Pergamon

Tetrahedron Letters, Vol. 37, No. 47, pp. 8601-8604, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01966-1

Low Temperature X-Ray Diffraction Analysis of 4,5,10,11-Tetramethylheptacyclo[8.2.1.1^{2,5}.1^{4,7}.1^{8,11}.0^{1,8}.0^{2,7}]hexadecane: DSC, MM2 and ^{1}H NMR Study of its [2 + 2]Retrocycloaddition to an Isomeric Diene

Pelayo Camps,*[a] Mercè Font-Bardia,[b] Francesc Pérez,[a] Lluis Solà,[c] Xavier Solans[b] and Santiago Vázquez[a]

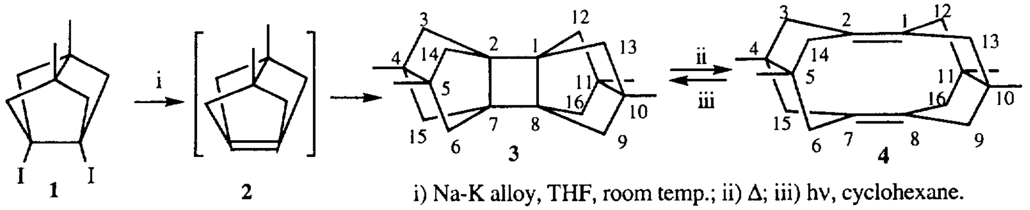
[a]Laboratori de Química Farmacèutica, Facultat de Farmàcia, Universitat de Barcelona, Av. Diagonal s/n; E-08028 Barcelona, Spain. [b]Departament de Cristal.lografia, Mineralogia i Dipòsits Minerals, Facultat de Geologia, Universitat de Barcelona, Av. Martí Franqués; E-08028 Barcelona, Spain. [c]Servei de Calorimetria de Reacció, Departament de Química Orgànica, Facultat de Química, Universitat de Barcelona, Av. Martí Franqués 1; E-08028 Barcelona, Spain.

Abstract: The synthesis of pure **3** has been achieved by deiodination of **1** with Na-K alloy at r.t. and by [2+2] photocyclization of diene **4**. X-ray diffraction analysis at -30°C of the thermally unstable **3** shows the cyclobutane ring to be highly rectangular with large central and short lateral bonds. Also, the C4-C5 and C10-C11 bonds in **3** and diene **4** are very large. A clear neat DSC conversion of **3** to **4** allowed us to obtain the ΔH and the Ea values for this transformation. ΔH is in good agreement with MM2 calculations, while Ea compares well with kinetic measurements in $CDCl_3$ solution.

Last year, we published[1] the first synthesis of 3,7-dimethyltricyclo[3.3.0.0^{3,7}]oct-1(5)-ene, **2**, by reaction of diiodo derivative **1** with *t*-butyllithium in THF or with melted sodium in dioxane under reflux. This highly reactive pyramidalized alkene was trapped with 1,3-diphenylisobenzofurane and with 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene and, in the absence of a trapping agent, cyclobutane dimer **3** or diene **4** were formed depending on the reaction conditions. Diene **4** was cleanly obtained in high yield as the only reaction product when deiodination was carried out with sodium in refluxing dioxane, whereas we were unable to obtain pure **3** in the reaction of **1** with *t*-butyllithium at low temperature due to the formation of by-products derived from the reaction of **2** with the reagent.

Recently Borden[2] published a review on pyramidalized alkenes of a series of which **2** is a dimethyl derivative of its consummate member, what prompt us to publish our results on both **2** and its demethylated analogue in this and the following paper.

In this paper, we describe the preparation of pure cyclobutane dimer **3** by two alternative procedures. The first one implies the reaction of diiodo derivative **1** with sodium-potassium alloy (22/78)[3] in anhydrous THF (Scheme 1). Since this alloy is liquid at room temperature and more reactive than sodium alone, deiodination of **1** under these conditions takes place smoothly at room temperature, thus preventing the [2 +2] retrocycloaddition of **3** to diene **4**. Purification of the product was easily carried out by crystallization of the crude product from chloroform, avoiding at any moment heating of the solution. Alternatively, compound **3** was obtained quantitatively from diene **4** by photocyclization in cyclohexane solution, using a quartz photoreactor and a low-pressure 125 W mercury lamp. Compound **3** has shown to be stable for extended periods of time at low temperature (-30 °C). However, in $CDCl_3$ solution at 20 °C, **3** transforms into **4**, 50% conversion being attained after 50 h, a percentage conversion which is attained in only 2 h at 50 °C. Complete conversion of **3** into **4** is observed after 3 h refluxing in dioxane solution.



i) Na-K alloy, THF, room temp.; ii) Δ; iii) hv, cyclohexane.

Scheme 1. Preparation and reactions of cyclobutane dimer **3**.

In spite of the fact that **3** is thermally unstable, we have been able of fully characterize this compound[4], including an X-ray diffraction analysis performed at -30 °C (Figure 1)[5,6]. As can be seen from Figure 1, the cyclobutane ring of **3** is quite rectangular with large central (1.594 ± 0.004 Å) and short lateral bonds (1.535 ± 0.004 Å). Also, large C4-C5 and C10-C11 bonds (1.649 ± 0.004 Å) (systematic numbering) are observed. The large values of the central cyclobutane and C4-C5 (C10-C11) bonds seem to be partly due to their position into the tricyclo[3.3.0.0^{3,7}]octane subunit, as it is the case for the same kind of bonds in the Diels-Alder adduct of **2** with 11,12-dimethylene-9,10-dihydro-9,10-ethanoanthracene[1]. The short lateral cyclobutane bonds of **3** together with the large central ones is in accord with the easy conversion of **3** to diene **4**. X-ray diffraction analysis of diene **4** (Figure 2)[6,7] also shows large C4-C5 (C10-C11) bonds (1.622 ± 0.004 Å), a fact that must contribute to reduce the crowding around these bonds.

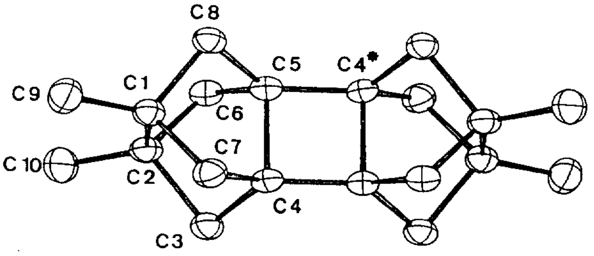


Figure 1. Crystal structure (ORTEP) of cyclobutane dimer 3. The numbering is that used for the X-ray analysis. Selected distances [Å]: C1-C2 1.649(4), C4-C5 1.594(4), C5-C4* 1.535(4).

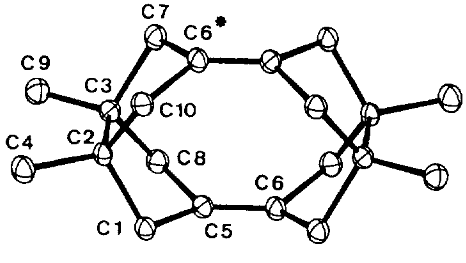


Figure 2. Crystal structure (ORTEP) of diene 4. The numbering is that used for the X-ray analysis. Selected distances [Å]: C2-C3 1.622(4), C5-C6 1.336(3), C5/C6* 2.989(3).

The neat thermally induced conversion of **3** into **4** could be nicely followed by Differential Scanning Calorimetry[8] working in both dynamic and isothermal modes[9] in closed capsules which allowed us to evaluate the reaction enthalpy, the activation energy and the Arrehnius preexponential factor.

The dynamic experiments were carried out at different heating rates (5, 7.5, 10 and 15 K min^{-1}) using similar amounts of sample (around 0.4 mg). Rather small amounts of products were used in the DSC experiments in order to minimize temperature gradients inside the sample. In a typical experiment, when **3** was heated at a heating rate of 10 K min^{-1}, two exothermic processes around 375 and 431 K were observed prior to the endothermic melting process around 460 K which was preceded by another much less endothermic process at around 440 K (Figure 3a). When heating was stopped just after the first and more exothermic process and the sample thus obtained was analyzed by ^{1}H NMR spectroscopy, the only observed product was diene **4** as it was the case after the melting process. When solid diene **4** was submitted to similar DSC conditions, only the second exothermic process and the two endothermic ones were observed (Figure 3b). The second exothermic process was not observed, when a sample of cyclobutane dimer **3** or diene **4** was submitted to DSC analysis, after having been melted in a DSC experiment and then allowed to solidify. This second exothermic process and the first endothermic one might be associated to changes in the crystalline form.

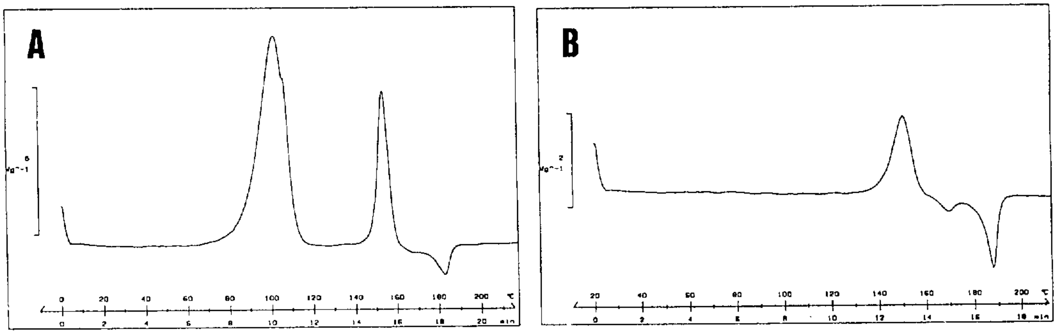


Figure 3. A) DSC diagram^a of cyclobutane dimer **3**. B) DSC diagram^a of diene **4**.
^{a}Heating rate: 10 K min^{-1}; Reaction heat: W g^{-1}.

The heat of the reaction was determined from the integration of the heat flow signal over the studied temperature range (Table 1). Since the heat capacity change during the reaction is small, the heat of the reaction can be identified with the enthalpy of reaction. A mean value of -45.6 ± 1.1 kcal mol^{-1} for ΔH_r was obtained. By applying the isoconversion method of Vyazovkin[10], in which no kinetic model is assumed, to the data arising from the dynamic experiments, an activation energy of 24.4 ± 0.5 kcal mol^{-1} was obtained. Following Ozawa's method[11] and assuming a first order kinetic model, an almost coincident activation energy value of 24.9 ± 0.5 kcal mol^{-1} and a logarithmic Arrehnius preexponential factor of 29.1 were obtained.

Moreover, three isothermal runs were performed at 373, 368 and 363 K. Blank curves were determined by using the same sample after reaction had taken place. This approach ensures an optimum result since a sample with exactly the same mass and very similar heat capacity is used as the blank. A mean value of - 44.4 ± 0.5 kcal mol^{-1} was obtained in this way for ΔH_r in the isothermal runs (Table 1). By applying a first order kinetic model to the corresponding data sets, an activation energy of 25.9 ± 4.2 kcal mol^{-1} and a logarithmic Arrehnius preexponential factor of 30.7 ± 5.8 were obtained. As can be seen from Table 1, a very good agreement between the data obtained from the dynamic and the isothermic experiments has been found.

Dynamic experiments		Isothermic experiments	
Heating rate (K min^{-1})	Δ_rH (kcal mol^{-1})	Temperature (K)	Δ_rH (kcal mol^{-1})
5	-45.2	363	-44.3
7.5	-45.7	368	-44.0
10	-44.5	373	-45.0
15	-47.1	-	-

Table 1. Enthalpy of the conversion of **3** to **4**, obtained by DSC under dynamic and isothermic conditions.

These results are in good agreement with force-field calculations carried out with the MM2 (91) program, which predicts a $\Delta H_f = -1.35$ kcal mol^{-1} and a $E_{str} = 48.07$ kcal mol^{-1} for diene **4** and a $\Delta H_f = 41.81$ kcal mol^{-1} and a $E_{str} = 129.35$ kcal mol^{-1} for cyclobutane dimer **3**, being thus $\Delta\Delta H_f = \Delta H_r = -43.16$ kcal mol^{-1} and $\Delta\Delta E_{str} = -81.28$ kcal mol^{-1} for the retrocycloaddition process.

The kinetic of this transformation was also followed by ^{1}H NMR in $CDCl_3$ solution at 20 and 50 °C. The ratio **3**:**4** was easily obtained by integration of the clearly resolved methylene signals of both compounds. The plot of ln[**3**] *vs* time for both temperatures gave straight lines (first order kinetics) ($r^2 = 0.990$, $n = 9$ for the process at 20 °C and $r^2 = 0.998$, $n = 16$ for the process at 50 °C) with rate constant values of $K_{20} = 1.43$ min^{-1} and $K_{50} = 5.29$ min^{-1}. From these rate constant values, by using the Arrehnius equation, an activation energy of 22.7 kcal mol^{-1} was calculated, in good agreement with the value obtained by DSC for the conversion of **3** to **4** in the solid state.

In the following paper, the synthesis, chemical trapping and dimerization of the demethyl derivative of **2**, the consummate member of this series of pyramidalized alkenes is described, the cyclobutane dimer being much unstable in this case.

Acknowledgements

We thank the *Serveis Científico-Tècnics* of the University of Barcelona and particularly Dr. *A. Linares* for recording the NMR spectra and Dr. *A. Marín* for registering the MS spectra. We also thank the *Comissionat per a Universitats i Recerca* (Generalitat de Catalunya) for Grants GRQ 94-1035 and 1995SGR 00583.

References and Notes

1. Camps, P.; Font-Bardia, M.; Pérez, F.; Solans, X.; Vázquez, S., *Angew. Chem.* **1995**, *107*, 1011-1012; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 912-914.
2. Borden, W. T., *Synlett* **1996**, 711-719.
3. Sodium-potassium alloy was purchased from Aldrich.
4. Analytical data of **3**: M.p. 161-162 °C; IR (KBr) ν: 2950 (s), 2922 (s), 2870 (s), 1476 (m), 1448 (m), 1373 (m), 1278 (m), 1192 (w), 1135 (w) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.09 (s, CH_3), 1.35 (d, J = 6.9 Hz) and 1.70 (d, J = 6.9 Hz) (CH_2). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ: 16.5 (CH_3), 50.9 (C), 51.8 (C), 54.9 (CH_2). GC/MS (electron impact, 70 eV): The GC rt and the MS spectra of **3** coincides with those previously obtained for diene **4**[1], into which it must be converted in the GC/MS conditions.
5. Crystal data for **3**: monoclinic, $P2_1/a$, a = 610.5(4), b = 1232.2(2), c = 1009.50(9) pm [$\alpha = \gamma = 90°$, $\beta = 92.13(2)°$]; 2221 measured reflections all of them independent, of which 1001 with $I > 2\sigma(I)$ were used for the refinement; $R = 0.0699$, $wR = 0.1820$.
6. Further details of the crystal structure investigations may be obtained from the Cambridge Crystallographic Data Centre.
7. Crystal data for **4**: monoclinic, $P2_1/n$, a = 683.7(8), b = 1188.2(8), c = 964.8(6) pm [$\alpha = \gamma = 90°$, $\beta = 94.93(7)°$]; 2271 measured reflections all of them independent, of which 1065 with $I > 2\sigma(I)$ were used for the refinement; $R = 0.0471$, $wR = 0.1126$.
8. Cammenga, H. K.; Epple, M., *Angew. Chem.* **1995**, *107*, 1284-1301; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1171-1187.
9. Duswalt, A. A., *Thermochim. Acta* **1974**, *8*, 57-68.
10. a) Vyazovkin, S. V.; Lesnikovick, A. I., *Thermochim. Acta* **1992**, *203*, 177-185. b) Vyazovkin, S. V.; Linert, W., *Anal. Chim. Acta* **1994**, *295*, 101-107.
11. Ozawa, T., *J. Thermal Anal.* **1970**, *2*, 301-324.

(*Received in UK* 26 *September* 1996; *revised* 2 *October* 1996; *accepted* 4 *October* 1996)