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Studies in the Diazine Systems I. The Infrared Spectra of 3,6-Disubstituted Pyridazines

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Although there has recently been a great increase in the number of publications concerning the pyridazine ring system, the spectral properties of this nucleus has received only cursory attention. A few authors have mentioned that pyridazines have spectra similar to those of the pyridines and pyrimidines (1,2), but useful generalizations have not yet appeared.

A series of closely related alkoxy pyridazine derivatives was examined in an effort to deduce spectral correlations which would be useful for identification of the nucleus. The absorptions believed to be most useful are given in Table I. In addition, the literature was reviewed to determine whether these correlations are applicable to other types of pyridazine derivatives. Surprisingly few pyridazine spectra have been published, but enough are available to convince us that the assignments made with alkoxy and halo derivatives can be applied even when other substituents are present (3).

The assignments listed in Table I are based upon individual spectra recorded on a Perkin-Elmer Model 337 spectrophotometer as potassium bromide wafers. The significant spectral bands of each compound are listed in Table II. Also included in Table II are the spectra of a few compounds recorded on a Perkin-Elmer Model 127 spectro-

photometer. These materials were not available for study with the high resolution instrument, but are included here for reference.

All of the compounds used in this study were prepared by a standard method (4), but several of them have not been reported in the literature. Table III is a listing of melting points and literature references for the known compounds together with the elemental analysis of the new materials.

Some explanation of the spectral assignments may be helpful. All of the compounds studied are 3-halo-6-alkoxy pyridazines. Therefore, the observations in the C-H stretch region are limited to the hydrogen atoms at the 4 or 5 positions. A somewhat broader range is to be expected when the 3 or 6 positions also are unsubstituted (pyridazine itself has a series of bands ranging from 3138 to 2980 cm^{-1} (5,6). The change from chloro through bromo to iodo substituents shows a trend to shift about 10 cm^{-1} (toward lower energy) in the C-H stretch frequency for each change.

Three of the bands arising from the pyridazine nucleus itself have been found in all of the available spectra, and are of considerable use in the identification of the ring system. These are the bands at 1600 to 1540 cm^{-1} , 1325 to 1295 cm^{-1} and 1065 to 935 cm^{-1} . These bands occurring together are good evidence for the presence of a pyridazine ring in the compound. The series of bands in the 1450 to 1400 cm^{-1} region are often helpful, but are subject to many interfering factors, rendering them less consistent.

The hydrogen in-plane and out-of-plane deformation bands also appear to be consistent, and as in the benzene series, are quite useful in determining the substitution pattern. They occur at 1150 to 1100 cm^{-1} and (for two adjacent hydrogens in a tetra substituted benzene) 860 to 830 cm^{-1} . These patterns are necessarily confused if other aromatic systems are present.

It is hoped that the generalizations presented here will help other workers in the identification of new pyridazines. We are preparing a much more extensive series of derivatives designed to fill in some of the obvious gaps in the present work.

EXPERIMENTAL

General Procedure.

Sodium hydride (1.1 mole) was dissolved in the appropriate alcohol and the resulting slurry or solution was added slowly to a

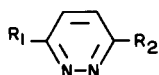
TABLE I

Infrared Spectral Assignments
for 3,6-Disubstituted Pyridazines

Frequency (cm^{-1})	Assignment
3070 to 3010	C-H Stretch (4 and 5 position hydrogen atoms only)
1600 to 1540	C=C and C=N Stretch
1430 to 1395	
1325 to 1295	
1150 to 1100	In-plane CH deformation
1065 to 935	"Ring breathing frequency"
860 to 830	Out-of-plane CH deformation (two adjacent hydrogen atoms)

TABLE II

Significant Infrared Peaks of 3,6-Disubstituted Pyridazines

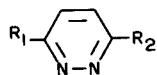


R ₁	R ₂	Significant Bands (cm ⁻¹) (a)					
Chloro	Methoxy	3060	1592	1309	1143	1010	848
	Ethoxy	3050	1592	1310	1149	1033	858
	<i>n</i> -Propoxy	3030	1587	1307	1134	995	852
	Isopropoxy	3035	1585	1309	1142	1065	855
	<i>n</i> -Butoxy	3040	1585	1316	1147	1019	855
	Isobutoxy	3040	1587	1316	1140	1005	855
	<i>t</i> -Butoxy	3045	1585	1305	1136	1041	854
	<i>n</i> -Pentyloxy	3040	1590	1314	1138	990	850
	Isopentyloxy	3040	1587	1316	1139	995	851
	<i>n</i> -Hexyloxy	3040	1590	1323	1142	1012	854
	Cyclohexyloxy	3030	1585	1305	1142	1016	840
	<i>n</i> -Octyloxy (b)	3030	1580	1300	1130	1005	835
	<i>n</i> -Decyloxy	3030	1580	1299	1129	1002	842
	Bromo	Methoxy	3067	1585	1307	1120	1006
Ethoxy (b)		3030	1543	1304	1111	1019	854
<i>n</i> -Propoxy		3030	1568	1301	1124	1053	850
Isopropoxy		3040	1577	1312	1105	1057	858
<i>n</i> -Butoxy		3030	1580	1312	1120	1020	858
Isopentyloxy		3020	1577	1302	1121	1053	857
Iodo	Methoxy	3040	1577	1300	1120	1005	848
	Ethoxy	3020	1565	1302	1124	1027	855
	<i>n</i> -Propoxy (b)	3050	1575	1316	1124	1053	848
	Isopropoxy	3020	1565	1295	1116	1044	853
	<i>n</i> -Butoxy	3030	1567	1300	1109	1031	849
	<i>n</i> -Pentyloxy	3030	1580	1309	1114	990	830
	<i>n</i> -Hexyloxy (b)	3020	1567	1302	1111	1010	854

(a) All spectra except those marked (b) were recorded on a Perkin-Elmer Model 337 spectrophotometer. (b) Recorded on a Perkin-Elmer Model 127 spectrophotometer.

TABLE III

Melting Points and Analytical Data of Compounds used in Study



R ₁	R ₂	M.P. °C Found	M.P. °C Lit.	Purification Procedure Used	% Yield	Elemental Analysis Calcd. % N	Found % N
Chloro	Methoxy	90-91	90 (a)	A			
	Ethoxy	59-61	63 (b)	A			
	<i>n</i> -Propoxy	72-73	65 (e)	A	84.2	16.23	16.20
	Isopropoxy	83-85	83-84 (a)	A			
	<i>n</i> -Butoxy	47-49	47-48 (c)	B			
	Isobutoxy	84-85	66 (e)	C	73.3	15.02	14.95
	<i>t</i> -Butoxy	86-89	90-92 (a)	C	34.0	15.02	14.88
	<i>n</i> -Pentyloxy	61-63		B	64.5	13.96	13.81
	Isopentyloxy	60-62	58-59 (e)	C	61.2	13.96	13.83
	<i>n</i> -Hexyloxy	54-56		C	58.8	13.05	12.92
	Cyclohexyloxy	105-107	108-110 (c)	B			
	<i>n</i> -Octyloxy	34-36		C	25.4	11.54	11.43
<i>n</i> -Decyloxy	43-44		C	23.1	10.35	10.21	
Bromo	Methoxy	104-105	103-104 (a)	A			
	Ethoxy	68-70		A	86.2	13.80	13.75
	<i>n</i> -Propoxy	62-63		A	75.9	12.91	12.86
	Isopropoxy	64-65		A	81.3	12.91	12.80
	<i>n</i> -Butoxy	59-62		C	62.7	12.12	12.01
	Isopentyloxy	48-50		C	58.4	11.43	11.59
Iodo	Methoxy	104-105	104-105 (d)	A			
	Ethoxy	90-91		A	76.4	11.21	11.14
	<i>n</i> -Propoxy	65-66		A	72.7	10.61	10.53
	Isopropoxy	95-97		A	63.4	10.61	10.48
	<i>n</i> -Butoxy	65-66		C	51.2	10.08	9.86
	<i>n</i> -Pentyloxy	51-52		C	46.4	9.59	9.44
	<i>n</i> -Hexyloxy	56-57		C	43.3	9.15	9.03

(a) Reference 4. (b) Reference 9. (c) Reference 8. (d) Reference 7. (e) Reference 10.

stirred solution of the appropriate 3,6-dihalopyridazine (1.0 mole) in the same alcohol. The resulting mixture was refluxed with continuous stirring for 24 hours (reflux for 48 hours was required for complete reaction with the higher alcohols). At this point different procedures depending on the properties of the alcohols were employed.

Procedure A. Water Miscible Alcohols:

The reaction mixture was filtered through glass filter paper, and the precipitate washed with fresh alcohol. The filtrate was evaporated under reduced pressure at a temperature less than 70°. The residue was taken up in boiling ligroine, decolorized and cooled. The product crystallized and was purified by recrystallization from ligroine.

Procedure B. Water Immiscible Alcohols:

The reaction mixture was washed with three 25 ml. portions of 0.1 *N* acetic acid, and the volume of alcohol was reduced under vacuum as much as possible. The residue was taken up in boiling ethanol and water was added until the solution clouded. Upon cooling an oil was generally recovered. This process was repeated several times until a solid was obtained. Recrystallization from the same solvent afforded final purification.

Procedure C. Water Immiscible Alcohols:

The reaction mixture was washed with three 25 ml. portions of water, mixed with an equal part of benzene and dried over sodium carbonate. The solvents were removed *in vacuo*, the oily residue was taken up in a small amount of benzene and placed on an

alumina column. Elution with 1:1 benzene-petroleum ether removed first unreacted alcohol followed by the product. The product was purified by recrystallization from petroleum ether.

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