Pergamon

Tetrahedron Letters, Vol. 37, No. 47, pp. 8605-8608, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01967-3

Synthesis, Chemical Trapping and Dimerization of Tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene, the Consummate Member of a Series of Pyramidalized Alkenes

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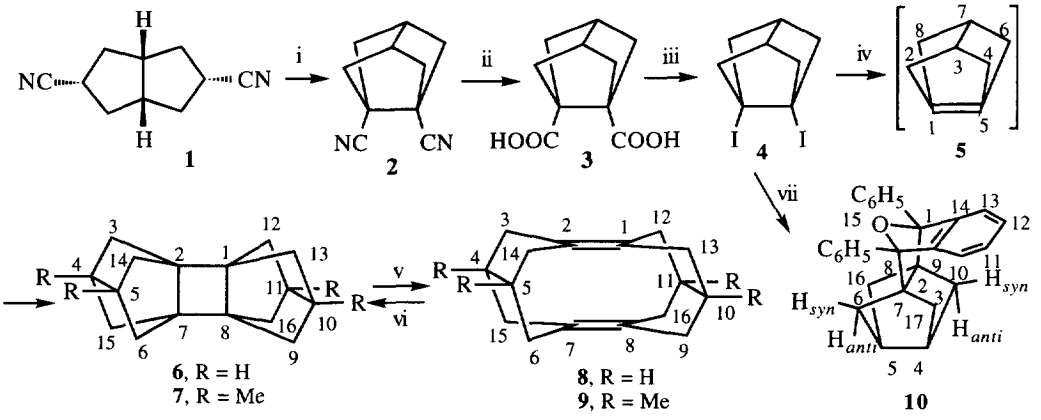
Abstract: The synthesis of tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene, **5**, the consummate member of a series of pyramidalized alkenes, has been carried out by deiodination of **4** in different ways. Reaction of **4** with sodium in boiling dioxane gave in good yield diene **8**, whose formation can be easily explained through the intermediacy of **5** and its cyclobutane dimer **6**. Reaction of **4** with *t*-butyllithium in THF at -78 °C in the presence of 1,3-diphenylisobenzofurane gave **10**, a Diels-Alder adduct derived from **5**.

Last year we published[1] the synthesis of the 3,7-dimethyl derivative of the pyramidalized alkene **5** by reaction of the corresponding dimethyl derivative of diiodide **4** with *t*-butyllithium in THF at -78 °C or with sodium in boiling dioxane. This highly pyramidalized alkene could be trapped as Diels-Alder adduct with different dienes, while in the absence of trapping agents, it dimerized to cyclobutane derivative **7**, which experienced a thermal [2 + 2] retrocycloaddition reaction to diene **9**. In the preceding communication[2] we have published alternative procedures to obtain cyclobutane dimer **7** in pure form, by reaction of the corresponding diiodide with sodium-potassium alloy in THF or by photocyclization of diene **9**. Also, the low temperature X-ray diffraction analysis of **7** and a DSC study of its [2 + 2] retrocycloaddition to **9** has been described in this paper.

In the present paper we describe the synthesis of tricyclo[3.3.0.0^{3,7}]oct-1(5)-ene, **5**, the consummate member of a series of pyramidalized alkenes, to which Borden recently devoted a review[3].

The methodology used for the preparation of **5** is similar to that previously developed for the synthesis of its 3,7-dimethyl derivative. Dinitrile **1**[4] was transformed into tricyclo[3.3.0.0^{3,7}]octane-1,5-dicarbonitrile, **2**, in 28.5 % yield, by reaction with two equivalents of solid lithium diisopropylamide in anhydrous THF followed by iodine-induced oxidative intramolecular coupling, in a similar manner to that previously described for the corresponding dimethyl ester[4]. Basic hydrolysis of **2** gave diacid **3** in 80 % yield, which was alternatively obtained in 97 % yield by saponification of the corresponding dimethyl ester[4]. Although the global yield of both procedures for the preparation of diacid **3** from dinitrile **1** are similar, the one passing through dinitrile **2** is two steps shorter, and consequently more convenient. Iododecarboxylation of **3** with iodosobenzene diacetate and iodine, following the Moriarty[5] modification of the Suárez[6] procedure gave 1,5-diiodotricyclo[3.3.0.0^{3,7}]octane, **4**, in 34% yield. This low yield compared with that obtained in the preparation of the corresponding 3,7-dimethyl derivative (65 %)[1] might be due to the greater volatility of **4**. Reaction of **4** with *t*-butyllithium in anhydrous THF in the presence of 1,3-diphenylisobenzofurane gave compound **10** in 75 % yield.

Reaction of **4** with sodium in dioxane under reflux gave diene **8** in 80% isolated yield, purified by column chromatography (60-200 μm silica gel / hexane) and crystallization from chloroform. These results are very similar to those previously observed starting from the 3,7-dimethyl derivative of **4**. Moreover, irradiation of a cyclohexane solution of **8** in a quartz reactor using a 125 W medium-pressure mercury lamp, followed by



i) a) LDA, THF, b) I_2; ii) a) KOH, MeOH, H_2O, Δ, b) HCl; iii) Iodosobenzene diacetate, I_2, hν; iv) Na, dioxane, reflux; v) Δ; vi) hν; vii) *t*-BuLi, THF, 1,3-Diphenylisobenzofurane.

Scheme 1. Synthesis, chemical trapping and dimerization of tricyclo[3.3.0.$0^{3,7}$]oct-1(5)-ene, **5**.

concentration and crystallization from chloroform avoiding heating at any moment gave a mixture of cyclobutane **6** and diene **8** in the approximate ratio 8:2. We were unable to obtain pure **6** due to its easy conversion into **8**. A $CDCl_3$ solution of the above 8:2 mixture of **6** and **8** at 20 °C was completely converted into **8** in 18-20 h.

The new compounds herein described (**2**, **3**, **4**, **6**, **8** and **10**) have been fully characterized on the basis of their spectroscopic data (IR, ^1H and ^{13}C NMR and MS)[7] and elemental analysis (C, H, N, I: ±0.3%). Assignment of the NMR spectra was straightforward, except for **10** which was assigned by comparison with its 4,5-dimethyl derivative[1].

The greater instability of cyclobutane dimer **6** in front of diene **8** as compared with its tetramethyl derivative **7** (see preceding paper) can be understood on the basis of theoretical calculations. Table 1 shows the enthalpy differences between the cyclobutane dimers **6** and **7** and the corresponding dienes **8** and **9**. For the *ab initio* calculations, the geometries were optimized at the HF/3-21G level[8]. Frequency analysis was performed to verify the minimum-energy nature of the stationary points. Single-point calculations were carried out by using the HF/3-21G optimized geometry at the MP2 level[9] with the 3-21G and 6-31G* basis sets[10]. Zero-point energy and thermal (298 K) corrections were determined from the HF/3-21G geometries by using the standard formula for harmonic oscillator-rigid rotor as implemented in Gaussian 94[11]. Moreover, the differences in energy were determined from MM2 calculations.

Both HF and MP2 results indicate a clear preference for diene **9** *vs* cyclobutane derivative **7**. The enthalpy difference is around - 41 kcal mol^{-1} at the MP2 level irrespective of the basis set. This value is slightly lower than that calculated by MM2 (around -43.2 kcal mol^{-1}) and all of them are in acceptable agreement with the values obtained by DSC[2] (-45.6 ± 1.1 and -44.4 ± 0.5 kcal mol^{-1} for the dynamic and isothermic experiments, respectively). Such an enthalpy difference must be mostly associated to the release of internal strain, due to the opening of the cyclobutane ring.

Worthy of note, the calculated enthalpy differences for the opening of the demethylated cyclobutane derivative **6** to diene **8** is consistently 3-4 kcal mol^{-1} larger in absolute value than that calculated for the conversion of **7** to **9**. This fact is likely related to the relative destabilization of diene **9** due to overcrowding around the C4-C5 (C10-C11) bonds. Table 2 collects the carbocyclic C-C bond lengths of these compounds calculated by MM2 and *ab initio* procedures, together with the experimental values obtained for **7** and **9**, which show a reasonable agreement between them. As can be seen from Table 2, the length of the C4-C5 (C10-C11) bonds decreases in passing from cyclobutane derivatives **6** and **7** to dienes **8** and **9**, respectively. The experimental length of these bonds in diene **9** is 0.027 Å shorter than the corresponding bond length in **7** and

thus, an specially significant increase of the overcrowding in diene **9** due to the tetrasubstituted nature of the carbon atoms implicated in these bonds, must be expected. The relative unstabilization of **7** in passing to **9** as compared with the corresponding conversion of **6** to **8** must be also apparent, although not in the same degree, in their transition states, which could explain the greater kinetic stability of **7** as compared with **6**.

$\Delta\Delta H_f$	MM2	HF/3-21G	HF/6-31G*	MP2/3-21G	MP2/6-31G*
ΔH_f**8** - ΔH_f**6**	-46.1	-51.5	-61.1	-44.2	-45.6
ΔH_f**9** - ΔH_f**7**	-43.2	-47.7	-53.9	-41.6	-41.2

Table 1. Calculated enthalpy differences (kcal mol^{-1}) for the [2+2]retrocycloadditions of the cyclobutane dimers **6** and **7** to the corresponding dienes **8** and **9**.

Compound	Bond	X-Ray[a]	MM2	HF/3-21G
6	C1-C2	-	1.519	1.546
	C1-C8	-	1.606	1.620
	C1-C12	-	1.528	1.544
	C3-C4	-	1.545	1.561
	C4-C5	-	1.584	1.632
7	C1-C2	1.535(4)	1.519	1.546
	C1-C8	1.594(4)	1.604	1.621
	C1-C12	1.524(4)	1.527	1.540
	C3-C4	1.543(4)	1.547	1.557
	C4-C5	1.649(4)	1.591	1.667
8	C1-C2	-	1.343	1.314
	C1-C12	-	1.507	1.518
	C3-C4	-	1.545	1.558
	C4-C5	-	1.559	1.587
9	C1-C2	1.336(3)	1.343	1.314
	C1-C12	1.515(4)	1.505	1.515
	C3-C4	1.539(4)	1.551	1.559
	C4-C5	1.622(4)	1.571	1.612

Table 2. Experimental and calculated bond distances (Å) for cyclobutane dimers **6** and **7** and dienes **8** and **9**.
[a] In some cases these values were averaged to remove slight deviations from D_{2h} symmetry in the crystal[12].

The generation and reactions of tricyclo[3.3.0.$0^{3,7}$]oct-1(5)-ene herein described open the way for a convergent synthesis of dodecahedrane[13].

Acknowledgements

We thank the *Serveis Científico-Tècnics* of the University of Barcelona and particularly Dr. *M. Feliz* and Dr. *A. Linares* for recording the NMR spectra, Dr. A. Marín for registering the MS spectra, the *Centre de Supercomputació de Catalunya* for computational facilities, Ms. *P. Domenech* from the *Centro de Investigación y Desarrollo* (C.I.D.) (Barcelona, Spain) for carrying out the elemental analyses, and the *Comissionat per a Universitats i Recerca* (Generalitat de Catalunya) for Grants GRQ 94-1035 and 1995SGR 00583.

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7. *Analytical data of the new compounds*:
Tricyclo[3.3.0.$0^{3,7}$]octane-1,5-dicarbonitrile, **2**: M.p. 156-157 °C (subl. 110 °C / 0.1 Torr); IR (KBr) ν: 2231 (CN st) cm^{-1}; MS (CI, NH_3), m/z (%): 160 (10), 159 (M^+ + 1, 100); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.95 (d, J = 7.7 Hz, 4 H) and 2.04 (d, J = 7.7 Hz, 4 H) [2(4,6,8)-H_2], 2.61 [broad s, 2 H, 3(7)-H]; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 36.6 [CH, C3(7)], 42.4 [C, C1(5)], 51.5 [CH_2, C2(4,6,8)], 118.6 (C, CN).
Tricyclo[3.3.0.$0^{3,7}$]octane-1,5-dicarboxylic acid, **3**: M.p. 130 °C (dec.) ($CHCl_3$); IR (KBr) ν: 3160 (OH st), 1700 (C=O st) cm^{-1}. ^1H NMR (200 MHz, DMSO-d_6) δ: 1.68 [s, 8 H, 2(4,6,8)-H_2] 2.35 [s, 2 H, 3(7)-H], 12.1 (broad signal, 2 H, COOH); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 37.3 [CH, C3(7)], 50.1 [CH_2, C2(4,6,8)], 57.7 [C, C1(5)], 179.6 (C, CO).
1,5-Diiodotricyclo[3.3.0.$0^{3,7}$]octane, **4**: M.p. 78-79 °C ($CHCl_3$); IR (KBr) ν: 2987, 2931, 2886, 1473, 1280, 1257, 1234, 1165, 1130, 1107, 1091, 995, 950, 926, 897, 801 cm^{-1}. MS (EI), m/z (%): 360 ($M^{\cdot+}$, 4), 233 (M^+ - I, 33), 106 (M^+ - 2I, 100), 105 (38), 91 (38), 79 (25), 78 (31), 77 (16), 65 (14); ^1H NMR (300 MHz, $CDCl_3$) δ: 2.03 [m, 6 H, 3(7)-H and 2(4,6,8)-H_a] 2.12 [broad d, J = 8.2 Hz, 4 H, 2(4,6,8)-H_b]; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 38.4 [CH, C3(7)], 44.3 [C, C1(5)], 59.4 [CH_2, C2(4,6,8)].
Heptacyclo[8.2.1.$1^{2,5}$.$1^{4,7}$.$1^{8,11}$.$0^{1,8}$.$0^{2,7}$]hexadecane, **6**: (Data from the spectra of a 8:2 mixture of **6** and **8**) ^1H NMR (300 MHz, $CDCl_3$) δ: 1.42 [broad d, J = 8.8 Hz, 8 H, 3(6,9,12,13,14,15,16)-H*exo*] 1.52 [d, J = 8.8 Hz, 8 H, 3(6,9,12,13,14,15,16)-H*endo*], 2.19 [broad s, 4 H, 4(5,10,11)-H]; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 39.4 [CH, C4(5,10,11)], 48.2 [CH_2, C3(6,9,12,13,14,15,16)], 49.4 [C, C1(2,7,8)].
Pentacyclo[8.2.1.$1^{2,5}$.$1^{4,7}$.$1^{8,11}$]hexadeca-1,7-diene, **8**: M.p. 165-168 °C ($CHCl_3$); IR (KBr) ν: 2944, 2924, 2894, 2864, 2836, 1697, 1451, 1311, 1254, 1146, 780, 741 cm^{-1}. MS (EI), m/z (%): 213 (16), 212 ($M^{\cdot+}$, 100), 197 (7), 169 (13), 143 (21), 131 (11), 130 (12), 129 (21), 128 (15), 117 (10), 115 (11), 107 (12), 106 (19), 105 (11), 91 (36), 79 (16), 77 (16), 65 (10); ^1H NMR (300 MHz, $CDCl_3$) δ: 2.17 [dd, J = 12.5 Hz, J' = 7.0 Hz, 8 H, 3(6,9,12,13,14,15,16)-H*exo*] 2.43 [d, J = 12.5 Hz, 8 H, 3(6,9,12,13,14,15,16)-H*endo*], 2.37 [m, 4 H, 4(5,10,11)-H]; ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 33.7 [CH, C4(5,10,11)], 39.7 [CH_2, C3(6,9,12,13,14,15,16)], 133.0 [C, C1(2,7,8)].
1,8-Diphenyl-15-oxahexacyclo[6.6.1.1^{2,5}.$1^{4,7}$.$0^{2,7}$.$0^{9,14}$]heptadeca-9,11,13-triene, **10**: M.p. 176 -177 °C (isopropanol); IR (KBr) ν: 3046, 3023, 3000, 2965, 2931, 2885, 1600, 1495, 1472, 1445, 1347, 1305, 1284, 1172, 1066, 980, 925, 887, 769, 747, 700, 671 cm^{-1}. MS (EI), m/z (%): 376 ($M^{\cdot+}$, 5), 334 (15), 272 (24), 271 (100), 270 (16), 241 (10), 229 (25), 215 (11), 165 (13), 105 (28), 77 (16); ^1H NMR (500 MHz, $CDCl_3$) δ: 0.91 [dd, J = 8.0 Hz, J' = 3.0 Hz, 2 H, 3(17)-H*syn*], 1.48 [dd, J = 8.0 Hz, J' = 3.0 Hz, 2 H, 6(16)-H*syn*], 1.57 [dd, J = 8.0 Hz, J' = 2.0 Hz, 2 H, 6(16)-H*anti*], 1.68 [dd, J = 8.0 Hz, J' = 2.0 Hz, 2 H, 3(17)-H*anti*], 2.42 [broad s, 2 H, 4(5)-H] 6.95 [m, 2 H, 11(12)-H], 7.09 [m, 2 H, 10(13)-H], 7.36 (t, J = 7.5 Hz, 2 H, H*para*), 7.44 (m, 4 H, H*meta*), 7.62 (d, J = 7.0 Hz, 4 H, H*ortho*); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 39.9 (CH, C4), 40.7 (CH, C5), 47.4 [CH_2, C6(16)], 47.5 [CH_2, C3(17)], 66.5 [C, C2(7)], 87.8 [C, C1(8)], 119.9 [CH, C11(12)], 125.8 (CH, Ar-C*ortho*), 126.4 [CH, C10(13)], 127.3 (CH, Ar-C*para*), 128.3 (CH, Ar-C*meta*), 138.3 (C, Ar-C*ipso*), 148.4 [C, C9(14)].

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(*Received in UK* 26 *September* 1996; *accepted* 4 *October* 1996)