HETEROCYCLES, Vol. 96, No. 7, 2018, pp. 1259 - 1265. © 2018 The Japan Institute of Heterocyclic Chemistry
Received, 26th April, 2018, Accepted, 8th June, 2018, Published online, 12th June, 2018
DOI: 10.3987/COM-18-13912

SYNTHESIS AND ELECTROCHEMICAL PROPERTIES OF 2,2'-BIGUAIAZULENE-BASED 1,2-DITHIIN AND THIOPHENE

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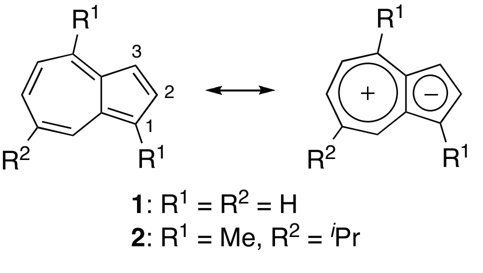
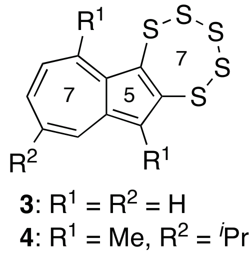
Abstract – The synthesis of diguaiazuleno[3,2-*c*:2',3'-*e*][1,2]dithiin was achieved by the reaction of 2,2'-biguaiazulene with disulfur dichloride/imidazole as a sulfuration reagent. Thermolysis of the dithiin afforded the corresponding desulfurized compound, diguaiazuleno[3,2-*b*:2',3'-*d*]thiophene. Cyclic voltammetry of the *S*-heterocycles showed one reversible wave at the reduction region, respectively.

Azulenes such as azulene (**1**) and guaiazulene (**2**) are one of the most interesting classes of non-benzenoid aromatics.[1] Particularly, electrochemical properties arising from their polarized structures attracted much attention. As for the azulene-based electron acceptors, 2,4,6,8-tetracyanoazulene,[2] azulenequinones[3] and tetracyanoazulenequinodimethanes[4] had been investigated. In the field of the electron donors, a few azulenes with tetrathiafulvalene moieties were reported.[5,6] Azulenes with sulfur groups[7,8] would be a precursor of functional electrochemicals, and we have already reported 7-5-7 ring condensed *S*-heterocycles, azulenopentathiepin (**3**)[8a] and its guaiazulene derivative (**4**).[8b]



1: $R^1 = R^2 = H$
2: $R^1 = Me, R^2 = {}^iPr$

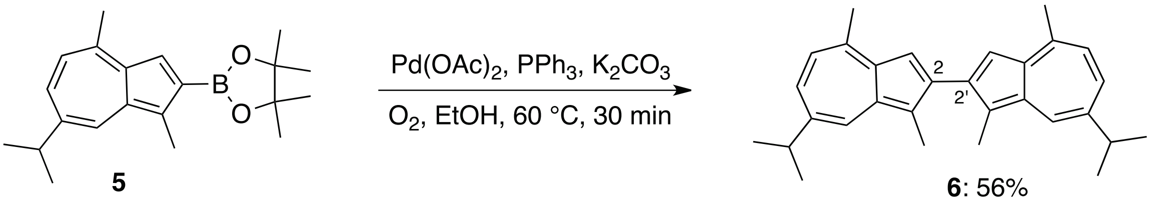


3: $R^1 = R^2 = H$
4: $R^1 = Me, R^2 = {}^iPr$

This paper is dedicated to Professor Kiyoshi Tomioka on the occasion of the 70th birthday.

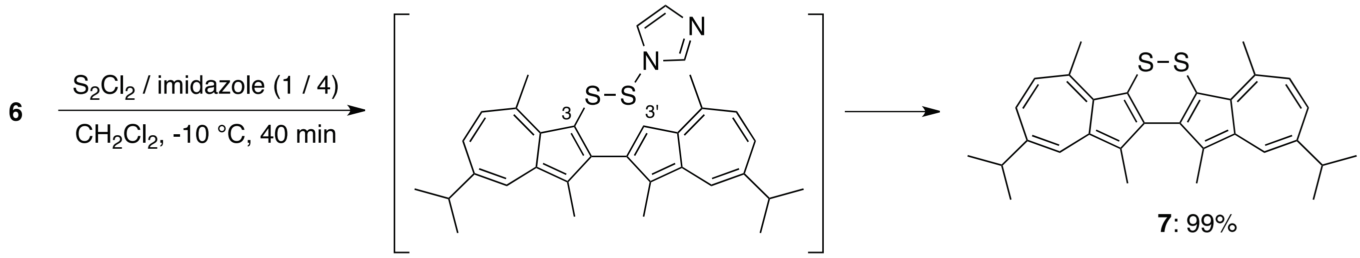
We next focused on introducing sulfur atom(s) into a framework of dimeric azulenes. Guaiazulene (**2**) is a low cost azulene derivative, and the alkyl substituents will cause restriction of reaction points.[9] Therefore, 2,2'-biguaiazulene (**6**), which is a dimer of **2** at the 2-position, could be a key compound for construction of *S*-heterocycles fused with two guaiazulene moieties. The interaction between the guaiazulene parts in redox behavior, arising from contribution of polarized structures, is of interest. We report herein the synthesis and electrochemical properties of novel skeletal *S*-heterocycles, diguaiazuleno[1,2]dithiin (**7**) and diguaiazulenothiophene (**8**).

While 2,2'-biguaiazulene (**6**) had been obtained by the reaction of 2-guaiazulenesulfonic acid with sulfuric acid in low yield,[10] efficient synthetic methods of biguaiazulenes have not been reported yet. As for the preparation of biaryls, widespread palladium catalyzed homo-coupling reaction with arylboronic acids was reported.[11] We would apply this method to prepare **6**, and chose 2-Bpin-guaiazulene (**5**, Bpin = 4,4,5,5-tetrametyl-1,3,2-dioxaborolan-2-yl)[9e,f] as a starting material. A substrate (**5**), prepared from **2** and B_2pin_2 with an iridium catalyst,[9f] was reacted with a mixture of palladium(II) acetate, triphenylphosphine and potassium carbonate in ethanol at 60 °C for 30 min under O_2 atmosphere (Scheme 1). The reaction mixture was purified by SiO_2 column chromatography to give **6** in 56% yield. The yield decreased in the case without O_2 as a reoxidant (6% yield).



Scheme 1

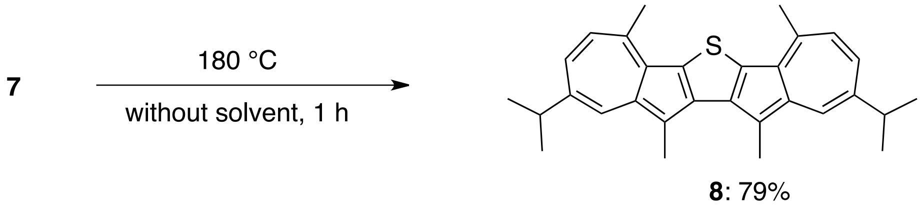
It is well known the 3-position of guaiazulene (**2**) has high reactivity towards electrophiles.[9c,d,g] Therefore, we expected that the 2,2'-dimer (**6**) should react with *S*-electrophiles at the 3-position to generate 3-*S*-substituted compounds (such as an intermediate in Scheme 2), which would cyclize at the 3'-position to give *S*-heterocycles with a 2,2'-biguaiazulene framework. We have already found that disulfur dichloride/imidazole were the reactive and efficient *S*-electrophiles in the course of preparation of guaiazulenopentathiepin (**4**).[8b] In refer to the results, **6** was treated with a mixture of disulfur dichloride and imidazole (1 / 4 molar ratio) in CH_2Cl_2 for 40 min at -10 °C. The reaction mixture was purified by SiO_2 column chromatography and recrystallization to afford diguaiazuleno[3,2-*c*:2',3'-*e*][1,2]dithiin (**7**) in almost quantitative yield, which has an interesting 7-5-6-5-7 ring condensed system, as expected.



Scheme 2

Diguaiazulenodithiin (**7**) was dark green crystals [mp 184-185 °C (dec.)]. The ^{1}H NMR spectrum showed three kinds of protons at δ 6.91 (2H), 7.30 (2H) and 8.19 (2H) with appropriate coupling constants (J = 10.4 and 2.0 Hz) as seven-membered ring moieties. The protons of the alkyl groups were observed at δ 1.36 (6H, ^{i}Pr), 1.37 (6H, ^{i}Pr), 2.63 (6H, Me), 3.04 (2H, ^{i}Pr) and 3.14 (6H, Me). Two doublet signals (δ 1.36 and 1.37) are due to diastereotopic methyl groups of *i*-propyl caused by the non-planarity of a 1,2-dithiin skeleton. The ^{13}C NMR spectrum showed fifteen kinds of carbons (two signals of diastereotopic methyl groups of *i*-propyl: δ 24.5 and 24.6). The longest wave-maximum of UV-VIS spectrum in CH_2Cl_2 appeared at 677 nm as a characteristic peak of azulene derivatives. The MS spectra gave molecular ion and fragment ion peaks [MALDI-TOF: *m/z* 456 (M^+), 424 (M^+-S)]. Together with the result of elemental analysis, those spectral data supported the proposed structure.

The dithiin (**7**) changed in color from dark green to ocher while the melting point was measuring. These phenomena should be caused by the thermolysis. Thereupon, **7** was heated at 180 °C for 1 h without solvent, and the residue was purified by recrystallization. Consequently, the desulfurization occurred to give 7-5-5-5-7 ring condensed diguaiazuleno[3,2-*b*:2’,3’-*d*]thiophene (**8**) in 79% yield (Scheme 3).



Scheme 3

Diguaiazulenothiophene (**8**, ocher solid, mp 202-203 °C) showed ^{1}H NMR peaks of seven-membered ring moieties at δ 7.11 (2H), 7.39 (2H) and 8.35 (2H) in $CDCl_3$. The protons of the alkyl groups were observed at δ 1.41 (12H, ^{i}Pr), 3.13 (6H, Me), 3.13 (2H, ^{i}Pr) and 3.23 (6H, Me), and the simple pattern was arising from the symmetrical and planar structure of **8**. The ^{13}C NMR spectrum in $CDCl_3$ showed thirteen kinds of carbons (carbons at δ 142.6 were overlapped), while in C_6D_6 appeared fourteen ones. The longest wave-maximum of UV-VIS spectrum (595 nm) was blue-shifted as compared with the dithiin (**7**).

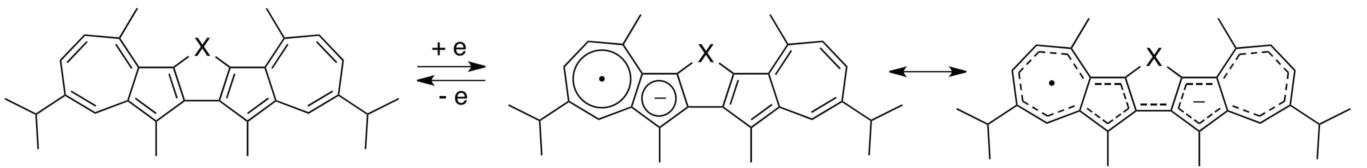
Together with the results of MS spectra [MALDI-TOF: *m/z* 424 (M^+)] and elemental analysis, physical data of **8** were consistent with the proposed structure.

In order to survey the electrochemical properties of diguaiazuleno[1,2]dithiin (**7**), diguaiazulenothiophene (**8**) and 2,2'-biguaiazulene (**6**), their cyclic voltammetry (CV) was measured (Table 1). All compounds showed one reversible wave at the reduction region [$(E_1^{red})_{1/2}$/V: **7**; -1.52, **8**; -1.76, **6**; -1.91] and one or three irreversible waves at the oxidation region (E_1^{ox}, E_2^{ox}, E_3^{ox}). In the reversible waves, the resulting radical anions (**9a**) were relatively stable as an electrochemical species caused by contribution of the delocalized resonance structures (**9b**) as shown in Scheme 4. That is, existence of the interaction between two guaiazulene parts in a 2,2'-biguaiazulene framework should be revealed. In view of electron donating ability, **8** showed considerable high ability than **6** and **7** under the influence of the thiophene ring [$(E_1^{ox})_{pa}$/V: **8**; +0.08, **6**; +0.36, **7**; +0.44].

Table 1. Redox potentials (E/V)[a] of diguaiazuleno[1,2]dithiin (**7**), diguaiazulenothiophene (**8**) and 2,2'-biguaiazulene (**6**)

Compound	$(E_1^{red})_{pc}$[b]	$(E_1^{red})_{1/2}$[c]	$(E_1^{red})_{pa}$[d]	$(E_1^{ox})_{pa}$[e]	$(E_2^{ox})_{pa}$[e]	$(E_3^{ox})_{pa}$[e]
1,2-dithiin **7**	-1.68	-1.52	-1.35	+0.44	-	-
thiophene **8**	-1.79	-1.76	-1.72	+0.08	+0.56	+0.97
2,2'-biguaiazulene **6**	-1.93	-1.91	-1.88	+0.36	-	-

[a] Obtained by cyclic voltammetry: V *vs.* Ag/Ag^+, 10^{-3} M in DMF with 0.1 M Bu_4NClO_4, 100 mV/s. [b] Reduction potentials by the cathodic peak. [c] Half-wave reduction potentials. [d] Reduction potentials by the anodic peak. [e] Oxidation potentials by the anodic peak.



6: X = H, H
7: X = SS
8: X = S

9a

9b

Scheme 4

In conclusion, we have succeeded in the preparation of novel 2,2'-biguaiazulene-based 1,2-dithiin (**7**) and thiophene (**8**), and evaluated their electrochemical properties. Further work aimed at chemical reactions of **7** and **8** (oxidation, reduction and so on) is now under investigation and will appear elsewhere.

EXPERIMENTAL

Mps were determined with a Laboratory Devices MEL-TEMP apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra ($SiMe_4$ as the internal standard) were obtained with Bruker AV500, AV500T, AV400 and/or AV300 spectrometers. Electronic spectra (UV-VIS) were obtained with a JASCO V-560 spectrophotometer. MS spectra were obtained with a Bruker AutoflexIII spectrometer. CV was obtained with an ALS-600 electrochemical measuring apparatus. Unless otherwise stated the spectra were taken in the following solvents/media: UV-VIS, CH_2Cl_2; ^{1}H and ^{13}C NMR, $CDCl_3$ and C_6D_6; MS spectra were taken at MALDI-TOF method; CV, V *vs*. Ag/Ag$^+$, GC, Pt wire, 0.1 M Bu_4NClO_4 in DMF. The progress of reactions was followed by TLC method using Merck Silica gel 60F$_{254}$.

Preparation of 2,2'-biguaiazulene (6): A mixture of **5**^{9e,f} (74 mg, 2.3 x 10^{-1} mmol), palladium(II) acetate (2.6 mg, 5.1 mol%), triphenylphosphine (6.0 mg, 10 mol%) and potassium carbonate (80 mg, 2.5 mol *eq*.) in EtOH (2.3 mL) was reacted at 60 °C for 30 min under O_2 atmosphere. After removal of the solvent *in vacuo* at rt, the resulting crude material was purified by SiO_2 column chromatography (hexane-EtOAc) to give **6** (25 mg, 56%).

2,2'-Biguaiazulene (6):[10] dark green crystals; mp 167-167.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.40 (d, *J* = 7.0 Hz, 12H), 2.71 (s, 6H), 2.88 (s, 6H), 3.12 (sept., *J* = 7.0 Hz, 2H), 7.06 (d, *J* = 10.5 Hz, 2H), 7.41 (dd, *J* = 10.5, 1.5 Hz, 2H), 7.43 (s, 2H), 8.29 (d, *J* = 1.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 11.9, 24.2, 24.8, 38.4, 115.2, 123.4, 125.7, 133.2, 134.3, 136.6, 137.5, 140.7, 143.7, 145.8; UV-VIS (log ε) λ_{max} 650 (3.06, sh), 610 (3.08), 4.08 (4.34), 328 (5.07), 253 (4.57); CV (V *vs*. Ag/Ag$^+$) $(E^{red})_{pc}$ -1.93, $(E^{red})_{1/2}$ -1.91, $(E^{red})_{pa}$ -1.88, $(E^{ox})_{pa}$ +0.36; MS (MALDI(+), dithranol) *m/z* 394 (M$^+$).

Preparation of diguaiazuleno[1,2]dithiin (7): To a solution of **6** (68 mg, 1.7 x 10^{-1} mmol) in dry CH_2Cl_2 (87 mL), a mixture of disulfur dichloride (2.1 x 10^{-2} mL, 1.5 mol *eq*.) and imidazole (70 mg, 6.0 mol *eq*.) in dry CH_2Cl_2 (86 mL) was added dropwise for 10 min at -10 °C under Ar. The solution was stirred for 40 min at the same temperature. The reaction mixture was quenched with water and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The resulting residue was purified by SiO_2 column chromatography (hexane-CH_2Cl_2) and recrystallization (EtOAc-EtOH) to give **7** (78 mg, 99%).

Diguaiazuleno[1,2]dithiin (7): dark green crystals; mp 184-185 °C (dec.); ^{1}H NMR ($CDCl_3$) δ 1.36 (d, *J* = 6.8 Hz, 6H), 1.37 (d, *J* = 6.8 Hz, 6H), 2.63 (s, 6H), 3.04 (sept., *J* = 6.8 Hz, 2H), 3.14 (s, 6H), 6.91 (d, *J* = 10.4 Hz, 2H), 7.30 (dd, *J* = 10.4, 2.0 Hz, 2H), 8.19 (d, *J* = 2.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 13.6, 24.5, 24.6, 28.6, 38.0, 121.8, 123.4, 128.1, 133.5, 134.5, 135.6, 139.9, 141.8, 143.5, 146.4; UV-VIS (log ε) λ_{max} 677 (2.81), 346 (4.40), 255 (4.09); CV (V *vs*. Ag/Ag$^+$) $(E^{red})_{pc}$ -1.68, $(E^{red})_{1/2}$ -1.52, $(E^{red})_{pa}$ -1.35, $(E^{ox})_{pa}$ +0.44; MS (MALDI(+), dithranol) *m/z* 456 (M$^+$), 424 (M$^+$-S). Anal. Calcd for $C_{30}H_{32}S_2$: C, 78.90; H, 7.06. Found: C, 79.26; H, 7.14.

Conversion into diguaiazulenothiophene (8) by thermolysis of 7: Under Ar, **7** (34 mg, 7.4 x 10^{-2} mmol) was heated at 180 °C for 1 h without solvent. The crude material was washed with hexane and the residue was purified by recrystallization (hexane-CH_2Cl_2) to give **8** (25 mg, 79%).

Diguaiazulenothiophene (8): ocher solid; mp 202-203 °C; ^{1}H NMR ($CDCl_3$) δ 1.41 (d, J = 6.8 Hz, 12H), 3.13 (s, 6H), 3.13 (m, 2H), 3.23 (br. s, 6H), 7.11 (d, J = 11.2 Hz, 2H), 7.39 (dd, J = 11.2, 1.6 Hz, 2H), 8.35 (d, J = 1.6 Hz, 2H); ^{1}H NMR (C_6D_6) δ 1.31 (d, J = 6.8 Hz, 12H), 2.92 (m, 2H), 3.03 (s, 6H), 3.18 (s, 6H), 6.88 (d, J = 11.2 Hz, 2H), 7.22 (dd, J = 11.2, 1.6 Hz, 2H), 8.41 (d, J = 1.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.4, 24.7, 26.4, 38.5, 117.2, 126.4, 130.2, 132.7, 133.5, 134.8, 137.1, 138.2, 142.6 (overlapped); ^{13}C NMR (C_6D_6) δ 14.3, 24.5, 26.1, 38.4, 117.4, 126.4, 130.8, 132.7, 134.0, 134.3, 137.6, 137.9, 142.4, 143.2; UV-VIS (log ε) λ_{max} 595 (2.93, sh), 550 (3.15, sh), 455 (4.45), 427 (4.25), 373 (4.91), 313 (4.54), 275 (4.36); CV (V *vs*. Ag/Ag$^+$) $(E^{red})_{pc}$ -1.79, $(E^{red})_{1/2}$ -1.76, $(E^{red})_{pa}$ -1.72, $(E^{ox})_{pa}$ +0.08, +0.56, +0.97; MS (MALDI(+), dithranol) *m/z* 424 (M$^+$). Anal. Calcd for $C_{30}H_{32}S\cdot 1/2CH_2Cl_2$: C, 78.42; H, 7.12. Found: C, 78.49; H, 6.94.

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