Pergamon

Tetrahedron Letters 40 (1999) 3749–3752

TETRAHEDRON
LETTERS

Homooxacalix[*n*]thiophenes: Their one-pot serial synthesis and X-ray structures

Naoki Komatsu,* Azusa Taniguchi, and Hitomi Suzuki

Department of Chemistry, Graduate School of Science, Kyoto University, Kitashirakawa, Sakyo-ku, Kyoto, 606-8224, Japan.

Received 29 October 1998; revised 18 March 1999; accepted 19 March 1999

Abstract

A series of homooxacalix[*n*]thiophenes ($\mathbf{1}_n$, n = 3~7) was prepared from 2,5-thiophenedimethanol in a one-pot way *via* acid-catalyzed dehydration under mild conditions. X-Ray crystallographic analysis revealed that homooxacalix[3]thiophene ($\mathbf{1}_3$) has helical chirality in the solid state.

Keywords: Thiophenes; Calixarenes; Crown ethers; X-Ray crystal structures

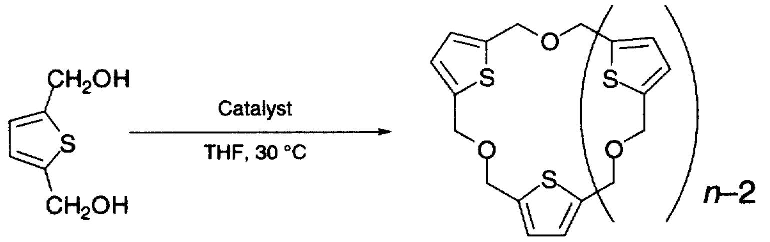
Homooxacalix[*n*]arenes represent the host molecules of current interest due to the dual characteristics of calixarenes and crown ethers. They exhibit specific affinity for alkali and alkaline-earth metal cations [1–3], ammonium ions [2–6], lanthanide ions [7,8], and buckminsterfullerene C_{60} [9,10]. Their heterocycle analogs, homooxacalix[3]furan [11,12] and -[*n*]pyridines (n = 2~4) [11,13,14], were prepared *via* a stepwise procedure by Cram about twenty years ago. However, oxacalix[*n*]thiophenes have not been prepared so far. In recent years, calix[*n*]thiophenes linked directly by sulfur [15,16], silicon [17,18] or phosphorus [18] have been prepared in 1–25 % yields, which prompt us to communicate our results as well. Herein, we report a one-pot preparation of a series of homooxacalix[*n*]thiophenes ($\mathbf{1}_n$, n = 3~7) *via* acid-catalyzed dehydration of 2,5-thiophenedimethanol. Furthermore, the solid state structures of $\mathbf{1}_3$ and $\mathbf{1}_4$ were elucidated by X-ray crystallography.

A typical experimental procedure is as follows: to a solution of 2,5-thiophenedimethanol (2.0 mmol) in dry THF (100 cm^3) was added trifluoromethanesulfonic acid (TfOH, 0.20 mmol) under an argon atmosphere. The mixture was magnetically stirred for 7 h at 30 °C, then quenched by the addition of several drops of dil. $NaHCO_3$ *aq.*, and concentrated to about 1/4 in volume. After the addition of dil. $NaHCO_3$ *aq.* (60 cm^3) to the concentrated mixture,

---

[*] E mail: komatsu@kuchem.kyoto-u.ac.jp

PII: S0040-4039(99)00600-0



$\mathbf{1}_n$ (n=3~7)

it was extracted with AcOEt (60 cm^3) three times. The combined extracts were concentrated and the residue was subjected to flash column chromatography on silica gel (hexane/AcOEt = 2/1) to give a mixture of homooxacalix[*n*]thiophenes, which were separated using GPC in the yields shown in Table 1. The isolated macrocycles were characterized by MALDI-TOF-MS spectra as well as by conventional analyses.[1]

A catalytic amount of Brønsted acid (TfOH) and/or Lewis acid such as Sn(OTf)$_2$ and Hf(OTf)$_4$ facilitated dehydration under mild conditions probably due to the π-electron-rich nature of the thiophene ring. This is in marked contrast to the preparation of homooxacalix[3]arene, where an excess amount of TfOH and high temperatures were required [19]. Although the isolated yields of $\mathbf{1}_n$ are not satisfactory at present,[2] a wide range of homooxacalix[*n*]thiophenes (n = 3~7) is directly obtainable in a one-pot procedure. The reaction time was optimized after the time-course plot of the yields of $\mathbf{1}_3$ and $\mathbf{1}_4$ under the conditions. Among several Lewis acids such as ZnCl$_2$, CeCl$_3$, and M(OTf)$_n$ (M = Ag, Hf, La, Sc, Yb) examined as catalyst or co-catalyst, Hf(OTf)$_4$ was found to improve the yields (run 3).

Table 1 One-pot preparation of homooxacalix[*n*]thiophenes ($\mathbf{1}_3$–$\mathbf{1}_7$).

Run	Catalyst (mol%)	Reaction time (h)	Yields (%)[a] $\mathbf{1}_3$	$\mathbf{1}_4$	$\mathbf{1}_5$	$\mathbf{1}_6$	$\mathbf{1}_7$	Total[b]
1	TfOH (10)	7	3.8	11.3	6.2	3.8	2.4	27.5
2	TfOH (5)/Sn(OTf)$_2$ (5)	6	8.1	8.0	4.8	1.9	0.8	23.6
3	Hf(OTf)$_4$ (10)	2	6.0	12.9	6.3	4.5	2.1	31.8

[a] Yields after GPC isolation. [b] Combined yields from $\mathbf{1}_3$ to $\mathbf{1}_7$.

---

[1] Selected data for $\mathbf{1}_n$: $\mathbf{1}_3$ white solid. ^{1}H NMR (200 MHz, CDCl$_3$) δ 4.73 (12H, s, CH$_2$), 6.77 (6H, s, ArH). ^{13}C NMR (50 MHz, CDCl$_3$) δ 66.9, 124.6, 143.0. MALDI–TOF–MS (pos) calcd for $C_{18}H_{18}O_3S_3$ 378.54. Found: 378.85 (M$^+$). Mp. 174–175 °C (from hexane/CH$_2$Cl$_2$) Anal. calcd for $C_{18}H_{18}O_3S_3$: C, 57.12; H, 4.79. Found: C, 56.89; H, 4.71; $\mathbf{1}_4$ white solid. ^{1}H NMR (200 MHz, CDCl$_3$) δ 4.69 (16H, s, CH$_2$), 6.86 (8H, s, ArH). ^{13}C NMR (50 MHz, CDCl$_3$) δ 66.5, 125.8, 141.8. MALDI–TOF–MS (pos) calcd for $C_{24}H_{24}O_4S_4Na$ 527.71. Found: 527.75 (M+Na$^+$). Mp. 162–164 °C (from hexane/CH$_2$Cl$_2$). Anal. calcd for $C_{24}H_{24}O_4S_4$: C, 57.12; H, 4.79. Found: C, 56.90; H, 4.78; $\mathbf{1}_5$ yellow oil. ^{1}H NMR (200 MHz, CDCl$_3$) δ 4.67 (20H, s, CH$_2$), 6.88 (10H, s, ArH). ^{13}C NMR (50 MHz, CDCl$_3$) δ 66.3, 126.2, 141.3. MALDI–TOF–MS (pos) calcd for $C_{30}H_{30}O_5S_5Na$ 653.88. Found: 653.30 (M+Na$^+$); $\mathbf{1}_6$ yellow oil. ^{1}H NMR (200 MHz, CDCl$_3$) δ 4.67 (24H, s, CH$_2$), 6.88 (12H, s, ArH). ^{13}C NMR (50 MHz, CDCl$_3$) δ 66.1, 126.3, 141.4. MALDI–TOF–MS (pos) calcd for $C_{36}H_{36}O_6S_6Na$ 780.06. Found: 779.67 (M+Na$^+$); $\mathbf{1}_7$ yellow oil. ^{1}H NMR (200 MHz, CDCl$_3$) δ 4.66 (28H, s, CH$_2$) 6.87 (14H, s, ArH). ^{13}C NMR (50 MHz, CDCl$_3$) δ 66.1, 126.3, 141.4. MALDI–TOF–MS (pos) calcd for $C_{42}H_{42}O_7S_7Na$ 906.24. Found: 906.17. (M+Na$^+$).

[2] The rest was considered to be linear and larger cyclic polyethers from the ^{1}H-NMR spectrum of the crude product.

The structures of compounds **1**$_3$ and **1**$_4$ were elucidated by X-ray crystallographic analyses and shown in Figure 1.[3]

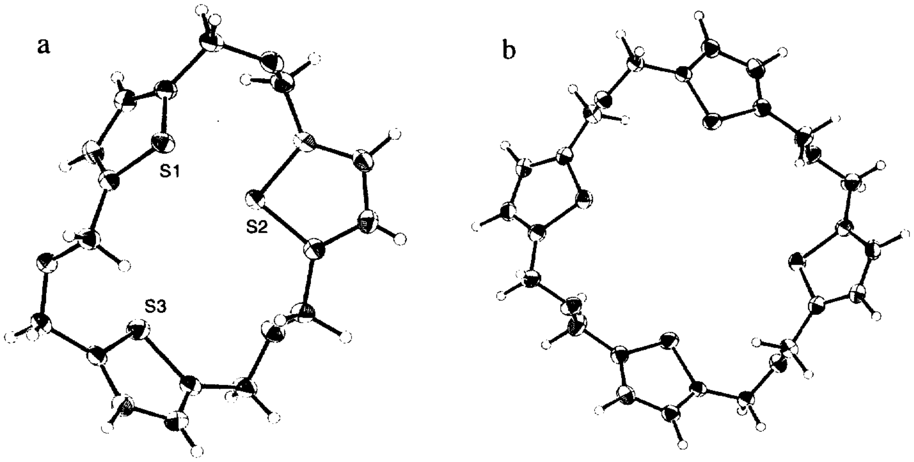


Figure 1. ORTEP drawings of **1**$_3$(a) and **1**$_4$ (b).

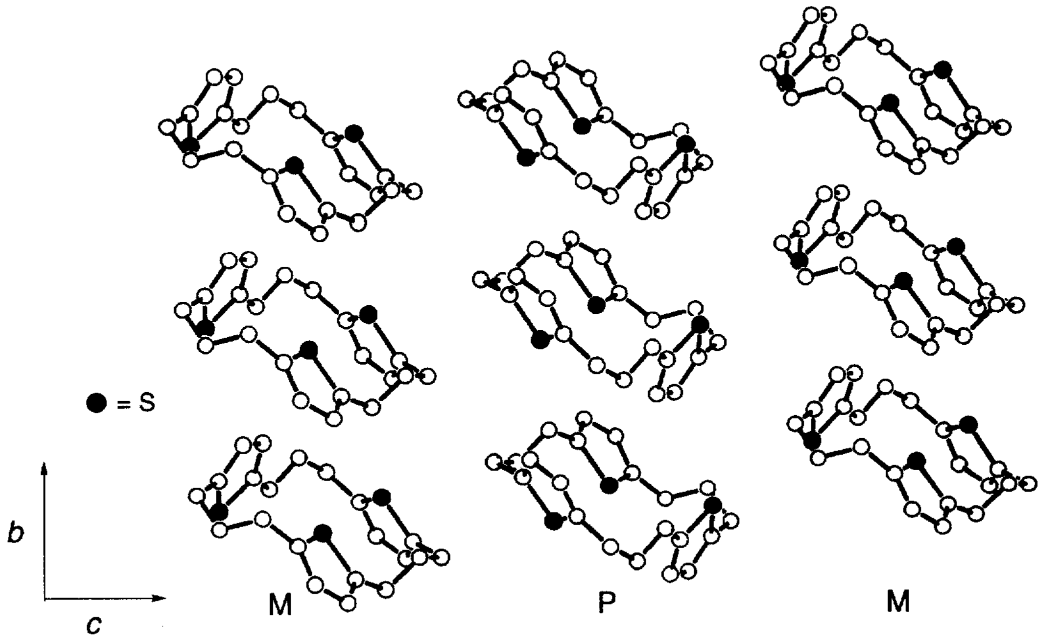


Figure 2. Molecular packing of **1**$_3$.

---

[3] Crystal data for **1**$_3$: $C_{18}H_{18}O_3S_3$, M = 378.54, monoclinic, *P2$_1$/n* (#14), *a* = 15.182(2), *b* = 5.774(2), *c* = 20.126(2) Å, β = 102.570(8)°, V = 1722.1(7) Å^3, Z = 4, prismatic, colorless, 0.24 × 0.06 × 0.24, ($Cu_{K\alpha}$) = 1.54178, of 2868 reflections collected, 2084 was taken as observed (I>3.0σ(I)). 272 parameters, R = 0.034, Rw = 0.053, GOF = 1.29. For **1**$_4$: $C_{24}H_{24}O_4S_4$, M = 504.72, monoclinic, *P2$_1$/a* (#14), *a* = 9.0613(8), *b* = 11.940(2), *c* = 11.2007(9) Å, β = 98.069(7)°, V = 1199.8(2) Å^3, Z = 2, prismatic, colorless, 0.20 × 0.20 × 0.10, ($Cu_{K\alpha}$) = 1.54178, of 1893 reflections collected, 1544 was taken as observed (I>3.0s(I)). 146 parameters, R = 0.037, Rw = 0.067, GOF = 1.49.

The ORTEP drawings (Figure 1) revealed that $\mathbf{1}_3$ has helical chirality, while $\mathbf{1}_4$ adopts a 1,2-alternate conformation in the solid state. Three thiophene rings of $\mathbf{1}_3$ make different dihedral angles to the plane defined by three oxygen atoms; 89.21, 29.03 and -58.10°, enforcing three sulfur atoms S1, S2 and S3 to point into the cavity in a helical manner, as shown in Figure 1a, where the *P* configuration is observed. In addition, the packing view of $\mathbf{1}_3$ (Figure 2) shows that the columns stacked along the *b* axis are constructed with either enantiomers, *M* or *P*, while each column along the *c* direction has the helix structure of alternately opposite sense. Although omitted from Figure 2 for clarity, every column along the *a* axis occupies the same configuration.

As for the functionality, a few homooxacalix[*n*]thiophenes were found to have inclusion ability for ammonium and pyridinium cations by ^{1}H-NMR and/or extraction experiments [12,13,20].

We are now making efforts to improve the yield of homooxacalix[*n*]thiophenes and thus elaborated conditions will be used for the preparation of homooxacalix[*n*]furans and -[*n*]pyrroles in future.

Acknowledgement: The present work was supported by a Grant-in-Aid for Scientific Research (No. 09750948) from the Ministry of Education, Science, Sports and Culture of Japan.

References

[1] Matsumoto H, Nishio S, Takeshita M, Shinkai S. Tetrahedron 1995;51:4647-4654.

[2] Araki K, Hashimoto N, Otsuka H, Shinkai S. J. Org. Chem. 1993;58:5958-5963.

[3] Araki K, Inada K, Otsuka H, Shinkai S. Tetrahedron 1993;49:9465-9478.

[4] Araki K, Inada K, Shinkai S. Angew. Chem. Int. Ed. Engl. 1996;35:72-74.

[5] Takeshita M, Inokuchi F, Shinkai S. Tetrahedron Lett. 1995;36:3341-3344 and references cited therein.

[6] Masci B. Tetrahedron 1995;51:5459-5464.

[7] Daitch CE, Hampton PD, Duesler EN, Alam TM. J. Am. Chem. Soc. 1996;118:7769-7773.

[8] Arnaud-Neu F. Chem. Soc. Rev. 1994:235-241.

[9] Ikeda A, Yoshimura M, Shinkai S. Tetrahedron Lett. 1997;38:2107-2110.

[10] Tsubaki K, Tanaka K, Kinoshita T, Fuji K. Chem. Commun. 1998:895-896.

[11] Cram DJ, Cram JM. Acc. Chem. Res. 1978;11:8-14.

[12] Timko JM, Moore SS, Walba DM, Hiberty PC, Cram DJ. J. Am. Chem. Soc. 1977;99:4207-4219.

[13] Newcomb M, Timko JM, Walba DM, Cram DJ. J. Am. Chem. Soc. 1977;99:6392-6398.

[14] Newcomb M, Gokel GW, Cram DJ. J. Am. Chem. Soc. 1974;96:6810-6811.

[15] Nakayama J, Katano N, Sugihara Y, Ishii A. Chem. Lett. 1997:897-898.

[16] König B, Rödel M, Dix I, Jones PG. J. Chem. Res. (M) 1997:555-563.

[17] König B, Rödel M, Bubenitschek P, Jones PG. Angew. Chem. Int. Ed. Engl. 1995;34:661-662.

[18] König B, Rödel M, Budenitschek P, Jones PG, Thondorf I. J. Org. Chem. 1995;60:7406-7410.

[19] Hampton PD, Bencze Z, Tong W, Daitch CE. J. Org. Chem. 1994;59:4838-4843.

[20] Araki K, Hisaichi K, Kanai T, Shinkai S. Chem. Lett. 1995;569-570.