UDC 582.852.3.07

126. **Yoshihiro Nitta and Fumio Yoneda**: Pyridazine Derivatives. II.[*1] Infrared Spectra of O-, N-Mono- and O,N-Dibenzyl Compounds of Maleic Hydrazide.

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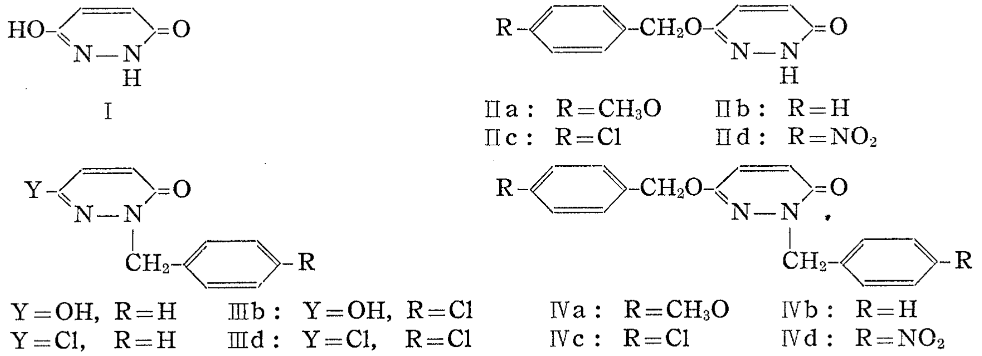
In the previous paper,[*1] we reported that the products arising from reaction of maleic hydrazide with substituted benzylchloride were O-benzyl compounds (II). The present investigation has been carried out to confirm the previous results, from the comparison of the infrared spectra of O-, N-mono and O,N-dibenzyl compounds, and some correlations between them will also be presented.



I

IIa: $R=CH_3O$ IIb: $R=H$
IIc: $R=Cl$ IId: $R=NO_2$

IIIa: $Y=OH$, $R=H$ IIIb: $Y=OH$, $R=Cl$
IIIc: $Y=Cl$, $R=H$ IIId: $Y=Cl$, $R=Cl$

IVa: $R=CH_3O$ IVb: $R=H$
IVc: $R=Cl$ IVd: $R=NO_2$

Chart 1.

The 3000 cm^{-1} Region——Useful informations about the structures of these compounds can be obtained from this region. O,N-Dibenzyl compounds (IV) arising from reaction of maleic hydrazide with 2 moles of benzylchloride or of substituted benzylchloride do not show any NH or OH stretching vibration, as would be expected. A broad weak band near 2500 cm^{-1}, however, appears only in the N-benzyl hydroxy compounds, IIIa and IIIb, which show no bands in the region of 3000~3500 cm^{-1}, as shown in Fig. 1. On deuteration this band disappears, and a similar broad band appears at 1900 cm^{-1}, thus showing that this band is assigned to the bonded OH stretching vibration (OH···N). The N-benzyl chloro compounds, IIIc and IIId, arising from replacement of OH group with Cl group show no bands in this region.

A structure of N-benzyl compounds (III) is expected from condensation of maleic acid with benzyl hydrazide. This is now supported, in addition to the above results, by further observations as will be mentioned later, and by the fact that maleic hydrazide arising from reaction of maleic acid with hydrazine has been shown to exist predominantly as I.[1,2]

On the other hand, in the 3000 cm^{-1} region the parent compound arising from reaction of maleic hydrazide with benzyl chloride exhibits a broad band having four peaks at 3130, 3055, 2940 and 2840 cm^{-1} in the solid state, which would be expected from bonded N-H stretching mode of the NH-CO group, and two of four peaks masked the C-H stretching bands. On deuteration of this compound, these bands moved to 2215, 2180 cm^{-1} and some weak bands (Fig. 2). In concentrated chloroform solution (0.1 mol./L.),

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[*1] Part I. F. Yoneda, Y. Nitta: This Bulletin, **11**, 669 (1963).

[*2] Takataminami-cho, Toshima-ku, Tokyo (新田義博, 米田文郎).

1) Cheinker, Gortinskaia, Sycheva: J. Chim. phys., **55**, 217 (1958).

2) D.M. Miller, R.W. White: Can. J. Chem., **34**, 1510 (1956).

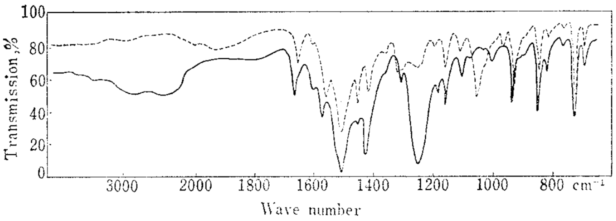

Fig. 1. Infrared Spectrum
——: 1-benzyl pyridazinone-6
⋯⋯: deuterated 1-benzyl pyridazinone-6

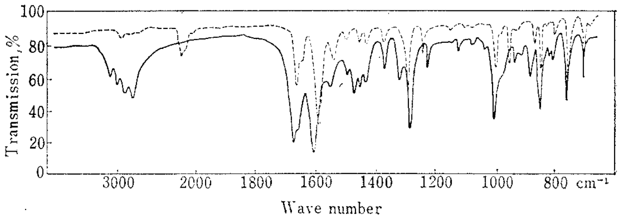

Fig. 2. Infrared Spectrum
——: 3-benzyloxy pyridazinone-6
⋯⋯: deuterated 3-benzyloxy pyridazinone-6

TABLE I. The C=O and the Ring Stretching Frequencies in the Region of 1600～1500 cm^{-1}

Compound	C=O	Ring stretching				
Ⅱa	1669 s	1655 sh	1601 s	1558 w	1514 s	
Ⅱb	1672 s	1657 sh	1605 s	1562 w	1498 w	
Ⅱc	1677 s	1655 sh	1602 s	1555 m	1497 w	
Ⅱd	1680 s	1660 sh	1600 s	1552 w	1475 w	
Ⅲa	1657 m		1600 w	1562 m	1498 s	
Ⅲb	1657 m		1600 w	1562 m	1497 s	
Ⅲc	1653 s		1599 w	1572 s	1509 w	1494 w
Ⅲd	1653 s		1580 s	1559 sh	1516 w	1489 w
Ⅳa	1660 s		1590 s	1535 m	1497 m	
Ⅳb	1666 s		1596 s	1543 w	1496 w	
Ⅳc	1663 s		1592 s	1542 m	1492 s	
Ⅳd	1669 s		1596 s	1547 m	1499 m	

s: strong m: medium w: weak sh: shoulder

a sharp and weak N-H stretching band at 3400 cm^{-1}, a weak and broad band near 3100 cm^{-1}, a medium intense band at 3015 cm^{-1}, and a weak band at 2890 cm^{-1} are observed. But, as the concentration is lowered, the intensity of the 3400 cm^{-1} band increases and that of the 3015 cm^{-1} band decreases because hydrogen bonding contributing to formation of a dimer is here strongly diminished.[*3], 3)

The C=O Stretching Frequencies——The carbonyl stretching frequencies of these compounds examined are listed in Table I. O-Monobenzyl, O,N-dibenzyl and N-monobenzyl compounds show a strong band near 1675, 1665 and 1655 cm^{-1}, respectively. It is of interest that the difference of frequencies between these compounds is approximately 10 cm^{-1}. Thus, the following series are observed for the C=O bond order; O-monobenzyl compounds>O,N-dibenzyl compounds>N-monobenzyl compounds.

The C=C and C=N Stretching Vibrations of the Ring——In the region of 1600～1500 cm^{-1}, the absorption bands due to the benzene ring and the pyridazinone ring are expected. The ring stretching frequencies of these compounds examined are listed in Table I.

It is noteworthy that O-benzyl compounds commonly show a strong band near 1600 cm^{-1}, and some of these show a medium or weak band near 1500 cm^{-1}, while N-benzyl hydroxy compounds show a very weak band near 1600 cm^{-1}, a medium band near 1560 cm^{-1}, and a wide and strong band near 1495 cm^{-1}. The first band is due to the benzene ring, and the others may be due to the pyridazinone ring. On the other

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[*3] Compound (Ⅱb) shows a shoulder at 1657 cm^{-1} in addition to a strong band at 1672 cm^{-1} in the solid state. The corresponding two bands are also observed at 1657 and 1677 cm^{-1} in chloroform solution, respectively, but as the concentration is lowered, the 1657 cm^{-1} shoulder soon disappears and the 1677 cm^{-1} band does not change.

3) Infrared Spectra of 2-Pyrolidone and its Deuterated Compounds. K. Kurosaki: J. Chem. Soc. Japan., 82, 1691 (1961).

hand, N-benzyl chloro compounds show a very weak band near 1600 cm^{-1}, a strong band near 1580 cm^{-1}, and two weak bands near 1515 and 1490 cm^{-1}. O,N-Dibenzyl compounds show a strong band near 1595 cm^{-1}. Two compounds containing a NO_2 group exhibit a strong band near 1520 cm^{-1} which is attributed to the NO_2 asymmetric stretching vibration.

From these observations, it has been found that O-substituted compounds such as O-benzyl and O,N-dibenzyl compounds are characterized by a strong band found near 1600 cm^{-1} which show distinct difference from N-benzyl compounds.

The Region of 1300$\sim$1200 cm^{-1}——The aromatic C–O stretching frequencies are in general expected in this region. Frequencies of the relatively strong band in the 1300$\sim$1200 and the 1100$\sim$1000 cm^{-1} region are listed in Table Ⅱ.

O-Benzyl compounds and O,N-dibenzyl compounds show a characteristically strong band near 1285 cm^{-1} accompanied by a strong band near 1260 cm^{-1} in some of these compounds. The band at 1288 cm^{-1} of O-benzyl compound (Ⅱb) does not disappear on deuteration, thus showing that this band may be assigned to the aromatic C–O stretching vibration. However, on this deuteration, disappearance of two bands at 1472 and 1314 cm^{-1} is observed. This fact shows that the 1472 and 1314 cm^{-1} bands may be attributed to the pure NH in plane deformation mode and to the NH in plane deformation including the C–N stretching mode, respectively.[3]

On the other hand, N-benzyl hydroxy compounds show a strong band near 1245 cm^{-1}, and N-benzyl chloro compounds do not show this band, but exhibit a medium band near 1300 cm^{-1} not shown by N-benzyl hydroxy compounds. The band near 1245 cm^{-1} of N-benzyl hydroxy compounds disappears on deuteration, thus showing that this band may be due to the OH bending mode. This band is of interest, but it is impossible at the present time to assign this band to any particular mode of molecular vibrations. However, these results also indicate the difference between O-benzyl compounds and N-benzyl compounds.

Table Ⅱ. The Relatively Strong Band in the 1300$\sim$1200 cm^{-1} and the 1000$\sim$900 cm^{-1} Regions

Compound	1300$\sim$1200 cm^{-1}		1000$\sim$900 cm^{-1}
Ⅱa	1284 s	1252 s	995 s
Ⅱb	1288 s		1002 s
Ⅱc	1284 s		995 s
Ⅱd	1283 s	1257 m	996 s
Ⅲa		1243 s	936 m
Ⅲb		1246 s	920 m
Ⅲc	1295 s		938 m
Ⅲd	1295 s		932 m
Ⅳa	1293 s	1259 s	980 s
Ⅳb	1283 s	1269 s	1004 s
Ⅳc	1282 s	1264 s	1003 s
Ⅳd	1283 s		1017 m

s : strong m : medium

The Region of 1200$\sim$1000 cm^{-1}——O-Benzyl and O,N-dibenzyl compounds are characterized by a strong band near 1000 cm^{-1}, not shown by N-bezyl compounds. This band may be due to the Ar–O–C symmetric stretching vibration. On the other hand, N-benzyl compounds exhibit a medium intensity band near 930 cm^{-1}.

As mentioned above, we confirmed that the products arising from reaction of maleic hydrazide with substituted benzyl chloride are O-benzyl compounds (Ⅱ), and found that N-benzyl compounds exist in the hydroxy form structure (Ⅲ), thus indicating that the structure (Ⅰ) of maleic hydrazide is now supported.

Experimental

The spectra were all recorded in KBr discs, on a Hitachi EPI 2 (NaCl optics). The preparations of the compounds examined have been given in the previous paper.[*1] All compounds were recrystallized before measurement. Deuterated compounds : Replacement of the hydroxy hydrogen or the NH hydrogen by deuterium was accomplished by adding a mixture of an excess of D_2O and a little Me_2CO, evaporating the D_2O and Me_2CO in vacuum, and these procedures were repeated three times.

The authors wish to thank Mr. G. Tatsui of director of this laboratory for his encouragement during this work, and Miss Tomii for the measurement of infrared spectra.

Summary

Infrared spectra confirmed that the products arising from reaction of maleic hydrazide with substituted benzyl chloride are O-benzyl compounds.

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127. **Fumio Yoneda, Takayuki Ohtaka, und Yoshihiro Nitta** : Pyridazinderivate. III.[1] Synthese der Anilinopyridazine.

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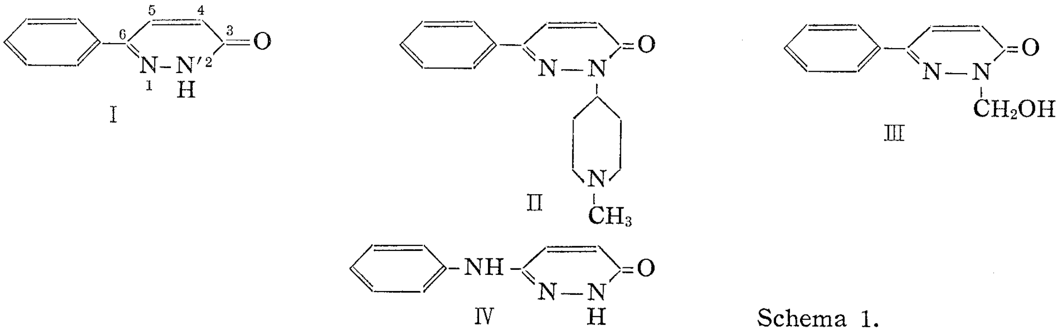
In den letzten Jahren wurde eine ziemliche Anzahl von pharmakologisch interessanten Verbindungen aus den Abkömmlingen des 6-Phenyl-3(2*H*)-pyridazinons (I), das selbst schon vorzeiten hergestellt wurde, aufgefunden. Einige von ihnen, besonders solche mit einem N-Methylpiperidyl-(4)-rest (II)[2] und mit einem Hydroxymethylrest (III)[3] in 2-Stellung des I besitzen starke analgetische Wirkung. Auch in dieser Reihe wurden mehrere Verbindungen mit amöbicider Wirksamkeit bereits beschrieben.[4]

Wir haben nun die Derivate des 6-Anilino-3(2*H*)-pyridazinons (IV), die Analoga von I, in welchem der Phenylrest in 6-Stellung durch den Anilinorest ersetzt ist, herge-



Schema 1.

[*1] Takataminami-cho, Toshima-ku, Tokio (米田文郎, 大高孝之, 新田義博).

[1] II. Mitt. : Dieses Bulletin, **11**, 737 (1963).

[2] E. Jucker, R. Süess : Helv. Chim. Acta, **42**, 2506 (1959).

[3] Brit. Pat. 840522. C.A., **55**, 3627 (1961).

[4] E.A. Steck, R.P. Brundage, L.T. Fletcher : J. Am. Chem. Soc., **75**, 1117 (1953).