Stereochemical Applications of Mass Spectrometry

1—The Utility of Electron Impact and Chemical Ionization Mass Spectrometry in the Differentiation of Stereoisomeric Benzoin Oximes and Phenylhydrazones

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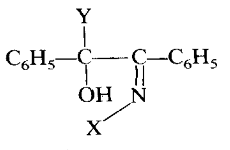
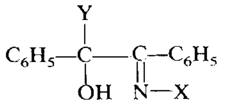
A study of the electron impact and chemical ionization (H_2, CH_4 and iso-C_4H_{10}) mass spectra of stereoisomeric benzoin oximes and phenylhydrazones indicates that while the former can be distinguished only by their chemical ionization mass spectra the latter are readily distinguishable by both their electron impact and chemical ionization mass spectra. The electron impact mass spectra of the isomeric oximes are practically identical; however, the chemical ionization spectra show that the *E* isomer forms more stable $[MH]^+$ and $[MH-H_2O]^+$ ions than the *Z* isomer for which both the $[MH]^+$ and $[MH-H_2O]^+$ ions are relatively unstable. In electron impact the *Z*-phenylhydrazone shows a lower $[M]^{+\cdot}$ ion abundance and more facile loss of H_2O than does the *E* isomer. This more facile H_2O loss also is observed for the $[MH]^+$ ion of the *Z* isomer under chemical ionization conditions.

Benzoin oximes and phenylhydrazones find wide application in synthetic,[1] mechanistic[2] and analytical[3] fields. While the stereoisomeric oximes have firmly established structures,[4] the phenylhydrazones lack unambiguous configurational assignments, even though both classes of compounds have been known for many years.[5] Mass spectrometry has been applied extensively to stereochemical problems;[6] however, there has been only a single report[7] concerned with the mass spectral features of stereoisomeric molecules containing the $>C=N-$ function. Therefore we have undertaken a study of the electron impact (EI) and chemical ionization (CI) mass spectra of benzoin derivatives to investigate configurational effects on the mass spectra of molecules containing the $>C=N-$ function.

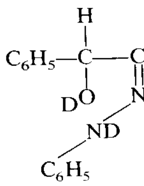
The compounds examined are indicated below. The stereochemical (and chemical) purity of each compound was confirmed by thin-layer chromatography. In the EI mass spectra elemental compositions of the ions have been determined by accurate mass measurements, while metastable peaks, where observed, are indicated by asterisks in the proposed fragmentation schemes. Throughout the following discussion, the designation *Z* represents those isomers in which the OH of the oxime or the NHC_6H_5 of the phenylhydrazone is *syn* to the hydroxybenzyl moiety, while the designation *E* represents those isomers with the *anti* configuration.



1: Y = OH, Y = H
3: $X = NHC_6H_5$, Y = H
5: $X = NHC_6H_3D_2$, Y = H
7: $X = NHC_6H_5$, Y = D



2: X = OH, Y = H
4: $X = NHC_6H_5$, Y = H
6: $X = NHC_6H_3D_2$, Y = H
8: $X = NHC_6H_5$, Y = D
9: X = OH, Y = D



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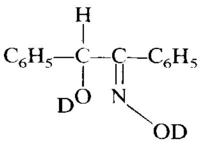

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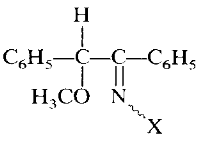

12: X = OH
13: $X = NHC_6H_5$

EI mass spectra of oximes

The EI mass spectra of the *Z*(**1**) and *E*(**2**) oxime isomers of benzoin are essentially identical, with the spectrum of **2** being shown in Fig. 1 as an example. The spectra observed are rationalized by the fragmentation shown in Scheme 1. The molecular ions are of low abundance, resembling the behaviour of benzoin and its methyl ether,[8] while the $[C_7H_7O]^+$ ion (*m/z* 107, shifting to *m/z* 108 for **9**), suggested as having the hydroxytropylium structure *a*, is the base peak in the EI spectra. The abundant benzaldehyde radical ion (*c*) and benzonitrile radical ion (*e*) arise from fragmentation of $[M-H_2O]^{+\cdot}$, by a process resembling the Beckmann fission observed[9] for these compounds in solution. In contrast to the usual Beckmann rearrangement, the Beckmann fission is observed for α-hydroxy, α-oxo and other related α-substituted ox-

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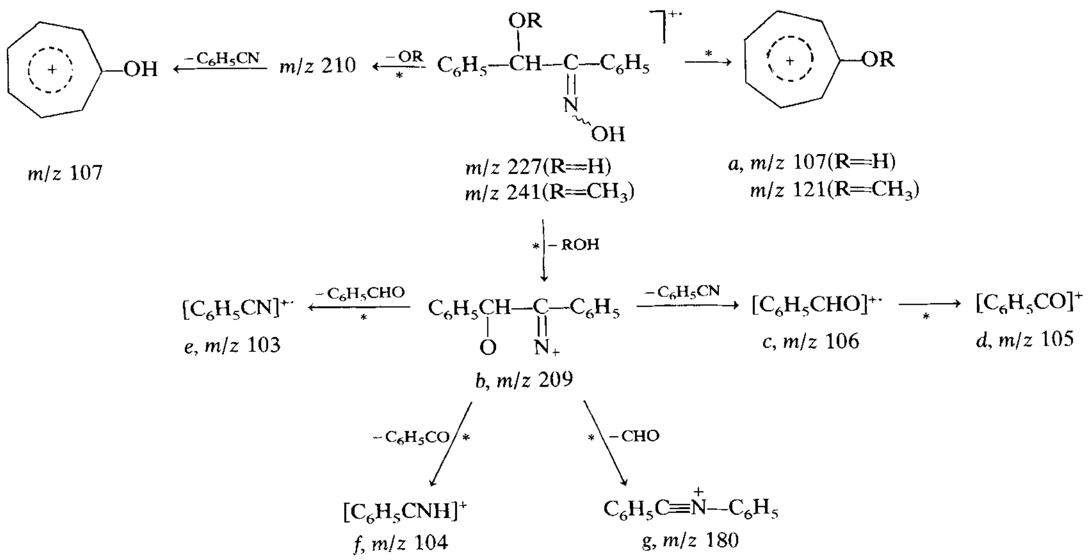
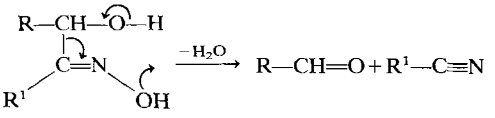


Scheme 1

imes,[10] and has been shown to yield carbonyl compounds and nitriles in the case of α-hydroxyketoximes. The mechanism[11] is indicated in Scheme 2 and involves the hydrogen of the α-hydroxyl group and the oxime hydroxyl in the water lost.



Scheme 2

The protonated benzonitrile ion $f(m/z\ 104)$ originates from the $[M-H_2O]^{+\cdot}$ fragment and involves migration of the benzylic hydrogen to the CN group, as shown by the shift of f to m/z 105 in the mass spectrum of **9** and its retention at m/z 104 for **11**. The ion g (m/z 180) originates from the $[M—H_2O]^{+\cdot}$ fragment ion and involves a phenyl group migration with elimination of CHO.

The EI mass spectrum of **12**, the single benzoin methyl ether oxime isolated, also shown in Fig. 1, is similar to the spectra of the oximes and can be rationalized by the same fragmentation scheme. The Beckmann fission in this case finds a direct parallel in solution chemistry.[12] The base is observed at m/z 121, corresponding to a ($R=CH_3$); however, an additional fragmentation mode noted for **12** is the formation of m/z 107 by loss of the methoxy group followed by migration of the oxime hydroxyl with benzonitrile elimination.

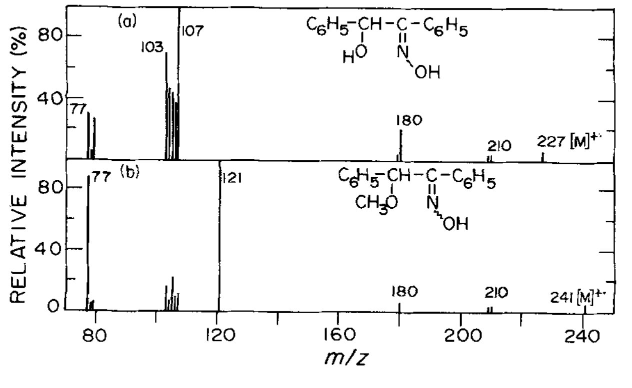


Figure 1. EI mass spectra of (a) benzoin oxime (**2**) and (b) benzoin methyl ether oxime (**12**).

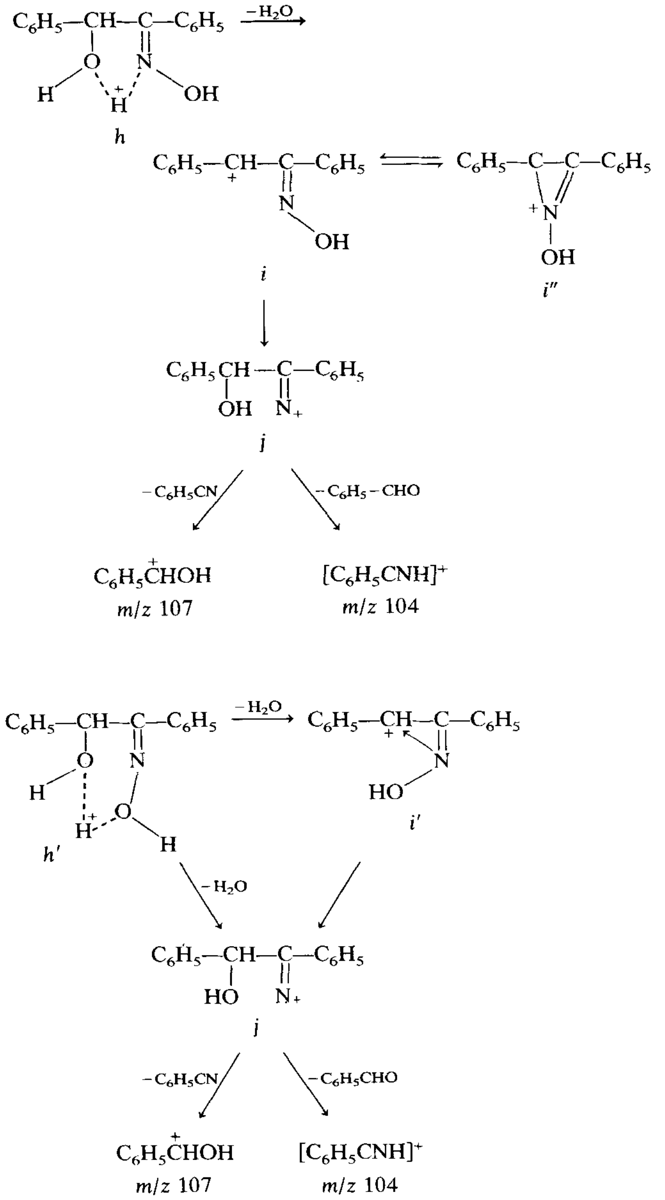
CI mass spectra of oximes

In contrast to the EI mass spectra, the hydrogen, methane and isobutane CI mass spectra of the stereoisomers **1** and **2** show substantial differences, as indicated by the spectra summarized in Table 1. These differences are manifested in the H_2 and CH_4 CI mass spectra by a much higher $[MH-H_2O]^+/[MH]^+$ ratio for the E isomer **2**. In the iso-C_4H_{10} CI mass spectra the differences are manifested by a much higher $[MH]^+$ ion abundance, coupled with much lower m/z 107 and m/z 104 fragment ion abundances for the E isomer **2** (see note in Experimental). These results show that both the $[MH]^+$ ion and the $[MH-H_2O]^+$ fragment ion are more stable for the E isomer **2** than for the Z isomer **1**. The likely explanation for this difference is that protonation of **2** occurs at the benzylic hydroxyl group to form h (Scheme 3) which is stabilized by internal hydrogen bonding. Water loss from h forms the stable benzylic ion i which can undergo further fragmentation only after migration of the oxime hydroxyl group to form j, a migration which requires prior rotation about the C=N double bond. In addition the ion i may be further stabilized by formation of the azirene ion i'', the mass spectrum of 2,3-diphenyl-1-azirine exhibiting the molecular ion as its base peak.[13] On the other hand protonation of **1** probably forms h' which apparently is less stabilized by internal hydrogen bonding and, furthermore, may form j directly by loss of the oxime hydroxyl as water. Alternatively, loss of the benzylic OH as water forms i' which has the oxime hydroxyl favourably disposed

Table 1. CI mass spectra of benzoin oximes

	Benzoin-*Z*-oxime (1)			Benzoin-*E*-oxime (2)			Benzoin methyl ether oxime (12)		
m/z	H_2Cl	CH_4Cl	iso-$C_4H_{10}Cl$	H_2Cl	CH_4Cl	iso-$C_4H_{10}Cl$	H_2Cl	CH_4Cl	iso-$C_4H_{10}Cl$
242							5	20	100
228	32	6	28	10	9	100			
224							—	15	14
211	7	—	—	15	10	—	8	—	—
210	44	16	28	90	100	42	63	88	49
195	4	7	—	16	15	—	9	10	—
121							100	100	83
107	100	87	100	87	98	14	24	16	29
106	—	4	8	15	6	—	—	—	—
105	15	11	10	22	21	3	8	5	10
104	87	100	80	100	99	4	40	29	64

towards migration to the benzylic position. Additionally, for the *Z* isomer **1**, the *m/z* 104 ($[C_6H_5CNH]^+$) ion may arise in part from protonation at the oxime nitrogen followed by elimination of $H_2O + C_6H_5CHO$, since the *Z* isomer has a favourable configuration for fragmentation in this manner.



Scheme 3

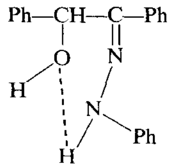
Attempts to distinguish the hydroxyl group lost following chemical ionization by selective deuteration of the hydroxyl groups failed with both **1** and **2**; however, it should be noted that the methyl ether oxime shows peaks for the loss of both CH_3OH (*m/z* 210) and H_2O (*m/z* 224) in the CH_4 and iso-C_4H_{10} CI spectra. In addition, the methyl ether spectra also show a peak at *m/z* 107 resulting from migration of the oxime hydroxyl group to the benzylic position following CH_3OH loss from $[MH]^+$. The CH_4 CI of the d_2-*E* oxime **11** showed predominant loss of HOD, while the CD_4 CI of **2** also showed predominant loss of HOD, both consistent with Scheme 3. However, in attempts to obtain the CD_4 CI spectrum of **1** it was observed that there was extensive exchange of the hydroxylic hydrogens with the deuterium of the reagent gas, with the result that the isotopic composition of the water lost could not be established clearly.

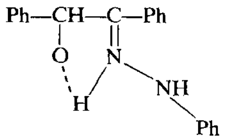
The configuration of the single benzoin methyl ether oxime **12** is not clearly established. Its nuclear magnetic resonance (NMR) spectrum showed a methine proton signal at 5.0δ which is closer to the methine proton signal of the *E* oxime **2** ($5.5\delta^{4a}$) than that of the *Z* oxime **1** ($6.1\delta^{4a}$). In addition, the benzoin *E*-phenylhydrazone shows a methine proton signal at $\sim 5\delta$ (see later discussion). These observations suggest the *E* configuration for the methyl ether oxime. Consistent with this assignment, the iso-C_4H_{10} CI mass spectrum of **12** shows $[MH]^+$ as the base peak, while the CH_4 CI spectrum shows an abundant $[MH-CH_3OH]^+$ peak, both analogous to the behaviour of the *E* oxime **2**. On the other hand, the fragment ion intensities (*m/z* 121, 107 and 104) in the iso-C_4H_{10} CI spectrum are much higher than one would have predicted from the iso-C_4H_{10} CI mass spectrum of the *E* oxime **2**, and are more in line with those observed for the *Z* oxime **1**. It may be that interconversion of the two stereoisomeric forms is particularly facile for the methyl ether oxime.

Configuration of benzoin phenylhydrazones

In contrast to the oximes, the configurations of the stereoisomeric benzoin phenylhydrazones have not been assigned unambiguously, although studies of their ultraviolet,[14] infrared(IR)[15] and NMR[16] spectra have been reported. The situation is further complicated by the fact that, in addition to stereoisomers, several tautomers also are theoretically possible.[17] In the present study the higher melting benzoin phenyl hydrazone (A, m.p. 162 °C) has been assigned the Z configuration, while the lower melting isomer (B, m.p. 101 °C) has been assigned the E configuration. These assignments are based on the following evidence.

(i) The IR spectrum of B displays a sharp NH band at 3320 cm^{-1} along with a broad peak centred at 3420 cm^{-1} (OH), while the corresponding absorptions for A appear at 3300 cm^{-1} (broad, NH) and 3600 cm^{-1} (sharp, OH). These are consistent with the hydrogen bonding anticipated for the Z(A) and E(B) forms.


Z(A)


E(B)

(ii) The phenylhydrazone A shows NMR signals ($CDCl_3$ solvent) at 2.9δ (OH) and $9.7_0\delta$(NH), while B exhibits signals at 5.30δ (OH) and $7.7_0\delta$(NH). For comparison, benzyl alcohol shows a hydroxy proton signal at 3.1δ, whereas 2-hydroxymethylpyridine, in which the hydroxyl H hydrogen bonds to the pyridine N, shows the hydroxyl proton signal at 5.0δ. Unless otherwise stated the NMR data are taken from Ref. 18. An intramolecularly bonded aromatic NH appears between 10–11δ while the aromatic NH of several phenylhydrazones are between 7.5 and 8.0δ. Taking the NH signal of benzaldehyde phenylhydrazone (known to have an almost exclusive E configuration[19]) as a standard (9.16δ), the H bonding of the NH proton to the hydroxyl in the Z form shifts the signal to 9.7δ for A, while reduced deshielding by C=N (owing to the H bonding of the N to hydroxyl) in the E form shifts the NH signal to 7.7δ for B.

(iii) According to Karabatsos and co-workers,[20] due to deshielding effects, the shift in the α-methine proton signal of a phenylhydrazone on moving from an aliphatic to an aromatic solvent is greater with the *cis*-NHPh(Z) orientation than with the *trans*(E) configuration. The α-methine proton shift on changing from $CDCl_3$ to C_6D_6 was observed to be 30 ppm for A and 18 ppm for B, consistent with the E and Z assignments respectively. Thus, the higher melting isomer A has the Z configuration **3** while the lower melting isomer has the E configuration **4**.

EI mass spectra of phenylhydrazones

In contrast to the benzoin oximes, the stereoisomeric benzoin phenylhydrazones **3** and **4** show substantial differences in their EI spectra as shown in Fig. 2. At high source temperatures the differences were much less noticeable indicating thermally induced isomerizations. The E isomer **4** shows a much more pronounced $[M]^{+\cdot}$ ion signal and reduced ion intensities at m/z 284, ($[M-H_2O]^{+\cdot}$, m/z 180 ($[C_{13}H_{10}N]^+$) and m/z 179 ($[C_{14}H_{11}]^+$), with stronger ion signals at m/z 104 ($[C_6H_5CNH]^+$) and m/z 92 ($[C_6H_5NH]^+$) compared with **3**. In addition, the high resolution studies showed that while the m/z 105 ion for **3** consisted entirely of the $[C_7H_5O]^+$ ion the spectrum of **4** showed the m/z

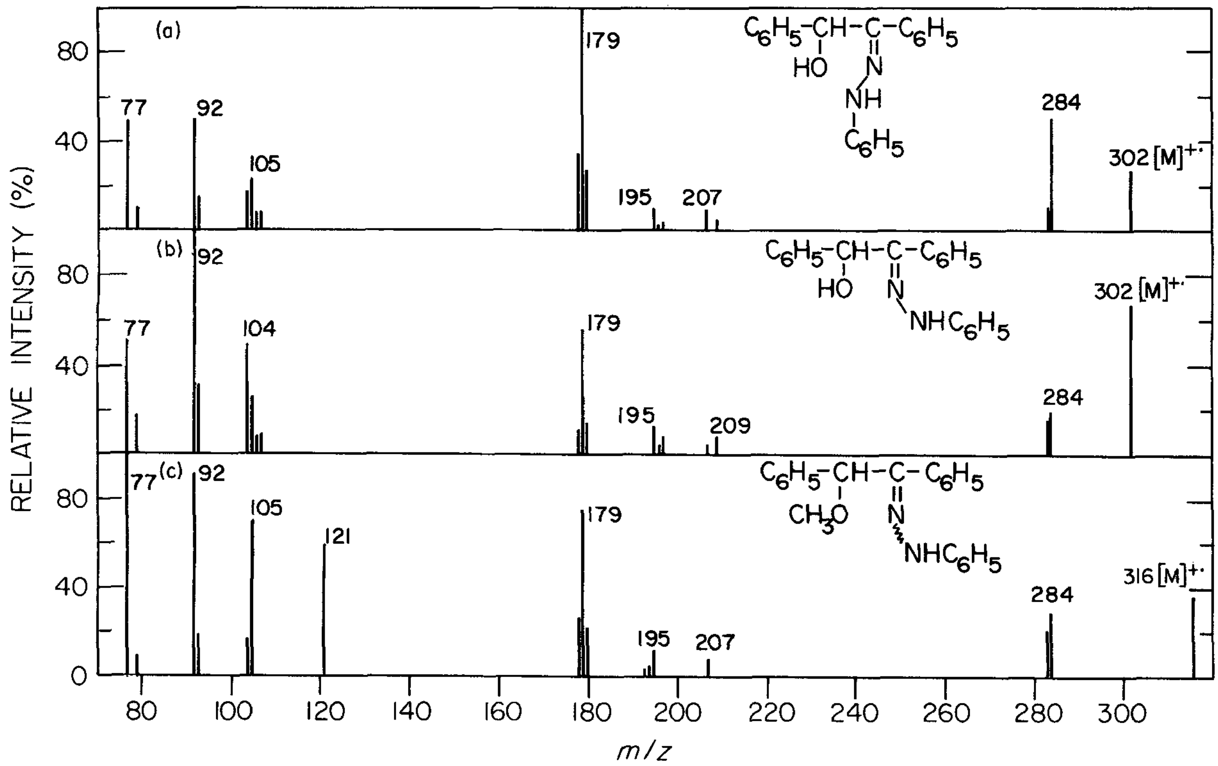
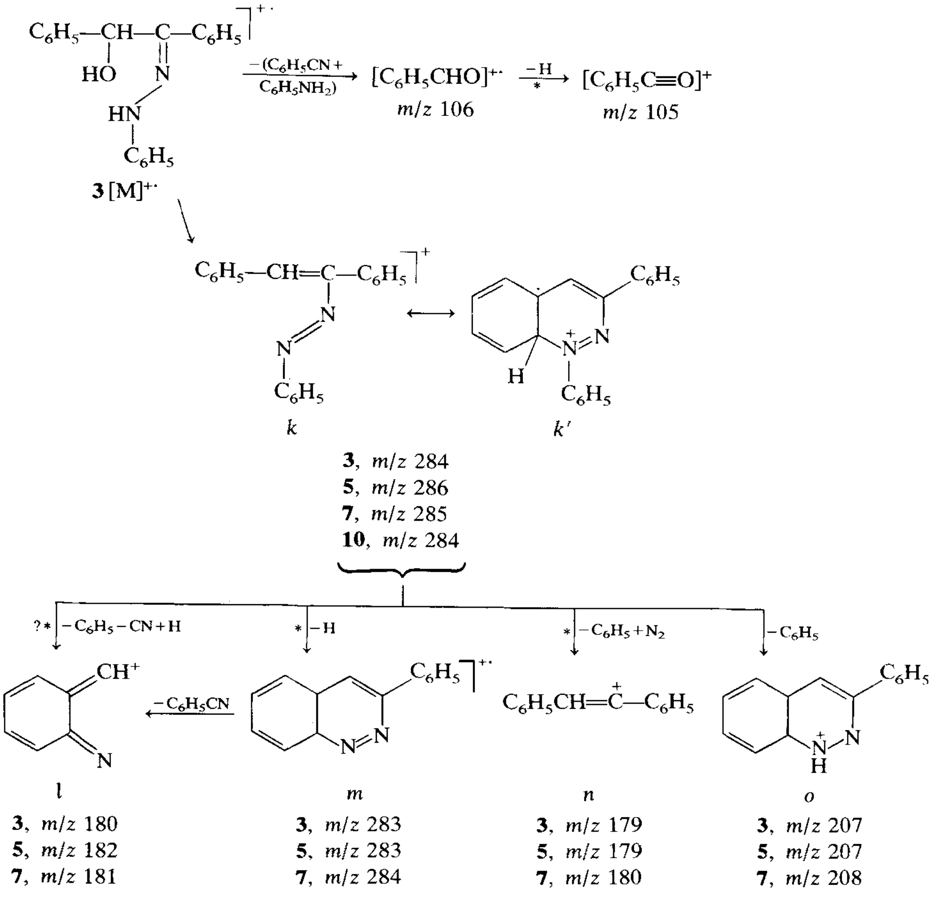


Figure 2. EI mass spectra of (a) Z-benzoin phenylhydrazone (**3**), (b) E-benzoin phenylhydrazone (**4**) and (c) benzoin methyl ether phenylhydrazone (**13**).



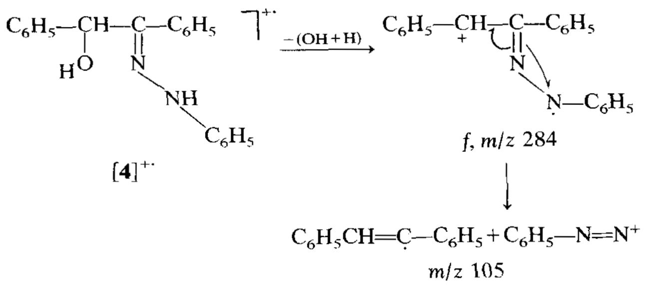
Scheme 4

105 ion to be $[C_7H_5O]^+$ and $[C_6H_5N_2]^+$ in the ratio 1:2. With increasing residence time of **4** on the solid sample probe this ratio changed slowly to 1:1, indicating a slow thermal isomerization of **4** to **3**.)

The proposed fragmentation scheme for **3** as deduced from isotopic labelling and observation of metastable ions is given in Scheme 4. The relative instability of the molecular ion of **3** can be attributed to its configuration which is suitable for an E_2-*cis* elimination of water, analogous to the pyrolytic E_i elimination,[21] with a 6-membered transition state that does not require coplanarity of the atoms concerned. *trans* Isomers do not exhibit such pyrolytic behaviour. The EI spectrum of **10** indicates that the water elimination involves exclusively the benzylic hydroxyl group and the amino hydrogen. The $[M-H_2O]^{+\cdot}$ ion from **3** is postulated to have, at least in part, the cyclic structure *k'* to rationalize the formation of the *m/z* 180 product *l* which contains a nitrogen as well as the hydrazino phenyl group. This fragment may arise either directly from the $[M—H_2O]^{+\cdot}$ ion or by intermediacy of the *m/z* 283 fragment, the energy resolution in the metastable peak measurements being insufficient to distinguish between the two possibilities. The loss of H from *k'* or *k* finds analogy in the EI induced fragmentation of chalcones[21] and their oximes.[22] Formation of the benzaldehyde radical cation, the precursor of the benzoyl cation (*m/z* 105) also probably results from a *cis*-E_i pyrolysis-type elimination similar to the loss of H_2O but with the neutrals eliminated being aniline and benzonitrile.

These elimination processes would not be expected for the *E* isomer **4** and it is possible that the molecular ion of **4** in part isomerizes to $[\mathbf{3}]^{+\cdot}$ prior to fragmentation. This is supported by the observation that the metastable peaks (first field free region) for the fragmentation reaction $[M]^{+\cdot} \rightarrow [M-H_2O]^{+\cdot}$, *m/z* 284 → *m/z* 179, and *m/z* 284 → *m/z* 180 showed identical kinetic energy releases for **3** and **4**. Such $E \rightarrow Z$ isomerizations have been reported photochemically[24] and, further, with *E*-salicylaldehyde phenylhydrazone the activation energy for the thermal isomerization has been found to be 39.3 kJ mol^{-1}.[24] The observation of a higher molecular ion intensity for **4**, along with the less facile H_2O elimination and the observation of $[C_6H_5NH]^+$ (shifting to *m/z* 94 for **6**) indicates an activation barrier for the process $[\mathbf{4}]^{+\cdot} \rightarrow [\mathbf{3}]^{+\cdot}$. The mechanism of formation of the $[C_6H_5N_2]^+$ ion, unique to the isomer **4**, is not clear but may involve stepwise elimination of OH+H to give the *trans* azo-stilbene structure *p* (Scheme 5) rather than the *cis* structure proposed for **3** (Scheme 4) with the *trans* structure fragmenting, in part, to form $[C_6H_5N_2]^+$ rather than cyclizing as proposed for the *cis* structure.

The EI mass spectrum of the benzoin methyl ether phenylhydrazone **13** is also shown in Fig. 2. In solution **13** was found to be a 1:1 mixture of the *E* and *Z* isomers on the basis of the methine proton NMR signals (see Experimental). The EI mass spectrum of **13** is similar to that of the phenylhydrazones **3** and **4** and shows fragment ion abundances (particularly *m/z* 179 and *m/z* 92) characteristic of both isomeric forms.



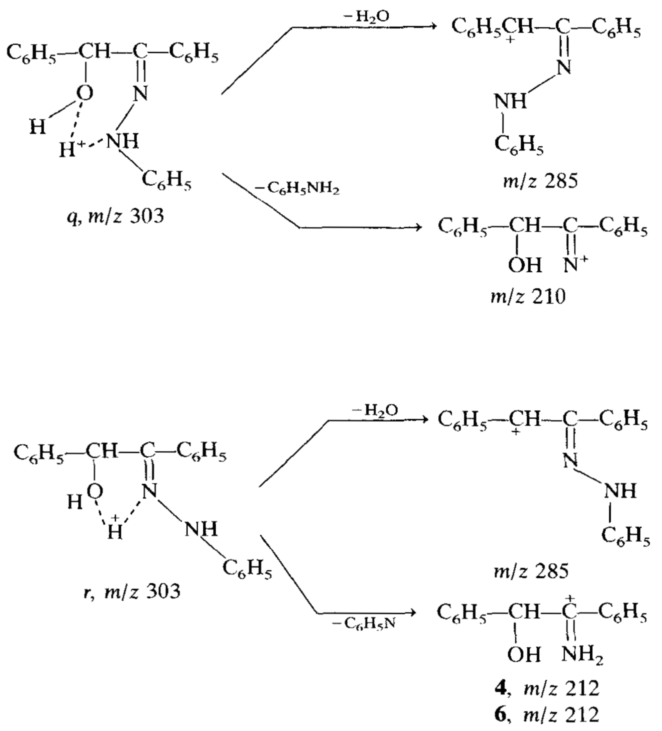
Scheme 5

Thus, it is likely that for **13** both stereoisomeric forms are present in the gas phase as well.

CI mass spectra of benzoin phenylhydrazones

The H_2, CH_4 and iso-C_4H_{10} CI mass spectra of the benzoin phenylhydrazones **3** and **4** and the methyl ether phenylhydrazone **13** are summarized in Table 2. The spectra of the stereoisomeric pair **3** and **4** show substantial differences, particularly in the CH_4 and iso-C_4H_{10} CI. Indeed, the spectra show a similarity to the spectra of the oximes in that the *E* isomer **4** shows a more stable $[MH]^+$ ion with less fragmentation by loss of H_2O. Further differences are the formation of $[MH-C_6H_5NH_2]^+$ (*m/z* 210) observed only for the *Z* isomer **3** and formation of *m/z* 212 ($[MH-91]^+$) which is observed only in the CH_4 and iso-C_4H_{10} mass spectra of the *E* isomer **4**. In contrast to the oximes the extent of further fragmentation of the $[MH-H_2O]^+$ ion shows little dependence on the stereoisomeric form.

The results can be rationalized by assuming that protonation of the *Z* isomer **3** forms the hydrogen bonded species *q* (Scheme 6) which may fragment by loss of either H_2O or $C_6H_5NH_2$. In agreement with this formulation the CD_4 CI mass spectrum of **3** showed loss of H_2O: loss of $HDO \simeq 2:1$ compared with a ratio of 1:2 for the *E* isomer **4**. For the latter,



Scheme 6

Table 2. CI mass spectra of benzoin phenylhydrazone

	Benzoin-*Z*-phenylhydrazone (3)			Benzoin-*E*-phenylhydrazone (4)			Benzoin methyl ether phenylhydrazone (13)		
m/z	H_2CI	CH_4CI	iso-C_4H_{10}CI	H_2CI	CH_4CI	iso-C_4H_{10}CI	H_2CI	CH_4CI	iso-C_4H_{10}CI
317							29	100	100
316							85	38	9
303	17	76	83	18	100	100			
302	100	16	10	65	25	10			
287	13	9	12	—			10	25	
286	17	5	3	28	4	2	6	7	7
285	74	100	100	100	80	31	100	82	51
226	—	—	—	—			4	9	18
224	—	—	—	—			2	4	
212	—	—	—	—	15	17			
210	8	30	29	—	—				
197	8	8	2	9	8	5		4	6
196	8	5	5	8	4	8	15	13	27
195	21	13	3	19	23		11	6	
182	29	15	—	38	5		27	5	
167	16	6	—	21	—				
121	—	—	—	—	—		46	48	45
107	22	22	16	20	41	30	5	48	61
106	5	3	—	9	8	5	11	6	—
105	21	24	3	11	4	3	12	10	—
104	27	16	6	28	29	14	56	75	38
94	46	69	40	55	61	41	93	88	89
93	28	12	4	23	12	7	38	17	18
92	21	9	—	14			14		
91	6	4	—	7			12		
79	22	7	—	41			56		

protonation at the hydroxylic oxygen presumably leads to the hydrogen bonded structure *r* (Scheme 6), which appears to be more stable and obviously cannot lead readily to elimination of $C_6H_5NH_2$. The fragmentation of *r* by loss of a neutral fragment of *m/z* 91 is unusual since it corresponds to loss of the diradical C_6H_5N, as shown by the fact that the CI spectra of the d_2 isomer **6** showed no shift in mass of the *m/z* 212 product. A similar loss of C_6H_5N in the CI spectra of simple aldehyde phenylhydrazones also is observed.[25]

The CI mass spectra of the benzoin methyl ether phenylhydrazone **13** resemble the spectra of the *E*-benzoin phenylhydrazone in terms of the relative intensities of the $[MH]^+$ and $[MH-CH_3OH]^+$ ions, the latter being analogous to the $[MH-H_2O]^+$ fragment. However, the ether also shows fragment ions at *m/z* 224 ($[MH-C_6H_5NH_2]^+$) and *m/z* 226 ($[MH-C_6H_5N]^+$) which by comparison with **3** and **4** are indicative of the *Z* and *E* configurations respectively. This lends further support to the conclusion that **13** exists in both stereoisomeric forms in the gas phase.

CONCLUSIONS

The identity of the EI mass spectra of the stereoisomeric benzoin oximes suggests a ready interconversion of the molecular ions in the gas phase to form the same equilibrium mixture of ions. Photochemical results[26] on oximes are indicative of photostationary states. By contrast isomerization appears to be much less facile under the gentler CI conditions and distinct differences are observed for the diastereomeric oximes. On the other hand, distinct differences are observed in both the EI and CI mass spectra of the diastereomeric phenylhydrazones indicating that even under EI conditions the interconversion of these isomers is much less facile. The present results suggest that chemical ionization mass spectrometry may be a fruitful approach to investigate the stereochemistry of α-hydroxy carbonyl derivatives of acyclic or cyclic nature.

EXPERIMENTAL

Low resolution mass spectra were obtained using either Dupont 21–490 mass spectrometers or an AEI MS 902 mass spectrometer at 70 eV ionizing electron beam energy with a source temperature of 130–150 °C. Samples were admitted using a solids insertion probe operated at 50–80 °C for the 21–490 instrument and heated by radiation from the source for the MS 902. High resolution mass spectra were obtained using an AEI MS 30 mass spectrometer interfaced to a DS-50 data system. The accurate mass measurements and doublet compositions were checked by peak matching using the AEI MS 902 instrument at a resolution $M/\Delta M = 10\,000$. Metastable peaks were observed for fragmentation reactions in the first field free region of the MS 902 mass spectrometer by scanning the ion accelerating voltage at constant electric sector voltage and magnetic field.

Chemical ionization mass spectra were recorded using a Dupont 21–490 mass spectrometer equipped with a high pressure source. The source temperature was 100–110 °C and samples were introduced by the direct insertion probe using a probe temperature of 50–80 °C. Reagent gas pressures were ~0.5 Torr for H_2 and ~0.3 Torr for CH_4, CD_4 and iso-C_4H_{10}.

We noted that the iso-C_4H_{10} CI mass spectrum of **2**, particularly, was very sensitive to traces of H_2O in the reagent gas stream. Addition of small amounts of H_2O lowered the $[MH]^+$ ion signal markedly amd made $[MH-H_2O]^+$ the base peak, apparently as a result of the more exothermic protonation of **2** by $[H_3O]^+$. Thermochemical considerations show that the reaction

$$[H_3O]^+ + \text{iso-}C_4H_{10} \rightarrow [C_4H_9]^+ + H_2 + H_2O$$

is probably slightly endothermic. As a result it may occur only slowly and $[H_3O]^+$ may persist as a reagent ion in isobutane CI studies unless precautions are taken to exclude H_2O.

NMR spectra were recorded on a Varian T-60 spectrometer in $CDCl_3$ and C_6D_6 solvents using TMS as an internal reference. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrophotometer in chloroform solution using polystyrene standard.

Synthesis of compounds

The oximes **1, 2** and **12,** as well as the phenylhydrazones **3, 4** and **13** were prepared by literature procedures.[5,16]

E-Benzoin oxime-*O*-d_2 (**11**) was prepared by dissolving the parent oxime **2** (0.1 g) in 1% NaOD (prepared by reacting sodium metal with D_2O) and reprecipitating after some time by addition of dilute D_2SO_4. Three such operations yielded **11** (m.p. 157 °C) with an isotopic purity of 90% as determined by mass spectrometry.

O,N^2-d_2-*Z*-Benzoin phenylhydrazone (**10**) was prepared by refluxing **3** (0.1 g) for 4 h with methanol-*O*-*d* (5 cm^3) containing a trace of NaOD and concentrating *in vacuo*. Recrystallization afforded **10** (m.p. 162 °C) with an isotopic purity of 70–75%.

The procedure for preparing the α-*d* oxime **9** and phenylhydrazones **7** and **8** was adapted from that used by Bachmann[27] for preparation of unlabelled benzoin from benzil. Benzil (3 g) was shaken for 5 h with sodium amalgam (2%, 35 g) in a mixture of anhydrous ether (30 cm^3) and dry benzene (30 cm^3) under nitrogen. The orange coloured precipitate was carefully decomposed with D_2O (excess) while cooling in ice. The resulting solid was recrystallized from ethanol to yield white crystals of the α-*d*-benzoin (2.8 g, m.p. 137 °C). Mass spectral analysis indicated an isotopic purity of ~98%. The oxime and phenylhydrazones were made from this α-*d*-benzoin by standard procedures.

The benzoin-d_2-phenylhydrazones **5** and **6** were obtained during an attempted preparation of the corresponding d_5 isomers. Aniline-d_5 was diazotized and converted into phenylhydrazine as per literature directions[28] for the unlabelled compound. The mass spectrum of the product analysed for $C_6H_6D_2N_2$ (85%)

$C_6H_5D_3N_2$ (10%) and $C_6H_4D_4N_2$ (5%) indicated extensive interchange of the phenyl hydrogens in the diazotization procedure.

NMR data

Benzoin-Z-phenylhydrazone (3). $CDCl_3$ solution: 2.9δ (1H, broad), 6.10δ (1H, s), 9.69δ (1H, broad), 7.25 & 7.60δ (15H, m). C_6D_6 solution: 2.10δ (1H, broad), 5.61δ (1H, s), 9.80δ (1H, broad), 7.05 & 7.45δ (15H, m).

Benzoin-E-phenylhydrazone (4). $CDCl_3$ solution: 4.66δ (1H, d), 5.26δ (1H, d), 7.66δ (1H, broad), 7.20δ (15H, m). C_6D_6 solution: 4.33δ (1H, d), 5.43δ (1H, d), 7.60δ (1H, broad), 7.05δ (15H, m).

Benzoin methyl ether oxime (12). $CDCl_3$ solution: 3.50δ (3H, s), 5.03δ (1H, s), 7.76δ (1H, broad), 7.25δ (10H, m).

Benzoin methyl ether phenylhydrazone (13). $CDCl_3$ solution: 3.50δ (3H, d), 5.08δ ($\frac{1}{2}$H, s), 5.70δ ($\frac{1}{2}$H, s). 7.70δ ($\frac{1}{2}$H, broad), 9.8δ ($\frac{1}{2}$H, broad), 7–7.6δ (15H, m).

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