Differential Geometry and Organic Chemistry; the Bonnet Transformation Applied to the Racemization of Tri-*o*-thymotide and Isomerization of Cyclophenes

Zoltan Blum,[a] Sven Lidin[a] and Lennart Eberson[b]

[a]Inorganic Chemistry 2 and [b]Organic Chemistry 3, Chemical Center, University of Lund, P.O. Box 124, S-221 00 Lund, Sweden

Concepts borrowed from differential geometry, minimal surfaces and the Bonnet transformation are applied to molecular reorganizations in organic chemistry. Both racemization and *E*/*Z*-isomerization of double bonds can be interpreted in terms of transformations of surfaces.

Solid-state structures can advantageously be viewed as infinite arrangements of surface elements. The periodic recurrence of discrete entities enables the mind to vizualise particular surfaces, the characteristics of which can be exploited descriptively. Recently, a number of solid-state structures have been described on the basis of infinite periodic minimal surfaces.[1-4] The features of these surfaces, as described by the concepts of differential geometry, have been used to illuminate various properties of the structures.[5-7]

A minimal surface is characterized by every point in it being a saddle point. In the terminology of curvature, the Gaussian curvature is always negative and the mean curvature is zero.[18] Minimal surfaces can be interconverted through the Bonnet transformation[8] (Fig. 1), the most restrictive of all topological transformations. It is isometric (angles and line-segment lengths are preserved) and can be visualized as a bending of one surface into another. If operating on a chemical structure, residing on a minimal surface, the transformation of one structure into another can be reduced to the bending, i.e. a *combined* translation *and* rotation, of the surface; bond angles and lengths will be kept intact, along the surface, during the entire process and the atoms will move along elliptical paths.[9] Furthermore, any solvent shell, with solvent molecules attached to consecutive parallel surfaces, will remain essentially unperturbed.[10] Chemical structures must often be regarded as more or less close approximations to surfaces. As a result, during the transformation some congestion and perturbation is unavoidable and hence strict adiabaticity will be unattainable.
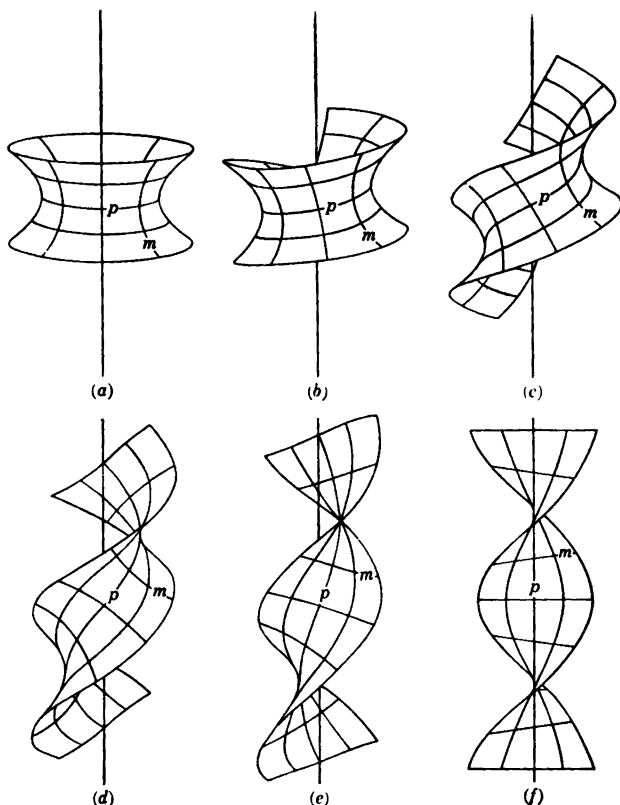
A close examination of the Bonnet transformation when applied to the catenoid-helicoid interconversion (see Fig. 1.) reveals *i* that the two helicoidal "end-points" have opposite chirality, and *ii* that straight lines become plane lines of curvature and vice versa. When the Bonnet transformation is applied to more elaborate surfaces the result is a transformation of, e.g., the P (Primitive) to the D (*D*iamond) surface, both achiral, the chiral G (*G*yroid) surface appearing *en route* [Fig. 2, (eqn. 1)].

$$P \rightleftharpoons G(+) \rightleftharpoons D \rightleftharpoons G(-) \rightleftharpoons P \rightleftharpoons \ \rightleftharpoons \text{etc.} \qquad (1)$$
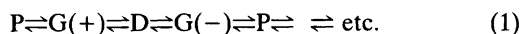
Discussion

Two examples of Bonnet-related transformations of chemical structures have been identified so far, viz. the martensite transformation[9] and the packing of DNA into chromatine.[10] In the case of the martensite transformation, the *fcc* austenite structure is transformed to the *bcc* structure of

Fig. 1. The Bonnet transformation of a
catenoid (a) to a helicoid (b).

martensite. This can be described as a Bonnet transformation of the D-minimal surface into the gyroid minimal surface. The DNA packing can be described as two consecutive Bonnet transformations in the helicoid to catenoid system.

Given these illustrative examples, both depicting reorganization of polyatomic systems, a search for similar transformations of organic molecules was undertaken. Noting the salient qualities of the Bonnet transformation, chiral lability, especially in so-called high symmetry chiral molecules, and E/Z isomerizations of double bonds should be suitable phenomena for investigation.
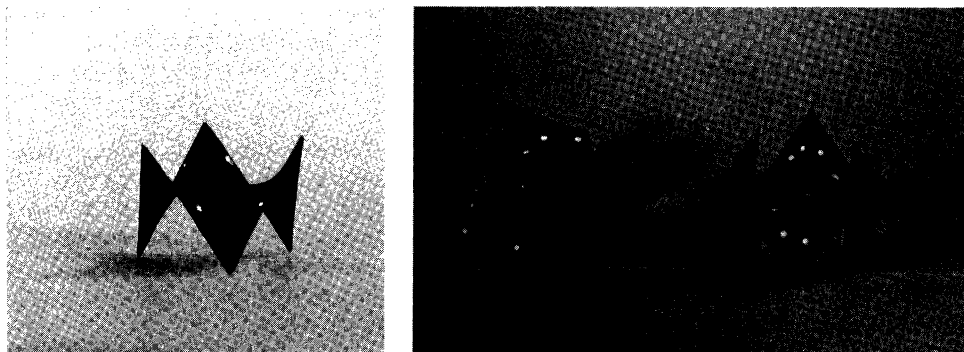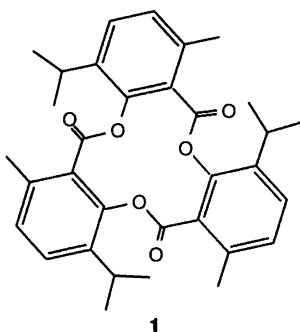

Fig. 2. The Bonnet transformation of the P-saddle to the D-saddle via the G-saddle (left to right).
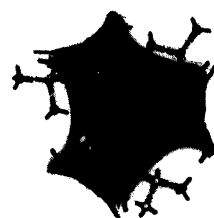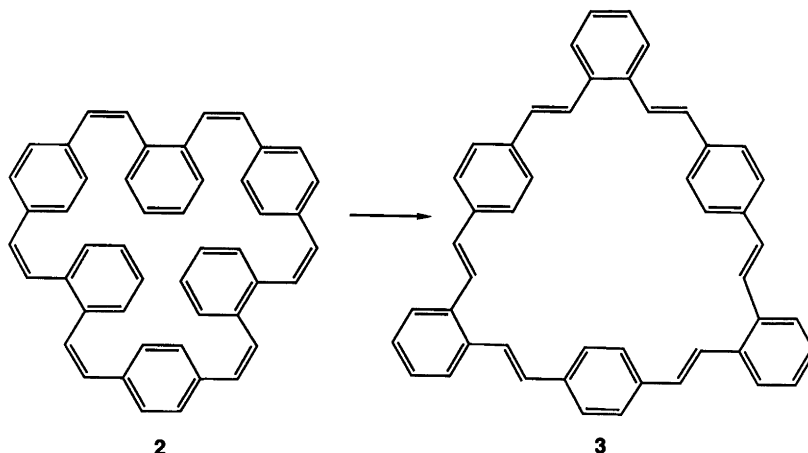
Scheme 1.

1

a

b

Fig. 3. Tri-*o*-thymotide; a: space filling model showing the substantial crowding; b: a tentative fitting to the G-saddle; the carbonyl groups are on the other side of the surface.

*Racemization.*Tri-*o*-thymotide (1, 4,10,16-triiso-propyl-1,7,13-trimethyl-6*H*,12*H*, 18*H*-tribenzo-trione), [*b,f,j*][1,5,9]trioxacyclododecin-6,12,18 an archetypal chirally labile compound, is a tri-meric lactone of 2-methyl-5-isopropylsalicylic acid.[11] It is described as a three-bladed propeller[12] and is surprisingly easy to synthesize by trimer-ization of the monomer in spite of the formation of a 12-membered ring. Both the appearance of the molecule and its ease of formation can be accounted for by assuming a strong drive to form the molecular equivalent of the monkey saddle of the G-minimal surface (Fig. 3). The central part of the molecule embraces the surface with the three carbonyl oxygens situated above the sur-face on one side, and the remaining three ox-ygens are located on the other side of the surface. Although an exact alignment to the G-monkey saddle involves non-planar benzene rings, there is ample precedence for such non-planarity in the literature.[13] In this context it is pertinent to real-ize that if a chemical structure could be fitted *exactly* to a Bonnet-related chiral minimal surface any *observable* chirality would vanish in that the structure would very rapidly equilibrate between the enantiomeric (energetically equivalent) end-points.

Establishing the structure of tri-*o*-thymotide as closely related to the G-surface suggests that it should be able to undergo the Bonnet transform-ation and hence readily racemize. Indeed, en-antiomerically pure tri-*o*-thymotide is reported to racemize in solution with $t_{1/2} \simeq 3.5$ min.[14] DNMR studies of conformational changes in tri-*o*-thymo-tide[15] revealed that the racemization is a stepwise process in which the enantiomers are intercon-verted via two rapidly equilibrating, also enantio-meric, intermediates. Theoretically, the Bonnet transformation should be continuous along the

particular surface. In this case, and in fact analo-gously to the martensite transformation, owing to severe congestion the transformation is undertak-en stepwise. Clearly, the crowding in the mole-cule does not permit a concerted inversion of all three *trans* ester bonds. After the first inversion the molecule attains a helical shape retaining the original chirality. As the transformation propaga-tes, a second helical form with opposite chirality appears, setting the stage for a final inversion. This mechanism seems to be general for related chirally labile compounds and may be responsible for the observed gear effect in crowded mole-cules.

E/Z isomerizations. All-*Z*[2_6]-orthoparacyclo-phene (2) isomerizes to the all-*E* analogue (3) upon irradiation[15] (Scheme 1). The all-*Z* isomer can be fitted to the D-monkey saddle and by a 90° bending, i.e. a Bonnet transformation, of the *surface* the all-*E* isomer can be fitted to the re-sulting P-monkey saddle (cf. Fig. 3). The mole-cular organization in the two isomers is such that the all-*Z* isomer is quite congested and the all-*E*

Scheme 1.   2   3

is extended (Fig. 4), in accordance with the general features of the respective monkey saddles. Thus, the observed exothermicity of the isomerization is explained in terms of release of steric strain and increased availability for solvation. If one allows for the interactive impact of curved surfaces (see Ref. 6), the exothermicity is self-evident as the amount of exposed curved area is approximately duplicated in the all-E isomer.

a

b

Fig. 4. Space filling model of a: all-Z [2$_6$]-orthoparacyclophene, and b: all-E [2$_6$]-orthoparacyclophene.

In the photoisomerization of [2$_6$]-paracyclophenes 4 and 5,[16] two different minimal surfaces are employed. Compound 4 can be fitted to a part of the helicoid and the isomerization proceeds toward the catenoid (cf. Fig. 1). However, the formation of a catenoid would require isomerization of the four Z double bonds to E and the two E double bonds to Z. This would create a highly congested and strained molecule, and hence the transformation only proceeds to the level where all the double bonds are slightly twisted. At this level the identity of the individual double bonds is lost, and when the molecule reverts to the original helicoid the deuterium labels have become scrambled.
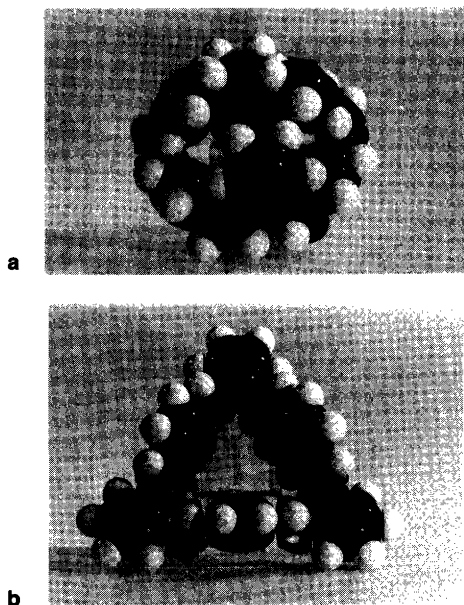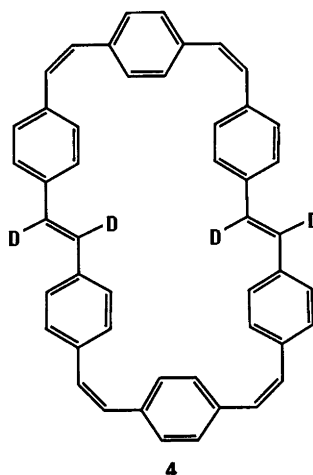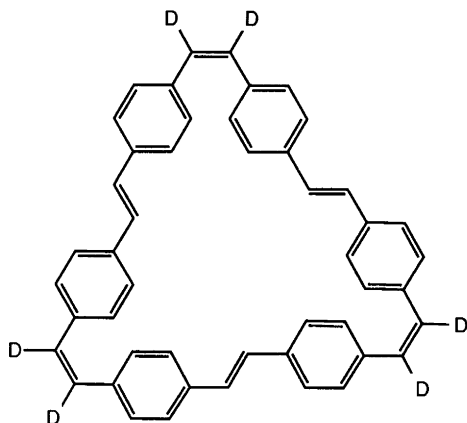
Scheme 2.   4

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Scheme 3.

5

Compound **5** can be fitted to the G-monkey saddle and is isomerized analogously to tri-*o*-thymotide but in a concerted fashion.

Both these latter *E/Z* isomerizations interconvert energetically equivalent isomers; the first case is a double-bond permutation, the second is a racemization (if one disregards the deuterium substitution!). Generally, in photoisomerizations, one can assume that upon irradation a more accurate alignment to the particular minimal surfaces is achieved. This assumption is based on the known conformational mobility of excited states.[17]

Conclusion

Chirality interconversions, racemization and inversion, and to some extent *E/Z* isomerizations are commonly encountered in organic chemistry. Differential geometry provides a way to explain and understand the underlying mechanistic requirements. The Bonnet transformation is the only "non-destructive" pathway to inversion available to a chiral structure in which the chirality is a result of hindered rotation around critical, formally rotationally unrestricted bonds. By regarding large, formally planar, unsaturated systems as nets tesselating minimal surfaces, the products of isomerization can be understood in terms of new minimal surfaces resulting from Bonnet transformations of the starting surfaces.

Fitting molecules to non-Euclidian surfaces and moving atoms and groups on ellipses rather than circles may seem to violate consensual rules.

In order to mitigate possible criticism the doubtful reader is advised to consult a recent review[18] on the role and impact of differential geometry in contemporary chemistry.

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