Photocycloaddition of Dimethyl Acetylenedicarboxylate to Activated Indoles

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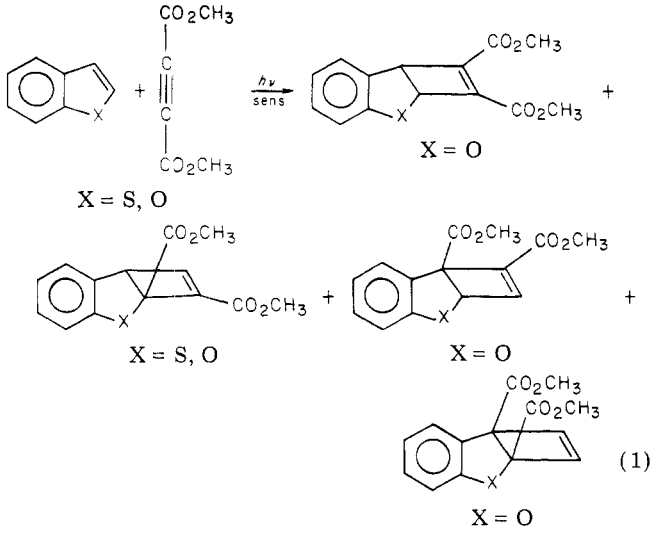
Received October 5, 1979

Photocycloaddition reactions of *N*-methylindoles to dimethyl acetylenedicarboxylate (DMAD) yield derivatives of cyclobutenes: 9,10-bis(methoxycarbonyl)-2-methyl-3,4-benzo-2-azatricyclo[3.3.2.0]deca-3,9-dienes. No secondary photorearrangements are prevalent, but ring opening of the formed cyclobutenes is effected at moderate temperatures.

Background

The photocycloaddition reactions of acetylene esters to the fused heterocycles benzo[*b*]thiophene and benzo[*b*]furan are fraught with unusual rearrangements.[1] Benzo[*b*]thiophene and its alkyl derivatives with acetylene esters give secondary photochemical allylic rearrangement products, and these are formed as the major isolable photoproducts;[2-5] benzo[*b*]furans give allylic rearrangement products as well as those deriving from other skeletal rearrangement processes (eq 1).[6-8]



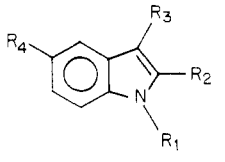
(1)

As part of a general study begun because of the observed secondary photorearrangements occurring when acetylene esters are added to the fused heterocycles benzo[*b*]thiophene and benzo[*b*]furan, we initiated, some years ago, a study of benzo[*b*]pyrrole (indole). Its photochemistry is complicated by interesting, though different, avenues of degradative achievement.[9]

Results and Discussion

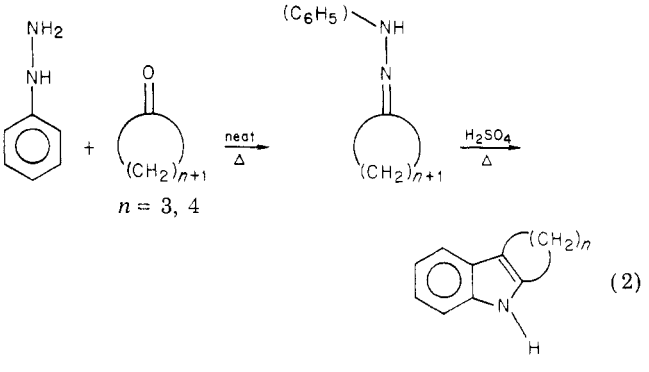
N-Methylindoles were selected for study, largely because nonalkylated indoles undergo photochemical N–H bond scission and oxidize,[10] the result of which is a tarry, disrespectable mixture. The specific indoles reported on in this and the subsequent paper are listed in Table I. All except Ic and Id were synthesized from known indoles by N-methylation using standard procedures. The bridged indole precursors of Ic and Id were synthesized by a standard Fisher indole synthesis as shown in eq 2.[11] The

Table I. Activated Indoles



I

a, $R_1 = CH_3$, $R_2 = R_3 = R_4 = H$	*N*-methylindole
b, $R_1 = R_2 = CH_3$, $R_3 = R_4 = H$	1,2-dimethylindole
c, $R_1 = CH_3$, R_2, $R_3 = -(CH_2)_3-$, $R_4 = H$	1-methyl-2,3-trimethyleneindole
d, $R_1 = CH_3$, R_2, $R_3 = -(CH_2)_4-$, $R_4 = H$	6,7,8,9-tetrahydro-1-methylcarbazole
e, $R_1 = CH_3$, $R_2 = R_4 = H$, R_3 = *tert*-butyl	3-*tert*-butyl-1-methylindole
f, $R_1 = R_3$ = *tert*-butyl, $R_2 = R_4 = H$	1,3-di-*tert*-butylindole



(2)

phenylhydrazones of cyclopentanone and cyclohexanone, respectively, were treated with dilute sulfuric acid under reflux for 1 h, and the N–H derivatives of Ic and Id were isolated in high yields (85 and 90%, respectively). The indoles 3-*tert*-butylindole and 1,3-di-*tert*-butylindole (If), were prepared by the synthetic route shown in eq 3.[12] Indolylmagnesium iodide, prepared from indole and methylmagnesium iodide, is known to undergo primarily 3-alkylation.[13] In the presence of excess *tert*-butyl

(1) Tinnemans, A. H. A.; Neckers, D. C. *J. Org. Chem.* **1978**, *43*, 2493.
(2) Neckers, D. C.; Dopper, J. H. *J. Org. Chem.* **1971**, *36*, 3755.
(3) Tinnemans, A. H. A.; Neckers, D. C. *J. Org. Chem.* **1977**, *42*, 2374.
(4) Sasse, W. H. A. *Aust. J. Chem.* **1969**, *6*, 1257.
(5) Reinhoudt, D. N.; Kouvenhaven, C. G. *Tetrahedron Lett.* **1972**, 5203.
(6) Hofmann, H.; Gauke, H. *Justus Liebigs Ann. Chem.* **1977**, 1874.
(7) Reinhoudt, D. N.; Kouvenhoven, G. G. *Tetrahedron* **1974**, *30*, 2431.
(8) Schultz, A. G.; Napier, J. J.; Lee, R. *J. Org. Chem.* **1979**, *44*, 663.
(9) Davis, P. D.; Neckers, D. C. *Tetrahedron Lett.* **1978**, 2979.
(10) Santus, R.; Grossweiner, L. I. *Photochem. Photobiol.* **1972**, *15*, 101.
(11) Perkin, W. H.; Plant, S. G. P. *J. Chem. Soc.* **1923**, *123*, 3242.
(12) Smith, G. F.; Waters, A. E. *J. Chem. Soc.* **1961**, 940.

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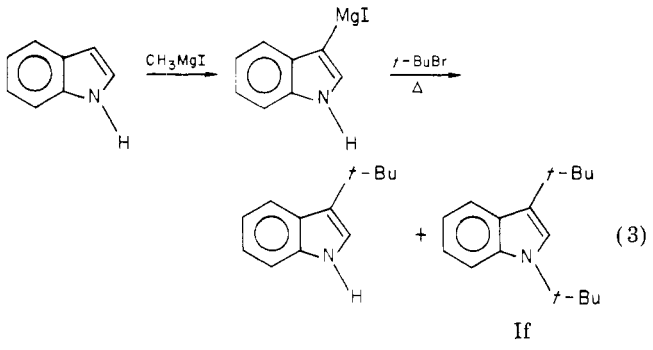
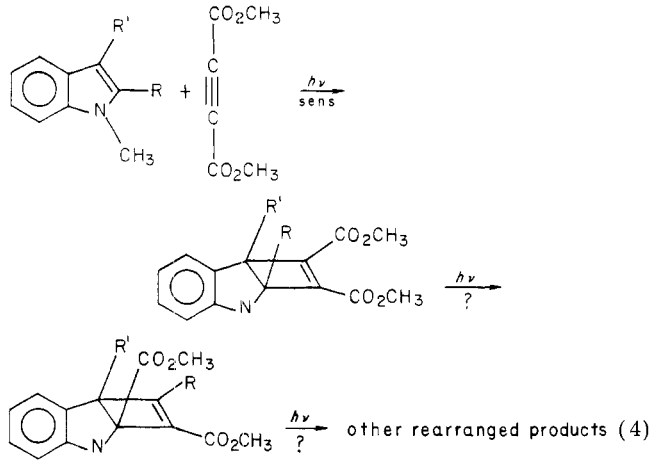


(3)

If

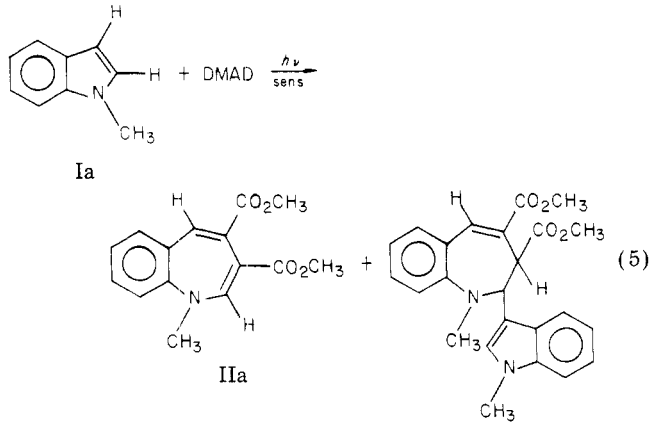
bromide, the initially formed 3-*tert*-butylindole presumably undergoes N-*tert*-butylation.

Photochemical Reactions of Activated Indoles and Dimethyl Acetylenedicarboxylate. On the basis of observations with the sulfur and oxygen isosteres, sensitized photocycloaddition of dimethyl acetylenedicarboxylate (DMAD) to activated indoles is expected to produce rearranged products (eq 4). Such does not occur.



(4)

The photocycloaddition of DMAD and *N*-methylindole (Ia) carried out at ambient temperatures gave the benzazepine 3,4-dimethoxycarbonyl-1-methyl-6,7-benzo-1-azepine (IIa) and its *N*-methylindole addition product (eq 5).

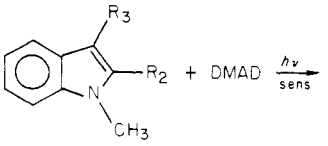


(5)

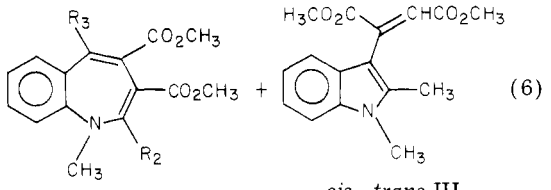
Ia

IIa

These products are identical with those reported by Acheson and co-workers[14] from the thermal cycloaddition reaction (6 days in refluxing acetonitrile). The analogous benzazepine, IIb, was also isolated from 1,2-dimethylindole and DMAD along with the mixture of isomers III (eq 6).



Ib, $R_2 = CH_3$, $R_3 = H$



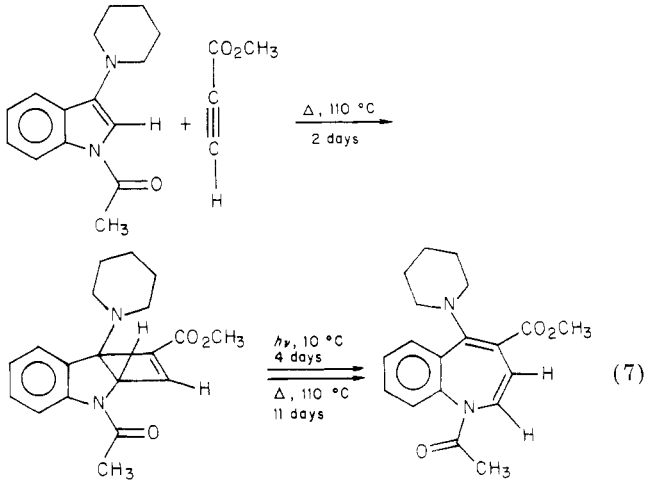
(6)

IIb

cis-, *trans*-III

III was shown not to be a photochemical product, but is formed thermally during the workup procedures.

On the basis of an earlier report[15] (eq 7), we suspected



(7)

that the cyclobutenes we sought from the photocycloaddition reactions should be *thermally* stable under our reaction and workup conditions. That the cyclobutenes were *photolabile* and ring-open to the benzazepine[16] was thereby suggested. The disrotatory ring opening predicted for the photochemical electrocyclic reaction might be favored over the thermal conrotatory process (giving the cis–trans diene) when the allylic rearrangement is not a competing secondary photochemical process. 2-Acetyl-6-(methoxycarbonyl)-5-piperidyl-3,4-benzo-2-azabicyclo-[3.2.0]hepta-3,6-diene (IV) was prepared by using the known procedure.[15] Photolysis of IV (4 days, 10 °C, 10^{-2} M, in benzene) led quantitatively to ring opening and to the benzazepine 1-acetyl-4-(methoxycarbonyl)-5-piperidyl-6,7-benzo-1-azepine. Thus it was confirmed that the benzazepines might derive from a similar secondary photoprocess in the indole series.

With photochemical ring opening to the benzazepine as a potential result, we sought to build a molecule(s) in which photochemical cyclobutene formation, if occurring, could be guaranteed and benzazepine formation, either thermally or photochemically, repressed. The possibility of testing for secondary photochemical rearrangements as observed in the benzo[*b*]thiophene and benz[*b*]furan isosteres was more likely if the ring opening could be prevented. 1-

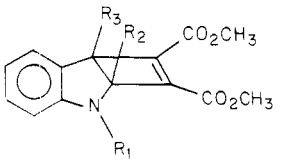
(13) (a) Powers, J. C. In "The Chemistry of Heterocyclic Compounds"; Weissberger, A., Taylor, E. C., Eds.; "Indoles"; Houlihan, W. J., Ed.; Interscience: New York, 1972; Part II, Chapter 5, pp 143–147. (b) Sebastian, J. F. Ph.D. Thesis, University of California, Riverside, June 1965. (c) Heacock, R. A.; Kasparek, D. *Adv. Heterocycl. Chem.* **1969**, *10*, 43. (d) Jackson, A. H.; Smith, A. E. *Tetrahedron* **1965**, *21*, 989. (e) Acheson, R. M.; Hands, A. R. *J. Chem. Soc.* **1961**, 744.

(14) Acheson, R. M.; Bridson, J. N.; Cameron, T. S. *J. Chem. Soc., Perkin Trans. 1* **1972**, 968.

(15) Lin, M. S.; Snieckus, V. *J. Org. Chem.* **1971**, *36*, 647.

(16) For example, see Reinhoudt, D. N. *Adv. Heterocycl. Chem.* **1977**, *22*, 254.

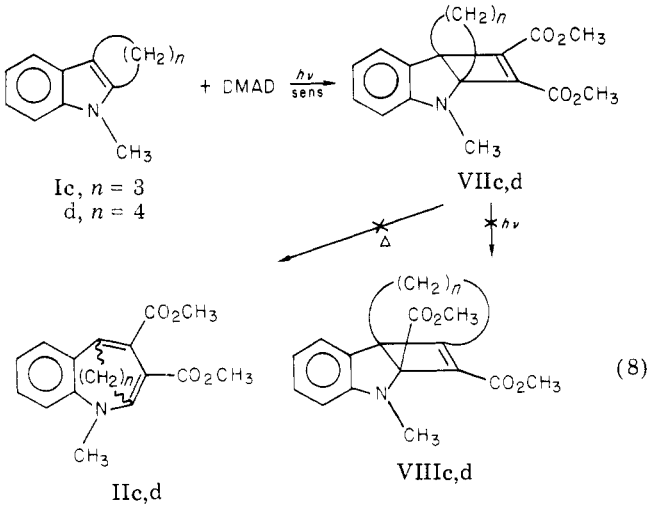
Table II. Yield of Products from the Sensitized Irradiation of Indoles and DMAD



VII

I	% yield of VII
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
c, $R_1 = CH_3$, R_2 and $R_3 = -(CH_2)_3-$	c, 71
d, $R_1 = CH_3$, R_2 and $R_3 = -(CH_2)_4-$	d, 82
e, $R_1 = CH_3$, $R_2 = H$, $R_3 = tert$-butyl	e, 77
f, $R_1 = tert$-butyl, $R_2 = H$, $R_3 = tert$-butyl	f, 85

Methyl-2,3-trimethyleneindole (Ic) and 6,7,8,9-tetrahydro-1-methylcarbazole (Id) were chosen as ideal candidates. The selection was based on the unlikelihood of



Ic, $n = 3$
d, $n = 4$

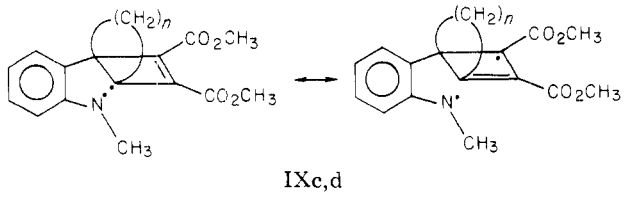
VIIc,d

IIc,d

VIIIc,d

(8)

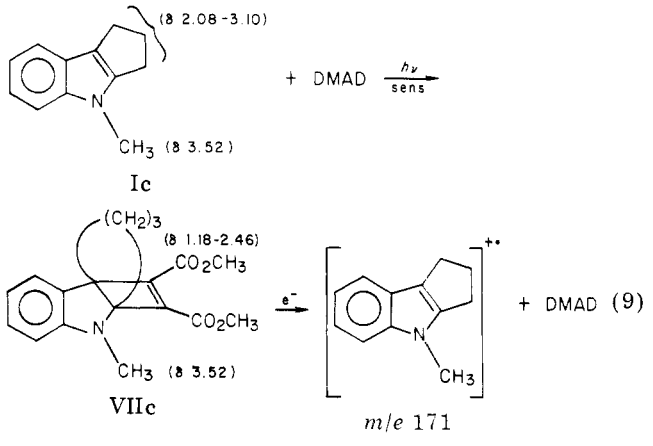
dual bridgehead double bond formation (Bredt's rule) upon thermal or photochemical ring opening of the incipient cyclobutenes, VIIc and VIId (eq 9). If ring opening is eliminated, the secondary photochemical allylic rearrangement can be considered. However, these secondary reactions, we suspected, might be inhibited by the added strain in the rearranged product(s), VIIIc and VIIId, and/or by the potential for sterically inhibited resonance in the biradical intermediates, IXc and IXd. A significant



IXc,d

allylic contribution in this biradical is necessary for rearrangement to be a facile process, and Bredt's rule considerations might also prevent it from occurring.

Accordingly, irradiation of 1-methyl-2,3-trimethyleneindole (Ic), and DMAD in the presence of acetophenone gave one product by gas chromatography. This *blood-red* compound was isolated and purified by TLC and could be collected unchanged through a GC column at 200 °C (injector, 250 °C; detector, 300 °C). The product was shown to be the cyclobutene 9,10-bis(methoxycarbonyl)-2-methyl-3,4-benzo-2-azatricyclo[3.3.2.0]deca-3,9-diene (VIIc) on the basis of the NMR, mass spectral, and UV data. The NMR spectrum of Ic is characterized by the *N*-methyl singlet absorption at δ 3.52 and a complex set of absorptions between δ 2.08 and 3.10 assigned to the six methylene hydrogens ($-(CH_2)_3-$). In the product these absorptions occur at δ 2.95 and from δ 1.18 to δ 2.46, respectively. The upfield shifts indicate an absence or diminution of the aromatic anisotropic effect in the heteroatomic ring system. In the mass spectrum the major fragment is at m/e 171, indicating loss of 142 mass units, the equivalent of one molecule of DMAD (eq 9). The cyclobutenes derived from



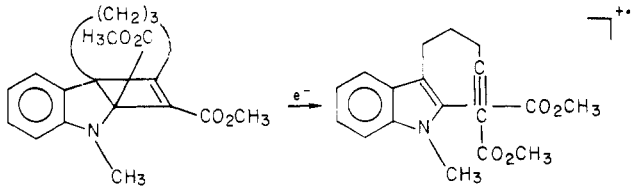
Ic

VIIc

m/e 171

(9)

benzo[*b*]thiophene and benzo[*b*]furan characteristically lose an acetylenic fragment (which acetylene loss depends on the degree of secondary rearrangement of the product) as the major fragmentation, with M^+ – acetylene: $M^+ < 1$.[1-4] The ratio $(M^+ - 142):M^+$ is approximately three,



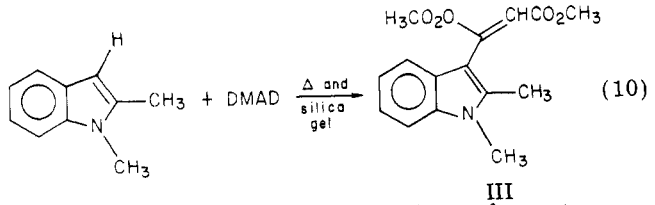
VIIIc

m/e 313

indicating acetylene loss in the fused indoles to be a more facile process than that in the sulfur- and oxygen-fused systems. The acetylene loss in the rearranged product, VIIIc, would be the equivalent of an intramolecular cycloreversion and would not show an efficient loss of acetylene, but an enhanced molecular ion. The UV data are also inconsistent with a rearranged product. Similar assignments and conclusions were made for the cycloadduct product isolated in the sensitized irradiation of Id and DMAD. *From these results we can conclude that the (2 + 2) cycloadduct is the primary isolable photochemical product in the system Id + DMAD where no benzazepine formation is possible.*

General (2 + 2) Photocycloadditions to Indoles: Physical and Chemical Characteristics. Sensitized photocycloaddition generally gives ($_\pi2 + _\pi2$) cycloadducts from the indoles Ia–f and DMAD, and these adducts are easily isolated under appropriate conditions. The yields, based on recovered starting material, are reported in Table II, and NMR data are given in Table III.

The yield of VIIb is notably low. VIIb must be separated from the substitution products, *cis*- and *trans*-III, formed during workup. These are formed very rapidly, both thermally and on silica gel (eq 10). In fact, at 10 °C it is difficult to suppress completely the thermal reaction. (Thermally, the fumarate, *trans*-III, is favored, whereas the maleate, *cis*-III, is formed predominately on silica gel. No cyclobutenes and/or benzazepines are formed in the

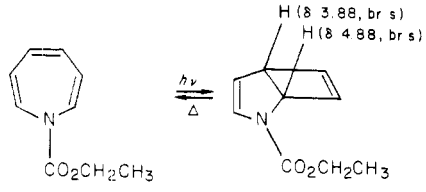


(10)

III
trans-; fumarate
cis-; maleate

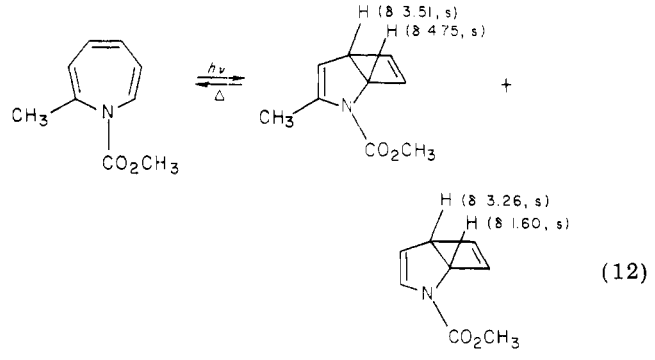
dark reaction. Even in refluxing benzene (>24 h) no detectable amounts of the *cycloadducts* (and benzazepines) are formed.)

Paquette and co-workers[17] have observed the photochemical ring closure in the 1*H*-azepine (and oxepine) ring systems to give bicyclo[3.2.0]hepta-3,6-dienes, which thermally (>150 °C) revert to the seven-membered ring (eq 11). The disubstituted azepine 1-(methoxy-



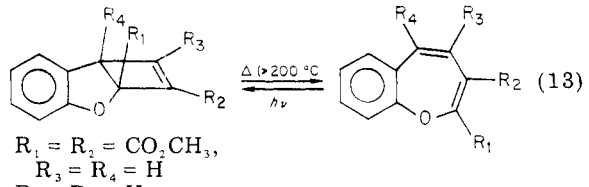
(11)

carbonyl)-2-methyl-1-azepine (eq 12) gives the two possible



(12)

products, the product with less angular strain predominating. Tinnemans and Neckers[1] have made similar observations in the fused benzo[*b*]furan cyclobutenes (eq 13).



(13)

$R_1 = R_2 = CO_2CH_3$, $R_3 = R_4 = H$
$R_1 = R_2 = H$, $R_3 = CO_2CH_3$

An analogous situation might be anticipated for the fused indole cyclobutenes and benzazepines. Irradiation of several benzazepines does in fact lead to formation of the corresponding cyclobutenes (Table IV). A limiting factor in these photocyclizations is a slow but competitive cycloreversion of the cyclobutene to starting materials.

All of the cyclobutenes isolated are highly colored, ranging from deep orange to blood red, because of an intramolecular charge-transfer (CT) absorption in the visible region of the absorption spectrum (Table V).[18] *Intermolecular* CT complexes can be eliminated if the extinction coefficient of the CT band does not change as the solution containing the complex is diluted, as the equi-

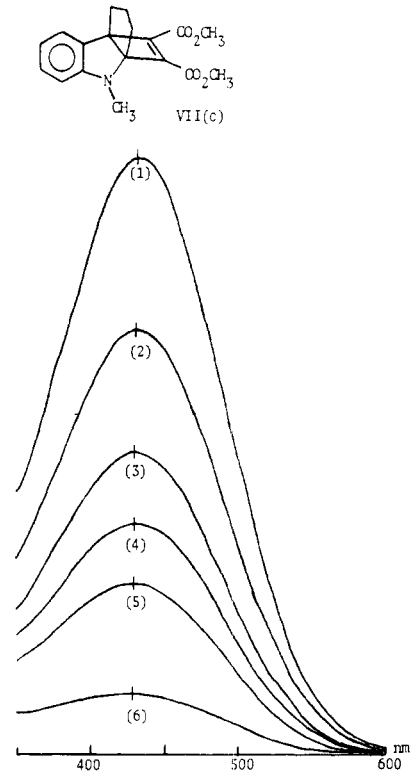


Figure 1. Effect of VIIc concentrations on the molar extinction coefficient of the charge-transfer absorption.

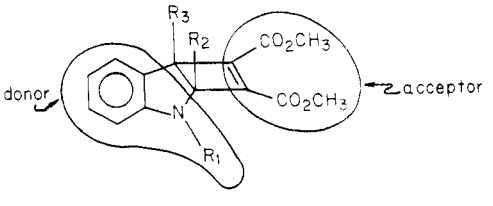
librium between complexes and free species is shifted to the left (eq 14). The extinction coefficient of an *intra-*

$$\underset{\text{donor}}{D} + \underset{\text{acceptor}}{A} \rightleftarrows \underset{\text{CT complex}}{[D{\cdot}A]} \qquad (14)$$

molecular CT complex should be independent of concentration if the interacting donor and acceptor chromophores are held in a specific and rigid geometry.

The compound chosen for detailed study is VIIc because of its thermal stability. The charge-transfer absorption for VIIc occurs at 435 nm (log ε 2.88) and does not change over concentrations ranging from 4.79×10^{-4} M to 3.45×10^{-5} M (Figure 1).

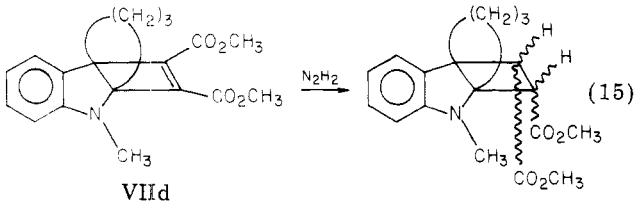
The interacting chromophores are assumed to be the electron-deficient cyclobutene olefinic double bond and the electron-rich, substituted-aniline-derived, aromatic portion of the molecule. Reduction of the double bond



is expected to cause disappearance of the CT band.[19] Thus diimide reduction destroys the 435 nm λ_{max} of VIId (Figure 2), and leads to an approximately equal mixture of the *endo*- and *exo*-dihydrobenzoazatricyclo[3.3.2.0]-decenes, X (eq 15).

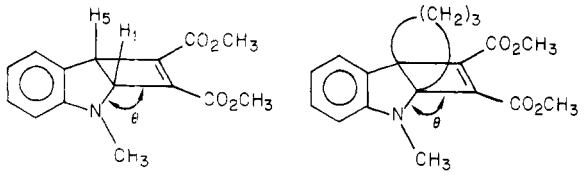
The position of the λ_{max}^{CT} has been related to the distances of separation between interacting chromophores,[20] where changes in distance are not accompanied by changes in electronic effects. We expect the electronic differences

(17) (a) Paquette, L. A.; Kuhla, D. E. *J. Org. Chem.* **1969**, *34*, 2885. (b) Paquette, L. A.; Barrett, J. B. *J. Am. Chem. Soc.* **1966**, *88*, 1718.
(18) Foster, R. "Organic Charge-Transfer Complexes"; Academic Press: New York, 1969.
(19) (a) Mulliken, R. S. *J. Am. Chem. Soc.* **1952**, *74*, 811. (b) Cram, D. J.; Cram, J. M. *Acc. Chem. Res.* **1971**, *4*, 204 and references therein.
(20) Hoffman, Jr., J. M.; Schlessinger, R. H. *J. Chem. Soc. D* **1971**, 1245.

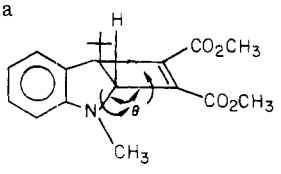


VIId

between the cyclobutenes VII to be negligible and propose reasons that the relative positions of the λ_{max}^{CT} for VIIa, VIIc, and VIIe are 375, 435, and 411 nm, respectively. Using VIIc as a model, we propose that in VIIa an increase



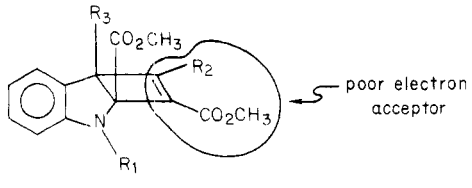
VIIa



VIIe

in θ results from the minimal strain between the angular 1 and 5 hydrogens and the smaller occupied space vs. the three methylene groups in VIIc and a subsequent increase in chromophoric distance. The hypsochromic shift in VIIe is presumably caused by the steric bulk of the 5-*tert*-butyl substituent. Steric strain leading to a decrease in θ would lead to a bathochromic shift in the CT absorption. Molecular models indicate that a torsional distortion, as indicated above in the bicyclo[3.2.0]heptadiene ring system, leads to both steric relief and an increase in chromophoric distance.

The identification of the intramolecular CT complex is significant in product verification. The electron-deficient double bond in a secondary rearrangement photoproduct, e.g., VIII, is a much poorer electron acceptor than it is in the unrearranged cyclobutenes, VII. Large charge-transfer character is not expected in VIII.



VIII

Comparison of the ultraviolet spectra of VII with those from the benzo[*b*]furan and benzo[*b*]thiophene systems, which show weaker CT character, point to the potential importance of electron availability in the aromatic "substituted aniline" portion of our complexes.

Conclusion

In summary, acetophenone-sensitized photocycloadditions of activated *N*-methylindoles and DMAD produce ($_{\pi}2 + _{\pi}2$) adducts which can be encouraged to undergo thermal ring opening to benzazepines. Yields are high in almost every case investigated, and the potential applications include a high-yield, one-step formation of benzazepine from a two-carbon fragment and indole. In contrast to the corresponding additions to benzo[*b*]furans and benzo[*b*]thiophenes in which secondary allylic photorearrangement is observed, the ($_{\pi}2 + _{\pi}2$) addition to activated indoles gives no secondary allylic rearrangement products.

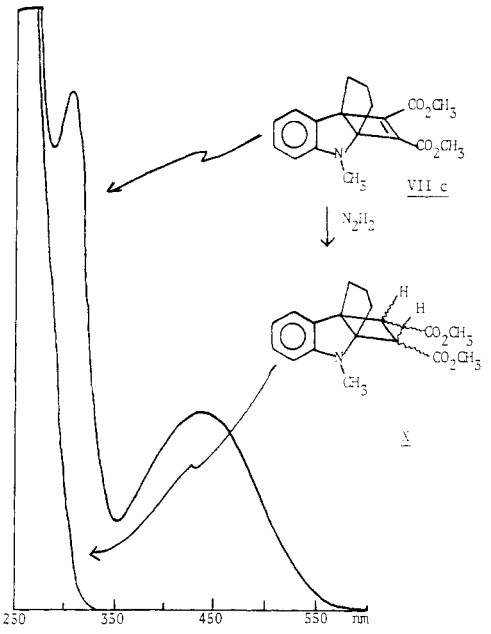


Figure 2. The UV spectra of VIIc and its diimide reduction products, *exo*- and *endo*-X.

Experimental Section

A. General. ^1H and ^{13}C NMR spectra were recorded on Varian A-60 and CFT-20 spectrometers. Unless otherwise indicated, $CDCl_3$ is used as the solvent with Me_4Si (tetramethylsilane) as the internal standard, coupling constants (J) are in hertz, and chemical shifts are in δ values. Infrared (IR) spectra are obtained on a Perkin-Elmer 337 spectrophotometer, mass spectra on a Varian MAT CH7 spectrometer, and ultraviolet (UV) spectra on a Beckman Acta IV spectrophotometer. Vapor-phase chromatography (GC) is carried out on a Hewlett-Packard Model 5710A chromatograph equipped with dual columns and a flame ionization detector (analytical) and on a Varian Model 90-P chromatograph with a thermal conductivity detector (preparative). A 6 ft × 0.25 in. column packed with 10% SE-30 adsorbed on Chromosorb W is used for both analytical and preparative purposes. Chromatograms are recorded on either a Houston Instruments Omniscribe Model A-5213-15 or a Hewlett-Packard Model 33805 integrator. Melting points are taken on a Thomas–Hoover capillary melting point apparatus and are uncorrected.

Indole, 2-methylindole, 3-methylindole (skatole), 2,3-dimethylindole, 5-methoxyindole, and dimethyl acetylenedicarboxylate (DMAD) were purchased from Aldrich Chemical Co. and used without further purification, with the exception of DMAD which was carefully distilled and stored in the refrigerator. Methyl propiolate was purchased from Pfaltz and Bauer. 3-*tert*-Butylindole (and 1,3-di-*tert*-butylindole),[12] 2,3-trimethyleneindole,[11] 6,7,8,9-tetrahydrocarbazole,[11] and 1-acetyl-3-piperidinoindole[15] were prepared as described. Useful spectral properties (especially ^1H NMR) of the N-methylated indoles (and 1,3-di-*tert*-butylindole) are summarized below. Routine analytic data not reported are on file with the principal investigator.

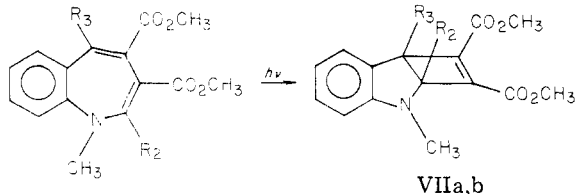
B. General Procedure for the N-Methylation of Indoles. Into a 1-L 3-neck round-bottom flask cooled with a dry ice–acetone bath and equipped to be stirred magnetically is condensed over 30–45 min approximately 500 mL of anhydrous ammonia. The ammonia is introduced to the flask via a 6-mm glass tube for rapid condensation. Approximately 100 mg of ferric nitrate nonahydrate, $Fe(NO_3)_3 \cdot 9H_2O$, is added to the liquid ammonia and allowed to dissolve, giving an orange–brown solution. Ten grams (0.435 mol) of sodium cut into small pieces is added. One gram or less is added initially, followed approximately 15 min later by rapid piecewise addition of the remainder. The cooled ammonia solution is stirred vigorously until the deep blue color disappears (1–3 h). To the gray slurry is added an ether solution of indole (0.345 mol). If the indole is insoluble in ether, it can be added

Table III. NMR Data of Cyclobutenes[a]

compd	N-R_1	R_2	R_3	CO_2CH_3	aromatic
VIIa	3.04	4.66, q (AB), 2 H		3.87	6.4-7.5 (6.39, 6.52, 6.70, 6.83), m, 4 H
VIIb	2.96	1.67	4.04, s, 1 H	3.83	6.35-7.4 (6.35, 6.49, 6.66, 6.78), m, 4 H
VIIc	2.98	1.18-2.46, m, 6 H		3.80	6.3-7.55 (6.31, 6.43, 6.64, 6.77), m, 4 H
VIId	2.96	1.28-2.66, m, 8 H		3.87	6.35-7.45 (6.35, 6.48, 6.66, 6.78), m, 4 H
VIIe	3.02	4.52, s, 1 H	1.11, s, 9 H	3.79, 3.83	6.4-7.6 (6.38, 6.52, 6.69, 6.82), m, 4 H
VIIf	1.50, s, 9 H	4.88, s, 1 H	1.08, s, 9 H	3.80	

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

Table IV. Photocyclization Conversions of Some Benzazepines to Cyclobutenes



IIa,b VIIa,b

	time, h	% VII[a]
IIa	24	30
IIb	9	45

[a] % conversion to 5% cycloreversion.

Table V. UV Data of Cyclobutenes (VII)[a]

compd	CT_{max}, nm	other, nm
VIIa	375	
VIIb	427	285, 253
VIIc	438 (2.88)	304 (3.18), 249 (3.68)
VIId	432	302, 250
VIIe	411 (2.81)	295 (3.21), 252 (3.62)
VIIf	408	

[a] 95% EtOH.

directly as a solid. Stirring is continued for 1 h. To the resulting dark solution (usually black) is added dropwise 100 mL of an ether solution containing 68 g (0.527 mol) of methyl iodide. Stirring is continued while the solution warms to ambient temperature (-34 °C). The excess ammonia is evaporated by placing a cool-water bath under the flask and stirring overnight. Water (250 mL) is added and extracted at least three times with 75-100 mL portions of ether. The combined extracts are washed with water (3 × 50 mL) and dried over $MgSO_4$. All N-methylated indoles are purified by column chromatography over Florisil. Yields are routinely between 80 and 90%, and that the conversion to the N-methylated product is complete is determined by ^1H NMR integration. All N-methylated indoles must be stored in the refrigerator or under N_2 as they are readily oxidized.

(a) *N*-Methylindole (Ia): liquid at room temperature; ^1H NMR (δ, $CDCl_3$) 3.32 (s, 3, N-CH_3), 6.50 (d, J_{23} = 3 Hz, 1, C(3)-H), 6.80 (d, J_{23} = 3 Hz, 1, C(2)-H), 7.0-7.8 (m, 4, aromatic); mass spectrum, *m/e* 131 (M^+).

(b) 1,2-Dimethylindole (Ib): mp 57-58 °C; ^1H NMR (δ, $CDCl_3$) 2.42 (s, 3, C(2)-CH_3), 3.63 (s, 3, N-CH_3), 6.24 (s, 1, C(3)-H), 6.85-7.62 (m, 4, aromatic); mass spectrum, *m/e* 145 (M^+).

(c) 1-Methyl-2,3-trimethyleneindole (Ic): ^1H NMR (δ, $CDCl_3$) 2.12-3.06 (m, 6, C(2)-$(CH_2)_3$-C(3)), 3.51 (s, 3, N-CH_3), 6.94-7.58 (m, 4, aromatic); mass spectrum, *m/e* 173 (M^+).

(d) 6,7,8,9-Tetrahydro-1-methylcarbazole (Id): mp 48.5-50 °C; ^1H NMR (δ, $CDCl_3$) 1.70-2.13 (bq, *J* = 3 Hz, 4, C(7)H_2-C(8)H_2), 2.42-2.90 (m, 4, C(6)-H_2 and C(9)-H_2), 3.49 (s, 3, N-CH_3), 6.79-7.62 (m, 4, aromatic); mass spectrum, *m/e* 185 (M^+).

(e) 3-*tert*-Butyl-1-methylindole (Ie): ^1H NMR (δ, $CDCl_3$) 1.45 (s, 9, C(3)-*tert*-butyl), 3.43 (s, 3, N-CH_3), 6.68 (s, 1, C(2)-H), 6.95-8.05 (m, 4, aromatic); mass spectrum, *m/e* 187 (M^+).

(f) 1,3-Di-*tert*-butylindole If: ^1H NMR (δ, $CDCl_3$), 1.47 (s, 9, C(3)-*tert*-butyl), 1.63 (s, 9, N-*tert*-butyl), 6.82-8.03 (m, 5, aromatic and C(2)-H); mass spectrum, *m/e* 229 (M^+).

C. General Procedure for the Sensitized Photocycloaddition of Activated Indoles with Dimethyl Acetylenedicarboxylate. All preparative scale reactions are carried out using a standard borosilicate (Pyrex) photochemical immersion well (Ace 7857-05) with a 450-W, medium-pressure, quartz, mercury-vapor lamp as the light source (Ace 7825-34). The reaction vessel is equipped with a gas inlet tube (fritted disk) and has a capacity of 1.0 L. The reactions are carried out under a constant stream of nitrogen and at ambient temperatures or in a constant temperature bath, 9 ± 4 °C. Reagent grade benzene is used as the solvent in all cases. All preparative irradiations are carried out for at least 24 h and are sensitized with acetophenone (25 mol % of acetylene). The workup requires the removal of solvent under pressure (for easily ring-opened cyclobutenes, especially VIIa and VIIb, the temperature is held below 10 °C), followed by separation of unreacted starting materials on Florisil through a 45 × 45 cm column. The indole is removed with a low-boiling petroleum ether (20-40 °C, Baker 9272), and the DMAD and acetophenone with 5% ether-petroleum ether. The product(s), cyclobutene and/or benzazepine, are removed with ether and further purified, if necessary, by preparative TLC on 20 × 20 cm × 2 mm silica gel plates [E. Merck HF-254 (type 60) for TLC]. Listed below are representative preparative reactions with the spectral properties of the cyclobutenes (and benzazepines) produced.

(a) 6,7-Bis(methoxycarbonyl)-2-methyl-3,4-benzo-2-azabicyclo[3.2.0]hepta-3,6-diene (VIIa). *N*-Methylindole (1.50 g, 1.15×10^{-2} M) and 2.5 g of DMAD (1.76×10^{-2} M) upon sensitized irradiation gave 2.25 g of VIIa and IIa, 3,4-bis(methoxycarbonyl)-1-methyl-6,7-benzo-1-azepine (yield, 72%). When heated, VIIa is converted completely to IIa. Even refrigeration at 0 °C does not stop this conversion completely.

(i) VIIa: deep orange oil; ^1H NMR (δ, $CDCl_3$), 3.04 (s, 3, N-CH_3), 3.87 (s, 6, C(6)- and C(7)-CO_2CH_3), 4.66 (ABq, 2, C(1)-H, C(5)-H), 6.4-7.5 (m, 4, aromatic); UV (λ_{max}, nm, 95% EtOH) 375 (CT absorption).

(ii) IIa: orange crystals; mp 83-84 °C; ^1H NMR (δ, $CDCl_3$), 3.07 (s, 3, N-CH_3), 3.72, 3.80 (s, 6, C(3)- and C(4)-CO_2CH_3), 6.7-7.4 (m, 6, aromatic, C(2)- and C(5)-H); UV (λ_{max}, nm (log ε), 95% EtOH) 239 (4.20), 259 (4.39), 293 (4.10), 317 (3.54); mass spectrum, *m/e* 273 (M^+).

(b) 6,7-Bis(methoxycarbonyl)-1,2-dimethyl-3,4-benzo-2-azabicyclo[3.2.0]hepta-3,6-diene (VIIb). Sensitized irradiation of 1.50 g (1.03×10^{-2} M) of 1,2-dimethylindole Ib and 2.5 g (1.76×10^{-2} M) of DMAD at 10 °C gives, after workup and separation, 326 mg of VIIb and IIb, 3,4-bis(methoxycarbonyl)-1,2-dimethyl-6,7-benzo-1-azepine (11%). Incomplete reaction because of internal filtering by product) hampers the workup on Florisil since Ib and DMAD react thermally on this surface to give the maleate and fumarate substitution products. VIIb is smoothly converted to IIa above 40 °C (no $\tau_{1/2}$ measured).

(i) VIIb: blood-red oil; ^1H NMR (δ, $CDCl_3$), 1.67 (s, 3, C-(1)-CH_3), 2.96 (s, 3, N-CH_3), 3.83 (s, 6, C(6)- and C(7)-CO_2CH_3), 4.04 (s, 1, C(5)-H), 6.35-7.4 (m, 4, aromatic); UV (λ_{max}, nm, 95% EtOH), 253, 285, 427.

(ii) IIb: yellow cubes, mp 141-142 °C; ^1H NMR (δ, $CDCl_3$) 2.31 (s, 3, C(2)-CH_3), 3.12 (s, 3, N-CH_3), 3.68, 3.82 (s, 6, C(3)- and C(4)-CO_2CH_3), 6.9-7.5 (m, 4, aromatic), 7.89 (s, 1, C(5)-H); mass spectrum, *m/e* 287 (M^+); UV (λ_{max}, nm (log ε), 95% EtOH) 220 (4.06), 258 (4.32), 292 (3.90), 370 (2.91).

(c) 9,10-Bis(methoxycarbonyl)-2-methyl-3,4-benzo-2-azatricyclo[3.3.2.0]deca-3,9-diene (VIIc). The sensitized irradiation of 1.50 g (8.77×10^{-3} M) of Ic and 2.50 g (1.76×10^{-2} M) of DMAD gives 1.58 g (5.04×10^{-3} mol) (71% yield based on recovered starting material) of VIIc.

VIIc: blood-red liquid; ^1H NMR (δ, $CDCl_3$), 1.18-2.46 (m, 6, C(6)-(8)-H_2), 2.98 (s, 3, N-CH_3), 3.80 (s, 6, C(9) and C(10)

CO_2CH_3), 6.3–7.55 (m, 4, aromatic); mass spectrum, *m/e* 313 (M^+, 5), 171 (100, base peak); UV (λ_{max}, nm (log ϵ), 95% EtOH) 249 (3.68), 304 (3.18), 438 (2.88).

(d) 10,11-Bis(methoxycarbonyl)-7-methyl-8,9-benzo-7-azatricyclo[4.3.2.0]undeca-8,10-diene (VIId). Sensitized irradiation of 1.50 g (8.11×10^{-3} M) of Id and 2.50 g (1.76×10^{-2} M) of DMAD gives 1.78 g (5.44×10^{-3} mol) of VIId (82% yield, based on recovered starting material).

VIId: blood-red liquid: ^1H NMR (δ, $CDCl_3$) 1.28–2.66 (m, 8, C(2)–C(5)H_2), 2.96 (s, 3, N–CH_3), 3.87 (s, 6, C(10)– and C(11)–CO_2CH_3), 6.35–7.45 (m, 4, aromatic); UV (λ_{max}, nm, 95% EtOH) 250, 302, 432.

(e) 5-*tert*-Butyl-6,7-bis(methoxycarbonyl)-2-methyl-3,4-benzo-2-azabicyclo[3.2.0]hepta-3,6-diene (VIIe). Sensitized irradiation of 1.50 g (8.02×10^{-3} M) of Ie and 2.50 g (1.76×10^{-2} M) of DMAD gives 1.32 g (4.01×10^{-3} mol) of VIIe (77% yield, based on recovered starting materials).

VIIe: red liquid; ^1H NMR (δ, $CDCl_3$) 1.11 (s, 9 C(5)-*tert*-butyl), 3.02 (s, 3, N–CH_3), 3.79, 3.83 (s, 6, C(6)– and C(7)–CO_2CH_3), 4.52 (s, 1, C(1)–H), 6.4–7.6 (m, 4, aromatic); mass spectrum, *m/e* 329 (M^+, base peak), 187 (90); UV (λ_{max}, nm (log ϵ), 95% EtOH) 252 (3.62), 295 (3.21), 411 (2.81).

(f) 2,5-Di-*tert*-butyl-6,7-bis(methoxycarbonyl)-3,4-benzo-2-azabicyclo[3.2.0]hepta-3,6-diene (VIIf). Sensitized irradiation of 1.50 g (6.55×10^{-3} M) of If and 2.50 g (1.76×10^{-2} M) of DMAD gives 480 mg of a mixture containing 75% VIIf (15% yield, not based on recovered starting material).

VIIf: deep orange liquid; ^1H NMR (δ, $CDCl_3$) 1.08 (s, 9, C-(5)-*tert*-butyl), 1.50 (s, 9, *N*-*tert*-butyl), 3.80 (s, 6, C(6)– and C(7)–CO_2CH_3), 4.88 (s, 1, C(1)–H, 6.3–7.5 (m, ?, aromatic); UV (λ_{max}, nm) 408 (CT absorption).

Photochemical Ring Closure of Some Substituted 3,4-Bis(methoxycarbonyl)-1-methyl-6,7-benz-1-azepines. (a) IIa $\xrightarrow{h\nu}$ VIIa. Under the direct irradiation of 1.10 g (4.02×10^{-3} M) of IIa, ^1H NMR indicates a 30% conversion to VIIa, and 205 mg (18%) of Va is isolated by preparative TLC. The temperature is carefully kept below 15 °C at *all* times during workup and isolation. The original crude reaction mixture contains not less than 5% (by NMR) Ia (TLC corroborates this observation).

(b) IIb $\xrightarrow{h\nu}$ VIIb. Direct irradiation of 300 mg of IIb (1.05×10^{-3} M) for 9 h indicates a 45% conversion to VIIb by NMR. VIIb (126 mg, 42%) is isolated by preparative TLC (10% ether–petroleum ether, three elutions). Less than 5% cycloreversion to Ib can be detected by NMR (and TLC).

Diimide Reduction of VIIc to *exo*-and *endo*-9,10-Bis(methoxycarbonyl)-2-methyl-3,4-benzo-2-azatricyclo[3.3.2.0]deca-3-ene (*exo*- and *endo*-X). To 10 mL of tetrahydrofuran containing 0.500 g (1.16 mol) of the red VIIc are added 3.10 mL (64 mmol) of hydrazine hydrate (97%), 6 drops of saturated copper sulfate solution, and 6 drops of glacial acetic acid; this solution is added dropwise to a solution of 1.71 g of sodium metaperiodate in 16 mL of water (2.5 h).[20] The reaction mixture is added to 50 mL of water and extracted 3 × 25 mL with ether, and the ether extracts are dried over $MgSO_4$ and removed at reduced pressure, leaving a pale yellow residual oil. Preparative TLC of the reaction mixture (20% ether–petroleum ether) indicates the presence of at least four distinct bands, two with relatively large R_f values. The first gives 50 mg of Id, 1-methyl-2,3-trimethyleneindole, followed by 120 mg of a colorless oil, a mixture of *exo*- and *endo*-VIId-red: ^1H NMR (δ, $CDCl_3$) 1.60 (d, 1), 1.5–2.5 (m, 6), 2.73, 2.78 (s, 3), 3.59, 3.66, 3.72 (s, 6) 6.22–7.54 (m, 5); mass spectrum, *m/e* 315 (M^+, 7), 171 (100, base peak); UV (λ_{max}, nm, 95% EtOH) 235, 255, 290. By NMR the mixture contains 50% of each isomer, exo and endo. The slow moving bands are not fully characterized, but they have molecular ions at *m/e* 385 in the mass spectrum and puzzling and complicated NMR spectra.

Photochemical Ring Opening of 2-Acetyl-6-(methoxycarbonyl)-5-piperidino-3,4-benzo-2-azabicyclo[3.2.0]hepta-3,6-diene. 2-Acetyl-6-(methoxycarbonyl)-5-piperidino-3,4-benzo-2-azabicyclo[3.2.0]hepta-3,6-diene is prepared by the procedure of Lin and Snieckus,[15] but it cannot be triturated, and it required preparative TLC separation from the thermally ring-opened product prior to purification. The bicycloheptadiene (115 mg) is irradiated in 6 mL of benzene solution for 4 days at 10 °C (no thermal ring is observed in the dark experiment). ^1H NMR shows a quantitative conversion to 1-acetyl-4-(methoxycarbonyl)-5-piperidino-6,7-benzo-1-azepine.

Acknowledgment. This work was supported by the National Institutes of Health (1-TO1 NS 14883-01) and the Petroleum Research Fund, administered by the American Chemical Society. The authors are grateful for these funds. Fruitful discussions with Drs. Roger Card and A. H. A. Tinnemans, as well as with Professors J. C. Dalton and T. H. Kinstle, are also acknowledged.

Registry No. Ia, 603-76-9; Ib, 875-79-6; Ic, 52751-31-2; Id, 6303-88-4; Ie, 46270-99-9; If, 28864-80-4; IIa, 34132-46-2; IIb, 69496-54-4; IV, 27150-56-7; VIIa, 69496-49-7; VIIb, 69496-50-0; VIIc, 69594-36-1; VIId, 69594-37-2; VIIe, 69496-52-2; VIIf, 69496-53-3; *endo*-X, 72121-26-7; *exo*-X, 72151-26-9; indole, 120-72-9; 2-methylindole, 95-20-5; 3-*tert*-butylindole, 19013-51-5; 2,3-trimethyleneindole, 2047-91-8; 6,7,8,9-tetrahydro-9*H*-carbazole, 942-01-8; DMAD, 762-42-5; 1-acetyl-4-(methoxycarbonyl)-5-piperidino-6,7-benzo-1-azepine, 27150-47-6.

Photocycloaddition of Dimethyl Acetylenedicarboxylate to 1,3-Dimethylindole

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Received October 5, 1979

In contrast to the clean photoaddition of activated indoles to dimethyl acetylenedicarboxylate (DMAD) reported in the previous paper,[1] the reaction of 1,3-dimethylindole produces seven different products. In this paper the structures of these seven products are reported, and mechanistic considerations of the photocycloaddition of dimethyl acetylenedicarboxylate to activated indoles are discussed.

Background

In addition to the predominant (2 + 2) reaction of DMAD with a variety of activated indoles,[1] we have identified six other products, several of which present interesting structure elucidation problems from reaction of 1,3-dimethylindole with DMAD. In this paper we discuss the reaction of 1,3-dimethylindole with DMAD, the products formed, and the mechanistic information the reaction provides about the photochemical reaction of

(1) Davis, P. D.; Neckers, D. C. *J. Org. Chem.*, preceeding paper in this issue.

0022-3263/80/1945-0462$01.00/0