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CYCLOOCTENONE PHOTOCYCLOADDITIONS

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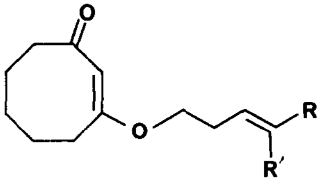
Abstract: The first intramolecular [2+2] photocycloadditions of cyclooctenones have been achieved using substituted 3-butenyloxy cyclooctenones.

The photochemical [2+2] cycloaddition of an enone to an olefin has been found to be a very versatile tool in the synthesis of natural products.[1] It is well understood that the ease of rotational relaxation has a profound effect on the lifetime of the triplet enone.[2] For efficient cyclo-addition the lifetime must be sufficiently long. Thus an enone in a rigid cyclic system should be a good substrate for photochemical [2+2] cycloaddition. This is indeed the case, 5- and 6-membered ring enones being excellent substrates for such reactions. In larger rings or acyclic systems, rotational relaxation to the ground state cis- or trans-enone becomes a more facile process, thus shortening the excited state lifetime.[2] A few intramolecular photocycloadditions are known in acyclic or macrocyclic systems, which presumably are due to the unimolecular nature of the reaction and the fact that both the cis- and trans-enones are conjugated.[3] However, in 7- or 8-membered ring enones the trans-enones formed by rotational relaxation are known to be non-conjugated. Both have been observed spectroscopically.[4] Since conjugation of the enone chromophore is a requirement for [2+2] photocycloaddition, these trans enones are inert.

In this Letter we wish to report that incorporation of an oxygen atom on the 3-position of the enone chromophore overcomes this barrier. Upon the irradiation of 3-alkoxycyclooctenones, no trans-enone is observable.[4] Thus the presence of oxygen causes relaxation to the cis-enone.[5] In order to explore further the possibility of intramolecular photocycloaddition in these compounds, a series of substituted 3-butenyloxy cyclooctenones was synthesized.

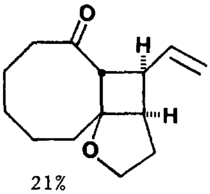
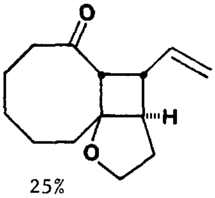
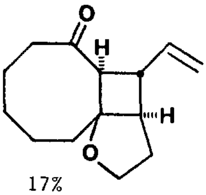
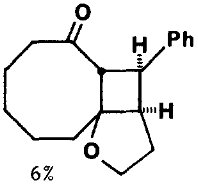
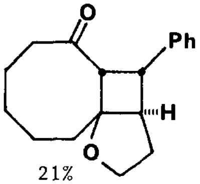
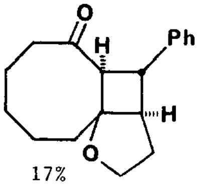
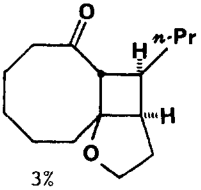
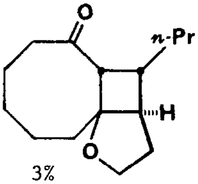
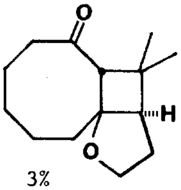
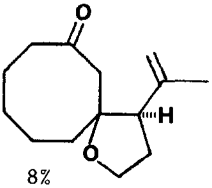
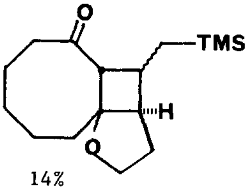
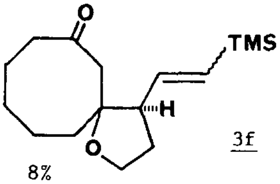
Cyclooctane-1,3-dione is prepared in 77% yield by the subjection of diethyl pimelate to the silyl acyloin reaction (5eq. Na sand, 4.2 eq. TMSCl, toluene, N_2, 4d) followed by treatment of the resulting bis(trimethylsiloxy)-cycloheptene with bromocarbene (2 eq. $CHBr_3$, 2 eq. Et_2Zn added over 1h, 0°, toluene, N_2). Aqueous ammonium chloride work-up and Kugelrohr distillation (80-85°, 1.5 torr) gives the dione. Preparation of the 3-butenyloxycyclooctenones is achieved by O-alkylation of the potassium enolate (tBuOK or $KN(TMS)_2$) of the dione with the corresponding butenyltosylate in DME solution (60°, 16h, N_2). Dilution with dry Et_2O, filtration, and evaporation of the solvents gives the sensitive enol ethers (1), which were purified by chromatography through neutral alumina.[6]



(1)

1	R	R′	Yield (%)
a	H	H	66
b	$CH{=}CH_2$	H	61
c	Ph	H	51
d	*n*-Pr	H	52
e	CH_3	CH_3	82
f	H	CH_2SiMe_3	35

Irradiations were performed on degassed 0.01M solutions of enone (1) in cyclohexane at 350 nm in a Rayonet photoreactor. An unusual substituent effect is observed. When 1a is irradiated under a wide variety of conditions (solvent, time, temperature, sensitizer, additives) no intramolecular cycloadduct is observed.[5] However, upon substitution of a vinyl (1b), or phenyl (1c) group on the olefin, the cycloaddition proceeds efficiently ($\Phi = 0.26$ for 2b) to give diastereomeric mixtures of cycloadducts 2b and 2c respectively.[7] Irradiation of enone 1d gives a mixture of cycloadducts 2d in lower yield after a much longer time. The dimethyl enone 1e again gives a low yield of cycloadduct 2e and in addition the photo-ene product 3e. Similarily the allyl silane 1f gives a mixture of cyclobutane and ene products, 2f and 3f respectively. The mechanistic aspects of this reaction and the origin of the substituent effect will be discussed in a full paper.

ENONE(1)	TIME	CYCLOADDUCT(2)		
1a	-	-		
1b	6h	 21%	 25%	 17%
1c	6h	 6%	 21%	 17%
1d	7 days	 3%	 3%	
1e	7 days	 3%	 8% 3e	
1f	7 days	 14%	 8% 3f	

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References and Notes

1. Oppolzer, W., Acc. Chem. Res., (1982), 15, 135; Baldwin, S.W., Org. Photochem., (1981), 5, 123; Bauslaugh, P., Synthesis, (1970), 257; Weedon, A.C., in "Synthetic Organic Photochemistry"; Horspool, W.M., Ed.; Plenum Press; New York, 1984; p 61.

2. Bonneau, R., J. Am. Chem. Soc., (1980), 102, 3816; Wagner, P.J., Bechek, D.J., Ibid., (1969), 91, 5090; de Mayo, P., Acc. Chem. Res., (1971), 4, 41.

3. Wolff, S., Agosta, W., J. Am. Chem. Soc., (1983), 105, 1292 and references therein; Heathcock, C.H., Badger, R., Chem. Commun., (1968), 1510; Scheffer, J., Boire, B., Tetrahedron Lett., (1969), 4005.

4. Corey, E.J., Tada, M., LeMaiheu, R., Libit, L., J. Am. Chem. Soc., (1965), 87, 2051; Eaton, P., Liu, K., Ibid., (1964), 86, 2087; Eaton, P., Liu, K., Ibid., (1965), 87, 2052; Bonneau, R., Fornier de Violet , P., Joussot-Dubieu, J., Nouv. J. Chim., (1977), 1, 37; Goldfarb, T.D., J. Photochem., (1978), 8, 29.

5. Results in collaboration with Professor N. Pienta, University of Arkansas, confirm that no trans-enone is observed on flash photolysis. In addition, oxygen substitution is known to shorten the triplet excited state lifetime: Peters, K., Freilich, S., J. Am. Chem. Soc., (1981), 103, 6255; Zimmt, M.B., Doubleday, C., Jr., Gould, I.R., Turro, N.J., Ibid., (1985), 107, 6724.

6. All new compounds gave satisfactory NMR, IR, and high resolution MS data. For enone 1a: ^{1}H NMR (300MHz, $CDCl_3$): 1.40-1.80 (6H, m), 2.45 (2H, tq, J = 6.5, 1.2), 2.65-2.90 (4H, m), 3.80 (2H, t, J = 6.5), 5.07 (1H, dq, J = 16.6, 1.4), 5.08 (1H, tq, J = 10.7, 1.2), 5.58 (1H, s), 5.82 (1H, ddt, J = 17.4, 11.0, 6.7).

7. Stereochemical assignments were made on the basis of NOEDS and LIS data. It has been suggested that the trans product observed for enones 1b and 1c may have arisen via a thermal reaction of the trans enone. However, trans products have been observed for enones that cannot form trans isomers.[1] Two pieces of evidence favour a photochemical origin for the trans product; (a) the diastereomeric ratio does not show a significant temperature dependence, and (b) 3-phenyl-3-butenyloxy-cyclooctenone cyclizes to give exclusively a trans [6.2.0] product whose regio-chemistry is incompatible with a thermal reaction.

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