

R. E. van der Stoep, H. C. van der Plas* and G. Geurtsen

Laboratory of Organic Chemistry, Agricultural University, Wageningen, The Netherlands

Received April 25, 1980

¹H- and ¹³C-nmr spectroscopy is presented showing that photolysis of 4-(*p*-trifluoromethylphenyl)-1,4-(3,4)-dihydropyrimidine yields 6-(*p*-trifluoromethylphenyl)-2,4-diazabicyclo[3.1.0]hex-2(3)ene.

J. Heterocyclic Chem., **17**, 1617 (1980).

In previous papers (1a,2) we reported the photochemical rearrangement of 4-*R*-1,4-(3,4)dihydropyrimidines (**1**) into 5-*R*-1,2-(2,3)dihydropyrimidines (**3**). Indirect chemical evidence was presented that this isomerization involves a di- π -methane photorearrangement of **1** into 2,4-diazabicyclo[3.1.0]hex-2(3)ene (**2**) and a subsequent thermal rearrangement of **2** into **3**. The suggested intermediacy of 1,6-diphenyl-2,4-diazabicyclo[3.1.0]hex-2(3)ene (**2a**) in the photoisomerization of 4,6-diphenyl-1,4-(3,4)dihydropyrimidine (**1a**) could not be confirmed by nmr spectroscopy (2). Its existence, however, was substantiated by the 57% of deuterium incorporation in position 2 of the product 4,5-diphenylpyrimidine (**4a**), obtained when **1a** was irradiated in an acetone/deuterium oxide mixture and the reaction product was subsequently oxidized (3). It was also observed that when the irradiation of **1a** was carried out in acetone and deuterium oxide was added to the acetone mixture after photolysis, still 11% of deuterium was found in **4a**. Evaporation of the solvent after irradiation of **1a** in acetone, and then addition of deuterium oxide did not lead to incorporation of deuterium.

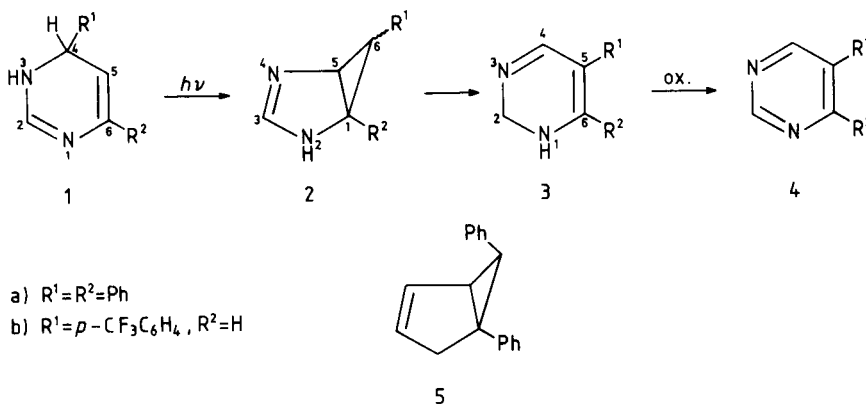
Based on these observations it was concluded that **2a** existed for some time in the photolysis mixture after irradiation and did not rearrange immediately. However, the gentle heating necessary for evaporation of the acetone caused **2a** to be converted completely into the

1,2-(2,3)dihydropyrimidine (**3a**). By recording spectra immediately after a very careful evaporation of the acetone we tried to obtain spectroscopic evidence for the intermediacy of the bicyclic compound **2**. We wish to present in this paper the results of a spectroscopic study on the structure of an intermediate in the photolysis of 4-(*p*-trifluoromethylphenyl)-1,4-(3,4)dihydropyrimidine (**1b**).

When a solution of **1b** in acetone was irradiated and the ¹H-nmr spectrum of the reaction mixture was immediately taken, a doublet at δ 3.75 was observed with a small coupling constant ($J = 1.7$ Hz) and a triplet at δ 0.90, intensity ratio doublet/triplet 2:1. The high field position of the latter signal was considered as an indication for the presence of a compound with a three-membered ring (4,5), and was tentatively ascribed to H-6 on **2b**. Tautomerism in the -N=C-NH-moiety, as was also observed in the 1,2-(2,3)-dihydropyrimidines (2), caused H-1 and H-5 to appear as one signal, and the doublet at δ 3.75 with twice the intensity of the triplet at δ 0.90 supports structure **2b**.

Further support for the correctness of these assignments was provided by the proton-decoupled ¹³C-nmr spectrum of the irradiation mixture (Figure 1b). Recording the spectrum in the proton coupled mode afforded the ¹J(CH) coupling constants (see Table 1). The signal at high field for a tertiary carbon atom (δ 23.3) and large coupling

Scheme I



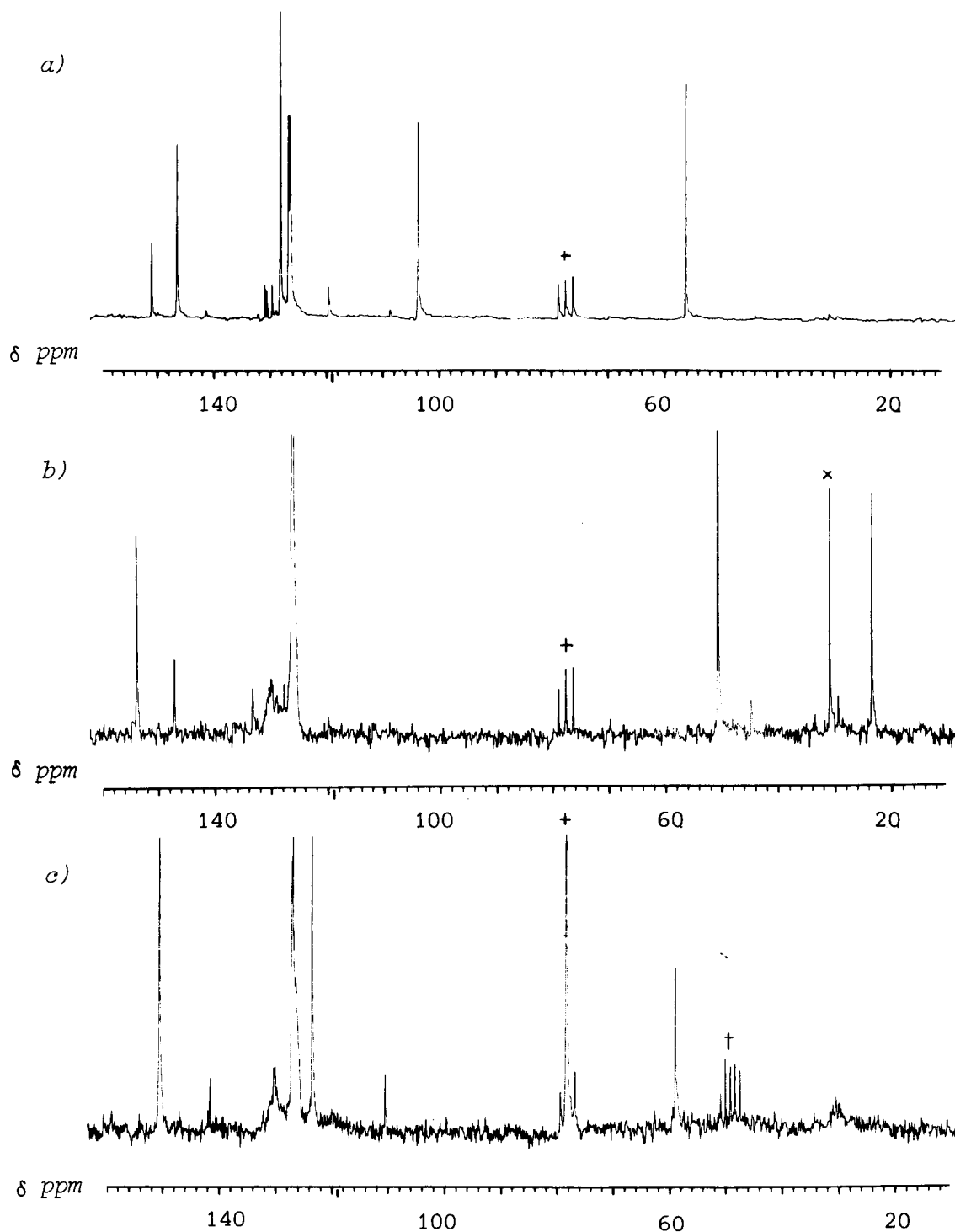


Figure 1. Proton decoupled ^{13}C -nmr spectra of a) compound **1b**; + = CDCl_3 ; b) irradiation mixture (**2b**); + = CDCl_3 , x = acetone; c) after addition of $\text{KOH}/\text{CD}_3\text{OD}$ (**3b**); + = $\text{CDCl}_3/\text{CHCl}_3$, † = CD_3OD

constant (165 Hz) was attributed to C-6 of **2b**; thus it can be considered as additional proof for the bicyclic structure (5,6). The doublet at δ 50.5 was ascribed to C-1,5; due to

tautomerism in the $\text{N}=\text{C}-\text{NH}$ moiety the carbon atoms C-1 and C-5 appear as one signal in the spectrum. This doublet lies at lower field than the C-6 signal at δ 23.3 due

Table 1

¹³C Chemical Shifts of Starting Material **1b**, Intermediate **2b** and Final Product **3b** (¹J(CH) in Parenthesis)

	1b	2b	3b
C-1	---	50.5 (187)	---
C-2	145.8 (194)	---	58.6 (152)
C-3	---	153.0 (197)	---
C-4	56.1 (144)	---	149.5 (173)
C-5	103.3 (167)	50.5 (187)	109.9
C-6	125.7 (160)	23.3 (165)	149.5 (173)
CF ₃	124.5 (273) (a)	(b)	(b)
C ₁ phenyl	150.3 —	146.4 —	148.8 —
C _{ortho}	127.5 (160)	125.4 (160)	125.8 (160)
C _{meta}	125.9 (160)	125.2 (160)	122.6 (162)
C _{para}	129.6 (32) (c)	(b)	129.3 (160)

(a) ¹J(CF), (b) Intensity too low to be observed in the spectrum. (c) ²J(CF)

to the presence of the adjacent nitrogen atom. Moreover the presence of nitrogen enhances the coupling constant (6) as is observed (187 Hz). The position of the *p*-trifluoromethylphenyl group in the bicyclic compound **2b** was determined to be *exo*, based on comparison of the vicinal proton to proton coupling constant J_{1,6} with those of related bicyclic systems published in literature (7). In **2b** the coupling J_{1,6} constant is small (1.7 Hz). In related carbocyclic compounds the *trans* coupling constant (J_{1,6n}) is always smaller than the *cis* coupling constant (J_{1,6x}) (J_{1,6n} = 4 Hz, J_{1,6x} = 7-9 Hz). Although replacement of the CH group in 2 position by a nitrogen atom is known to affect these coupling constants, in a 2-azabicyclo[3.1.0]hexene J_{1,6n} is still smaller (1.6-2.8 Hz) than J_{1,6x} (6.5-8.5 Hz) (8). Based on these data the coupling constant of 1.7 Hz, found in **2b**, most likely is a *trans* coupling constant (J_{1,6n}) and consequently the aromatic substituent is in *exo* position.

This stereochemical assignment is in contrast to the preferred formation of the *endo* stereoisomer **5** formed in the di- π -methane rearrangement of 5,5-diphenyl-1,3-cyclohexadiene (9) and similar related systems as reported in literature (10-13). In these cases, however, the steric interaction of the two bulky phenyl groups strongly determines the *endo* stereochemistry of the photochemical process.

Addition of a solution of potassium hydroxide in methanol-*d*₆ to the above mentioned ¹³C-nmr sample of the irradiation of **1b** caused an immediate change in the nmr spectra. The signals attributed to compound **2b** disappeared completely. In the proton coupled ¹³C-nmr spectrum besides the signals of the aromatic carbons a triplet at δ 58.6, a singlet at δ 109.9 and a doublet at δ 149.5 appeared. The chemical shifts of these signals agree well with those reported for 5-phenyl-1,2-(2,3)dihydropyrimidine (**3**, R¹ = Ph, R² = H) (2). The ¹H-nmr spectrum of the mixture obtained after addition of potassium hydroxide

(singlets at δ 4.63 and δ 7.52 of equal intensity) further supports the formation of 5-(*p*-trifluoromethylphenyl)-1,2-(2,3)dihydropyrimidine (**3b**) (2).

Neutralization and subsequent oxidation with potassium permanganate gave 5-(*p*-trifluoromethylphenyl)pyrimidine (**4b**).

EXPERIMENTAL

General experimental conditions were as described in previous papers (1a,2). Uv spectra were taken of solutions in 96% ethanol, ir spectra of solutions in chloroform and ¹H- and ¹³C-nmr spectra of solutions in deuteriochloroform with TMS as the internal standard. Column chromatography was performed with Merck silica gel 60 (70-230 mesh ASTM) as the stationary phase.

Preparation of 4-(*p*-Trifluoromethylphenyl)-1,4(3,4)-dihydropyrimidine (**1b**).

4-Bromobenzotrifluoride (2.82 g., 12.5 mmoles) in 10 ml. of ether was added to 8 ml. of a 1.6M solution of *n*-butyllithium in hexane at -70° (14). The reaction mixture was warmed to 0° during 30 minutes and 1.00 g. (12.5 mmoles) of pyrimidine in 10 ml. of ether was added at this temperature. After the addition of a mixture of water and methanol and separation of both layers, the aqueous phase was extracted with chloroform (2 times). The combined organic layers were dried over magnesium sulfate, filtered and then the solvents were evaporated *in vacuo*. The residual oil was subjected to column chromatography with a mixture of petroleum ether (b.r. 40-60°)/acetone/diethylamine (10:10:1) as the eluant and gave 1.65 g. of orange oil (58%); ir: 3240, 3225 (sh), 3175, 1690 (sh), 1683, 1640, 1622 and 1587 cm⁻¹; uv: λ max 283 nm (log ϵ 3.12); ¹H-nmr: δ 7.51, d (*p*-CF₃C₆H₄, *m*-H), 7.37 d (*p*-CF₃C₆H₄, *o*-H), 6.91, s (H-2), 5.99, d (H-6), 5.12, d (H-4) and 4.59, dd (H-5), J_{o,m} = 8.0, J_{4,5} = 3.0, J_{5,6} = 7.5 Hz.

Oxidation of **1b** with a solution of potassium permanganate in acetone gave 4-(*p*-trifluoromethylphenyl)pyrimidine; ¹H-nmr: δ 9.22, d (H-2), 8.75, d (H-6), 8.15, d (*p*-CF₃C₆H₄, *o*-H), 7.68, d (*p*-CF₃C₆H₄, *m*-H) and 7.68, dd (H-5), J_{2,5} = 1.0, J_{5,6} = 5.0, J_{o,m} = 8.0 Hz.

The picrate had m.p. 133° (from aqueous ethanol).

Anal. Calcd. for C₁₇H₁₀F₃N₂O₂: C, 45.04; H, 2.22. Found: C, 45.2; H, 2.0.

Irradiation of 4-(*p*-Trifluoromethylphenyl)-1,4(3,4)dihydropyrimidine (**1b**).

Nitrogen was bubbled through a solution of 0.50 g. of **1b** in 500 ml. of acetone in a quartz vessel for 1 hour before and during irradiation. This solution was irradiated for 1.75 hours in a Rayonet RPR-208 preparative photoreactor equipped with eight RUL 300 lamps at ambient temperature. The solvent was subsequently evaporated *in vacuo* while the heating bath was kept below 30°. The results of the ¹H- and ¹³C-nmr study are discussed above. For the formation of 5-(*p*-trifluoromethylphenyl)pyrimidine (**4b**) the residue was oxidized with a solution of potassium permanganate in acetone and subsequently subjected to column chromatography with a mixture of chloroform and ethyl acetate (4:1) as the eluant, yield 0.21 g. of **4b** (41%), m.p. 114° (from petroleum ether, b.r. 40-60°); ¹H-nmr: δ 9.15, s (H-2), 8.88, s (H-4,6) and 7.67, s (*p*-CF₃C₆H₄).

Anal. Calcd. for C₁₁H₆F₃N₂: C, 58.93; H, 3.15. Found: C, 59.2; H, 2.9.

REFERENCES AND NOTES

- (1a) Photoreactions of Diazines. Part 10. For Part 9, see R. E. van der Stoel and H. C. van der Plas, *J. Chem. Soc., Perkin Trans. I*, 2393 (1979); (b) Pyrimidines, Part LXXXII. For Part LXXXI see N. J. Kos and H. C. van der Plas, *Rec. Trav. Chim.*, submitted.
- (2) R. E. van der Stoel and H. C. van der Plas, *J. Chem. Soc., Perkin Trans. I*, 1228 (1979).

(3) Compounds containing the 2,4-diazabicyclo[3.1.0]hexene structure have also been suggested as intermediates in the reaction of imidazoles with carbenes yielding pyrimidines. In these reactions the bicyclic intermediates were not detected either [R. E. Busby, *J. Chem. Soc. D*, 1344 (1969)].

(4) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd Ed., Pergamon Press, Oxford, 1972, p. 196.

(5) F. van Rantwijk, R. E. van der Stoel and H. van Bekkum, *Tetrahedron*, **34**, 569 (1978).

(6) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley-Interscience, New York, N.Y.,

1972.

(7) D. Gravel, C. Leboeuf and S. Caron, *Can. J. Chem.*, **55**, 2373 (1977); and references therein.

(8) J. F. Biellmann and M. P. Goeldner, *Tetrahedron*, **27**, 1957 (1971).

(9) J. S. Swenton, A. L. Crumrine and T. J. Walker, *J. Am. Chem. Soc.*, **92**, 1406 (1972).

(10) H. E. Zimmerman, P. Hackett, D. F. Jeurs, J. M. McCall and B. Schröder, *ibid.*, **93**, 3653 (1971).

(11) H. E. Zimmerman and G. Samuelson, *ibid.*, **91**, 5307 (1969).

(12) H. E. Zimmerman and G. Samuelson, *ibid.*, **89**, 5971 (1967).

(13) H. E. Zimmerman and G. A. Epling, *ibid.*, **92**, 1411 (1970).

(14) J. D. Cook and B. J. Wakefield, *J. Chem. Soc. C*, 2376 (1969).