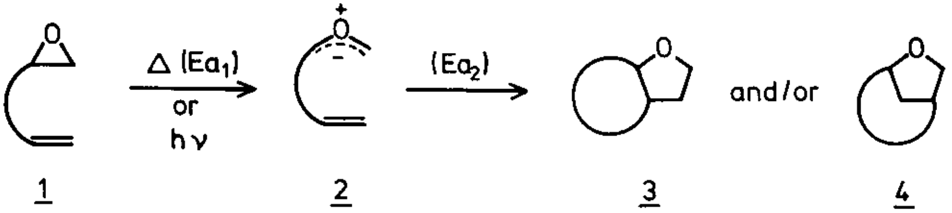
INVESTIGATIONS ON INTRAMOLECULAR CYCLOADDITION REACTIONS OF PHOTOCHEMICALLY GENERATED CARBONYL YLIDES

Jürgen Brokatzky-Geiger and Wolfgang Eberbach *
Institut für Organische Chemie und Biochemie der Universität
Albertstr. 21, D-7800 Freiburg, Germany

Abstract – Upon photoexcitation of appropriately substituted oxiranes ring opening leads to carbonyl ylides which undergo intramolecular cycloaddition reactions affording annelated and/or bridged tetrahydrofurans.

The transformation of ene-oxiranes 1 into tetrahydrofuran derivatives 3/4 takes place in two steps involving C/C-bond cleavage of the epoxide ring and subsequent intramolecular cycloaddition of the 1,3-dipolar intermediate 2.

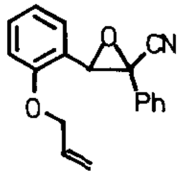
(1)



We have studied this reaction in some detail using different types of carbonyl ylides which were generated so far by thermal ring opening of the oxirane precursors [1,2]. Although the cyclisation step 2 ⟶ 3/4 seems to be rate determining in many cases, the relatively high activation barrier to the formation of 2 [3] not only complicates the mechanistic interpretation but might also be responsible for the formation of appreciable amounts of side products in certain examples [2]. Therefore we undertook intramolecular cycloaddition experiments with carbonyl ylides which were obtained by electronic excitation of selected ene-oxiranes in the temperature range between -57 and +80 °C [4].

In the present communication we describe our results with the compounds 5 - 7 as starting materials [5].

According to the uv-spectra of the ene-oxiranes, which show the long-wavelength absorption maxima at about 280 nm ($\varepsilon \sim 4000$), direct excitation may be performed either by the 253.7 Å line of a low pressure mercury lamp or using the pyrex-/vycor-filtered radiation of a high pressure mercury light source.



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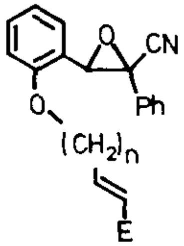
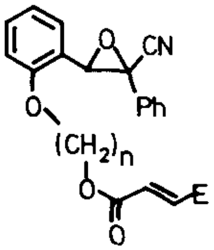


6a (n=1)
6b (n=5)
6c (n=10)



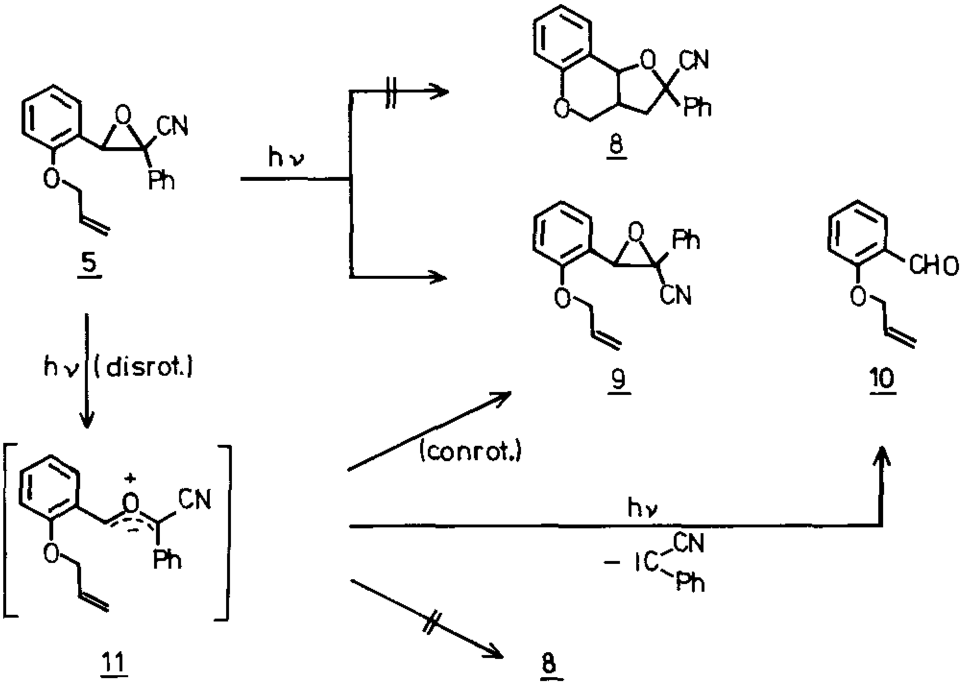
7a (n=2)
7b (n=3)
7c (n=11)

$E = CO_2CH_3$

The photoconversion of the O-allyl derivative 5 proceeds very slowly: after irradiating a solution of 100 mg of 5 in acetonitrile for 8 h (Hanau Q81, 80 W, λ >280 nm) the reaction mixture contains still ca. 30 mg of starting material as well as ca. 10 mg of its geometrical isomer 9 . Only one further monomeric product could be identified after careful thin layer chromatography (tlc), namely the aldehyde 10, the yield being ca. 30%. No indication was obtained for the formation of the intramolecular cycloadduct 8, even when the photolysis was executed at 80 °C.

The occurrence of 9 and 10 as photoproducts may be best explained by the intermediacy of carbonyl ylide 11 which either undergoes conrotatory ring closure to

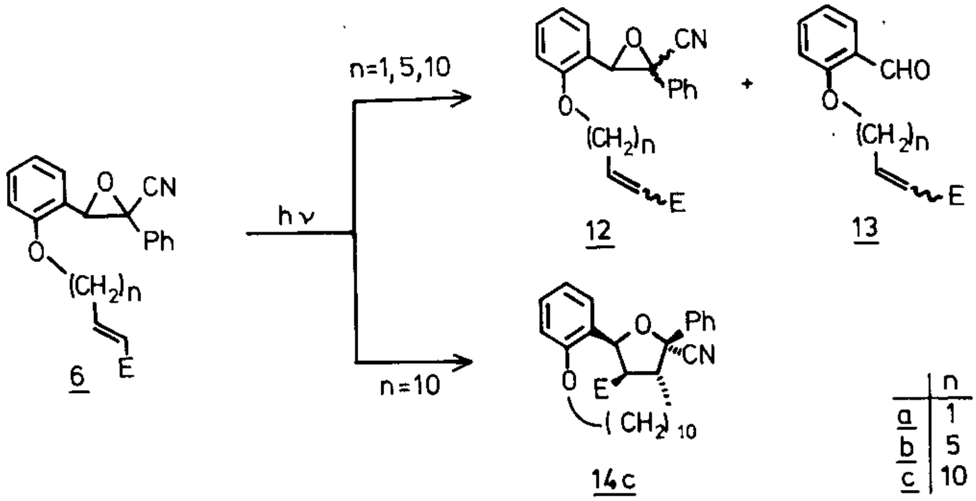
(2)



the isomer 9 (ground state reaction) or photofragmentation leading to 10 and phenyl-cyano-carbene [4,6]. Very similar results have been reported by Huisgen and coworkers with *cis*- and *trans*-diphenyl-cyano-stilbene oxide [3a,7]. On the other side, bimolecular trapping studies with photochemically formed carbonyl ylides like 11, carried out by the Munich workers as well as by our own group [2], indicated that for a successful intramolecular cycloaddition the olefinic unit of the oxirane derivatives should be substituted by electron withdrawing groups in order to reduce the activation energy Ea_2 (see equation 1).

However, irradiation experiments with 6a and 6b afforded merely a mixture of geometrical isomers of 12 and 13. It was only 6c in this series which on photoexcitation was transformed, at least to a small extent, to a cycloadduct: besides 12c/13c as the main products, the bridged tetrahydrofuran derivative 14c could be isolated in about 10% yield.

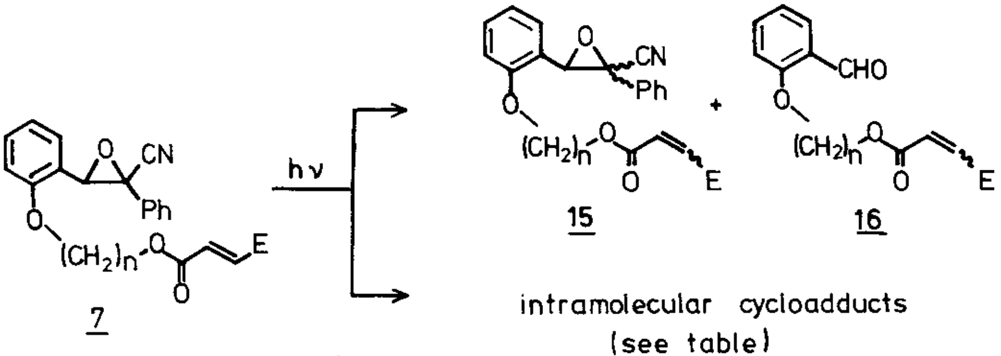
(3)



Interestingly the latter compound (14c) proved to be identical with the major product obtained on thermolysis of 6c [1b]. Therefore the cycloaddition step during the photoreaction must be slower than the C/O-bond rotation in the primary ylide (*i.e.* *exo*,*endo*- to *exo*,*exo*-isomerisation of the 1,3-dipole [8]).

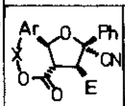
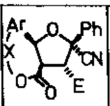
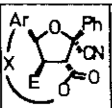
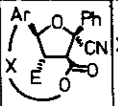
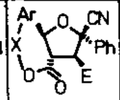
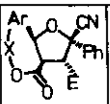
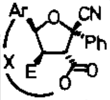
Consequently, a further enhancement of the cycloaddition process should be possible using ene-oxiranes with an olefinic unit activated by two electron attracting substituents. This assumption turned out to be correct: the photoreactions of the derivatives 7a - 7c were found to proceed significantly faster than in the other cases and to produce higher amounts of intramolecular cycloadducts (35 - 44%). Depending on the irradiation conditions (see table) 40 - 50% conversion was reached after 30 to 60 min. The product analysis was carried out by means of detailed ^{1}H-nmr investigations, including double resonance experiments, of tlc fractions containing varying quantities of reaction products [9] .

(4)



	a	b	c
n	2	3	11

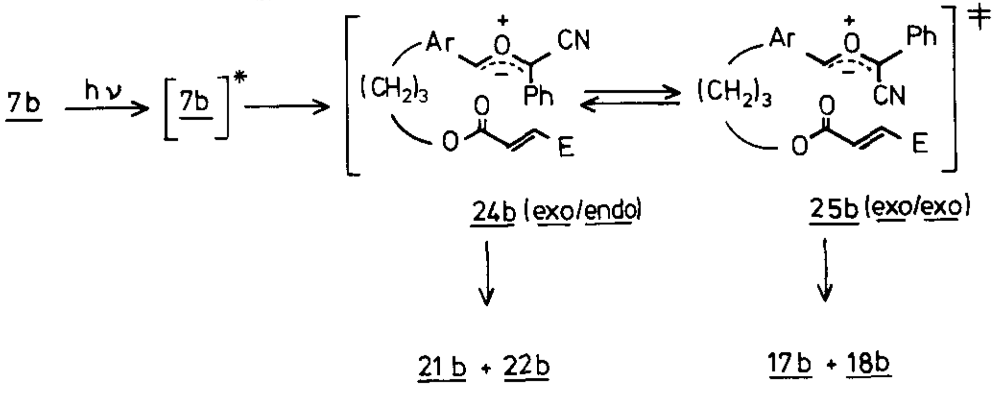
Table. Intramolecular Cycloadducts of the Ene-Oxiranes 7a, 7b and 7c

	Photolysis Conditions a)	C.[b] (%)	Y.[c] (%)	Cycloadducts [d]						
				 17	 18	 19	 20	 21	 22	 23 [e]
7a	254nm [f] 45min/20°C	39	36	50	-	-	-	50	-	-
7b	254nm[f] 45min/20°C	45	44	48	2	-	-	48	2	-
7b	> 230nm[g] 30min/20°C	50	40	39	7	-	-	53	1	-
7b	> 230nm[g] 30min/-57°C	50	40	35	4	-	-	48	13	-
7c	254nm[f] 60min/20°C	45	35	7	-	40	3	-	-	50

[a] Each run is performed with 100 mg of 7 in 100 ml solvent. [b] Conversion. The re-isolated fractions of oxiranes consist of the respective ring and double bond isomers (see structure 15). [c] Yield, related to conversion of 7. In addition to 17 - 23 , traces of the aldehydes 16 are formed as well as further adducts with unknown stereochemistry in 3 - 4% yield. [d] Numbers in %, related to the total yield of cycloadducts 17 - 23. Ar = oC_6H_4-O-, X = $(CH_2)_n$, E = CO_2CH_3. [e] Structure assignment still ambiguous. [f] Hanau NK 6/12 (6 W); CH_3CN as solvent. [g] Hanau TQ 150 (150 W); CH_3OH as solvent.

The results with 7a - 7c are summarized in the table. Whereas the annelated tetrahydrofuran derivatives 17 and 21 are formed as the exclusive or predominant cycloadducts during the photoreactions of 7a and 7b, photolysis of 7c leads preferentially to the bridged compounds 19 and 23. The prevalence of "crossed" addition has been likewise observed for the ene-oxirane 6c [1b] (*vide supra*).

According to the general scheme for intramolecular cycloadditions of ene-oxiranes (equation 1), it is reasonable to suggest that the reaction temperature might exert a strong influence on the yield of the cycloadducts (for instance, the thermal conversion of the dipole intermediate of 7b to 17/18 requires a temperature of about 120 °C) [2]. Therefore it was a rather surprising outcome of our investigations that the corresponding phototransformation turned out to be almost temperature independent (see table): in the range between +20 and -57 °C not only the total yield but also the relative amounts of cycloadducts remained nearly unchanged (the slight decrease of the adducts (17 + 18) in favor of the isomers (21 + 22) at lower temperature is in agreement with the expected diminuation of the rate for the C/O-bond rotation process 24 → 25. This result may be explained by the assumption that the cycloaddition step takes place from a vibrationally excited state [11] of the carbonyl ylide intermediate (see equation 5 with the reaction sequence for 7b).



(5)

In conclusion, we have shown that photochemical ring opening of appropriately substituted ene-oxiranes leads to carbonyl ylides which subsequently undergo intramolecular cycloaddition to the olefinic unit. However, due to various side reactions the yields are usually modest. According to the result at different temperatures, the cycloaddition step is assumed to take place from a vibrationally excited state of the dipole intermediate.

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4. For pertinent reviews on the photochemistry of oxiranes see: G.W.Griffin and A.Padwa, 'Photochemistry of Heterocyclic Compounds', Wiley-Interscience, New York, 1976, p. 41; M.Nastasi and J.Streith, 'Rearrangements in Ground and Excited States', Academic Press, New York, 1980, p. 445.
5. The synthesis of compounds *5* - *7* [2] will be reported in our full paper.
6. G.W.Griffin, *Angew.Chem.*, 1971,**83**, 604; *Angew.Chem.,Int.Ed.Engl.*, 1971,**10**, 537; K.Nishiyama, K.Ishikawa, I.Sarkar, D.C.Lankin and G.W.Griffin, *Heterocycles* 1977, **6**, 1337, and references therein.
7. V.Markowski and R.Huisgen, *Tetrahedron Lett.*, 1976, 4643.
8. The terms *exo*/*exo*- and *exo*/*endo*-ylide refer to the arrangement of the aryl and phenyl groups.
9. Amongst the various criteria for the structural assignments the different coupling constants of vicinal ring protons as well as the significant shielding effect of aryl groups on *cis*-located hydrogens are especially valuable[10]. Moreover, some of the cycloadducts have been already identified during our thermal investigations [1,2].
10. For a more detailed discussion see: W.Eberbach and B.Burchardt, *Chem.Ber.*, 1978,**111**,3665; J.Brokatzky-Geiger and W.Eberbach,*Heterocycles*,1981,**16**, 1907.
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