3-Aroylmethyl Derivatives of 2(1*H*)Quinoxalinone and 2*H*-1,4-Benzoxazin-2-ones Existing in the Enamine Form (1)

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Seventeen derivatives of 2(1*H*)quinoxalinone and 2*H*-1,4-benzoxazin-2-one have been synthesized for structural study. All of the compounds having a substituted phenacyl, isonicotinoylmethyl, or 2-furoylmethyl side chain are shown to exist in the enamine form with an internal chelation both in the crystalline and solution states as evidenced by the ir and pmr spectra, respectively. In the gas phase, however, *o*-hydroxyphenacyl derivatives can exist in another type of intramolecularly hydrogen-bonded form which is supported by their mass spectra.

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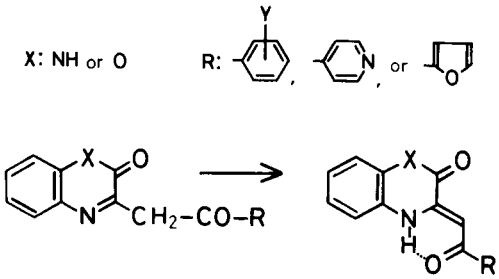
We have shown that several nitrogen heterocycles with a β-carbonyl side chain at a position adjacent to the nitrogen atom exist in the tautomeric α,β-unsaturated carbonyl form (2). This tautomeric change seems to be facilitated by the intramolecular hydrogen bonding thereby permitted (3). However, some exceptions have also been known (4).

Seventeen heterocycles were prepared by the condensation of *o*-phenylenediamine or *o*-aminophenol with an ethyl aroylpyruvate, in which the aromatic or heteroaromatic group is shown in Table I. Infrared and pmr spectra gave adequate information as to their existing modes, which are herein referred to as the enamine and imine forms, respectively.



Imine form Enamine form

The carbonyl in the imine form should give a normal aroyl absorption, but it exhibited a band in the region 1628-1612 cm^{-1}. The shift to lower frequencies is consistent with the occurrence of an α,β-unsaturated aroyl C=O involved in hydrogen bonding (Table II). Their enamine structures were further supported by the pmr spectra; the signal of =CH-, instead of $-CH_2-$, appeared together with that of hydrogen-bonded NH at the lowest field (Table II). Enolization of the ketone could also cause the formation of =CH- group. However, it is most unlikely in these compounds. The carbonyl adjacent to the phenyl ring would displace the *ortho* proton signals downfield. The band at around 8.00 ppm is probably due to this effect. Correspondingly, the signals of typical isonicotinoyl or 2-furoyl protons were also exhibited in the case of **14-17**.

When the pmr spectra of these compounds were measured in methanol-d_4 or in dimethyl sulfoxide-d_6 with the addition of deuterium oxide, the signal of =CH- did not disappear by deuterium exchange (3). In this respect, no exception was found even for *o*-hydroxyphenacyl derivatives (**3** and **11**) which attracted our special attention because of the possibility of the existence of another type of hydrogen bonding leading to the imine form. Therefore, the compounds could probably not exist as an equilibrium mixture of the imine and enamine tautomers, but were fixed in the enamine form. The infrared spectra taken in the solid state (nujol mull) also showed no indications of the imine form. From these results, we may conclude that these compounds exist in the hydrogen-bonded form exclusively both in the solution and crystalline states. Hence, it is more practical to designate them as phenacylidene, isonicotinoylmethylene, and 2-furoylmethylene derivatives of the heterocycles, respectively.

A further interesting point which emerges is that the possibility of the two *o*-hydroxyphenacyl compounds **3** and **11** existing in the imine form was substantiated

Table I

Melting Points and Analytical Data of the Products

Compound Number	X	R	M.p., °C	Yield, %	Empirical Formula	Analysis Calcd./Found C	H	N
1	NH	*p*-chlorophenyl	275-276	86	$C_{16}H_{11}N_2O_2Cl$	64.33 64.42	3.71 3.72	9.38 9.15
2	NH	*p*-bromophenyl	276-277	73	$C_{16}H_{11}N_2O_2Br$	56.00 55.86	3.23 3.41	8.16 8.03
3	NH	*o*-hydroxyphenyl	309-310	58	$C_{16}H_{12}N_2O_3$	68.57 68.72	4.32 4.31	9.99 9.65
4	NH	*m*-hydroxyphenyl	294-295*	50	$C_{16}H_{12}N_2O_3$	68.57 68.52	4.32 4.47	9.99 9.91
5	NH	*p*-hydroxyphenyl	323-324	83	$C_{16}H_{12}N_2O_3$	68.57 68.30	4.32 4.45	9.99 9.95
6	NH	*o*-methoxyphenyl	231-232	77	$C_{17}H_{14}N_2O_3$	69.38 69.47	4.79 4.92	9.52 9.50
7	NH	*m*-methoxyphenyl	228-229	84	$C_{17}H_{14}N_2O_3$	69.38 69.35	4.79 4.86	9.52 9.50
8	NH	*p*-methoxyphenyl	243-244	68	$C_{17}H_{14}N_2O_3$	69.38 69.42	4.79 4.80	9.52 9.33
9	O	*p*-chlorophenyl	180	80	$C_{16}H_{10}N\ O_3Cl$	64.12 63.97	3.36 3.37	4.67 4.58
10	O	*p*-bromophenyl	213-214*	77	$C_{16}H_{10}N\ O_3Br$	55.84 55.97	2.93 3.18	4.07 3.95
11	O	*o*-hydroxyphenyl	255*	68	$C_{16}H_{11}N\ O_4$	68.33 68.05	3.94 3.88	4.98 5.00
12	O	*m*-hydroxyphenyl	269*	42	$C_{16}H_{11}N\ O_4$	68.33 68.15	3.94 4.06	4.98 4.92
13	O	*p*-hydroxyphenyl	233	67	$C_{16}H_{11}N\ O_4$	68.33 68.37	3.94 3.98	4.98 5.02
14	NH	4-pyridyl	260 subl.	68	$C_{15}H_{11}N_3O_2$	67.92 67.98	4.18 4.46	15.84 15.62
15	O	4-pyridyl	188.5-189	71	$C_{15}H_{10}N_2O_3$	67.67 67.65	3.79 4.00	10.52 10.59
16	NH	2-furyl	301-302	76	$C_{14}H_{10}N_2O_3$	66.14 65.82	3.96 4.22	11.02 11.15
17	O	2-furyl	169*	65	$C_{14}H_9N\ O_4$	65.88 65.95	3.55 3.66	5.49 5.77

The compounds with *mark were recrystallized from 1-butanol, and the others all from ethanol.

by their mass fragmentation pattern. The most important fragmentation pathway that was common to all the compounds **1-17** (not only phenacyl derivatives but also isonicotinoylmethyl and 2-furoylmethyl derivatives) was initiated from ring cleavage with loss of CO. The resultant ion of M-28 species in turn lost hydrogen atom to afford M-29 species (1,5,6). However, these two processes, especially the latter, were quite inconspicuous in the case of two *o*-hydroxyphenacyl derivatives **3** in the quinoxalinone series (X = NH) and **11** in the benzoxazinone series (X = O). Instead of the latter dehydrogenation process, dehydroxylation from the M-28 species (m/e 252 for **3** and m/e 253 for **11**) became sizable giving ions m/e 235 and 236, respectively. On the other hand, *m*-hydroxyphenacyl derivatives **4** (X = NH) and **12** (X = O) behaved similarly with other derivatives, except **3** and **11**. The elimination of a phenyl group from the molecular ions also occurred to yield ions of m/e 187 in quinoxalin-

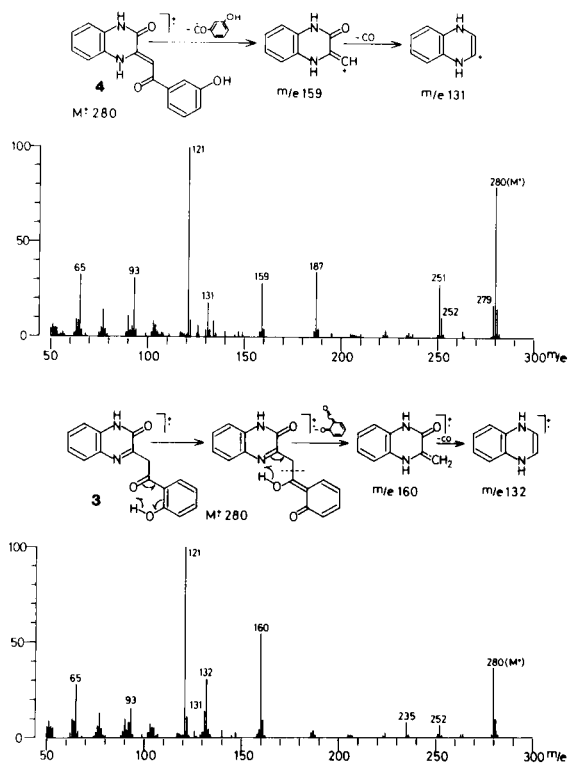


Figure 1. Mass spectra of compounds **4** (above) and **3** (below), and main difference between their fragmentation processes revealed thereby.

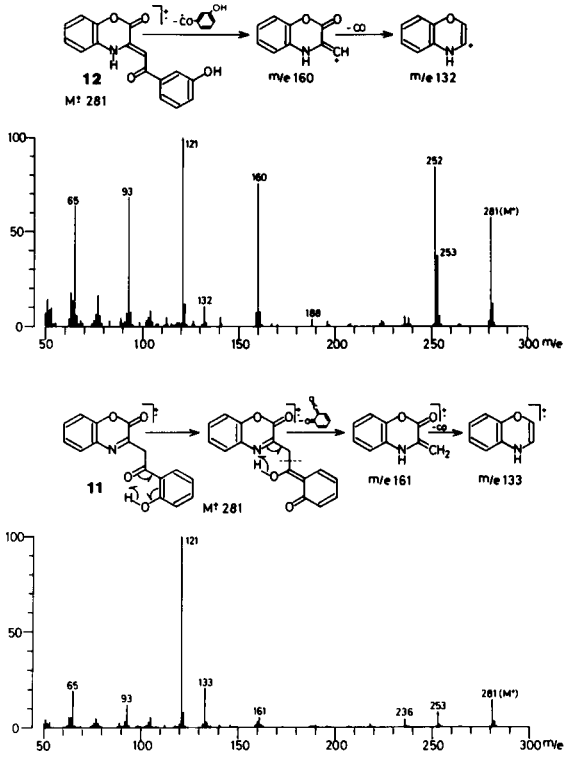


Figure 2. Mass spectra of compounds **12** (above) and **11** (below), and main difference between their fragmentation processes revealed thereby.

ones (X = NH) and m/e 188 in benzoxazinones (X = O), but to a lesser extent in the X = O series.

Further, considerable difference between *o*- and *m*-hydroxyphenacyl derivatives was found in an alternative pathway starting from loss of a benzoyl group. *m*-Hydroxyphenacyl and other derivatives simply lost the respective benzoyl groups to yield ions of m/e 159 (X = NH) or m/e 160 (X = O), while *o*-hydroxyphenacyl derivatives underwent a decisively distinct fission to give ions of m/e 160 (X = NH) or m/e 161 (X = O). The observed fragmentation pattern of the latter compounds **3** and **11** may be interpreted to mean that these two exceptional compounds can tautomerize into the imine form in the gas phase, since a hydrogen transfer to cause the ions of m/e 160 (X = NH) or m/e 161 (X = O) probably occurs more easily in the imine form as illustrated in Figures 1 and 2.

EXPERIMENTAL (7)

The methods for the preparation of the compounds are similar with those for the simpler derivatives reported previously (2), and the data are collected in Table I. In addition to those of the ir and pmr spectra summarized in Table II, some important portions of the mass spectral data are shown in Figures 1 and 2.

Acknowledgement.

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REFERENCES AND NOTES

(1) Part V in the series Heterocycles Structurally Influenced by a Side Chain; Part IV: Y. Iwanami, T. Inagaki, and H. Sakata, *Org. Mass Spectrom.*, presented for publication.

(2) Y. Iwanami, T. Seki, and T. Inagaki, *Bull. Chem. Soc. Japan*, **44**, 1316 (1971), and references cited therein.

(3) Y. Iwanami, *ibid.*, **44**, 1311 (1971).

Table II

Characteristic Absorptions in the Infrared and Pmr Spectra

Compound Number	Ir (cm^{-1}, Nujol) ν c=o Lactone	Lactam	Ketone	ν c=c	=CH	Pmr (δ ppm, DMSO-d_6) Benzoyl (*ortho*)	NH
1		1678	1619	1603	6.94	*ca.* 8.18	12.26 13.94
2		1683	1617	1602	6.89	*ca.* 8.00	12.19 13.83
3		1678	1615	1606	7.00	*ca.* 8.08	12.23 (OH) 13.03, 13.32
4		1674	1620	1601	6.85		9.78 (OH) 12.11, 13.79
5		1670	1620	1600	6.85	*ca.* 8.03	10.27 (OH) 12.02, 13.74
6		1689	1613	1602	6.80	*ca.* 7.65	11.90 13.61
7		1679	1612	1603	6.82		12.07 13.79
8		1683	1621	1602	6.81	*ca.* 8.02	11.98 13.67
9	1753		1627	1597	6.89	*ca.* 8.12	12.94
10	1752		1628	1610	7.05	*ca.* 8.25	13.14
11	1757		1627	1603	7.07	*ca.* 7.96	12.15
12	1758		1623	1600	6.99		9.92 (OH) 13.15
13	1760		1624	1598	6.94	*ca.* 8.06	10.41 (OH) 12.93
14		1694	1621	1614	6.94		12.45 14.17
15	1757		1625	1598	6.98		13.27
16		1687	1615	1601	6.73		12.07 13.21
17	1763		1621	1600	6.86		12.82

(OH); One of the signals is due to hydroxyl proton.

(4) Y. Iwanami, *ibid.*, **44**, 1314 (1971).
(5) T. Inagaki and Y. Iwanami, *Org. Mass Spectrom.*, in press.
(6) Y. Iwanami and M. Akino, *Tetrahedron Letters*, 3219 (1972).
(7) The ir spectra were determined on a Hitachi EPI-G3 spectrophotometer. The pmr spectra were measured on a Hitachi H-60 spectrometer using tetramethylsilane as the external reference. The mass spectra were recorded with a Hitachi RMS-4 mass spectrometer by the use of direct inlet method. All the melting points are uncorrected.