Organic Structures from 2D NMR Spectra

Instructor's Guide and Solutions Manual

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WILEY

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PREFACE

This book is the Instructor's Guide and Solutions Manual to the problems contained in the text *Organic Structures from 2D NMR Spectra*.

The aim of this book is to teach students to solve structural problems in organic chemistry using NMR spectroscopy and in particular 2D NMR spectroscopy. The basic philosophy of the book is that learning to identify organic structures using spectroscopy is best done by working through examples. This book contains a series of about 60 graded examples ranging from very elementary problems through to very challenging problems at the end of the collection.

We have assumed a working knowledge of basic structural organic chemistry and common functional groups. We also assume a working knowledge of the rudimentary spectroscopic methods which would be applied routinely in characterising and identifying organic compounds including infrared spectroscopy and basic 1D ^{13}C and ^{1}H NMR spectroscopy.

The Instructor's Guide contains a worked solution to each of the problems contained in *Organic Structures from 2D NMR Spectra*. At the outset, it should be emphasised that there are always many paths to the correct answer – there is no single process to arrive at the correct solution to any of the problems. We do not recommend a mechanical attitude to problem solving – intuition, which comes with experience, has a very important place in solving structures from spectra; however, students often find the following approach useful:

(i) **Extract as much information as possible from the basic characterisation data which is provided:**

- *(a)* **Note the molecular formula** and any restrictions this places on the functional groups that may be contained in the molecule.
- *(b)* From the molecular formula, **determine the degree of unsaturation**. The degree of unsaturation can be calculated from the molecular formula for all compounds containing C, H, N, O, S and the halogens using the following three basic steps:
  1. Take the molecular formula and replace all halogens by hydrogens.

2. Omit all of the sulfur and/or oxygen atoms.

3. For each nitrogen, omit the nitrogen and omit one hydrogen.

After these three steps, the molecular formula is reduced to C_nH_m, and the degree of unsaturation is given by:

$$\text{Degree of Unsaturation} = n - {}^{m}/_{2} + 1$$

The degree of unsaturation indicates the number of π bonds and/or rings that the compound contains. For example, if the degree of unsaturation is 1, the molecule can only contain one double bond or one ring. If the degree of unsaturation is 4, the molecule must contain four rings or multiple bonds. An aromatic ring accounts for four degrees of unsaturation (the equivalent of three double bonds and a ring). An alkyne or a C≡N accounts for two degrees of unsaturation (the equivalent of two π bonds).

(c) **Analyse the 1D ^{1}H NMR spectrum** if one is provided and note the relative numbers of protons in different environments and any obvious information contained in the coupling patterns. Note the presence of aromatic protons, exchangeable protons, and/or vinylic protons, all of which provide valuable information on the functional groups which may be present.

(d) **Analyse the 1D ^{13}C NMR spectrum** if one is provided and note the number of carbons in different environments. Note also any resonances that would be characteristic of specific functional groups, *e.g.* the presence or absence of a ketone, aldehyde, ester or carboxylic acid carbonyl resonance.

(e) **Analyse any infrared data** and note whether there are absorptions characteristic of specific functional groups, *e.g.* C=O or –OH groups.

(ii) **Extract basic information from the 2D COSY, TOCSY and/or C–H correlation spectra**.

(a) The COSY will provide obvious coupling partners. If there is one identifiable starting point in a spin system, the COSY will allow the successive identification (*i.e.* the sequence) of all nuclei in the spin system. The COSY cannot jump across breaks in the spin system (such as where there is a heteroatom or a carbonyl group that isolates one spin system from another).

(b) The TOCSY identifies all groups of protons that are in the same spin system.

(c) The C–H correlation links the carbon signals with their attached protons and also identifies how many –CH–, $–CH_2–$, $–CH_3$ and quaternary carbons are in the molecule.

(iii) **Analyse the INADEQUATE spectrum** if one is provided, because this can sequentially provide the whole carbon skeleton of the molecule. Choose one signal as a starting point and sequentially work through the INADEQUATE spectrum to determine which carbons are connected to which.

(iv) **Analyse the HMBC spectrum.** This is perhaps the most useful technique to pull together all of the fragments of a molecule because it gives long-range connectivity.

(v) **Analyse the NOESY spectrum** to assign any stereochemistry in the structure.

(vi) **Continually update the list of structural elements** or fragments that have been conclusively identified at each step and start to pull together reasonable possible structures. Be careful not to jump to possible solutions before the evidence is conclusive. Keep assessing and re-assessing all of the options.

(vii) When you have a final solution which you believe is correct, **go back and confirm that all of the spectroscopic data are consistent with the final structure** and that every peak in every spectrum can be properly rationalised in terms of the structure that you have proposed.

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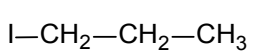
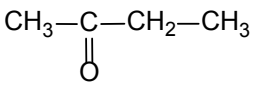
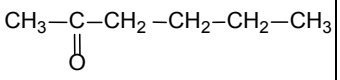
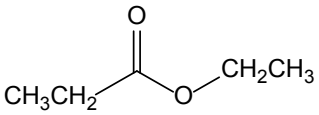
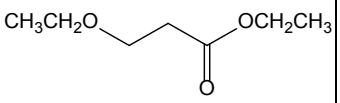
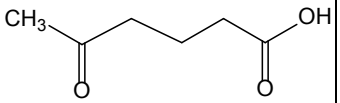
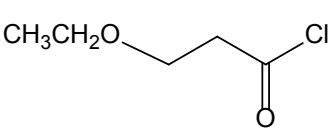
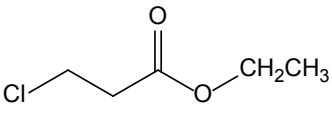
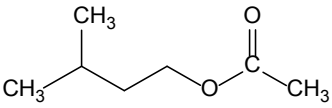
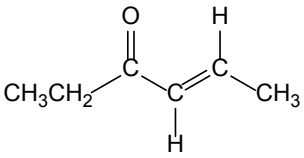
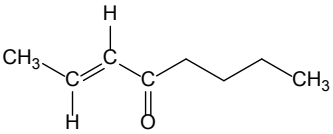
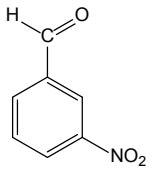
A. M. Magill
January 2015

1	 1-iodopropane C_3H_7I	LABEL COSY HSQC HMBC INADEQUATE
2	 2-butanone C_4H_8O	LABEL COSY HSQC HMBC INADEQUATE
3	 2-hexanone $C_6H_{12}O$	COSY HSQC HMBC
4	 ethyl propionate $C_5H_{10}O_2$	SIMULATE COSY HSQC HMBC
5	 ethyl 3-ethoxypropionate $C_7H_{14}O_3$	LABEL COSY HSQC HMBC
6	 4-acetylbutyric acid $C_6H_{10}O_3$	ASSIGNMENT HSQC HMBC

7	 3-ethoxypropionyl chloride $C_5H_9ClO_2$	COSY HSQC HMBC ISOMER (2)
8	 ethyl 3-chloropropionate $C_5H_9ClO_2$	COSY HSQC HMBC ISOMER (2)
9	 isoamyl acetate $C_7H_{14}O_2$	LABEL COSY HSQC HMBC INADEQUATE
10	 *trans*-4-hexen-3-one $C_6H_{10}O$	LABEL COSY HSQC HMBC NOESY
11	 *trans*-2-octen-4-one $C_8H_{14}O$	COSY HSQC HMBC NOESY
12	 3-nitrobenzaldehyde $C_7H_5NO_3$	LABEL COSY HSQC HMBC NOESY INADEQUATE

Problem 19

Question:

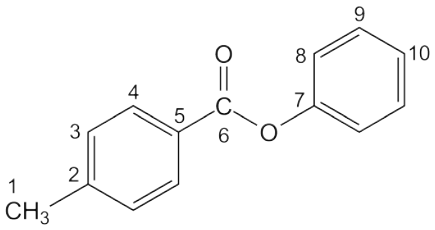
Identify the following compound.

Molecular Formula: $C_{14}H_{12}O_2$

IR: 1720 cm^{-1}

Solution:

Phenyl *p*-toluate



1. The molecular formula is $C_{14}H_{12}O_2$. Calculate the degree of unsaturation from the molecular formula: ignore the O atoms to give an effective molecular formula of $C_{14}H_{12}$ (C_nH_m) which gives the degree of unsaturation as $(n - m/2 + 1) = 14 - 6 + 1 = 9$. The compound contains a combined total of nine rings and/or π bonds.
2. The ^1H NMR spectrum indicates that the compound has nine aromatic protons and three aliphatic protons.
3. The presence of nine aromatic protons suggests two aromatic rings.
4. The three aliphatic protons are equivalent and have no visible splitting so these must be an isolated methyl group.
5. IR and 1D NMR spectra establish that the compound is an ester (quaternary ^{13}C resonance at 165.2 ppm).
6. The presence of two aromatic rings and an ester carbonyl satisfies the degree of unsaturation, so there are no more functional groups with double bonds or rings.
7. The methyl resonance in the ^1H and ^{13}C spectra (2.44 and 21.7 ppm, respectively) eliminates the possibility of a methyl ester, since for a methoxy group both the ^1H and ^{13}C signals would appear significantly further downfield.
8. The ^1H NMR spectrum shows five unique signals in the aromatic region.

Problem 39

Question:

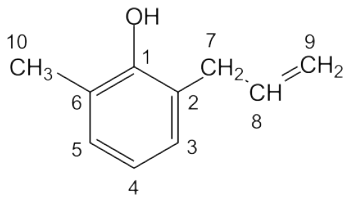
Identify the following compound.

Molecular Formula: $C_{10}H_{12}O$

IR: 3600 (br), 1638, 1594, 1469 (s) cm^{-1}

Solution:

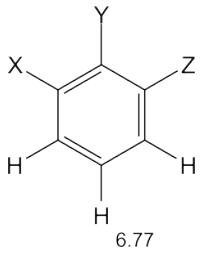
2-Allyl-6-methylphenol



1. The molecular formula is $C_{10}H_{12}O$. Calculate the degree of unsaturation from the molecular formula: ignore the O atom to give an effective molecular formula of $C_{10}H_{12}$ (C_nH_m) which gives the degree of unsaturation as $(n - m/2 + 1) = 10 - 6 + 1 = 5$. The compound contains a combined total of five rings and/or π bonds.

2. 1D spectra establish that the compound is a trisubstituted benzene. The aromatic ring accounts for four degrees of unsaturation and the remaining degree of unsaturation is accounted for by a double bond (alkene ^1H resonances at 5.99 and 5.15 ppm).

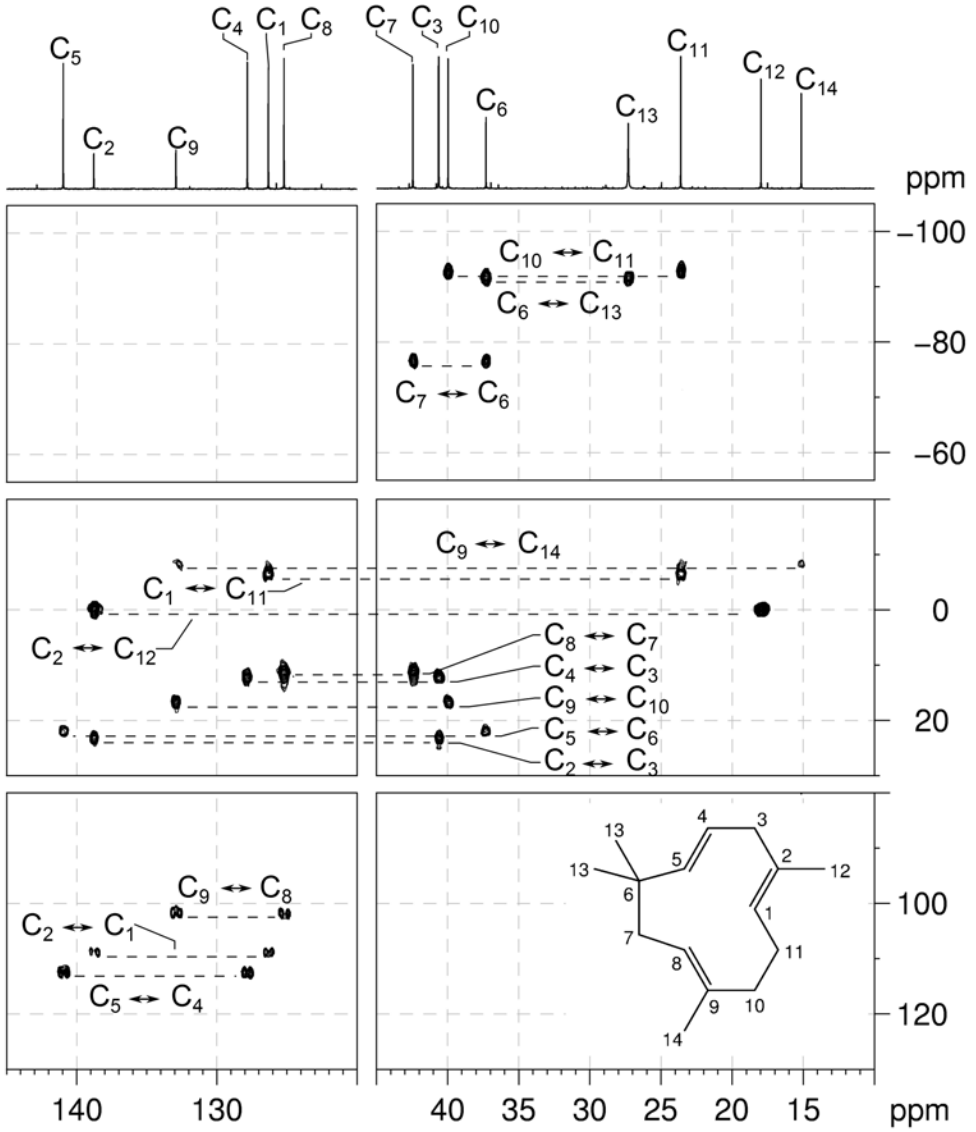
3. The coupling pattern in the aromatic region of the ^1H NMR spectrum shows that the three protons on the aromatic ring must occupy adjacent positions. The proton at 6.77 ppm is the proton at the middle of the spin system since it has two large splittings (*i.e.* it has two *ortho*-protons) whereas the other two aromatic protons each have only one large splitting.



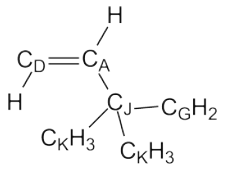
4. The three substituents on the aromatic ring must therefore be in adjacent positions *i.e.* this compound is a "1,2,3-trisubstituted benzene".

5. 1D spectra establish that two of the substituents are an –OH substituent (^1H resonance at 4.99 ppm, exchangeable) and a $–CH_3$ group (three proton resonance at 2.21 ppm).

INADEQUATE spectrum of α-humulene ($C_2D_2Cl_4$, 150 MHz, 338 K)



7. We will only work in one direction, so let us work from C_J. This resonance has two further correlations in the INADEQUATE spectrum – one to the resonance at 27.3 ppm (C_K, which, according to the integrations in the ^{1}H NMR spectrum, corresponds to a pair of geminal methyl groups) and the second to the resonance at 42.4 ppm (C_G, a methylene group).



8. C_K has no further correlations as it is a pair of terminal geminal methyl groups.