Determination of Double Bond Position and Geometry of Olefins by Mass Spectrometry of Their Diels–Alder Adducts

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The Diels-Alder reaction of olefins with ketals of tetrachlorocyclopentadiene produces adducts, the mass spectra of which clearly identify the position and geometry of the original double bond. The loss of either substituent determines the position of the olefin, and the relative abundances of the resultant lons can be related to the geometry. These ions are at least 5-fold more abundant in the product derived from the Z-olefin. The spectra are simpler than the spectra of other derivatives previously used for this purpose and the sensitivity of the technique is such that it can be applied at the microgram level. The ions indicative of the molecular weight of the adduct are very prominent even though the molecular ion is absent.

The electron impact (EI) mass spectra of isomeric olefins are often very similar, if not identical, making it almost impossible to determine the position and geometry of the double bond. Most methods devised to provide this information have relied upon the prior chemical derivatization of the olefin, frequently by osmium tetraoxide oxidation to the vicinal diol and subsequent derivatization of the resulting diol. Trimethylsilyl and isopropylidine derivatives have been most widely used (1-3). However, the mass spectra of the trimethylsilyl derivatives are insensitive to the geometry of the olefin and while the spectra of the isopropylidine derivatives do contain information about the geometry of the original double bond, the corresponding ions are of low abundance and difficult to locate. These earlier chemical derivatization techniques have been critically reviewed (4).

Recently various laboratories have reported limited success in determining the position and geometry of double bonds by chemical ionization mass spectrometry (CI) of the underivatized olefin. Chemical ionization has the advantage over EI in generating far simpler spectra. Budzikiewicz and Busker (5) used primarily isobutane as the reagent gas whereas Jennings et al. (6) used vinyl methyl ether (VME) either as such or diluted with CO_2 (7). Chai and Harrison (8) have improved upon the work of Jennings by using a $N_2/CS_2/VME$ mixture as the reagent gas. This gas mixture yields somewhat simplified mass spectra, compared to other CI spectra, and the location of the double bond is easily determined. However, none of these CI techniques produce information containing the geometry of the double bond.

We have developed a one-step derivatization technique which is simpler than the osmium tetraoxide oxidation and can be carried out with a few micrograms of olefin. The resulting derivatives exhibit EI spectra which are less complex than even the CI spectra of other derivatives. Furthermore, unlike in the CI spectra, the geometry of the original olefin can clearly be determined. As opposed to other methods, this derivatization is also applicable to alkynes.

EXPERIMENTAL SECTION

5,5-Dimethoxy-1,2,3,4-tetrachlorocyclopentadiene (1). The procedure of Newcomer and McBee (9) was used for the preparation of this compound. After two distillations through a 25-cm Vigreux column the yellow liquid crystallized on standing at 0

 $^{\circ}$ C and was >99% pure (by GC). Compound 1 is also commercially available (Aldrich).

1.2.3.4-Tetrachlorocyclopentadienone Ethylene Ketal (2). To a 2-L three-neck flask equipped with mechanical stirrer, condenser, dropping funnel, and argon inlet was added 280 g (5 mol) of KOH and 1.2 L of ethylene glycol and the solution cooled in ice. To the stirred solution was added 136 g (0.5 mol) of hexachlorocyclopentadiene (3) over a 10-min period and the mixture stirred for 24 h at 0 °C. The mixture was diluted with 1.5 L of water and extracted with two 500-mL portions of ether. The organic layer was dried over Na_2SO_4 and concentrated. The solution contains 2 and small amounts (<10% by GC) of 3 and can be used directly or rapidly distilled to yield 20 g (15%) of a white solid (bp 110-111 °C, 1.8 mm, mp 45-55 °C). The wide melting range was attributed to inadvertent impurities of 3. If not distilled rapidly only the dimer is obtained. Compound 2 dimerizes in solution within a few months at 0 °C and within 1 h at 100 °C. The solid crystalline monomer is stable for at least 1 year when stored at 0 °C.

Derivatization. when the reaction is carried out on a larger scale, 0.5 mg of the olefin dissolved in methanol or CH_2Cl_2 was placed in a 4 × 200 mm Pyrex tube. To this solution was added 200 μ L of 1 or 2. The tube was sealed and heated for 12–24 h at 200 °C for compound 1 or 160 °C for compound 2. The tube is then cooled and opened and 1 μ L analyzed by GC/MS.

Derivatization of Double Bonds on a Micro Scale. Six micrograms of the olefin in CH_2Cl_2 (2 μL) was placed in a melting point capillary and 2 μL of a 50% (v/v) solution of 2 in CH_2Cl_2 was added. The liquid was spun down and the tube sealed and heated at 160 °C for 12–24 h. The tube was cooled, the liquid again spun down, the tube opened, and the solution analyzed by GC/MS.

Derivatization of Alkynes. Alkyne (0.5 mg) and 0.5 mL of CH_2Cl_2 were placed in a 4 × 200 mm Pyrex tube. To this solution was added 0.5 mL of 1 or 2. The tube was sealed and heated for 12 h at 130 °C, cooled, and opened and 1 μ L was analyzed by GC/MS. The dialkyltetrachlorobenzenes may be purified by chromagraphy on silica gel using hexane as eluent. Compound 1 gave a much cleaner reaction than compound 2.

Dechlorination of the Dialkyltetrachlorobenzenes. Purified dialkyltetrachlorobenzene (ca. 10 mg) was dissolved in 25 mL of 2-methyl-2-propanol and a 10-fold excess of sodium added. The mixture was refluxed overnight and the excess sodium destroyed by slowly adding methanol. Then the solution was poured into 50 mL of 10% HCl and extracted with two 50-mL portions of CH_2Cl_2 and the organic layer analyzed by GC/MS.

Instrumentation. The products of large scale reactions were identified by using a 6 ft \times ¹/₄ in. glass column packed with 3% OV-17 on 100/120 Supelcoport (Supelco, Bellefonte, PA) in a Perkin-Elmer 990 GC interfaced to a Hitachi RMU-6L mass spectrometer. The GC was programmed from 100 to 330 °C at 24 °C/min with helium as the carrier gas at a flow rate of 40 cm³/min. The solutions obtained in the micro scale experiments were injected (on column) onto a 15 m \times 0.32 mm SE52 fused silica column (J & W Scientific Inc., Rancho Cordova, CA) in a Varian 3700 GC interfaced to a Finnigan-MAT 212 mass spectrometer. The GC was programmed from 100 to 280 °C at 5 °C/min with helium as the carrier gas at a flow rate of 1.2 cm³/min. Both mass spectrometers were operated at an ion source temperature of 200 °C and a ionizing voltage of 70 eV.

RESULTS AND DISCUSSION

The reaction involved in the derivatization is outlined in Scheme I. Figure 1 shows the mass spectra of the derivatives

Table I. Representative Ratios of the Ions from the Adducts of 1 and 2 with Various Olefins

compound	adduct	ion intensity				
		A	В	C	D	E
(Z)-2-pentene	1	100	26	27	7	3
(E)-2-pentene	1	100	3	4	20	6
1-hexene	1	100	а	а	12	18
1-hexene	2	100	a	а	10	19
(Z)-2-decene	1	100	47	51	20	10
(Z)-3-decene	1	100	69	70	17	13
(E)-3-decene	1	100	5	6	12	10
(Z)-4-decene	1	100	72	73	26	14
(E)-4-decene	1	100	2	7	12	13
1-dodecene	1	100	а	а	6	37
(Z)-methyl 6-octadecenoate	2	100	51	56	28	28
(Z)-methyl 9-octadecenoate	2	100	38	52	27	23
(E)-methyl 9-octadecenoate	2	100	7	11	25	22
(E)-methyl 9-octadecenoate	1	100	6	7	8	18
(Z)-methyl 11-octadecenoate	2	100	40	52	16	18
(E)-methyl 11-octadecenoate	2	100	12	16	30	40

Scheme I. Reaction of 1 and 2 with Olefins



Scheme II. Fragmentation Proposed for the Derivatives Resulting from the Addition of 1 or 2 to Olefins



Intensity Selative с m/z 100 200 300 400 с Relative Intensity m/z 200 Relative Intensity з 200 m/z 300 100 400 500 m/z 100 200 300 400 500 Relative

Figure 1. Mass spectra of adducts of (1) (E)-4-decene and 1, (2) (Z)-4-decene and 1, (3) (E)-methyl 9-octadecenoate and 2, (4) (Z)-methyl 9-octadecenoate and 2, (5) (Z)-methyl 9-octadecenoate and 1.

soo

400

500

of (E)- and (Z)-methyl 9-octadecenoate and of (E)- and (Z)-4-decene. The most striking features of these spectra are the chlorine isotope clusters as well as the high abundance of ion A which is due to the loss of a chlorine radical from the molecular ion, itself absent. The major fragmentation pathways are outlined in Scheme II and were confirmed for the

adduct of methyl oleate by linked scanning (10, 11).

200

m/z

100

Compound 1 reacts somewhat faster with olefins than compound 2 so that lower temperatures or shorter reaction times may be used in the derivatization. The spectra of the adducts of both 1 and 2 with (Z)-methyl 9-octadecenoate are shown in Figure 1 and the ions of interest are listed in Table I. Except for the expected mass shifts of the m/z values, both reagents give very similar spectra, with ions B and C enhanced in the adducts derived from 1.

Ion A is the precursor of a number of characteristic ions (see Scheme II). It can lose either of the two R groups along with a hydrogen radical (ions B and C), the elements of HCl (ion D), or both R groups (ion E). For locating the position of the double bond, the formal loss of HR and HR' is the fragmentation of interest. The differences in mass between ion A and ions B and C, respectively, indicate the size of the two R groups and define the location of the double bond in the original olefin. There is the advantage of redundancy in the spectra, the sum of the masses of ions B and C should equal the mass of ion A + 251 (for derivatives with 1) or 249 (for derivatives with 2).

The ratio of the abundance of ions B or C to ion A is indicative of the geometry of the olefin. These ions are at least five times as abundant in the derivatives of Z olefins compared to the E isomers. Representative values of these ratios are listed in Table I. Although the data I show a remarkable consistency in a given series for the ratio of ions B or C to ion A, these data should be used with caution. On truly unknown materials, the ion intensity ratio should always be compared to a closely related material before deducing the geometry of the olefin. However, one does not necessarily need an E/Zpair.

The spectra of the adducts of all olefins also show an ion (E) at m/z 251. (As always the m/z value given is for the ³⁵Cl containing ions even though this may not be the largest ion in a given isotope cluster.) This can be used in conjuction with mass chromatograms to locate the compounds of interest in a complex mixture. Since ion D contains the ethylene ketal moiety, this ion will be found at m/z 253 in the adducts of compound 2.

Whether RH is lost as a neutral molecule or as two radicals (as shown in Scheme II) is open to question. Linked scanning (10, 11) of ion A showed that fragment ions B, C, and D arise directly from it. Most likely, two successive radicals are lost, primarily due to geometric considerations. If the two R groups are cis in ion A, the hydrogen and the R group lost must necessarily be trans. It is hard to envision how the R group and the hydrogen could come within bonding distance, with such a geometry, to be lost in a concerted manner. Although there are many instances in the literature where two radicals are lost successively (12), this is one of the few cases where fragmentation proceeds by loss of three radical groups from the molecular ion. The driving force for these otherwise energetically unfavorable processes (the loss of the second radical) is the formation of an aromatic system or a highly stabilized ion. Thus, it is not too surprising that three radical groups could be lost; the first producing the highly conjugated and stable ion A and the second two groups lost forming the aromatic rings in ions B through E.

In addition to olefins this derivatization method should also be applicable to alkynes. Alkynes are known to react with 1 forming the initially expected adducts (see below). These adducts, under the conditions of their formation, rapidly lose the ketal bridge forming ortho-disubstituted tetrachlorobenzenes (13).



These, like other alkylbenzenes show prominent molecular ions and peaks due to the cleavage of either of the two benzylic bonds, the larger group being most easily lost. This fragmentation is outlined in Scheme III. If both alkyl chains are Scheme III. Fragmentation Proposed for Dialkyltetrachlorobenzenes Derived from Reaction of 1 or 2 with Alkynes and of Their Dechlorination Products



Figure 2. Mass spectra of products from reaction of 1 and (1) 3-decyne, (2) 4-decyne, (3) 5-decyne, and (4, 5) the dechlorination products of the derivatives of 3-decyne and 4-decyne.

longer than three carbons, the rearrangement ion (ion I in Scheme III) becomes the base peak. This facile fragmentation of ions of type H, derived from cleavage of either of the two benzylic bonds, greatly reduces their abundance in favor of ions I. Since these are the ions characteristic for the position of the original triple bond, these derivatives are much less useful for alkynes than alkenes. Figure 2 depicts the spectra of three tetrachlorobenzenes from 3-, 4-, and 5-decyne as well as the corresponding dechlorinated materials. As can be seen, ion H is the base peak for the adduct from 3-decyne, which does not undergo this rearrangement, but for the adducts from 4- and 5-decyne this ion is very small.

SCOPE AND LIMITATIONS

In molecules with polar functional groups, the Diels-Alder reaction is known to be highly sterospecific (14). On the other hand, with nonpolar, unsymmetrical olefins one would expect a mixture of both endo and exo products greatly complicating the GC trace.



Yet under the conditions of the derivatization, only one peak was observed on a capillary column. This may be due either to the known, high temperature reversibility of the Diels-Alder reaction yielding only the thermodynamically more stable product or to the coelution of the two isomers. In any event, the mass spectra of both endo and exo products are expected to be very similar.

In addition to the possibility of generating exo-endo isomers, pairs of enantiomers may also be formed. For example:



This poses no problem as long as the original olefin does not have a chiral center since the enantiomers would not be separated on normal, achiral column packings. On the other hand, with an optically active olefin a mixture of diastereomers would result that may then be separated and used to advantage in the determination of the absolute configuration of an optically active olefin.

The derivatization technique described in this paper works quite well for the disubstituted olefins but is not satisfactory for highly hindered olefins such as (E)-2-methyl methylbut-2-enoate which gave no adduct with either 1 or 2 even after heating for 48 h. Although some trisubstituted olefins such as 2-methyl-2-heptene do produce adducts with 2, the mass spectra of these adducts are dominated by ion A and the other fragments are not of sufficient intensity to allow the position or substitution of the original double bond to be determined.

The large increment in mass upon derivatization of double bonds is somewhat of a problem. It makes the method less useful for polyenes, because the polyadduct would be difficult to elute from a gas chromatographic column. This limitation may diminish in the future with the availability of high temperature, thinly coated, capillary columns which transmit even n-C₅₅H₁₂₂ (15).

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Analysis of the Chemical Ionization Reagent Plasma Produced in Liquid Chromatography/Mass Spectrometry by Direct Liquid Introduction Mass Spectrometry/Mass Spectrometry

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A tandem quadrupole mass spectrometer is used to identify Ion-molecule reaction products in two common reversedphase solvents, acetonitrile/water and methanol/water. The collision-induced dissociation spectra of normal and isotopic labeled solvents and high-resolution data provide the information to deduce the empirical formulas and structures for the cluster ions. The solvent effect on sample protonation and fragmentation is discussed. This solvent reagent study represents the first steps in understanding the spectra obtained by direct liquid introduction LC/MS.

The advantages of liquid chromatography over gas chro-

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matography as a means of sample separation for classes of compounds which are thermally labile, very polar, or nonvolatile have justified the increasing interest in liquid chromatography/mass spectrometry (LC/MS) (1, 2). A variety of interfaces developed to introduce the effluent from the LC into the mass spectrometer include the moving belt (3), silicone membrane separator (4), direct liquid introduction (DLI) (5), atmospheric pressure ionization (6), and the heated wire (7). The DLI method utilizes the solvent as the reagent gas for chemical ionization. Very little has appeared in the literature on the nature of this reagent plasma. Insight into the processes that occur in the source that give rise to analyte ions, the degree of fragmentation observed for the analyte, and the identity of the many solvent cluster ions observed will provide information needed to optimize the technique. This information is important if one wants to choose the best conditions