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HEXAMETHYLENE BRIDGED CYCLOHEPTATRIENES AND TROPONE

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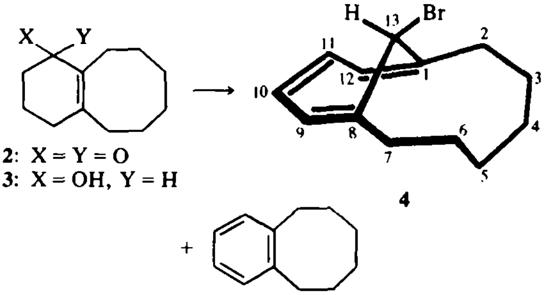
Abstract—The novel, bridged bromocycloheptatriene (**4**) is obtained by the thermolysis of a tricyclo[6.4.1.$0^{1,8}$]tridecane derivative (**6**), and the observed anti stereochemistry of the Br atom on C(13) is accounted for by assuming the suprafacial [1,5] hydrogen shift in the intermediate **7**. The mother hydrocarbon (**8**) and syn-methyltropylidene (**9**), as well as tropone (**10**), are derived from **4**, and the structures of these products are examined spectrometrically. The covalent C–Br bond of **4** remains intact under various reaction conditions of nucleophilic substitution, and this is ascribed to the conformational rigidity constrained by the short hexamethylene bridge. The attempted transformation of **4** or **10** to the corresponding tropylium ion **12** or **14** fails to success and this is again attributed to the bridge effect.

The aromatic ring of a phane can be distorted from a plane in the presence of very short aliphatic chain bridging the nonvicinal positions, and much of the extraordinary behaviour has been ascribed to the bridge effect.[1] We have synthesized the title compounds in order to examine: (1) the bridge effect prohibiting the planarity of the 7-membered, potential aromatic ring[2] and (2) the structures and reactive behaviour including the problem of cycloheptatriene-norcaradiene tautomerism.[3] This article offers a discussion and experimental details.[4]

Synthesis of bridged tropylidenes and tropone. The 7-membered, potential aromatic ring was constructed by thermal opening of a norcarane framework.† Base-catalyzed intramolecular aldol condensation of cyclododecane-1,5-dione (**1**)[6] gave a bicyclic enone (**2**), which was reduced to an allylic alcohol (**3**) with LAH. Cycloaddition of dibromocarbene to **3** followed by thermolysis *in vacuo* afforded 13-bromobicyclo[6.4.1]trideca-8,10,12-triene (**4**, 33%) along with a by-product (**5**, *ca*. 10%).[7] It is assumed that the thermal cleavage of the cyclopropane ring under dehydration and dehydrobromination gives initially a labile bromocycloheptatriene (**7**), which is transformed to the less strained isomer (**4**) by the suprafacial [1,5] hydrogen shift.[8]‡

This mechanism is strongly supported by the configuration of C(13), whose Br atom spectrometrically proved to be anti to the tropylidene ring (*vide infra*). In order to corroborate the stereochemistry of C(13), related compounds were prepared and examined spectrometrically.

Reduction of **4** with LAH gave the desired hydrocarbon, bicyclo[6.4.1]trideca-8,10,12-triene (**8**), along with **5** and two unidentified hydrocarbons.[10]§ The formation of these by-products was minimized by use of n-Bu$_3$SnH as a reducing agent, which gave chiefly **8**, the ratio of **8**:**5** being 5/1. The magnetic nonequivalence of the two hydrogens at C(13) indicated the absence of the conformational flipping of the hexamethylene chain, which apparently is not sufficiently long to induce the aliphatic bridge flipping up



2: X = Y = O
3: X = OH, Y = H

4

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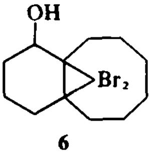

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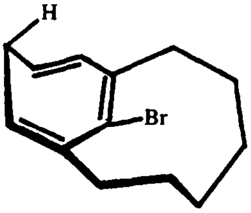

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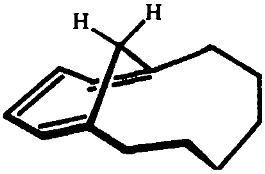

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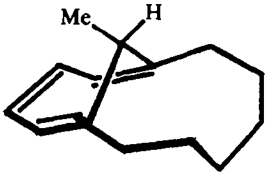

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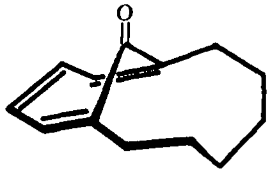

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†The tropylidene ring is conventionally constructed in such manners as: (1) [6 + 1], Ref. 5a–c, (2) [5 + 2], Ref. 5d, e, (3) [4 + 3], Ref. 5f–h.

‡According to the Bredt's Rule the strain accumulated at the bridgehead must be the motive force of the transformation (see Ref. 9).

§The low deuterium incorporation (d_1 < 25% on ms) observed upon LiAlD$_4$ treatment of **4** may suggest the existence of radical intermediates (see Ref. 11).

and down the tropylidene ring, even though the bond angle between C(1)-H and C(6)-H of tropylidene itself is smaller than that of *meta* hydrogens of the benzene ring.† The conformational rigidity remained unchanged even at 210°C.

Treatment of **4** with MeLi in ether-HMPA (10/1) gave *syn*-Me derivative (**9**) as a sole product. The stereochemistry is based on the PMR signal appearing at δ 0.63 (3H), which is characteristic of the *syn*-Me protons.[13] Negligible formation of a lithiated derivative was demonstrated by the absence of deuterium incorporation upon quenching with deuterium oxide.[14] The complete inversion of the configuration on C(13) is ascribed to a push-pull S_N2 mechanism[15] or alternatively to a radical-type one. Oxidation of **4** with CrO_3·2Py complex in dichloromethane afforded 2,7-hexamethylene bridged tropone (**10**) in 16% yield.[16]

Bridge effects on the reactivities of **4**. Bromotropylidene itself is known to be labile, easily transformed into tropylium bromide (**11**), and therefore is soluble only in polar solvents such as methanol, ethanol or water.[17] In sharp contrast, however, **4** was dissolved freely into hydrocarbon solvents and exhibited molecular peaks (*m/e* 252, 254) in the MS. Remarkably, **4** remained unchanged even after treatment with NaOMe or NaOH,[18] and attempted Kornblum's DMSO oxidation in existence of $AgClO_4$[19] also resulted in the recovery of **4**. Attempts to obtain a bridged tropylium ion (**12**) were also made without success by treatment of **4** with $AgClO_4$ or $AgBF_4$.‡ The covalent C–Br bond thus survived under both S_N1 and S_N2 reaction conditions and this probably originates from the rigid structure constrained by the short hexamethylene bridge as well as from the steric hindrance. The bent 7-membered ring is fixed by the bridge and accordingly the conjugation of three double bonds and the carbonium ion on C(13) is considerably inhibited. The successful synthesis of [6]metacyclophane (**13**)[12] was previously recorded and the difference clearly indicates the less aromatic stabilization of tropylium ion[21] as compared with that of the benzene ring. The IR spectra of tropone (**10**) appeared at 1656 cm⁻¹, which was characteristic of the vibrational absorption of carbonyl C=O bond in a bent tropone system.[22] The constraint introduced by the hexamethylene bridge was also indicated by the unsuccessful attempt at transforming **10** into the corresponding hydroxytropylium ion (**14**) by means of CF_3COOH. In contrast to **10**, 2,7-nonamethylenetropone (**15**) afforded the aromatic hydroxytropylium ion (**16**) under the same condition and the diamagnetic ring current was evidenced by its PMR spectra.[2c]

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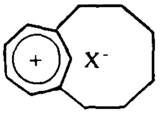
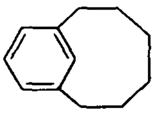


12: $X^- = ClO_4^-$ or BF_4^-



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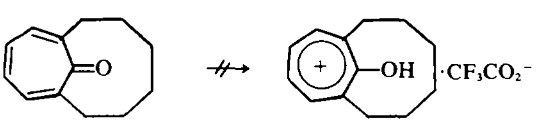
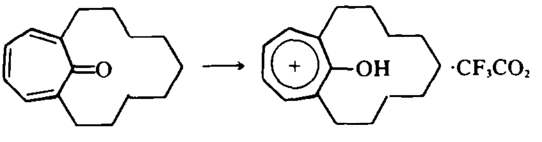


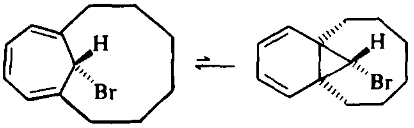
10 **14**



15 **16**

Stereochemistry of the tropylidenes. The energy barrier of the conversion from **4** to the corresponding norcaradiene isomer (**17**) was so high that no evidence for the existence of **17** had been obtained.[3] In the PMR spectra of **4** the observed parameter N of the olefinic A_2B_2 system[23] was 5.9 Hz, which was characteristic of the cycloheptatriene system.§

In the CMR spectra C(1) and C(8) absorbed at 132.3 and C(13) at 58.8 ppm, which clearly eliminated the presence of cyclopropane ring in the system.[24] According to the Hoffmann's theory[25] it is plausible for the electron-donating Br atom to destabilize the bond between C(1) and C(8) of **17**.



4 **17**

The *anti* stereochemistry of the C–Br bond of **4** was at first deduced from the reaction course and the reactivity of bromine. More strict assignment was achieved by the spectral data. (1) One of the allylic protons on C(2) or C(7) is considerably deshielded in terms of the anisotropy of the neighbouring Br atom which is *anti* to the tropylidene ring.[12,26] (2) The double irradiation technique as applied to PMR spectra of **8** or **9** indicated that the *anti* proton on C(13) coupled (J = 1.5 Hz) with protons on C(9) and C(12), while the *syn* proton did not. The *anti* stereochemistry of Br atom was again supported by the fact that the proton on C(13) appeared as a singlet. (3) The stereochemistry on C(13) was more clearly indicated by the UV spectra. While **9** absorbed at 283 nm, **4** and **8** absorbed at 271 and 272 nm, respectively. The bathochromic shift of **9** is ascribed into the bulky *syn*-Me group which is responsible for spreading out the cycloheptatriene ring in a flat boat form.[27]

EXPERIMENTAL

2,3-*Hexamethylene-2-cyclohexenone* (**2**). A mixture of **1** (14.3 g, 0.073 mol) and 4% methanolic NaOH (6.0 g in MeOH 180 ml) was heated at reflux for 3 hr under N_2. Removal of the solvent *in vacuo*, followed by usual work-up and distillation, gave **2** (11.9 g, 92%), b.p. 100°/2.5 mm. IR (neat): 1661 and 1629 cm⁻¹, PMR (CCl_4): δ 2.8–1.9 (m, 8H) and 2.0–1.1 (m, 10H), MS: *m/e* 178 (P^+). (Found: C, 81.0; H, 10.0. Calcd for $C_{12}H_{18}O$: C, 80.9; H, 10.2%).

2,3-*Hexamethylene-2-cyclohexenol* (**3**). The bicyclic enone (**2**) (9.88 g, 0.056 mol) was reduced by means of LAH (1.05 g, 0.028 mol) in refluxing ether (80 ml) for 1.5 hr. Work-up afforded **3** (8.96 g, 90%), b.p. 108°/2.5 mm, IR (neat): 3350 and 969 cm⁻¹, PMR (CCl_4): δ 3.9 (m, 1H), 2.8–1.7 (m, 7H) and 1.9–1.2 (m, 12H). (Found: C, 79.8; H, 11.1. Calcd for $C_{12}H_{20}O$: C, 79.9; H, 11.2%).

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†The conformational inflexibility of **4** is accounted for by the sp^3 hybridization at C(13) rather than sp^2 of metacyclophanes. As for the conformational flipping of [n]metacyclophanes (see Ref. 12).

‡It was reported that only the *endo*-chloro rather than *exo*-chloro moiety was abstracted with Ag^+ in cycloocta-1,3,5-triene system (see Ref. 20).

§No essential change in the PMR spectra of **4** was observed even at temperatures as low as −125°C.

13-*Bromobicyclo*[6.4.1]*trideca*-8,10,12-*triene* (**4**). To a mixture of **3** (7.95 g, 0.044 mol) and t-BuOK (34.6 g, 71% K, 0.22 mol) suspended in anhyd n-hexane (280 ml), $CHBr_3$ (55.7 g, 0.22 mol) was added at −20° under N_2 and the mixture was allowed to warm up to room temp over a period of 4 hr. Work-up followed by distillative thermolysis (150°/0.2 mm) provided **4** (3.67 g, 33%), together with **5** (*ca.* 0.73 g, 10%). The triene **4** formed a colourless oil, b.p. 125°/0.1 mm, IR (neat): 3030, 3012, 1595, 1508, 864 and 739 cm^{-1}, PMR ($CDCl_3$): δ 6.60 (dd, C(10,11)-H), 6.03 (m, C(9,12)-H), 3.85 (s, C(13)-H), 2.93, 2.41 (m, allylic, 4H) and 2.0–1.0 (m, 8H). Unless otherwise stated CMR data (in $CDCl_3$ with TMS internal standard) are given in the order of chemical shift, intensity, off-resonanced signal: 132.3 (90, s, C(1,8)), 130.1 (173, d), 120.7 (148, d), 58.8 (92, d, C(13)), 32.4 (190, t), 28.5 (176, t) and 25.1 ppm (152, t). MS *m*/*e* (relative abundance): 254, 252 (1.2, P^+), 173 (100, P^+–Br), 131 (11), 117 (17), 115 (13), 105 (11), 103 (11) and 91 (28), UV (cyclohexane): λ_{max} ($\log \epsilon$) 214 (4.23) and 271 nm (3.62). (Found: C, 61.8; H, 6.6. Calcd for $C_{13}H_{17}Br$: C, 61.7; H, 6.8%). The IR (neat) of **5** was completely in accord with the published data.[28]

Bicyclo[6.4.1]*trideca*-8,10,12-*triene* (**8**)

(a) *Reduction of* **4** *with LAH.* Compound **4** (380 mg, 1.5 mmol) was treated with LAH (230 mg, 6.0 mmol) in refluxing THF (25 ml) for 30 hr under N_2. Work-up and distillation yielded a mixture (235 mg) of **8**, **5** and two unidentified products having the same MS mol. wt. of 174 in a ratio of 5:4:3:1. Preparative TLC on silica gel–$AgNO_3$ (n-hexane–CH_2Cl_2 3:1) gave analytical samples. The triene **8** formed an oil, b.p. 120°/4 mm, IR (neat): 3012, 1619 and 734 cm^{-1}. PMR ($CDCl_3$): δ 6.43 (dd, C(10, 11)-H), 5.94 (m, C(9, 12)-H), 2.95 (dt, C(13)-H*anti*, J = 11.9, 1.5 Hz), 2.47 (m, allylic, 4H), 1.78 (d, C(13)-H*syn*, J = 11.9 Hz) and 1.8–1.2 (m, 8H), MS *m*/*e* (relative abundance): 174 (41, P^+), 159 (7), 145 (18), 131 (41), 117 (42), 105 (51), 104 (100) and 91 (49), UV (n-hexane): λ_{max} ($\log \epsilon$) 216 (4.11) and 272 nm (3.54). (Found: C, 89.6; H, 10.5. Calcd for $C_{13}H_{18}$: C, 89.6; H, 10.4%).

(b) *Reduction of* **4** *with* n-Bu_3SnH. A mixture of **4** (100 mg, 0.40 mmol) and n-Bu_3SnH (580 mg, 2.0 mmol) was heated at 50° for 4 hr under N_2. Preparative TLC on silica gel furnished a mixture (30 mg, n-hexane, R_f = 0.7) which was resolved successively into components **8** (16 mg, 23%, R_f = 0.5) and **5** (3 mg, 5%, R_f = 0.8) by means of preparative TLC on SiO_2–$AgNO_3$ (n-hexane–CH_2Cl_2 3:1).

13-*Methylbicyclo*[6.4.1]*trideca*-8,10,12-*triene* (**9**). Reaction of **4** (253 mg, 1.0 mmol) with MeLi (prepared from Li (42 mg, 6.0 mmol) and MeI (426 mg, 3.0 mmol)) in dry ether (10 ml) and HMPA (1 ml) at −20° for 20 min, followed by work-up and distillation, afforded **9** as an oil (125 mg, 67%), b.p. 120°/4 mm, IR (neat): 3013, 1623, 839 and 729 cm^{-1}. PMR ($CDCl_3$): δ 6.32 (dd, C(10, 11)-H), 5.96 (m, C(9, 12)-H), 3.23 (qt, C(13)-H, J = 7.2, 1.5 Hz), 2.43 (m, allylic, 4H), 1.9–1.1 (m, 8H) and 0.63 (d, Me, J = 7.2 Hz), MS *m*/*e* (relative abundance): 188 (65, P^+), 173 (41), 159 (56), 145 (49), 131 (64), 119 (52), 118 (100), 117 (87), 105 (60) and 91 (68). UV (cyclohexane): λ_{max} ($\log \epsilon$) 220 (4.17) and 283 nm (3.56). (Found: C, 89.4; H, 10.8. Calcd for $C_{14}H_{20}$: C, 89.3; H, 10.7%).

2,7-*Hexamethylenetropone* (**10**). Bromotropylidene **4** (300 mg, 1.19 mmol) was oxidized with $CrO_3 \cdot 2Py$[29] (prepared from CrO_3 (1.78 g, 17.8 mmol) and pyridine (2.82 g, 35.5 mmol) in dry CH_2Cl_2 (45 ml)) for 20 hr at room temp under N_2. Work-up and purification (preparative TLC on SiO_2 (PhH–n-hexane 1:1, R_f = 0.3) and GLC (SE 30, 30% on chromosorb)) gave **10** (28 mg, 16% considering the recovery of **4** (74 mg, 25%)). The tropone **10** formed an oil, b.p. 125°/5 mm, IR (neat): 3016, 1656, 1613, 1515, 1114 and 727 cm^{-1}, PMR ($CDCl_3$): δ 6.62 (s, 4H), 3.28, 2.48 (m, allylic, 4H) and 2.0–0.8 (m, 8H), PMR ($CDCl_3$–1.5 eq of CF_3COOH): δ 6.76 (s, 4H), 3.29, 2.55 (m, allylic, 4H) and 2.0–0.8 (m, 8H). MS *m*/*e* (relative abundance): 188 (43, P^+), 159 (67), 145 (92), 131 (80), 117 (80), 104 (100) and 91 (84), UV (n-hexane): λ_{max} ($\log \epsilon$) 202 (4.01), 238 (4.00) and 284 nm (3.62). (Found: *m*/*e* 188.1188. Calcd for $C_{13}H_{16}O$: *m*/*e* 188.1201).

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