A Study of the Fragmentation Processes of Some

N-Acyl-2-indolinols Upon Electron Impact *

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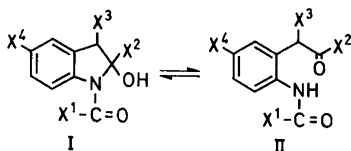
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A mechanistic rationalization for the origin of the principal peaks in the mass spectra of ten indolinols (I) is presented. Evidence was found from an examination of the mass spectra of these compounds and certain models for the preferential occurrence in the gas phase of the open chain tautomer II.

A previous study[1] indicated that very little or no tautomerism occurred in the product ions of the McLafferty rearrangement of two cyclic ketones and a substituted malonic ester. N-Acyl-2-indolinols (I) represent an interesting class of compound since it has been shown[2,3] that they exist in a tautomeric equilibrium with species II. The ring tautomers (I) were found[2] to be preferred when X^2=H, whereas the corresponding chain tautomers (II) were the more stable species in both solution and the crystalline form when X^2=CH_3. It was of interest to examine the mass spectrometric fragmentation of N-acyl-2-indolinols as no investigation of this class of compound has as yet appeared in the literature. An additional impetus for this work was the possibility of being able to determine mass spectrometrically which of the two tautomeric forms (I and II) was the more stable one in the gas phase.

A priori one would predict different mass spectra for each tautomeric partner on the basis of the different functional groups present. Thus the indolinol form I which contains a hydroxyl substituent would be expected to exhibit in its mass spectrum a facile loss of water from both the molecular ion and some fragment ions containing this group, whereas the open chain

	X^1	X^2	X^3	X^4
a:	H	H	H	H
b:	H	H	H	CH_3
c:	H	H	H	OCH_3
d:	CH_3	H	H	H
e:	CH_3	CH_3	H	H
f:	CH_3	H	CH_3	H
g:	CH_3	CH_3	CH_3	H
h:	C_6H_5	H	H	H
i:	C_6H_5	CH_3	H	H
j:	C_6H_5	H	CH_3	H

tautomer II should not show abundant ions corresponding to the expulsion of water. To investigate this we have determined the mass spectra [4] of ten indolinols and chain tautomers (Ia—d, f, h, j, and IIe, g, and i) using the direct inlet procedure and minimal sample heating to reduce thermal dehydration of those compounds existing in the N-acyl-2-indolinol form (I).

Discussion of mass spectra. The molecular ion of N-formyl-2-indolinol (Ia) can be represented as either a or b or a mixture of both species depending upon which tautomer is preferred in the gas phase. In view of the almost negligible peak (m/e 145; 1 % relative abundance, Fig. 1) due to the loss of water from the molecular ion it would appear that species b predominates as the molecular ion and it is likely that N-formyl-2-indolinol preferentially exists in the gas phase as II.

Carbon monoxide is ejected [5] from the molecular ion of N-formyl-2-indolinol (production of m/e 135, (c, d or d')) and this ion(s) then probably eliminate(s) a hydrogen atom (m/e 134 in Fig. 1) rather than the alternative loss of a formyl radical directly from the molecular ion. This conclusion was reached from an examinaion of the low voltage spectrum of Ia in which the
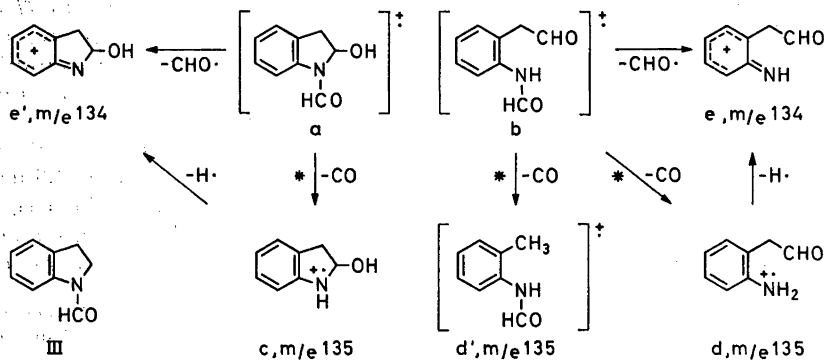
intensity of the M—29 species (e or e') declines more rapidly than that of the M—28 ion (m/e 135), while no metastable ions were observed to clarify the origin of the M—29 species. It is pertinent to note that the most abundant ion (100 % relative abundance) in the mass spectrum of N-formylindoline (III) arises from the elimination of 29 mass units from the molecular ion and that the ejection of 28 mass units (CO as shown by exact mass measurements) is very small (8 % relative abundance).

Two important ions of mass 118 and 117 are present in the spectrum (Fig. 1) of N-formyl-2-indolinol (Ia) and both could formally arise by the expulsion of a hydroxyl radical from the M—28 (c, d or d') and M—29 (e and e') ions, respectively. Since d' represents the ionized form of N-formyl-o-toluidine (IV), its mass spectrum was determined and found to display a loss [5] of a hydroxyl radical (13 % relative abundance) from the molecular ion. In view of this expulsion of a hydroxyl radical from IV it is not necessary to postulate the intervention of the cyclic species c or e' as precursors of the ions of mass 118 and 117 in Fig. 1. Their appearance, therefore, need not be taken as evidence for c and e', but can be rationalized equally well in terms of the loss of a hydroxyl radical from d, d', and e. Since cyclization may well be involved in this elimination, representations f and g may be plausible, which would then lose HCN to yield the fragments of mass 91 and 90. The elimination of HCN from g parallels the behaviour of indole itself.[6]

m/e 91 ←—HCN—— f, m/e 118   IV   g, m/e 117 —*—HCN→ C₇H₆⁺· m/e 90
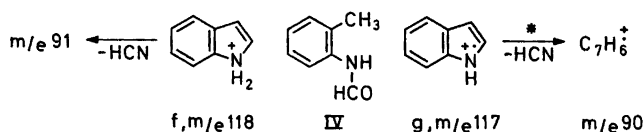
The original M—CO ion (or ions) of mass 135 in the spectrum (Fig. 1) of N-formyl-2-indolinol (Ia) can again expel carbon monoxide [5] to yield a fragment of mass 107 and this decomposition mode can be accommodated more easily in ions d and d' (generation of h) than from the alternative species c. In addition the mass spectra of N-formyl-o-toluidine (IV)[7] and of phenylacetaldehyde (V) contain peaks of 28 % and 24 % relative abundance due to the expulsion of carbon monoxide from their respective molecular ions, thus offering support in favour of the postulated origin of the ion h from the species d or d'.


h, m/e 107   V
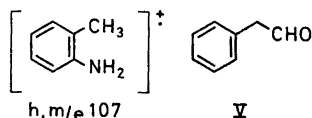
Three possible origins exist for the ion of mass 106 in the spectrum (Fig. 1) of N-formyl-2-indolinol (Ia). First, the ejection of a formyl radical from d or d'; second, loss of carbon monoxide from e or e', and third loss of a hydrogen radical from h. No metastable ions could be found to distinguish between these possible modes of formation. However, the mass spectra of IV and V contain
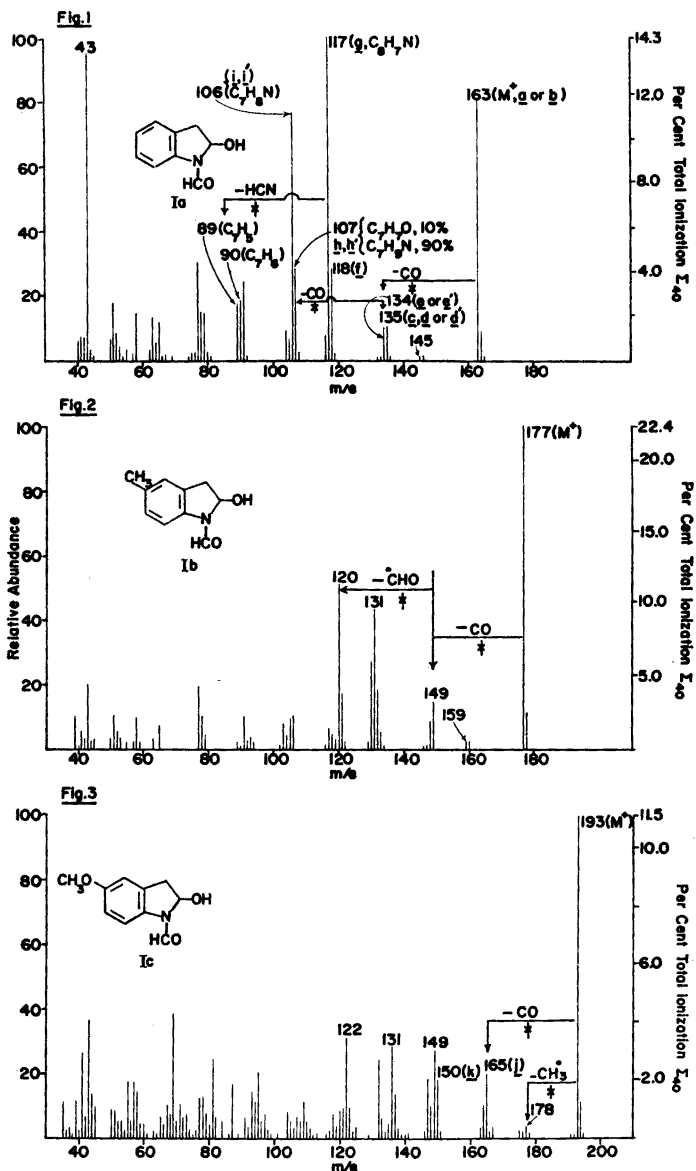
Figs. 1—3. Mass spectra of 1 N-formyl-2-indolinol (Ia), 2 N-formyl-5-methyl-2-indolinol (Ib), 3 N-formyl-5-methoxy-2-indolinol (Ic).

fragments (100 % relative abundance) derived from the expulsion of a formyl radical from their molecular ions thus supplying some support for the postulate that loss of this entity from d or d' is responsible for the species i and i' (m/e 106) or their ring expanded counterparts in the spectrum (Fig. 1) of Ia.
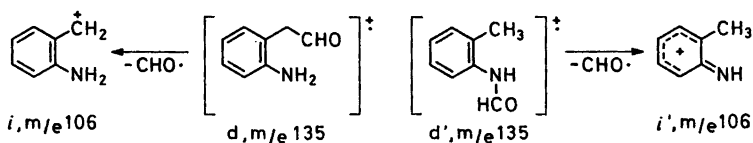
The mass spectra (Figs. 1 and 2) of *N*-formyl-2-indolinol (Ia) and its 5-methylated analog (Ib) show a strong resemblance with the major peaks displaced fourteen mass units higher in the latter instance and thus no detailed analysis of Fig. 2 is warranted.

N-Formyl-5-methoxy-2-indolinol (Ic) yields a mass spectrum (Fig. 3) similar to those previously encountered with Ia and Ib thereby suggesting that the 5-methoxy derivative predominately exists in the gas phase in the open chain form IIc. In addition we now observe with Ic the influence of the methoxyl function superimposed on the fragmentation pattern of the 2-indolinol ring system. This is exemplified by the elimination of a methyl radical from the initial M—CO species and can be rationalized by IIc→j→k (*m/e* 150). An alternative explanation for the origin of the ion of mass 150 in Fig. 3 would involve loss of carbon monoxide from the M—CH₃ species at mass 178. In this instance expulsion of carbon monoxide could incorporate the methoxyl oxygen.
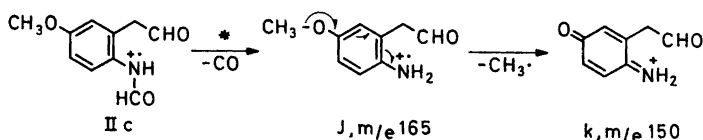

Virtually no loss of water (*m/e* 159, Fig. 4) occurs from the molecular ion of *N*-acetyl-2-indolinol (Id) suggesting that this compound also exists in the gas phase as the open chain tautomer IId. Expulsion of carbon monoxide [5] from the molecular ion of Id is a relatively unimportant process (*m/e* 149, Fig. 4) and probably arises from the aldehyde group of IId in view of this same loss from the molecular ion of phenylacetaldehyde (V) and the absence of an M—CO peak in acetanilide itself. Ejection of ketene [5] (analogous to the behaviour of acetanilide) from the molecular ion of Id is responsible for the base peak at *m/e* 135 (c or d) in the mass spectrum (Fig. 4) of this compound while the presence of the abundant ions at mass 118 (*f*), 117 (*g*), 107 (*h*), and 106 (*i*) can be rationalized by paths identical to those detailed for *N*-formyl-2-indolinol (Ia).

o-Acetamidophenylacetone (IIe), which primarily exists in the open form as a solid as well as in solution,[2] upon electron impact (Fig. 5) suffers dehydration [5] to only a limited extent suggesting no appreciable concentration of the cyclized form Ie in the gas phase. Loss of water from IIe can be rationalized by assuming intervention of the enolized molecular ion of IIe, dehydration of which could yield *m* (*m/e* 173). Subsequent elimination of ketene from *m* rationalizes the formation of the ion of mass 131 (*n*) in Fig. 5.
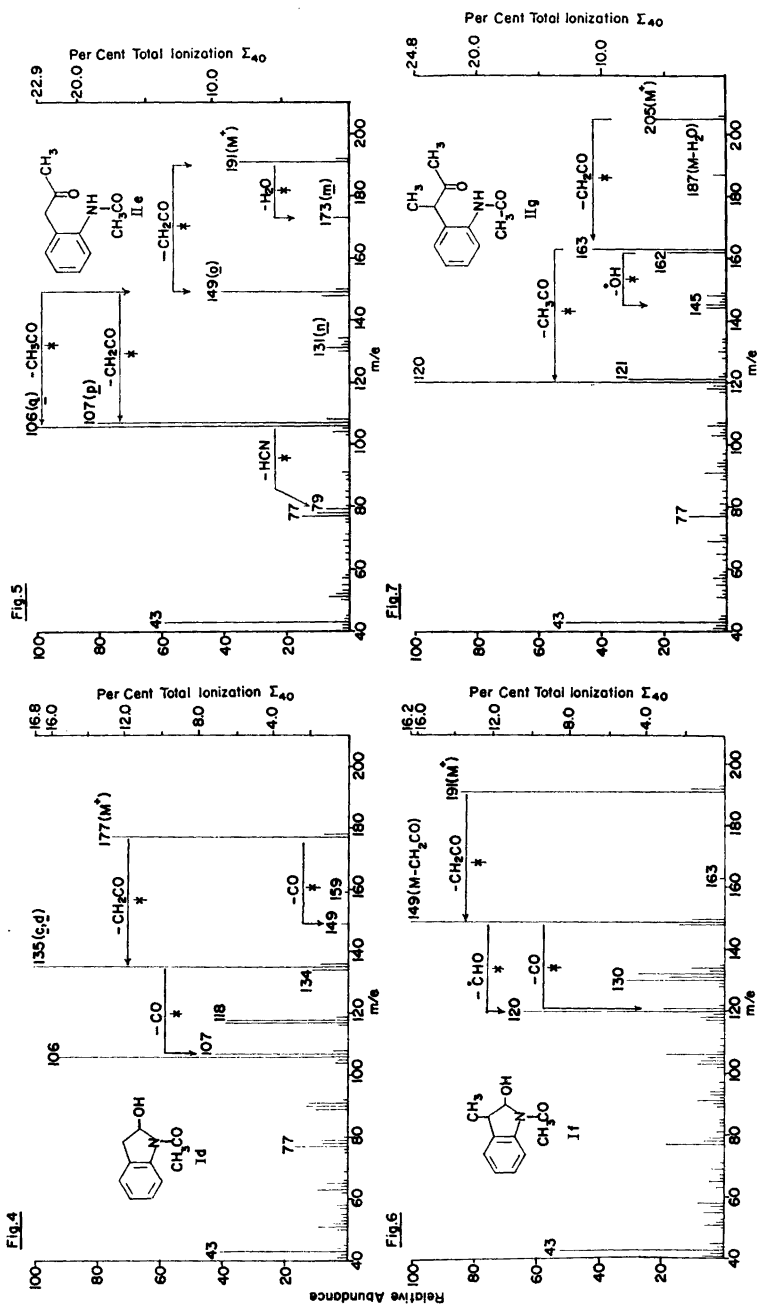
Figs. 4—7. Mass spectra of *4* N-acetyl-2-indolinol (Id), *5* o-acetamidophenylacetone (IIe),
    6 N-acetyl-3-methyl-2-indolinol (If), *7* 3-(o-acetamidophenyl)-2-butanone (IIg).

VI   m, m/e 173   n, m/e 131
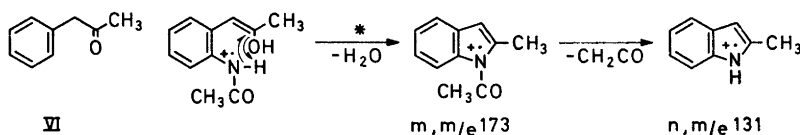
A second fragmentation pathway of the molecular ion of IIe is the expulsion of ketene (o and o', m/e 149) which then expels [5] either a second molecule of ketene (p, m/e 107) or an acetyl radical,[5] by benzylic cleavage to generate i (m/e 106) or its ring expanded counterpart. The formulation o as a possible fragment derived by loss of ketene from the molecular ion of IIe is supported by the observation that the mass spectrum of phenylacetone (VI) contains peaks (8 % and 58 % relative abundance, respectively) due to the elimination of ketene and an acetyl radical from the parent ion of VI. However, o' would not be expected to be as abundant as the species o (m/e 149). Elimination of HCN from i then yields the ion of mass 79 in Fig. 5.

i, m/e 106   o, m/e 149   p, m/e 107   o', m/e 149
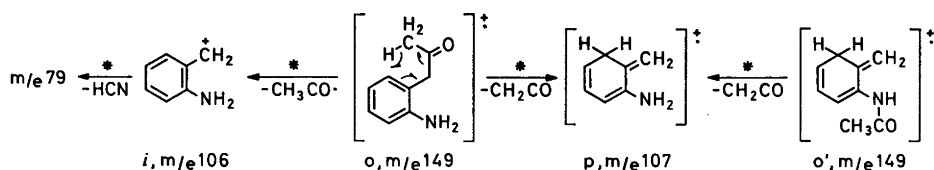
The electron impact promoted decomposition (Fig. 6) of N-acetyl-3-methyl-2-indolinol (If) parallels that of Id, the major peaks being displaced to higher mass by 14 mass units and a decomposition sequence analogous to that proposed for Id accounts for the abundant ions in Fig. 6. It is noteworthy that If does not lose water to any significant extent upon electron impact as the appropriate ion is of less than 1 % relative abundance.

3-(o-Acetamidophenyl)-2-butanone (IIg) fragments subsequent to electron impact (Fig. 7) in a manner similar to its demethylated homolog IIe (Fig. 5) all the major peaks being displaced by 14 mass units; hence their origins can be rationalized by processes used previously for IIe.

Decomposition subsequent to electron impact (Figs. 8, 9, and 10) of N-benzoyl-2-indolinol (Ih) and its methylated derivatives IIi and Ij are dominated by the fragments of mass 105 (C_6H_5CO) and 77 (C_6H_5). Ions of low abundance corresponding to the elimination of water (1 % and 3 % relative abundance, Figs. 8 and 9) from the molecular ion of Ih and IIi are observed and may be taken as evidence for these compounds existing preferentially as the open chain tautomers II in the gas phase. The elimination of carbon monoxide and ketene from the parent ions of Ih and IIi can be rationalized from the open chain tautomers (II) in each instance.

A mechanistically interesting peak occurs at m/e 117 (M—122) in the mass spectrum (Fig. 8) of Ih and a metastable ion indicated that at least a portion of this fragment arose directly from the molecular ion. Furthermore at low ionizing voltage this peak attained 54 % relative abundance. One rationalization would be to invoke participation of the enol form of the open chain tautomer IIh which by concerted elimination would yield ionized indole g
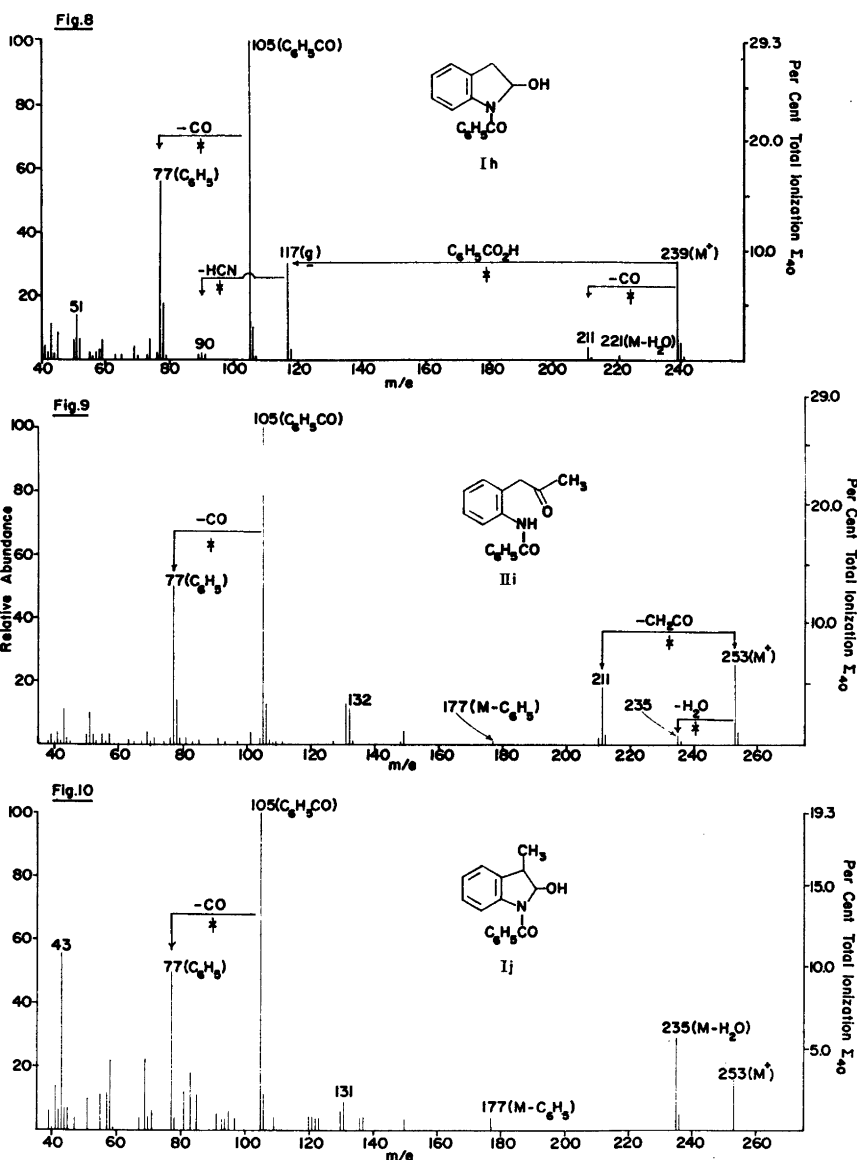
Figs. 8—10. Mass spectra of 8 N-benzoyl-2-indolinol (Ih), 9 o-benzamidophenyl-acetone (IIi), 10 N-benzoyl-3-methyl-2-indolinol (Ij).

(m/e 117) and benzoic acid. It is pertinent to observe that the mass spectra (Figs. 9 and 10) of the two methyl homologs IIi and Ij of N-benzoyl-2-indolinol (Ih) contain peaks at m/e 131 which can be assigned to the molecular ion of 2-methyl- and 3-methylindole, respectively. Both of these ions were present

at low ionizing voltages but no metastable ions could be identified in these instances to verify a direct parent-daughter relationship with the molecular ions of IIi and IIj.
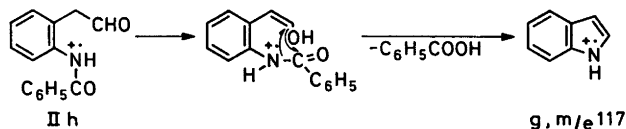
Of the ten indolinols subjected to mass spectral scrutiny N-benzoyl-3-methyl-2-indolinol (Ij, Fig. 10) displays the greatest ion yield corresponding to loss of water from the parent ion. This may be due to a larger concentration of the cyclized tautomer Ij in the gas phase in this instance. Support for this thesis is the lack of an M—CO fragment in Fig. 10 since this elimination was shown to be a common decomposition mode of all the open chain forms of those indolinols which contained the substituted phenylacetaldehyde grouping.

In summary, our investigation of the mass spectra of ten indolinols (Ia—Ij) affords evidence that these compounds exist preferentially in the gas phase as the open chain tautomers II with the exception of Ij which may exist preferentially as the cyclized form (I).

EXPERIMENTAL

Low resolution mass spectra were obtained with an Atlas CH-4 instrument using direct sample insertion into the TO-4 ion source and 70 eV electrons unless otherwise noted. To ensure more even evaporation the samples were mixed with charcoal. High resolution mass measurements (Fig. 1) were carried out by Mr. R. G. Ross on an MS-9 mass spectrometer using the direct inlet system and were accurate to within ±3 ppm. The N-acyl-2-indolinols used in this investigation were prepared by published procedures.[2,3]

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4. Use of an all glass heated inlet system (200°) in conjunction with a C.E.C. 103C mass spectrometer resulted in thermal degradation of the samples in the inlet system.
5. The occurrence of this process is supported by the presence of the appropriate metastable peak in the mass spectrum. This is indicated with an asterisk in the degradation schemes.
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