J. Org. Chem. 1991, 56, 1879–1882 1879

A Reinvestigation of the Reactions Occurring upon Photoexcitation of Cyclohexenone in the Presence of Triethylamine

David I. Schuster* and Anthony M. Insogna

Department of Chemistry, New York University, New York, New York 10003

Received August 6, 1990

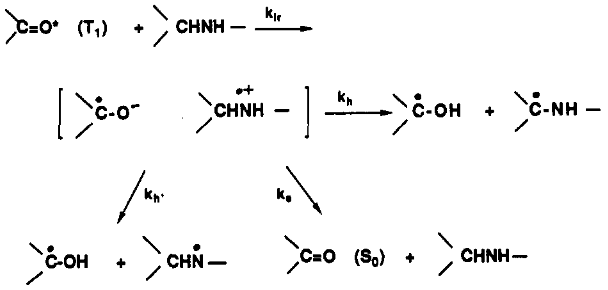
It had been previously reported that the distribution of products from irradiation of cyclohexenone (CH) in the presence of triethylamine (TEA) required the intermediacy of a triplet excimer intermediate derived from the enone. Reinvestigation of this reaction has given results removing the necessity of postulating such an intermediate. Specifically, the reaction results in the products previously reported, namely cyclohexanone, photodimers (two major, two minor), and a pair of 1:1 enone–amine adducts, as well as previously unobserved products from reductive dimerization of the enone (3-(3-oxocyclohexyl)cyclohexanone) and from condensation of two enone and one amine moieties. The photodimer yields decreased dramatically as the amine concentration was increased, and the product ratios were dependent on the CH concentration, findings which are contrary to the earlier report but understandable if there is a competition between TEA and ground-state CH for capture of monomeric CH triplets. The mechanism for formation of the products derived from interaction of TEA involves an initial electron-transfer step to give a pair of radical ions, followed immediately by proton transfer to a ketyl and an α-aminoalkyl radical, which yield the observed products by subsequent radical combination and H-abstraction reactions. These results are consistent with published laser flash kinetic data from this laboratory, and earlier studies of the photochemical behavior of other ketones in the presence of amines.

Introduction

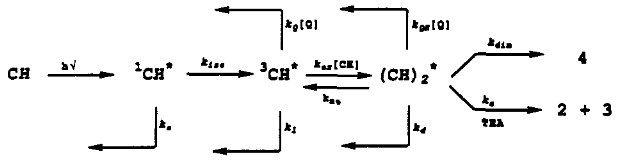
The photochemical reactions of cyclic enones have been a subject of extensive investigation.[1] These reactions include photodimerization, photorearrangements, photoreduction, and photocycloaddition to alkenes and dienes; all proceed via triplet excited states. Triplet excited states of a large number of cyclic enones have been directly detected using nanosecond flash photolysis, and their lifetimes have been shown to vary as a function of molecular structure in a way which implicates twisting around the C=C bond as the principal relaxation mode of the lowest π,π^* triplet.[2,3] This conclusion is supported by recent measurements of triplet energies of a series of cyclic enones using time-resolved photoacoustic calorimetry.[4] Using flash techniques, rate constants have been measured for interaction of these enone triplets with a wide variety of reagents, including oxygen,[3] aromatic hydrocarbons,[3] alkenes[5] and amines.[6,7] Amines with appropriately low ionization potentials quenched monomeric triplet states of cyclohexenones by a process involving electron transfer from the amine to the enone to generate a radical ion pair,[6,7] in agreement with results of studies of quenching of aromatic ketone triplets by amines.[8]

Cohen and co-workers have carried out extensive investigations of the photoreduction of aromatic ketones by amines.[9] They showed that initial electron transfer (ET) to generate a radical ion pair is followed by proton transfer to give a ketyl radical and either an α-aminoalkyl or an N-centered radical, depending on the amine (see Scheme I).[9] This radical pair can undergo disproportionation to regenerate starting materials, in competition with radical combination, dimerization of ketyl radicals to give pinacols, and reaction of the α-aminoalkyl radicals (particularly from tertiary amines) or N-centered radicals (from primary and secondary amines) with ground-state ketone to give an imine and another ketyl radical. Variations in quantum efficiencies for photoreduction can be satisfactorily explained by competition between these reaction pathways, which are shown in Scheme I.[9]

Scheme I



Scheme II



* See ref 11.

Cookson and co-workers were apparently the first to report the formation of 1:1 adducts between amines and photoexcited α,β-unsaturated carbonyl compounds.[10] They assumed the reaction proceeded via enone triplets but provided no supporting evidence. Sometime later, Pienta and McKimmey investigated the reactions occurring on photoexcitation of 2-cyclohexenone (CH, 1) in the presence of TEA, as a function of the concentration of both

---

[1] For a recent review of enone photochemistry, see: Schuster, D. I. In *The Chemistry of Enones*; Patai, S., Rappoport, Z., Eds.; John Wiley and Sons, Ltd.: Chichester, U.K., 1989; pp 623–756.

[2] Bonneau, R. *J. Am. Chem. Soc.* **1980**, *102*, 3816.

[3] Schuster, D. I.; Bonneau, R.; Dunn, D. A.; Rao, J. M.; Joussot-Dubien, J. *J. Am. Chem. Soc.* **1984**, *106*, 2706. Schuster, D. I.; Dunn, D. A.; Heibel, G. E.; Rao, J. M.; Bonneau, R. *Ibid.*, submitted for publication.

[4] Schuster, D. I.; Heibel, G. E.; Caldwell, R. A.; Tang, W. *Photochem. Photobiol.* **1990**, *52*, 645.

[5] Schuster, D. I.; Heibel, G. E.; Brown, P. B.; Turro, N. J.; Kumar, C. V. *J. Am. Chem. Soc.* **1988**, *110*, 8261.

[6] Dunn, D. A.; Schuster, D. I.; Bonneau, R. *J. Am. Chem. Soc.* **1985**, *107*, 2802.

[7] Dunn, D. A. Ph.D. Dissertation, New York University, 1985.

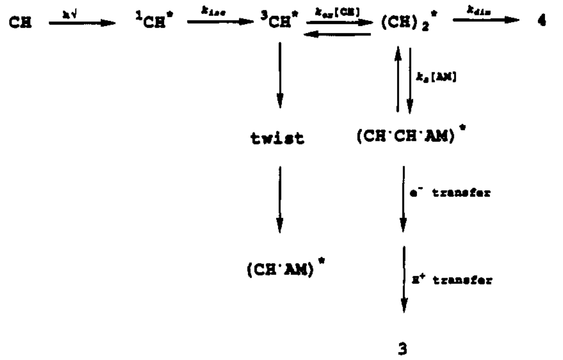
[8] Cohen, S. G.; Cohen, J. I. *J. Phys. Chem.* **1968**, *72*, 3782. Guttenplan, J. B.; Cohen, S. G. *J. Am. Chem. Soc.* **1972**, *94* 4040; *Tetrahedron Lett.* **1972**, 2163. Bartholomew, R. F.; Davidson, R. S.; Lambeth, P. F.; McKellar, J. F.; Turner, P. H. *J. Chem. Soc., Perkin Trans. 2* **1972**, 577. Cohen, S. G.; Parola, A. H.; Parsons, G. H., Jr. *Chem. Rev.* **1973**, *73*, 141. Arimitsu, S.; Masukara, H.; Mataga, N.; Tsubomura, H. *J. Phys. Chem.* **1975**, *79*, 1255. Simon, J. D.; Peters, K. S. *J. Am. Chem. Soc.* **1981**, *103*, 6403 and earlier papers cited.

[9] See: Inbar, S.; Linschitz, H.; Cohen, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 1048 and earlier papers.

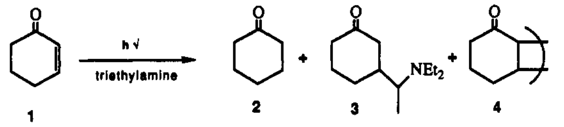
[10] Cookson, R. C.; Hudec, J.; Mirza, N. A. *J. Chem. Soc., Chem. Commun.* **1968**, 180.

0022-3263/91/1956-1879$02.50/0

Scheme III



CH and TEA, in either acetonitrile or TEA as solvent.[11] The products detected, shown in eq 1, were cyclohexanone



(1)

(2), a pair of diastereomeric 1:1 adducts (3), and a mixture of [2 + 2] photodimers (4). They found that, as expected, the yields of the products attributable to interaction of CH triplets with TEA, namely 2 and 3, increased and the yield of 4 decreased when the amine concentration was increased from 0.99 to 7.17 M (neat amine), although dimer yields were reported to be appreciable even in neat amine. When the enone concentration was increased from 65 mM to 2.0 M in neat TEA, the absolute quantum yields of all the products increased, and the ratio of (2 + 3)/4 was reported to be essentially constant. Therefore, a mechanism was postulated in which all three products arise by competitive reactions of an enone triplet excimer, with little if any product arising by direct interception of the monomeric triplet by TEA (see Scheme II).

This conclusion is at odds with analogous studies of aromatic ketones (see above), where the monomeric triplet is the species intercepted by amines.[8,9] Pienta obtained flash kinetic data which provided support for the mechanism shown in Scheme II.[12] Specifically, the CH transient lifetime at 280 nm, in the wavelength range characteristic of enone triplet absorption,[2,3] was reported to increase when the TEA concentration was increased in acetonitrile as solvent. This finding suggested formation of a second longer lived transient with absorption at 280 nm, thought to be an enone–amine triplet exciplex, which is in rapid equilibrium with the monomeric CH triplet.[12] The transient decay profiles at 280 nm changed markedly as a function of either TEA or diazabicyclooctane (DABCO) concentration, consistent with the formation of two additional transient species with lifetimes in the microsecond domain. The relative importance of these slowly decaying transients grew as the amine concentration was increased, eventually obliterating the contribution of the nanosecond transient to the total decay profile. These and other data were interpreted according to Scheme III, in which both twisted monomeric CH triplets and CH triplet excimers are intercepted by TEA, the former path being unproductive as far as product formation is concerned. The microsecond transients were postulated to be radical ions or ion pairs and/or the terplex derived from the CH triplet excimer and the amine.

The incompatibility of Scheme III with our findings regarding quenching of a variety of cyclohexenones by amines in flash[6,7] and steady-state investigations[13] prompted a reexamination of the interactions of electronically excited cyclohexenones and amines. Our flash kinetic studies,[14] which included a particularly careful analysis of the nanosecond portion of the transient decay profiles at 280 nm following excitation of five cyclohexenones in the presence of TEA, DABCO, and diphenylamine, established that the lifetime of the enone triplet definitely *decreased* as the amine concentration was increased, contrary to the earlier report.[12] At high amine concentrations, the fast component decay could no longer be analyzed because of the absorption by the long-lived transient. No evidence for formation of enone-amine exciplexes was obtained in these flash studies, which does not rule out their possible involvement in these reactions.

Since the flash kinetic data[14] indicated that monomeric triplets of cyclohexenones were indeed being quenched by TEA and the other amines, the steady-state findings which led to the mechanism shown in Scheme II[11] were called into question. In order to resolve this discrepancy, we decided to repeat the study of the steady-state photochemical behavior of cyclohexenone in the presence of TEA as a function of both enone and TEA concentration.

Results

Irradiation of CH in acetonitrile in the presence of low concentrations of TEA indeed led to the formation of the reduction product 2 (identified by comparison with an authentic sample), a mixture of diastereomeric 1:1 adducts 3 (identified by NMR and mass spectral analysis), and a mixture of photodimers 4, identical with photodimers formed in the absence of TEA. We observed four photodimer peaks (according to GC/MC analysis), two major and two minor, suggesting that trans- as well as cis-fused [2 + 2] head-to-head and head-to-tail dimers are formed.[15] As reported by Pienta,[11] the product distribution indeed changed upon increasing the TEA concentration, but not in the manner described in the earlier report. At CH concentrations below 0.1 M and TEA concentrations above 1.0 M, photodimerization does not occur. At high concentrations of both CH and TEA, the yield of photodimers is sharply reduced, and additional products not reported by Pienta[11] were detected. Prominent among these are products with *m/e* 194, corresponding to reductive dimerization of CH. The GC retention times and mass spectra of these products were identical with authentic samples of 3-(3-oxocyclohexyl)cyclohexanone (5) synthesized (as a mixture of diastereomers) according to a literature procedure.[16] Analogous reductive dimerization of isophorone using a silylamine has been reported.[17] Since the GC peaks due to 5 appear between the four peaks due to CH photodimers under our analytical conditions, yields of 5 may have been erroneously incorporated into the photodimer yield in the earlier study.[11]

The results of one of many studies of the product distribution as a function of CH concentration in neat TEA are shown in Table I. It is readily apparent that the

---

[11] Pienta, N. J.; McKimmey, J. E. *J. Am. Chem. Soc.* **1982**, *104*, 5502.

[12] Pienta, N. J. *J. Am. Chem. Soc.* **1984**, *106*, 2704.

[13] Tucker, P. C. Ph.D Dissertation, New York University, 1988.

[14] Weir, D.; Scaiano, J. C.; Schuster, D. I. *Can. J. Chem.* **1988**, *66*, 2595.

[15] Wagner, P. J.; Bucheck, D. J. *J. Am. Chem. Soc.* **1969**, *91*, 6090. Ruhlen, J. L.; Leermakers, P. A. *Ibid.* **1967**, *89*, 4944. Eaton, P. E. *Acc. Chem. Res.* **1968**, *1*, 50.

[16] Cahiez, G.; Alami, M. *Tetrahedron Lett.* **1986**, *27*, 569 and references cited therein.

[17] Hasegawa, E.; Xu, W.; Mariano, P. S.; Yoon, U.; Kim, J. *J. Am. Chem. Soc.* **1988**, *110*, 8099.

Scheme IV

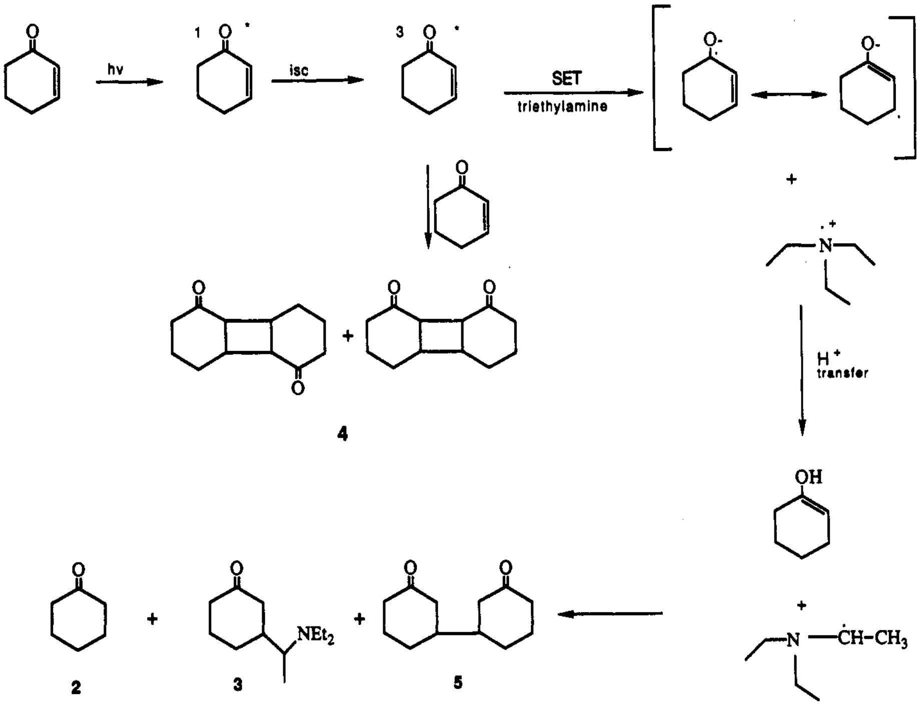


Table I. Yields of Products on Irradiation of Cyclohexenone in Neat Triethylamine

[cyclohexenone], M	% yield[a,b]			
	2	3	4	(2 + 3)/4
2.02	5.5	30.5	32.5	1.1
1.22	4.5	36.6	21.9	1.9
0.50	5.2	48.4	9.9	5.4
0.25	14.8	54.0	6.3	10.9
0.10	7.7	66.7	5.7	13.1
0.066	8.4	66	4.6	16.2
0.035	7.9	91	*c*	∞
0.026	*c*	85	*c*	∞

[a] Yields determined by capillary gas chromatographic analysis relative to dodecane as internal standard. See the Experimental Section. [b] Yields reported at 15–30% conversion of CH. [c] None detectable.

product ratio (**2** + **3**)/**4** is not constant, as reported earlier,[11] but varies as expected if electron transfer to the enone triplet from TEA (to give ultimately **2**, **3**, and **5**) is competitive with interaction of the triplet with CH ground states to give photodimers. Thus, at low CH concentrations, the yield of photodimers is negligible and the yield of enone–amine adducts **3** is maximal.

At high CH concentrations secondary photoproducts were noted, corresponding to a group of poorly resolved peaks with long GC retention times. Mass spectral analysis gave an *m/e* value of 293 for M^+, corresponding to a 2:1 enone–amine adduct. Structure **6**, which corresponds to several diastereomers, is proposed for this group of products, based upon the mass spectral fragmentation depicted in Figure 1.

Discussion

The results of the present study together with the recent laser flash studies[14] refute the claim[11,12] that a chemically reactive dimeric enone intermediate must be involved in the photochemical reactions of cyclohexenone in the presence of triethylamine. Thus, there is no longer any valid basis for invoking the mechanisms shown in Schemes II and III involving a CH triplet excimer. The much simpler mechanism shown in Scheme IV, analogous to that formulated in Scheme I for other ketone triplets, suffices to rationalize the results of the product as well as the kinetic studies in the present case.

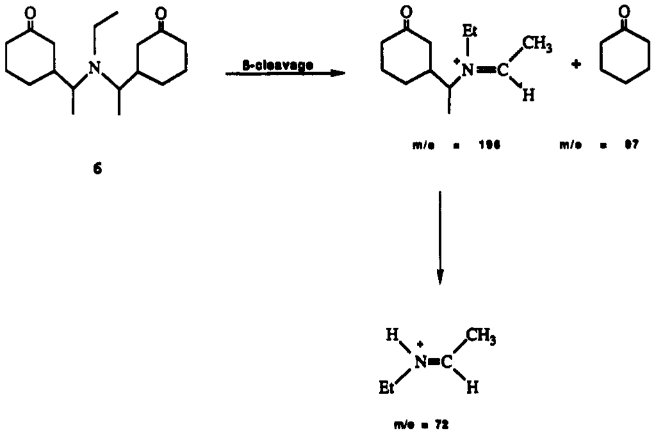


Figure 1. Mass spectral analysis of the secondary photoproduct.

The first step in the overall process involves electron transfer (ET) from TEA to monomeric CH triplets to give a radical ion pair. Such a mechanism is directly supported by the observation by Dunn et al.[6] of the generation of DABCO radical cations on laser flash excitation of CH in the presence of DABCO; this particular radical cation is very long-lived and consequently readily detectable because of the structural prohibition to subsequent proton transfer. Data from CIDNP studies[18] supports an initial ET step in the CH–TEA system. Such a mechanism has also been suggested for interactions of CH triplets and silylamines[17] and is completely consistent with the photochemical behavior of other ketones in the presence of amines.[8,9]

The ET step is followed by proton transfer from C_α of the TEA radical cation to the oxygen of the CH radical anion to generate the aminoalkyl and ketyl radicals shown in Scheme IV. The formation of this particular CH-derived radical as opposed to other possible alternative

---

[18] Smith, D. W.; Pienta, N. J. *Tetrahedron Lett.* **1984**, *25*, 915.

structures is supported by the subsequent radical combination reactions, which afford the 1:1 adducts **3** and the dihydro dimers **5**, as well as the 2:1 adducts **6**. It is likely that **6** is formed as a secondary product from interaction of CH triplets with **3**, but we have no direct evidence to require this mechanism.

There is clearly competition between TEA and ground-state enone for interception of monomeric CH triplets. Increasing the enone concentration favors the photodimerization pathway, while increasing the TEA concentration favors the electron-transfer pathway. Thus, all the primary products formed in this model system arise from monomeric triplet states of cyclohexenone.

Experimental Section

Materials. 2-Cyclohexenone (Aldrich, 99+%) was fractionally distilled under vacuum before use and showed no extraneous peaks in the gas chromatogram. Triethylamine (Aldrich, 99+%) was purified before use by reflux over NaOH and distillation. Acetonitrile (Aldrich, anhydrous, 99+%) was freshly purified before use by heating to reflux over sodium hydride and then distillation from sodium hydride.

Ultraviolet Irradiations. Solutions in Pyrex test tubes sealed with rubber septa were purged with Argon for 8 min and then irradiated in a Rayonet Reactor (New England Ultraviolet Co.) equipped with blacklight lamps whose output is centered at 350 nm. The reactor is equipped with a cooling fan which keeps the temperature at 30–35 °C. When more than one sample needs to be irradiated simultaneously, a rotating turntable ("merry-go-round") is utilized.

Gas Chromatography. All GC analyses were carried out on a Hewlett-Packard Model 5890 gas chromatography equipped with an HP 3396A integrator. Detection was by flame ionization. The capillary column used in all analyses was an Alltech no. 932530 Heliflex RSL-150 column, 30 m × 0.25 mm, with a maximum allowable temperature of 330 °C. The following temperature program was utilized: initial column temperature 100 °C, final column temperature 290 °C, temperature ramp 8 °C/min, injection port 250 °C. Most analyses were carried out in duplicate or triplicate, using dodecane as an internal standard.

Gas chromatography/mass spectral analysis was carried out an HP 5992 GC/MS system equipped with a 20 × 0.25 mm cross-linked methylsilica column. Additional analyses were carried out on a GC/MS system at Columbia University consisting of an HP gas chromatograph, HP5988 mass selective detector, and HP 9216 work station.

Column chromatography of mixtures after irradiation was carried out on silica gel columns using various proportions of hexane and ethyl acetate to isolate the photoproducts.

Preparative-scale thin-layer chromatography of irradiation mixtures after concentration and removal of TEA by extraction was carried out on Alltech silica gel GF plates using a mixture of 95% chloroform/5% ethyl acetate to isolate the photoproducts.

NMR Spectra. ^{1}H and ^{13}C NMR spectra were obtained on a GE-Nicolet QE-300 300-MHz NMR spectrometer. All spectra were obtained in deuteriochloroform.

Synthesis of 3-(3-Oxocyclohexyl)cyclohexanone (5). The method of Cahiez and Alami was utilizied.[16] Anhydrous tetrahydrofuran (THF) from Aldrich was dried over lithium aluminum hydride and distilled under nitrogen immediately prior to use. Dry THF (10 mL) was added to 1.2 g (0.1 mol) of magnesium turnings. Isopropyl chloride (5.5 mL, 0.06 mol) was dissolved in anhydrous THF, and 3 mL of this soln. was added dropwise to the Mg suspension with stirring. A few drops of 1,2-dibromoethane was added to initiate formation of the Grignard reagent. In a separate apparatus, 3.17 g (0.025 mol) of manganese chloride in 50 mL of THF was stirred for 15 min under nitrogen. The Grignard reagent was added to the $MnCl_2$ suspension using a canula under nitrogen, and the mixture was stirred for 5 min. To this was slowly added 4.96 g (0.05 mol) of 2-cyclohexenone, and the mixture was then stirred at room temperature for 30 min. The reaction mixture was neutralized with 0.5% HCl and then extracted with ether. The extracts were concentrated under vacuum, and the resulting oil was subjected to GC analysis. This analysis demonstrated the presence of only two set of peaks: one peak due to unreacted starting materials and two with retention times identical with the photoproducts concluded to result from reductive dimerization of CH on the basis of MS data.

Acknowledgment. This study was supported in part by a grant from the National Science Foundation, CHE-8900099, and a small grant from the Exxon Undergraduate Research Program Award to New York University. A.M.I. also wishes to thank Dr. George Heibel and Mr. Robert Nodar for technical assistance. A.M.I. is also thankful for an award for this research from the NYU Chapter of Sigma Xi.

A General Synthetic Route to Isobenzofurans Bearing a Functionalized C-1 Substituent

Sanath K. Meegalla and Russell Rodrigo*

Guelph-Waterloo Centre for Graduate Work in Chemistry, Department of Chemistry, University of Waterloo, Waterloo, Ontario, Canada N2L 3G1

Received July 18, 1990

Aromatic *o*-formyl acetals undergo base-catalyzed Claisen–Schmidt condensation with nitro compounds, ketones, methyl acetate, and acetonitrile to produce functionalized styrenes. Hydrolysis of the acetal and cyclization of the product in methanol provide methoxy phthalans **8** which are used to generate isobenzofurans bearing a functionalized substituent at C-1. The Diels–Alder reactions of these isobenzofurans with several dienophiles have been studied. Conjugated exo-methylene phthalans **20** have been isolated, and an unusual elimination of nitrous acid from nitroalkyl phthalans **8E** and **8F** has been observed.

The last decade has witnessed rapid advances in the chemistry of isobenzofuran (IBF).[1,2] Many versatile routes for IBF generation have been devised, and multisubstituted IBF's have been employed in the synthesis of aromatic and hydroaromatic natural products.[2] Our continuing interest in this area has led us to seek methods that will further broaden the utility of IBF in synthesis. To this end, we have directed our efforts at developing a general procedure for the production of IBF's with C-1 substituents bearing various common functional groups that can be manipulated in a synthetically useful manner. We now report the results of these investigations.

---

(1) Rickborn, B. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; JAI Press Inc.: Greenwich, CT, 1989.

(2) Rodrigo, R. *Tetrahedron* 1988, *44*, 2093–2135.

0022-3263/91/1956-1882$02.50/0