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SYNTHESIS OF A NOVEL NON-BENZENOID QUINONE, 3,10-DIHYDRO-2,4-DIMETHYL-7,13-METHANOCYCLOHEPTA[11]-ANNULENE-3,10-DIONE, FROM 8H-7,9-BIS(METHOXYCARBONYL)-5,11-METHANO[11]ANNULENO[c]FURAN-8-ONE

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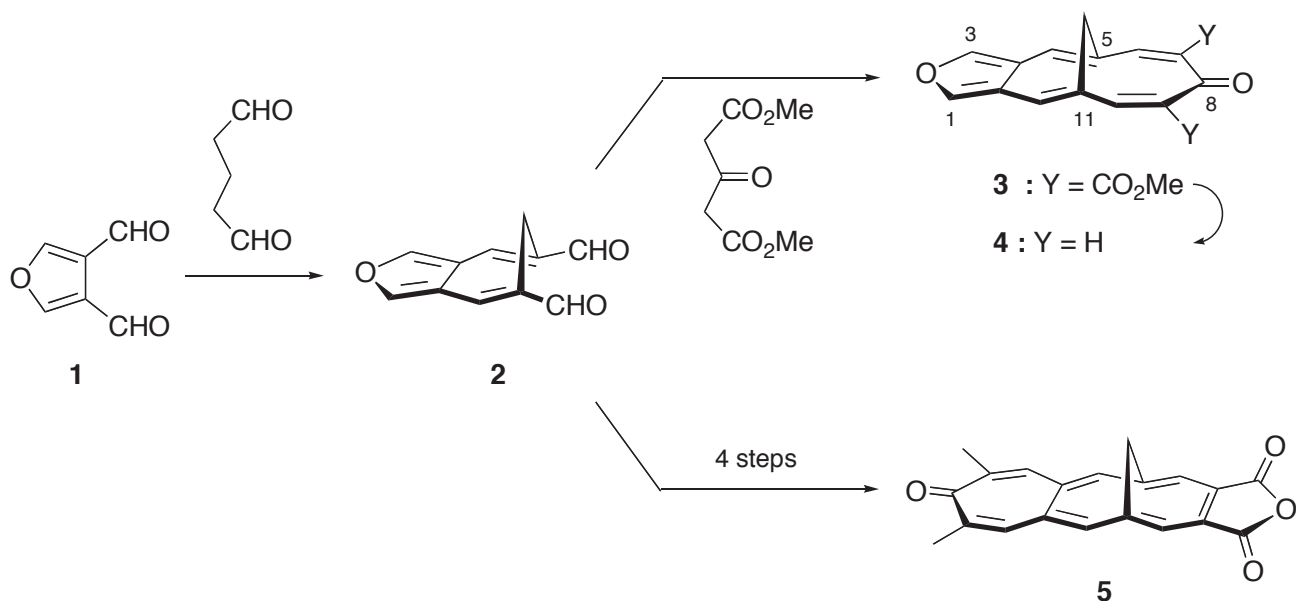
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Abstract – 8H-7,9-Bis(methoxycarbonyl)-5,11-methano[11]anuleno[c]furan-8-one (**3**) undergoes [4+3] cycloaddition with an oxyallyl species generated from 2,4-dibromo-3-pentanone in the presence of KI and copper, followed by dehydration in fluorosulfuric acid to give cyclohepta[11]annulenedione diester **9**. After hydrolysis of the ester groups, decarboxylation yielded the title quinone **6**. The ¹H NMR spectrum of **6** in D₂SO₄ indicates generation of its protonated dicationic species.

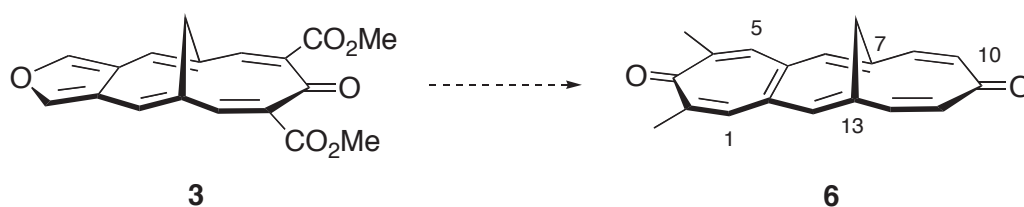
This paper is dedicated to Professor Dr. Ei-ichi Negishi on the occasion of his 77th birthday

We have previously found the efficient synthesis of 6H-cyclohepta[c]furan-5,7-dicarbaldehyde (**2**) from furan-3,4-dicarbaldehyde (**1**) by aldol condensation with pentanedial and developed a novel synthetic method for bridged [11]annulenes, 8H-7,9-bis(methoxycarbonyl)-5,11-methano[11]anuleno[c]furan-8-one (**3**) and its nor-ester compound **4** from **2**. We also disclosed [4+2] cycloaddition of **3** and **4** with dimethyl acetylenedicarboxylate (DMAD) at their furan ring to present potentiality for extension of their carbon framework.¹ Later, we reported that the furan moiety of **2**, after modification of their formyl groups, undergoes [4+3] cycloaddition with an oxyallyl species² generated from 2,4-dibromo-3-pentanone and, then, was converted into a tropone-annulated methano[10]annulene derivative **5**.³ These results



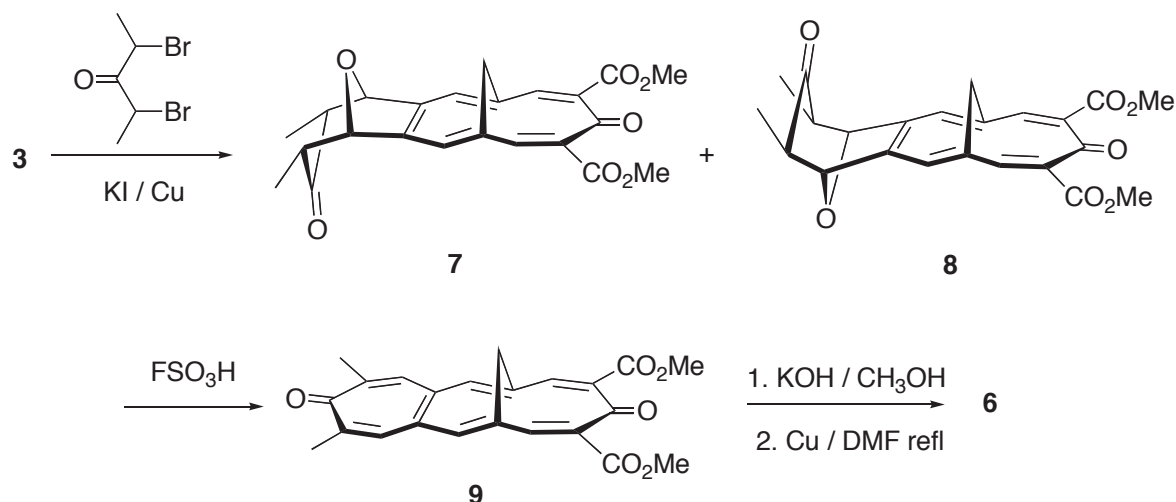
Scheme 1. Our previous synthetic work for methano[11]annulenes from **2**

indicate that the formyl groups and the furan functionality of compound **2** are advantageous to elaborate π -bond-extended methano-bridged compounds. In this short paper, we describe synthesis of a new non-benzenoid quinone⁴ of bridged cyclohepta[11]annulene, 3,10-dihydro-2,4-dimethyl-7,13-methanocyclohepta[11]annulene-3,10-dione (**6**), based on the reactivity of **2**, and its protonation.

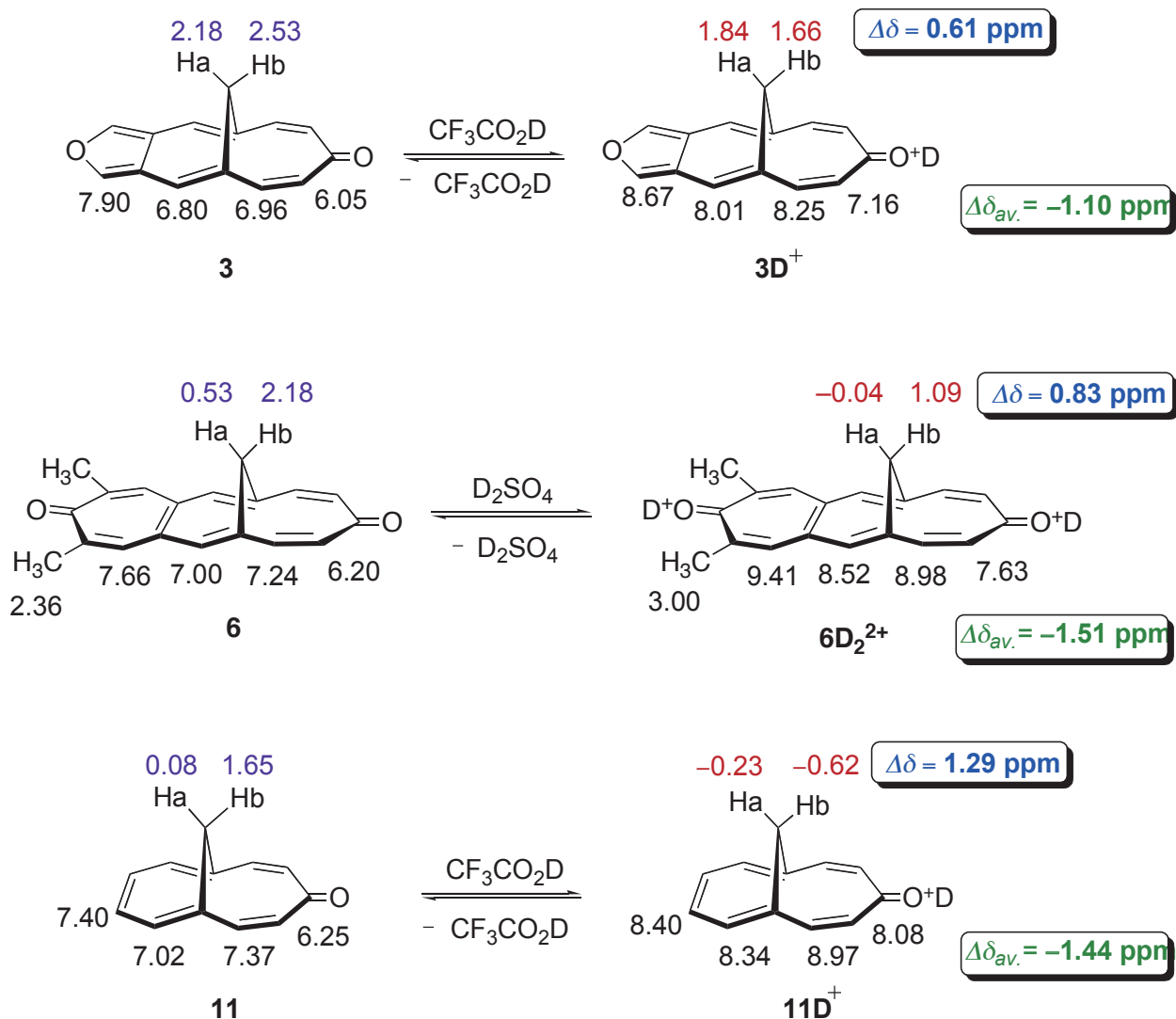


Scheme 2. Synthetic work in this study

The synthesis of **6** from **3** is shown in Scheme 3. Compound **3** undergoes [4+3] cycloaddition with an oxyallyl reagent generated from 2,4-dibromo-3-pentanone in the presence of KI and copper. The product was isolated as a mixture of two inseparable stereoisomers in 95% yield. The ¹H NMR spectrum of this mixture indicates that it constitutes two stereoisomers in ratio of 4:1. Signals for the two methyl groups on the seven-membered ring appear to be equivalent for both stereoisomers and those of the two methyl groups of the esters do in the same way, suggesting that these isomers are symmetrical through a plane containing bridging methylene carbon and hydrogens. Since both isomers have coupling constants of 4.4 Hz between adjacent methine protons on the seven-membered ring, relative stereochemistry between the methyl groups and the ether group is assigned as trans (**7** and **8**) for both isomers, based on previously

Scheme 3. Synthesis of **6**

analyzed NMR data by Hoffmann *et al.*⁶ However, the stereochemical relationship between the oxa and methano bridges for each product is obscure from these spectral data. Dehydration of a mixture of **7** and **8** in fluorosulfuric acid gave diketo-diester **9** in 58% yield. Finally, two ester groups in **9** were removed by hydrolysis in KOH/MeOH and subsequent thermal decarboxylation in the presence of copper metal to give the title compound **6** in 40% yield. Compound **6** was isolated as stable yellow microcrystals. Its structure was confirmed by spectroscopic analysis. Typical features are as follows; the carbonyl and C=C absorption bands in the IR spectrum were observed at 1576 and 1608 cm⁻¹, respectively.⁷ The bridging methylene protons in the ¹H NMR spectrum in CDCl₃ resonate at 0.53 and 2.18 ppm with a coupling constant of 11.6 Hz.⁸ The long-wave absorption in the UV-vis spectrum of **6** in CH₂Cl₂ was found at 438 nm. Generation of the cationic species was studied by ¹H NMR analysis. The chemical shifts in the ¹H NMR spectrum of **6** in CDCl₃ and acid media are shown in Scheme 4, accompanied with those of **3**¹ and 4,9-methano[11]anulenone (**11**).⁹ As seen in heptalenediones,^{5,10} sufficient duplicated protonation of **6** was not observed in CF₃CO₂D, probably because of retardation in the second protonation. Acidity of D₂SO₄ was found strong enough to generate the dicationic species.^{11,12} The ¹H NMR spectrum in D₂SO₄ shows clear a down-field shift of the peripheral ring protons and a up-field shift of the bridging methylene protons, indicating that **6D**₂²⁺ is diatropic and exist as a full conjugated 14π-electronic dicationic structure. Beside shift values for all protons, changes of average shifts of the bridging and peripheral protons are also shown in Scheme 4. The magnitude of these shifts in **6** is greater than that seen in **3**. While the down-field shift of the peripheral protons for **6** is greater than that of **11**, the up-field shift of the bridging methylene protons for **6** is less than that for **11**, probably because of a deshielding effect by the neighboring tropylium ring.



Scheme 4. Chemical shifts of **3**, **6**, and **10** in neutral (left, in CDCl_3) and acidic media (right, in acid)

We have demonstrated that the title cyclohepta[11]annulenedione **6** can be synthesized from **3** and protonation of **6** generates diatropic dicationic species **6D₂²⁺**. As far as we know, **6D₂²⁺** is the first example of a 14π -electronic dicationic structure having a methano-bridged [7]annuleno[11]annulene system. Completion of the synthesis of **6** in this study and our previous syntheses of **4** and **5** through cyclization using two formyl groups and the furan moiety prove importance of **2** as a versatile synthetic precursor for bridged annulenes and annulenones.

EXPERIMENTAL

Melting points were measured on a Yanaco MP-3. IR spectra were recorded on a Perkin-Elmer Spectrum RX 1 spectrometer. UV spectra were measured on a Shimadzu UV-1600 spectrometer. ^1H and ^{13}C NMR spectra were recorded with tetramethylsilane as internal standard on a JEOL $\alpha 400$ NMR instrument.

Mass spectra were measured on a JMS-700 mass spectrometer. Column chromatography was done with Merck Kieselgel 60 Art 7734. Compound **3** was prepared by the previously reported method.¹

[4+3] Cycloaddition reaction of **3** with 2,4-dibromo-3-pentanone in the presence of KI and copper

A mixture of KI (452 mg, 2.76 mM) and copper powder (177 mg, 2.76 mM) was charged in a 50 mL three-necked flask and heated under vacuum at 150 °C on an oil bath for 3 h. After being cooled to room temperature, the flask was fitted with a condenser and dropping funnel, and 2,4-dibromo-3-pentanone (1.11 g, 4.60 mM), **3** (300 mg, 0.920 mM), and 30 mL of dry MeCN was added to the flask. This mixture was refluxed for 2 h under nitrogen atmosphere. Solids were removed by filtration and the filtrate was poured into 40 mL of water and extracted with CH₂Cl₂ (30 mL x 3). The combined organic layer was washed with brine and was dried over MgSO₄. The solvent was removed and the residue was purified by silica gel column chromatography with AcOEt/Hexane (20/80) to give 395 mg (95% yield) of a mixture of **7** and **8** (4:1) as yellow solids. Mp 85–98 °C. ¹H NMR (CDCl₃) of the major stereoisomer in the mixture, δ = 8.04 (s, 2H), 7.19 (s, 2H), 5.26 (d, J = 4.4 Hz, 2H), 3.85 (s, 6H), 3.14 (qd, J = 7.2, 4.4 Hz, 2H), 2.03 (d, J = 12.0 Hz, 1H), 0.93 (d, J = 7.2 Hz, 6H), –0.16 (d, J = 12.0 Hz, 1H) ppm; ¹³C NMR (CDCl₃) of the major stereoisomer in the mixture, δ = 207.5, 191.9, 164.3, 145.6, 139.9, 125.3, 123.8, 116.5, 86.5, 52.6, 50.7, 32.9, 9.8 ppm; ¹H NMR (CDCl₃) of the minor stereoisomer in the mixture, δ = 8.00 (s, 2H), 7.09 (s, 2H), 5.39 (d, J = 4.4 Hz, 2H), 3.85 (s, 6H), 3.25 (qd, J = 7.2, 4.4 Hz, 2H), 2.10 (d, J = 12.0 Hz, 1H), 1.21 (d, J = 7.2 Hz, 6H), 0.12 (d, J = 12.0 Hz, 1H) ppm; ¹³C NMR (CDCl₃) of the minor stereoisomer in the mixture, δ = 207.0, 192.4, 164.3, 145.6, 140.0, 126.3, 123.0, 119.7, 84.0, 52.6, 49.5, 31.9, 9.8 ppm; IR (KBr) of the mixture, ν_{\max} = 1712s, 1698vs, 1691vs, 1681vs, 1574m, 1360s, 1282s, 1236s, 1282s, 755s cm⁻¹; UV-vis (CH₂Cl₂) of the mixture, λ_{\max} = 260 (log ϵ = 4.75), 302 (5.00), 377 (4.18) nm; MS (70 eV) of the mixture, m/z (rel int) = 410 (M⁺, 100), 353 (65), 326 (9), 267 (9), 239 (9), 168 (17), 152 (9). HRMS m/z Calcd for C₂₃H₂₂O₇ (M⁺) 410.1366, found 410.1360.

3,10-Dihydro-9,11-bis(methoxycarbonyl)-2,4-dimethyl-7,13-methanocyclohepta[11]anulene-3,10-dione (9)

To a solution of a mixture of **7** and **8** (705 mg, 1.72 mM) in 10 mL of CH₂Cl₂ at 0 °C was added dropwise 1.72 g (17.2 mM) of fluorosulfuric acid and the mixture was stirred at the same temperature for 2 h. Then, the resulted reddish brown mixture was poured into 100 mL of water and was extracted with CH₂Cl₂ (30 mL x 3). The combined organic layer was washed with a saturated aqueous NaHCO₃ solution and brine. After dryness over MgSO₄, the solvent was removed and the residue was purified by silica gel column chromatography with AcOEt/Hexane (25/75) to give 391 mg (58% yield) of **9** as yellow powder. Mp 275–277 °C. ¹H NMR (CDCl₃), δ = 7.89 (s, 2H), 7.62 (s, 2H), 7.14 (s, 2H), 3.86 (s, 6H), 2.55 (d, J = 13.0 Hz, 1H), 2.38 (s, 6H), 0.58 (d, J = 13.0 Hz, 1H) ppm; ¹³C NMR (CDCl₃) δ = 193.7, 187.2, 164.4, 145.2, 140.5, 139.0, 138.0, 134.5, 127.9, 120.0, 52.9, 30.7, 23.5 ppm; IR (ART) ν_{\max} = 1725s, 1709s,

1665m, 1609m, 1593s, 1582m, 1432m, 1267s, 1223s cm^{-1} ; UV-vis (CH_2Cl_2) $\lambda_{\text{max}} = 260$ ($\log \epsilon = 4.75$), 302 (5.00), 377 (4.18) nm; MS (70 eV) m/z (rel int) = 392 (M^+ , 28), 364 (18), 336 (100), 305 (24), 277 (20), 202 (15). HRMS m/z Calcd for $\text{C}_{23}\text{H}_{20}\text{O}_6$ (M^+) 392.1260, found 392.1268.

3,10-Dihydro-2,4-dimethyl-7,13-methanocyclohepta[11]annulene-3,10-dione (6)

To a solution of **9** (100 mg, 0.255 mM) in 20 mL of MeOH and 1 mL of water was added 286 mg (0.510 mM) of potassium hydroxide. The mixture was refluxed on an oil bath for 2 h. Then, the resulted mixture was poured into 30 mL of 1M HCl and was extracted with EtOAc (20 mL x 3). The combined organic layer was washed with water and brine. After dryness over MgSO_4 , the solvent was removed and the residue was resolved in 5 mL of DMF. To this solution was added 32.6 mg (2.55 mM) of copper powder and the suspension was refluxed for 2.5 h. After removal of solids by filtration, the filtrate was mixed with 50mL of water and was extracted with AcOEt (20 mL x 3). The combined organic layer was washed with water and brine. After dryness over MgSO_4 , the solvent was removed and the residue was purified by silica gel column chromatography with AcOEt/Hexane (20/80) to give 28.1 mg (40% yield) of **6** as yellow microcrystals. Mp 228–229 °C. ^1H NMR (CDCl_3) $\delta = 7.66$ (s, 2H), 7.24 (d, $J = 12.4$ Hz, 2H), 7.00 (s, 2H), 6.20 (d, $J = 12.4$ Hz, 2H), 2.36 (s, 6H), 2.18 (d, $J = 11.6$ Hz, 1H), 0.53 (d, $J = 11.6$ Hz, 1H) ppm; ^{13}C NMR (CDCl_3) $\delta = 194.4$, 187.3, 144.0, 138.8, 138.7, 137.0, 130.3, 130.2, 127.7, 33.5, 23.5 ppm; IR (ART) $\nu_{\text{max}} = 1608\text{m}$, 1576s cm^{-1} ; UV-vis (CH_2Cl_2) $\lambda_{\text{max}} = 238$ ($\log \epsilon = 4.37$), 250 (4.38), 321 (5.10), 367 (4.34), 438 (3.37) nm; MS (70 eV) m/z (rel int) = 276 (M^+ , 48), 220 (100), 219 (36), 205 (64), 189 (21). HRMS m/z Calcd for $\text{C}_{19}\text{H}_{16}\text{O}_2$ (M^+) 276.1150, found 276.1155.

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11. The solution of **6** in D₂SO₄ appeared red, having $\lambda_{\text{max}} = 242$ (log $\epsilon = 4.27$), 279 (3.92), 361 (4.89), 469 (3.90) nm.
12. Compound can be recovered from the D₂SO₄ solution by neutralization with NaHCO₃ and subsequent extraction with CH₂Cl₂.