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A GENERALISED ROTATION RULE FOR HETEROCYCLIC AND AROMATIC COMPOUNDS

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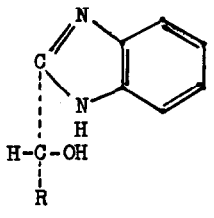
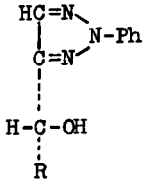
A common feature of both the benzimidazole rule[1] and phenylosotriazole rule[2] is that the sign of rotation of these compounds (I&II) is determined by the configuration of the asymmetric carbon atom attached to the ring, irrespective of the configuration of the other asymmetric carbon atoms. In both rules, we also find that when the hydroxyl group on the asymmetric carbon atom α- to the ring is to the right in the usual Fischer projection formula, the compound is dextro-rotatory and conversely it is levo-rotatory when this hydroxyl group is to the left.



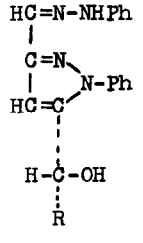
I

R=-$(CHOH)_nCH_2OH$ or -$(CHOH)_nCH_3$



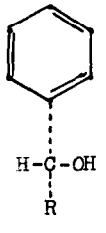
II

R=-$(CHOH)_nCH_2OH$ or -$(CHOH)_nCH_3$



III

R=CH_2OH or CH_3



IV

R=CH_3, CO_2H, $CONH_2$, CO_2Me or -$(CHNHCH_3)CH_3$

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1 N.K. Richtmyer and C.S. Hudson, J. Amer. Chem. Soc., 64, 1612 (1942).

2 H. El Khadem, J. Org. Chem., 1963, in press.

The benzimidazole and phenylosotriazole rules apply without exceptions to more than sixty compounds, some of which possess up to five asymmetric carbon atoms in the molecule. It seems therefore likely that these relationships are of a general nature and can be applied to other ring systems.

We have now verified this with the dianhydrophenylosazones[3] (III) recently prepared in this laboratory. These compounds have a pyrazole ring attached to an asymmetric hydroxyl bearing carbon atom, and as expected the isomers having the hydroxyl group to the right were dextrorotatory and their enantiomorphs levo-rotatory. This relationship was found to hold for aromatic compounds as well; thus for example, in phenyl-methyl and acetylcarbinol, mandelic acid, its amide and ester, in the ephedrines and chloramphenicol, whenever the hydroxyl group α- to the benzene ring is to the right, the rotation is positive, provided the ring is on top (IV). As with benzimidazoles and phenylosotriazoles, if the molecule has more than one asymmetric carbon atom, the sign of rotation depends on the configuration of the asymmetric carbon atom α- to the ring.

The above relationships may be stated in the following generalised form:

1. The sign of rotation of a heterocyclic or aromatic compound having more than one asymmetric carbon atom depends only on the configuration of the asymmetric carbon atom attached to the heterocyclic or benzene ring provided no other ring is present in the molecule.
2. If the asymmetric carbon atom is represented in the Fischer projection formula with the ring on top and the latter together with the main carbon chain below the plane of the paper, then the rotation

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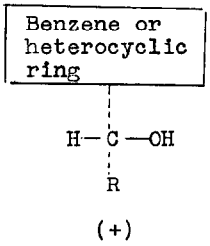
3 H. El Khadem and M.M. Mohamed-Aly, J. Chem. Soc., 1963, in press.

is positive when the hydroxyl group is to the right and negative when it is to the left.



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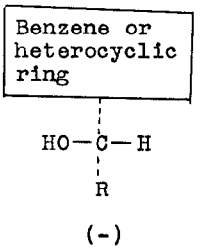

(-)

3. The hydroxyl groups may be methylated or acetylated without influencing the sign of rotation, but benzoylation may yield a derivative having an opposite sign of rotation[4] specially if several hydroxyl groups are present in an opposite direction to that of the asymmetric carbon α- to the ring.

Although Brewster's rule[5] is able to predict satisfactorily the sign of rotation of compounds having one asymmetric carbon atom, yet the present rules offer a simple approach and should find application in determining the configuration of compounds having more than one asymmetric carbon atom.

4 H. El Khadem, Adv. Carbohydrate Chem., 18, 99 (1963).

5 J.H. Brewster, J. Amer. Chem. Soc., 81, 5475 (1959).