ^{1}H NMR ($CDCl_3$): δ 6.76 (d, J = 3.3 Hz, 1H), 6.58 (d, J = 3.3 Hz, 1H), 6.52 (d, J = 3.3 Hz, 1H), 6.47 (d, J = 3.3 Hz, 1H), 4.14 (m, 1H, methine), 3.72 (m, 1H, methine), 2.78 (m, 2H), 2.38 (m, 6H), 1.90 (m, 2H), 1.25 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 149.23, 147.79, 147.72, 145.81, 124.88, 124.48, 122.83, 122.18, 43.80, 40.91, 30.54, 30.47, 29.73, 29.61, 26.93, 22.09; HRMS (FAB): calcd for $C_{16}H_{18}S_2$ (M^+) 274.0850; found 274.0867.

3d: yield 34%; white solid; mp 54–55 °C (from hexane); ^{1}H NMR ($CDCl_3$): δ 6.69 (d, J = 3.3 Hz, 2H), 6.56 (d, J = 3.3 Hz, 2H), 3.98 (m, 2H, methine), 2.59 (m, 4H), 2.49 (m, 2H), 2.32 (m, 2H), 1.46 (m, 4H), 1.19 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 145.46, 144.46, 124.21, 123.99, 43.06, 32.67, 29.81, 25.77, 22.91; HRMS (FAB): calcd for $C_{17}H_{20}S_2$ (M^+) 288.1007; found 288.1004; Anal. Calcd for $C_{17}H_{20}S_2$: C, 70.78; H, 6.99; found C, 71.10; H, 7.11.

REFERENCES and NOTES

1. J. Nishimura, H. Doi, E. Ueda, A. Ohbayashi, and A. Oku, *J. Am. Chem. Soc.*, 1987, **109**, 5293; J. Nishimura, A. Ohbayashi, H. Doi, K. Nishimura, and A. Oku, *Chem. Ber.*, 1988, **121**, 2019.
2. J. Nishimura, M. Takeuchi, H. Takahashi, E. Ueda, Y. Matsuda, and A. Oku, *Bull. Chem. Soc. Jpn.*, 1989, **62**, 3161; M. Takeuchi and J. Nishimura, *Tetarhedron Lett.*, 1992, **33**, 5563.
3. P. M. Keehn and S. M. Rosenfeld, "Cyclophanes," Academic Press, New York, 1983; F. Vögtle, "Supramolecular Chemistry," Wiley, Chichester, 1991.
4. H. E. Winberg, F. S. Fawcett, W. E. Mochel, and C. W. Theobald, *J. Am. Chem. Soc.*, 1960, **82**, 1428; Y. Ito, S. Miyata, M. Nakatsuka, and T. Saegusa, *J. Org. Chem.*, 1981, **46**, 1043; W. Baker, K. M. Buggle, J. F. W. McOmie, and D. A. M. Watkins, *J. Chem. Soc.*, 1958, 3594; H. J. J.-B. Martel and M. Rasmussen, *Tetrahedron Lett.*, 1971, 3843; K.-J. Przybilla and F. Vögtle, *Chem. Ber.*, 1989, **122**, 347.
5. T. Shinmyozu, Y. Hirai, and T. Inazu, *J. Org. Chem.*, 1986, **51**, 1551.
6. F. F. Blicke and J. H. Burckhalter, *J. Am. Chem. Soc.*, 1942, **64**, 477.
7. R. M. Kellogg, A. P. Schaap, E. T. Harper, and H. Wynberg, *J. Org. Chem.*, 1968, **33**, 2902.

8. M. Kosugi, K. Sasazawa, Y. Shimizu, and T. Migita, *Chem. Lett.*, 1977, 301; D. R. McKean, G. Parrinello, A. F. Renaldo, and J. K. Stille, *J. Org. Chem.*, 1987, **52**, 422; A. M. Echavarrenand and J. K. Stille, *J. Am. Chem. Soc.*, 1987, **109**, 5478.

9. The computations were performed with MM3 program, graphically facilitated by CAChe® 3.1 from Sony/Tektronics Co. The program was developed by N. L. Allinger and coworkers, University of Georgia.

10. $\Delta G^{\ddagger} = 4.576Tc(10.32 + \log Tc - \log k_c)$, $k_c = \pi(\Delta\nu^2 + 6J^2)^{1/2}/2^{1/2}$, where $\Delta\nu$ and J denote the difference in frequency between the two methine protons and the coupling constant, respectively. A. J. Gordon and R. A. Ford, The Chemists Comapanion – A Handbook of Practical Data, Techniques, and References, Wiley-Interscience, New York, 1972, p. 136.

Received, 13th January, 1999