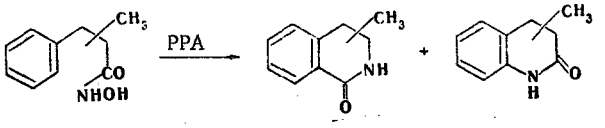
DIFFERENCES IN THE MASS SPECTRA OF ISOMERIC BENZOLACTAMS

P. B. Terent'ev, L. D. Solov'eva,
V. M. Dem'yanovich, O. A. Popova,
and V. M. Potapov

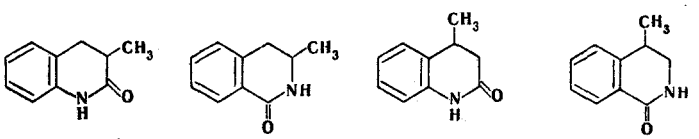
UDC 547.831.8'833.7:54.51'422.25.4.6

It is shown that 3- and 4-substituted dihydro-2-quinolones can be distinguished from the isomeric dihydro-1-isoquinolones by mass spectrometry. The $[M - CO]^+$ ion is characteristic for the mass spectra of dihydroquinolone derivatives, whereas retrodiene fragmentation of the molecular ion is characteristic for dihydroisoquinolone derivatives. The intense $[M - R]^+$ and $[M - R, -H_2O]^+$ ion constitute evidence that the substituent is located in the 3 (for dihydroisoquinolones) or 4 (for dihydroquinolones) position. The processes that occur in the fragmentation were confirmed by data from the high-resolution mass spectra, an analysis of the observed metastable ions, and an analysis of the mass spectra of 3-methyl-3,4-dihydro-1-isoquinolone and 4-methyl-3,4-dihydro-2-quinolone containing deuterium attached to the nitrogen atoms.

The Beckmann, Pearson, and Schmidt rearrangements in aromatic ring-substituted α-indanones proceed ambiguously and lead to mixtures of both substituted dihydro-2-quinolones and substituted dihydro-1-isoquinolones (for example, see [1, 2]). In the present research we have demonstrated that similar mixtures are also formed in the cyclization of aralkylhydroxamic acids, although the formation of only 1-quinolone has been indicated in the literature [3]:



Considering that the identification of such isomeric compounds on the basis of their IR, UV, and PMR spectra is not always reliable, we studied the mass spectral behavior of 3- and 4-methyl-3,4-dihydro-2-quinolones (I and III) and 3- and 4-methyl-3,4-dihydro-1-isoquinolones (II and IV):



I II III IV

There is no information in the literature regarding the dissociative ionization of such compounds. It is known only that oxindoles under the influence of electron impact eliminate a molecule of CO with subsequent ejection of a hydrogen atom and a molecule of HCN [4].

An analysis of the mass spectra obtained (Table 1) and the intensities of the peaks of the characteristic ions (Table 2) makes it possible to conclude that although the molecular ions of I, III, and IV are rather stable, the introduction of a methyl group in the α position relative to the amide nitrogen atom appreciably destabilizes the molecular ion (II). Intense peaks of $[M - CO]^+$ and $[M - HCO]^+$ ions are characteristic for the mass spectra of dihydroquinolones, whereas these ions are absent in the mass spectra of dihydroisoquinolones (Schemes 1 and 2).

M. V. Lomonosov Moscow State University, Moscow 117234. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 246-249, February, 1979. Original article submitted July 5, 1978.

 0009-3122/79/1502-0208$07.50

TABLE 1. Mass Spectra of I-IV

Compound	m/e values (relative intensities of the ion peaks, %)†
I	161 (96), 146 (6), 133 (43), 132 (100), 131 (7), 130 (8), 128 (6), 118 (68), 117 (22), 116 (64), 115 (13), 106 (19), 105 (8), 104 (38), 103 (10), 93 (6), 92 (43), 91 (23), 90 (11), 89 (13), 78 (28), 77 (30).
II	161 (5), 147 (11), 146 (100), 128 (36), 119 (6), 118 (75), 91 (19), 90 (72), 89 (35), 77 (7).
III	161 (60), 147 (9), 146 (100), 133 (11), 132 (12), 130 (6), 129 (7), 128 (77), 119 (10), 118 (82), 117 (30), 116 (6), 115 (7), 103 (9), 92 (6), 91 (60), 90 (23), 89 (20), 78 (11), 77 (47).
IV	161 (42), 133 (8), 132 (100), 131 (14), 128 (6), 105 (8), 104 (82), 103 (28), 102 (6), 91 (6), 89 (6), 78 (32), 77 (28).

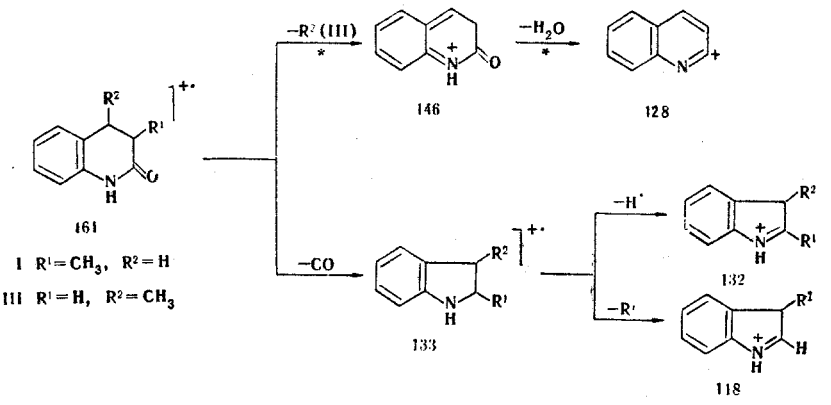
†The molecular ions and the ions whose peaks have intensities > 5% are presented.

TABLE 2. Intensities of the Characteristic Ions in the Mass Spectra of I-IV (% Σ_{39})

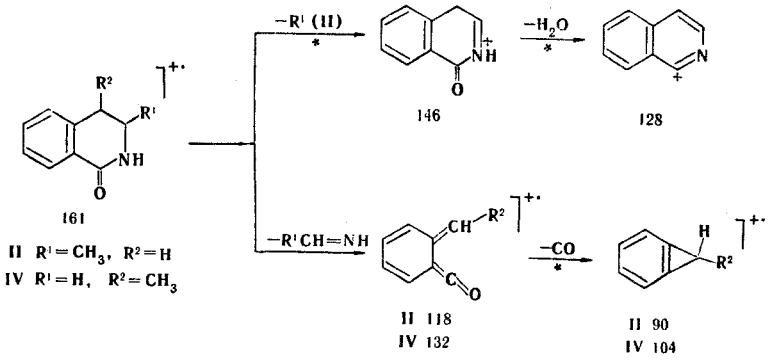
Compound	W_M	$[M-CH_3]^+$	$[M-CO]^+$	$[M-HCO]^+$	$[M-CH_3, -H_2O]^+$	$[M-CH_3, -CO]^+$	$\frac{J_{[M-CH_3]^+}}{J_{M^+}}$
I	10,5	0,7	4,6	10,8	0,6	7,4	0,06
II	1,1	19,3	—	—	6,9	14,5[a]	17,5
III	6,3	9,8	1,1	1,2	7,5	8,0	1,5
IV	9,5	0,6	—	20,1[b]	1,1	0,4	0,06

[a]The $[M - CH_3CH{=}NH]^+$ ion. [b]The $[M - CH_2NH]^+$ ion.

Scheme 1



Scheme 2



Note. The asterisk indicates the existence of a metastable ion that confirms the process. The numbers under the formulas characterize the m/e values of the ions.

TABLE 3. Metastable Ions in the Mass Spectra of I-IV

Compound	m* found	m* calculated	Transition	Fragment eliminated
II, III	132,4	132,39	161→146+15	CH_3
II, III	112,2	112,21	146→128+18	H_2O
II (D), III (D)	111,5	111,45	147→128+19	HDO
IV	108,2	108,22	161→132+29	CH_2NH
II	88,0	88,01	90→89+1	H
IV	81,9	81,93	132→104+28	CO
II	68,2	68,64	118→90+28	CO
IV	58,2	58,50	104→78+26	C_2H_2

It was established by means of the high-resolution mass spectra that the intensive process involving the loss of 29 amu by the molecular ion of IV is explained exclusively by the elimination of a CH_2NH fragment (retrodiene fragmentation, Scheme 2). An analogous process in the fragmentation of II leads to an intense ion peak with m/e 118.

Although an $[M - CH_3]^+$ ion peak was observed in the mass spectra of all of the investigated compounds, the $J_{[M - CH_3]^+}/J_{M^+}$ value is greater than unity only for II and III, in which the resulting carbonium ion is capable of stabilization through the pair of p electrons of the nitrogen atom.

Processes involving the loss of a molecule of water by the $[M - CH_3]^+$ ion that proceed with the participation of the amide nitrogen atom are also characteristic for the mass spectra of these compounds; this was proved by an analysis of the mass spectra of the II(D) and III(D) compounds,* which contain deuterium attached to the nitrogen atom, by the data from the high-resolution mass spectra, and by an analysis of the observed metastable ions (Table 3). Similar processes involving the loss of water were also observed in the dissociative ionization of 3-methyl-3-chlorooxindole [5].

Thus 3- and 4-substituted dihydro-2-quinolones can be successfully distinguished from the isomeric 3- and 4-substituted dihydro-1-isoquinolones by mass spectrometry. The $[M - CO]^+$ ion is characteristic for the mass spectra of dihydroquinolone derivatives, whereas retrodiene fragmentation of the molecular ion is characteristic for dihydroisoquinolone derivatives. The intense $[M - R]^+$ and $[M - R, - H_2O]^+$ ion constitute evidence that the substituent is located in the 3 (for dihydroisoquinolones) or 4 (for dihydroquinolones) position.

EXPERIMENTAL

The mass spectra of the compounds were recorded with an MKh-1303 spectrometer with direct introduction of the samples into the ion source at an ionizing-electron energy of 50 eV, 40°C, an emission current of 1.5 mA, and an accelerating voltage of 2 kV. The high-resolution mass spectra were recorded with a JEOL JMS-01-SG-2 spectrometer with double focusing at an ionizing-electron energy of 75 eV.

Compounds I-IV were obtained by the method described in [3]. Compounds II and IV were identical to (+)-3-methyl- [6] and (-)-4-methyl-3,4-dihydro-1-isoquinolones [7], which were previously synthesized by independent methods. The structures of I and III were confirmed by their IR, UV, and PMR spectra.

A mixture of 2 g of methylbenzylacetylhydroxamic acid and 40 g of polyphosphoric acid (PPA) was heated at 110°C for 4 h, after which it was decomposed with ice water and extracted with benzene. The extract was dried with magnesium sulfate, and the solvent was removed by evaporation. The mixture of products was separated preparatively on aluminum oxide (neutral) plus a luminophore (LLD 6400 K) in a benzene–acetone system (7 : 3) with double passage of the solvent to give 3-methyl-3,4-dihydro-2-quinolone (I), with mp 127-128°C,† and 3-methyl-3,4-dihydro-1-isoquinolone (II) with mp 130-131°C [8].

*Obtained by two recrystallizations of the appropriate compounds from CH_3OD.
†For the optically active compound.

4-Methyl-3,4-dihydro-2-quinolone (III), with mp 98°C [9], and 4-methyl-3,4-dihydro-1-isoquinolone (IV), with mp 81°C* [8], were similarly obtained from α-phenylethylacetylhydroxamic acid and PPA.

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*For optically active compounds.

INVESTIGATION OF NITROGEN- AND SULFUR-CONTAINING HETEROCYCLES.

37.* REACTION OF o-AMINO MERCAPTO DERIVATIVES OF PYRIDINE AND PYRIMIDINE WITH ESTERS OF β-HALO-α,γ-DIKETO ACIDS

L. G. Levkovskaya, I. E. Mamaeva, O. S. Anisimova, and T. S. Safonova

UDC 547.822.7'825'853.3'869.2

The synthesis of two-ring 1,4-thiazine systems was previously accomplished on the basis of the reaction of o-amino mercapto derivatives of pyridine and pyrimidine with dicarbonyl compounds — halo β-keto esters and halo β-diketones. In the present paper it is shown that the primary products of this reaction are S-β-ketoalkylmercapto derivatives, which are subsequently cyclized to the corresponding hydroxy amino compounds. The latter are converted to N-acylamino-S-β-carbethoxy (keto)alkylmercapto derivatives under the influence of an alkaline agent. The indicated compounds were isolated and characterized [2, 3].

Continuing our recent research [2, 3] to obtain biologically active substances among derivatives of two-ring 1,4-thiazine systems we investigated the reaction of o-amino mercapto derivatives of pyridine and pyrimidine with tricarbonyl compounds — esters of β-halo α, γ-diketo acids.

We have shown that the reaction of 2-mercapto-3-amino-6-chloropyridine (I) and 4-methoxy-5-amino-6-mercaptopyrimidine (II) with esters of β-chloro-β-acylpyruvic acids in the presence of a slight excess of alkaline agents such as KOH, NaH, and triethylamine leads to the formation of the previously unknown heterocyclic systems — oxazolidino[3,2-d]pyrido[2,3-b]- and oxazolidino[3,2-d]pyrimido[4,5-b]-1,4-thiazines (VIIa-g).

In analogy with the reaction of o-amino mercapto derivatives of pyridine and pyrimidine with dicarbonyl compounds, we assumed that the initial step in the reaction of I and II with esters of β-halo α, γ-diketo acids is evidently alkylation of the sulfur atom to give intermediate III (see the scheme below), which subsequently undergoes cyclization to hydroxy amino compound IV. The conditions for the destructive cleavage of IV at the C_6-C_7 bond, as a result of which the corresponding N-oxamoyl-S-β-ketoalkylmercapto derivatives Va-e (Table 1) are

*See [1] for communication 36.

S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Moscow 119021.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 250-253, February, 1979. Original article submitted April 21, 1978.