

ORTHO- AND PARA-PHOTOCYCLOADDITIONS OF 3-METHOXY-
N-METHYLPHTHALIMIDE TO n-HEXENE

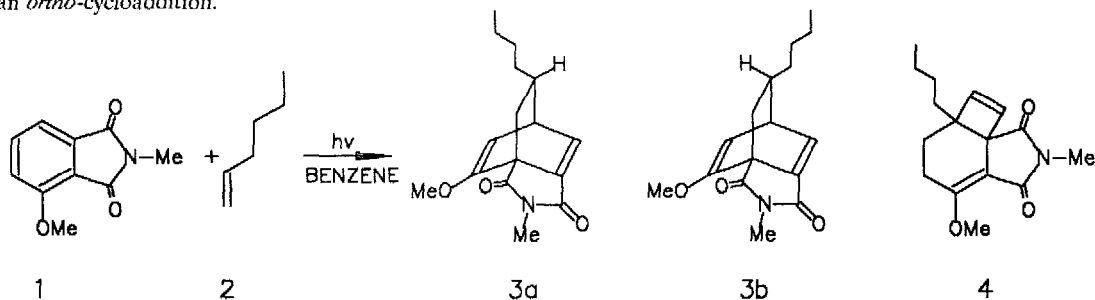
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Abstract: Photocycloaddition of 3-methoxy-N-methyl-phthalimide to n-hexene results in the formation of 8-butyl-N-methyl-6-methoxy bicyclo[2,2,2]octa-2,5-diene-1,2-carboximide and 6-butyl-N-methyl-3-methoxy bicyclo[4,2,0]octa-2,7-diene-1,2-dicarboximide through regioselective para and ortho-cycloadditions respectively.

One important and well established process in the photochemistry of phthalimides with alkenes is the addition to give benzazepinediones after ring expansion.¹ Although several processes can compete with the photocycloaddition² the reaction has been found to depend on the nitrogen substituent³, while 4-aryl substitution (MeO-, Me-, Cl-, MeOOC-) does not affect the cycloaddition and the concerted nature of the reaction has been proposed from the observed regioselectivity.⁴

However, it has been recently reported that the irradiation of N-methylphthalimide/cyclohexene system does not display the expected imide photoreactivity but *para*-cycloaddition to the benzene moiety is observed as the main reaction.⁵

In the present paper we wish to report the photoreactivity of 3-methoxy-N-methylphthalimide (1) and n-hexene (2) that gave a regioselective *para*-cycloaddition product and a new photo process probably initiated with an *ortho*-cycloaddition.



A solution containing 10.5 mM of **1**, 129 mM of **2**, and 200 mL of benzene was irradiated (125 W mercury lamp, pyrex filter, N₂) for 64 hours. HPLC analysis of the reaction mixture showed the almost complete disappearance of the starting phthalimide and the formation of two isomeric adducts **3** and **4** in 59% and 25% yield respectively.⁶

Compound **3** isolated as an oil was showed to be a mixture of two epimers **3a** and **3b** (4:1 ratio respectively). The pmr (table 1) suggested the bicyclo[2,2,2]-octadiene structure, in agreement with the absence of aromatic protons and the high field methoxy signal. The MS supported this assumption since an easy retro Diels-Alder fragmentation was observed (M⁺ at m/e 275, less than 2%) giving prominent ions at m/e 215 (M⁺ - HC≡C-OMe) and m/e 191 (M⁺ - C₆H₁₂).

That the *para*-cycloaddition occurred regioselectively between positions 1 and 4 of the aromatic nucleus of **1**, was clear from the cmr spectrum (table 1) showing a olefinic bond substituted with an electron donor (C-5 and C-6) and a second olefinic bond conjugated with a carbonyl group (C-2 and C-3). The stereochemistry at C-8 was established from the steric effect of the side chain on the chemical shifts of H-3 and H-5.

TABLE 1

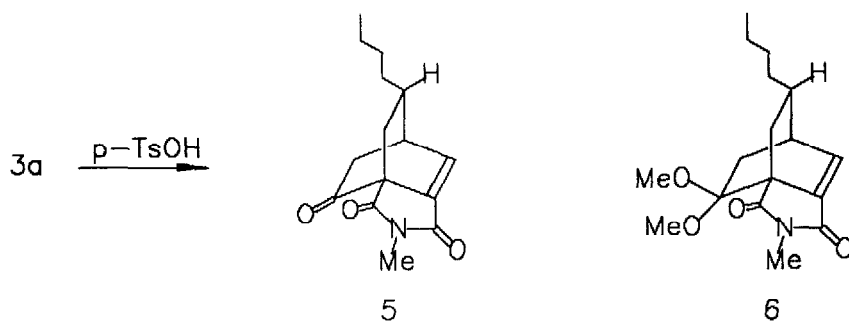
	3a	3b	5	6
H-3	7.2 d (5.1)	7.3 d (5.1)	7.3 d (6.4)	7.08 d (6.4)
H-4	3.6 ddd (6.7, 5.1 and 2)	----	3.2 m (*)	2.8 m (**)
H-5	5.0 d (6.7)	4.8 d (6.7)	2.2 bd (2.4)	1.61 dd (12.9 and 2.8)
O-Me	3.50 s	3.55 s	----	3.44 and 3.00 two s
C-2	138.3	----	132.7	138.6
C-5	140.3	----	138.5	136.4
C-3	98.1	94.0	40.2	41.0
C-6	165.0	----	202.2	105.2

Coupling constants in Hz are in parenthesis. Chemical shifts are in δ values

(*) J_{4,3}=6.2; J_{4,8}=2.0; J_{4,5}=2.7; and J_{4,5'}=2.9

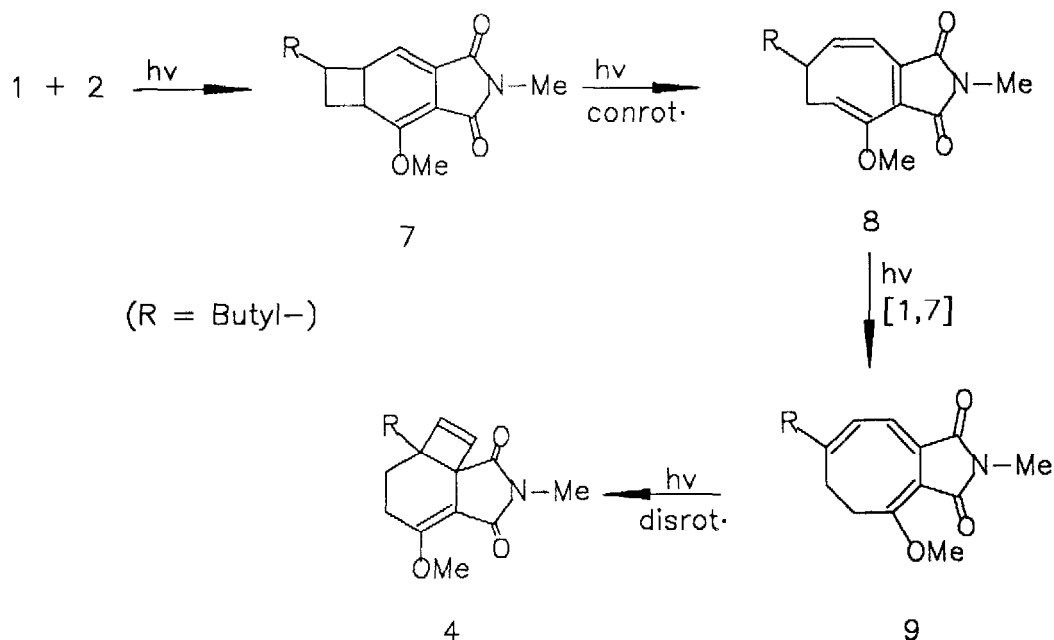
(**) J_{4,3}=6.4; J_{4,8}=1.9; J_{4,5}=2.8; and J_{4,5'}=3.1

In agreement with the enol-ether functionality, a sample of **3a** (almost pure isomer) was treated with wet benzene and p-TsOH to give the expected ketone **5** and a minor amount of the dimethoxyketal **6**. NOE difference and 2D NOESY experiments on this last compound confirmed the proposed stereochemistry.



The photoadduct **4** was obtained as a single isomer and analyzed for $C_{16}H_{21}NO_3$ (HRMS). Its pmr, cmr and 2D-COSY spectra revealed the presence of the imide function ($\delta = 2.9$ ppm, N-Me) and the absence of aromatic hydrogens. Instead, two vicinally coupled vinylic protons with a small coupling constant ($J = 2.8$ Hz) and a large C-H coupling constant ($J = 171.2$ and 179.5 Hz) were attributed to a cyclobutene ring. Two quaternary aliphatic carbon atoms ($\delta = 57.13$ and 56.12 ppm) and a conjugated double bond containing a methoxy substituent ($\delta = 164$ and 102 ppm) connected to a well resolved $-\text{CH}_2-\text{CH}_2-$ system ($\delta = 2.38\text{--}1.24$ ppm) supported the bicyclic [4,2,0] structure with a butyl side chain.

Although the mechanism of formation of **4** is uncertain, it can be rationalized as the result of an initial [2+2] photoaddition followed by an electrocyclic ring opening of the cyclohexadiene **7** (probably a photochemical step) to the cyclooctatriene structure **8** which must experiment a photochemical [1,7] sigmatropic rearrangement to the isomeric cyclooctatriene **9** and finally ring closure to **4**, none of these processes are without precedents in related systems ⁷.



This observed change in the reactivity of the phthalimide system from the imide function to the aromatic ring is most unusual. From the aromatic photoreactivity point of view the absence of *meta* photoaddition imply some charge transfer character in the reaction, more in agreement with the observed *ortho* and *para* cycloadditions.⁸ That those results were not due to the benzene sensitization was checked by carrying out the reaction with acetonitrile as solvent, both **3** and **4** were also formed although a slightly slower rate.

Further work taking into account this unexpected aspect of the photochemistry of phthalimides is in progress.

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