6 Assignment of Proton and Carbon Signals
Proton NMR Spectroscopy

Emperical Correlations for Predicting Chemical Shifts

Alkanes
Shoolery's Rule

for a disubstituted methane

$$X - CH_2 - Y$$

$$\delta(CH_2) = 0.23 + S_x + S_y \quad [ppm]$$

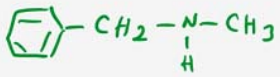
نقطه برج جابجایی شیمیایی پروتون‌های مورد نظر است

* انگیزه سازمات تجربی هستند
empirical equation

Table 6-1.
Substituent increments S for estimating ^1H chemical shifts in disubstituted methanes X-CH_2-Y using *Shoolery's rule*:

$$\delta(CH_2) = 0.23 + S_x + S_y \text{ [ppm]} \qquad (6\text{-}1)$$

Substituent	S	Substituent	S
$-CH_3$	0.47	$-NRR'$	1.57
$-CF_3$	1.14	$-SR$	1.64
$-CR=CR'R''$	1.32	$-I$	1.82
$-C\equiv CH$	1.44	$-Br$	2.33
$-COOR$	1.55	$-OR$	2.36
$-CONH_2$	1.59	$-Cl$	2.53
$-COR$	1.70	$-OH$	2.56
$-C\equiv N$	1.70	$-OCOR$	3.13
$-C_6H_5$	1.83	$-OC_6H_5$	3.23



$S_{phenyl} = 1.83$

$S_{NHR} = 1.57$

$\sum S = 3.40$

$\delta(CH_2) = 0.23 + 3.40 = 3.63$

مقدار تجربی مشاهده شده :

$\delta = 3.75$

Alkenes
Pascual-Meier-Simon rule

Table 6-2.
Substituent increments $S^{1)}$ for estimating ^1H chemical shifts in alkenes using the expression:

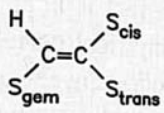
$$\delta(H) = 5.28 + S_{gem} + S_{cis} + S_{trans} \text{ [ppm]} \qquad (6\text{-}2)$$

Substituent	S_{gem}	S_{cis}	S_{trans}
$-H$	0	0	0
$-CH_3$ (alkyl)	0.44	−0.26	−0.29
$-F$	1.51	−0.43	−1.05
$-Cl$	1.00	0.19	0.03
$-Br$	1.04	0.40	0.55
$-I$	1.11	0.78	0.85
$-NR_2$ (aliph.)	0.69	−1.19	−1.31
$-OAlkyl$	1.18	−1.06	−1.28
$-OCOCH_3$	2.09	−0.40	−0.67
$-C_6H_5$	1.35	0.37	−0.10
$-CH=CH_2$ (conj.)	1.26	0.08	−0.01
$-COOH$ (conj.)	0.69	0.97	0.39
$-NO_2$	1.84	1.29	0.59

[1] Data from [1] and [2].

$$\delta(H) = 5.28 + S_{gem} + S_{cis} + S_{trans} \text{ [ppm]} \qquad (6\text{-}2)$$

نقطه مرجع در اینجا جابجایی شیمیایی پروتون نیاد در اتیلن است



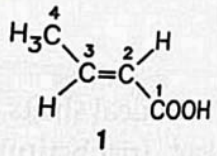
این مقادیر از طریق محاسبه با برنامه spectool حاصل شده اند

Example 1: trans-crotonic acid (1)

δ(H-2) = 5.28 + S_{gem} (COOH) + S_{cis} (CH_3)
= 5.28 + 0.69 − 0.26 = 5.71 (5.83)
experimental value: 5.82

δ(H-3) = 5.28 + S_{gem} (CH_3) + S_{cis} (COOH)
= 5.28 + 0.44 + 0.97 = 6.69 (6.68)
experimental value: 7.04

Also: δ(CH_3) = 1.89; δ(COOH) ≈ 12

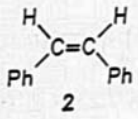


1

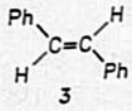
این مقادیر از طریق محاسبه با برنامه spectool حاصل شده اند

cis-stilbene (**2**):
δ(H) = 5.28 + S_{gem} (Ph) + S_{trans} (Ph)
= 5.28 + 1.35 − 0.1 = 6.53 (6.56)
experimental value: 6.55

trans-stilbene (**3**):
δ(H) = 5.28 + S_{gem} (Ph) + S_{cis} (Ph)
= 5.28 + 1.35 + 0.37 = 7.00 (6.99)
experimental value: 7.1



2



3

در این سری ترکیبات استخلافهای وینیل را از مقادیر $^3J_{(H,H)}$ نیز می‌توان مشخص نمود

در هر دو ایزومر دو پروتون اولفینی تکیان مشتقه و شاکله پیک سینگلت می‌دهند

Benzene Derivatives

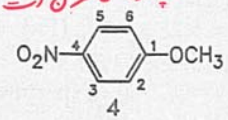
Table 6-3.
Substituent increments S[1] for estimating ^1H chemical shifts in arenes using the expression:
$\delta(H) = 7.27 + \Sigma S$ [ppm] (6-3)

Substituent	S_o	S_m	S_p
$-CH_3$	−0.17	−0.09	−0.18
$-CH_2CH_3$	−0.15	−0.06	−0.18
−F	−0.30	−0.02	−0.22
−Cl	+0.02	−0.06	−0.04
−Br	+0.22	−0.13	−0.03
−I	+0.40	−0.26	−0.03
−OH	−0.50	−0.14	−0.4
$-OCH_3$	−0.43	−0.09	−0.37
$-OCOCH_3$	−0.21	−0.02	0.0
$-NH_2$	−0.75	−0.24	−0.63
$-N(CH_3)_2$	−0.60	−0.10	−0.62
$-C_6H_5$	+0.18	0.0	+0.08
−CHO	+0.58	+0.21	+0.27
$-COCH_3$	+0.64	+0.09	+0.3
$-COOCH_3$	+0.74	+0.07	+0.20
$-NO_2$	+0.95	+0.17	+0.33

[1] Data from [3].

$$\delta(H) = 7.27 + \Sigma S \text{ [ppm]} \qquad (6\text{-}3)$$

نقطه مرجع در اینجا جابجایی شیمیایی پروتونهای بنزن است



این ثابتها از طریق محاسبه با برنامه spectool حاصل شده اند

Example: p-nitroanisole (4)

δ(H-2,6) = 7.27 + S_o (OCH_3) + S_m (NO_2)
= 7.27 − 0.43 + 0.17 = 7.01 (7.04)
experimental value: 6.88

δ(H-3,5) = 7.27 + S_o (NO_2) + S_m (OCH_3)
= 7.27 + 0.95 − 0.09 = 8.13 (8.12)
experimental value: 8.15

Also: $\delta(OCH_3) = 3.90$

تجربه نشان داده که انحراف بین ثابتهای محاسبه شده و ثابتهای تجربی در موارد زیر بیشتر میشود:

- افزایش تعداد استخلافها
- استخلافهای اورتو
- استخلافهای حجیم

- Decoupling Experiments
- Effects of solvent and Temperature
- Altering the chemical structure of the sample
  - replacement of hydrogen by deuterium

- حذف سیگنال پروتون ها از طیف
- ساده تر شدن سیگنال های پیچیده تا حدی که قبلاً با پروتون جابجایی با دوتریم حذف نشده
- تبادل پروتون (OH ، NH ، SH) - حذف سیگنال پروتون در اثر تبادل با دوتریم (شناسایی از D_2O)

  - derivatization
- شل استیله کردن گروه OH در گروه هیدروکسیل (تغییر سیگنال - تغییر حلالیت)

Assignment of Proton and Carbon Signals
Carbon-13 NMR Spectroscopy

Emperical Correlations for Predicting Chemical Shifts

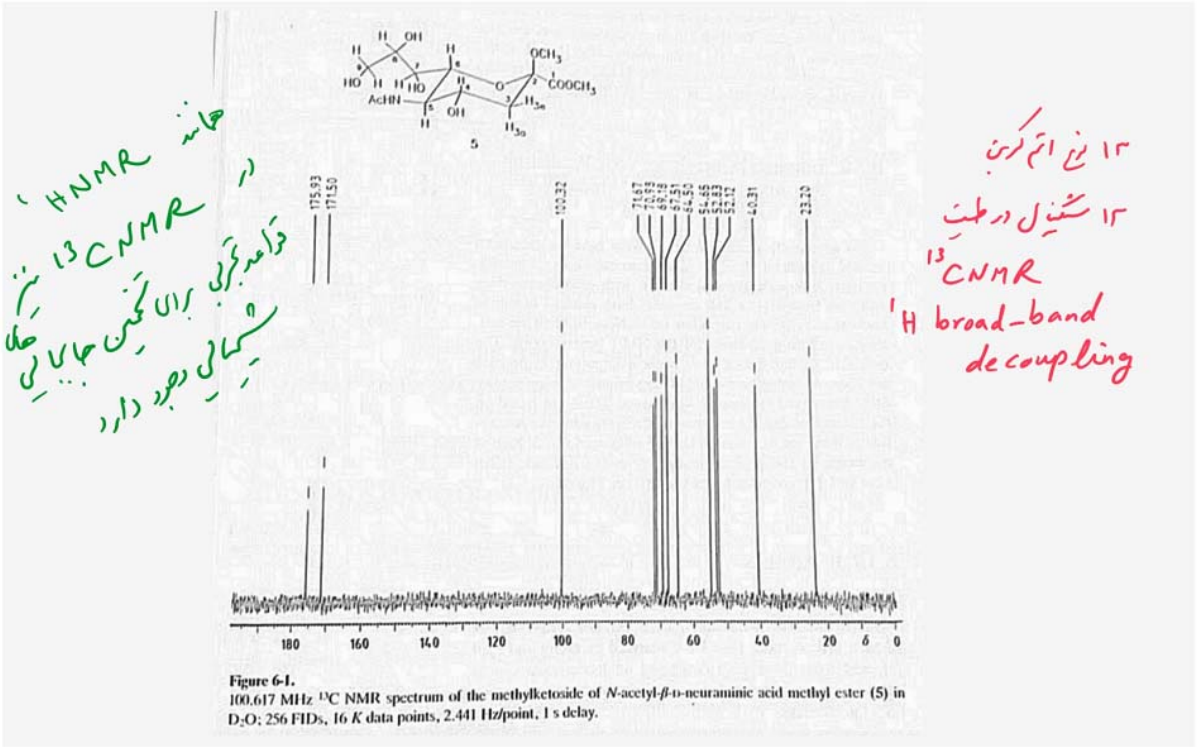


Figure 6-1.
100.617 MHz ^{13}C NMR spectrum of the methylketoside of *N*-acetyl-β-D-neuraminic acid methyl ester (5) in D_2O; 256 FIDs, 16 *K* data points, 2.441 Hz/point, 1 s delay.

Alkanes

Linear and Branched Alkanes

(Grant & Paul)

$$\delta_i = -2.3 + 9.1\,n_\alpha + 9.4\,n_\beta - 2.5\,n_\gamma + 0.3\,n_\delta + 0.1\,n_\varepsilon + \Sigma S_{ij} \text{ [ppm]} \qquad (6\text{-}4)$$

where:

δ_i = chemical shift of the carbon nucleus of interest

n = numbers of carbon atoms in the α-, β-, γ-, δ- and ε-positions relative to this nucleus

S_{ij} = steric correction terms taking account of branching.

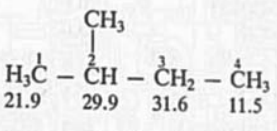
Table 6-4.
Steric correction factors S_{ij}[1] for estimating ^{13}C chemical shifts in branched alkanes by the method of Ref. [5].

i \ j	primary	secondary	tertiary	quaternary
primary	0	0	− 1.1	− 3.4
secondary	0	0	− 2.5	− 7.5
tertiary	0	−3.7	− 9.5	−15.0
quaternary	−1.5	−8.4	−15.0	−25.0

i = observed nucleus; J = neighbor nucleus
[1] from [6].

$$\delta_i = -2.3 + 9.1\,n_\alpha + 9.4\,n_\beta - 2.5\,n_\gamma + 0.3\,n_\delta + 0.1\,n_\varepsilon + \Sigma S_{ij}\ [\text{ppm}]$$

Example: 2-methylbutane (6)



6

C-1: $n_\alpha = 1, n_\beta = 2, n_\gamma = 1$
Steric corrections: primary with adjacent tertiary → − 1.1
S_{ij} = − 1.1
δ(C-1) = − 2.3 + (9.1 x 1) + (9.4 x 2) − (2.5 x 1) − 1.1 = 22.0 (22.3)

C-2: $n_\alpha = 3, n_\beta = 1$
Steric corrections: 1. tertiary with adjacent primary → 0
2. tertiary with adjacent secondary → − 3.7
S_{ij} = − 3.7
δ(C-2) = − 2.3 + (9.1 x 3) + (9.4 x 1) − 3.7 = 30.7 (30.1)

C-3: $n_\alpha = 2, n_\beta = 2$
Steric corrections: 1. secondary with adjacent tertiary → − 2.5
2. secondary with adjacent primary → 0
S_{ij} = − 2.5
δ(C-3) = − 2.3 + (9.1 x 2) + (9.4 x 2) − 2.5 = 32.2 (32.0)

C-4: $n_\alpha = 1, n_\beta = 1, n_\gamma = 2$
Steric corrections: primary with adjacent secondary → 0
S_{ij} = 0
δ(C-4) = − 2.3 + (9.1 x 1) + (9.4 x 1) − (2.5 x 2) = 11.2 (11.5)

* تفاوت در اعداد پرانتز با استفاده از برنامه Spectool محاسبه شده اند
* با این محاسبات C-1 و C-4 دقت به نسبت قابل قبولی دارند
* درباره تاثیر استریک های C-2 و C-3 مشکل وجود دارد چرا تفاوت کم است

Substituted Alkanes

ابتدا شادیر که با استفاده از رابطه زیر برای هیدروکربن بدون اکتلات شاخه محاسبه می‌شود سپس با استفاده از شادیر جدول ۵-۶ تصحیح انجام می‌گیرد

$$\delta_i = -2.3 + 9.1\,n_\alpha + 9.4\,n_\beta - 2.5\,n_\gamma + 0.3\,n_\delta + 0.1\,n_\varepsilon + \Sigma S_{ij}\ [\text{ppm}] \qquad (6\text{-}4)$$

where:

δ_i = chemical shift of the carbon nucleus of interest

n = numbers of carbon atoms in the α-, β-, γ-, δ- and ε-positions relative to this nucleus

S_{ij} = steric correction terms taking account of branching.

Table 6-5.
Substituent increments S^1 for estimating ^{13}C chemical shifts in substituted alkanes $X - C_\alpha - C_\beta - C_\gamma - C_\delta$.

Substituent	S_α	S_β	S_γ	S_δ
−D	−0.4	−0.12	−0.02	–
$-CH_3$	9.1	9.4	−2.5	0.3
$-CH{=}CH_2$	22.3	6.9	−2.2	0.2
$-C{\equiv}CH$	4.5	5.5	−3.5	–
$-C_6H_5$	22.3	8.6	−2.3	0.2
−CHO	31.9	0.7	−2.3	–
$-COCH_3$	30.9	2.3	−0.9	2.7
−COOH	20.8	2.7	−2.3	1.0
−CN	3.6	2.0	−3.1	−0.5
$-NH_2$	28.6	11.5	−4.9	0.3
$-NO_2$	64.5	3.1	−4.7	−1.0
−OH (prim.)	48.3	10.2	−5.8	0.3
−OH (sec.)	44.5	9.7	−3.3	0.2
−OH (tert.)	39.7	7.3	−1.8	0.3
−OR	58.0	8.1	−4.7	1.4
$-OCOCH_3$	51.1	7.1	−4.8	1.1
−SH	11.1	11.8	−2.9	0.7
−F	70.1	7.8	−6.8	–
−Cl	31.2	10.5	−4.6	0.1
−Br	20.0	10.6	−3.1	0.1
−I	−6.0	11.3	−1.0	0.2

[1] Adapted from [4] and [6].

Example: isobutanol (7)

$$\underset{20.4}{(\overset{3}{C}H_3)_2}\underset{32.0}{\overset{2}{C}H} - \underset{70.2}{\overset{1}{C}H_2} - OH \qquad 7$$

We treat this as being formally derived from isobutane (8) by substitution of a hydroxyl group.

$$\underset{24.6}{(CH_3)_2}\underset{23.3}{CH} - \underset{24.6}{CH_3} \qquad 8$$

For 8, by the method used in the example of 2-methylbutane (6), we calculate the following δ-values:

$\delta\,(CH_3) = 24.5$
$\delta\,(CH) = 25.0$

Using the values $S_\alpha = 48.3$, $S_\beta = 10.2$ and $S_\gamma = -5.8$, as given in Table 6-5 for a (primary) OH group, we obtain

$\delta\,(C\text{-}1) = 24.5 + 48.3 = 72.8$
$\delta\,(C\text{-}2) = 25.0 + 10.2 = 35.2$
$\delta\,(C\text{-}3) = 24.5 - 5.8 = 18.7$

Unsaturated hydrocarbons: The chemical shifts of alkenes can be calculated from Equation (6-5) [7].

$$C_\gamma - C_\beta - C_\alpha - \overset{1}{C} = \overset{2}{C} - C_{\alpha'} - C_{\beta'} - C_{\gamma'}$$

↑ ^{13}C nucleus being observed

$$\delta(\text{C-1}) = 123.3 + 10.6n_\alpha + 7.2n_\beta - 1.5n_\gamma - 7.9n_{\alpha'} - 1.8n_{\beta'} + 1.5n\gamma' + \Sigma S \text{ [ppm]} \quad (6\text{-}5)$$

where n is the number of neighbor carbon atoms of each type and S is a steric term given by:

$S = 0$ if C_α and $C_{\alpha'}$ are in the *E*-configuration ($\alpha\alpha'$, *trans*)
$S = -1.1$ if C_α and $C_{\alpha'}$ are in the *Z*-configuration ($\alpha\alpha'$, *cis*)
$S = -4.8$ for two alkyl substituents at C-1 ($\alpha\alpha$)
$S = +2.5$ for two alkyl substituents at C-2 ($\alpha\alpha'$)
$S = +2.3$ for two or three alkyl substituents at $C_{\beta'}$

Alkenes Unsaturated Hydrocarbons

$$\delta(\text{C-1}) = 123.3 + 10.6n_\alpha + 7.2n_\beta - 1.5n_\gamma - 7.9n_{\alpha'} - 1.8n_{\beta'} + 1.5n\gamma' + \Sigma S \text{ [ppm]}$$

Example: 2-methylbut-1-ene (9)

C-1: $n_{\alpha'} = 2$, $n_{\beta'} = 1$, $S = +2.5$

$$\delta(\text{C-1}) = 123.3 - (7.9 \times 2) - (1.8 \times 1) + 2.5 = 108.2$$

(108.2)

C-2: $n_\alpha = 2$, $n_\beta = 1$, $S = -4.8$

$$\delta(\text{C-2}) = 123.3 + (10.6 \times 2) + (7.2 \times 1) - 4.8 = 146.9$$

(146.9)

22.5
CH_3
$H_2\overset{1}{C} = \overset{2}{C} - \overset{3}{CH_2} - \overset{4}{CH_3}$
109.1 147.0 31.1 12.5

9

Table 6-6.
Substituent increments S_i[1] for estimating ^{13}C chemical shifts for the double-bonded carbon nuclei in alkenes using the expression:
$\delta = 123.3 + \Sigma S_i$ [ppm]

$X - \overset{1}{C}H = \overset{2}{C}H_2$

Substituent	S_1	S_2	Substituent	S_1	S_2
$-H$	0	0	$-OCH_3$	29.4	−38.9
$-CH_3$	10.6	− 7.9	$-OCOCH_3$	18.4	−26.7
$-CH_2CH_3$	15.5	− 9.7			
			$-C_6H_5$	12.5	−11.0
$-F$	24.9	−34.3	$-CH=CH_2$	13.6	− 7.0
$-Cl$	2.6	− 6.1	$-COOH$	4.2	8.9
$-Br$	− 7.9	− 1.4			
$-I$	−38.1	7.0	$-NO_2$	22.3	− 0.9

[1] Data from [6].

Substituted Alkenes

Example: crotonic acid (**10**)

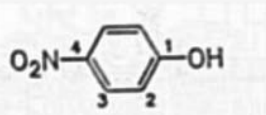
δ(C-2) = 123.3 + S_1(COOH) + S_2(CH_3)
= 123.3 + 4.2 − 7.9 = 119.6 (120.5)

δ(C-3) = 123.3 S_1(CH_3) + S_2(COOH)
= 123.3 + 10.6 + 8.9 = 142.8 (142.5)

$H_3\overset{4}{C} - \overset{3}{C}H = \overset{2}{C}H - \overset{1}{C}OOH$
18 147 122 172
(16.4) (170.0)

10

Benzene Derivatives



11

Example: p-nitrophenol (11)

δ(C-1) = 128.5 + S_i(OH) + S_p(NO_2) = 128.5 + 26.9 + 6.1 = 161.5 Exp.: 161.5 (163.4)

δ(C-2) = 128.5 + S_o(OH) + S_m(NO_2) = 128.5 − 12.8 + 0.9 = 116.6 115.9 (116.6)

δ(C-3) = 128.5 + S_m(OH) + S_o(NO_2) = 128.5 + 1.4 − 4.9 = 125.0 126.4 (125.0)

δ(C-4) = 128.5 + S_p(OH) + S_i(NO_2) = 128.5 − 7.4 + 19.9 = 141.0 141.7 (141.0)

Table 6-7.
Substituent increments S[1] for estimating ^{13}C chemical shifts in substituted benzenes using the expression:
$\delta = 128.5 + \Sigma S$ [ppm] (6-7)

Substituent	S_i	S_o	S_m	S_p
$-CH_3$	9.2	0.7	−0.1	− 3.1
$-CH_2CH_3$	15.6	− 0.5	0.0	− 2.7
−F	34.8	−13.0	1.6	− 4.4
−Cl	6.3	0.4	1.4	− 1.9
−Br	− 5.8	3.2	1.6	− 1.6
−I	−34.1	8.9	1.6	− 1.1
−OH	26.9	−12.8	1.4	− 7.4
$-OCH_3$	31.4	−14.4	1.0	− 7.7
$-OCOCH_3$	22.4	− 7.1	0.4	− 3.2
$-NH_2$	18.2	−13.4	0.8	−10.0
$-N(CH_3)_2$	22.5	−15.4	0.9	−11.5
$-C_6H_5$	13.1	− 1.1	0.4	− 1.1
−CHO	8.4	1.2	0.5	5.7
$-COCH_3$	8.9	0.1	−0.1	4.4
$-COOCH_3$	2.0	1.2	−0.1	4.3
$-NO_2$	19.9	− 4.9	0.9	6.1

[1] Data from [4].

- Decoupling Experiments
- T_1 Measurements
- Solvent and Temperature Effects and shift Reagents
- Chemical changes to the Sample
  - ^{13}C enrichment
  - Specific deuteration (synthesis or H,D exchange)
  - derivatization

سازمان پژوهشهای علمی و صنعتی ایران حسین رحمانی پژوهشکده فناوریهای شیمیایی