

Photoinduced Alcoholysis of the Trichloroacetyl Group¹

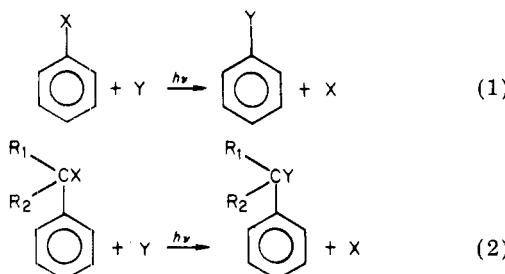
Yasuji Izawa, Hideo Tomioka,* Masashi Natsume, Shinji Beppu, and Hideo Tsujii

Department of Industrial Chemistry, Faculty of Engineering, Mie University, Tsu, Mie 514, Japan

Received April 17, 1980

Irradiation of α,α,α -trichloroacetophenone (**1a**) in methanol afforded alcoholysis products methyl benzoate (**2**; X = H, R = Me) and methyl benzoylformate (**3**; X = H, R = Me) along with dichloroacetophenone. Formation of **2** was greatly favored in the presence of oxygen, whereas that of **3** was favored by the sensitization. Quenching studies showed that both alcoholysis products are derived from different excited triplet states. Reaction mechanisms involving the exciplex between **1** and oxygen are discussed.

Since light-induced heterolytic solvolysis reactions of nitrophenyl phosphates were first discovered by Havinga, de Jongh, and Dorst in 1956,² the related reactions were found to occur with other aromatic esters, ethers, halogeno compounds, etc.³ Interest has increased in this new domain of chemistry not only from the standpoint of the reaction mechanism but also from a synthetic viewpoint because the reactions often proceed in good yields to give products which are sometimes difficult to prepare by other reactions. Most of the investigations thus far reported in this field, however, have been focused on the aromatic photosubstitution reactions, S_NAr^* (eq 1). Photohetero-



lytic side-chain reactions have been relatively limited. The photosolvolytic reaction of benzyl acetates carrying electron-donating ring substituents in aqueous dioxane to form benzyl alcohols⁴ is one of the most well-understood reactions of this type and is explained in terms of the activating effect of a meta group (meta transmission) in the excited-state molecules.⁴ Recently, it has been reported⁵ that a trifluoromethyl group attached to an aromatic nucleus with electron-releasing substituents (i.e., OH and NH₂) is also exceptionally susceptible to a photohydrolysis reaction which yields the corresponding benzoic acid. More recently, it has been demonstrated⁶ that α,α,α -trichlorotoluene itself undergoes a photochemical alcoholysis, forming an alkyl benzoate even under neutral conditions. This is especially noteworthy since irradiation of the monosubstituted α,α,α -trifluorotoluenes^{5b} in methanol leads to very low reaction rates and no identified product and since trifluorotoluene itself shows hardly any reactivity under irradiation even under acidic or basic conditions. Such a reactivity difference has been explained⁶ in terms of the difference in electrophilicity of the benzylic carbon.

Table I. Yields of **2a**-**4a** from Irradiation of **1a**^a

alcohol	yield, % ^b		
	2a	3a	4a
MeOH	10.6	9.7	12.3
EtOH	4.4	9.7	8.0
<i>i</i> -PrOH	3.8	8.7	7.1
<i>t</i> -BuOH	1.7	5.0	7.3

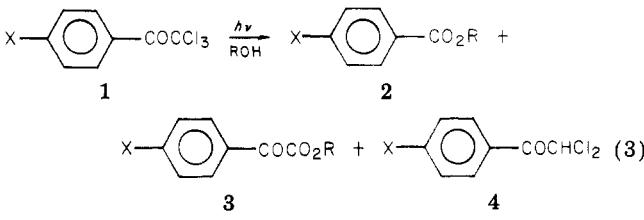
^a All irradiations were carried out on 25 mM solutions of **1a** in nondegassed alcohol in a Pyrex tube at 25 °C for 1.0 h.

^b Determined by GC analysis of aliquots removed from the irradiation mixture. Other minor products detected were chloroacetophenone and acetophenone.

As a part of an investigation⁷ into the photochemical behavior of the trichloromethyl group, we became interested in the photoinduced alcoholysis of the trichloroacetyl group and now report the results of experiments on the photo-reactivity of α,α,α -trichloroacetophenones in alcohols. Our results clearly indicate (i) that the final products from irradiation in alcohol are derived from heterolytic rather than homolytic fission, (ii) that not only the carbonyl but also the trichloromethyl carbon undergoes nucleophilic attack in the excited state, and (iii) that oxygen plays an important role in the present photoalcoholysis.

Results and Discussion

Irradiation Products. A nondegassed solution of α,α,α -trichloroacetophenone (**1a**, 1.0 g) in methanol (150 mL) was irradiated with a high-pressure mercury lamp through a Pyrex filter. After irradiation for 16.5 h, silica gel chromatography of the reaction mixture provided methyl benzoate (**2a**, R = CH₃; 0.139 g, 22.7%), methyl benzoylformate (**3a**, R = CH₃; 0.037 g, 5.0%), and α,α -dichloroacetophenone (**4**; 0.051 g, 6.0%). The identity of



a, X = H; b, X = Me; c, X = Cl

these products was confirmed by comparison with authentic samples. This photoinduced alcoholysis was observed also in a wide variety of alcohols. Yields determined by GC are given in Table I for irradiation in other alcohols. The appropriate control experiments showed that there was no reaction under identical conditions in the absence

(7) Y. Ogata, Y. Izawa, and T. Ukiyai, *Bull. Chem. Soc. Jpn.*, **46**, 1009 (1973); N. Suzuki, T. Kawai, S. Inoue, N. Sano, and Y. Izawa, *ibid.*, in press.

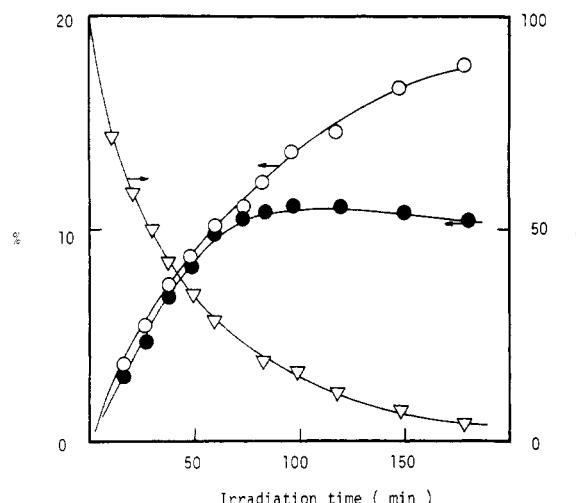


Figure 1. Yields of **2a** (○) and **3a** (●) during irradiation of **1a** (inverted triangle) in nondegassed methanol.

Table II. Effects of Oxygen and Sensitizer on the Yields of **2a** and **3a** from Irradiation of **1a** in Methanol^a

runs	condi-tions	[Ph ₂ C=O], mM	yield, % ^b		ratio of 2a/3a
			2a	3a	
1	N ^c	0	2.5	3.5	0.71
2	O ^d	0	8.3	4.3	1.93
3	O ^d	25	6.5	8.5	0.76
4	O ^d	131	6.0	15.8	0.38
5	D ^e	0	~1	3.1	~0.32
6	D ^e	25	1.5	9.8	0.15
7	D ^e	131	1.4	19.3	0.07

^a All irradiations were conducted on 25 mM solutions of **1a** in methanol at 25 °C for 1.0 h. ^b Determined by GC. ^c The solution was purged with nitrogen for 30 min before irradiation. ^d The solution was purged with oxygen for 30 min. ^e The solution was degassed in three freeze-thaw cycles at 10⁻⁵ mmHg.

of light. Plots of the product yields as a function of irradiation time in methanol (Figure 1) indicate that both **2a** and **3a** are the primary photoproducts of trichloroaceto-phenone but that **3a** is somewhat more photolabile than **2a**. Control experiments showed, however, that only a trace (<1%) amount of **2a** was formed from **3a** even after more than 50% of the **3a** was photodecomposed in methanol.

Effects of Oxygen. Since oxygen has been shown⁶ to have a marked effect on the photoinduced alcoholysis of α,α,α -trichlorotoluene, we next examined the effect of oxygen on the present photoalcoholysis reaction. The results are shown in Table II. The irradiation was interrupted at about 30% completion in order to minimize the error associated with the product photodecomposition. As can be seen in Table II, oxygen has a marked effect on the product ratio; thus, the formation of **2a** was substantially increased by irradiation in an oxygenated solution but suppressed by irradiation in a degassed solution. Compound **3a** was relatively unaffected by oxygen. Control experiments indicated that both the products were not unduly reactive under irradiation in the presence of oxygen.

Quenching and Sensitization Studies. The extent of conversion of ketone **1a** to **2a** and **3a** in degassed methanol was studied as a function of the concentration of piperylenes as quencher. The data are presented graphically in Figure 2 in the usual form of a plot of relative quantum yield for product appearance vs. quencher concentration. Interestingly, the two alcoholysis products

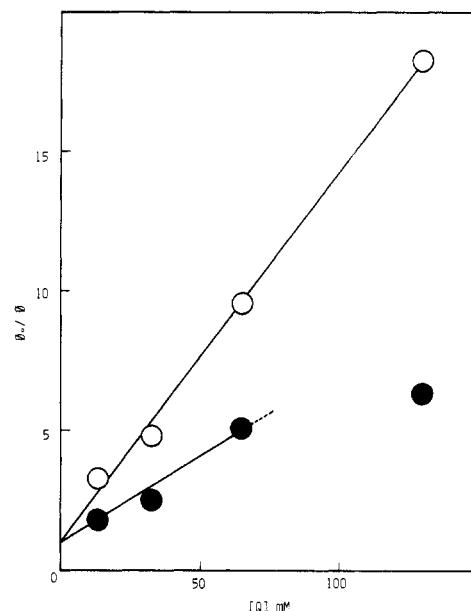


Figure 2. Effect of piperylene on the quantum yield for formation of **2a** (○) and **3a** (●) from **1a** in degassed methanol.

Table III. Effects of Ring Substituents on the Photoalcoholysis of **1a** in Methanol^a

substituent	irradn time, h	% conv ^b	yield, % ^b		
			2	3	4
none (H)	1.0	70	10.6	9.7	12.3
p-Me	0.25	93	7.0	7.7	9.9
p-Cl	2.0	82	6.8	4.8	9.2

^a Irradiations were performed on 25 mM solutions of ketone in nondegassed methanol at 25 °C. ^b Determined by GC. See also footnote ^b in Table I.

show differential quenching. Thus, the formation of benzoate is quenched substantially faster ($k_{q\tau} = 132 \text{ M}^{-1}$) than the formation of formate ($k_{q\tau} = 63 \text{ M}^{-1}$), indicating that the esters **2a** and **3a** are derived from different excited states.

When the irradiation with monochromatic light of 366 nm was carried out in the presence of benzophenone as a sensitizer, both esters were formed but in a different ratio from that observed in direct photolysis. As indicated in Table II, the effect of the benzophenone concentration on the product ratio is particularly intriguing. Thus, the yield of **2a** was essentially unaltered with the sensitizer concentration, whereas that of **3a** increased as the concentration increased. The sensitizer was receiving >98% of the 366-nm light when a 5 molar excess of benzophenone was present.

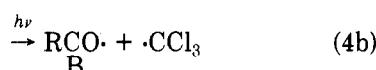
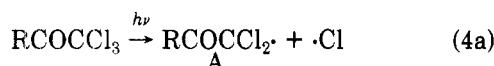
Effects of Ring Substituents. Since correlation of the effects of substituents on the reactivity of aromatic photosubstitution is one of the principal weapons of mechanistic study,³ para-substituted ketones listed in Table III were irradiated in methanol, and the product yields were determined by GC analysis.

Reaction Mechanism. It is evident from the sensitization and quenching studies that the photochemistry of **1** is essentially derived from the triplet excited state but that **2** and **3** are formed from different triplet states. Similar differential quenching has been also observed in the photochemical addition of 2-cyclohexenones⁸ and 9-

(8) O. L. Chapman, T. H. Koch, F. Kleine, P. J. Nelson, and E. L. Brown, *J. Am. Chem. Soc.*, **90**, 1657 (1968).

anthraldehyde⁹ and in photodimerization of isophorone¹⁰ and has been explained in terms of the two-triplets mechanism. The nature of the two chemically distinct triplets which lead, respectively, to **2** and **3** is not clear at present. They may differ in electronic configuration, geometry, or structure.³ The effect of oxygen on the product ratio is especially noteworthy in this connection. The marked acceleration of the photoalcoholysis of α,α,α -trichlorotoluene by oxygen has been explained⁶ in terms of the involvement of the normally forbidden $S_0 \rightarrow T_1$ transition of trichlorotoluene due to the trichlorotoluene–oxygen charge-transfer complex. In the present reaction, however, only the formation of **2** was accelerated by oxygen whereas that of **3** was essentially unchanged. This suggests that **2** may be formed from the exciplex of **1** with oxygen while **3** is derived from the “free” triplet excited state of **1**. Such an assumption also explains the preferential effect of the sensitizer on the formate formation. Presumably, the exciplex may be generated from a contact charge-transfer complex¹¹ of **1** with oxygen in the ground state. Thus, the sensitization should result in an increase only in the generation of triplet excited state, a precursor for **3**, but not affect the generation of the exciplex formation. Although attempts to observe such a charge-transfer band in the oxygen-saturated solution of **1** were unsuccessful, such complexes of organic compounds with oxygen have been frequently observed¹¹ and are responsible for some photochemical reactions¹² in the presence of oxygen.

The experimental results obtained above clearly establish that the photolysis of **1** in alcohol results in the formation of two esters, and this is in sharp contrast with the analogous thermal reaction¹³ with base, where only benzoate is formed. It is very interesting to note here that most aromatic ketones are known¹⁴ to undergo photoreduction especially in good hydrogen donating solvents, e.g., 2-propanol, to give the corresponding pinacols and/or alcohols presumably via hydrogen abstraction by an excited carbonyl group. Moreover, it has been demonstrated¹⁵ that the primary processes of photolysis of most trichloroacetyl groups involve cleavage of the carbon-chlorine bond and cleavage of the bond between the trichloromethyl and carbonyl groups, creating radicals A and B, respectively. Indeed, the formation of dichloroaceto-



phenone (**4**), presumably via radical A, as a byproduct from photolysis implies that the homolytic fission takes place as a competing reaction pathway. It is very important, then, to examine the exact reaction step for the formation of the esters **2** and **3**. Libman, Sprecher, and Mazur have

(9) N. C. Yang, R. Loeschen, and D. Mitchell, *J. Am. Chem. Soc.*, **89**, 5465 (1967).

(10) O. L. Chapman, P. J. Nelson, R. W. King, D. J. Trecker, and A. A. Griswold, *Rec. Chem. Prog.*, **28**, 167 (1967).

(11) H. Tsubomura and R. S. Mulliken, *J. Am. Chem. Soc.*, **82**, 5966 (1960); H. Ishida, H. Takahashi, H. Sato, and H. Tsubomura, *ibid.*, **92**, 275 (1970).

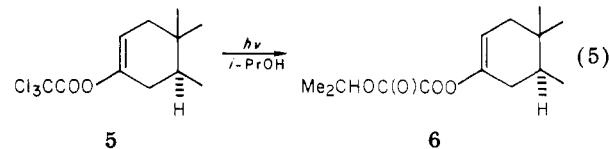
(12) (a) K. S. Wei and A. H. Adelmann, *Tetrahedron Lett.*, 3297 (1969); (b) C. von Sonntag, K. Neuwald, H.-P. Schuchmann, F. Weeke, and E. Janssen, *J. Chem. Soc., Perkin Trans. 2*, 171 (1975).

(13) R. B. Wagner and H. D. Zook, “Synthetic Organic Chemistry”, Wiley, New York, 1953, p 488.

(14) See for example N. J. Turro, “Modern Molecular Photochemistry”, W. A. Benjamin/Cummings, Menlo Park, CA, 1978, p 362.

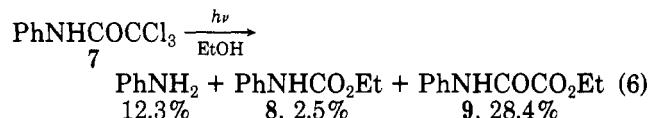
(15) J. R. Majer and J. P. Simons, *Adv. Photochem.*, **2**, 137 (1964).

reported¹⁶ that photolysis of enol trichloroacetate (**5**) derived from 17β -acetoxy- 5α -androstan-3-one in 2-propanol results in the formation of a solvent addition product (eq 5), which has been tentatively assigned as oxalic acid de-



rivatives **6**, a quite analogous product to **3** in the present photoalcoholysis. However, they have explained its formation in terms of a combination of a radical of type A with 2-propanol and a subsequent conversion to **6** probably occurring during the isolation procedure in the dark. This scheme seems less likely, however, as a route for the benzoylformate formation in the present system because (i) **3** was formed even in the irradiation of **1** in *tert*-butyl alcohol, in which the oxalic acid derivative is not formed¹⁶ as in the photolysis of **5**, and (ii) irradiation of methyl trichloroacetate under the present conditions did not produce either oxalate or carbonate, although the starting material was photodecomposed. A more probable explanation must include the nucleophilic attack of the alcohol on the excited trichloromethyl carbon, followed by the thermal alcoholysis of the intermediary benzoylformyl chloride, as has been proposed to explain the analogous alcoholysis of α,α,α -trifluoro-⁵ and -trichlorotoluenes.⁶

Photoalcoholysis of Other Trichloroacetyl Compounds. In order to know the scope and limit of the present novel photoalcoholysis reactions, we attempted the photolysis of several other trichloroacetyl compounds briefly in alcohol. Irradiation of methyl trichloroacetate in methanol through quartz did not result in the formation of expected alcoholysis product, i.e., carbonate and/or oxalate. Hexachloroacetone also did not lead to the alcoholysis reaction upon irradiation in alcohol. These results seemed to suggest that the phenyl group adjacent to the trichloroacetyl might play an important role in the photoalcoholysis. However, irradiation of trichloroacetanilide (**7**) in ethanol (eq 6) through a Pyrex filter afforded aniline, ethyl *N*-phenylcarbamate (**8**), and ethyl oxanilate (**9**).



Experimental Section

IR spectra were recorded on a JASCO IR-G recording spectrometer, and NMR spectra were determined with a JEOL JNM-MH-100 NMR spectrometer in CDCl_3 with Me_4Si as an internal reference. UV spectra were measured with a Shimadzu UV 250 recording spectrometer. GC analyses were performed on a Yanagimoto Model F 1800 instrument using a $2.0 \text{ m} \times 5.0 \text{ mm}$ column packed with (A) 5% PEG 6000 and (B) 5% SE-30 on 60–80-mesh Diasolid L. Woelm silica gel (activity III) was always used for column chromatography.

Materials. Di-(4a–c)¹⁷ and trichloroacetophenones (1a–c)¹⁸ were prepared by chlorination of corresponding acetophenones. Benzoylformates were prepared¹⁷ from 4 followed by esterification. Trichloroacetanilide (**7**) was obtained¹⁹ in the reaction of hexa-

(16) J. Libman, M. Sprecher, and Y. Mazur, *J. Am. Chem. Soc.*, **91**, 2062 (1969).

(17) J. G. Aston, J. D. Newkirk, D. M. Jenkins, and J. Dorsky, “Organic Syntheses”, Collect. Vol. III, Wiley, New York, 1955, p 538.

(18) S. G. Cohen, H. T. Wolosinski, and P. J. Scheuper, *J. Am. Chem. Soc.*, **72**, 3952 (1950).

chloroacetone with aniline. Ethyl oxanilate (9) was prepared²⁰ by the reaction of diethyl oxalate with aniline. Satisfactory spectroscopic data have been obtained on all compounds.

Piperylenes were distilled and stored at -5 °C. Benzophenone was used as obtained from the Tokyo Kasei Co. Absolute alcohols were prepared in the usual way just before use. All other reagents were obtained from commercial sources and used as received.

Irradiations for Product Identification. In a typical run, a solution of 1a (1.0 g) in methanol (150 mL) was placed in a Pyrex well equipped with a thermometer and a water-cooled condenser. A high-pressure, 300-W, Hg lamp with a water-cooled quartz jacket was used as an external light source. The reaction vessel and light source were immersed in a water bath. The progress of the reaction was monitored by removal of aliquots with a syringe and examination by TLC. After irradiation for 16.5 h, the irradiation mixtures were concentrated on a rotary evaporator and chromatographed on a 2.0 × 30 cm silica gel (Woelm, activity III) column with chloroform as eluent to afford methyl benzoate (0.139 g, 22.7%), methyl benzoylformate (0.047 g, 6.4%), and dichloroacetophenone (0.051 g, 6.0%) which had the same NMR spectra and GC retention times as authentic samples.

Irradiation for Analytical Purposes. All irradiations outlined in Tables I-III and Figures 1 and 2 were carried out on 25-mM solutions of 1 in alcohol in a Pyrex tube of 5.0-mL capacity at 25 °C. The progress of reaction was monitored by GC analysis of aliquots removed from the irradiation mixture. The irradiation was generally interrupted at about 30% completion in order to minimize error associated with the product decomposition. The identity of the products was confirmed by GC comparison with authentic samples prepared as above.

(19) B. Sukornick, "Organic Syntheses", Collect. Vol. V, Wiley, New York, 1973, p 1074.

(20) J. S. Pierce, C. D. Lunsford, R. W. Raiford, Jr., J. L. Rush, and D. W. Riley, *J. Am. Chem. Soc.*, **73**, 2595 (1951).

Sensitized irradiations were conducted by using a Ritsu MC-20 radiating monochromator (250-W xenon arc lamp) so as to assure absorption of most of incident light by the photosensitizer. Thus, when sensitized irradiation was carried out in Pyrex tubes containing 131 mM benzophenone (ϵ ~70 at 366 nm) and 25 mM 1a (ϵ ~0.7 at 366 nm) with light of 366-nm wavelength from the monochromator, more than 98% of the incident light was absorbed by the sensitizer.

For quenching studies, a stock solution of 1 in methanol was prepared, and 3-mL portions were added to Pyrex tubes containing varying amounts of piperylene. The tubes were then corked and placed in the "merry-go-round" for irradiation.

Degassing was accomplished by subjecting the samples to a minimum of three freeze-degas-thaw cycles at a pressure near 10⁻⁵ mmHg. A purge of the samples with the gas (N₂ or O₂) was carried out at 0 °C with vigorous stirring by a magnetic stirring bar.

Irradiation of Trichloroacetanilide (7) in Ethanol. A solution of 7 (1.0 g) in ethanol (150 mL) was irradiated and worked up as described above to afford ethyl N-phenylcarbamate (8; 15.8 mg, 2.5%) and ethyl oxanilate (9; 213.5 mg, 28.4%). GC analysis of the reaction mixture showed that aniline (12.3%) was present as a major byproduct.

Attempted Irradiation of Other Trichloroacetyl Compounds. Irradiation of hexachloroacetone (25 mM) in nondegassed methanol in a quartz tube was carried out with the unfiltered 300-W Hg lamp. GC monitoring of the reaction indicated that neither methyl trichloroacetate nor methyl trichloropyruvate was detected even after more than 70% of the starting material was consumed. Similar irradiation of methyl trichloroacetate resulted in no detection of methyl carbonate or methyl oxalate.

Registry No. 1a, 2902-69-4; 1b, 36930-95-7; 1c, 27704-37-6; 2a, 93-58-3; 2b, 99-75-2; 2c, 1126-46-1; 3a, 15206-55-0; 3b, 34966-53-5; 3c, 37542-28-2; 4a, 2648-61-5; 4b, 4974-59-8; 4c, 5157-57-3; 7, 2563-97-5; 8, 101-99-5; 9, 1457-85-8; aniline, 62-53-3.

Unusual Germacranolides from *Inula eupatorioides*¹

Robindra N. Baruah, Ram P. Sharma, and Gopalakrishna Thyagarajan

Regional Research Laboratory, Jorhat 785 006, Assam, India

Werner Herz* and Serengolam V. Govindan

Department of Chemistry, The Florida State University, Tallahassee, Florida 32306

John F. Blount

Research Division, Hoffmann-La Roche Inc., Nutley, New Jersey 07110

Received June 23, 1980

Three new germacranolides, ineupatolide, ineupatorolide A, and ineupatorolide B, were isolated from *Inula eupatorioides* DC. Structures were deduced by chemical transformations and X-ray crystallography. The absolute configurations are discussed.

The sesquiterpene lactones so far found in *Inula* species (tribe Inuleae, Compositae)²⁻⁴ are relatively simple germacra-1(10),4,5-dien-8,12-olides or substances formed from them by cyclization and subsequent scission processes which have been adumbrated elsewhere.^{5,6} Best known

are alantolactone and its congeners from several *Inula* species including *I. helenium* (elecampane), an article of commerce. We now report isolation from *I. eupatorioides*

(5) Herz, W. *Isr. J. Chem.* 1977, 16, 32.

(6) Seeming exceptions to the rule that lactone ring closure toward C-8 prevails in *Inula* (as it generally does in *Inulae sensu lato*) are germanin from *I. germanica*,⁷ several herbolide A analogues among the plethora of lactones in *I. helenium*⁸ and *I. royleana*,⁸ and 8-hydroxyeremanthin in *I. aschersonia*.⁹

(7) (a) Chugunov, P. V.; Pakalns, D.; Shreter, A. M. *Khim. Prir. Soedin.* 1970, 6, 478. (b) Konovalova, O. A.; Rybalko, K. S.; Sheichenko, V. I. *Ibid.* 1974, 10, 578.

(8) Bohlmann, F.; Mahanta, P. K.; Jakupovic, J.; Rastogi, R. C.; Natu, A. A. *Phytochemistry* 1978, 17, 1165.

(9) Papanov, G. Y.; Malakov, P. H.; Bohlmann, F. *Phytochemistry* 1980, 19, 152.

(1) Work at the Florida State University was supported in part by a United States Public Health Service grant (CA-13121) through the National Cancer Institute.

(2) Fischer, N. H.; Olivier, E. J.; Fischer, H. D. *Fortschr. Chem. Org. Naturst.* 1979, 38, 47, ref 97, 111, 115, 163, 259, 560, 583, 583a, 768-773, 847, 850e, 921, 1003.

(3) Mukhametzhanov, M. N.; Abdurakhmanov, O. A.; Adekenov, S. N. *Teor. Osn. Pererab. Miner. Org. Syr'ya* 1976, 3, 104; *Chem. Abstr.* 1979, 91, 123889.

(4) Pyrek, J. *St. Rocz. Chem.* 1977, 51, 1277.