

Contents

<i>1</i>	<i>Introduction to NMR Spectroscopy</i>	<i>1</i>
1.1	Nuclear Magnetism	1
1.2	Nuclear Precession	2
1.3	Nuclear Magnetic Energy Levels	3
1.4	Nuclear Magnetic Resonance	4
1.5	Relaxation	5
1.5.1	Equilibrium of Nuclear Spins in the B_0 Field	5
1.5.2	Spin-Lattice Relaxation	5
1.5.3	Spin-Spin Relaxation	6
1.5.4	Saturation	6
1.6	Magnetization Vectors	7
1.7	Bloch Equations	8
1.7.1	Motion of the Magnetization Vector in a Fixed Coordinate System	8
1.7.2	Motion of the Magnetization Vector in the Rotating Coordinate System	9
1.7.3	NMR in the Rotating Frame of Reference	10
1.7.4	Relaxation in the Rotating Frame of Reference	12
1.8	NMR Spectra	13
1.8.1	Nuclear Induction	13
1.8.2	Absorption and Dispersion Spectra	13
1.8.3	Magnitude Spectra	14
1.9	Chemical Shift	15
1.9.1	Shielding of Nuclei in Atoms and Molecules	15
1.9.2	Calibration of NMR Spectra	16
1.9.3	Reference Standard	17
1.10	Spin-Spin Coupling	17
1.10.1	Multiplicity of Signals	17
1.10.2	Coupling Constants	18

1.10.3	Comparison between Chemical Shifts and Coupling Constants	18
1.10.4	Origin of Spin-Spin Coupling.	18
2	<i>Instrumental Methods of ^{13}C NMR Spectroscopy</i>	21
2.1	Sensitivity of ^{13}C NMR Spectroscopy	21
2.2	Methods of Sensitivity Enhancement in ^{13}C NMR Spectroscopy. . . .	21
2.3	Continuous Wave NMR Spectroscopy	22
2.4	Pulsed NMR Spectroscopy	22
2.4.1	Magnetization	22
2.4.2	90°_x Pulse.	22
2.4.3	Transverse Magnetization	23
2.4.4	Free Induction Decay	24
2.4.5	Pulse Interferograms.	25
2.5	Pulse Fourier Transform (PFT) NMR Spectroscopy	28
2.5.1	FID Signal and NMR Spectrum as Fourier Transforms	28
2.5.2	Position, Width and Phase of FT NMR Signals	29
2.5.3	Acquisition of Pulse Interferograms for Fourier Transformation	30
2.5.3.1	Digitization	30
2.5.3.2	Dwell Time and Pulse Interval	30
2.5.3.3	Filtering of Frequencies Outside of the Spectral Width	30
2.5.4	Optimization of Pulse Interferograms for Fourier Transformation . . .	31
2.5.4.1	Adjustment of Pulse Frequency	31
2.5.4.2	Adjustment of Pulse Width.	32
2.5.5	Data Transformation and Subsequent Manipulations.	33
2.5.5.1	Fourier Transformation	33
2.5.5.2	Phase Correction	33
2.5.5.3	Computation of Magnitude Spectra	36
2.5.6	Controlling Signal to Noise and Resolution in PFT NMR Spectroscopy.	36
2.5.6.1	Digital Filtering.	36
2.5.6.2	Number of FID Data Points and Digital Resolution	36
2.5.7	Spin-Lattice Relaxation and Signal to Noise in PFT NMR Spectroscopy.	39
2.5.8	Comparison between CW and PFT	41
2.6	Double Resonance Techniques used in ^{13}C NMR Spectroscopy as Assignment Aids	43
2.6.1	Basic Concept of Spin Decoupling.	43
2.6.2	Proton Broad Band Decoupling in ^{13}C NMR Spectroscopy.	44
2.6.3	Nuclear Overhauser Effect in $^{13}\text{C}\{^1\text{H}\}$ NMR Experiments	46
2.6.4	Quenching Nuclear Overhauser Effects in $^{13}\text{C}\{^1\text{H}\}$ NMR Experiments	47
2.6.5	Proton Off-Resonance Decoupling.	47
2.6.6	Pulsed Proton Broadband Decoupling	50
2.6.6.1	Measurement of NOE Enhanced Coupled ^{13}C NMR Spectra	50

2.6.6.2	Measurement of Proton-Decoupled ^{13}C NMR Spectra with Suppressed NOE	50
2.6.6.3	Measurement of Nuclear Overhauser Enhancements	51
2.6.7	Selective Proton Decoupling	53
2.7	Measurement of ^{13}C Relaxation Times.	55
2.7.1	Spin-Lattice Relaxation Times	55
2.7.1.1	Inversion-Recovery or 180° , τ , 90° Method.	55
2.7.1.2	Saturation-Recovery Method	59
2.7.1.3	Progressive Saturation or 90° , τ ,... Method.	60
2.7.2	Spin-Spin Relaxation Times	63
2.7.2.1	CPMGSE Experiments	63
2.7.2.2	Spin-Locking Fourier Transform Experiments.	66
2.8	Instrumentation.	67
2.8.1	Magnet	69
2.8.2	Stabilization Channel (Lock)	70
2.8.3	Observation Channel	71
2.8.4	Decoupling Channel.	71
2.8.5	Sample	71
2.9	From the First to the Second Dimension of ^{13}C NMR Spectroscopy.	73
2.9.1	The Spin-Echo	73
2.9.2	J -Modulated Spin-Echo	75
2.9.3	Polarization Transfer	78
2.9.3.1	Selective Polarization Transfer	79
2.9.3.2	Non-Selective Polarization Transfer	80
2.9.4	Measurement of Carbon-Carbon Coupling Constants Without ^{13}C Enrichment: INADEQUATE.	84
2.10	The Second Dimension	87
2.10.1	Basic Concept	87
2.10.2	J -Resolved Two-Dimensional ^{13}C NMR Spectra	89
2.10.3	Two-Dimensional Carbon-Proton Shift Correlation	92
2.10.4	Two-Dimensional Proton-Proton Shift Correlation: The COSY Experiment	96
2.10.5	Two-Dimensional $\text{C}_\text{A}\text{H}_\text{A} - \text{C}_\text{X}\text{H}_\text{X}$ Correlation: The RELAY Experiment.	100
2.10.6	Two-Dimensional Carbon-Carbon Shift Correlation: The Second Dimension of the INADEQUATE Experiment	102
2.10.7	Carbon-13 NMR Spectroscopy: Strategy for Structure Elucidation.	104
3	^{13}C NMR Spectral Parameters and Structural Properties.	107
3.1	Chemical Shifts	107
3.1.1	Comparison of ^{13}C and ^1H Shifts	107
3.1.2	Referencing ^{13}C Chemical Shifts	108

3.1.3	Survey of ^{13}C Chemical Shifts	110
3.1.3.1	Carbon Hybridization	111
3.1.3.2	Electronegativity	111
3.1.3.3	Crowding of Alkyl Groups and Substituents	112
3.1.3.4	Unshared Electron Pairs at Carbon	112
3.1.3.5	Electron Deficiency at Carbon	113
3.1.3.6	Mesomeric Effects.	113
3.1.3.7	Conjugation	114
3.1.3.8	Steric Interactions.	115
3.1.3.9	Electric Fields of Charged Substituents.	116
3.1.3.10	Anisotropic Intramolecular Magnetic Fields	116
3.1.3.11	Heavy Atoms.	117
3.1.3.12	Isotope Effect	117
3.1.3.13	Intramolecular Hydrogen Bonding.	117
3.1.3.14	Substituent Increments and Functional Group Shifts	118
3.1.4	Medium Shifts	120
3.1.4.1	Dilution Shifts	120
3.1.4.2	Solvent Shifts.	120
3.1.4.3	pH Shifts	121
3.1.5	Isotropic Shifts	123
3.1.6	Intramolecular Mobility and Temperature Dependence of ^{13}C Chemical Shifts and Line Widths	127
3.1.6.1	Introduction	127
3.1.6.2	Temperature Dependence of ^{13}C NMR Spectra	131
3.2	^{13}C Coupling Constants	133
3.2.1	Basic Theoretical Considerations	133
3.2.2	Carbon-Proton Coupling.	134
3.2.2.1	One-Bond Coupling (J_{CH})	134
3.2.2.2	Longer-Range Carbon-Proton Couplings: The $J_{\text{CH}}/J_{\text{HH}}$ Ratio	140
3.2.2.3	Two-Bond Coupling ($^2J_{\text{CH}}$)	141
3.2.2.4	Three-Bond Coupling ($^3J_{\text{CH}}$)	143
3.2.3	Carbon-Deuterium Coupling	147
3.2.4	Carbon-Carbon Coupling	147
3.2.4.1	One-Bond Coupling (J_{CC}).	147
3.2.4.2	Longer-Range Carbon-Carbon Couplings ($^2J_{\text{CC}}$, $^3J_{\text{CC}}$)	152
3.2.5	$^{13}\text{C}-^{15}\text{N}$ Coupling Constants	155
3.2.5.1	One-Bond Couplings (J_{CN})	155
3.2.5.2	Longer-Range Couplings ($^2J_{\text{CN}}$, $^3J_{\text{CN}}$)	157
3.2.6	Coupling between Carbon and Other Heteronuclei X (X $\neq$ C, H, D)	160
3.3	Spin-Lattice Relaxation Times	163
3.3.1	Mechanisms of ^{13}C Spin-Lattice Relaxation	163
3.3.1.1	Relaxation Resulting from Chemical Shift Anisotropy (CSA Mechanism).	163
3.3.1.2	Relaxation by Scalar Coupling (SC Mechanism).	163
3.3.1.3	Relaxation by Spin Rotation (SR Mechanism)	163

3.3.1.4	Relaxation by Internuclear Dipole-Dipole Interaction (DD Mechanism)	164
3.3.1.5	Electron Spin-Nucleus Interactions and Consequences	165
3.3.2	Influence of Molecular Motion on Dipole-Dipole Relaxation	166
3.3.3	Information Content of ^{13}C Spin-Lattice Relaxation Times	168
3.3.3.1	Degree of Alkylation and Substitution of C Atoms	168
3.3.3.2	Molecular Size and Relaxation Mechanisms	168
3.3.3.3	Anisotropy of Molecular Motion	169
3.3.3.4	Internal Molecular Motion	172
3.3.3.5	Association and Solvation of Molecules and Ions	178
3.3.3.6	Determination of Quadrupole Relaxation Times and Coupling Constants from ^{13}C Spin-Lattice Relaxation Times	180
3.3.4	Medium and Temperature Effects	181
4	<i>^{13}C NMR Spectroscopy of Organic Compounds</i>	183
4.1	Saturated Hydrocarbons	183
4.1.1	Alkanes	183
4.1.2	Cycloalkanes	186
4.1.3	Polycycloalkanes	189
4.2	Alkenes	192
4.2.1	Open-Chain Alkenes and Dienes	192
4.2.2	Cycloalkenes	194
4.3	Alkynes and Allenes.	196
4.4	Halides	198
4.4.1	Alkyl Halides.	198
4.4.2	Cycloalkyl Halides	203
4.4.3	Alkenyl Halides.	205
4.4.4	Carbon-Fluorine Coupling Constants in Alkyl and Cyloalkyl Fluorides	205
4.5	Alcohols	206
4.5.1	Alkanols.	206
4.5.2	Cycloalkanols	209
4.6	Ethers	213
4.6.1	Dialkyl Ethers	213
4.6.2	Enol Ethers and Alkynyl Ethers.	215
4.7	Carbonyl Compounds	215
4.7.1	General	215
4.7.2	Aldehydes and Ketones	216
4.7.3	Quinones and Annulenones.	222
4.7.4	Carboxylic Acids and Derivatives	226

XIV *Contents*

4.8	Aliphatic Organosulfur Compounds	233
4.9	Aliphatic Organonitrogen Compounds	236
4.9.1	Amines	236
4.9.2	Enamines, Enaminoaldehydes, Cyanines	238
4.9.3	Imines	240
4.9.4	Nitriles and Isonitriles	242
4.9.5	Azacumulenes	244
4.9.6	Nitroso and Nitro Compounds	246
4.10	Organophosphorus Compounds	247
4.10.1	Survey of Carbon-13 Shifts	247
4.10.2	Carbon-Phosphorus Couplings	250
4.11	Aromatic Compounds	254
4.11.1	General	254
4.11.2	Substituted Benzenes	255
4.11.3	Substituted Naphthalenes	263
4.11.4	Benzocycloalkenes and Hydroaromatic Compounds	264
4.11.5	Fused and Bridged Aromatic Rings	265
4.11.6	Typical Coupling Constants	266
4.11.7	¹³ C- and ¹² C-Enriched Aromatic Compounds for Structural Assignments and Mechanistic Studies	270
4.12	Heterocyclic Compounds	272
4.12.1	Heterocycloalkanes	272
4.12.2	Non-Aromatic Heterocycles with <i>sp</i> ² Ring Carbons	276
4.12.3	Heteroaromatic Compounds	281
4.12.4	Typical Coupling Constants	286
4.13	Organometallic Compounds	293
4.13.1	General	293
4.13.2	Group I Organometallic Compounds	295
4.13.3	Group II Organometallic Compounds	295
4.13.4	Group III Organometallic Compounds	296
4.13.5	Group IV Organometallic Compounds	297
4.13.6	Organo-Transition-Metal Compounds	300
4.14	Ions	302
4.14.1	Carbocations	302
4.14.2	Carbanions	305
4.15	Synthetic Polymers	308
4.15.1	Tacticity	308
4.15.2	Configurational Isomerism	311
4.15.3	Segmental Mobility	313
4.16	Substituent Increments: Summary and Application	313
4.16.1	Substituted Alkanes	314
4.16.2	Substituted Cyclohexanes and Bicyclo[2.2.2]heptanes	316

4.16.3	Substituted Alkenes	318
4.16.4	Substituted Benzenes	319
4.16.5	Substituted Pyridines	322
4.16.6	Nitrogen Increments in Fused Heterocycles	322
5	<i>¹³C NMR Spectra of Natural Products</i>	327
5.1	Terpenes	327
5.2	Steroids	337
5.2.1	Androstanes, Pregnanes and Estranes	338
5.2.2	Cholestanes and Cholanes	340
5.2.3	Cardenolides and Sapogenins	358
5.3	Alkaloids	360
5.4	Carbohydrates	379
5.4.1	Monomeric Aldoses and Ketoses	380
5.4.2	Di- and Polysaccharides	394
5.4.3	Polyols	397
5.4.4	Aldonic Acids	397
5.4.5	Inositols	400
5.5	Nucleosides and Nucleotides	401
5.5.1	Assignment of the Purine Resonances	402
5.5.2	Assignment of the Pyrimidine Resonances	409
5.5.3	Assignment of the Isoalloxazine Resonances	409
5.5.4	Assignment of the Sugar and Polyol Carbon Atoms	409
5.5.5	Correlations of ¹³ C Chemical Shifts with Other Physicochemical Parameters.	410
5.5.6	Nucleic Acids.	412
5.6	Amino Acids	414
5.6.1	¹³ C Chemical Shifts of Amino Acids.	414
5.6.2	pH-Dependence of the ¹³ C Chemical Shift Values of Amino Acids.	420
5.6.3	Prediction of Carbon Shifts and their Correlation with Other Physicochemical Parameters.	421
5.7	Peptides	422
5.7.1	Oligopeptides.	422
5.7.2	Homopolymeric Polypeptides.	436
5.7.3	Proteins	437
5.8	Porphyrins	441
5.9	Coumarins	41
5.10	Flavonoids	450
5.11	Elucidation of Biosynthetic Pathways	457
5.11.1	Radicinin	457

XVI *Contents*

5.11.2	Asperlin	457
5.11.3	Cycloheximide	457
5.11.4	Averufin, Versicolorin A and their Relation to Aflatoxin B ₁	459
5.11.5	Virescenosides	459
5.11.6	Methyl Palmitoleate	459
5.11.7	Sepedonin	462
5.11.8	Antibiotic X-537 A	463
5.11.9	Cephalosporin	463
5.11.10	Prodigiosin.	465
5.11.11	Myxovirescin A ₁	465
5.12	Appendix	467
6	<i>References</i>	469
	<i>Subject Index</i>	499