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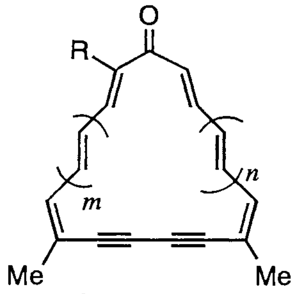
Synthesis and Properties of a Bismethano-bridged Bisdehydro[21]annulenone. Conformation in Solution and in the Crystalline State

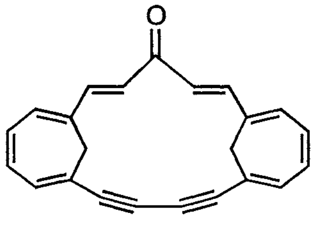
Hiroyuki HIGUCHI, Seiken KIYOTO, Chiaki SAKON, Naoki HIRAIWA, Kaori ASANO,
Jūro OJIMA,* Katsuya INOUE,† and Gaku YAMAMOTO*,†
Department of Chemistry, Faculty of Science, Toyama University, Gofuku, Toyama 930
†Department of Chemistry, School of Science, Kitasato University, Kitasato, Sagamihara, Kanagawa 228

A bismethano-bridged bisdehydro[21]annulenone, tricyclo[15.4.1.1^{6,11}]tricosa-6,8,10,12,15,17,19,21-octaene-2,4-diyn-14-one, was synthesized. X-ray crystallography reveals the syn orientation of the two methano bridges. Two conformers are present in solution in a 97:3 ratio, the major isomer being the one existing in the crystalline state. Paratropicity of this compound in CDCl$_3$ and in CF$_3$CO$_2$D is discussed.

It has been confirmed that the dimethyl- or trimethyl-bisdehydroannulenones **1** (m=0–3, n=0–3) with 13- to 25-membered rings show the alternation of the tropic nature between (4n+2)π- and 4nπ-electron systems arising from polarization of the carbonyl group.1) However, annulenone derivatives to show the ring current effect in which the ring size is higher than 25 are yet unknown.2) Since a methano-bridge contributes to keeping the annulene perimeter rigid and planar3) and a cycloheptatriene ring has three conjugated double bonds, we noticed that the bismethano-bridged bisdehydroannulenone **2**, which is formally derived from the lowest member of **1**, the [13]annulenone (m=n=0), by replacing two double bonds with two cycloheptatriene rings, has the same number of double bonds as the bisdehydro[21]annulenone **1** (m=n=2). Thus we expected that annulenone derivatives larger than the bisdehydro[25]annulenone **1** (m=n=3) would possibly be prepared taking advantage of bismethano-bridging.



1 R=H or Me
m=0–3, n=0–3



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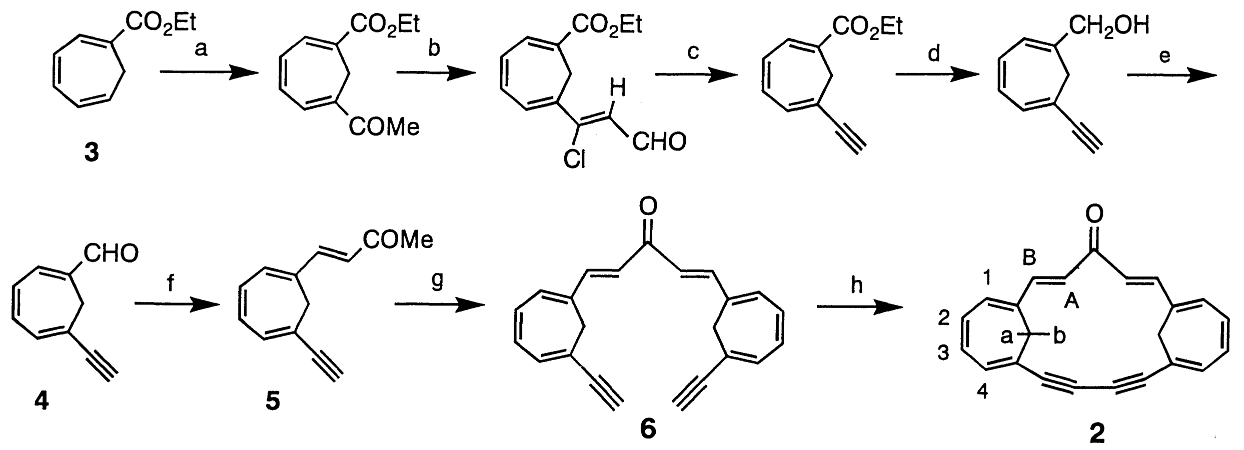
Bearing these in mind, we were interested in testing whether the bismethano-bridged bisdehydro[21]annulenone **2** would show the same degree of paratropicity with that observed in the dimethylbisdehydro-[21]annulenone **1** (R=H, m=n=2).4)

The key intermediate for the synthesis of **2** was 6-ethynyl-1,3,5-cycloheptatriene-carbaldehyde (**4**),5) which was derived in five steps from the known ester, ethyl 1,3,5-cycloheptatrienecarboxylate (**3**)6) as illustrated in Scheme 1. Compound **4** was condensed with acetone to afford the ketone **5**, which was then condensed with the aldehyde **4** to give the bisethynyl compound **6**. Finally an intramolecular oxidative coupling of the two ethynyl groups of **6** afforded the desired annulenone **2**, mp 185–187 °C (dec).



Scheme 1.

a) AcCl, $AlCl_3$, CH_2Cl_2 (66%). b) $POCl_3$, DMF-C_6H_6 (57%). c) aq KOH, DMF (49%). d) DIBAH, C_6H_6 (93%). e) $Ba(MnO_4)_2$, CH_2Cl_2 (78%). f) acetone, NaOH-EtOH (58%). g) **4**, NaOEt, Et_2O (78%). h) $Cu(OAc)_2$, Py-Et_2O (66%).

Compound **2** exists in $CDCl_3$ at 26 °C as a mixture of two isomers in a ratio of ca. 97:3. The ^1H NMR spectrum of the major isomer was unambiguously analyzed as follows (Table 1). The methylene protons appear as a pair of doublets, and this suggests that the molecule is symmetric (C_s or C_2) and the flipping of the methano bridge through the average plane of the macrocyclic ring is slow on the NMR time scale but the relative disposition of the two methano bridge, *syn* or *anti*, is not determined from the data. The higher field doublet at δ 2.05 is assigned to H^a located above the seven-membered ring from several lines of evidence. The -CH^A=CH^B- moieties also afford a pair of doublets and the lower-field doublet at δ 7.73 was assigned to H^A located α to the carbonyl group from the CH-COSY spectrum.[7] This may seem anomalous because a β-proton usually resonates at a lower field than an α-proton in α,β-unsaturated ketones and be understood in terms of the paramagnetic ring-current effect and the anisotropy of the diacetylene moiety judging from the structure revealed below. The H^A signal shows an intensity enhancement (NOE) upon irradiation of the lower-field methylene proton at δ 4.20, which indicates that H^A should be close to H^b and thus inside the ring. The H^B signal at δ 7.03 shows NOE upon irradiation of the doublet at δ 6.46, which is thus assigned to H^1. Therefore the two-dimensional structure **2** is assigned to the isomer, leaving the two possibilities, *syn* (**2a**) and *anti* (**2b** and its enantiomer). As for the minor isomer, no clear information about the structure and conformation is obtained because of the low population.

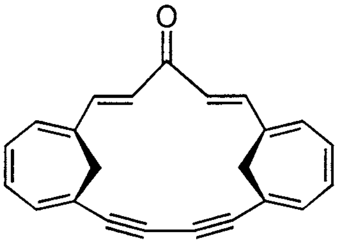
Interconversion between these isomers is slow on the NMR time scale at 26 °C as judged from the sharp NMR signals. Elevation of the temperature, however, causes broadening of the signals. When measured in toluene-d_6, the signals due to the minor isomer begins to broaden around 70 °C and disappeared around 100 °C because of the coalescence with the signals due to the major isomer, while the broadening of the major isomer signals occurs above 90 °C. At 115 °C the methylene proton signals appear as a pair of broad doublets. These findings indicate that the equilibrium between **2a** and **2b** is attained at 26 °C and that the interconversion takes place on the NMR time scale at higher temperatures, although no quantitative estimation of the rate can be made.

In order to obtain the further details of the molecular structure of **2**, X-ray crystallographic analysis was performed. The crystal of compound **2** contains two independent molecules of **2** in a unit cell, but the structures

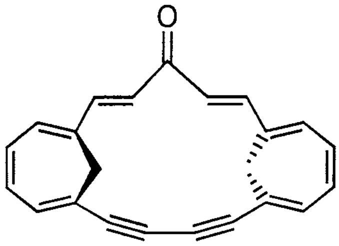
Table 1. ^{1}H NMR Data of Isomers of Compound **2** at 25 °C [a)]

	major isomer **2a**		minor isomer **2b**	
	$CDCl_3$	CF_3CO_2D	$CDCl_3$	CF_3CO_2D
H^a	2.049 d (12.5)	3.093 d (13.0)	1.769 d (12.8)	1.90 d (13)
H^b	4.200 d (12.5)	5.344 d (13.0)	3.549 d (12.8)	3.88 d (13)
H^A	7.733 d (15.7)	9.532 d (15.3)	7.141 d (15.9)[b)]	7.71 d (16)[c)]
H^B	7.028 d (15.7)	7.271 d (15.3)	6.970 d (15.9)[b)]	7.38 d (16)[c)]
H^1	6.463 d (5.9)	6.279 d (6.0)	6.534 d (5.8)[d)]	e)
H^2	6.689 dd (11.1, 5.9)	6.679 dd (11.2, 6.0)	6.775 dd (11.3, 5.8)[f)]	e)
H^3	6.610 dd (11.1, 5.9)	6.606 dd (11.2, 6.0)	6.832 dd (11.3, 5.8)[f)]	e)
H^4	6.370 d (5.9)	6.679 d (6.0)	6.567 d (5.8)[d)]	e)

a) Obtained at 500 MHz. Chemical shifts are given in δ. In parentheses are coupling constants in Hz. b) Assignments are mutually exchangeable. c) Assignments are mutually exchangeable. d) Assignments are mutually exchangeable. e) Not clearly identified. f) Assignments are mutually exchangeable.



2a



2b

are quite similar to each other and one of them is shown in Fig. 1.[8)] The crystal structure reveals that compound **2** adopts the *syn* conformation **2a** in the crystalline state. It will therefore be reasonable to assign **2a** to the major isomer in solution and **2b** to the minor isomer. The higher stability of the *syn*-isomer **2a** than the *anti*-isomer **2b** may be due to the more effective conjugation of the π-system in **2a** as judged from the molecular model considerations, and this is consistent with the higher tropicity of **2a** than **2b** as described below.

Comparison of the ^{1}H chemical shifts of compound **2** with those of its open-chain counterpart **6**[9)] reveals that isomer **2a** shows some paratropicity because the methylene protons and the inner olefinic proton H^A show

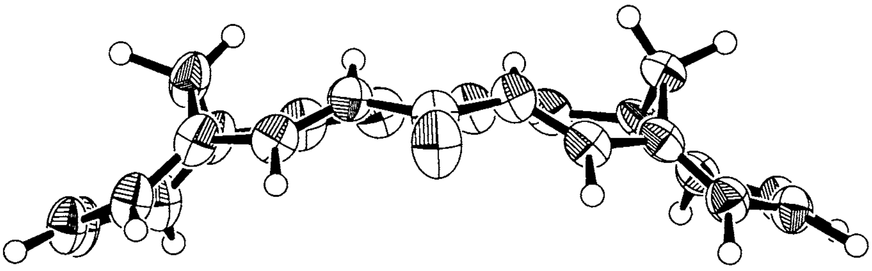


Fig. 1. The perspective drawing of compound **2**.

downfield shifts and the outer olefinic protons, H^B and H^1–H^4, show slight upfield shifts, while isomer **2b** shows no tropicity at all. The difference between the two isomers is magnified when the NMR spectrum is measured in CF_3CO_2D. The methylene protons shift further downfield by 1.1 and 0.2 ppm on the average in **2a** and **2b**, respectively. The inner H^A moves downfield by 1.8 and 0.6 ppm in **2a** and **2b**, respectively, while the outer olefinic protons of **2a** show no significant shifts, while H^B in **2b** shifts downfield, reflecting the addition and cancellation of the downfield effect due to the cation formation and the paratropicity effect for the inner and outer protons, respectively.

Compound **1** shows the averaged chemical shift difference between the inner and outer protons of 1.80 ppm in $CDCl_3$ and upon changing the solvent from $CDCl_3$ to CF_3CO_2D the outer protons shift upfield by 0.6 ppm on the average and the inner protons shift downfield by 4.1 ppm. It is therefore concluded that compound **2** shows smaller tropicity than **1** and this will be ascribed to the low planarity of the π-system compared with compound **1**, which is revealed by the crystal structure of **2** (Fig. 1).

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7) The CH-COSY spectrum of the isomer **2a** reveals that the proton at δ 7.03 is bonded to the carbon at δ 138.71, while the proton at δ 7.73 is bonded to the carbon at δ 130.69. The carbon chemical shifts reflects the electron densities more directly than proton chemical shifts and the carbon signal at the lower field is reasonably assigned to carbons located β to the carbonyl group.

8) X-ray crystallographic data for compound **2**: $C_{23}H_{16}O$, FW=308.38, triclinic, $P\bar{1}$ (#2), a =13.160(3), b =15.942(3), c =7.918(2) Å, α=97.41(2), β=92.39(2), γ=93.50(2) °, V=1642.3(6) Å^3, Z =4, D_{calc}=1.247 g/cm^3, R =0.063, R_w=0.045, 3071 unique reflections with $I > 3.0\sigma(I)$.

9) ^{1}H NMR spectrum ($CDCl_3$, 500 MHz) of compound **6**: δ 7.441 (2H, d, J=15.6 Hz), 6.800 (2H, d, J=15.6 Hz), 6.732 (2H, dd, J=11.0 and 6.0 Hz), 6.670 (2H, dd, J=10.9 and 6.0 Hz), 6.623 (2H, d, J=6.0 Hz), 6.573 (2H, d, J=6.0 Hz), 2.940 (2H, s), 2.753 (4H, s).

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