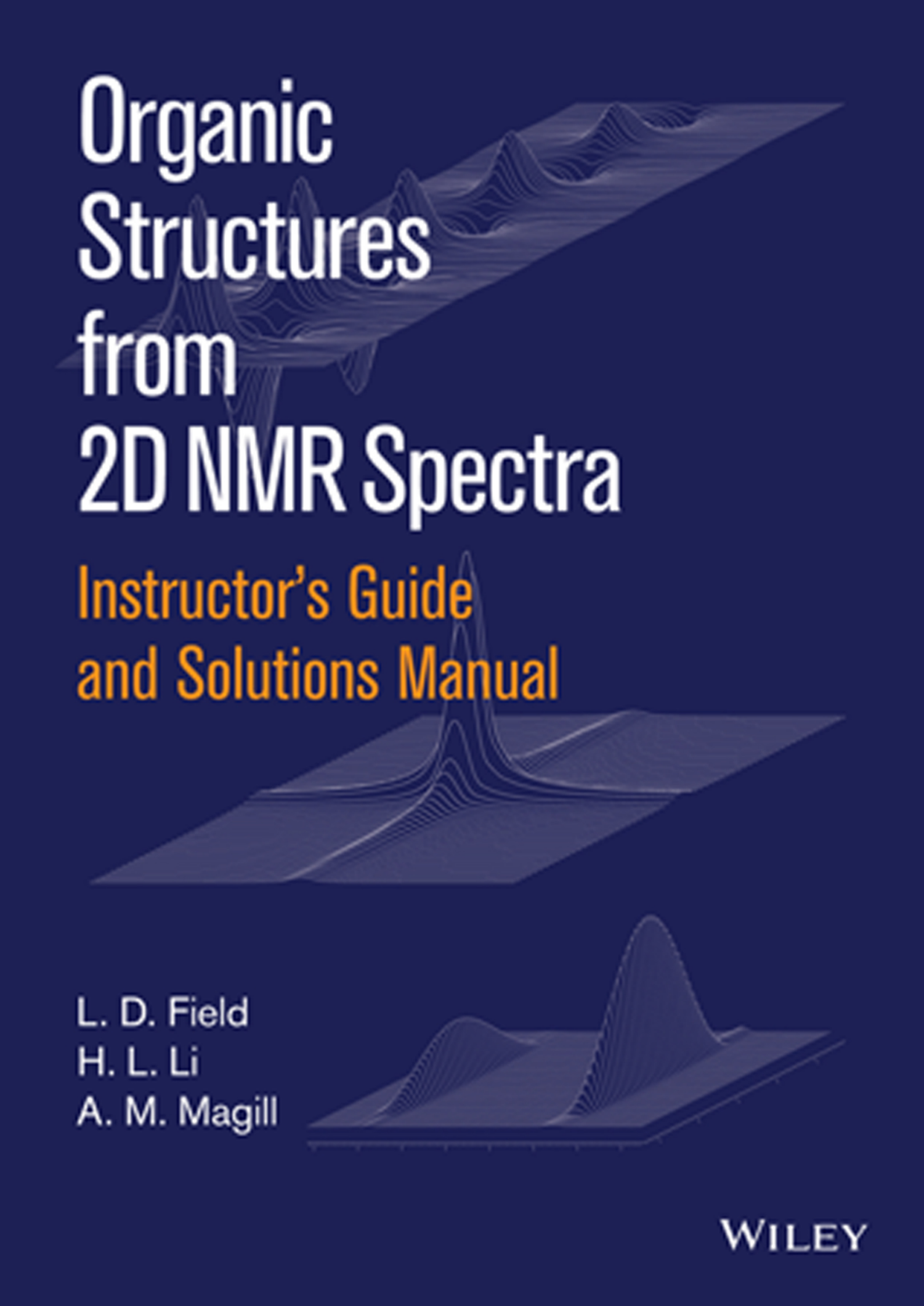


Organic Structures from 2D NMR Spectra

The background of the cover features three stylized, 3D-rendered 2D NMR spectra. The top spectrum shows a series of peaks of varying heights. The middle spectrum shows a single, sharp, prominent peak. The bottom spectrum shows two distinct peaks, one broader and one sharper.

Instructor's Guide and Solutions Manual

L. D. Field
H. L. Li
A. M. Magill

WILEY

Instructor's Guide and Solutions
Manual to Organic Structures
from 2D NMR Spectra

Instructor's Guide and Solutions Manual to Organic Structures from 2D NMR Spectra

L. D. Field, H. L. Li and A. M. Magill

School of Chemistry, University of New South Wales, Australia

WILEY

This edition first published 2015
© 2015 John Wiley & Sons Ltd

Registered office

John Wiley & Sons Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, United Kingdom

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com.

The right of the author to be identified as the author of this work has been asserted in accordance with the Copyright, Designs and Patents Act 1988.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the publisher.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book.

Limit of Liability/Disclaimer of Warranty: While the publisher and author have used their best efforts in preparing this book, they make no representations or warranties with respect to the accuracy or completeness of the contents of this book and specifically disclaim any implied warranties of merchantability or fitness for a particular purpose. It is sold on the understanding that the publisher is not engaged in rendering professional services and neither the publisher nor the author shall be liable for damages arising herefrom. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

Library of Congress Cataloging-in-Publication Data

Field, L. D.

Instructor's guide and solutions manual to organic structures from 2D NMR spectra /
L.D. Field, H.L. Li and A.M. Magill.

pages cm

ISBN 978-1-119-02725-6 (pbk.)

1. Nuclear magnetic resonance spectroscopy—Problems, exercises, etc. 2. Spectrum analysis—Problems, exercises, etc. I. Li, H. L. (Hsiu L.) II. Magill, A. M. (Alison M.) III. Title. IV. Title: Organic structures from 2D NMR spectra. Instructor's guide and solutions manual. V. Title: 2D NMR spectra.

QD96.N8F54 2015b

543'.66—dc23

2015009524

A catalogue record for this book is available from the British Library.

ISBN: 9781119027256

Set in 12/18pt Times New Roman by Aptara Inc., New Delhi, India.

CONTENTS

Preface	ix
Solutions Summary	1
Problem 1 (1-iodopropane)	7
Problem 2 (2-butanone)	11
Problem 3 (2-hexanone)	15
Problem 4 (ethyl propionate)	19
Problem 5 (ethyl 3-ethoxypropionate)	23
Problem 6 (4-acetylbutyric acid)	28
Problem 7 (3-ethoxypropionyl chloride)	32
Problem 8 (ethyl 3-chloropropionate)	36
Problem 9 (isoamyl acetate)	40
Problem 10 (<i>trans</i> -4-hexen-3-one)	45
Problem 11 (<i>trans</i> -2-octen-4-one)	50
Problem 12 (3-nitrobenzaldehyde)	55
Problem 13 (3-iodotoluene)	61
Problem 14 (8-hydroxy-5-nitroquinoline)	64
Problem 15 (2-bromo-3-picoline)	69
Problem 16 (<i>trans</i> -anethole)	72
Problem 17 (<i>cis</i> -2-pentene)	75
Problem 18 (<i>p</i> -tolyl benzoate)	79
Problem 19 (phenyl <i>p</i> -toluate)	86
Problem 20 (4-biphenyl acetate)	93
Problem 21 (4'-phenoxyacetophenone)	99
Problem 22 (4'- <i>tert</i> -butylacetophenone)	106

Contents

Problem 23 (2,2,4'-trimethylpropiophenone)	110
Problem 24 (<i>trans</i> -2-methyl-3-phenyl-2-propen-1-ol)	114
Problem 25 (methyl 4-ethoxybenzoate)	119
Problem 26 (methyl 3-(<i>p</i> -tolyl)propionate)	123
Problem 27 (4-(4'-methoxyphenyl)-2-butanone)	127
Problem 28 (ethyl 6-bromohexanoate)	132
Problem 29 (piperonal)	135
Problem 30 (<i>cis</i> -3-hexenyl benzoate)	139
Problem 31 (<i>trans</i> -2, <i>cis</i> -6-nonadienal)	146
Problem 32 (allyl glycidyl ether)	155
Problem 33 (3,4-epoxy-4-methyl-2-pentanone)	159
Problem 34 (dl-methionine)	162
Problem 35 (<i>N</i> -acetyl- <i>l</i> -leucine)	165
Problem 36 (isoamyl valerate)	170
Problem 37 ((<i>E</i>)-4-methyl-4'-nitrostilbene)	173
Problem 38 (2- <i>tert</i> -butyl-6-methylphenol)	181
Problem 39 (2-allyl-6-methylphenol)	186
Problem 40 (2-hydroxy-4-methoxybenzaldehyde)	194
Problem 41 (2'-hydroxy-5'-methylacetophenone)	198
Problem 42 (3'-fluoro-4'-methoxyacetophenone)	203
Problem 43 (<i>trans</i> -ferulic acid)	209
Problem 44 (sec-butyl 3-hydroxycinnamate)	215
Problem 45 (1-benzosuberone)	221
Problem 46 (dimethyl (3-bromopropyl)phosphonate)	228
Problem 47 (caffeine)	233
Problem 48 (benzyloxypropionitrile)	238
Problem 49 (cineole)	242
Problem 50 (thymoquinone)	246

Problem 51 (4-bromo-1-indanol)	251
Problem 52 (1-bromo-4-methylnaphthalene)	257
Problem 53 (carvacrol)	264
Problem 54 (acetoacetanilide)	272
Problem 55 (ethyl acetamidocyanoacetate)	277
Problem 56 (α-humulene)	283
Problem 57 (3,4-dihydro-2<i>H</i>-benzopyran-3-carboxylic acid)	289
Problem 58 (quinidine)	296
Problem 59 (salbutamol)	312
Problem 60 (2-hydroxy-1-naphthaldehyde)	322
Problem 61 (6-methyl-4-chromanone)	329
Problem 62 (citronellal)	336
Problem 63 ((+)-<i>cis</i>-2-oxabicyclo-[3.3.0]oct-6-en-3-one)	344
Problem 64 (melatonin)	349
Problem 65 (carvone)	362
Problem 66 (haloperidol)	370

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 ^1H 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:

$$\text{Degree of Unsaturation} = n - \frac{m}{2} + 1$$

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 $C \equiv N$ accounts for two degrees of unsaturation (the equivalent of two π bonds).

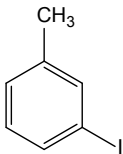
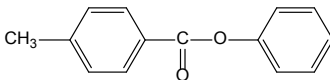
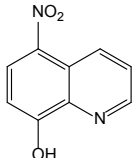
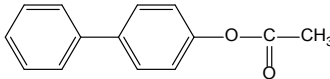
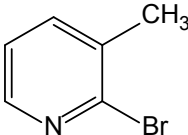
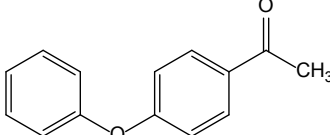
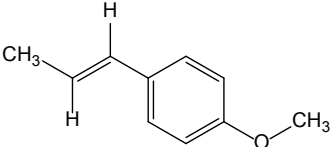
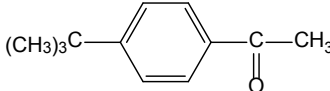
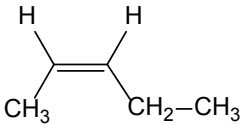
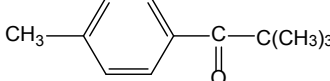
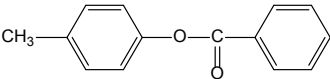
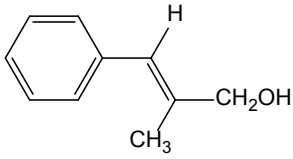
- (c) **Analyse the 1D 1H NMR spectrum** if one is provided and note the relative numbers of protons in different environments and any obvious information contained in the coupling patterns. Note the presence of aromatic protons, exchangeable protons, and/or vinylic protons, all of which provide valuable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

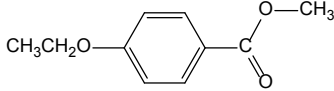
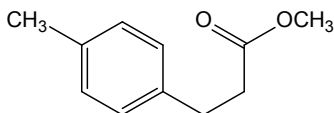
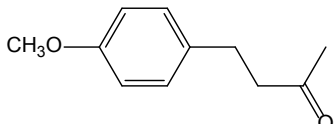
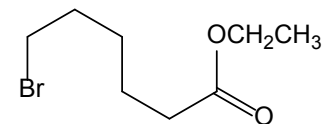
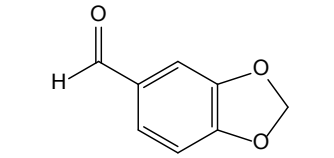
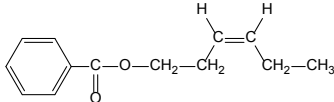
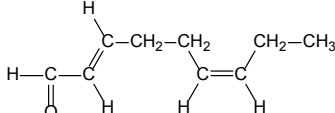
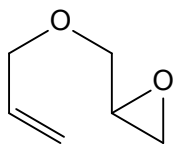
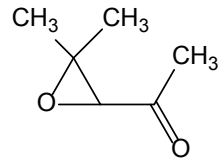
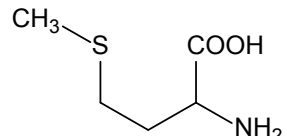
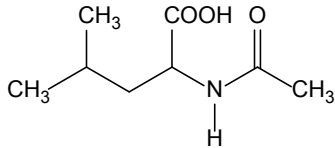
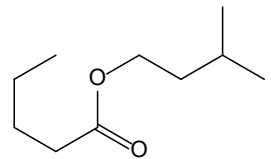
- (b) The TOCSY identifies all groups of protons that are in the same spin system.
- (c) The C–H correlation links the carbon signals with their attached protons and also identifies how many –CH–, –CH₂–, –CH₃ and quaternary carbons are in the molecule.
- (iii) **Analyse the INADEQUATE spectrum** if one 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.

L. D. Field
H. L. Li
A. M. Magill
January 2015

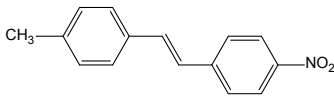
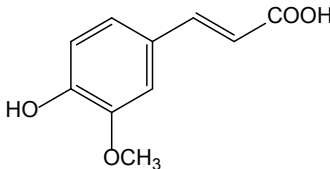
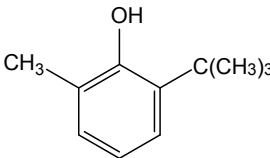
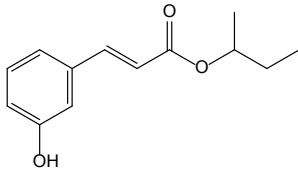
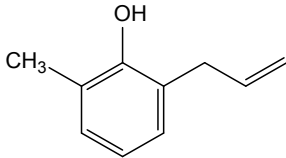
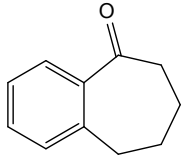
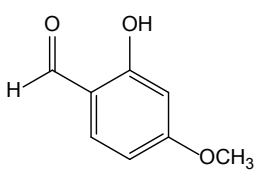
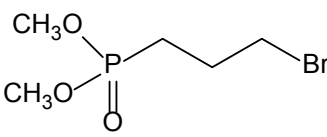
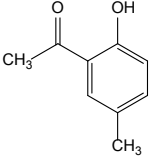
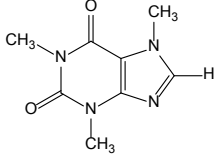
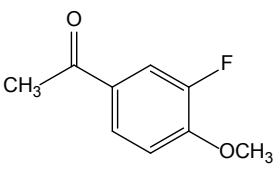
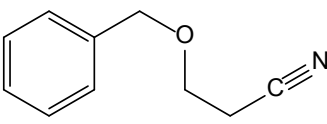
1	$\text{I}-\text{CH}_2-\text{CH}_2-\text{CH}_3$ 1-iodopropane $\text{C}_3\text{H}_7\text{I}$	LABEL COSY HSQC HMBC INADEQUATE
2	$\text{CH}_3-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_3$ 2-butanone $\text{C}_4\text{H}_8\text{O}$	LABEL COSY HSQC HMBC INADEQUATE
3	$\text{CH}_3-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$ 2-hexanone $\text{C}_6\text{H}_{12}\text{O}$	COSY HSQC HMBC
4	$\text{CH}_3\text{CH}_2-\text{C}(=\text{O})-\text{O}-\text{CH}_2\text{CH}_3$ ethyl propionate $\text{C}_5\text{H}_{10}\text{O}_2$	SIMULATE COSY HSQC HMBC
5	$\text{CH}_3\text{CH}_2\text{O}-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{O}-\text{CH}_2\text{CH}_3$ ethyl 3-ethoxypropionate $\text{C}_7\text{H}_{14}\text{O}_3$	LABEL COSY HSQC HMBC
6	$\text{CH}_3-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{OH}$ 4-acetylbutyric acid $\text{C}_6\text{H}_{10}\text{O}_3$	ASSIGNMENT HSQC HMBC
7	$\text{CH}_3\text{CH}_2\text{O}-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{Cl}$ 3-ethoxypropionyl chloride $\text{C}_5\text{H}_9\text{ClO}_2$	COSY HSQC HMBC ISOMER (2)
8	$\text{Cl}-\text{CH}_2-\text{CH}_2-\text{C}(=\text{O})-\text{O}-\text{CH}_2\text{CH}_3$ ethyl 3-chloropropionate $\text{C}_5\text{H}_9\text{ClO}_2$	COSY HSQC HMBC ISOMER (2)
9	$\text{CH}_3-\text{CH}(\text{CH}_3)-\text{CH}_2-\text{CH}_2-\text{O}-\text{C}(=\text{O})-\text{CH}_3$ isoamyl acetate $\text{C}_7\text{H}_{14}\text{O}_2$	LABEL COSY HSQC HMBC INADEQUATE
10	$\text{CH}_3\text{CH}_2-\text{C}(=\text{O})-\text{CH}=\text{CH}-\text{CH}_3$ <i>trans</i> -4-hexen-3-one $\text{C}_6\text{H}_{10}\text{O}$	LABEL COSY HSQC HMBC NOESY
11	$\text{CH}_3-\text{CH}=\text{CH}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_3$ <i>trans</i> -2-octen-4-one $\text{C}_8\text{H}_{14}\text{O}$	COSY HSQC HMBC NOESY
12	$\text{H}-\text{C}(=\text{O})-\text{C}_6\text{H}_4-\text{NO}_2$ 3-nitrobenzaldehyde $\text{C}_7\text{H}_5\text{NO}_3$	LABEL COSY HSQC HMBC NOESY INADEQUATE

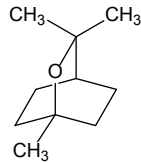
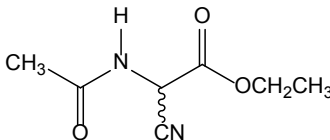
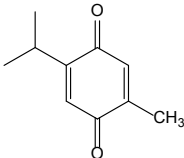
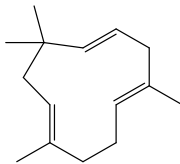
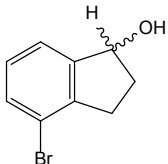
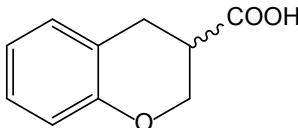
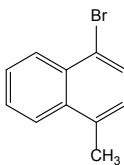
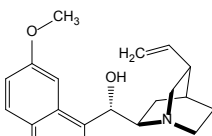
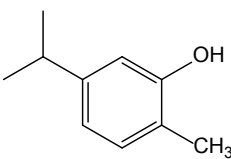
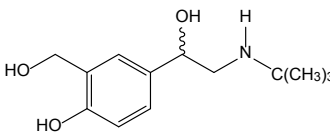
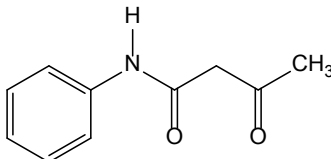
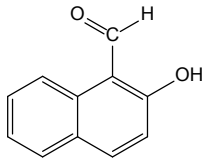
Organic Structures from 2D NMR Spectra

13  <p>3-iodotoluene</p> <p>C_7H_6I</p>	SIMULATE HSQC HMBC	19  <p>phenyl <i>p</i>-toluate</p> <p>$C_{14}H_{12}O_2$</p>	COSY HSQC HMBC ISOMER (4)
14  <p>8-hydroxy-5-nitroquinoline</p> <p>$C_9H_6N_2O_3$</p>	LABEL COSY HSQC HMBC INADEQUATE	20  <p>4-biphenyl acetate</p> <p>$C_{14}H_{12}O_2$</p>	COSY HSQC HMBC ISOMER (4)
15  <p>2-bromo-3-picoline</p> <p>C_6H_6BrN</p>	HSQC HMBC	21  <p>4'-phenoxyacetophenone</p> <p>$C_{14}H_{12}O_2$</p>	COSY HSQC HMBC ISOMER (4)
16  <p><i>trans</i>-anethole</p> <p>$C_{10}H_{12}O$</p>	SIMULATE COSY NOESY	22  <p>4'-<i>tert</i>-butylacetophenone</p> <p>$C_{12}H_{16}O$</p>	HSQC HMBC ISOMER (2)
17  <p><i>cis</i>-2-pentene</p> <p>C_5H_{10}</p>	COSY HSQC NOESY	23  <p>2,2,4'-trimethylpropiophenone</p> <p>$C_{12}H_{16}O$</p>	HSQC HMBC ISOMER (2)
18  <p><i>p</i>-tolyl benzoate</p> <p>$C_{14}H_{12}O_2$</p>	COSY HSQC HMBC ISOMER (4)	24  <p><i>trans</i>-2-methyl-3-phenyl-2-propen-1-ol</p> <p>$C_{10}H_{12}O$</p>	COSY HSQC HMBC NOESY

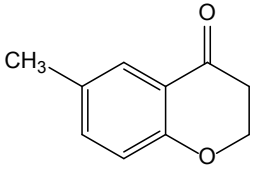
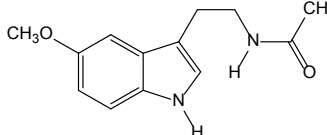
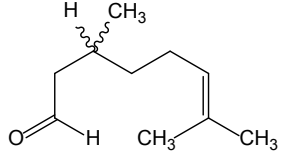
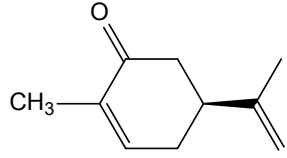
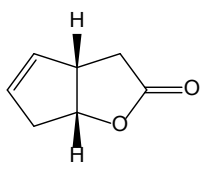
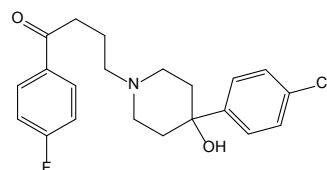
25  methyl 4-ethoxybenzoate $C_{10}H_{12}O_3$	COSY HSQC HMBC
26  methyl 3-(p-tolyl)propionate $C_{11}H_{14}O_2$	COSY HSQC HMBC ISOMER (2)
27  4-(4'-methoxyphenyl)-2-butanone $C_{11}H_{14}O_2$	HSQC INADEQUATE ISOMER (2)
28  ethyl 6-bromohexanoate $C_8H_{15}BrO_2$	ASSIGNMENT COSY HSQC
29  piperonal $C_8H_6O_3$	SIMULATE HSQC HMBC
30  cis-3-hexenyl benzoate $C_{13}H_{16}O_2$	COSY HSQC HMBC NOESY
31  trans-2,cis-6-nonadienal $C_9H_{14}O$	COSY HSQC HMBC NOESY
32  allyl glycidyl ether $C_6H_{10}O_2$	COSY HSQC HMBC ISOMER (2)
33  3,4-epoxy-4-methyl-2-pentanone $C_6H_{10}O_2$	HSQC HMBC ISOMER (2)
34  dl-methionine $C_5H_{11}NO_2S$	IDENTIFY 1 HSQC HMBC
35  N-acetyl-L-leucine $C_8H_{15}NO_3$	COSY HSQC HMBC
36  isoamyl valerate $C_{10}H_{20}O_2$	TOCSY HSQC

Organic Structures from 2D NMR Spectra

37  <p>(<i>E</i>)-4-methyl-4'-nitrostilbene</p> <p>$C_{15}H_{13}NO_2$</p>	ASSIGNMENT COSY HSQC HMBC	43  <p><i>trans</i>-ferulic Acid</p> <p>$C_{10}H_{10}O_4$</p>	COSY HSQC HMBC
38  <p>2-<i>tert</i>-butyl-6-methylphenol</p> <p>$C_{11}H_{16}O$</p>	HSQC HMBC	44  <p><i>sec</i>-butyl 3-hydroxycinnamate</p> <p>$C_{13}H_{16}O_3$</p>	COSY HSQC HMBC
39  <p>2-allyl-6-methylphenol</p> <p>$C_{10}H_{12}O$</p>	COSY HSQC HMBC	45  <p>1-benzosuberone</p> <p>$C_{11}H_{12}O$</p>	ASSIGNMENT COSY HSQC HMBC
40  <p>2-hydroxy-4-methoxybenzaldehyde</p> <p>$C_8H_8O_3$</p>	HSQC HMBC	46  <p>dimethyl (3-bromopropyl)phosphonate</p> <p>$C_5H_{12}BrO_3P$</p>	COSY HSQC P-H HMBC HETEROATOM
41  <p>2'-hydroxy-5'-methylacetophenone</p> <p>$C_9H_{10}O_2$</p>	HSQC HMBC	47  <p>caffeine</p> <p>$C_8H_{10}N_4O_2$</p>	ASSIGNMENT HSQC HMBC N-H HSQC HETEROATOM
42  <p>3'-fluoro-4'-methoxyacetophenone</p> <p>$C_9H_9FO_2$</p>	HSQC NOESY HETEROATOM	48  <p>benzyloxypropionitrile</p> <p>$C_{10}H_{11}NO$</p>	COSY HSQC HMBC

49  <p>cineole</p> <p>$C_{10}H_{18}O$</p>	HSQC INADEQUATE	55  <p>ethyl acetamido- cyanoacetate</p> <p>$C_7H_{10}N_2O_3$</p>	COSY HSQC HMBC N-H HSQC N-H HMBC
50  <p>thymoquinone</p> <p>$C_{10}H_{12}O_2$</p>	IDENTIFY 1 HSQC HMBC	56  <p>α-Humulene</p> <p>$C_{15}H_{24}$</p>	HSQC INADEQUATE
51  <p>4-bromo-1-indanol</p> <p>C_9H_9BrO</p>	COSY HSQC HMBC	57  <p>3,4-dihydro-2<i>H</i>-benzo- pyran-3-carboxylic acid</p> <p>$C_{10}H_{10}O_3$</p>	COSY HSQC HMBC
52  <p>1-bromo-4-methylnaphthalene</p> <p>$C_{11}H_9Br$</p>	ASSIGNMENT COSY HSQC HMBC	58  <p>quinidine</p> <p>$C_{20}H_{24}N_2O_2$</p>	ASSIGNMENT COSY HSQC HMBC NOESY
53  <p>carvacrol</p> <p>$C_{10}H_{14}O$</p>	COSY HSQC HMBC	59  <p>salbutamol</p> <p>$C_{13}H_{21}NO_3$</p>	COSY HSQC HMBC NOESY N-H HMBC HETEROATOM
54  <p>acetoacetanilide</p> <p>$C_{10}H_{11}NO_2$</p>	HSQC HMBC NOESY	60  <p>2-hydroxy-1-naphthaldehyde</p> <p>$C_{11}H_8O_2$</p>	COSY HSQC HMBC

Organic Structures from 2D NMR Spectra

<p>61</p>  <p>6-methyl-4-chromanone</p> <p>$C_{10}H_{10}O_2$</p>	<p>HSQC HMBC INADEQUATE</p>	<p>64</p>  <p>melatonin</p> <p>$C_{13}H_{16}N_2O_2$</p>	<p>COSY HSQC HMBC NOESY N-H HSQC N-H HMBC HETEROATOM</p>
<p>62</p>  <p>citronellal</p> <p>$C_{10}H_{18}O$</p>	<p>COSY HSQC HMBC</p>	<p>65</p>  <p>carvone</p> <p>$C_{10}H_{14}O$</p>	<p>COSY HSQC HMBC</p>
<p>63</p>  <p>(+)-cis-2-oxabicyclo- [3.3.0]oct-6-en-3-one</p> <p>$C_7H_8O_2$</p>	<p>COSY HSQC HMBC NOESY</p>	<p>66</p>  <p>haloperidol</p> <p>$C_{21}H_{23}ClFNO_2$</p>	<p>ASSIGNMENT COSY HSQC HMBC HETEROATOM</p>

Problem 1

Question:

The ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of 1-iodopropane ($\text{C}_3\text{H}_7\text{I}$) recorded in CDCl_3 solution at 298 K and 400 MHz are given below.

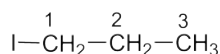
The ^1H NMR spectrum has signals at δ 0.99 (H_3), 1.84 (H_2) and 3.18 (H_1) ppm.

The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum has signals at δ 9.6 (C_1), 15.3 (C_3) and 26.9 (C_2) ppm.

Also given on the following pages are the ^1H - ^1H COSY, ^1H - ^{13}C me-HSQC, ^1H - ^{13}C HMBC and INADEQUATE spectra. For each 2D spectrum, indicate which correlation gives rise to each cross-peak by placing an appropriate label in the box provided (e.g. $\text{H}_1 \rightarrow \text{H}_2$, $\text{H}_1 \rightarrow \text{C}_1$).

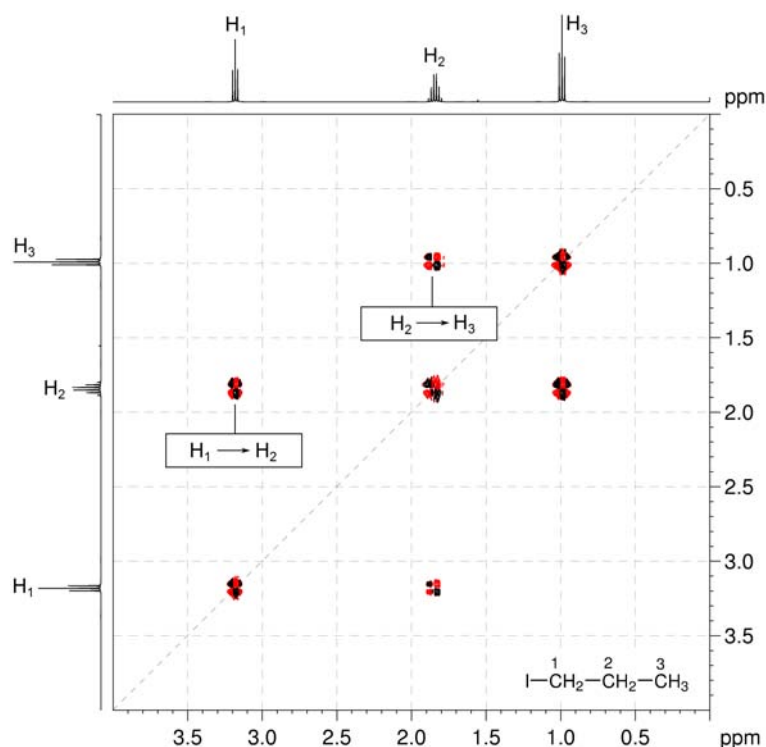
Solution:

1-iodopropane



- ^1H - ^1H COSY spectra show which pairs of protons are coupled to each other. The COSY spectrum is always symmetrical about a diagonal. In the COSY spectrum, there are two $^3J_{\text{H-H}}$ correlations above the diagonal ($\text{H}_1 \rightarrow \text{H}_2$ and $\text{H}_2 \rightarrow \text{H}_3$). There are no long-range correlations.

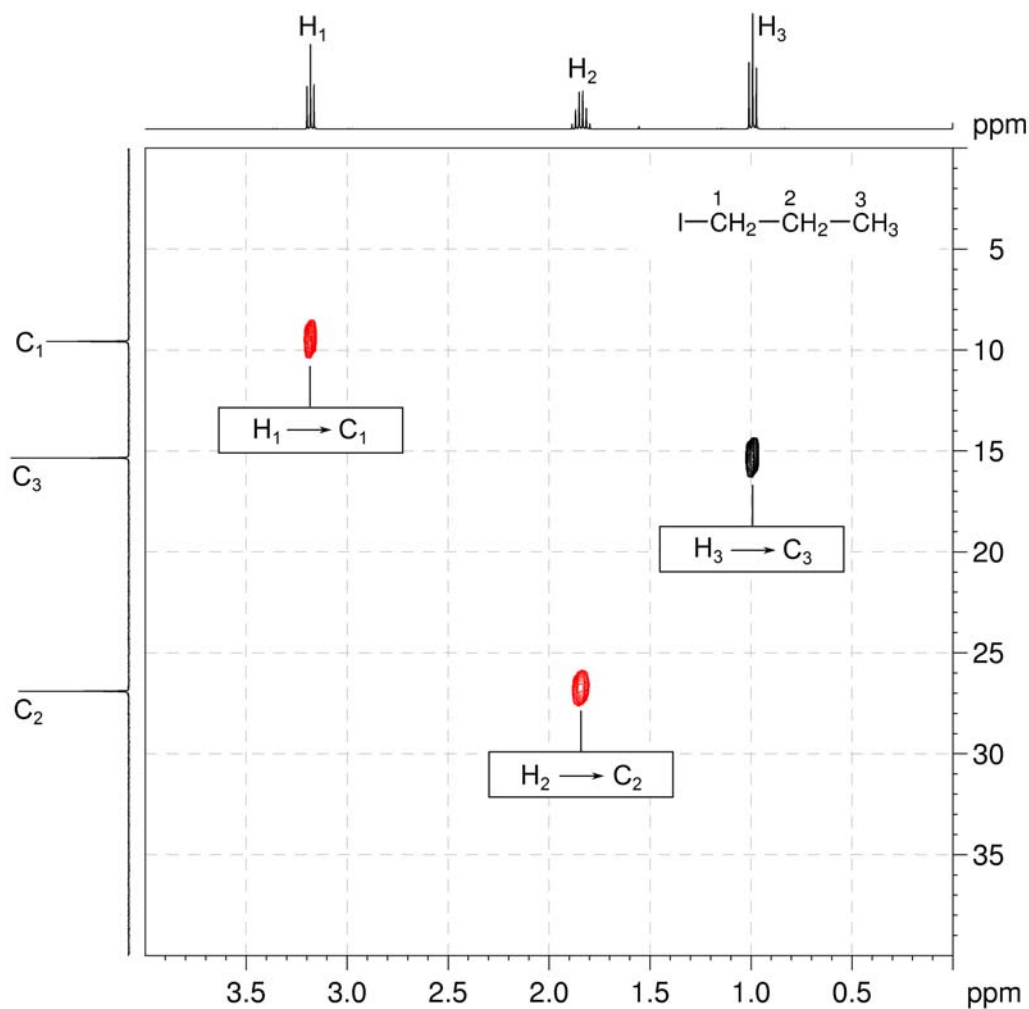
^1H - ^1H COSY spectrum of 1-iodopropane (CDCl_3 , 400 MHz)



Organic Structures from 2D NMR Spectra

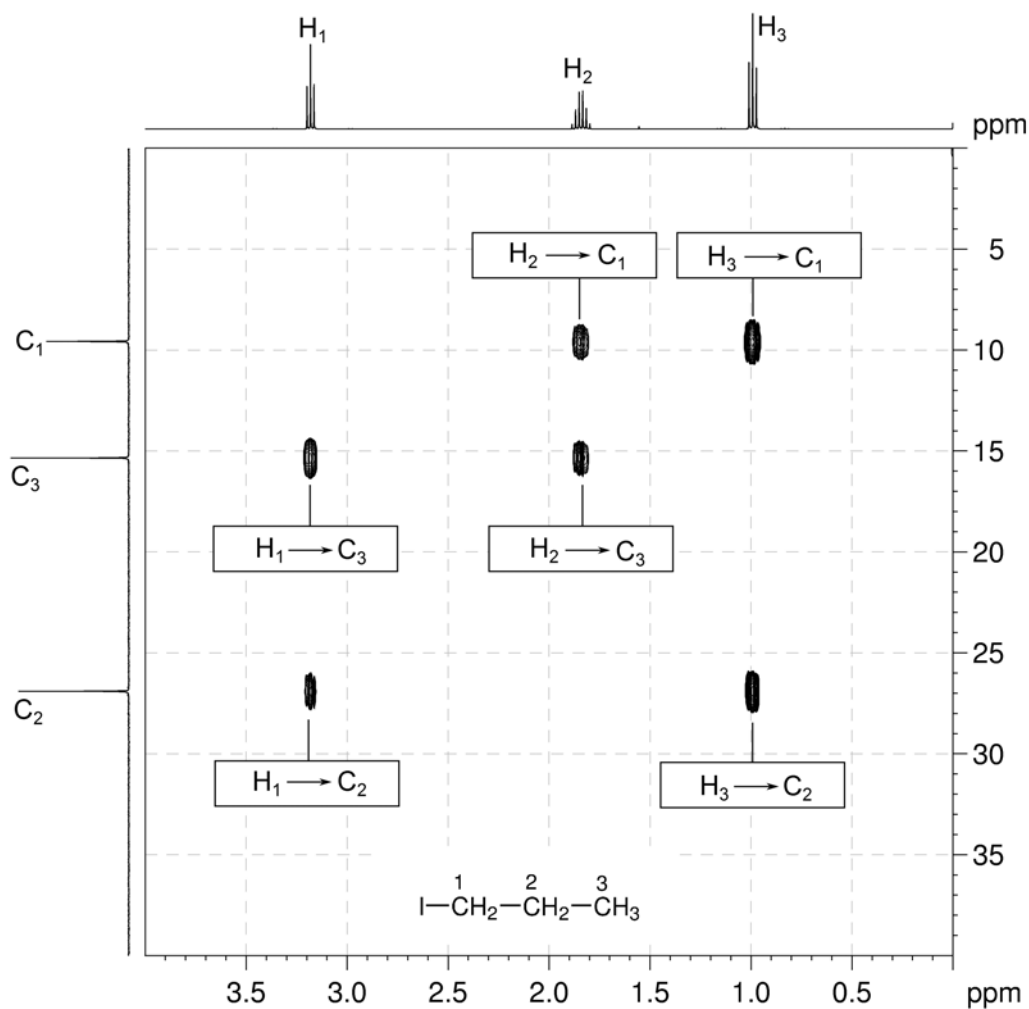
2. The ^1H - ^{13}C me-HSQC spectrum shows direct (one-bond) correlations between proton and carbon nuclei, so there will be cross-peaks between H_1 and C_1 , H_2 and C_2 and also between H_3 and C_3 . As the spectrum is multiplicity edited, the cross-peaks corresponding to CH_2 groups are shown in red and are of opposite phase to those for CH_3 groups.

^1H - ^{13}C me-HSQC spectrum of 1-iodopropane (CDCl_3 , 400 MHz)



3. In HMBC spectra, remember that, for alkyl systems, both two- and three-bond C–H coupling can give rise to strong cross-peaks.
4. H_1 correlates to C_2 and C_3 . H_2 correlates to C_1 and C_3 . H_3 correlates to C_1 and C_2 .

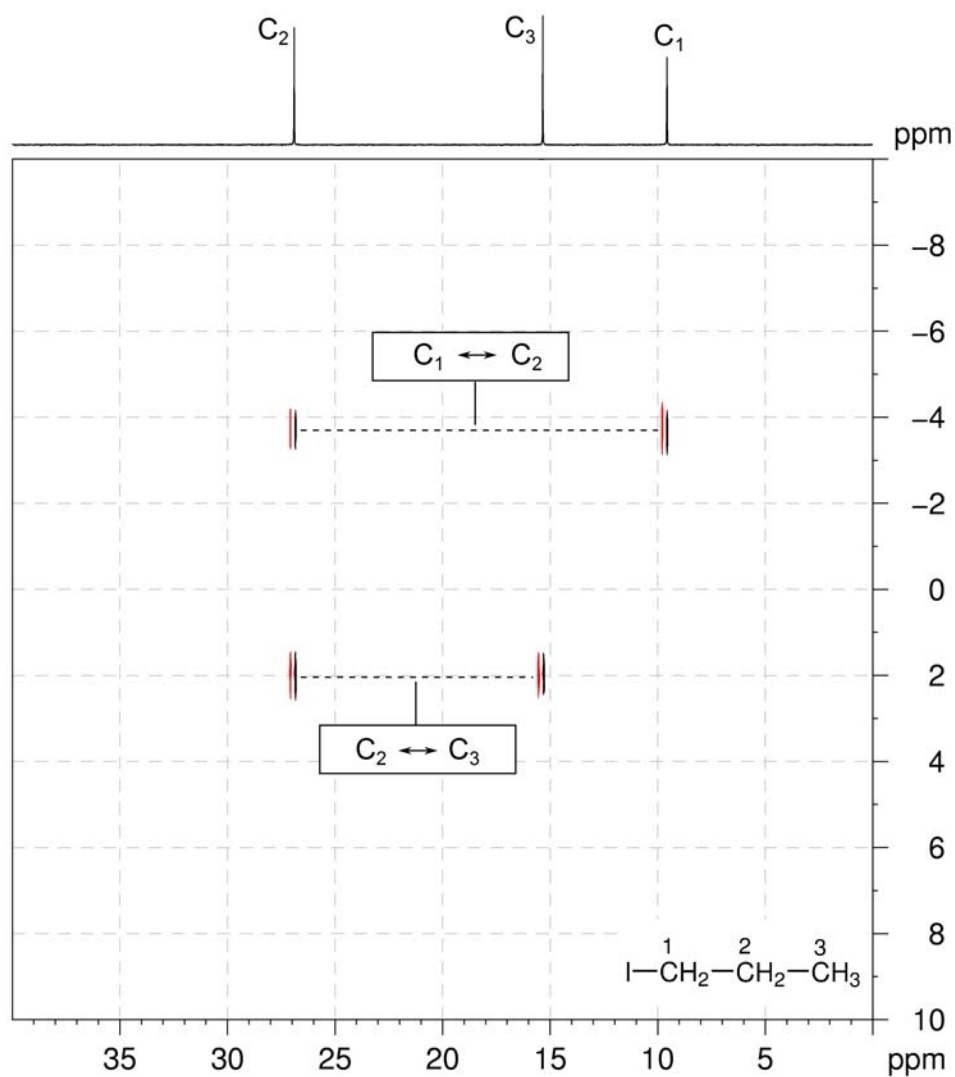
^1H – ^{13}C HMBC spectrum of 1-iodopropane (CDCl_3 , 400 MHz)



Organic Structures from 2D NMR Spectra

5. The INADEQUATE spectrum shows one-bond ^{13}C - ^{13}C connectivity. There are correlations between C_1 and C_2 , and C_2 and C_3 .

INADEQUATE spectrum of 1-iodopropane (CDCl_3 , 150 MHz)



Problem 2

Question:

The ^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of 2-butanone ($\text{C}_4\text{H}_8\text{O}$) recorded in CDCl_3 solution at 298 K and 400 MHz are given below.

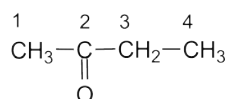
The ^1H NMR spectrum has signals at δ 1.05 (H_4), 2.14 (H_1) and 2.47 (H_3) ppm.

The $^{13}\text{C}\{^1\text{H}\}$ NMR spectrum has signals at δ 7.2 (C_4), 28.8 (C_1), 36.2 (C_3) and 208.8 (C_2) ppm.

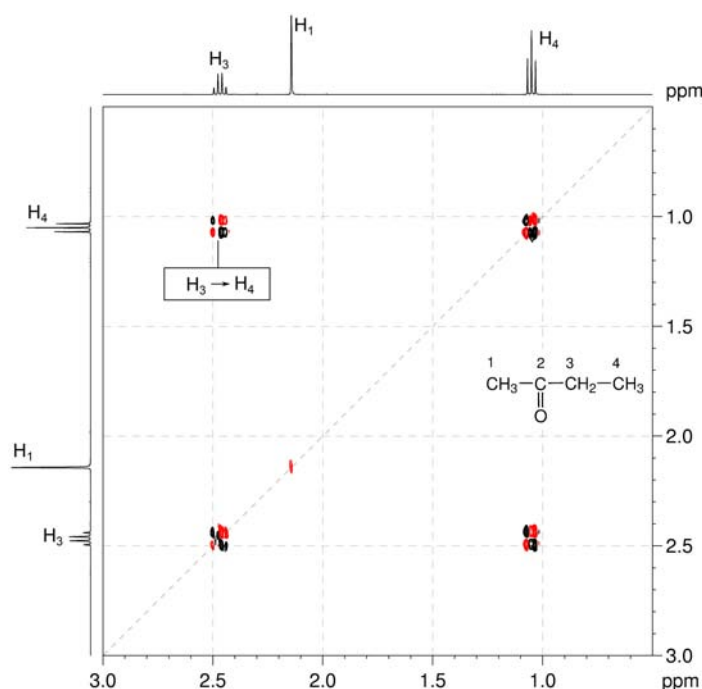
Also given on the following pages are the ^1H - ^1H COSY, ^1H - ^{13}C me-HSQC, ^1H - ^{13}C HMBC and INADEQUATE spectra. For each 2D spectrum, indicate which correlation gives rise to each cross-peak by placing an appropriate label in the box provided (*e.g.* $\text{H}_1 \rightarrow \text{H}_2$, $\text{H}_1 \rightarrow \text{C}_1$).

Solution:

2-Butanone



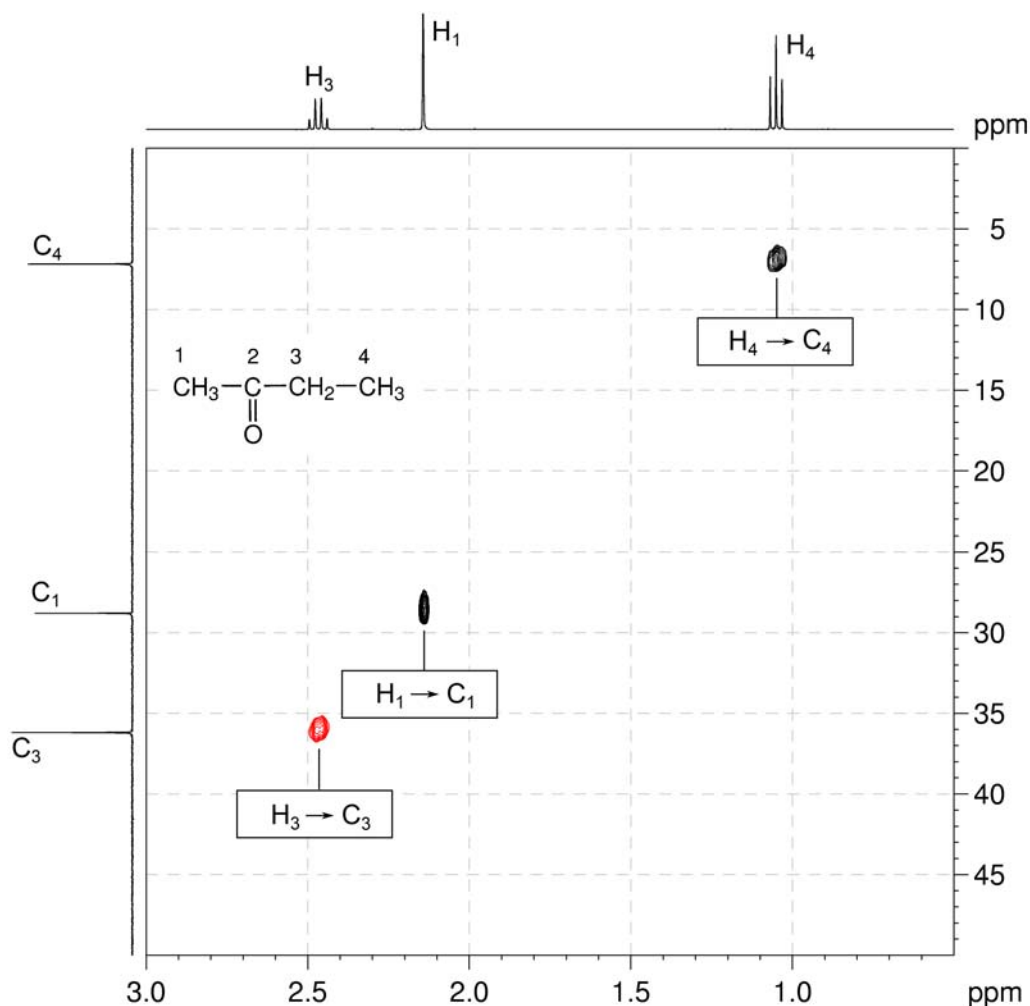
- ^1H - ^1H COSY spectra show which pairs of protons are coupled to each other. The COSY spectrum is always symmetrical about a diagonal. In the COSY spectrum, there is only one $^3J_{\text{H-H}}$ correlation above the diagonal ($\text{H}_3 \rightarrow \text{H}_4$). There are no long-range correlations.

 ^1H - ^1H COSY spectrum of 2-butanone (CDCl_3 , 400 MHz)

Organic Structures from 2D NMR Spectra

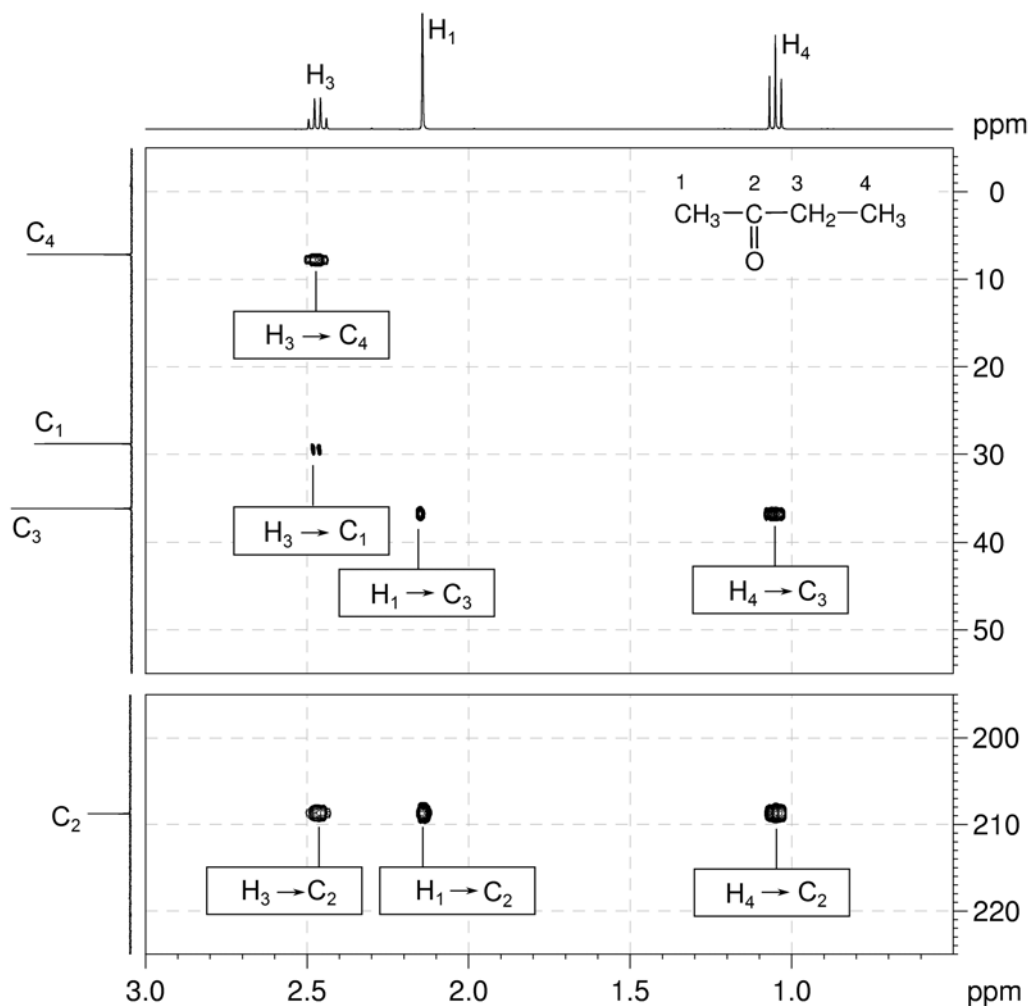
2. The ^1H - ^{13}C me-HSQC spectrum shows direct (one-bond) correlations between proton and carbon nuclei, so there will be cross-peaks between H_1 and C_1 , H_3 and also between C_3 and H_4 and C_4 . As the spectrum is multiplicity edited, the cross-peaks corresponding to CH_2 groups are shown in red and are of opposite phase to those for CH_3 groups.

^1H - ^{13}C me-HSQC spectrum of 2-butanone (CDCl_3 , 400 MHz)



- In HMBC spectra, remember that, for alkyl systems, both two- and three-bond coupling can give rise to strong cross-peaks. There are no one-bond C–H correlations.
- H₁ correlates to C₂ and C₃. H₃ correlates to C₁, C₂ and C₄. H₄ correlates to C₂ and C₃.

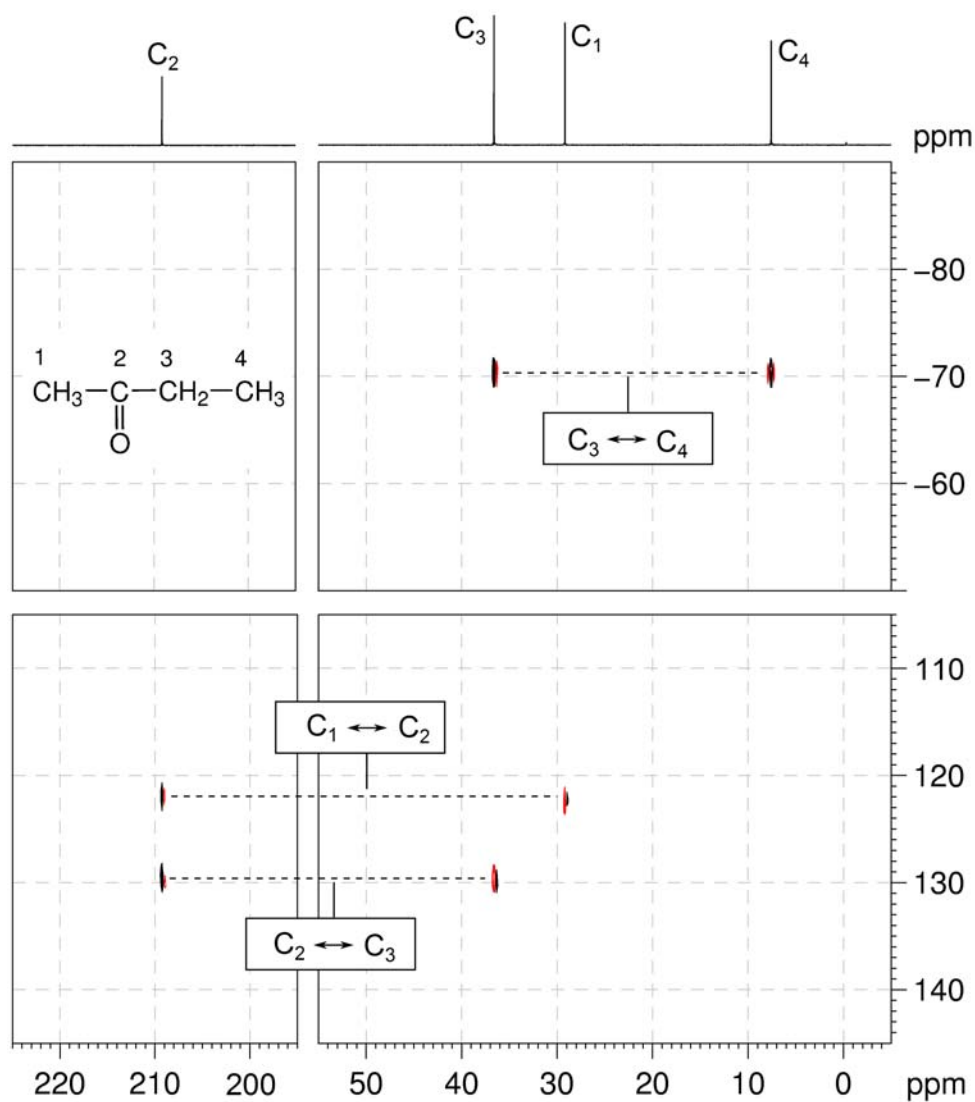
¹H–¹³C HMBC spectrum of 2-butanone (CDCl₃, 400 MHz)



Organic Structures from 2D NMR Spectra

5. The INADEQUATE spectrum shows one-bond ^{13}C – ^{13}C connectivity. There are correlations between C_1 and C_2 , C_2 and C_3 and C_3 and C_4 .

INADEQUATE spectrum of 2-butanone (CDCl_3 , 150 MHz)



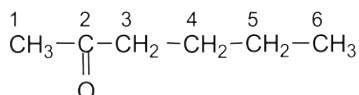
Problem 3

Question:

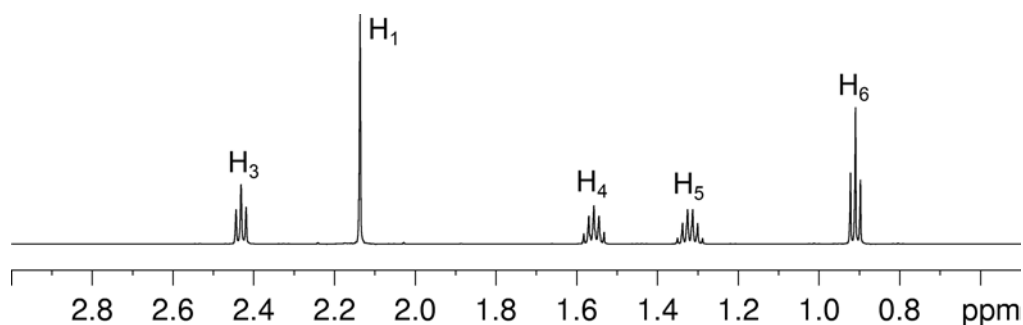
Identify the following compound.

Molecular Formula: $C_6H_{12}O$

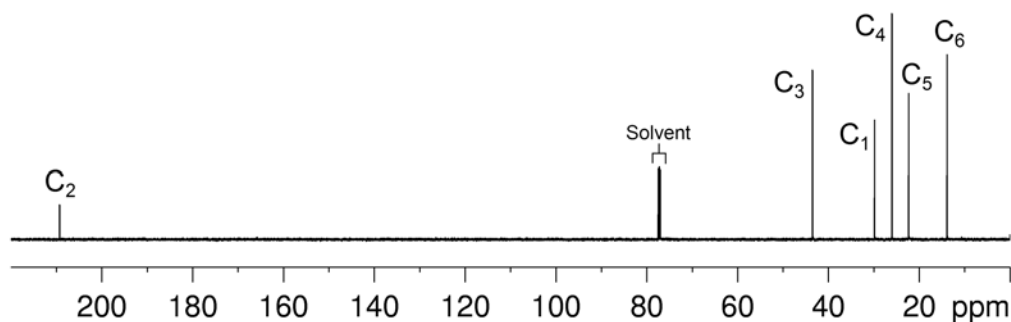
IR: 1718 cm^{-1}

Solution:**2-Hexanone**

1. The molecular formula is $C_6H_{12}O$. Calculate the degree of unsaturation from the molecular formula: ignore the O atom to give an effective molecular formula of C_6H_{12} (C_nH_m) which gives the degree of unsaturation as $(n - m/2 + 1) = 6 - 6 + 1 = 1$. The compound contains one ring or one functional group containing a double bond.
2. The $^{13}\text{C}\{^1\text{H}\}$ spectrum establishes that the compound contains a ketone (^{13}C resonance at 209.3 ppm). There can be no other double bonds or rings in the molecule because the $\text{C}=\text{O}$ accounts for the single degree of unsaturation.
3. 1D NMR spectra establish the presence of three CH_2 groups and two CH_3 groups. The multiplicities of the signals can be verified using the me-HSQC spectrum.

 ^1H NMR spectrum of 2-hexanone (CDCl_3 , 600 MHz)

$^{13}\text{C}\{^1\text{H}\}$ NMR spectrum of 2-hexanone (CDCl_3 , 150 MHz)



- The COSY spectrum shows a single spin system – $\text{H}_3 \rightarrow \text{H}_4$, $\text{H}_4 \rightarrow \text{H}_5$ and $\text{H}_5 \rightarrow \text{H}_6$ for a $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ fragment.
- H_1 does not couple to any of the other protons in the molecule and therefore does not show any correlations in the COSY spectrum.

$^1\text{H}-^1\text{H}$ COSY spectrum of 2-hexanone (CDCl_3 , 600 MHz)

