Tetrahedron Letters No. 33, pp 2979-2982.
0040-4039/78/0808-2979$02.00/0

PHOTOCYCLOADDITION OF DIMETHYLACETYLENE DICARBOXYLATE TO ACTIVATED INDOLES

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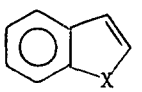
Photochemical cycloaddition reactions of acetylene esters and fused ring heteroaromatic compounds of the general structure (I) have been under extensive investigation in our laboratories.[1-3] Our results demonstrate that sensitized photocycloaddition to benzo(b)thiophene



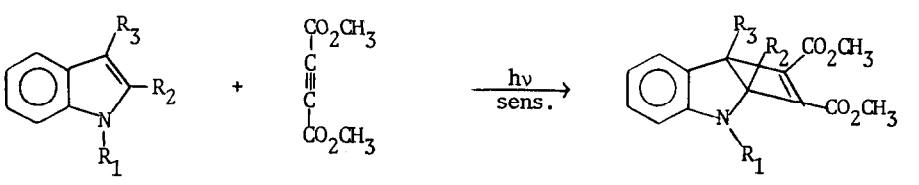
(I)

X=O,S,N-R; R=alkyl

and many of its alkylated derivatives, as well as the anologus benzo(b)furans, give $[2\pi+2\pi]$ adducts which are capable of secondary photochemical allylic rearrangements.

As part of the continuing study, we have now investigated the comparable reactions of N-alkylindoles, and find significant differences from the sulfur and oxygen isosteres.

We report herein preliminary results on the photocycloaddition of dimethyl acetylenedicarboxylate (DMAD) to activated N-alkylindoles, (1). The products listed in Table I are those expected from the $[2\pi+2\pi]$ photocycloaddition reactions. Though no attempt has been made to maximize the yields, the photoreactions are remarkably clean and in most of the cases examined, cyclobutenes constituted the major product.

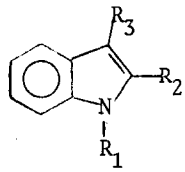


(1)

1 DMAD 2

Table I

Yield of Products from the Sensitized Photolysis of Indoles and DMAD



		% Yield of 2
1(a)	R_1=CH_3, R_2=R_3=H	(a) 72
(b)	R_1=CH_3, R_2=CH_3, R_3=H	(b) 11[a,b]
(c)	R_1=CH_3, R_2=H, R_3=CH_3	(c) 2-12[a,c]
(d)	R_1=CH_3, R_2 and R_3=-$(CH_2)_3$-	(d) 71[b]
(e)	R_1=CH_3, R_2 and R_3=-$(CH_2)_4$-	(e) 82[b]
(f)	R_1=CH_3, R_2=H, R_3=t-butyl	(f) 77[b]
(g)	R_1=t-butyl, R_2=H, R_3=t-butyl	(g) 15[a,b]

a Isolated; not based on recovered starting material even though irradiations typically proceed to only 25-40% conversion

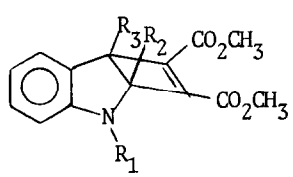
b <5% substitution products

c Yield is a function of [1(c)] / [DMAD], 2:1 adducts predominate as the ratio is increased to >1.

A typical photochemical run is carried out in benzene solution, which is 0.015 M in indole, 0.012 M in DMAD and .006 M in acetophenone. This solution is degassed and then irradiated with a 450-W medium pressure Hg lamp through pyrex while held at 9±4° C and kept under a constant flow of nitrogen. After 24 hrs. the solvent is removed under reduced pressure and the reaction mixture separated by column chromatography on Florisil. Elution with petroleum ether allows removal of starting indole, increasing amounts of ether (>5%) removal of sensitizer, the acetylene ester, and substitution products, followed by the cyclobutene (and/or benzazepine). These materials are further purified by TLC.

Table II

NMR Data of Cyclobutenes



	N-R_1	R_2	R_3	CO_2CH_3	Aromatic
2(a)	3.04	4.66,q(AB),2H		3.87	6.4-7.5,m,4H
(b)	2.96	1.67	4.04,s,1H	3.83	6.35-7.4,m,4H
(c)	3.06	4.33,s,1H	1.66	3.84	6.4-7.4,m,4H
(d)	2.98	1,18-2,46,m,6H		3.80	6.3-7.55,m,4H
(e)	2.96	1.28-2.66,m,8H		3.87	6.35-7.45,m,4H
(f)	3.02	4.52,s,1H	1.11,s,9H	3.79, 3.83	6.4-7.6,m,4H
(g)	1.50,s,9H	4.88,2,1H	1.08,s,9H	3.80	

δ,$CDCl_3$; unless otherwise indicated all peaks are singlets (3H)

The nmr and uv data for all the cyclobutenes thereby prepared are listed in Table II. The nmr spectra are characterized by (1) a shielding of the N-alkyl substituent relative to the corresponding starting indole, (2) a shielding of R_2 and/or R_3, for both alkyl and allylic proton substituents, and (3) a very characteristic set of four peaks in the region (in $CDCl_3$) between 6.3 and 6.8δ. The uv spectra are distinguished by the presence of an intramolecular charge-transfer (C-T) absorption. Log ε is constant at 2.88 for the C-T

Table III

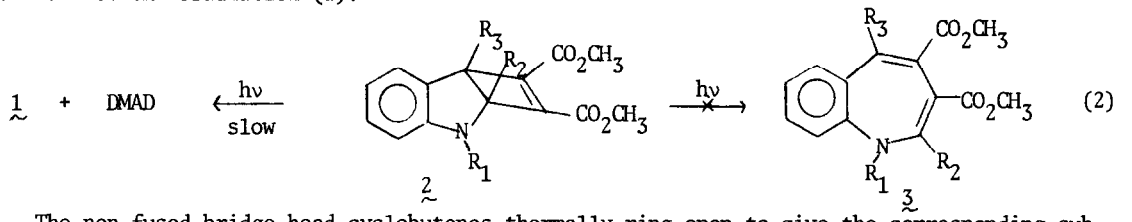
UV Data of Cyclobutenes (2)

	C-T λ_{max}	Other
2(a)	375	---
(b)	427	285, 253
(c)	435 (2.79)	302 (3.14), 251 (3.61)
(d)	438 (2.88)	304 (3.18), 249 (3.68)
(e)	432	302, 250
(f)	411 (2.81)	295 (3.21), 252 (3.62)
(g)	408	---

95% EtOH

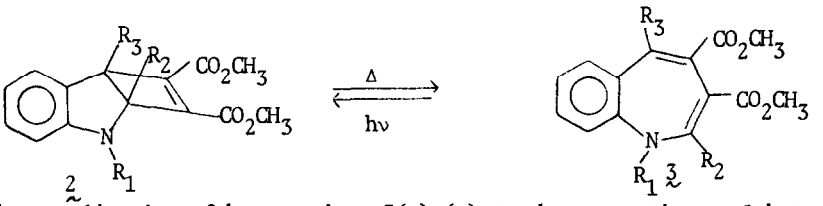
band belonging to 9,10-dimethoxycarbonyl-2-methyl-3,4-benzo-2-azatricyclo [3.3.2.0] deca-3,9-diene, 2(d), at 435 nm over concentrations ranging from 4.79×10^{-4} M to 3.45×10^{-5} M. This C-T absorption disappears upon reduction with diimide. The presence of these C-T absorptions in the visible region means that the cyclobutenes are colored, ranging from a very deep orange to a blood red. These intramolecular charge transfer complexes are unique in that the donor and acceptor portions of the molecule are held in a specific geometry. Since the distance between and relative orientation of the donor and acceptor portions is controlled, it is of interest to study the effect of substituents on the intensity and position of the charge transfer band. Further work in this area is in progress.

All of the cyclobutenes isolated are stable to photochemical ring opening under direct and sensitized irradiation, although they do undergo a slow cycloreversion to starting materials under direction irradiation (2).



(2)

The non-fused bridge head cyclobutenes thermally ring open to give the corresponding substituted benzazepines, 3. As expected, 2(d) and 10,11-dimethoxycarbonyl-7-methyl-8,9-benzo-7-azatricyclo [4.3.2.0] undeca-8,10-diene, 2(e), are relatively thermally stable because of the fused bridge head ring system. The relative ease of ring opening is substituent dependent. The cyclobutene photoadduct of 1,3-dimethylindole, 2(c), has a $\tau_{1/2}$ (58°)=60 min., while that derived from 3-t-butyl-1-methylindole, 2(f), has a $\tau_{1/2}$ (92°)=90 min.



The photocyclization of benzazepines 3(a)-(c) to the respective cyclobutenes occurs at the rates indicated in Table IV. The concentrations typically used are approximately $5x10^{-3}$ M, Slow, but competitive photocycloreversion also takes place. Paquette, for example, has carried out similar studies in the 1H-azepine systems, where unlike the present benzazepine systems, more than one cyclobutene can be obtained. In this case, the regioselectivity of ring closure is substituent dependent.[4,5]

Table IV

Photocyclization Conversions of Some Benzazepines

	t(hr.)	% 2*
3(a)	24	30
(b)	9	45
(c)	12	71

* % conversion

The cyclobutene, 6,7-dimethoxycarbonyl-2,5-dimethyl-3,4-benzo-2-azabicyclo [3.2.0] hepta-3,6-diene, 3(c), has previously been suggested as an intermediate in the reaction of 1,3-dimethylindole with DMAD in the presence of $BF_3 \cdot Et_2O$, but was neither isolated nor characterized.[6]

The observed photostability of 2 towards rearrangement contrasts with the photolabile C-heteroatom bond cleavage process which occurs in the sulfur and oxygen systems, leading to molecular rearrangements.

We are presently carrying out mechanistic studies on this system, details of which will be published elsewhere.

Acknowledgement

This work has been supported in part by the Petroleum Research Fund, administered by the American Chemical Society. We gratefully acknowledge the donors of these funds.

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(Received in USA 25 April 1978; received in UK for publication 20 June 1978)