Photodecarboxylation of Cyanohydrin Esters. Models for Pyrethroid Photodecomposition

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Benzyl esters in which the α position has been substituted with a cyano group give upon irradiation in either methanol or hexane products resulting from photoelimination of carbon dioxide. The relative amount of photoeliminated product formed is dependent upon intermediate free-radical stability. The α-substituted and unsubstituted esters examined may serve as models for photodecomposition studies of pyrethroid insecticide chemicals in organic solvents.

The favorable characteristics of the natural pyrethrin esters of having high insecticidal activity and low mammalian toxicity have been recognized for decades (Casida, 1973, pp 3ff). The use of these natural esters has been limited, however, due primarily to their photolability (Casida, 1973, p 311). During the past few years several synthetic analogues (pyrethroids) have been introduced which have retained the favorable toxicity ratio between insects and mammals but which are considerably more stable toward photodegradation. Three of these new pyrethroid esters currently being investigated for commercial use are NRDC-143 (Elliott et al., 1973), NRDC-161 (Elliott et al., 1974), and S-5602 (Matsuo et al., 1976) shown in Figure 1. The acid portions of these pyrethroids differ in the type of halogens and the presence or absence of a cyclopropane ring, whereas the alcohol moiety differs only by a cyano group on the benzylic carbon atom.

Previous studies of the photodecomposition of pyrethroids indicate that ester bond cleavage is an important reaction pathway for degradation (Ueda et al., 1974). Thus, it was of interest whether or not the cyano group α to the ester linkage gave either additional stability to the overall molecule or yielded unique products upon irradiation.

This study describes the photolytic behavior of several benzyl esters and their α-cyano derivatives including acetates of the alcohol portions of the pyrethroids shown in Figure 1.

MATERIALS AND METHODS

Chemicals. All chemicals used including the various acid chlorides, benzaldehyde, and benzyl alcohol (Aldrich Chemical Co., Milwaukee, Wis.) were of reagent grade quality and used without further purification. The 1,3-cyclohexadiene (Aldrich) utilized in the quenching experiments was distilled prior to use.

Cyanohydrin Preparation. The cyanohydrins examined were prepared by the addition of excess KCN and glacial acetic acid to an ethanolic solution of benzaldehyde with compounds **1**–**7** and 3-phenoxybenzaldehyde with **9**. Workup consisted of pouring the reaction mixture into water and extracting several times with ether. After normal extraction procedures and removal of the ether and any ethanol remaining using a vacuum rotary evaporator, the resulting cyanohydrin was used directly to prepare the esters as described below.

Compounds 1–9 and S-5602. The esters were prepared in the usual manner by addition of the appropriate acid chloride to a cooled solution of the cyanohydrin or benzyl alcohol in benzene and pyridine. After workup, the esters were distilled under vacuum and characterized by ^{1}H NMR and mass spectrometry. Compound **8** was prepared by reacting acetyl chloride in the normal manner with α-ethynyl benzyl alcohol prepared from a method similar to that described by Skattebol et al. (1963) utilizing ethynylmagnesium chloride and benzaldehyde (5 g, 0.047 mol). After workup, the residual liquid was distilled under reduced pressures to give 3.5 g (43% yield) of **8**. S-5602 was prepared by the addition of 1-(4′-chlorophenyl)-3-methyl butyryl chloride (Miyakado et al., 1975) to the cyanohydrin of 3-phenoxybenzaldehyde in the usual manner. The product was purified on a Florisil column by eluting with hexane. ^{1}H NMR showed four isomers to be present (i.e., *R*,*R*, *S*,*S*, *R*,*S*, and *S*,*R*): ^{1}H NMR (CCl$_4$, internal Me$_4$Si) δ 0.70 (d, 3 H, J = 6.0 Hz), 0.72 (d, 3 H, J = 6.0 Hz), 0.95 (d, 3 H, J = 6.0 Hz), 1.05 (d, 3 H, J = 6.0 Hz), 2.30 (br m, 1 H), 3.19 (d, 1 H, J = 10.5 Hz), 6.24 (s, 1 H), 6.29 (s, 1 H), and 7.5–6.8 ppm (br m, 13 H, aromatic); CI-MS (isobutane) m/e (relative intensity) *442* (33.3), *421* (100) $[M + 1]^+$, *278* (26.4), *208* (65.3), *169* (30.5), *167* (88.8).

Analysis. *Routine GC–MS and MS.* The Finnigan Model 9500 GC coupled to a Finnigan 1015D mass spectrometer with a chemical ionization (CI) source was used in combination with a System Industries Model 150 control system for qualitative product analysis. A U-shaped column of 2 m length and 2 mm i.d. containing 3% Dexil on Varaport-30 (100–120 mesh) was operated with temperature programming and a helium flow rate of 15–20 ml/min. Isobutane or methane was used as reagent gas with a source pressure of 0.5–1.5 Torr. Electron impact (EI) mass spectra were obtained at 70 eV with a CEC Model 21-110 instrument using the direct insertion technique and a sample volatilization temperature of 150 °C.

Quantitative GC Measurements. The Hewlett-Packard Model 5754 instrument equipped with a thermal conductivity detector and a coiled stainless steel column, 2 m × 2 mm i.d., containing 10% UCW-86 on Gas-Chrom G (100–120 mesh) was operated in the programming mode from 130 to 250 °C at 10 °C/min with a helium flow rate of 15 ml/min. The quantitative values in Table I were obtained using a Hewlett-Packard Model 3380A recording integrator attached to the above H.P. instrument.

Routine Proton Magnetic Resonance (^{1}H NMR) and Infrared (IR) Measurements. Characterizations of products and reactants were aided by the use of a Perkin-Elmer Model R-32 90-MHz ^{1}H NMR instrument with spin-decoupling capabilities and a Perkin-Elmer Model 457 IR spectrophotometer.

Photolysis. The photodecomposition studies were carried out by placing 1–2 ml of 0.1 M methanol or hexane solution of the compound (**4**, **6**, and **7** were not readily soluble in hexane) in quartz NMR tubes (Wilmad Glass

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Table I. Percent Decarboxylated Product Formed upon Irradiation of Various Esters

	$C_6H_5C(-R)HOC(O)R'$			% products[a]		
No.	R	R′	Solvent	Starting ester	$C_6H_5C(-R)HR'$	Other[b]
1	CN	CH_3	Methanol	35.6	57.3	7.1
			Hexane	57.8	37.7	4.5
1a	H	CH_3	Methanol	100		
2	CN	n-C_3H_7	Methanol	31.8	55.7	12.5
			Hexane	67.6	24.5	7.9
3	CN	i-C_3H_7	Methanol	31.1	56.5	12.4
			Hexane	68.4	22.6	7.9
4	CN	c-C_3H_5	Methanol	55.8	38.5	5.7
5	CN	$CH_2C(CH_3)_3$	Methanol	26.5	67.8	5.7
			Hexane	63.8	27.2	9.0
5a	H	$CH_2C(CH_3)_3$	Methanol	91.4		8.6
6	CN	C_6H_5	Methanol	87.4		12.6
7	CN	$CH_2C_6H_5$	Methanol	10.2	73.8	16.0
7a	H	$CH_2C_6H_5$	Methanol	98.2		1.8
8	C≡CH	CH_3	Methanol	78.9	7.7	13.4
			Hexane	86.1	8.1	5.8
9	m-$C_6H_5OC_6H_5C(CN)HOC(O)CH_3$		Methanol	16.1	77.8	6.1
9a	m-$C_6H_5OC_6H_5CH_2OC(O)CH_3$		Methanol	98.2		1.8

[a] Values given are based on GC areas and are approximate since all esters were irradiated as 0.1 M solutions. [b] Determined to be benzylnitrile for compounds 1–3 and 7.

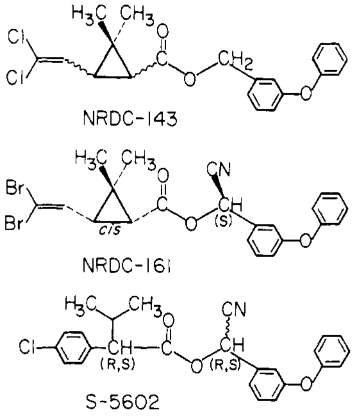


Figure 1. Structures of the synthetic pyrethroids NRDC-143, NRDC-161, and S-5602.

Co., Buena, N.J.). The tube(s) was attached to a quartz immersion well and irradiated at room temperature for 2 h using a 200-W Hanovia lamp with a Vycor filter (>220 nm). Identical products to those described in Table I were obtained using Corex (>260 nm) or Pyrex (>290 nm) filters with only the rate of disappearance of starting ester differing. The resulting solution after irradiation was analyzed directly by GC and GC–MS. Preparative photolyses were accomplished by dissolving 1–2 g of starting ester in 180 ml of anhydrous methanol and irradiating using the lamp and filter described above. Isolation of the products was carried out using a combination of column and preparative thin-layer chromatography.

Spectral Data for Compound 10. As in the case with S-5602, four different isomers of 10 were obtained: ^1H NMR (CCl_4, internal Me_4Si) δ 0.85 (d, 3 H, J = 6 Hz), 0.90 (d, 3 H, J = 6 Hz), 0.93 (d, 3 H, J = 6 Hz), 1.23 (d, 3 H, J = 6 Hz), 2.40 (br m, 1 H), 2.45 (d of d, 1 H, J = 13.0, 9.0 Hz), 2.95 (d of d, 1 H, J = 9.0, 5.5 Hz), 4.05 (d, 1 H, J = 9.0 Hz), 4.30 (d, 1 H, J = 5.5 Hz), and 6.5–7.4 ppm (br m, 13 H, aromatic); EI-MS, m/e (relative intensity) *375* (5.5), *209* (47.7), *169* (31.1), *167* (100), *127* (26.0), *125* (77.3), *115* (11.6); the mass spectrum gave a parent ion at 375.1408 (calcd for $C_{24}H_{22}NOCl$, 375.1390); CI-MS (methane), m/e (relative intensity) *416* (7.9) $[M + 41]^+$, 404 (18.9) $[M + 29]^+$, 376 (88.4) $[M + 1]^+$, 210 (10.5), *169* (36.8), *167* (100), *127* (5.2), *125* (15.8).

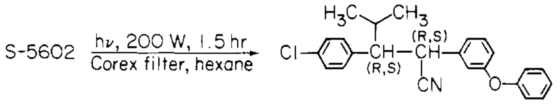
RESULTS

The various esters studied and the major product(s) obtained in the photolysis are shown in Table I. The reaction mixtures were relatively simple with only one to four components being observed. The major photoproduct obtained from compound 1 was identified by ^1H NMR, mass spectral, and IR comparison with an authentic standard (Aldrich Chemical Co., Milwaukee, Wis.) as α-methylbenzyl cyanide. The major photoproduct from compounds 2–4, 7, and 9 was also identified to be that formed from photoelimination of CO_2 from the parent esters. This product was also observed in slightly smaller amounts upon irradiation of these esters in hexane. Compound 6 gave none of the photodecarboxylated product but only components with short GC retention times and starting material. Compound 8, where the cyano group is replaced with an ethynyl group, also gave the corresponding CO_2 photoeliminated product but in considerably smaller amounts with larger amounts of unidentified material. Compound 9, the acetate ester of the alcohol portion of NRDC-161 and S-5602, also gave upon irradiation large amounts of a product identified as that due to photoelimination of CO_2.

In contrast to compounds 1–9 compounds **1a**, **5a**, **7a**, and **9a**, the unsubstituted analogues, did not give the photodecarboxylated product under the conditions used, and, with **1a**, only starting material was observed.

Compounds 1–3 and 5 gave similar product distributions while the cyclopropyl analogue 4 gave slightly less of the decarboxylated product and the benzyl system 7 and compound 9 slightly more. The relative percents in Table I are only approximate, however, since in this product study, the molar absorptivities of the esters were not taken into consideration.

The reaction of 1 using the standard conditions in the presence of 1,3-cyclohexadiene was quenched completely. No other photoproducts were formed, and the initial concentration of 1 remained unchanged. This suggests that the quenching arises from excited state deactivation and not by chemical processes (i.e., reaction of starting material or products with quencher). Compound 1 photolyzed in the presence of a 50-fold molar excess of benzophenone using a Pyrex filter did not show any increase in product



10 (75%)

Figure 2. Photolysis of S-5602 in hexane for 1.5 h utilizing a Corex filter.

formation. Failure to sensitize by benzophenone may be the result of an unfavorable triplet–triplet energy gap between substrate and sensitizer.

DISCUSSION

Photodecarboxylation of simple esters is one pathway available to the excited state with the relative importance depending upon the structure of the ester and the photolytic conditions (Calvert and Pitts, 1966). Loss of CO_2 has been observed as the major photochemical pathway in the photolysis of *p*-methoxybenzyl acetate (Zimmerman and Sandel, 1963) and in benzene solutions of benzyl acetate (Van Dusen and Hamill, 1962). Extensive mechanistic studies have been carried out on the photodecarboxylation of benzyl phenyl acetate (Givens and Oettle, 1972), benzhydryl esters (Fujita et al., 1972), and naphthol esters (Matoszewski et al., 1973). These results indicate that the photoelimination process with esters occurs via discrete radical intermediates which are formed by stepwise loss of CO_2, possibly from the triplet state of the starting ester, with subsequent recombination of the radicals within a solvent cage.

Our results with the esters **1**–**9** indicate that they also undergo rapid elimination of CO_2 upon irradiation yielding products formed from recombination of free radicals. Within the series of compounds examined, the amount of major product and starting ester remaining parallels the stability of the free radical formed both on the acid and alcohol portions of the molecule. Thus, compounds in which simple alkyl radicals would be formed (i.e., **1**–**3** and **5**) give similar amounts of product and remaining starting ester whereas **7** yielding the stable benzyl radical and **6** the unstable phenyl radical give substantially greater and smaller amounts of the major products, respectively. Substitutions on the alcohol portion also affect the amount of recombined products formed. For example, the free radical resulting from compound **8** where the α-cyano group has been replaced by an ethynyl group is stabilized to a lesser degree, a fact which is reflected in the relative amounts of recombined products as is seen in Table I. Substitution on the aromatic ring with an electron-donating substituent as is the case with **9** increases the amount of major product, since the intermediate radical formed would be stabilized to a greater degree. A similar observation has been made by other workers (Givens and Oettle, 1972).

It was expected that the decarboxylated material formed from compound **4** would contain a mixture of cyclopropyl and allyl products resulting from the isomerization of the intermediate cyclopropyl radical. This, however, was not the case since examination by ^1H NMR of the product produced on a preparative scale in methanol demonstrated the absence of a double bond giving absorptions due to the cyclopropane ring at 0.7 (br m, 4 H) and 1.25 ppm (br m, 1 H). This result indicates that the combination of the individual free radicals after loss of CO_2 is either extremely rapid or possibly a concerted process.

The utility of model systems or compounds such as those in Table I is dependent, in part, on their similarity, both mechanistically and in the products formed, to the actual pesticide chemical under consideration. Thus, when S-5602 was irradiated in hexane utilizing either a Corex or Pyrex filter at room temperature for 1.5 h (Figure 2), the major product formed was the decarboxylated material, compound **10** (see Materials and Methods). Evidence for a decarboxylated product upon irradiation of NRDC-161 in methanol has also recently been observed (Ruzo et al., 1977).

This preliminary study indicates that pyrethroid insecticide chemicals which contain an α-cyano or any radical stabilizing group α to the ester linkage such as NRDC-161 and S-5602 may increase not only the rate of photodecomposition relative to unsubstituted derivatives (NRDC-143), but also, at least in organic solvents, may produce in substantial amounts products due to photoelimination of CO_2.

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