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Description of Steric Relationships Across Single Bonds

By W. KLYNE[1] and V. PRELOG[2]

The growth of interest and knowledge regarding the steric relationships between atoms and groups connected by single bonds makes some agreed system of nomenclature desirable. At present different terms are used by different schools eg. *syn, anti, cis, trans, skew, gauche, opposed, staggered*, etc.; all of these have other meanings in other circumstances.

Relative position of two atoms or groups across a single bond. Let us consider the general system of four linked atoms A–X–Y–B (I), in which the middle bond XY is single, although the other two bonds AX and YB may be single or double. (For the sake of convenience, they will be shown as single in most of this discussion.) If this system is projected on to a plane at right angles to XY, it may be represented as IA[3]. The essential parameter, which defines the relative position of A and B across the bond X–Y, is the angle τ i.e. the angle AXYB, the *torsion angle* between A and B across the bond XY.

To distinguish between enantiomeric types the angle τ is considered as *positive* when it is measured *clockwise* from the *front* substituent A *to the rear* substituent B, (I) and *negative* when it is measured *anticlockwise* (II)[4].

Partial conformations. The partial conformation of two bonded atoms (X, Y) with all their substituents across the bond (X–Y) may be defined in terms of the *torsion angle between the two most preferred substituents* (one on each atom).

The most preferred substituents are chosen by means of the *Sequence Rules* of CAHN, INGOLD, and PRELOG[5]; the following additional rules are necessary for special cases.

(i) If all substituents on one of the two bonded atoms are identical, the *smallest* of the possible torsion angles is chosen to define the conformation.

(ii) If on a tetrahedral atom (X or Y) there are two like substituents *aa* and one unique substituent *b*, the position of the *unique substituent b* determines the conformational designation, *without reference to the sequence rule.*

These conventions suffice to deal with all combinations of tetrahedral, trigonal, or digonal atoms (X, Y), whereas most of the terms previously used – e. g., skew, gauche, opposed, staggered – apply only to one type of structure (e.g., two tetrahedral atoms).

Approximate description of conformations. It is often necessary to discuss the relative positions or conformations of groups across a bond X–Y, when the exact angles are not known. A combination of three almost self-explanatory simple terms may be used to describe the angle τ approximately. The terms *periplanar* and *clinal* are introduced to indicate 'approximately planar' and 'inclined', cf. (III). The terms *syn* and *anti* are used to indicate $\tau < 90°$ and $\tau > 90°$ (cf. IV). If the dividing lines shown in formulae III and IV are combined (as in V) the circle is divided into sextants[6]. (Abbreviations are shown in the Table). The use of *plus* and *minus* signs, where required to differentiate between enantiomeric conformations, has been discussed above (cf. VI); the combination of this distinction with the two previous ones gives the terms shown in formula VII and in the Table.

$0° \pm 30°$	$\pm$ syn-periplanar	($\pm$ sp)
$+60° \pm 30°$	+ syn-clinal	(+ sc)
$+120° \pm 30°$	+ anti-clinal	(+ ac)
$180° \pm 30°$	$\pm$ anti-periplanar	($\pm$ ap)
$-120° \pm 30°$	– anti-clinal	(– ac)
$-60° \pm 30°$	– syn-clinal	(– sc)

Examples. Since torsion angles play an important role in discussions of stabilities, reaction mechanisms, optical rotatory dispersion, and other stereochemical problems, the proposed description of positions and conformations can often be used to define the geometry without the necessity for expensive diagrams (which are often not on the same page as the text). The following examples are taken from the recent literature. It

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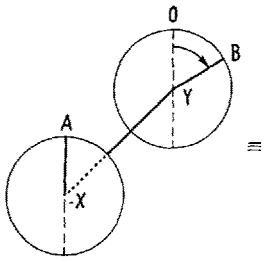
[3] In projection formulae of type (IA), Y should lie directly behind X; for the sake of legibility it is printed immediately to one side. It is convenient to show the valency bonds of the rear atom Y by dashed lines (– – –).

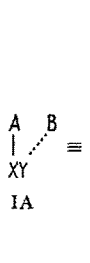
[4] The same sign is obtained if one condiders the system from the opposite direction – e. g. IB is I looked at from the direction B-Y to X-A; τ is still positive.

[5] R. S. CAHN, C. K. INGOLD, and V. PRELOG, Exper. *12*, 81 (1956).

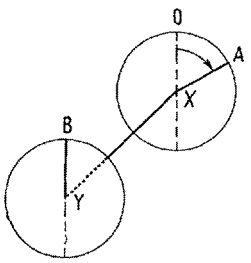
[6] Sextants have been chosen because in the important case of two tetrahedral atoms (X, Y), the potential energy curve has six extrema.



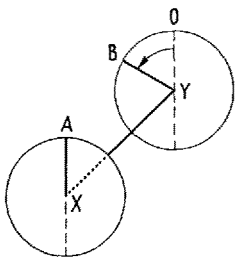
I τ positive



IA

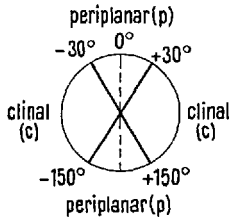


IB

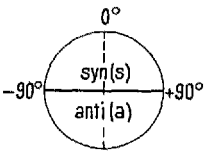


II τ negative

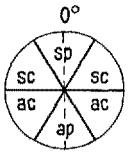
IIA



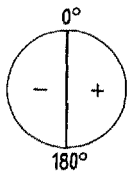
III



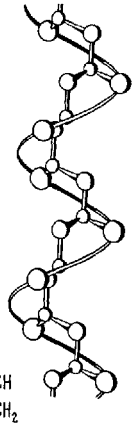
IV

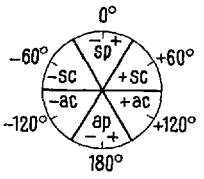


V

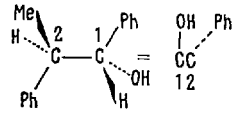


VI

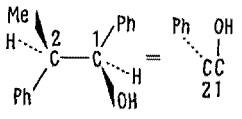




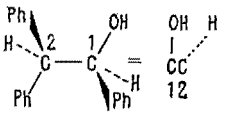
VII



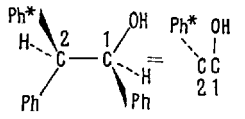
VIII (erythro)
$\tau \sim +60°$ (+ sc)



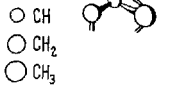
IX (threo)
$\tau \sim -60°$ (− sc)

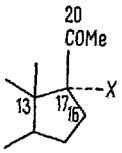


X unlabelled
τ (H, OH) $\sim +60°$ (+ sc)

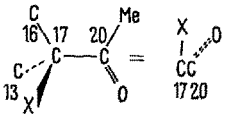


XI ^{14}C-labelled
τ (Ph*, OH) $\sim -60°$ (− cs)

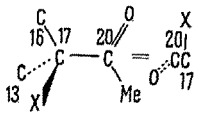




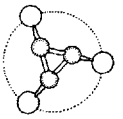
XII



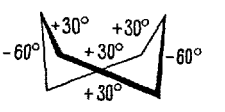
XIII
(τ X, O) $\sim +60°$ (+ sc)



XIV
τ (X, O) $\sim -120°$ (− ac)



XV



XVI Twist or skewed conformation of cyclohexane.

should be noted that the *configurations* of asymmetric atoms are *not included* in the description of the conformation.

A simple illustration of the use of these conventions is given by formulae VIII and IX and the designations under them. These two formulae represent, according to ABD ELHAFEZ and CRAM[7], the preferred conformations across the C-1, C-2 bond of the diastereoisomers of 1,2-diphenylpropan-1- ol.

A second example which shows (a) the treatment of identical groups and (b) the treatment of isotopically labelled groups according to the Sequence Rule[5] is taken from the work of COLLINS and BONNER[8] on the 1,2,2-triphenylpropan-1-ols. In the unlabelled compound (X), the two phenyl groups on C-2 are identical, and the conformational designation is therefore based on the relative positions of H(C-2) and OH(C-1): (+ sc). In the ^{14}C-labelled compound (XI), however, the phenyl groups are not identical; the labelled group Ph* takes precedence over the unlabelled; and the conformational designation is based on the relative positions of Ph* (C-2) and OH(C-1): (− sc).

The third example introduces a trigonal atom. DJERASSI *et al.*[9] have inferred from rotatory dispersion measurements that the favoured conformation of the acetyl side chain in 17α-halo-17β-acetyl steroids (17α-halo-20-oxo-pregnanes; XII) is that shown in formula XIV (C–17, C-20: − ac) and not XIII (C-17, C-20: + sc).

The proposed description of partial conformations is particularly convenient for defining and memorizing the geometry of helices and rings, which are often difficult to remember, e.g. the helix of fibrous sulphur is built from $+76°$ or from $-76°$ partial conformations (PAULING[10]), and the helix of isotactic polypropylene can be described as $(+60°, 180°)_n$ or $(-60°, 180°)_n$ (NATTA[11]; cf. XV).

[7] F. ABD ELHAFEZ and D. J. CRAM, J. Amer. chem. Soc. *74*, 5846 (1952).

[8] C. J. COLLINS and W. A. BONNER, J. Amer. chem. Soc. *77*, 96 (1955).

[9] C. DJERASSI, I. FORNAGUERA, and O. MANCERA, J. Amer. chem. Soc. *81*, 2385 (1959).

[10] L. PAULING, Proc. nat. Acad. Sci., Wash. *35*, 495 (1949).

[11] G. NATTA, Exper. Suppl. *7*, 28 (1957).

The partial conformations of cyclohexane are as follows: chair form $(+60°, -60°)_3$, twist or skewed form[12] (XVI) $(+30°, +30°, -60°, +30°, +30°, -60°)$ and the boat form $(+60°, -60°, 0°)_2$.

One of the two conformations of cyclononylamine hydrobromide, as determined by X-rays (BRYAN and DUNITZ[13]) can be described as follows, starting with the torsion angle for the C-1, C-2 bond; $-73°$, $-65°$, $+67°$, $+48°$, $-94°$, $+86°$, $-104°$, $+43°$, $+84°$. The stable conformation of cyclodecane (as found in 1,6-trans-diaminocyclodecane dihydrochloride; HUBER-BUSER and DUNITZ[14]) can be easily memorized as $-sc$, $-sc$, $+ap$, $-sc$, $-sc$, $+sc$, $+sc$, $-ap$, $+sc$, $+sc$. The enantiomeric conformations of cyclododecane (DUNITZ and SHEARER[15]) are $(-sc, -sc, +ap)_4$, and $(+sc, +sc, -ap)_4$.

It may be noted that torsion angles of partial conformations related by a pure rotation or screw axis have the same sign, whereas those related by a centre of symmetry or a mirror plane have opposite signs.

Zusammenfassung

Es werden Konventionen vorgeschlagen, welche erlauben, die Lage von zwei Atomen oder Gruppen A B an zwei mit einfacher Bindung verbundenen Atomen X Y durch die Angabe des Torsionswinkels τ eindeutig zu bezeichnen. Durch Kombination dieser Konventionen mit den früher vorgeschlagenen Rangordnungsregeln[5] wurden eindeutige Bezeichnungen für partielle Konformationen (Konstellationen) abgeleitet.

[12] P. HAZEBROEK and L. J. OOSTERHOFF, Disc. Faraday Soc. *10*, 87 (1951). – R. E. REEVES, Ann. Rev. Biochem. *27*, 17 (1958). – K. E. HOWLETT, J. chem. Soc. *1957*, 4353. – N. L. ALLINGER, J. Amer. chem. Soc. *81*, 5727 (1959). – R. D. STOLOW, J. Amer. chem. Soc. *81*, 5806 (1959).

[13] R. BRYAN and J. D. DUNITZ, Helv. chim. Acta *43*, 3 (1960).

[14] E. HUBER-BUSER and J. D. DUNITZ, Helv. chim. Acta *43*, 760 (1960).

[15] J. D. DUNITZ and H. M. M. SHEARER, Helv. chim. Acta *43*, 18 (1960).

Chemische Konstitution und mutagene Wirkung. Klassifizierungsversuch chemischer Mutagene

Von G. RÖHRBORN*

«Wissenschaftsgebiete, die sich in sehr rascher und intensiver Entwicklung befinden, lassen sich schwer zusammenfassen. Das gilt besonders für die experimentelle Mutationsforschung...». Diese Worte prägte TIMOFÉEFF-RESSOVSKY[1] bereits 1937, also mehrere Jahre bevor die ersten klar wirksamen chemischen Mutagene gefunden wurden[2,3,4]. Seither sind von vielen Forschern an den verschiedensten Objekten zahlreiche Verbindungen mit signifikanter mutagener Wirkung erprobt und beschrieben worden. Es ist deshalb im Rahmen der vorliegenden Arbeit unmöglich, alle mutagenen Chemikalien abzuhandeln. Ausgehend von einem Vorschlag LEDERBERGS[5], die chemischen Mutagene in drei Gruppen, nämlich die alkylierenden Agenzien, die Peroxyde und eine gemischte Gruppe zu unterteilen, soll vielmehr versucht werden, die chemischen Mutagene unter dem Gesichtspunkt gemeinsamer Beziehungen in Konstitution und Wirkungsweise zu ordnen und die wichtigsten Vertreter jeder Gruppe zu erörtern. Zu diesem Zweck wurden aus der sogenannten gemischten Gruppe mehrere neue Gruppen gebildet und als gleichberechtigt neben die alkylierenden Agenzien und Peroxyde gestellt. Soweit dies aus klassifikatorischen Gründen nötig erschien, wurden innerhalb der einzelnen Gruppen Untergruppen eng verwandter Verbindungen gebildet.

A. Alkylierende Agenzien

Biologisch wirksame alkylierende Agenzien sind hochreaktive Verbindungen, die auf andere Moleküle oder Atome einen Alkylrest übertragen können. In diese, bei weitem umfangreichste und biochemisch bestuntersuchte Gruppe gehören die stärksten chemischen Mutagene. Ihre Mutagenität wurde an Metazoen, höheren Pflanzen und Mikroorganismen übereinstimmend nachgewiesen. Eine Sonderstellung innerhalb dieser Gruppe nehmen die sogenannten *Radiomimetika* ein; sie sollen deshalb zuerst behandelt werden.

Der Begriff radiomimetisch hat seit seiner Prägung durch DUSTIN[6] mancherlei Wandlungen durchgemacht und wird heute oft unterschiedlich gebraucht. Wir wollen nach KOLLER[7] nur solche Stoffe als Radiomimetika bezeichnen, die mit ionisierenden Strahlen folgende Ef-

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[1] N. W. TIMOFÉEFF-RESSOVSKY, *Mutationsforschung in der Vererbungslehre* (Steinkopff, Dresden und Leipzig 1937).

[2] C. AUERBACH, Proc. Roy. Soc. Edinburgh *B 62*, 211 (1946).

[3] F. OEHLKERS, Z. Vererbungslehre *81*, 313 (1943).

[4] I. A. RAPOPORT, Dok. Akad. Nauk. USSR *10*, 12 (1946).

[5] L. LEDERBERG, Bacter. Rev. *21*, 133 (1957).

[6] P. DUSTIN, Nature *159*, 794 (1947).

[7] P. KOLLER, Progr. Biophys. *4*, 195 (1954).