Photochemistry of Pesticides. 9.[1] Further Studies on the Photochemistry of *O,O*-Diethyl *O*-(3-Chloro-4-methyl-2-oxo-2*H*-1-benzopyran-7-yl) Thiophosphate (Coumaphos)

Wafaa M. Abdou,[2] Mahmoud M. Sidky, and Heinrich Wamhoff*

The photodimerization of Coumaphos (1) has been studied in detail, varying solvents and concentrations. In all cases, three dimeric products 2–4 have been isolated: head-to-tail anti dimer 2, its oxidation product 3, and head-to-tail syn dimer 4. 3 was independently made by irradiation of Coroxon (5). A biological evaluation was carried out for the main product 2.

It has been previously reported (Abdou et al., 1987) that UV irradiation of the pesticide (Gunther and Gunther, 1971; Büchel, 1983) *O,O*-diethyl *O*-(3-chloro-4-methyl-2-oxo-2*H*-1-benzopyran-7-yl) thiophosphate (1, Coumaphos; also marketed under the trade names Bayer 21/199, Asuntol, Resitox, and Muscatox) reveals a rather different cycloaddition behavior in comparison to the unsubstituted coumarin molecule. Thus, irradiation of an 1% $CHCl_3$ solution of 1 in the presence or absence of singlet oxygen results in a regioselective photodimerization to afford a head-to-tail anti dimer 2, whose structure was established by single-crystal X-ray diffraction analysis. Since it has been reported (Anet, 1962; Hammond et al., 1964; Krauch et al., 1966; Morrison et al., 1966; Hoffman et al., 1971) that both solvent and concentration show a remarkable effect on the course of the photodimerization of coumarins, we have now extended our study on the photodimerization of Coumaphos (1) with variation of the solvents and concentrations employed (cf. Tables I and II). Moreover, a biological evaluation of the dimer 2 seemed to be of great interest, with regard to the general question if the biological activity of a known active principle, such as 1, is decreased or increased upon photodimerization to 2 (cf. Table III).

RESULTS AND DISCUSSION

An 1% MeOH solution of 1 was irradiated with a Hg high-pressure lamp in a Pyrex reactor ($\lambda > 313$ nm) for ca. 300 h. The photolysate was carefully chromatographed over silica gel to give products 2–4 in sequence (Scheme I).

As in the previous work (Abdou et al., 1987), the head-to-tail anti dimer 2 was obtained as main product in 30% yield and was confirmed by comparison with the previous reported data. Product 3 was obtained as colorless needles in 10% yield. We discuss for 3 the constitutional formula of a head-to-tail anti dimer with oxidation at the thiophosphate moiety of 2 for the following reasons: (a) The elemental analysis and MS are consistent with the constitutional formula of 3, while electron impact MS show a significant peak at m/z 346 (348) corresponding to the monomeric form (i.e., compound 5), which reflects, likely to 2, the instability of the dimer 3 on electron impact, and the novel dual-beam ionization technique (Bütfering et al., 1986, 1987) reveals $[M + H]^+$ at m/z 693. (b) The IR spectrum reveals a new strong band at 1265 cm^{-1} typical for the >P=O group (Hesse et al., 1979). (c) The ^{31}P NMR shift δ –6.66 is definitively within the range expected for the phosphate shift (Crutchfield et al., 1967). (d) The NMR data (^1H, ^{13}C) of 3 are in close relationship to those of dimer 2, the latter one being established unambiguously (cf. Tables IV and V). In ^1H NMR, the methyl signal at δ 1.63 indicates clearly the methyl group being attached to a bridgehead C atom (Hesse et al., 1987). Supplementary evidence for assigned structure 3 has been gained from the close similarity of $^1H_{ar}$ and $^{13}C_{ar}$ signals in 2 and 3. An additional support for this structure was obtained by preparing and UV irradiation of *O,O*-diethyl *O*-(3-chloro-4-methyl-2-oxo-2*H*-1-benzopyran-7-yl) phosphate (5, Coroxon; i.e. the phosphate analogue of Coumaphos (1); Amin and Christian, 1974). The photolysate was chromatographed on silica gel to afford colorless needles possessing the identical melting point (111–112 °C) and proved to be head-to-tail anti dimer 3 (melting point, mixed melting point, and comparative spectral data; cf. Scheme I).

Most obviously, Coumaphos (1) shows a *fast* dimerization rate but a comparatively *slow* oxidation (air) rate toward Coroxon (5), the latter shows due to its UV absorption at shorter wavelengths a much decreased dimerization tendency to form product 3. This is confirmed by independent irradiation of the dimeric thiophosphate 2 in MeOH or $CHCl_3$ for ca. 100 h, where in no case any change could be observed; additionally, no cross dimer of 1 and 5 could be detected.

Then, the third product 4 was obtained as colorless crystals (8% yield, mp 145 °C). Even though this product 4 shows the same analysis, molecular weight, and conse-

Table I. Effect of Solvent on the Photodimerization of 1

solvent	yield,[a] % 2	3	4
$CHCl_3$	20	5	4
EtOAc	25	8	5
MeCN	25	5	7
MeOH	30	10	8

[a] Based on the amount of the starting material (100% disappearance of 1; TLC).

Table II. Effect of Concentration on the Photodimerization of 1

concn, mM	yield,[a] % 2	3	4
10	30	10	8
50	22	7	8
100	19	3	5

[a] Based on the amount of the starting material used (100% disappearance of 1; TLC).

Institut für Organische Chemie und Biochemie, Universität Bonn, Gerhard-Domagk-Strasse 1, D-5300 Bonn 1, FRG.

[1] Part 8: Wamhoff, H.; Abdou, W. M.; Zahran, M. *J. Agric. Food Chem.* 1988, *36*, 205.

[2] Research Fellow, National Research Centre, Cairo, A.R. Egypt.

0021-8561/88/1436-1291$01.50/0

Table III. Results of Some in Vitro Tests of 2 in Comparison with Asuntol (1; Applied as 16% E.C.).

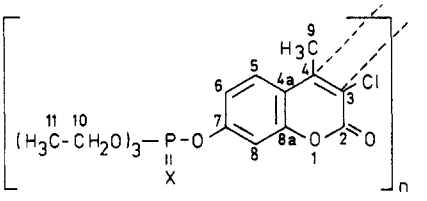
concn, ppm a.i.	inhib of egg deployment act., %: female *Boophilus microplus* (OP-sens. Yeerongpilly-St.)		kill rate, %: blowfly larvae of *Lucilia cuprina* (OP-sens. Elberfeld st.)		kill rate, %: *Musca autumnalis* and *Stomoxys calcitrans*	
	2	Asuntol	2	Asuntol	2	Asuntol
10000	0	100	100	100	0	100
3000	0	100	100	100	0	100
1000	0	100	100	100	0	100
300	0	100	0	100	0	0
100	0	50	0	100		
30	0	50	0	100		
10	0	0	0	100		
3			0	100		
1			0	0		

Table IV. Physical Constants and IR, ^{1}H NMR ($CDCl_3$, δ, TMS Internal Standard), ^{31}P NMR ($CDCl_3$, ppm), MS, and Analytical Data of 1–4

no.	mp, °C	formula (MW)	MS: *m/z* (rel intens)	elemental anal: calcd (found) C	H	Cl	IR (KBr), cm^{-1} C=O	P=O	P—O—R	^{31}P NMR	^{1}H NMR: δ (*J*, Hz)
1	93[a]	$C_{14}H_{16}ClO_5PS$ (362.8)	362 (100)[d] 364 (33)[d]				1735		1015	+62.55	1.42 (dt, 6 H, CH_3CH_2, J_{HH} = 7.5, $^4J_{PH}$ = 1.1), 2.62 (d, 3 H, CH_3, $^4J_{HH}$ = 0.6), 4.28 (dq, 4 H, CH_2CH_2, J_{HH} = 7.5, $^3J_{PH}$ = 10.2), 7.42 (m, 3 H_{ar})
2	124[a]	$C_{28}H_{32}Cl_2O_{10}P_2S_2$ (725.6)	362 (100)[d] 364 (33)[d] 727 $[M + H]^+$[e]	46.35 (46.42)	4.44 (4.55)	9.77 (9.67)	1760		1035	+62.51	1.30 (dt, 12 H, CH_3CH_2, J_{HH} = 8.0, $^4J_{PH}$ = 1.2), 1.66 (d, 6 H, CH_3, $^4J_{HH}$ = 0.5), 4.25 (dq, 8 H, CH_3CH_2, J_{HH} = 8.0, $^3J_{PH}$ = 10.8), 7.30 (m, 6 H_{ar})
3	112[b]	$C_{28}H_{32}Cl_2O_{12}P_2$ (693.4)	346 (100)[d] 348 (33)[d] 693 $[M + H]^+$[e]	48.49 (48.50)	4.65 (4.71)	10.22 (10.60)	1760	1265	1045	−6.66	1.37 (dt, 12 H, CH_3CH_2, J_{HH} = 7.8, $^4J_{PH}$ = 1.4), 1.63 (d, 6 H, CH_3, $^4J_{HH}$ = 0.5), 4.03 (dq, 8 H, CH_3CH_2, J_{HH} = 7.8, $^3J_{PH}$ = 10.6), 7.28 (m, 6 H_{ar})
4	145[c]	$C_{28}H_{32}Cl_2O_{10}P_2S_2$ (725.6)	362 (100)[d] 364 (33)[d] 727 $[M + H]^+$[e]	46.35 (46.47)	4.44 (4.48)	9.77 (9.72)	1750		1020	+62.31	1.42 (dt, 12 H, CH_3CH_2, J_{HH} = 7.6, $^4J_{PH}$ = 1.2), 1.62 (d, 6 H, CH_3, $^4J_{HH}$ = 0.5), 4.30 (dq, 8 H, CH_3CH_2, J_{HH} = 7.6, $^3J_{PH}$ = 10.4), 7.19 (m, 6 H_{ar})

[a] Crystallization solvent: EtOH. [b] Crystallization solvent: $CHCl_3$. [c] Crystallization solvent: MeOH. [d] Electron impact. [e] Dual-beam ionization technique (Bütfering et al., 1986, 1987).

Table V. ^{13}C NMR Data of 1–4 in $CDCl_3$ [ppm, TMS Internal Standard (J_{PC}, Hz)]



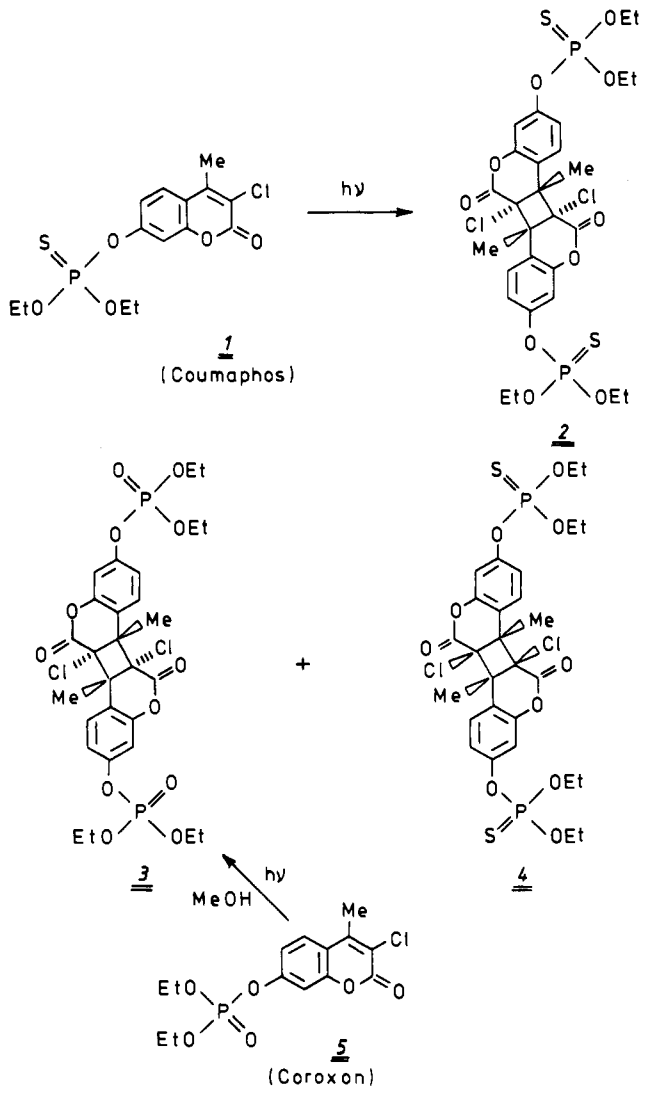
1: X = S, *n* = 1
2: X = S, *n* = 2
3: X = O, *n* = 2
4: X = S, *n* = 2

no.	C-2 (C-2′)	C-3 (C-3′)	C-4 (C-4′)	C-4a (C-4a′)	C-5 (C-5′)	C-6 (C-6′)	C-7 (C-7′)	C-8 (C-8′)	C-8a (C-8a′)	C-9 (C-9′)	C-10 (C-10′)	C-11 (C-11′)
1	156.5	119.8	147.3	117.5 d (1.7)	126.1	118.4 d (5.1)	152.9 d (6.6)	116.8 d (5.2)	151.9	16.4	64.9 d (6.6)	15.7 d (7.4)
2	161.0	69.8	54.5	117.4 d (1.4)	129.4	118.3 d (5.1)	152.4 d (6.6)	110.4 d (5.1)	150.8	24.9	65.4 d (5.9)	15.8 d (8.0)
3	161.0	69.7	54.3	117.4 d (1.3)	129.8	119.4 d (5.1)	152.1 d (5.8)	109.8 d (5.4)	151.0	24.8	65.7 d (5.7)	15.7 d (8.0)
4	161.1	69.9	54.7	117.3 d (1.5)	130.3	118.4 d (5.0)	152.7 d (5.4)	110.1 d (5.4)	150.9	25.1	65.5 d (6.0)	15.9 d (7.4)

quently the same elemental composition $C_{28}H_{32}Cl_2O_{10}P_2S_2$ as 2, the physical properties as well as the spectral data (IR, ^{31}P, ^{1}H, ^{13}C NMR) of both compounds turned out to be rather different (cf. Tables IV and V). Nevertheless, 4 is an isomer of 2. From the spectral data, we assume 4 to be a head-to-tail syn dimer, and due to steric and electronic effects of the substituents (thiophosphate, Cl, Me) a potential formation of head-to-head dimers can be excluded.

In order to study any so vent effect on the photo-

Scheme I



dimerization course, the irradiation of Coumaphos (1) was carried out in several solvents of different polarity ($CHCl_3$, EtOAc, MeCN, MeOH), maintaining the general conditions as in the first experiment (cf. Table I).

Similarly, the influence of the concentration on the individual yield of 2–4 was studied as well by carrying out the irradiation of 1 in MeOH in the same way but with different molarities; the results are depicted in Table II.

From the data shown in Tables I and II, it is obviously that Coumaphos (1) undergoes photodimerization, preferentially to give the head-to-tail anti dimer 2, which always dominates the side products 3 and 4. Moreover, it has been demonstrated that the polarity and the molarity only affect the amount of converted Coumaphos (1): Polar solvents increase slightly the amount of conversion; high concentrations, however, diminish the rate of conversion (self-quenching?). From this behavior and previous results (Abdou et al., 1987), we can conclude that the dimerization mechanism for Coumaphos (1) and Coroxon (5) is completely different from that of nonsubstituted coumarin. Because of the internal heavy-atom effect of Cl, no singlet seems to be involved. The head-to-tail anti formation of dimers 2 and 3 is a product of a coumarin triplet state. As a consequence, solvent polarity and concentration effects (Anet, 1962; Hammond et al., 1964; Krauch et al., 1966; Morrison et al., 1966; Hoffman et al., 1971) play only a very limited role. Additionally, a steric governing effect of the (thio)phosphate group might be discussed.

BIOLOGICAL EVALUATION

Table III shows the results of the biological assay of the dimer 2 against Asuntol (as 16% E.C. commercial product) as standard. Except for a rather weak activity against blowfly larvae, 2 shows no significant activities against typical test parasites studied. [We thank Prof. Dr. H. Hulpke and Dr. W. Stendel of the Bayer AG, Leverkusen and Wuppertal, for carrying out the biological evaluation.]

This result is not surprising as in most cases photoreactions, photooxidations, and photodegradations of active principles cause complete elimination of their previous biological activities. Thus, consequently, upon UV irradiation Asuntol (Coumaphos, 1) loses largely its biological activities; it is photochemically deactivated.

EXPERIMENTAL SECTION

Melting points are uncorrected. Technical Coumaphos (1) was supplied by the Bayer AG D-5090 Leverkusen and was recrystallized from MeOH before use. IR (KBr): Perkin-Elmer 157-G. ^1H NMR ($CDCl_3$) and ^{31}P NMR ($CDCl_3$, vs 85% H_3PO_4): Varian CFT-20. ^{13}C NMR ($CDCl_3$): Bruker WH-90. MS (70 eV): MS-50 of Kratos (AEI). Microanalysis: Mikroanalytisches Laboratorium Pascher, Remagen. Photolyses were carried out in a Pyrex photoreactor equipped with a Hg high-pressure lamp (Philips HPK 125).

Photodimerization of Coumaphos (1) in MeOH. Coumaphos (1; 3 g, 8 mmol) was exposed in MeOH solution (300 mL) to UV irradiation using a Pyrex filter. After 300 h, the solvent was evaporated to dryness in the presence of silica gel (7 g), and then the mixture was separated by chromatography on silica gel with light petroleum ether, then with toluene as eluent, and finally with toluene–ethyl acetate (9.5:0.5, 8:2, 6:4) to give the photoproducts 2, unchanged 1, and 3 and 4 in sequence. For physical and analytical data of 2–4, cf. Tables IV and V.

Photodimerization of Coroxon (5) in $CHCl_3$. Coroxon (5) was prepared as described before (Amin and Christian, 1974), and 5 (3 g, 8.6 mmol) was irradiated in $CHCl_3$ (300 mL) for 200 h. The reaction mixture was worked up as mentioned above. The chromatography was carried out with the following eluents: toluene and then toluene containing increasing amounts of EtOAc. The fraction (up to 9.5:0.5) eluted 1.5 g (50%) of a yellow substance, recrystallized from cyclohexane to give a yellowish white solid (mp 65 °C) and proved to be unchanged Coroxon (5; Amin and Christian, 1974).

The fraction (up to 8:2) afforded 600 mg (20%) of colorless needles (mp 111–112 °C), confirmed to be dimer 3 (melting point, mixed melting point, and comparative spectra). Cf. Tables IV and V.

Irradiation of Dimer 2 in MeOH and $CHCl_3$. The dimeric thiophosphate 2 (1 g, 1.3 mmol) was irradiated in MeOH and/or $CHCl_3$ (150 mL) for 100 h. TLC analysis showed no trace of any photoproduct, and only starting material (0.96 g, 96%) was recovered after the usual workup.

Dimerization Studies in Different Solvents. In three parallel experiments, irradiation of Coumaphos (1) was carried out in $CHCl_3$, EtOAc, and MeCN, similar to the photoreaction of 1 in methanol, employing the same amounts. The reaction mixture was worked up in the usual way and chromatography on silica gel gave products 2–4. For comparative yields, cf. Table I.

Dimerization Studies in Different Concentrations. In three parallel experiments 1 (1.1, 5.4, 10.8 g) was dissolved in MeOH (300 mL) to give 0.01, 0.05, and 0.1 M solutions. After irradiation of the individual solutions for 300 h, it was worked up in the usual manner; 2–4 were

isolated by chromatography (cf. Table II).

ACKNOWLEDGMENT

This work was supported by the Fonds der Chemischen Industrie, the ASRT Cairo, and the Bayer AG. W.M.A. thanks the Heinrich-Hertz-Stiftung for granting a research fellowship.

Registry No. 1, 56-72-4; 2, 116257-45-5; 3, 116149-75-8; 4, 116257-46-6; 5, 321-54-0.

LITERATURE CITED

Abdou, W. M.; Born, L.; Hulpke, H.; Mahran, M. R.; Sidky, M. M.; Wamhoff, H. "Photochemistry of Pesticides, 7. Regioselective Photodimerization of *O,O*-Diethyl-*O*-(3-chloro-4-methylcoumarin-7-yl)-thiophosphate (Coumaphos)". *Phosphorus Sulfur* **1987**, *29*, 179.

Amin, C. G.; Christian, C. M. "Pesticides. *O,O*-Diethylphosphato- and -Thiophosphato Derivatives from Coumarins and Flavonols". *Indian Chem. Manuf.* **1974**, *12*, 22; *Chem. Abstr.* **1975**, *83*, 58.596.

Anet, R. "The Photodimers of Coumarin and Related Compounds". *Can. J. Chem.* **1962**, *40*, 1249.

Büchel, K. H., Ed. *Chemistry of Pesticides*; Wiley-Interscience: New York, 1983; p 82.

Bütfering, L.; Schmelzeisen-Redeker, G.; Röllgen, F. W. "A Dual Beam Thermospray Vaporizer for On-line H.P.L.C.-Mass Spectrometry Coupling". *J. Chem. Soc., Chem. Commun.* **1986**, 579.

Bütfering, L.; Schmelzeisen-Redeker, G.; Röllgen, F. W. "Studies with a Dual-Beam Thermospray Interface in High Performance Liquid Chromatography-Mass Spectrometry". *J. Chromatogr.* **1987**, *394*, 109.

Crutchfield, M. M.; Dungan, C. H.; Letcher, J. H.; Mark, V.; Van Wazer, J. R. *^{31}P Nuclear Magnetic Resonance*; Wiley-Interscience: New York, 1967.

Gunther, F. A.; Gunther, J. O., Eds. *Chemistry of Pesticides*; Springer: New York, 1971; p 341.

Hammond, G. S.; Stout, C. A.; Lamola, A. A. "Mechanisms of Photochemical Reactions. XXV. The Photodimerization of Coumarin". *J. Am. Chem. Soc.* **1964**, *86*, 3103.

Hesse, M.; Meier, H.; Zeeh, B. *Spektroskopische Methoden in der Organischen Chemie*; Thieme: Stuttgart, 1987.

Hoffman, R.; Wells, P.; Morrison, H. "Organic Photochemistry. XII. Further Studies on the Mechanism of Coumarin Photodimerization. Observation of an Unusual 'Heavy Atom' Effect". *J. Org. Chem.* **1971**, *36*, 102.

Krauch, C. H.; Farid, S.; Schenck, G. O. "Photo-C_4-Cyclodimerisation von Coumarin". *Chem. Ber.* **1966**, *99*, 625.

Morrison, H.; Curtis, H.; Mc Dowell, T. "Solvent Effects on the Photodimerization of Coumarin". *J. Am. Chem. Soc.* **1966**, *88*, 5415.

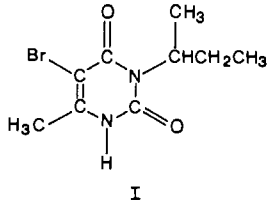
Received for review February 18, 1987. Accepted March 29, 1988.

Crystal and Molecular Structure of Herbicides. 5. Bromacil (Hyvar)

Russell G. Baughman* and Pei-Jan Yu

The crystal and molecular structure of bromacil (5-bromo-3-*sec*-butyl-6-methyluracil) [monoclinic; $P2_1/n$; a = 9.570 (2), b = 9.801 (1), c = 12.147 (3) Å; β = 106.41 (3)°; Z = 4; Mo Kα radiation; μ = 39.65 cm^{-1} (correction made)] has been determined by X-ray analysis. The structure was solved by the Patterson method and refined to a final R = 0.073 for 1004 observed reflections. Planar molecules form a dimer through NH···O intermolecular bonds. Addition of the Br and *sec*-butyl group causes a few significant bond length and angle changes in the uracil skeleton.

Bromacil (5-bromo-3-*sec*-butyl-6-methyluracil, I) is a substituted uracil herbicide. Members of this class of compounds were shown by Bucha et al. (1962) to be highly phytotoxic to a variety of plants. The mode of action of the uracils appears to be by their interference with the photosynthetic process in the plant, likely by competing with naturally occurring pyrimidines (Metcalf, 1971)



I

The structural study of bromacil is part of a series (Baughman et al., 1978, 1980a,b, 1981) being carried out in order to collect a body of precise structural parameters to eventually aid in drawing interferences regarding the nature of the interaction site(s) on the chloroplast.

Division of Science, Northeast Missouri State University, Kirksville, Missouri 63501.

EXPERIMENTAL SECTION

Crystal Data. At 27 °C with graphite-monochromated Mo Kα radiation (λ = 0.710 69 Å), a rectangular prismatic crystal with dimensions 0.36 × 0.10 × 0.16 mm yielded the following information: monoclinic; a = 9.570 (2), b = 9.801 (1), c = 12.147 (3) Å; β = 106.41 (3)°.

Intensity Data, Structure Determination, and Refinement. Four octants of data within a 2θ sphere of 45° were collected by the method and apparatus described by Rohrbaugh and Jacobson (1974). A total of 4095 reflections were recorded in the $\pm h,\pm k,l$ octants.

The intensity data were corrected for Lorentz and polarization effects, and since μ = 39.65 cm^{-1}, an absorption correction was applied with a ϕ-scan technique (Karcher and Jacobson, 1980). The estimated variance in each intensity was calculated by

$$\sigma^2(I) = [C_T + 2C_B + (0.03C_T)^2 + (0.03C_B)^2 + (0.03C_N)^2]/A^2$$

where C_T, C_B, and C_N represent the total, background, and net counts, respectively, A is the transmission factor, and

0021-8561/88/1436-1294$01.50/0