*Carbohydrate Research*, 111 (1982) 163–169
Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

## Note

# Linear relationship between molecular rotation and bond refraction in the α-D-mannopyranose, α-D-talopyranose, α-D-lyxopyranose, and α-D-rhamnopyranose series*

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(Received April 5th, 1982; accepted for publication, May 24th, 1982)

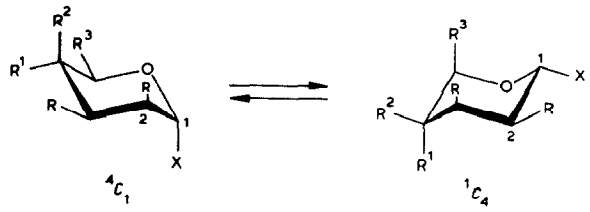
There exists a considerable amount of literature data on the molecular rotations ($[M]_D$) of carbohydrates. The lack of a satisfactory quantitative treatment of these data has prompted an exploration of the possibility of applying the simple empirical equation[1]

$$[M]_D = m\sum R_D + I \qquad (1)$$

to carbohydrates, where $\sum R_D$ is the sum of bond refractions, and m and I are constants for a given series of compounds. It has been shown[2] that this equation can correlate satisfactorily the molecular rotations of α-D-glucopyranose, α-D-galactopyranose, and α-D-xylopyranose derivatives having various C-1 substituents. An extension to α-D-mannopyranose (**1**, **2**, **7**), α-D-talopyranose (**3**, **4**), α-D-lyxopyranose (**5**, **6**), and α-D-rhamnopyranose (**8**, **9**) derivatives is now reported.

The method of calculating the $\sum R_D$ values has been described[2]. For the initial plots of $[M]_D$ against $\sum R_D$, the $\sum R_D$ values for **1**–**9** with the C-1 substituents shown in Table I (X = YZ, where Y = O, N, or S) were calculated from the Newman projection **10a** (viewed from C-1 along the C-1–Y bond). Where X = OH, OMe, $N_3$, SAlk, SAr, or OAr, the points deviate considerably from the line correlating the halogen atoms, OAc, $SCH_2Ar$, and $S(CH_2)_2Ar$ in all the plots of the literature data (Table I). The deviation is unlikely to be caused by the presence of a mixture of two chair conformers, because the compounds listed in Table I are expected to adopt mainly the $^4C_1$ conformation. The literature data[3–6] (Table II) on the conformational equilibria of α-D-lyxopyranose (**6**) and tetra-*O*-acetyl-α-D-lyxopyranose (**5**) derivatives show the preponderance of the $^4C_1$ conformer. This preponderance should be

*Linear Relationship Between Molecular Rotation and Bond Refraction in Carbohydrates, Part II. For Part I, see ref. 2.
**This work was carried out at the Max-Planck-Institut für Experimentelle Medizin, Göttingen, Germany.



$^4C_1$ $^1C_4$

1 R = $R^1$ = OAc, $R^2$ = H, $R^3$ = $CH_2OAc$
2 R = $R^1$ = OH, $R^2$ = H, $R^3$ = $CH_2OH$
3 R = $R^2$ = OAc, $R^1$ = H, $R^3$ = $CH_2OAc$
4 R = $R^2$ = OH, $R^1$ = H, $R^3$ = $CH_2OH$
5 R = $R^1$ = OAc, $R^2$ = $R^3$ = H
6 R = $R^1$ = OH, $R^2$ = $R^3$ = H
7 R = $R^1$ = OBz, $R^2$ = H, $R^3$ = $CH_2OBz$
8 R = $R^1$ = OBz, $R^2$ = H, $R^3$ = Me
9 R = $R^1$ = OAc, $R^2$ = H, $R^3$ = Me

TABLE I

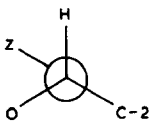
MOLECULAR ROTATIONS OF COMPOUNDS **1–9**

| *X* | $[M]_D$ | *X* | $[M]_D$ | *X* | $[M]_D$ |
|---|---|---|---|---|---|
| *Compounds* **1**[a] | | | | | |
| H | −139[9] | $OC_6H_4Me(m)$ | 318[15] | $SC_6H_4NHAc(p)$ | 486[17] |
| F | 75[10] | $OC_6H_4Me(p)$ | 304[15] | $SCH_2C_6H_4NO_2(p)$ | 918[14] |
| Cl | 330[10] | $OC_6H_4NO_2(o)$ | 571[15] | $SCH_2C_6H_4CN(p)$ | 881[14] |
| Br | 541[10] | $OC_6H_4NO_2(m)$ | 381[15] | $SCH_2C_6H_4Ph(p)$ | 869[14] |
| I | 873[10] | $OC_6H_4NO_2(p)$ | 492[16] | $SCH_2C_6H_4NHAc(p)$ | 756[14] |
| OAc | 215[11] | $OC_6H_4Br(m)$ | 380[15] | $S(CH_2)_2Ph$ | 721[14] |
| SMe | 352[12] | $OC_6H_4Br(p)$ | 365[15] | $S(CH_2)_6Me$ | 425[18] |
| OPh | 314[13] | $OC_6H_4OMe(p)$ | 435[15] | $S(CH_2)_6Cl$ | 445[18] |
| $OC_6H_4CN(o)$ | 232[14] | $OC_6H_4OEt(p)$ | 311[15] | $S(CH_2)_6CN$ | 434[18] |
| $OC_6H_4CN(p)$ | 414[14] | $OC_6H_4Bu^t(p)$ | 450[15] | $S(CH_2)_6SAc$ | 450[18] |
| $OC_6H_4Cl(p)$ | 355[15] | $SC_6H_4OMe(p)$ | −356[d14] | $N_3$ | 339[e19] |
| $OC_6H_4Et(p)$ | 318[15] | $SC_6H_4NO_2(p)$ | 692[17] | $OCOC_6H_{11}$ | 275[40] |
| *Compounds* **2**[b] | | | | | |
| H | −82[9] | $OC_6H_4OMe(p)$ | 351[c15] | $SCH_2C_6H_4NH_2(p)$ | 1132[c14] |
| F | 29[21] | $OC_6H_4OEt(p)$ | 321[c15] | $SCH_2C_6H_4NHAc(p)$ | 1163[c14] |
| OH | 54[22] | $OC_6H_4Cl(p)$ | 370[c15] | $SCH_2C_6H_4CN(p)$ | 1160[c14] |
| OMe | 153[22] | $OC_6H_4CN(o)$ | 142[c14] | $SCH_2C_6H_4CH_2$-$NH_2(p)$ | 964[c14] |
| $OC_6H_4NO_2(o)$ | 300[c15] | $OC_6H_4CN(p)$ | 410[c14] | | |
| $OC_6H_4NO_2(m)$ | 394[c15] | $OC_6H_4NH_2(p)$ | 350[c14] | $SCH_2C_6H_4Ph(p)$ | 1205[c14] |
| $OC_6H_4NO_2(p)$ | 437[16] | $OC_6H_4CH_2NH_2(o)$ | 215[14] | $S(CH_2)_2Ph$ | 1026[c14] |
| $OC_6H_4Me(m)$ | 313[c15] | $OC_6H_4CH_2NH_2(p)$ | 311[14] | $S(CH_2)_6Me$ | 556[c18] |
| $OC_6H_4Me(p)$ | 332[c15] | $SC_6H_4OMe(p)$ | 767[c14] | $S(CH_2)_6OH$ | 444[18] |
| $OC_6H_4Br(m)$ | 346[c15] | $SC_6H_4NHAc(p)$ | 533[c14] | $S(CH_2)_6NH_2$ | 348[18] |

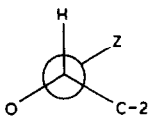
TABLE I *(continued)*

| *X* | $[M]_D$ | *X* | $[M]_D$ | *X* | $[M]_D$ |
|---|---|---|---|---|---|
| $OC_6H_4Br(p)$ | 383[c15] | $SC_6H_4NO_2(p)$ | 1008[c14] | $S(CH_2)_6Cl$ | 557[c18] |
| $OC_6H_4Et(p)$ | 302[c15] | $SC_6H_4NH_2(p)$ | 766[14] | $S(CH_2)_6CN$ | 552[c18] |
| $OC_6H_4Bu^t(p)$ | 345[c15] | $SCH_2C_6H_4NO_2(p)$ | 530[c,f14] | | |
| *Compounds* **3**[a] | | | | | |
| H | −54[9] | OAc | 265[24] | $SC_6H_4NHAc(p)$ | 626[25] |
| Br | 681[23] | $OC_6H_4NO_2(p)$ | 544[25] | | |
| $N_3$ | 442[19] | $SC_6H_4NO_2(p)$ | 788[25] | | |
| *Compounds* **4**[b] | | | | | |
| H | −19[9] | $OC_6H_4NO_2(p)$ | 564[c25] | $SC_6H_4NO_2(p)$ | 1049[c25] |
| OMe | 204[26] | $OC_6H_4NH_2(p)$ | 409[c25] | | |
| *Compounds* **5**[a] | | | | | |
| H | −193[9] | Br | 474[28] | OMe | 86[30] |
| F | −15[27] | $N_3$ | 155[19] | OCOPh | 200[31] |
| Cl | 265[28] | OAc | 80[29] | $OCH_2Ph$ | 195[29] |
| *Compounds* **6**[b] | | | | | |
| H | −132[9] | OH | 8[33] | | |
| OMe | 97[32] | $OCH_2Ph$ | 184[29] | | |
| *Compounds* **7**[a] | | | | | |
| F | −515[27] | Br | 77[34] | OMe | −412[34] |
| Cl | −188[34] | I | 317[34] | OCOPh | −130[34] |
| *Compounds* **8**[a,g] | | | | | |
| H | −1285[35] | Cl | −673[36] | I | 160[36] |
| F | −1104[27] | Br | −350[36] | OMe | −872[36] |
| *Compounds* **9**[a,g] | | | | | |
| H | −132[35] | Cl | 392[37] | OAc | 209[39] |
| OMe | 181[35] | Br | 566[38] | | |

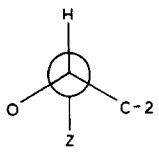
[a]In chloroform. [b]In water. [c]In methanol. [d]This value seems to be erroneous in sign. [e]In 1,4-dioxane; the $\Sigma R_D$ value (5.69) for X = $N_3$ is calculated for conformer **10b** for the resonance form C-N=N⁺=N⁻ with $R_D$ (N = N) = 4.12 (ref. 20). [f]This value seems to be erroneous, because it has only half the expected magnitude (*cf.* the corresponding $NH_2$, CN, NHAc, and Ph compounds). [g]Obtained from the α-L enantiomers.




10a




10b




10c

TABLE II

PERCENTAGE OF $^4C_1$ CONFORMER IN **5** AND **6**

| *X* | | $^4C_1$ (%) | *Reference* |
|---|---|---|---|
| **5** | OAc | 71[a]; 100[b] | 3,4 |
| | OMe | 83[a]; 100[b] | 3,4 |
| | OBz | 72[a] | 3 |
| | SAc | 64[a] | 3 |
| | Br | 96[b] | 3 |
| | Cl | 91[b] | 3 |
| | $N_3$ | 52[b] | 5 |
| **6** | OH | 75[c]; 50[c] | 4,6 |
| | OMe | 90[c] | 4 |

[a]In $CD_3COCD_3$. [b]In $CDCl_3$. [c]In $D_2O$.

TABLE III

CORRELATIONS OF MOLECULAR ROTATIONS WITH BOND REFRACTIONS[a] IN COMPOUNDS **1–9** BY USE OF EQUATION *1*

| *Compound* | *n*[b] | *r*[c] | *Slope (m)* | *Intercept (I)* | *Average deviation*[d] (%) |
|---|---|---|---|---|---|
| **1** | 34 | 0.944 | 55.7 | 25.0 | 13 |
| **2** | 35 | 0.954[e] | 93.3 | −212 | 32 (15)[f] |
| **3** | 6 | 0.985 | 56.7 | 106 | 5 |
| **4** | 4 | 0.998 | 94.7 | −109 | 4 |
| **5** | 8 | 0.951 | 56.0 | −80.4 | 22[g] |
| **6** | 3 | 0.998 | 101 | −227 | 4[h] |
| **7** | 6 | 0.954 | 60.5 | −535 | 42 (20)[i] |
| **8** | 5 | 0.996 | 93.7 | −1225 | 6 |
| **9** | 4 | 0.998 | 59.3 | 8.0 | 4 |

[a]For method of calculating $\Sigma R_D$, see ref. 2; conformer **10a** was used for X = $SCH_2Ar$ and $S(CH_2)_2Ar$; conformer **10b** was used for X = OH, OMe, SR, OAr, SAr, and $N_3$. [b]Number of points used in the correlations. The point for X = H is not used (see text). [c]Correlation coefficient. [d]Average deviation of observed molecular rotations from the corresponding values calculated from the correlation lines. [e]X = $SCH_2C_6H_4NO_2(p)$ is not used (see footnote *f* of Table I). [f]Excluding X = $OC_6H_4CN(o)$, OH, and F (the latter two give comparatively large % deviations because of their comparatively small molecular rotations). [g]Excluding X = F, which has a comparatively small molecular rotation. [h]Excluding X = OH, which has a comparatively small molecular rotation. [i]Excluding X = OBz.

greater for **1–4** and **7–9** because of the presence of an additional substituent at C-5. However, when the $\sum R_D$ values calculated for conformation **10b** (**10c** gives identical $\sum R_D$ values, but the contribution of this conformation is negligible because of steric hindrance[7]) are used for the former substituents, satisfactory plots are obtained (Table III). These results suggest that these substituents favour the conformation

TABLE IV

A COMPARISON OF THE INTERCEPTS (I) OF EQUATION *1* AND THE MOLECULAR ROTATIONS ($[M]_D$) OF THE 1,5-ANHYDRO-D-ALDITOLS

| *Compound* | $I - [M]_D$ | *Ref.* |
|---|---|---|
| 1,5-Anhydro-D-mannitol tetra-acetate (**1**, X = H) | 164 | This work |
| 1,5-Anhydro-D-talitol tetra-acetate (**3**, X = H) | 160 | This work |
| 1,5-Anhydro-D-lyxitol triacetate (**5**, X = H) | 113 | This work |
| 1,5-Anhydro-D-rhamnitol triacetate (**9**, X = H) | 140 | This work |
| 1,5-Anhydro-D-mannitol (**2**, X = H) | −130 | This work |
| 1,5-Anhydro-D-talitol (**4**, X = H) | −90 | This work |
| 1,5-Anhydro-D-lyxitol (**6**, X = H) | −95 | This work |
| 1,5-Anhydro-D-glucitol tetra-acetate | 121[a] | 2 |
| 1,5-Anhydro-D-galactitol tetra-acetate | 106[b] | 2 |
| 1,5-Anhydroxylitol triacetate | 68[c] | 2 |
| 1,5-Anhydro-D-glucitol | 19[d] | 2 |
| 1,5-Anhydro-D-galactitol | 61[e] | 2 |
| 1,5-Anhydroxylitol | 41[c] | 2 |

[a] $[M]_D = 130$ ($CHCl_3$); ref. 41. [b] $[M]_D = 160$ ($CHCl_3$); ref. 9. [c] $[M]_D = 0$ (*meso* compound). [d] $[M]_D = 70$ ($H_2O$); ref. 42. [e] $[M]_D = 126$ ($H_2O$); ref. 9.

**10b** rather than **10a**. This finding is surprising, because **10a** would be expected to be favoured as a result of the exo-anomeric effect. In the corresponding C-2 epimers (α-D-glucopyranose, α-D-galactopyranose, and α-D-xylopyranose derivatives), **10a** is favored over **10b** because of the exo-anomeric effect and steric factors[7], and our previous results[2] are in agreement with this fact. Another puzzling observation is the different behaviour of $S(CH_2)_nAr$ ($n$ = 1 or 2) from SAr and SAlk. The $O(CH_2)_nAr$ ($n$ = 1 or 2) substituent might be expected to show the trend of the corresponding thio substituents. The lack of literature data does not permit verification of this point or a check on whether the same trend persists for higher values of $n$.

The average value of m in the above equation is 57 ±2 for the acetate series (**1**, **3**, **5**, **9**), 77 ±16 for the benzoate series (**7**, **8**), and 96 ±5 for the three parent series (**2**, **4**, **6**). The constancy in the m values shows that the magnitude of m is independent of the position of the groups on C-3,4,5. This constancy is also observed in the corresponding C-2 epimers[2]. The average m value for the acetate series is identical to that[2] (57) of the corresponding C-2 epimers, but the average m value of the parent series is about twice that[2] (40) of the corresponding C-2 epimers.

Previously[2], $\sum R_D = 0$ was assigned for X = H. However, a more detailed analysis shows that the point for X = H generally deviates from the corresponding correlation line. This is probably due to the failure of the above equation when the centre is achiral[1]. It is observed that the $[M]_D$ value for X = H differs from the intercept of the corresponding correlation line by about the same magnitude in the acetate series as well as in the parent series. This trend is also observed in the corresponding C-2 epimers (Table IV).

The plots are not as good as those of the C-2 epimers, probably because of the presence of significant and different amounts of the $^1C_4$ conformations for various substituents. The compounds where X = $NHC_6H_4NO_2(p)$ and $N(Ac)C_6H_4NO_2(p)$ in **5** have the $^1C_4$ conformation, and their reported molecular rotations [$-48° \rightarrow -194°$ and $-771°$, respectively, (chloroform)][8] do not fit in the correlation line of **5** having the $^4C_1$ conformation.

ACKNOWLEDGMENTS

The Alexander von Humboldt Stiftung is acknowledged for a research fellowship, the Max-Planck-Institut für Experimentelle Medizin for its library facilities, and Professor W. Saenger for laboratory facilities.

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