

Regioselective Intramolecular Photocyclisation in the Prostaglandin Series

By PIERRE CRABBÉ,*† GUSTAVO A. GARCIA, and ESPERANZA VELARDE

(*Facultad de Química, Universidad Nacional Autónoma de México, México 20, D.F., México*)

Summary Irradiation of PGA₂ methyl ester (**1**) affords the cage compounds (**2**)—(**4**).

Irradiation of PGA₂ methyl ester (**1**) at -70° for 90 min, in tetrahydrofuran solution, affords a mixture of three isomeric cycloadducts.

THE broad outlines of the reaction pathway of the addition of photoexcited cyclopentenones to alkenes have been elucidated,^{1,2} and photochemical cycloadditions have been reported in numerous classes of natural products, including the prostaglandin family.³ In addition, it has been shown that intramolecular enone-ene photocyclisations can lead to substituted cyclobutane derivatives.^{1,4}

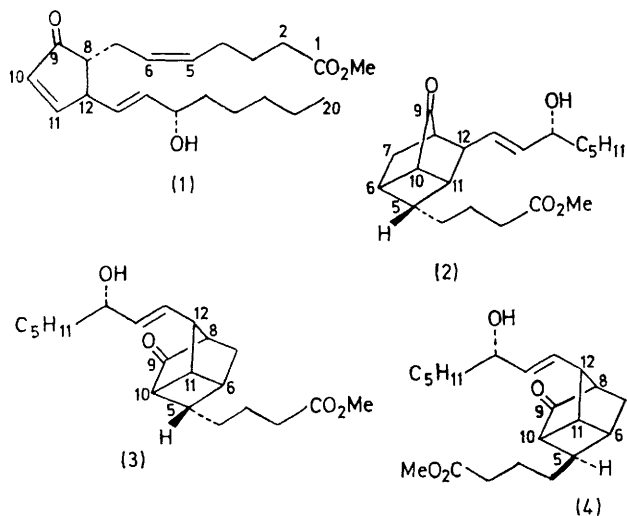
Preparative t.l.c. allows separation of the saturated ketone (**2**)‡ as the major component (18%). The structure of compound (**2**) is supported by the presence of an i.r. band at 1755 cm^{-1} , typical of similar cyclopentanones,⁵ the absence of intense u.v. absorption above 220 nm, and the n.m.r. spectrum which shows only two olefinic protons at *ca.* δ 5.48, compared to six in (**1**). Moreover, the c.d. curve exhibits a very weak negative Cotton effect ($[\theta]_{308} - 460$) because the molecule is almost completely symmetrical but for the four carbon chain at C-5 which seems to be located, at least partly, in a front octant.

Here we report an example of intramolecular photochemical cycloaddition occurring with the PGA₂ molecule, which provides optically active tricyclic cage compounds.

† Present address: Laboratoire de Chimie Organique, C.E.R.M.O., Université Scientifique et Médicale, Boite Postale 43, Grenoble-38.041, France.

‡ Satisfactory elemental analysis and/or mass spectra were obtained for all new compounds. I.r., u.v., and n.m.r. spectra were in agreement with the proposed structures.

The second component (15%) is the keto-derivative (3). In this tricyclic compound the saturated ketone is located



in a six-membered ring, so that the i.r. carbonyl band and the methyl ester absorption appear in the same region. The ketone (3) presents only two olefinic protons and exhibits a positive c.d. curve ($[\theta]_{295} + 5640$), since the C-12 carbon is twisted in a positive octant.

The third component (8%) of the reaction is a stereo-isomer of (3). Structure (4) is assigned to this substance. Its physical properties are reminiscent of these of its configurational isomer (3). Furthermore, as expected, compound (4) also presents a positive Cotton effect ($[\theta]_{295} + 5150$).

The formation of the major compound (2) can be rationalised as resulting from an intramolecular photochemical addition process, due to the stereoproximity of the *cis*-5,6-double bond⁶ which adds to positions C-11 and C-10, respectively, from the α -side of the PGA₂ methyl ester (1), through a stable biradical.^{2,7}

Isomers (3) and (4) result from internal photoinduced α -addition of the 5,6-*cis*-double bond to C-10 and C-11, respectively. The initial bond is formed between C-6 and C-11, and the diradical intermediate is rotationally equilibrated before ring closure.^{7§}

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§ During the previous photochemical additions no internal cycloaddition was detected.³ This may be due to the nature of the solvent,¹ the absence of external substrate with which to react, and/or to the fact that when the previously mentioned cycloadditions³ were very fast processes, the intramolecular photochemical additions reported here are slower reactions, thus allowing the formation of the requisite biradicals.

¹ See: P. G. Sammes, *Quart. Rev.*, 1970, **24**, 37; P. de Mayo, *Accounts Chem. Res.*, 1971, **4**, 41; P. G. Bauslaugh, *Synthesis*, 1971, **2**, 287.

² N. D. Epiotis, *J. Amer. Chem. Soc.*, 1972, **94**, 1941; R. O. Loufty, and P. de Mayo, *Canad. J. Chem.*, 1972, **50**, 3465; W. C. Herndon, *Chem. Rev.*, 1972, **72**, 157, and references therein.

³ P. Crabbé, G. A. Garcia, and C. Rius, *Tetrahedron Letters*, 1972, 2951; P. Crabbé, G. A. Garcia, and C. Rius, *J.C.S. Perkin I*, 1973, 810.

⁴ G. Ciamician and P. Silber, *Chem. Ber.*, 1908, **41**, 1928; G. Büchi and I. M. Goldman, *J. Amer. Chem. Soc.*, 1957, **79**, 4741.

⁵ See: J. L. Charlton, P. de Mayo, and L. Skattebøl, *Tetrahedron Letters*, 1965, 4697.

⁶ A n.m.r. study of prostaglandin complex with tris(dipivalomethanato)europium(III) has shown that no isomerisation of the double bonds occurs during these photochemical reactions: G. A. Garcia, E. Diaz, and P. Crabbé, *Chem. and Ind.*, 1973, in the press.

⁷ Cf. W. L. Dilling, T. E. Tabor, F. P. Boer, and P. P. North, *J. Amer. Chem. Soc.*, 1970, **92**, 1399, and references cited.