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THE PYROLYSIS OF ISOPROPYL 5-CHLORO-2-HYDROXYCARBANILATE DURING GAS CHROMATOGRAPHY*

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SUMMARY

Isopropyl 5-chloro-2-hydroxycarbanilate has been shown to thermally degrade to 5-chloro-2-benzoxazolinone and unidentified polymeric products. Isopropyl 2-acetoxy-5-chlorocarbanilate was thermally degraded to N-acetyl 5-chloro-2-benzoxazolinone and polymeric products. When isopropyl 2-acetoxy-5-chlorocarbanilate was pyrolyzed in the presence of dimethylamine isopropyl 2-hydroxy-5-chlorocarbanilate, 5-chloro-2-benzoxazolinone and 3-(2-hydroxy-5-chlorophenyl)-1,1-dimethylurea were isolated. The acetylated carbamate was shown to be thermally more stable than the hydroxy analog.

INTRODUCTION

In soybeans, the aglucone of a major water-soluble metabolite of isopropyl 3-chlorocarbanilate has been identified as isopropyl 5-chloro-2-hydroxycarbanilate[1]. Problems with chemical and thermal instability were encountered throughout the isolation and characterization of this metabolite. Gas–liquid chromatography (GLC) of the free phenol or the acetylated derivative yielded pyrolytic degradation products. ROMAGNOLI AND BAILEY[2] reported the instability of isopropyl 3-chlorocarbanilate at temperatures above 200°. FISHBEIN AND ZIELINSKI[3] reviewed the thermal degradation of a variety of alkyl- and aryl-substituted carbamates during GLC. MUKAIYAMA *et al.*[4,5] studied the thermal dissociation of *ortho*, *meta* and *para* (methyl-, methoxy-, chloro- or nitro-) substituted benzylcarbanilates in an amine solvent. Their data suggested the following sequence of reactions:

$$RNHCOOR' \rightleftarrows R\text{-}N{=}C{=}O + HO\text{-}R' \quad (1)$$

$$R\text{-}N{=}C{=}O + H_2NR'' \rightarrow RNHCONHR'' \quad (2)$$

Reaction 1 was shown to be the rate-determining step. DYER AND WRIGHT[6] extended the finding of MCKAY AND VAVASOUR[7] and studied the thermal degradation of ethyl, benzyl, and α-methylbenzyl carbanilates under nitrogen in the absence of solvent.

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Several investigators[6-8] have shown that carbamate esters of secondary and tertiary alcohols may decompose according to reaction 3 if the alcohol has a β-hydrogen.

$$C_6H_5NHCOOCH(CH_3)R' \rightarrow C_6H_5NH_2 + CO_2 + R'CH{=}CH_2 \quad (3)$$

Kinetic and chemical data[6] support an intramolecular degradation with a proposed carbanilic acid intermediate. None of these studies have been performed with *ortho*-hydroxy carbanilates. The appearance of several unknown materials was observed during the development of a suitable GLC method for the separation of the hydroxy or acetoxy carbanilates. These unknown materials had shorter retention times than the parent and their concentrations increased at elevated column temperatures. Recent reports[9,10] on the mass spectral analysis of isopropyl 2-hydroxy-5-chlorocarbanilates have proposed that 5-chloro-2-benzoxazolinone is a predominant fragment ion. Thus, the possibility of 2-benzoxazolinone formation by thermal degradation of isopropyl 5-chloro-2-hydroxycarbamate was considered.

EXPERIMENTAL

General procedures for degradations

Samples were placed in glass hydrolysis ampules with silanized glass wool, purged with nitrogen and sealed at atmospheric pressure. The ampules were heated either in a programmed GLC oven or a preheated silicone oil bath. Following the pyrolysis period the ampule was opened and the reaction mixture dissolved in 1,2-dimethoxyethane. The procedures for the separation of the reaction components are described in Table I.

A 10:1 splitter was employed to transfer samples from the effluent stream of the gas–liquid chromatograph. All samples were collected in capillary tubes from which the material could be removed for IR, NMR or mass spectral analysis. As a general practice IR spectroanalysis was conducted using semi-micro KBr pellets. After the IR data had been collected the KBr pellets were re-ground and placed in sample tubes for mass spectrometry by use of the solid sample probe. The mass spectra were measured with a Varian M-66 mass spectrometer equipped with a V-5500 console. The spectra were attained at 70 eV at a source temperature of 180° and a probe temperature of 25–50°.

NMR spectra were collected using a Varian A-60A with the aid of a Fabri-Tek computer of averaging transients. Samples were examined as solutions of carbon tetrachloride or acetone-D6.

All GLC data were exposed as peak area measured by using a Technicon-strip chart integrator. The quantitative data were based on standard curves as a function of peak area.

RESULTS

In a typical experiment the conditions of the gas–liquid chromatograph were simulated by charging a glass hydrolysis ampule with silanized glass wool, isopropyl 2-hydroxy-5-chlorocarbanilate or isopropyl 2-acetoxy-5-chlorocarbanilate, and sealed at atmospheric pressure under nitrogen. The samples were pyrolyzed for 10 min at 250–260°. The products of the thermal degradation were isolated by TLC and/or GLC (Table I) and assayed by IR, NMR, and mass spectroscopy.

TABLE I

CHROMATOGRAPHY OF DERIVATIVES OF ISOPROPYL-2-HYDROXY-5-CHLOROCARBANILATE ANALOGS

Conditions for thin-layer chromatography: layer, 250-μ Silica Gel HF; solvent system, benzene–chloroform–ethyl acetate (15:05:15). Conditions for gas chromatography: carrier gas, helium 60 cc/min; inlet temp., 220°; flame detector; temperature program, 15 min at 125°, then 1.0°/min to 160°; column, 1.8 m × 0.6 cm 3% Dexsil 300 on Gas-chrom Q, 80–100 mesh, or 3% OV-1 on Gas-chrom Q, 80–100 mesh.

Compound	*TLC R_F value*	*GLC retention time (min)*	
		3% OV-1	*3% Dexsil 300*
Isopropyl 2-acetoxy-5-chlorocarbanilate	0.52	13	19
Isopropyl 2-hydroxy-5-chlorocarbanilate	0.17		13
N-Acetyl isopropyl 2-acetoxy-5-chlorocarbanilate		30	15
Isopropyl 2-acetoxy-3-chlorocarbanilate		35	53
N-Acetyl isopropyl 2-acetoxy-3-chlorocarbanilate		38	50
Isopropyl 4-acetoxy-3-chlorocarbanilate		55	
N-Acetyl isopropyl 4-acetoxy-3-chlorocarbanilate		50	
Isopropyl 3-acetoxy-5-chlorocarbanilate		58	50
N-Acetyl isopropyl 3-acetoxy-5-chlorocarbanilate		50	
N-Acetyl 5-chloro-2-benzoxazolinone	0.60		21
5-Chloro-2-benzoxazolinone	0.30		31

Characterization of 5-chloro-2-benzoxazolinone

When isopropyl 2-hydroxy-5-chlorocarbanilate was subjected to elevated temperatures an unknown product was observed. This unknown pyrolytic product (unknown A) had a TLC R_F value of 0.30 and a GLC retention time of 31 min (Table I). The IR spectrum of unknown A, 2-isopropoxy-benzoxazole, 2-benzoxazolinone and 5,6-dichloro-2-benzoxazolinone were similar in several respects. A strong carbonyl at 1775 cm^{-1} indicated that unknown A had a carbonyl group similar to 2-benzoxazolinone.

Mass spectral data for unknown A and several possible structurally related compounds are reported in Table II. Unknown A had a strong parent ion and base peak at *m/e* 169 which fragments with the loss of two carbon monoxide fragments (−56) to yield a peak at *m/e* 113. This fragmentation pattern is comparable to the mass spectra of the two model compounds, 2-isopropoxy-benzoxazole and 2-benzoxazolinone. The 2-isopropoxy-benzoxazole then fragments with the loss of 42 to yield 2-benzoxazolinone (*m/e* 135) and the *m/e* 135 ion from both model compounds loses two carbon monoxide fragments (*m/e* 56) to yield a strong ion at *m/e* 79. A significant difference between unknown A, 2-benzoxazolinone and 2-isopropoxy-benzoxazole was a difference of 34 mass units in the parent ions. This may be accounted for by substitution of a hydrogen with a chlorine atom. The presence of chlorine in unknown A is confirmed by the 3:1 ratio for the chlorine cluster found in Table II. Therefore, 5-chloro-2-benzoxazolinone is proposed as the structure in unknown A.

Characterization of N-acetyl 5-chloro-2-benzoxazolinone

When isopropyl 2-acetoxy-5-chlorocarbanilate was thermally degraded unknown B was observed. Unknown B had a TLC R_F value of 0.60 and a GLC retention time of 21 min (Table I). The compound was unstable to TLC and GLC and yielded 5-chloro-2-benzoxazolinone. The IR spectrum of unknown B was similar to 5-chloro-

TABLE II

MASS SPECTRAL DATA: RELATIVE INTENSITIES

m/e	*Unknown*		*2-Benzoxazolinone*	*2-Isopropoxybenzoxazole*	*Isopropyl 2-acetoxy-5-chlorocarbanilate*	*Isopropyl 2-hydroxy-5-chlorocarbanilate*
	A	*B*				
41				6		
43		34		10	63	78
45					64	100
50				4		
51				4		
54			23			
55			5			
78	25			3	45	28
79	4		32	11		
80			5			
91			14	6		
113	21	10			31	20
114	7	3			10	16
115	7	4			13	10
135			100	100		
136			16	9		
143	30	9			100	93
144	5				12	13
145	18	3			32	33
169	100	100			91	93
170	10	9			10	15
171	30	32			30	23
177				9		
178				1		
187					22	27
188					3	
189					8	11
211		10				
213		3				
229					21	30
230					3	
231					7	12
271					5	
273					1	

2-benzoxazolinone with the exception of a strong carbonyl absorption at 1840 cm^{-1}. The carbonyl absorption at 1775 cm^{-1} observed in the 2-benzoxazolinone remained in this spectrum. The absorption for NH from 3300 cm^{-1} to 3100 cm^{-1} was diminished in the spectra of unknown B.

Mass spectral analysis of unknown B yielded a fragmentation pattern very similar to 5-chloro-2-benzoxazolinone (unknown A) with the exception of the parent ion at *m/e* 211, which was 42 mass units larger than 5-chloro-2-benzoxazolinone. These data are in good agreement with the predicted spectrum for N-acetyl 5-chloro-2-benzoxazolinone.

To test this hypothesis, a sample of unknown B was subjected to NMR analysis. These data are presented in Table III. Data from the model compounds, 2-benzoxazolinone (I, reported in the literature, and II, synthesized in this laboratory) and

2-isopropoxy-benzoxazole are in good agreement with unknown B for assignment of the aromatic hydrogens. The aromatic hydrogens in unknown B absorbed at 7.33 and 8.00 p.p.m. (δ). Integration of these two peaks showed that the area of the 7.33 hydrogens was double that of the 8.00 p.p.m. (δ) hydrogen. The protons at 2.60 p.p.m. (δ) E are assigned to the methyl of the N-acetyl derivative; this is supported by data from the spectrum of the model compound N-acetyl pyrolidone. The chromatographic, NMR, IR, and mass spectral data, all support the hypothesis that N-acetyl 5-chloro-2-benzoxazolinone is the structure of unknown B.

Thermal degradation in the presence of dimethylamine

The data presented in this report show that *ortho*-hydroxy carbanilates thermally degrade to yield 2-benzoxazolinone derivatives. These derivatives may result from the formation of an *ortho*-hydroxy isocyanate intermediate during pyrolysis. To test this hypothesis, isopropyl 2-acetoxy-5-chlorocarbanilate was pyrolyzed in the presence of excess dimethylamine. The pyrolytic products were separated by TLC, and three components were detected with R_F values of 0.20, 0.30, and 0.47, respectively. The first intermediate (R_F 0.47) had a GLC retention time identical to isopropyl 2-hydroxy-5-chlorocarbanilate (Table I). IR analysis and mass spectral fragmentation patterns of this component were identical to isopropyl 2-hydroxy-5-chlorocarbanilate.

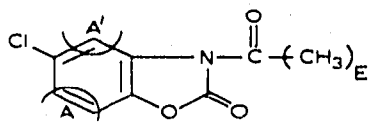
The GLC retention time, IR and mass spectral analysis of the unknown material (R_F 0.30) were identical to 5-chloro-2-benzoxazolinone.

When subjected to GLC, the unknown material (R_F 0.20) yielded predominantly 5-chloro-2-benzoxazolinone. Assuming that 2-hydroxy-5-chlorophenyl isocyanate was an intermediate in the thermal degradation process, the product with R_F 0.20 could have been 3-(2-hydroxy-5-chlorophenyl)-1,1-dimethylurea. Several workers have reported[3-5] that ureas are thermally unstable. If 3-(2-hydroxyphenyl)-1,1-dimethylureas are thermally degraded by a process similar to the *ortho*-hydroxy carbanilates, then the presence of 5-chloro-2-benzoxazolinone is in agreement with the proposed urea intermediate.

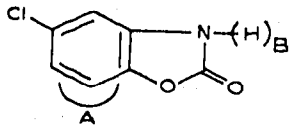
IR analysis of the R_F 0.20 material yielded a spectrum that was very similar to

BLE III

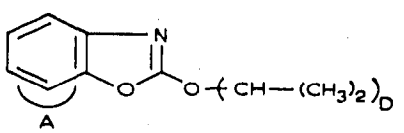
R DATA in p.p.m. (δ)



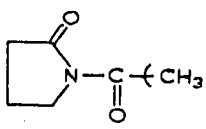
Unknown B



I[a]



II



A, 7.33; A', 8.00	7.31	7.27	7.27, 7.24	—
	0.04	0.00	—	—
	—	—	1.58, 1.48	—
	—	—	5.00, 5.10, 5.20, 5.30	—
			5.40, 5.50, 5.60	
2.60	—	—	—	2.50

[a] Sadtler spectrogram 668.
[b] Varian spectrogram 405.

TABLE IV

MASS SPECTRAL DATA OF UREA ANALOGS

m/e	*Unknown (Rf 0.20)*	*3-(4-Chlorophenyl)-1,1-dimethylurea*	
44	20	27	
45	34	6	
63	11	17	
72	100	100	
73	9	14	
78	20		
79	5		
99		10	
99		12	*
100		4	
101		4	
113	20	4	
114	10		
115	18		
125		10	
126		6	
127		5	
128		3	
143	30		
144	4		
145	10		
153		10	
154		5	
155		5	
169	70		
170	9		
171	25		
198		30	
199		3	
200		12	
214	11		
215	1		
216	4		

3-(4-chlorophenyl)-1,1-dimethylurea. The mass spectral fragmentation pattern of the unknown was compared with the model compound 3-(4-chlorophenyl)-1,1-dimethylurea (Table IV). The mass spectral fragmentation pattern of the unknown material yielded a base peak of *m/e* 72 and abundant ions at *m/e* 44 and *m/e* 45. These three ions are characteristic fragments from N,N-dimethylureas[11,12]. The fragmentation of the unknown compound (parent ion *m/e* 214) to the *m/e* 169 ion could be the same loss of *m/e* 45 $(CH_3)_2NH$ as seen in the spectrum of the model compound. There is, however, a striking difference between the fragmentation pattern of the *m/e* 169 ion and the *m/e* 153 ion. The *m/e* 169 ion resulted from the loss of two carbon monoxide fragments to yield *m/e* 113 (C_6H_4NCl) while the *m/e* 153 ion (4-chloro-phenyl isocyanate) fragmented to lose CO and CN to yield the *m/e* 90 ion (C_5H_4Cl). Both parent ions also lost dimethyl isocyanate (*m/e* 72) to yield the respective aniline ions, 2-hydroxy-5-chloroaniline (*m/e* 143) and 4-chloroaniline (*m/e* 127). The fragmentation data for the model urea compounds are in agreement with LOUDON *et al.*[13]. The mass spectrum of the unknown, *Rf* 0.20 material, is in good agreement with the proposed 3-(2-hydroxy-

5-chlorophenyl)-1,1-dimethylurea. This conclusion is supported by the presence of the unique fragmentation of the *m/e* 160 ion, which may be assumed to be 5-chloro-2-benzoxazolinone[10].

The data show that when isopropyl 2-acetoxy-5-chlorocarbanilate was thermally degraded in the presence of dimethylamine, the only compounds isolated were isopropyl 2-hydroxy-5-chlorocarbanilate, 5-chloro-2-benzoxazolinone and 3-(2-hydroxy-5-chlorophenyl)-1,1-dimethylurea.

Quantitative pyrolysis studies

Both isopropyl 2-acetoxy-5-chlorocarbanilate and isopropyl 2-hydroxy-5-chlorocarbanilate have been shown to be unstable to moderate thermal conditions. Quantitative studies were conducted to determine the thermal stability of the *ortho*-hydroxy carbanilate and 2-benzoxazolinone intermediates. Table I reports the GLC conditions used to separate the components of this quantitative study. Standard curves for isopropyl 2-acetoxy-5-chlorocarbanilate and isopropyl 2-hydroxy-5-chlorocarbanilate were linear in the concentration range from 0 to 14 μg.

The results of these pyrolysis studies are reported in Table V. Greater than 90 % of the starting acetylated derivative was recovered as unaltered carbanilate at 200° for 5 min. Under the same conditions only 70 % of isopropyl 2-hydroxy-5-chlorocarbanilate was recovered. The N-acetyl 5-chloro-2-benzoxazolinone derivative was present at 175° during the 10-min pyrolysis but did not accumulate at elevated temperatures. These data did not permit a comparison between the stability of the 5-chloro-2-benzoxazolinone and its acetylated analog, but they did indicate that both of these pyrolytic products were unstable and were converted to unidentified pyrolysis products. The identities of the final pyrolysis products of the carbamates and the 2-benzoxazolinone intermediates are not known. These unidentified pyrolysis products are non-polar and will not chromatograph in the GLC system used in this study.

TABLE V

PER CENT RECOVERY OF STARTING MATERIAL AND MAJOR PRODUCTS FROM PYROLYSIS

A = Isopropyl 2-acetoxy-5-chlorocarbanilate (starting material); B = N-acetyl 5-chloro-2-benzoxazolinone (product); C = isopropyl 2-hydroxy-5-chlorocarbanilate (starting material); D = 5-chloro-2-benzoxazolinone (product).

Duration of pyrolysis (min)	*Pyrolysis temp. (°C)*	*A*	*B*	*Total*	*C*	*D*	*Total*
5	25	100	0	100	100	0	100
	150	100	0	100	92	0	92
	175	90	0	90	92	0	92
	200	93	0	93	70	0	70
	225	71	2	73	50	0	50
	250	71	2	73	35	10	45
10	25	100	0	100	100	0	100
	150	98	0	98	80	0	80
	175	91	1	92	88	0	88
	200	85	1	86	67	0	67
	225	70	3	73	47	0	30
	250	47	7	54	16	13	29
20	250	16	16	32	—	—	—

DISCUSSION

A summary of the pyrolysis experiments is shown in Fig. 1. Pyrolysis of isopropyl 2-acetoxy-5-chlorocarbanilate in the presence of dimethylamine is described in reactions A, B, E, F, and G. Isopropyl 2-hydroxy-5-chlorocarbanilate was isolated from the reaction mixture indicating that there was cleavage of the acetoxy bond. The presence of the intermediate, 2-hydroxy-5-chlorophenyl isocyanate, is suggested by the formation of the urea[1-7]. It is not clear whether 5-chloro-2-benzoxazolinone is derived from 2-hydroxy-5-chlorophenyl isocyanate or is a thermal degradation product of the urea.

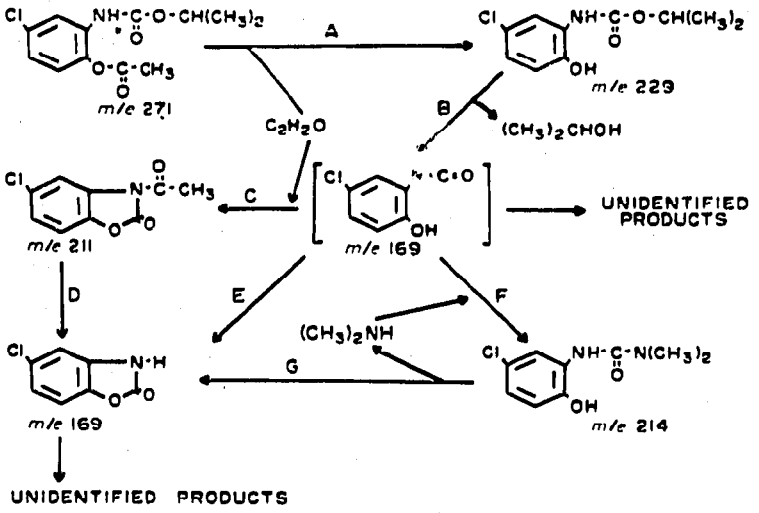


Fig. 1. Summary of pyrolysis experiments.

In the absence of dimethylamine the thermal degradation proceeds via reaction scheme A, B, C, and D. The attack of the phenyl isocyanate intermediate by a C_2H_2O ion, in these gas phase reactions, is speculative.

The transesterification of the starting material could result in accumulation of N-acetyl isopropyl 2-hydroxy-5-chlorocarbanilate. A conserted reaction mechanism where the isopropyl group leaves under the attack of the electro-negative phenol oxygen on the now electron-deficient carbonyl carbon to yield N-acetyl 5-chloro-2-benzoxazolinone could then be proposed. This reaction mechanism would bypass the phenyl isocyanate intermediate. SCOTT AND KEARSE[13] compared the mechanism for the preferential 2-benzoxazolinone formation in the Lossen rearrangement with the Curtius rearrangement that yielded only phenyl isocyanate. They proposed an $(R{-}\dot{N}{=}\dot{C}{-}O)$ intermediate that would be compatible with the concerted mechanism described above.

Regardless of the mechanism involved, isopropyl 2-hydroxy-5-chlorocarbanilate is thermally unstable and degrades, under nitrogen in an all-glass vessel, to yield the transient 2-benzoxazolinones. The low per cent recovery of *ortho*-hydroxy carbanilates at elevated temperatures is paralleled by the large accumulation of unidentified products (Table V). Several possibilities for these low recoveries are suggested in Fig. 1.

Non-volatile, polymeric materials were not removed during GLC analysis. If reaction 3 was a major route for thermal degradation, the reaction product, 2-amino-4-chlorophenol, would be unstable and would have led to the formation of polymeric products.

The data reported in these studies show that isopropyl 2-hydroxy-5-chlorocarbanilate and isopropyl 2-acetoxy-5-chlorocarbanilate undergo rapid thermal degradation to 5-chloro-2-benzoxazolinone and N-acetyl 5-chloro-2-benzoxazolinone. Information concerning relative rates of the reactions occurring during thermal degradation was not provided.

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