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2D ¹H and ¹³C NMR evidences of the [2 + 2] autodimerization of 2-benzyl-5-benzylidene cyclopentanone yielding two different diphenyl, dispiro cyclobutane derivatives

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Abstract

The ene-ene [2 + 2] cycloaddition of 2-benzyl-5-benzylidenecyclopentanone proceeds smoothly and spontaneously in benzene-d₆ or deuteriochloroform solution to give two different diphenyl dispiro [4.1.4.1] dodecan-4,11-diones. Detailed ¹H and ¹³C 2DNMR spectroscopy (COSY, HMQC, HMBC) were performed in order to prove the existence in solution of two cyclobutane derivatives, one a previously described photodimer obtained by the UV irradiation of crystals of 2-benzyl-5-benzylidenecyclopentanone. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

It is well known that [2+2] cycloaddition are not easy under thermal conditions. Under vigorous conditions, cycloaddition may occur by steps via diradicals and not in a concerted fashion.

Likewise, photochemical [2 + 2] cycloaddition are very common, although some of these proceed also by a stepwise sequence.

In cycloaddition, two new bonds are formed by use of π electrons of the reactants. The concerted

reaction results from overlaps of the orbital of one molecule with the orbital of the other.

On the other hand, the 1,4 cycloaddition [1,2] reactions have been known for many years. In the cases of 1,4 cycloaddition in benzylidenecycloalkanones, they yield dimers with structures well established and different from those of the [2 + 2] cycloaddition reaction.

During work on the stereochemistry of cyclic systems Cornubert et al. [3] investigated stereoisomerism in substituted cyclopentanones and cyclohexanones, preparing the 2-benzyl-5-benzylidene cyclopentanone (1). Compound 1 was unstable in light and upon irradiation Cornubert reported the formation of a phototrimer, however years later,

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G.C. Forward [4] established the correct structure of the irradiation product as the photodimer (2) and demonstrated a head-tail dimerization.

The low resolution ¹H NMR spectrum did not mention detailed features (δ ppm 7.37, 20H, aromatic; 4.28, 2H, cyclobutane protons and 0.8–3.0 multiplet, 14H, methylene). With new high resolution NMR spectra currently available, we undertook this work in order to demonstrate that the photodimer **2** described by Forward and Whiting [4] already exist in the NMR tube solution of 2-benzyl-5-benzylidene cyclopentanone **1**.

2. Results and discussion

In the course of our search of the reaction between 2,5-dibenzylidenecyclopentanone **3** with 6-amino-1,3-dimethyl uracil (**4**) using phase transfer conditions, we were able to isolate in good yields and identify by spectroscopic methods (NMR, MS, IR) the oxidized monoadduct **5**, as well as a reduced derivative whose structure was established as 2-benzyl-5-benzylidene cyclopentanone **1** in good yields. Thereby, we undertake, using 2D high resolution NMR spectra, the structural identification of compound (**5**) as well as of compounds (**2**) and (**6**), formed in solution at the expense of (**1**).

Compound 5 showed at MS a molecular ion m/zM⁺ 395 which match well with the molecular formula C₂₅H₂₁N₃O₂. The ¹H NMR spectrum showed a triplet $\delta = 7.67$, ⁴J = 2.7 Hz for the vinyl proton; two NMe groups at $\delta = 3.86$, s and 3.32, s, as well as ten aromatic protons between $\delta = 7.6$ and 7.1 assigned to the phenyl groups. At $\delta = 3.13$ and 2.78 four protons were observed corresponding to the methylenes of the five member ring. Using these data and the knowledge of the reaction mechanism previously proposed by us [5–8], we assigned the structure **5** for this adduct.

On the other hand, product 1, isolated as pale yellowish crystals, showed at MS a molecular ion m/z M⁺ 262 which matched well with molecular formula C₁₉H₁₈O. The ¹H NMR (C₆D₆) showed a triplet at $\delta = 7.66$, ⁴J = 2.7 Hz and the usual ten aromatic protons between $\delta = 7.3$ and 7.0. We also observed an AMX pattern of the benzylic methyl-

ene at $\delta_A = 3.34$, dd, J = 5.0, -14.0; $\delta_M = 2.51$, dd, J = 9.0; -14.0; $\delta_X = 2.26$ m and the remaining protons for the methylene groups of the cyclopentanone moiety at $\delta = 2.45$, m, 2.16, m; 1.63 and 1.15, m (Fig. 1a).

Surprisingly, the 1D 1 H NMR spectrum recorded in CDCl₃ and C₆D₆ of compound 1 was time depending due to the formation of two new products detected through the new protons signals displayed (Figs. 2 and 3).

2.1. $2D^{-1}H NMR$

At first, we should point out that the ratio between product 1 and the new products formed in solution was dependent upon the chosen solvent. In this way, compound 1 after 1 week in DMSO- d_6 solution at room temperature, displayed in its proton NMR spectrum only traces of the compound 2, easily recognized by the small singlet at $\delta = 4.19$, as well as the small multiples at $\delta = 3.06$, 2.37, 2.21, 1.92, 1.67, 1.37 and 0.91. When the NMR solvent was C_6D_6 and recorded immediately after dissolving, only traces of the product 2 were initially detected (see Fig. 1). After 12 h, the proton NMR spectrum displayed signals that enabled the assignment of the ratio 1:2 of $\approx 8:2$, respectively. Nevertheless, when the solvent was CDCl₃ and after 12 h at room temperature (see Fig. 2), a mixture of 1, 2 and 6 whose ratio was calculated as 16:61:23, respectively was detected.

In order to establish unambiguously that the new signals of the products formed in solution corresponded to the photoadducts 2 and 6, we prepared 2 through the UV irradiation of 2-benzyl-5-benzylidene cyclopentanone 1 (see Scheme 1) using the procedures described previously by Forward and Whiting [4].

The high resolution ¹H NMR spectrum (CDCl₃, 500 MHz) of compound **2** (see Fig. 3 Scheme 2) showed at $\delta = 6.86$, 2H_{ortho}, 7.10, 1H_{para} and 7.17, 2H_{meta} for the phenyl ring of the benzyl moiety. In addition, we observed the aromatic protons of the phenyls attached to the cyclobutane moiety at $\delta = 7.35$, 2H_{ortho}, 7.32, 2H_{meta} and 7.23, 1H_{para} (the assignment was made through a HMBC experiment), a sharp singlet at $\delta = 4.25$, assigned to both methine of the cyclobu-

tane ring and an AMX pattern at $\delta_A = 2.59$, dd, J = 4.5; -14.0; $\delta_M = 2.10$, m and $\delta_X = 1.08$, dd, J = 11.0; -14.0, assigned to the benzylic methylene and the methine where this was attached. The larger chemical shift difference between both protons of each benzylic methylene ($\Delta \delta = 1.51$) suggested that the benzylic proton at $\delta = 1.08$ suffered a symmetrical diamagnetic shielding for only one proton of each methylene through the magnetic anisotropy of the phenyl rings [9–11] attached to the cyclobutane moiety, as is shown in Fig. 4. This spectroscopic behaviour matched well with the structure previously established via X-ray crystallographic studies [12].

On the other hand, using the vertical enhancement of the signal at $\delta = 4.25$, we were able to observe two additional singlets at $\delta = 4.23$ and 4.18, that we assigned to traces of a new and non-described asymmetric photoadduct **6**. Thus, the two cyclobutane hydrogens with the previously mentioned chemical shifts were magnetically non-equivalent and were not observable coupled. As was observed through the COSY spectrum [13] (see Fig. 2, insert) of the mixture of **1**, **2** and **6**, which displayed cross peaks for the compound **6**; these signals enabled us to detect evidence of the chemical shifts from the protons of both benzylic methylene at $\delta = 1.14$, dd, J = 11.0; -14.0 and



Fig. 1. (a) ¹H NMR 500 MHz (C_6D_6) of compound 1 immediately as solved. (b) ¹H NMR 500 MHz (C_6D_6) of compound 1 after 12 h. (c) COSY spectrum of compound 1 after 12 h.



Fig. 2. (a) ¹H NMR 500 MHz (CDCl₃) of compound 1, 2 and 6 after 12 h. (b) Vertical enhancement of the 4.18-4.26 ppm chemical shift range of the spectrum (a). (c) COSY of the mixture of compounds 1, 2 and 6.

2.60 (overlapped) and $\delta = 2.91$, dd J = 4.5; -14.0and $\delta = 2.30$, dd, J = 10.0, -14.0, respectively. These chemical shifts suggested an asymmetric structure, where only one proton ($\delta = 1.14$) from both methylenes was shielded for one of the phenyl rings attached to the cyclobutane moiety and displaying the remaining benzylic methylene protons, the usual chemical shifts between $\delta =$ 2.91 and 2.30. Thus, the two benzylic units were unambiguously *cis* to each other (preserving the centre of symmetry as in compound **2**) (see Fig. 4).

2.1.1. 2D ¹³CNMR

The photodimer **2** displayed at ¹³C NMR a signal at $\delta = 218.1$ assigned to the carbonyls of cyclopentanone. Two signals of non-protonated carbons at $\delta = 139.9$ and 138.0 for both ipso carbons of the different phenyl rings. In addition, we observed the signals for the methines of the phenyl rings (DEPT) at $\delta = 130.7$, 128.5, 128.3 and 128.4 (methines *ortho* and *meta*) and finally, the signals assigned to the *para* carbons at $\delta = 127.5$ and 126.0.

At higher field, we observed a non-protonated

carbon at $\delta = 59.6$, the methine at $\delta = 54.7$ and 49.7, as well as the three methylene carbon signals (DEPT) [8] at $\delta = 35.2$, 34.7 and 25.4.

The HMQC [14] experiment enabled us to assign the proton singlet at $\delta = 4.25$, which correlates with the carbon signal at $\delta = 54.7$ and the multiplet at $\delta = 2.10$ with the methine at $\delta = 49.7$. The benzylic methylene protons displaying the higher chemical shift difference between both protons at $\delta = 1.08$ and 2.59 correlated with the signal at $\delta = 34.7$. Consequently, the methylene protons at $\delta = 1.40$ and 1.82 correlated with the carbon signal at $\delta = 25.4$.

At lower field, we were able to assign the proton doublet at $\delta = 6.86$ with the carbon signal at $\delta = 128.5$; the proton at $\delta = 7.10$ with the signal at $\delta = 126.0$ and the proton triplet at $\delta = 7.17$ with the carbon at $\delta = 128.2$. The proton triplet at $\delta = 7.23$ correlated with the carbon signal at $\delta = 127.5$ and the protons at $\delta = 7.35$ and 7.32 with the carbons at $\delta = 130.7$ and 128.4, respectively.

The HMBC [15] experiment allowed us to assign the aromatic non-protonated and protonated carbons. For example, the proton singlet at $\delta = 4.25$ correlated through 3s bond with the carbonyl signal at $\delta = 218.1$, with the ipso carbon at $\delta = 138.0$ and with the methine carbon at $\delta = 130.7$. This experiment enabled us to confirm the chemical shifts of the phenyl group carbons attached to the cyclobutane ring. Additional correlations through this methine signal were those observed at higher field with the non-protonated carbon at $\delta = 59.6$ and the methylene carbon at $\delta = 35.2$. Using the benzylic protons at $\delta = 1.08$ and 2.60, we observed the 2σ



Fig. 3. (a) ¹H NMR 500 MHz (CDCl₃) of compound **2**. (b) COSY spectrum of compound **2**.



Scheme 1.

and 3σ bond correlation with the carbonyl carbon at $\delta = 218.1$, the ipso carbon at $\delta = 139.9$ and the methine at $\delta = 128.5$, as well as with the methine carbon at $\delta = 49.7$ and the methylene carbon at $\delta = 25.4$. The triplet at $\delta = 7.17$ correlated with the ipso carbon at $\delta = 139.9$; the triplet at $\delta = 7.32$ was correlated with the ipso carbon at $\delta = 138.0$ and finally, the doublet at $\delta = 6.86$ correlated with the carbon signal at $\delta = 128.5$. The methylene protons at $\delta = 1.60$ and 2.75 correlated with the non-protonated carbon at $\delta = 59.6$, as well as the methines at $\delta = 54.7$ and 49.7 and the methylene at $\delta = 25.4$. The methylene protons at $\delta = 1.40$ and 1.82 correlated with the non-protonated carbon at $\delta = 59.6$, the methine at $\delta = 49.7$ and the methylene at $\delta = 35.2$.

In addition, because the ¹³C NMR experiment has the longer recording consuming time and in order to avoid the dimerization of compound 1, we chose as solvent DMSO- d_6 , which allowed us to detect exclusively the signals due to the compound 1. In this way, using the noise decoupling experiment and HMQC and HMBC experiments, we completed the assignments of protons and carbons of this compound.

3. Conclusions

It was reported in 1969 that the UV irradiation of 2-benzyl-5-benzylidene cyclopentanone yielded only one of four possible photodimer, the centrosymmetric photodimer.

In light of modern NMR spectroscopy, we were able to observe the interesting behaviour of 2-benzyl-5-benzylidene cyclopentanone and deduce the existence in solution of the well known photodimer 2, as well as a new centroasymmetric photodimer 6.

4. Experimental

Melting points were determined with a Kofler Hot Stage apparatus and were not corrected. The ¹H and ¹³C NMR spectra were recorded using a Varian Unity 300 spectrometer operating at ob-



Scheme 2.





servation frequency of 300.0 MHz for ¹H and 75.0 MHz for ¹³C.

The ¹H and ¹³C chemical shifts (δ) are given in ppm relative to tetramethyl silane (TMS).

High resolution NMR spectra were recorded on a Varian Unity 500 operating at 500.3 MHz for ¹H and 125.0 MHz for ¹³C. The experiments were performed using an inverse detection 5 mm probe. The COSY, HMQC and HMBC spectra were recorded by the usual Varian Unity software.

Mass spectra were recorded on instruments JEOL-JMS AX505HA and JEOL-JMS 10217 using standard FAB or CI/EI sources in glycerol or with CH_4 gas, respectively. The IR spectra were performed on Nicolet FX-SX and Nicolet 55-X in solution or KBr mode.

The 2,5-dibenzylidene cyclopentanone used as a starting material was prepared following the procedure described by Quilico [16].

The 2-benzyl-5-benzylidene cyclopentanone used for the UV irradiation was prepared by the method described by Forward and Whiting [4].

The 6-amino-1,3-dimethyl uracil, dichloro-

methane and Triton B were purchased from Aldrich Chemical and used as received.

4.1. General procedures for the synthesis of the adduct **5**

To a suspension of 2 mM of 6-amino-1,3dimethyl uracil in 3 ml of dichloromethane, 1 ml of Triton B (methanol solution) and 1 ml of distilled water were added, followed by 1 mM of 2,5-phenylidencyclopentanone in 5 ml of dichloromethane. The mixture was stirred at room temperature until the starting material was consumed (reaction was monitored by TLC). Usual work up followed by flash column chromatography (silica gel, Kieselgel 60, 230-400 mesh, Merck) or preparative thin layer chromatography (silica gel, Kieselgel GF-254, plates 20×20 , 2.0 mm thick) yielded the adduct 5 and the reduced 2-benzyl-5-benzylidenecyclopentanone 1, which were recrystallized from a mixture of dichloromethane/hexane.

Adduct **5** showed the followed physical constants:

Yellow solid m.p. 264–266 °C, MW 395 $(C_{25}H_{21}N_3O_2)$; MS EI, M⁺ m/z 395, 394 318, 304. IR v_{max} (KBr); 3025, 2931, 1702, 1658, 1554, 1492, 1448 and 1358 cm⁻¹.

4.1.1. Compound 2

The diphenyldispiro [4.1.4.1] dodecan-4,11dione (2) was prepared using the method described by Forward and Whiting [4]. The photodimer crystallized from dichloromethane gave colorless needles m.p. 242–243 °C (lit [3] m.p. 240–241 °C). IR v_{max} 1730, 700 cm⁻¹. MS m/z 524 M⁺, 262 (100%).

References

- J. Cologne, G. Descotes, in: J. Hamer (Ed.), 1,4 Cycloaddition Reactions, Academic Press, New York, 1967, p. 217 Chapter 9.
- [2] H.O. House, A.G. Hortmann, J. Org. Chem. 26 (1961) 2190.
- [3] R. Cornubert, M. de Demo, J. Roby, P. Louis, P. Robinet, A. Strébel, Bull. Soc. Chim. France 5 (1938) 513.
- [4] (a) G.C. Forward, D.A. Whiting, J. Chem. Soc. C, Part III, (1969) 1868;
 (b) V. Ramamurthy, K. Venkatesan, Chem. Rev. 87

(1987) 433.

- [5] E. Díaz, H. Barrios, A. Guzmán, D. Corona, A. Fuentes, C.K. Jankowski, Spectroscopy 14 (2000) 177.
- [6] E. Díaz, J.L. Nava, H. Barrios, B. Quiroz, A. Guzmán, L.

León, A. Fuentes, Spectrochim. Acta Part A 54 (1998) 567.

- [7] E. Díaz, H. Barrios, J.L. Nava, M.I. Chavez, A. Guzmán, J.F. Fuentes, A. Fuentes, Spectrosc. Lett. 31 (1998) 51.
- [8] E. Díaz, H. Barrios, J.L. Nava, R.G. Enriquez, A. Guzmán, L. León, J.F. Fuentes, A. Fuentes, A. Quintero, J.D. Solano, J. Heterocyc. Chem. 34 (1997) 1037.
- [9] C.E. Johnson, F.A. Bovey, J. Chem. Phys. 29 (1958) 1012.
- [10] E. Díaz, H. Barrios, F. Yuste, J.L. Aguilera, W.F. Reynolds, M.R. van Calsteren, C.K. Jankowski, J. Heterocyc. Chem. 30 (1993) 97.
- [11] E. Díaz, E. Galeazzi, J.L. Nava, J.M. Muchowski, A. Guzmán, M.R. van Calsteren, C.K. Jankowski, Mag. Res. Chem. 33 (1995) 581.
- [12] (a) C.R. Theocharis, W. Jones, Stud. Org. Sol. State Chem. 32 (1987) 47;
 (b) D.A. Whiting, J. Chem. Soc. C, Part III, (1971) 3396.
- [13] A. Derome, Modern Techniques for Chemistry Research, Pergamon Press, New York, 1987, p. 240.
- [14] (a) W.E. Hull, W.R. Croasmum, in: R.M.K. Carlson (Ed.), 2D NMR Spectroscopy for Chemist and Biochemist, VCH, New York, Chapter 2, 1994;
 (b) G.E. Martin, A.S. Sektzer, Two Dimensional NMR Methods for Establishing Molecular Connectivity, VCH, New York, 1988, p. 219.
- [15] (a) A. Bax, S. Subramanian, J. Mag. Res. 63 (1986) 565;
 (b) A. Bax, R. Freeman, J. Mag. Res. 44 (1981) 542;
 (c) H. Kessler, M. Gehrke, C. Griesinger, Angew Chem. Int. Ed. Engl. 27 (1988) 490;
 (d) A. Bax, M.F. Summers, J. Am. Chem. Soc. 108 (1986) 2093;
 (c) A. Bax, M.F. L. M., P. 44 (1985) 497.

(e) G.A. Pearson, J. Mag. Res. 64 (1985) 487.

[16] A. Quilico, The Chemistry of Heterocyclic Compounds, vol. 17, Wiley, New York, London, 1962.