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5-ARYLIDENETETRONATE AS A VERSATILE ELECTROPHORE FOR PI-EXTENDED ELECTRON ACCEPTORS

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Dedicated to Prof. Dr. Yasuyuki Kita on the occasion of his 77th Birthday

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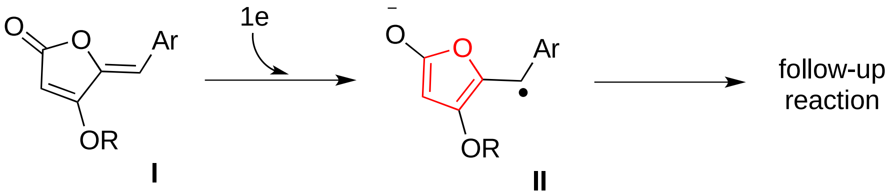
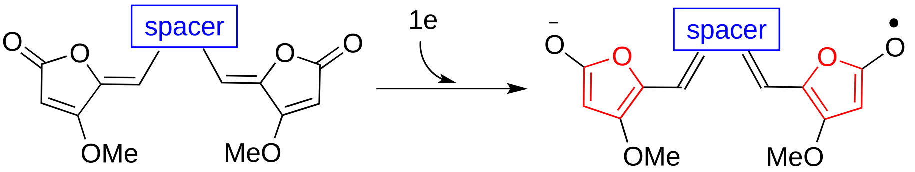
Abstract – Bis[4-methoxy-5-methylenefuran-2(5*H*)-one]-type electron acceptors with anthracene-9,10-diyl and thiophene-2,5-diyl spacer were prepared by one-pot condensation of methyl tetronate with the corresponding dialdehydes. They undergo reversible electrochemical reduction, thus showing the potential utility of 5-arylidenetetronate as an electrophore for developing novel electron acceptors.

5-Ylidenetetronic acid [4-hydroxy-5-methylenefuran-2(5*H*)-one] derivatives are attracting considerable recent attention from the viewpoint of potential chemotherapeutic agents with displaying interesting biochemical acitivity.[1,2] During our synthetic studies[3] on a series of 5-arylidenetetronate compounds (**I**), we have got interested in the redox reaction of them since they would undergo one-electron reduction to the corresponding anion radicals (**II**), which is facilitated by formation of aromatic furan ring (Scheme 1).



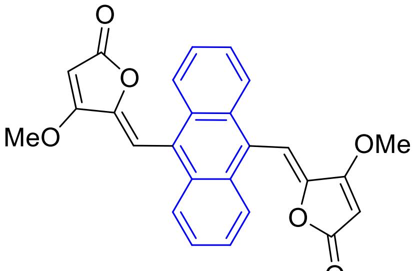
Scheme 1



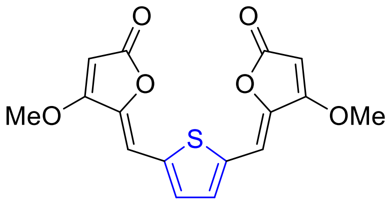
III

Scheme 2

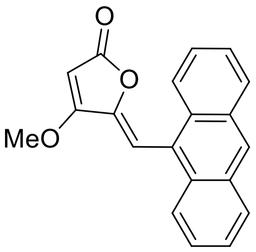
By combination with the molecular design that stabilizes the resulting anionic species, we envisaged that 5-arylidenetetronate could be used as a versatile redox-active chromophore (electrophore) to develop novel electron acceptors undergoing reversible electrochemical reduction. Since the dimerization of **II** at the ylidene carbon would be the main decomposition path, we designed here the bis(tetronic) molecules (**III**), in which the charge and spin can be delocalized over the two electrophores. Pi-extended structure is also favored to stabilize the charged species, and thus a certain pi-spacer is inserted between them (Scheme 2). Here we report preparation and redox properties of bis[4-methoxy-5-methylenefuran-2(5*H*)-one]s (**1a** and **1b**), in which anthracene-9,10-diyl or thiophene-2,5-diyl is used as a spacer, respectively.



1a



1b



2a

Acceptors **1a**[4] and **1b**[4] were prepared in respective yields of 43% and 23% through condensation of methyl tetronate with the corresponding dialdehyde by using DBU in MeCN.[5] They were isolated as stable yellow-orange crystalline solids. As a reference, 9-anthrylmethylidene compound **2a**[4] with only one tetronate unit was also prepared in 30% yield. Although the yields are not high, this one-pot procedure[3b] is more convenient than the multistep protocol starting with 2-lithiated tetronate.[6] In terms of the stereochemistry of the newly formed double bond, *Z*-configuration is assumed based on the results in the previous studies,[3] in which the endocyclic oxygen atom of the furanone ring is facing to the aryl group. The configuration of the double bond in **1b** and **2a** was finally confirmed to be *Z*,*Z* and *Z* by the X-ray analyses (Figures 1, S1 and S2).[7,8]

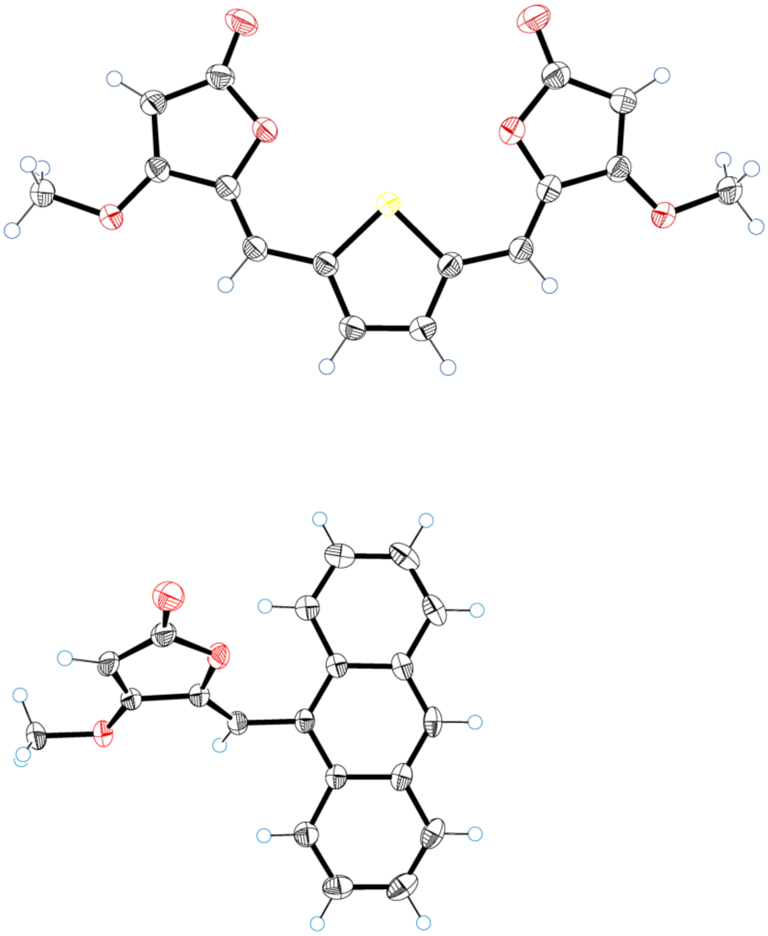


Figure 1. ORTEP drawings of **1b** (upper) and **2a** (lower) obtained by X-ray analyses at 150 K

According to the density functional theory (DFT) calculation [B3LYP/6-31G(d,p)] of the thiophenediyl derivative **1b**, *E,E*-isomer is higher in energy by about 10 kcal mol^{-1} than *Z,Z*-isomer (Table S1).[8] The *Z,Z*-isomer can adopt two conformations that can be interconverted by rotation of the thiophene ring. The more stable geometry is *Z,Z-anti*-form, exhibiting short C-H -- O contacts (2.41 Å) between H of the thiophene ring and the endocyclic O of the tetronate unit which can be assigned as weak hydrogen bonds.[9] The *Z,Z-syn*-form was actually found in the crystal of **1b**, which is higher in energy only by 0.31 kcal mol^{-1}. Both forms would coexist in solution. The HOMO and LUMO for both of *Z,Z-anti*- and *Z,Z-syn*-**1b** are similar to each other (Figure S3),[8] and coefficients are distributed over the thiophene ring as well as tetronate rings, as expected for the pi-extended acceptors. In contrast to the nearly planar geometry of **1b** in crystal, the tetronate unit and the anthracene unit cannot be located on the same plane in **2a** due to the steric repulsion. The dihedral angle of 53.3° can afford partial conjugation between the two units, which would hold true for bis(tetronate) **1a**.

By considering their low solubility in other solvents, the voltammetric studies on the newly prepared acceptors were conducted in DMSO (Figure 2). The reference compound **2a** with only one tetronate unit undergoes electrochemical reduction at the peak potential of –1.94 V *vs* Ag/Ag$^+$. Irreversibility of this process suggests that the **2a**$^{-\bullet}$ is unstable and undergoes some follow-up reaction(s) (Scheme 1). In contrast, bis(tetronate) **1a** undergoes reversible reduction at the peak potential of –1.73 V, and the less negative value by ca. 0.2 V comes from the interaction between two electrophores through the anthracene-9,10-diyl spacer. The peak current is twice as large as that for **2a**, showing that **1a** undergoes one-wave two-electron reduction. The similar two-electron process[10] has been reported for the dichromophoric redox systems with the anthracene-9,10-diyl spacer.[11] The slight anodic shift of the reoxidation peak (–1.34 V) results from the non-planar twisted geometry of **1a** as well as butterfly-shaped geometry of **1a**$^{2-}$. Such separation of redox peaks is often accompanied by the drastic geometrical change upon electron transfer in the anthracene-9,10-diyl/9,10-anthraquinodimethane skeleton[12] (Scheme 3).

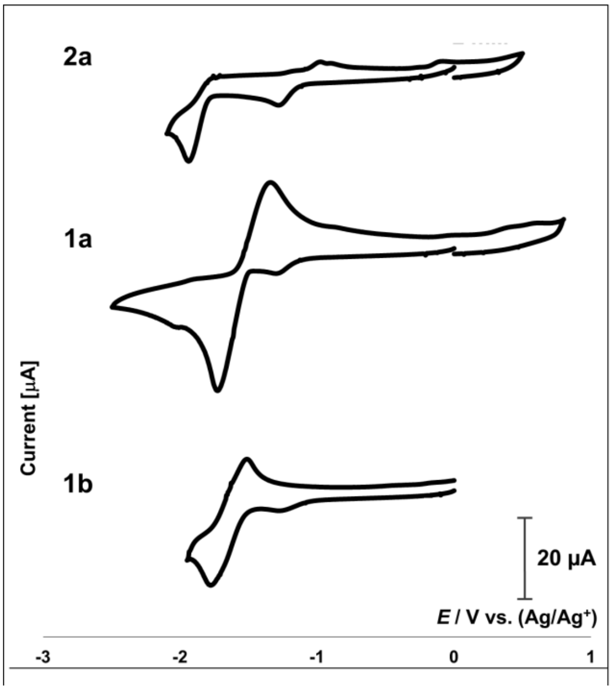
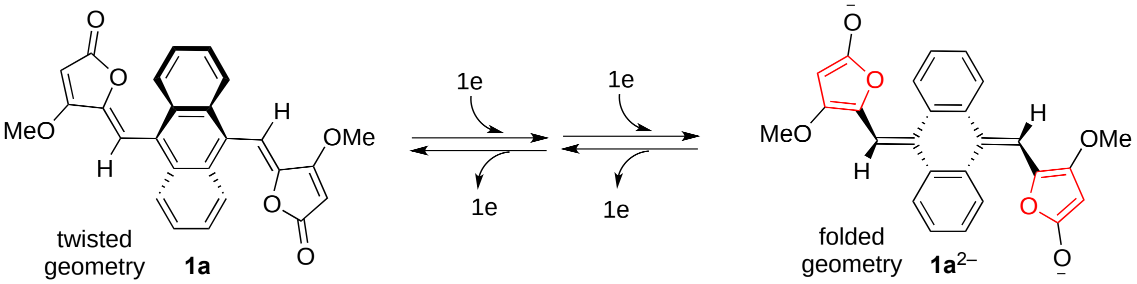
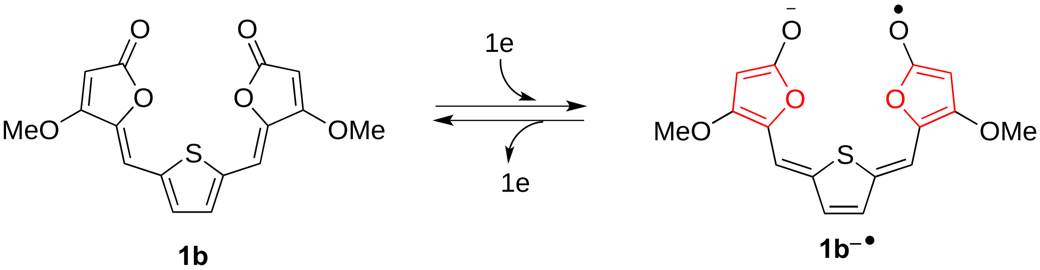


Figure 2. Cyclic voltammograms of **2a**, **1a**, and **1b** (2 mM) in DMSO containing 0.1 M Bu_4NPF_6 as a supporting electrolyte (scan rate 100 mV s^{-1}, glassy carbon electrode). The small cathodic peak around –1.3 V corresponds to the reduction process of O_2.

On the other hand, **1b** with a thiophene spacer undergoes reversible one-electron reduction at –1.66 V. Thus, negative charge and spin can be delocalized over the two tetronate units for **1b**$^{-\bullet}$ as shown in Scheme 4 thanks to coplanarity of the thiophene spacer and the tetronate units. Similar delocalization of charge and spin has been observed in other dichromophoric electron donors with the thiophene spacer.[13]



Scheme 3



Scheme 4

This work has revealed that methyl tetronate is a versatile electrophore to construct pi-extended electron acceptors. By connecting two units with a proper spacer such as anthracene-9,10-diyl or thiophene-2,5-diyl, the newly constructed acceptors undergo reversible electrochemical reduction. Further studies toward the molecular response systems based on bis(tetronate)s are now in progress.

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SUPPORTING INFORMATION

Supplementary data (X-ray, DFT calculation) associated with this article can be found, in the online version, at URL: https://wwwheterocycles.jp/newlibrary/downloads/PDFsi/26318/103/1.

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4. Data of new compounds are as follows. **1a**: mp > 300 °C; ^{1}H NMR (DMSO-d_6): δ/ppm 8.08 (4H, dd, J = 6.8 Hz, 3.3 Hz), 7.60 (4H, dd, J = 6.8 Hz, 3.3 Hz), 7.27 (2H, s), 5.89 (2H, s), 4.15 (6H, s); ^{13}C NMR (DMSO-d_6): δ/ppm 170.36 (2C), 168.19 (2C), 145.46 (2C), 129.21 (4C), 127.62 (2C), 126.75 (4C), 126.71 (4C), 103.91 (2C), 90.56 (2C), 60.71 (2C); HRMS (ESI$^+$): Calcd for $C_{26}H_{19}O_6$ $(M + H)^+$ 427.1176. Found 427.1175. **1b**: mp 153-160 °C (decomp.); ^{1}H NMR ($CDCl_3$): δ/ppm 7.41 (2H, s), 6.40 (2H, s), 5.29 (2H, s), 3.98 (6H, s); ^{13}C NMR ($CDCl_3$): δ/ppm 170.36 (2C), 167.79 (2C), 141.55 (2C), 138.95 (2C), 131.58 (2C), 101.09 (2C), 88.78 (2C), 59.33 (2C); HRMS (ESI$^+$): Calcd for $C_{16}H_{13}O_6S$ $(M + H)^+$ 333.0427. Found 333.0429. **2a**: mp 166-170 °C (decomp.); ^{1}H NMR ($CDCl_3$): δ/ppm 8.48 (1H, s), 8.03 (4H, m), 7.49 (4H, m), 7.16 (1H, s), 5.37 (1H, s), 4.11 (3H, s); ^{13}C NMR ($CDCl_3$): δ/ppm 169.90 (1C), 168.12 (1C), 144.76 (1C), 131.30 (2C), 129.83 (2C), 128.84 (2C), 128.35 (1C), 126.17 (2C), 125.74 (2C), 125.32 (1C), 125.31 (2C), 104.65 (1C), 89.48 (1C), 59.45 (1C); MS (ESI$^+$, relative intensity): 303 [BP, $(M + H)^+$], 325 [85, $(M + Na)^+$].
5. Experimental procedure: To a solution of methyl tetronate (322 mg, 2.80 mmol) and anthracene-9,10-dialdehyde (394 mg, 1.68 mmol) in MeCN (14 mL) was added DBU (0.84 mL, 5.6 mmol) under Ar atmosphere, and the mixture was heated at 65 °C for 18 h. After cooling, yellow precipitates were filtered and washed with MeCN and $CHCl_3$ to give pure **1a** (258 mg, y. 43%). By the similar procedure, **1b** and **2a** were also prepared, and the crude products were purified by SiO_2 column chromatography.
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7. Crystal data deposition numbers: **1b**, CCDC1982516; **2a**, CCDC1982517.
8. Supplementary Materials are available: Figures S1 and S2 showing details of X-ray analyses; Table S1 showing the energies and MO levels for various geometries and stereoisomers of **1b**; Figure S3 showing HOMOs and LUMOs of *Z,Z-anti*-**1b** and *Z,Z-syn*-**1b**.
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