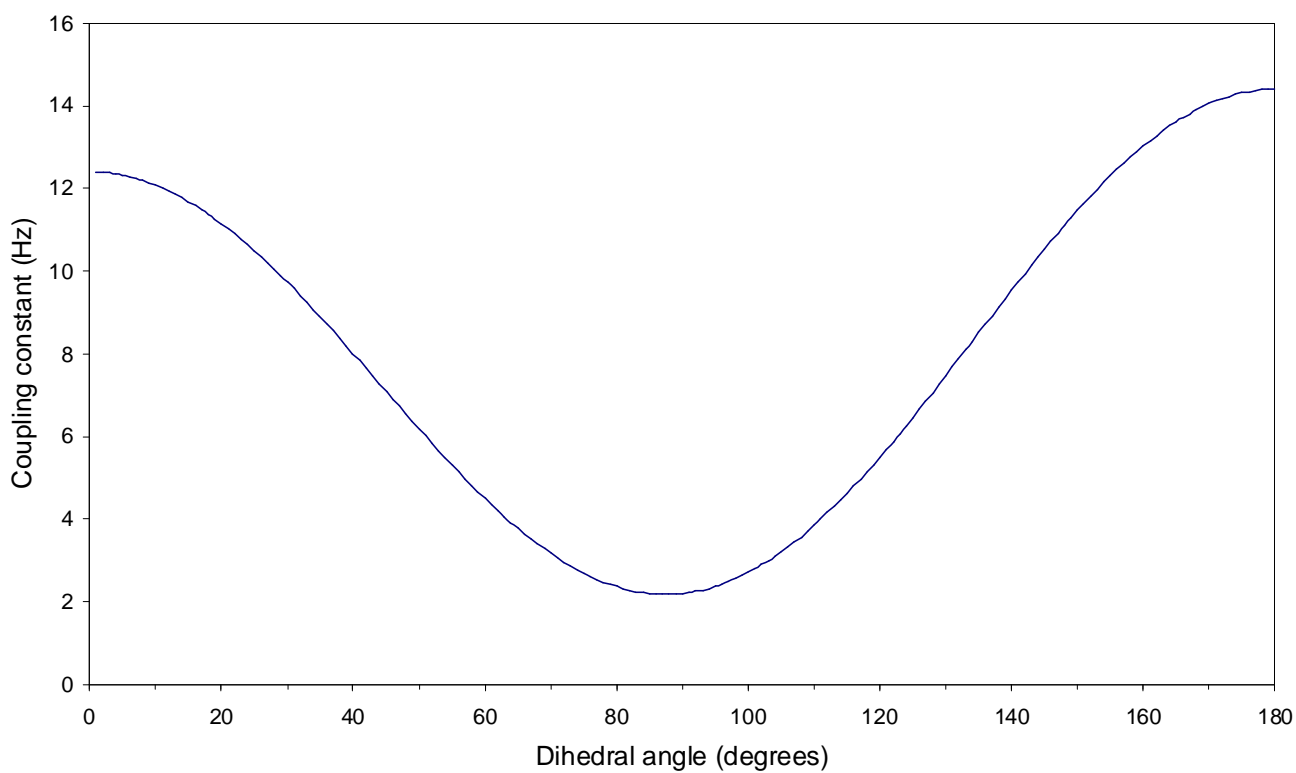


Problems for Organic Structure Analysis

Professor Marcel Jaspars

Throughout these problems use the following:

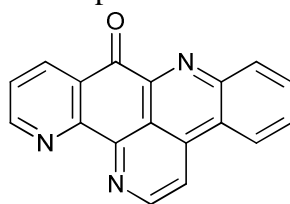
Karplus curve



Jan 2010 EAQ 1

The 1D (^1H , ^{13}C) and 2D NMR (^1H - ^1H COSY, ^1H - ^{13}C HMBC) data for the marine invertebrate compound ascididemin are given below.

- Use the ^1H - ^1H COSY data to construct three spin systems. Indicate on the structure of ascididemin where these belong. (4)
- Explain the multiplicities (coupling patterns) observed for each proton in the three spin systems. (4)
- Assign all the ^1H and ^{13}C NMR chemical shifts to the structure of ascididemin using the data provided. Explain your reasoning. Are there any chemical shifts that cannot be assigned using the data given? (10)
- Give an additional 2D NMR experiment that could provide additional data to confirm your assignment and explain how it would help. (2)



Ascididemin

1D and 2D NMR data of ascididemin in CDCl_3 at 400 MHz

Atom No	$\delta^{13}\text{C}/\text{ppm}$		$\delta^1\text{H}/\text{ppm}$	mult J/Hz	^1H - ^1H COSY H \rightarrow H	HMBC C \rightarrow H
1	181.9	C				C1-H9
2	155.7	CH	9.11	<i>dd</i> , 4.8, 1.8	H2-H9, H2-H14	C2-H9, C2-H14
3	152.5	C				C3-H2, C3-H9
4	149.9	CH	9.22	<i>d</i> , 5.6	H4-H18	C4-H18
5	149.8	C				C5-H4, C5-H18
6	146.1	C				C6-H11, C6-H16
7	145.9	C				
8	138.2	C				C8-H4, C8-H16
9	136.8	CH	8.70	<i>dd</i> , 8.0, 1.8	H9-H14	C9-H2
10	133.2	CH	8.52	<i>dd</i> , 7.7, 1.3	H10-H11	C10-H12
11	132.1	CH	7.94	<i>ddd</i> , 8.2, 7.7, 1.3	H11-H10, H11-H12	C11-H16
12	131.1	CH	7.89	<i>ddd</i> , 8.2, 7.7, 1.3	H12-H11, H12-H16	C12-H10
13	129.2	C				C13-H14
14	125.8	CH	7.60	<i>dd</i> , 8.0, 4.8	H14-H7, H14-H9	C14-H2
15	123.7	C				C15-H18
16	123.2	CH	8.63	<i>dd</i> , 7.7, 1.3	H16-H12	C16-H10
17	118.2	C				C17-H18
18	117.1	CH	8.48	<i>d</i> , 5.6	H18-H4	C18-H4

Jan 2010 EAQ2

A marine invertebrate derived compound contains C, H, O, N and I. The MS, 1D and 2D NMR data is given below.

- Use the data to calculate the molecular formula. (4)
- Use the COSY data to construct 2 spin systems. (6)
- Using the remaining atoms construct a final spin system, taking account of the symmetry and crucial HMBC correlations. (5)
- Using the remaining HMBC correlations, propose a structure that is consistent with all the data. (5)

MS (M^+) 506.9192 m/z

IR 1660, 1630 cm^{-1}

Atom label	δ_C (ppm)	δ_H (ppm) mult, int	1H - 1H COSY correlations	1H - ^{13}C HMBC correlations
A	167.7 C	-		A-h, A-k
B	157.7 C	-		B-c, B-j
C	140.2 2CH	7.76 s, 2H		C-c, C-l
D	138.9 C	-		D-k
E	134.6 C	-		E-g
F	131.8 CH	7.52 t, 1H	f-g	F-h
G	128.7 2CH	7.46 t, 2H	g-f, g-h	G-g
H	126.9 2CH	7.73 d, 2H	h-g	H-f, H-h
I	90.6 2C	-		I-c
J	60.7 CH_3	3.86 s, 3H		
K	41.0 CH_2	3.67 q, 2H	k-l, k-NH	K-l
L	34.0 CH_2	2.84 t, 2H	l-k	L-c
NH	-	6.14 bs	NH-k	

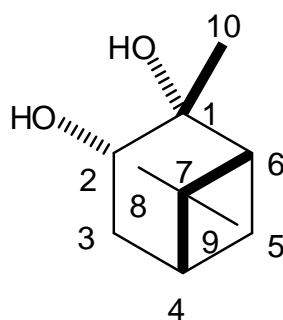
H = 1.0078; C = 12.0000; N = 14.0031; O = 15.9949; I = 126.9045

Jan 2009 EAQ1

The structure of pinanediol is given below together with 1D and 2D NMR data.

Use this data to:

- Assign all the ^1H and ^{13}C chemical shifts. Show how you have used the data to derive your conclusions. (12)
- Draw a clear conformational drawing of pinanediol and indicate how you can use the NOESY data to confirm your assignments in part a.) and use this data to determine the orientation of MeI and MeJ. Also determine the relative stereochemistry of protons f/f' and h/h'. (8)

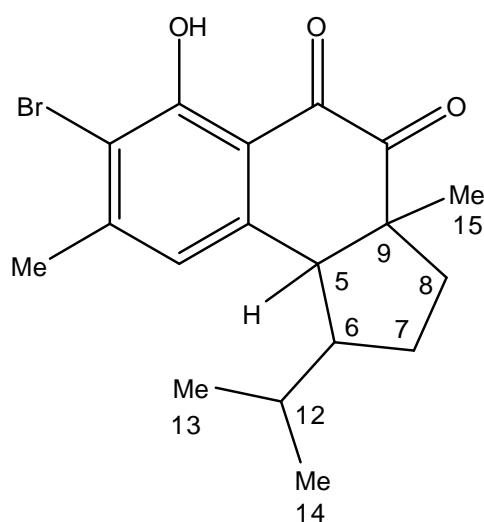


Pinanediol

Atom label	δ_{C} (ppm), mult	δ_{H} (ppm) mult, J/Hz	^1H - ^1H COSY correlations	^1H - ^{13}C long range correlations	^1H - ^1H NOESY correlations
A	73.9 s	-		A-f, A-h', A-g	
B	69.2 d	3.96 dd 5.1, 9.4	b-f/f'	B-f', B-g	b-f/f', b-g, b-j
C	54.0 d	1.99 t 5.7	c-d, c-h	C-i, C-j	
D	40.6 d	1.90 m	d-c, d-h	D-i, D-j	d-f/f'
E	39.0 d	-		E-f', E-h', E-i, E-j	
F	38.1 t	2.43 m	f-b, f-f'	F-h'	f-b, f-d, f-j
F'		1.62 m	f'-b, f'-f		f'-b, f'-d
G	29.7 q	1.28 s			g-b
H	28.2 t	2.17 m	h-c, h-d, h-h'	H-f/f'	h-h', h-i
H'		1.35 d 5.0	h'-h		h'-h
I	27.9 q	1.25 s	i-j		i-h
J	24.2 q	0.91 s	j-i	J-i	j-b, j-f

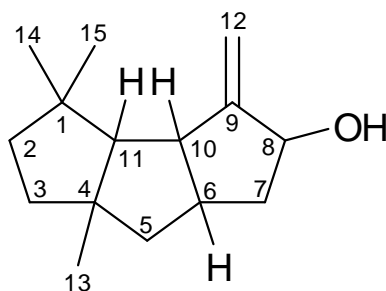
Jan 2009 EAQ2

- a.) Describe how proton-proton coupling constants and NOE data can be used to determine the relative stereochemistry of cyclic molecules. Use a specific example to illustrate your answer and give details of the process that needs to be carried out. (8)
- b.) Hamigeran B, isolated from a sponge has the plane structure given below. The ^1H NMR data with coupling constants as well as selected NOE data has been given in the table below.
 - i. Use the NOE data to determine the relative stereochemistry around the five membered ring. Draw a clear conformational drawing and explain your reasoning. (7)
 - ii. The coupling constant data for H5 and H8a are given in the table. Use the Karplus curve below and your answer to (b)(i) to explain the size of the H5 coupling constant and assign the coupling constants for H8a to specific coupling partners. (5)



Hamigeran B

Atom	δ_{H} (ppm, mult, J/Hz)	NOE correlations
5	3.39, d, 9.3	H6, H7a, H8a, Me15
6	2.31, m	
7a	1.81, m	
7b	1.69, m	8b, H12, Me14
8a	2.63, ddd, 13.0, 9.6, 5.4	
8b	1.56, m	
9	-	
12	1.21, m	
13	0.53, d, 6.5	
14	0.45, d, 6.5	
15	1.29, s	

*Capnellene*

Capnellene was isolated from the Indonesian soft coral *Capnella imbricata*. The ^1H NMR data has been provided below.

NMR data for capnellene at 400 MHz in CDCl_3

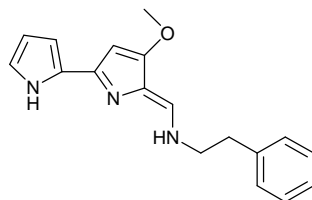
	$\delta^1\text{H}$ (mult, J Hz)	NOE data
H2	1.51 m	H2-H3b
H3a	2.09 m	
H3b	1.45 m	H3b-Me15, H3b-H2
H5a	1.79 dd 13.8, 8.4	
H5b	1.51 dd 13.8, 4.6	H5b-H6, H5b-Me15
H6	2.22 dddd 11.6, 8.4, 4.6, 3.5	H6-H5b
H7a	2.13 ddd 14.2, 8.4, 3.5	H7a-H11
H7b	1.39 dd 14.2, 4.2	
H8	4.74 dd 8.4, 4.2	
H10	2.36 dd 11.6, 3.3	
H11	1.75 d 3.3	H11-Me14, H11-H12a, H11-H7a, H11-Me13
H12a	5.05 d 2.5	H12a-H11,
H12b	4.96 d 2.5	
Me13	1.24 s	Me13-H11,
Me14	1.02 s	Me14-Me15, Me14-H11
Me15	0.82 s	Me15-Me14, Me15-H5b, Me15-H3b

- Draw the structure, labelling protons on carbons 5, 6, 7, 8, 10, 11. Use the data table above to indicate the coupling constants between these protons. Explain why one of the expected couplings between H6 and H7b is missing. (6)
- Use the information from part a. to propose two possible relative stereochemistries between protons H6, H10, H11. A Karplus curve is given below. (6)
- Use the NOE data given to confirm the relative stereochemistry determined in part b. and the relative stereochemistry of Me13, Me14, Me15. What is the stereochemistry of the ring junctions? Draw a clear stereochemical diagram to explain your answer. (8)

2007 EAQ1

The alkaloid tambjamine F was isolated from the marine invertebrate *Sigillina signifera*. The ^1H , ^{13}C , HSQC, COSY and HMBC data are given in Table 1 below. Use this information to:

- Assign all ^1H NMR shifts explaining your reasoning. (6)
- Assign all ^{13}C NMR shifts explaining your reasoning. (8)
- Indicate how the COSY data are consistent with your assignments. (2)
- Indicate how the HMBC data are consistent with your assignments. (4)



Tambjamine F

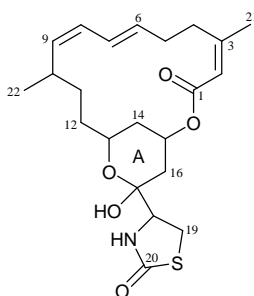
Table 1. 1D and 2D NMR spectral data for tambjamine F obtained in CDCl_3 at 400/100 MHz (δ in ppm).

Atom	δ ^{13}C /ppm	mult	δ ^1H /ppm, integral, mult, J/Hz	^1H - ^1H COSY (H \rightarrow H)	^{13}C - ^1H HMBC (C \rightarrow H)
C1	164.5	C			H-14
C2	143.7	C			H-10
C3	140.3	CH	7.07 (1H, d, 14.7)	NH2	H-15
C4	137.4	C			H-15, H-16, H-6
C5	129.1	CH	7.18 (2H, m)	H-6, H-7	H-6, H-7
(2C)					
C6	129.0	CH	7.26 (2H, m)	H-5	H-16, H-5, H-7
(2C)					
C7	127.1	CH	7.19 (1H, m)	H-5	H-5
C8	124.8	CH	7.07 (1H, bs)	H-12	
C9	122.5	C			H-8
C10	114.1	CH	6.72 (1H, bs)	H-12	H-8
C11	110.9	C			H-13, H-3
C12	110.9	CH	6.30 (1H, m)	H-10, H-8	H-8
C13	91.8	CH	5.92 (1H, d, 1.2)		
C14	58.5	CH_3	3.85 (3H, s)		
C15	52.7	CH_2	3.66 (2H, m)	NH2, H-16	H-16
C16	36.7	CH_2	2.98 (2H, t, 7.2)	H-15	H-15
NH1			11.60 (1H, bs)		
NH2			9.80 (1H, bs)	H-3, H-15	

2007 EAQ2

Latrunculin A is a complex metabolite isolated from the sponge *Latrunculia* and the seaslugs that feed on it. There are 5 stereocentres in this molecule and different approaches need to be employed to determine their relative stereochemistry. For the A ring the ^1H NMR data and coupling constants are given in the extract of the data table below.

- In some conformationally constrained systems, expected couplings may be missing. Using the Karplus curve below explain why this is the case. (3)
- Draw a diagram of ring A in your answer book and indicate the couplings between the protons. (4)
- Use the information from part a.) in conjunction with the Karplus curve to assign the correct relative stereochemistry at C-13 and C-15, and assign the diastereotopic protons at C-14 and C-16. Draw a clear conformational diagram to explain your answer. (8)
- An NOE correlation is observed between H16' and H18. Use this information to suggest the relative stereochemistry at C17. (3)
- Suggest how you might determine the relative stereochemistry at C-11. (2)



Latrunculin A

Table 1. Selected ^1H NMR and coupling data for latrunculin A obtained in $\text{DMSO}-d_6$ at 400 MHz.

No.	$\delta_{\text{H}}/\text{ppm}$ (integral, mult., J/Hz)
12	1.22 (2H, m)
13	4.28 (1H, t, 11.0)
14	1.42 (1H, d, 14.4)
14'	1.32 (1H, ddd, 3.2, 11.0, 14.4)
15	4.99 (1H, dd, 3.2, 4.8)
16	1.97 (1H, d, 14.8)
16'	1.53 (1H, dd, 4.8, 14.8)

2006 EAQ1

Spectroscopic data is given below for a potential drug molecule. The molecule contains two amides and a phenol-OH.

Use this information:

- To determine the molecular formula (4)
- Determine the correct structure of the molecule using the 1D and 2D NMR data. Draw structures indicating the COSY and HMBC correlations to confirm your conclusions. (10)
- Assign all the ^1H and ^{13}C NMR data. (6)

MS data: M^+ at 250.1317 m/z

(C = 12.0000, H = 1.0078, N = 14.0031; O = 15.9949)

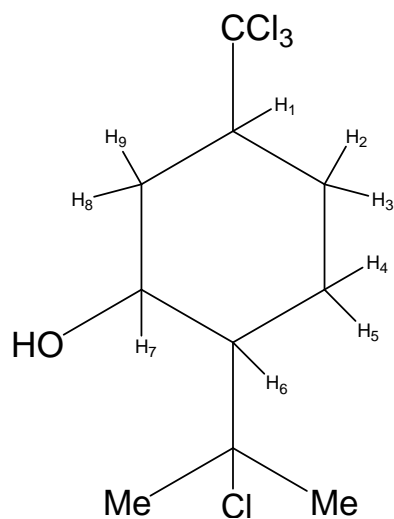
The IR spectrum shows major bands at 3630, 3314, 3256, 1692, 1608 cm^{-1}

	$\delta^{13}\text{C}/\text{ppm}$, mult	$\delta^1\text{H}/\text{ppm}$, mult, J	^1H - ^1H COSY data	HMBC data $\text{C} \rightarrow \text{H}$
1	176.5 s			C1-H7, 11, 14
2	172.0 s			C2-H8, 10, 13
3	152.9 s			C3-H5, 6
4	133.4 s			C4-H5, 6, 13
5	121.8 d (2C)	7.47 2H d 8 Hz	H5-H6	C5-H6, 13
6	115.9 d (2C)	6.71 2H d 8 Hz	H6-H5	C6-H5
7	36.5 t	2.18 2H t 7 Hz	H7-H11	C7-H9, 11, 14
8	33.9 t	2.23 2H t 7Hz	H8-H10	C8-H9, 10, 13
9	28.3 t	1.29 2H quint 7 Hz	H9-H10, H9-H11	C9-H7, 8, 10, 11
10	25.3 t	1.67 2H quint 7 Hz	H10-H8, H10-H9	C10-H8, 9, 11
11	25.0 t	1.57 2H quint 7 Hz	H11-H7, H11-H9	C11-H7, 9, 10
12		11.0 1H s		
13		8.0 1H bs		
14		6.0 2H bs		

2006 EAQ2

The ^1H NMR spectrum of the compound below has been analysed and selected ^1H - ^1H coupling data has been reported.

H	mult	J/Hz
1	dddd	12.3, 12.3, 3.3, 3.2
2	dddd	14.5, 4.6, 3.6, 3.3
3	dddd	14.5, 12.3, 10.6, 3.3
4	dddd	15.1, 12.4, 10.6, 3.6
5	dddd	15.1, 4.6, 4.3, 3.3
6	ddd	12.4, 10.4, 3.3
7	ddd	11.3, 10.4, 4.3
8	ddd	14.1, 12.3, 11.3
9	ddd	14.1, 4.3, 3.2



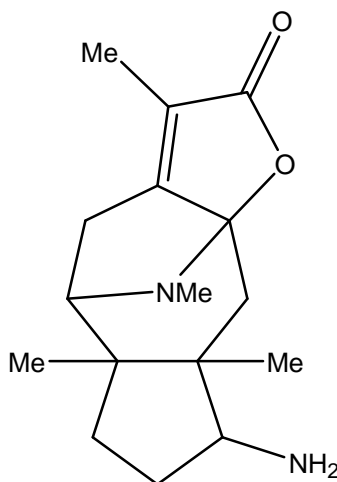
- Copy the structure into your answer book and indicate all the mutual coupling constants. (6)
- Use the information from part a.) together with the Karplus curve given below to assign the stereochemistry of H₁-H₉. Draw a conformational diagram to explain your reasoning and indicate the stereochemistry of the side groups. (10)
- NOE data shows enhancements for: H₁-H₄, H₁-H-7, H₃-H₆, H₄-H₇, H₆-H₈, H₈-H₃. rationalise this information using the conformation derived in part b.).

2006 EAQ 3

Hederacine B is a compound isolated from ground ivy (*Glechoma hederaceae*). The ^1H , ^{13}C and HMBC NMR data are given below. Using this information:

- Assign the ^1H and ^{13}C NMR data to the structure indicating your reasoning. Draw a structure indicating the HMBC correlations to confirm your conclusions. (14)
- Selected NOE correlations are given below. Use this information to assign the relative stereochemistry in the lower five-membered ring in hederacine B. (6)

NOE data: 3.11 – 1.40; 2.88 – 1.49; 2.13 – 1.29; 1.49 – 2.13; 1.29 – 1.40; 1.40 – 2.88



Hederacine B

Atom No	δ ^1H /ppm, mult	δ ^{13}C /ppm, mult	HMBC H \rightarrow C
1	–	170.5 s	–
2	–	130.5 s	–
3	–	156.0 s	–
4	2.82 m, 1H 2.37 m, 1H	22.5 t	C-2, C-12
5	3.37 m, 1H	59.0 d	C-12
6	–	46.5 s	–
7	2.13 m, 1H 1.26 m, 1H	35.1 t	C-9, C-10
8	2.01 m, 1H 1.49 m, 1H	24.5 t	C-6, C-10
9	2.88 m, 1H	67.5 d	C-6, C-11, C-14
10	–	55.5 s	–
11	2.85 m, 1H 1.30 m, 1H	48.2 t	C-6, C-9
12	–	110.0 s	–
13	3.11 s, 3H	49.5 q	C-12
14	1.40 s, 3H	17.0 q	C-6, C-9, C-11
15	1.29 s, 3H	15.0 q	C-5, C-7
16	1.90s, 3H	7.5 q	C-1, C-3

NH₂ data not shown

2006 EAQ4

A water-soluble compound containing an guanidinium group ($\text{HN}-(\text{C}=\text{NH})-\text{NH}_2$, $\delta_{\text{C}} \sim 157$ ppm) was isolated from a New Zealand hydroid.

The 1D and 2D NMR data is given below. The accurate mass measurement obtained by ESI-MS is $[\text{M}+\text{H}]^+ = 279.1452 \text{ m/z}$.

(C = 12.0000, H = 1.0078, N = 14.0031; O = 15.9949)

Use this information:

- d.) To determine the molecular formula (4)
- e.) To determine the correct structure of the molecule using the 1D and 2D NMR data and assign all the ^1H and ^{13}C NMR data. Draw structures indicating the COSY and HMBC correlations to confirm your conclusions.(12)
- f.) To explain the NOESY correlations observed for this compound. (4)

	$\delta_{\text{C}}/\text{ppm}$ mult	$\delta_{\text{H}}/\text{ppm}$ (H, mult, J/Hz)	^1H - ^1H COSY	HMBC (C \rightarrow H)	NOESY
1	189.4 s			H-9	
2	166.2 s			H-7, H-11	
3	164.1 s			H-9, H-10	
4	157.3 s			H-6	
5	125.0 s			H-10	
6	41.0 t	3.06 (2H, d, 6.0)	H-8, H-12		H-8, H-12
7	38.5 t	3.17 (2H, d, 6.0)	H-8, H-11	H-8, H-11	H-8, H-11
8	26.6 t (2C)	1.40 (4H, t, 2.8)	H-7, H-6	H-7, H-6	H-7, H-6, H-9
9	133.2 d (2C)	7.80 (2H, d, 8.8)	H-10		
10	116.3 d (2C)	6.80 (2H, d, 8.8)	H-9	H-9	H-9, H-13
11		8.70 (1H, t, 5.6)	H-7		H-7, H-9
12		7.40 (1H, t, 5.6)	H-6		H-6
13		10.80 (1H, bs)			H-10

Note: 3 additional exchangeable H are not visible in the ^1H NMR

2005 EAQ1

The Antarctic alga *Pantoneura plocamioides* produces an interesting monobrominated monoterpene called pantoisofuranoid A. The mass spectrometric and 1D and 2D NMR data are given below. To simplify your workings, you may assume that C3 and C6 are linked by an ether bridge.

MS data: M^+ at 264.0361 m/z

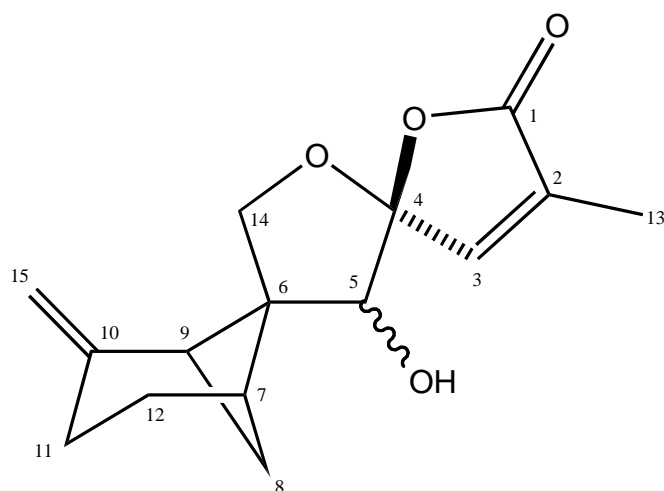
(C = 12.0000, H = 1.0078, O = 15.9949, ^{79}Br = 78.9180)

Label	δ ^{13}C (ppm), mult	δ ^1H (ppm), mult, J (Hz)	COSY data (H-H)	HMBC data (H to C)
1	105.9 d	6.31 d 13.6	H1-H2	H1-C2, H1-C3
2	141.3 d	6.17 d 13.6	H2-H1	H2-C1
3	88.3 s			
4	75.4 d	3.84 m	H4-H5	H4-C3, H4-C6
5	34.7 t	2.30 m	H5-H4,	H5-C3, H5-C6
		1.94 dd 14.0, 3.1	H5-H6	
6	83.4 d	3.84 m	H6-H5	H6-C3
7	71.7 s			
8	26.4 q	1.09 s		H8-C6, H8-C7, H8-C9
9	27.6 q	0.78 s		H9-C6, H9-C7, H9-C8
10	21.0 q	1.32 s		H10-C2, H10-C3, H10-C4

- Determine the molecular formula of pantoisofuranoid A. (4)
- Calculate the number of double bond equivalents. (2)
- What are the functional groups present in pantoisofuranoid A? Present your evidence for each one. (4)
- Using the 1D and 2D NMR data determine the structure of pantoisofuranoid A. Explain your reasoning at all stages. (10)

2005 EAQ2

Massarinolin A, a sesquiterpene isolated from an aquatic fungus *Massarina tunicata*, is shown below. ^1H NMR data and selective NOEs are given in the table below.



Position	^1H NMR data (δ /ppm, mult, J /Hz)	NOE correlations
3	6.95, q, 1.3	4.22
5	4.22, broad s	2.27, 3.14, 6.95
7	2.63, m	
8	2.27, ddd, 10.0, 5.7, 5.7	4.22
	1.57, d, 10.0	1.64
9	3.14, d, 5.7	4.22, 4.87
11	2.58, m	4.84
	2.22, ddd, 17.0, 9.4, 1.2	4.84
12	1.98, dddd, 12.0, 9.4, 4.2, 2.4	
	1.64, m	3.93
13	1.94, d, 1.5	
14	3.99, d, 9.6	1.98, 2.58, 3.14, 4.84, 4.87
	3.93, d, 9.6	2.63, 1.64
15	4.87, m	3.14, 3.99
	4.84, m	2.22, 3.99

- Using the Karplus curve below, assign the diastereotopic chemical shifts for positions 11 and 12 to equatorial and axial protons. Indicate the chemical shifts and all the coupling constants you can assign on a clear conformational drawing of the relevant part of the molecule. (5)
- Confirm your answer to part a.) using the NOE information provided. Indicate the relevant NOE correlations on a separate clear conformational drawing. (3)
- Using the coupling constant information, assign the diastereotopic protons at position 8. Explain why the signal at δ 1.57 ppm is only a doublet. Rationalise your assignments using the NOE information. (5)
- Use the NOE information provided to assign the diastereotopic protons at position 14. (4)
- Use the NOE information provided to determine the stereochemistry at position 5. (3)

2004 EAQ1

A natural product containing a chlorinated double bond shows a molecular ion cluster at m/z 188/190 in its mass spectrum. The ^1H and ^{13}C NMR data are given in the table below, as well as the ^1H - ^1H COSY and HMBC ($\text{C} \rightarrow \text{H}$, 2 and 3 bonds only) data.

(Hint – there are two isotopes of Cl, ^{35}Cl and ^{37}Cl)

^{13}C NMR (δ/ppm , multiplicity) at 100MHz and ^1H NMR (δ/ppm , proton count, multiplicity, J/Hz) at 400 MHz and ^1H - ^1H COSY and HMBC data in CDCl_3

	^{13}C	^1H	COSY H-H	HMBC $\text{C} \rightarrow \text{H}$
A	139.2 d	5.76 1H m	d/d', f	f, h
B	133.0 s			c, e, j
C	127.6 d	5.75 1H m	e, j	e, g, j
D	114.1 t	4.94 dq 17.1 1.8 4.88 dq 10.3 1.0	a, f	a, f
E	66.9 t	4.12 1H s	c, OH	c
F	33.7 t	2.00 2H q 7.1	a, d/d', h	a, d/d'
G	29.2 t	1.27 2H m	i, j	i, j
H	28.7 t	1.33 2H m	f, i	
I	28.4 t	1.36 2H m	g, h	h
J	28.1 t	2.16 2H q 7.2	c, g	c

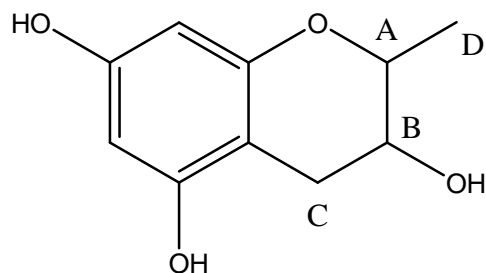
- a. The accurate mass of the molecule is 188.0968. Using the NMR data and the accurate mass, calculate the molecular formula. (4)

($^1\text{H} = 1.0078$, $^{12}\text{C} = 12.0000$, $^{16}\text{O} = 15.9949$, $^{35}\text{Cl} = 34.9689$)

- b. Calculate the double bond equivalents. (2)
- c. Besides the chlorinated double bond, what are the other functional groups present? (2)
- d. Generate a list of substructures consistent with your answer to c.) and the molecular formula. (4)
- e. Propose a structure for the natural product that is consistent with all the 1D and 2D NMR data given. Show how you used the 2D NMR data to generate your final structure. (8)

2004 EAQ2

- a. Explain the effect of chemical equivalence/magnetic non equivalence. Use chemical structures and draw spectra to illustrate your answer. (8)
- b. Selected ^1H NMR data is given for the structure below. Determine the relative stereochemistry of the OH and the Me groups. Assign the diastereotopic protons at C to the equatorial or axial position. (8)
- c. In addition, NOE spectra showed the following enhancements:
Irradiation at 1.43 ppm enhanced a peak at 2.70 ppm
Irradiation at 4.10 ppm enhance peaks at 3.94 and 2.32 ppm
Rationalise this information with respect to your answer to part b.)



	$\delta_{\text{H}}/\text{ppm}$	mult	J/Hz
A	3.94	dq	4.0, 6.8
B	4.10	ddd	10.3, 6.2, 4.0
C	2.70	dd	12.5, 10.3
	2.32	dd	12.6, 6.2
D	1.43	d	6.8

2003 EAQ1

^1H , ^{13}C , ^1H - ^1H COSY NMR, IR and MS data for an unknown compound is summarised below. Using this information:

- | | | |
|---|--|---|
| a | Determine the molecular formula of the unknown compound. | 3 |
| b | Determine the plane structure of the molecule. You may wish to use the ^1H - ^1H COSY data to construct a spin system. Is there more than one possible structure that is consistent with the data given? | 7 |
| c | Assign the ^1H and ^{13}C chemical shifts to the structure. | 4 |
| d | Given that there is a strong NOE detectable between peaks in the ^1H NMR spectrum at 4.6 and 4.2 ppm, use this information to determine the relative stereochemistry of the compound in question. | 3 |
| e | Explain the formation of the m/z 86 fragment in the MS and explain the fragmentation. | 3 |

Spectroscopic data:

IR: 3400 cm^{-1} (broad); 1620 cm^{-1} (strong)

MS: 131, 86 m/z

accurate mass: 131.0582

(C = 12.0000; H = 1.0078; O = 15.9949; N = 14.0031)

^{13}C NMR data (δ/ppm , mult): 175 (s); 69 (d); 60 (d); 53 (t); 38 (t).

^1H NMR data (δ/ppm , integral, mult, J/Hz)

4.55, H, m

4.18, H, dd, 10.6, 3.8

3.43, H, dm, 12.4

3.34, H, dd, 12.6, 3.8

2.47, ddd, H, 14.4, 10.2, 4.7

2.22, dm, H, 14.6

(dm = double multiplet, coupling constant given for doublet)

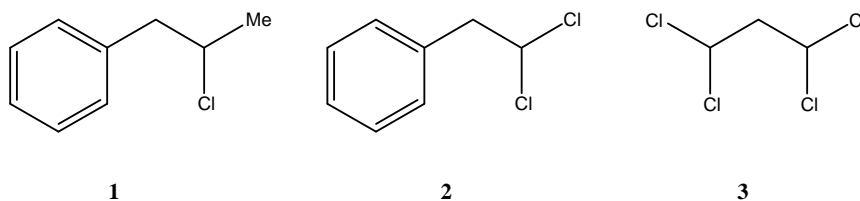
^1H - ^1H COSY data. There are correlations between peaks at the following chemical shifts:

4.55-3.43; 4.55-3.34; 4.55-2.47; 4.55-2.22; 4.18-2.47; 4.18-2.22; 3.43-3.34; 2.47-2.22

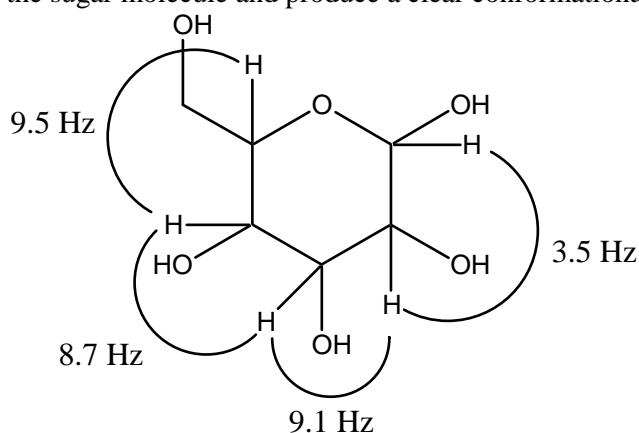
2003 EAQ2

Many natural compounds contain chiral centres, and this complicates the interpretation of ^1H NMR spectra as CH_2 groups become diastereotopic.

- a Using illustrative examples, briefly explain the terms homotopic, enantiotopic and diastereotopic. 4
- b For the three structures given below, indicate whether the CH_2 is homotopic, enantiotopic or diastereotopic. Draw the expected coupling pattern for the CH_2 in an achiral and in a chiral solvent. 8



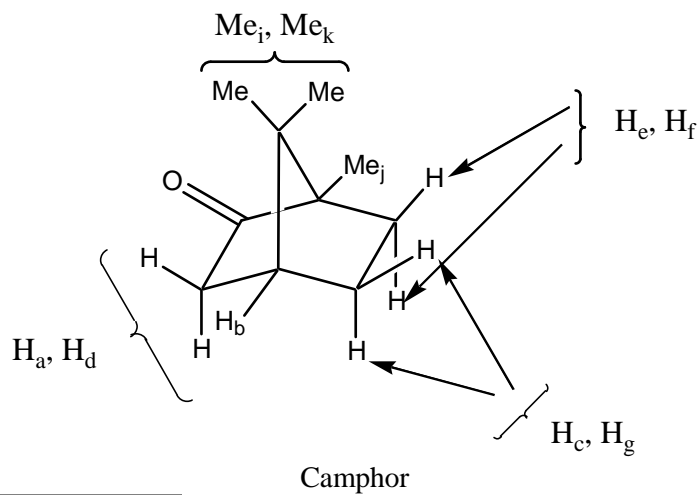
- c The general structure of a sugar molecule with relevant coupling constants is given below. Using your knowledge of axial-axial, axial-equatorial and equatorial-equatorial coupling constants for six membered rings, determine the relative stereochemistry of the sugar molecule and produce a clear conformational drawing. 8



2002 EAQ1

a. Give a brief qualitative description of the origin of the NOE effect between two protons I and S. Diagrams should form a large part of your answer. (8).

b. Non-stereospecific assignments for camphor are given on the structure below. Data acquired from a difference NOE spectrum is tabulated below. Using this data assign H_a , H_c , H_d , H_e , H_f , H_g , Me_i and Me_k stereospecifically. Give your reasoning. (12)



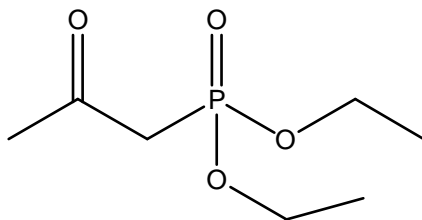
Irradiate	Enhancement
H_a	H_b, H_d, Me_k
H_c	H_b, H_e, H_f, H_g
Me_i	H_b, H_c, H_e
Me_k	H_a, H_b

2002 EAQ2

a. Which of the following nuclei is the most receptive in NMR at natural abundance? (4)

Nucleus	Natural abundance	Gyromagnetic ratio
^{13}C	1.1%	6.76
^{15}N	0.4%	2.70
^{19}F	100%	25.1
^{31}P	100%	10.8

b. Using your knowledge of ^{13}C NMR chemical shifts draw the expected ^{13}C NMR spectrum of the compound below. (8)



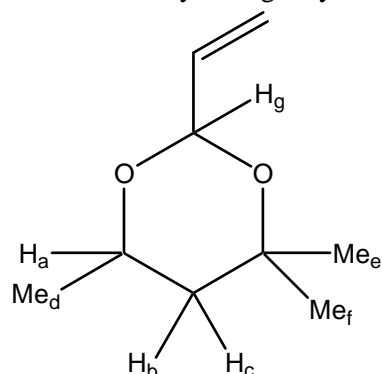
c. The ^1H NMR data for a compound $\text{C}_4\text{H}_{11}\text{O}_3\text{P}$ is given below. Determine the structure of the compound, and explain the coupling patterns observed. (8)

δ_{H} (ppm)	multiplicity (J, Hz)	No. of H
6.8	d, 692	1
4.2	dq, 9.1, 7.0	4
1.4	t, 7.0	6

2001 EAQ1

- a Briefly describe how the Karplus curve can be used to determine relative stereochemistry for rigid cyclic systems.

5



- b For protons H_a , H_b and H_c in the molecule above the coupling constants are:
 H_a , dd, $J = 14.0, 4.5$ Hz
 H_b , dd, $J = 15.0, 4.5$ Hz
 H_c , dd, $J = 15.0, 14.0$ Hz
- i Copy the structure into your answer book and indicate the magnitude of the couplings between H_a , H_b and H_c . 3
- ii Use the Karplus curve below to determine the possible values for the two relevant dihedral angles. 3
- iii Draw the above molecule in the chair conformation and indicate the relative stereochemistry of H_a , H_b and H_c . 4
- c NOE difference experiments were performed. When H_g was irradiated, the 1H NMR signals for H_a and Me_e were enhanced. In addition, irradiating H_c gave enhancements at H_b , Me_d and Me_f . Use this information to determine the relative stereochemistry of Me_d , Me_e , Me_f and H_g . 5

2001 EAQ2

A compound has the following IR, MS and NMR spectra:

IR:

2900-3000 cm^{-1} (s)

1600 cm^{-1} (s)

1200 cm^{-1} (s)

MS:

Low resolution electron impact m/z 100, 85, 56, 44

High resolution electron impact m/z 100.0888

(H = 1.0078; C = 12.0000; N = 14.0031; O = 15.9949)

^1H NMR:

6.44 ppm, 1H, dd $J = 14.0, 7.0$ Hz

4.18 ppm, 1H, dd $J = 14.0, 1.5$ Hz

3.94 ppm, 1H, dd $J = 7.0, 1.5$ Hz

3.61 ppm, 2H, t $J = 7.0$ Hz

1.63 ppm, 2H, quintet, $J = 7.0$ Hz

1.41 ppm, 2H, sextet, $J = 7.0$ Hz

0.97 ppm, 3H, triplet, $J = 7.0$ Hz

^{13}C NMR:

152 ppm CH

87 ppm CH_2

68 ppm CH_2

32 ppm CH_2

20 ppm CH_2

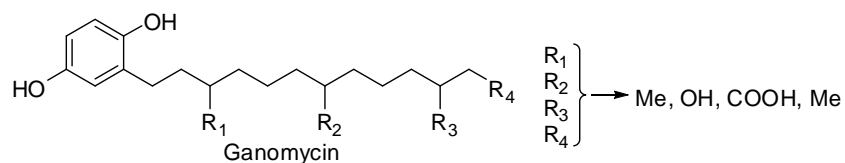
15 ppm CH_3

Use this information to:

- | | | | |
|---|----|---|---|
| a | i | Determine the molecular formula of the compound | 4 |
| | ii | Find the two functional groups present in the molecule | 2 |
| | ii | Elucidate the structure of the molecule | 8 |
| b | | Assign all the ^1H and ^{13}C NMR data to the structure, and explain the low resolution mass spectral fragmentations. | 6 |

One extra question:

The incomplete structure of ganomycin isolated from the basidiomycete fungus *Ganoderma pfeifferi* is given below. The side chain contains and additional three double bonds and groups R₁-R₄. Use the ¹H, ¹³C, ¹H-¹H COSY and HMBC data, acquired in CD₃OD, to place the three double bonds and groups R₁ – R₄ in their correct positions and fully assign the ¹H and ¹³C NMR data to this structure.



1D and 2D NMR spectral data for ganomycin obtained in CDCl₃ at 400/100 MHz (δ in ppm)

Atom	¹³ C (δ/ppm, mult)	¹ H (δ/ppm, mult, J/Hz)	¹ H- ¹ H COSY	HMBC (C-H, 2-3 bonds)
A	173 s			p
B	151 s			l
C	149 s			k, m, q
D	141 d	5.98 t 7.8	q	p
E	137 s			t
F	136 s			u
G	133 s			p, q
H	128 s			d
I	127 d	5.39 t 7.1	s	n, u
J	125 d	5.14 t 7.3	r	o, t
K	118 d	6.61 d 2.8	m	q
L	117 d	6.64 d 8.5	m	
M	115 d	6.52 dd 8.5 2.8	k, l	
N	69 t	3.94 s		i, u
O	40 t	2.00 t 7.8	s	j, t
P	36 t	2.33 t 7.2	r	d
Q	32 t	3.69 d 7.7	d	k
R	28 t	2.19 q 7.2	j, p	
S	27 t	2.10 q 7.5	i, o	
T	16 q	1.61 s		j, o
U	14 q	1.66 s		i, n