91. Photorearrangement of 4,4-Dimethylcyclohex-2-enones with Alkyl or Fluoro Substituents at C(5) and C(6): in Search of the Mechanism

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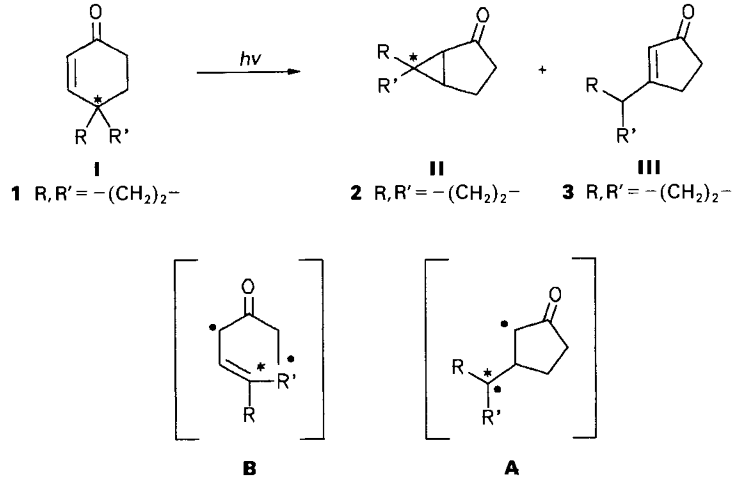
The photorearrangement of cyclohex-2-enones **4a–h** to bicyclo[3.1.0]hexan-2-ones **5** and cyclopent-2-enones **6** ($\lambda = 350$ nm, MeCN) was investigated. Both the quantum yield ($\Phi_{-4} = 0.004 - 0.024$) and the product ratio (**5**/**6** = 65:35–31:69) vary only over a rather small range, indicating the rearrangement to be relatively insensitive to substituents on C(5) or C(6). Compounds **4b**, **4c**, and **4g** with just one alkyl group at either C(6) or C(5) rearrange selectively to the diastereoisomer **5** with alkyl group and three-membered ring in *trans*-configuration, while 6-fluorocyclohex-2-enones **4d** and **4f** afford mixtures of diastereoisomeric bicyclohexanones. Mechanistic conclusions regarding an intermediate trimethylene biradical are presented.

Introduction. – The light-induced photoisomerization of 4,4-dialkylcyclohex-2-enones **I** with concomitant formation of bicyclo[3.1.0]hexan-2-ones **II** and cyclopent-2-enones **III** has been investigated in the past by several groups [1–6] and more recently quite thoroughly by *Schuster et al.* [7–10]. Nevertheless, the question of the mechanism of this rearrangement remains unanswered, both concerted and stepwise mechanisms having been proposed but not proven. The lifetime of an eventual propane-1,3-diyl-biradical intermediate **A** has to be short, as *a*) the reaction proceeds with retention of configuration at the dialkyl-disubstituted C(4) [7], and *b*) no products derived from cyclopropyl-

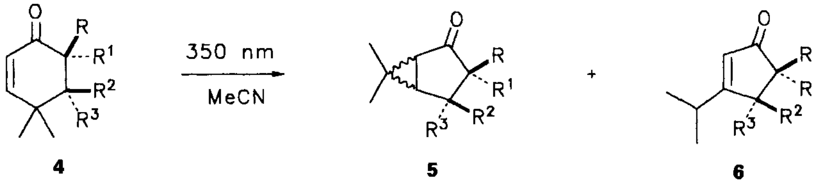
Scheme 1



carbinyl-radical-ring opening were detected in the rearrangement of **1** to **2** and **3** [5]. In a preliminary communication [11], we had discussed a hex-5-enyl-type radical **B** as possible precursor of **A** *(Scheme 1)*, based on the observed product configuration. In this paper, we report detailed results on the photolysis of 4,4-dimethylcyclohex-2-enones **4a–h**, the configuration of bicyclohexanones **5**, and correlate our experimental results with the most recent theoretical descriptions of the reaction of trimethylene biradicals affording cyclopropanes and propylenes [12] [13].

Results. – The quantum yields for disappearance of starting material (Φ_{-4}) and product distribution (**5** and **6**) for irradiations (λ = 350 nm) of **4** (10^{-1} M in MeCN) measured at 10–15% conversion are given in *Scheme 2*. The ^{1}H-NMR and MS data of photoproducts **5** and **6** are summarized in the *Table*.

Scheme 2



	R	R¹	R²	R³	Φ_{-4}					
4a	H	H	H	H	0.014	**5a**	65%		**6a**	35%
b	Me	H	H	H	0.009	**b**	54%		**b**	46%
c	CF_3	H	H	H	0.004	**c**	45%		**c**	55%
d	F	H	H	H	0.011	$\mathbf{d}_x$	29%;	$\mathbf{d}_y$ 30%	**d**	41%
e	Me	Me	H	H	0.017	**e**	51%		**e**	40%
f	F	Me	H	H	0.024	$\mathbf{f}_x$	40%;	$\mathbf{f}_y$ 20%	**f**	40%
g	H	H	Me	H	0.013	**g**	61%		**g**	39%
h	H	H	Me	Me	0.012	**h**	31%		**h**	69%

Discussion. – Several aspects regarding the results summarized in *Scheme 2* and in the *Table* are worth mentioning. The values of the quantum yield (Φ_{-4}) and the product ratio **5**/**6** do not show significant variations in dependence on the substituents on C(5) and C(6) of **4**. In bicyclohexanones **5b**, **5c**, **5e**, $\mathbf{5f}_y$, and **5g** the five-membered ring has a puckered conformation (*cf.* NMR data in the *Table*). In **5b** and **5c**, the alkyl group is in *quasi*-equatorial position and in **5g** in *quasi*-axial, *i.e.* always *trans*-oriented to the three-membered ring. In $\mathbf{5f}_y$, the F-atom is most probably in *quasi*-axial position ($^3J(F_{ax},H_{ax})$ = 37 Hz) and the Me group again *quasi*-equatorial. In 3-fluorobicyclohexanones **5d**, the cyclopentanone ring seems to be flexible, and, therefore, an unambiguous assignment of the configuration of $\mathbf{5d}_x$ and $\mathbf{5d}_y$ from the ^{1}H-NMR data is not possible. The fact that both fluoroenones **4d** and **4f** afford diastereoisomeric mixtures of bicyclohexanones **5** could be due to dipole-dipole interactions between the F-atom and the C=O bond somewhere on the reaction path.

The major goal of this investigation is to better understand the mechanism of the photorearrangement of **4** to **5** and **6**. The concept of two essentially concerted pathways from triplet **I** to **II** and **III**, requiring intersystem crossing to the singlet state, cleavage of one bond, and formation of two new bonds (for **5**), or the formation of one new bond and

Table. *Selected Spectroscopic Data of Photoproducts* **5** *and* **6**

Compound	^{1}H-NMR ($CDCl_3$) [ppm] (J(H,F) [Hz])					MS $[m/z]$ (%)
	H–C(1)	H–C(3)	H–C(4)	H–C(5)	CH_3–CF	
5a	1.65	2.25 (2 H)	2.18 (2 H)	1.82		124 (10, M^+), 82 (100)
5b	1.72	2.42	2.51 (H_{ax}); 1.77 (H_{eq})	1.80		138 (20, M^+), 67 (100)
5c	1.82	3.20 (9.9)	2.57 (H_{ax}); 1.97 (H_{eq})	1.88		192 (12, M^+), 82 (100)
5d$_x$	1.80 (3.0)	4.68 (51)	2.52 (10.8); 2.28 (36.0)	2.08		142 (20, M^+), 99 (100)
5d$_y$	1.70 (2.0)	4.73 (50)	2.72 (9.6); 1.90 (21.7)	1.76		142 (20, M^+), 99 (100)
5e	1.75	–	1.92 (H_{ax}); 1.60 (H_{eq})	1.70		152 (20, M^+), 67 (100)
5f$_x$	[a])					156 (15, M^+), 113 (100)
5f$_y$	1.90[b])	–	2.46 (37.2); 2.03[b])	1.95[b])	1.36 (23)	156 (15, M^+), 113 (100)
5g	1.65	2.35 (H_{ax})	2.26	1.70		138 (15, M^+), 96 (100)
5h	[a])					152 (1, M^+), 110 (100)

$J(3,3) = 19.2$, $J(4,4) = 12.6–14.8$
$J(1,5) = 5.2–5.5$, $J(3ax,4ax) = 11.8–13.0$, $J(3ax,4eq) = 5.4–9.4$
$J(3eq,4eq) = 3.0$, $J(4ax,5) = 6.8–7.2$, $J(4eq,5) = 0.8–1.8$

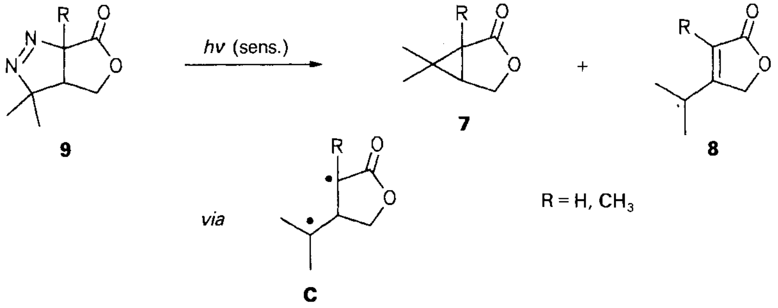
Compound	H–C(2)	H–C(4)	H–C(5)	CH_3–CF	MS $[m/z]$ (%)
6a	5.92	*cf.* [14]			124 (40, M^+), 82 (100)
6b	5.89	2.85	2.42		138 (45, M^+), 67 (100)
6c	5.95	2.91 2.75	3.15 (10.2)		192 (63, M^+), 82 (100)
6d	5.97	3.00 (6.8) 2.70 (22.4)	5.00 (51)		142 (30, M^+), 100 (100)
6e	5.84	2.46 (2 H)	–		152 (40, M^+), 139 (100)
6f	5.94	2.92 (20.8) 2.70 (10.0)	–	1.50 (22.6)	156 (60, M^+), 141 (100)
6g	5.89	2.98	2.65		138 (38, M^+), 95 (100)
6h	[a])				152 (41, M^+), 139 (100)

$J(4,4) = 18.0–19.0$, $J(5,5) = 18.4$
$J(4,5c) = 6.8–7.4$, $J(4,5t) = 2.0–3.4$
$J(2,4) = 0.8–1.5$

[a]) Not measured. [b]) Unresolved multiplet.

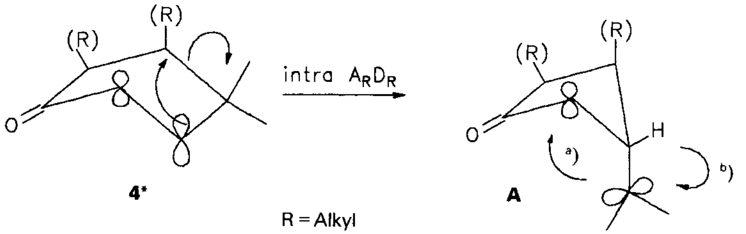
an 1,2-H shift (for **6**) is very hard to accept. Taking into consideration that in a very similar system *both* the oxabicyclohexanones **7** and the unsaturated lactones **8** are formed in the triplet-sensitized photolysis of oxa-diaza precursors **9**, undoubtedly *via* propane-1,3-diyl radical **C** [15] *(Scheme 3)*, it is safe to assume that formation of **5** and **6** from triplet **I** proceeds *via* a propane-1,3-diyl (triplet) radical **A**.

Scheme 3



The first question, thus, concerns the formation of triplet **A** from triplet **I**, *i.e.* the sequence of steps in this transformation. In [11], we had discussed a possible intermediate **B** as precursor of **A**, as **B** behaved as expected for a hex-5-enyl radical, a species known [16] [17] to undergo ring closure in the *exo*-mode to give five-membered rings selectively *and* to afford *trans*-disubstituted five-membered rings when bearing a substituent at C(2), *i.e.* C(6) of **4**. The fact that from **4g** again the *trans*-bicyclohexanone **5g** is formed selectively *clearly rules out such an intermediate*, as now a *cis*-disubstituted five-membered ring should be formed. The conversion of triplet **I** to triplet **A** is, therefore, best described as an intramolecular homolytic substitution (S_H2 reaction) with attack of the radical center C(3) on C(5), the leaving group, *i.e.* the dialkyl-substituted C(4), then being *trans* to the alkyl group at C(5) or C(6) *(Scheme 4)*. Examples of intermolecular displacement reactions by alkyl radicals at saturated C-atoms are rarely encountered, but intramolecular examples involving strained alicyclic rings are known [18]. According to the newest IUPAC recommendations for the representation of reaction mechanisms [19], such a sequence would be termed *intra* A_RD_R.

Scheme 4



[a]) Formation of **5**. [b]) Formation of **6**.

The fate of the propane-1,3-diyl (triplet) radical **A** is straightforward [12]. Once formed, it does *not* relax thermally on the triplet surface, *i.e.* it undergoes intersystem crossing very rapidly as shown by the observed retention of configuration at C(4) in these rearrangements. The barrier to H transfer on the singlet surface from singlet **A** to **6** is certainly lower than that of unsubstituted propane to propene, as the C=C bond formed is now conjugated to a C=O bond; this explains, why, in contrast to triplet-derived simple propane-1,3-diyl radicals, which give cyclopropane products and only very little propylenes, intermediates **A** afford more or less equal amounts of both **5** and **6**.

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Experimental Part

General. Anal. GC: 30-m *SE 30* cap. column. Prep. GC: 2-m 10% *QF1* on *Chromosorb* at 180°. ^{1}H, ^{1}H-COSY-NMR: at 400 MHz. MS: at 70 eV. *Photolyses. Rayonet RPR 100* photoreactor equipped with 350-nm lamps. *Starting Materials.* Cyclohexenones **4a** [20], **4b** [21], **4c** [11], **4d** [22], **4e** [23], **4f** [22], **4g** [20], and **4h** [24] were synthesized according to literature.

Prep. Irradiations. Ar-degassed solns. of **4** (1 mmol) in MeCN (10 ml) were irradiated for 12–50 h up to 40–90% conversion (GC) of starting material.

Irradiation of **4a**. *Cf.* [1] [7] [14].

Irradiation of **4b**. Prep. GC afforded two fractions, the first one containing trans-*3,6,6-trimethylbicyclo[3.1.0]hexan-2-one* (**5b**) of 65% purity and the second one *3-isopropyl-5-methylcyclopent-2-enone* (**6b**) of 85% purity.

Irradiation of **4c**. Prep. GC afforded trans-*6,6-dimethyl-3-(trifluoromethyl)bicyclo[3.1.0]hexan-2-one* (**5c**, 99% purity). Chromatography (SiO$_2$, benzene/AcOEt 95:5) afforded *3-isopropyl-5-(trifluoromethyl)cyclopent-2-enone* (**6c**) of 85% purity.

Irradiation of **4d**. Monitoring the reaction by GC/MS indicates the formation of two diastereoisomeric *3-fluoro-6,6-dimethylbicyclo[3.1.0]hexan-2-ones* **5d**$_x$ and **5d**$_y$ (initial ratio 1:1, final ratio 4:5) and **6d**. The isomer with the lower t_R (**5d**$_x$) also exhibits the higher R_f value. Chromatography (SiO$_2$, benzene/AcOEt 1:1) afforded two fractions: *A*) 110 mg, a mixture of 65% **4d**, 14% **5d**$_x$, and 21% **6d**, and *B*) 28 mg, 1:4 mixture of **5d**$_x$ and **5d**$_y$. Fraction *A* was rechromatographed (SiO$_2$, CH$_2$Cl$_2$) to give 50 mg of a 1:2 mixture of *5-fluoro-3-isopropylcyclopent-2-enone* (**6d**) and **4d**, and 10 mg of **5d**$_x$ of 65% purity.

Irradiation of **4e**. Chromatography (SiO$_2$, benzene/AcOEt 9:1) afforded 80 mg (53%) of *3,3,6,6-tetramethylbicyclo[3.1.0]hexan-2-one* (**2e**, [14]). A 2:1 mixture of *3-isopropyl-5,5-dimethylcyclopent-2-enone* (**6e**, [14]) and **4e** was obtained by prep. GC.

Irradiation of **4f**. Monitoring the reaction by GC/MS indicates the formation of two diastereoisomeric *3-fluoro-3,6,6-trimethylbicyclo[3.1.0]hexan-2-ones* (**5f**$_x$/**5f**$_y$; initial ratio 2:1, final ratio 1:1) and **6f**. The isomer with lower t_R (**5f**$_x$) decomposes during workup. Chromatography (SiO$_2$, benzene/AcOEt 9:1) affords two fractions: *A*) 30 mg of *5-fluoro-3-isopropyl-5-methylcyclopent-2-enone* (**6f**) of 89% purity, and *B*) 110 mg of a 1:1 mixture **4f**/**5f**$_y$. Fraction *B* was rechromatographed (SiO$_2$, CH$_2$Cl$_2$) to give 22 mg **5f**$_y$ of 85% purity.

Irradiation of **4g**. Chromatography (SiO$_2$, CH$_2$Cl$_2$) afforded 84 mg (60%) pure trans-*4,6,6-trimethylbicyclo[3.1.0]hexan-2-one* (**5g**) as colorless oil. Prep. GC gave a 5:1 mixture of *3-isopropyl-4-methylcyclopent-2-enone* (**6g**) and **4g**.

Irradiation of **4h**. Due to lack of material, this reaction was only pursued by GC/MS. The initial ratio of *4,4,6,6-tetramethylbicyclo[3.1.0]hexan-2-one* (**5h**) and *3-isopropyl-4,4-dimethylcyclopent-2-enone* (**6h**) was roughly 1:2. As in all irradiations described above, cyclopentenones **6** undergo slow photodecomposition on higher degree of conversion of **4**.

Actinometry. Solns. of **4** (0.1 mmol in 1 ml of MeCN) containing tetradecane as internal standard were irradiated using a 'merry-go-round' setup. The degree of conversion (10–15%) was monitored by GC. A MeCN soln. of *6-(prop-2-enyl)-4,4,6-trimethylcyclohex-2-enone* [25] was used as chemical actinometer.

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