Carbohydrate Research, 66 (1978) C4–C6

Preliminary communication

Circular dichroism of 3-(polyhydroxyalkyl) derivatives of 1-phenylpyrazolo-[3,4-*b*]quinoxalines

MOHAMMED A. E. SALLAM

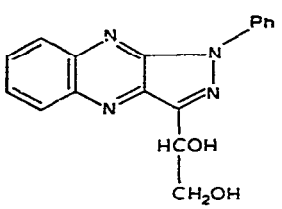
Department of Chemistry, Faculty of Science, Alexandria University, Alexandria (Egypt)

(Received May 26th, 1978; accepted for publication, June 13th, 1978)

The correlation of the optical rotation (at the D line of sodium) of heterocyclic derivatives of carbohydrates with the absolute configuration of the carbon atom adjacent to the heterocyclic ring has resulted in several useful rules that permit configurational assignment at this asymmetric center, the absolute configuration of which has the major influence on the sign of the rotation. Thus, the configuration at C-2 and C-3 of sugars can be established on the basis of the benzimidazole rule[1] and the osotriazole rule[2,3]. El Khadem and El Shafei[4] suggested the general applicability of the latter rule to all aromatic systems.

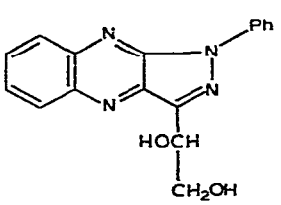
Observation of the Cotton effects in rotatory dispersion, or ellipticity extrema in circular dichroism (c.d.) spectra, of polyhydroxyalkyl-benzimidazoles, -quinoxalines[5], and -osotriazoles[6] provided a potential method of assigning the absolute stereochemistry at C-2 and C-3.

In the present work, five 3-(polyhydroxyalkyl) derivatives (**1**–**5**) of 1-phenylpyrazolo[3,4-*b*]quinoxaline were prepared, and subjected to spectropolarimetric study in order to make a correlation for the assignment of the absolute configuration at C-4 of the side chain. A systematic comparison of the optical rotation (at the D line of sodium) of compounds **1**–**5** in pyridine revealed no direct relationship between the optical rotation and the absolute configuration. However, c.d. studies of the compounds in 1,4-dioxane



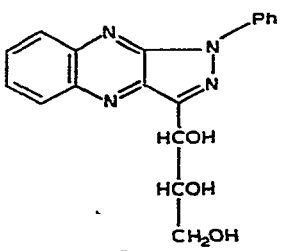
1

$[\alpha]_D^{22}$ + 8.1°



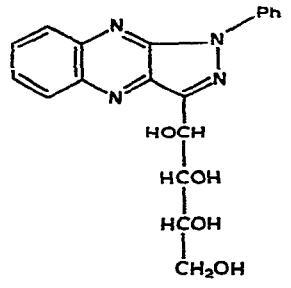
2

$[\alpha]_D^{22}$ −8.3°



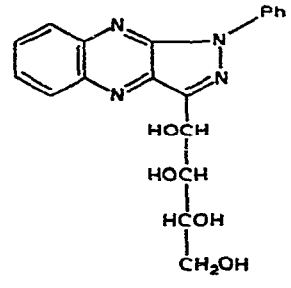
3

$[\alpha]_D^{22}$ −22.5°



4

$[\alpha]_D^{22}$ −30.4°



5

$[\alpha]_D^{22}$ +15.9°

showed multiple Cotton effects (see Fig. 1), and a direct correlation between the sign of the Cotton effect at the long-wavelength absorption and the absolute configuration at C-1′ was found. Those 1-phenyl-3-(polyhydroxyalkyl)pyrazolo[3,4-*b*]quinoxalines possessing *R* chirality at C-1′ (C-4 of the original sugar) in the Fischer projection formula have a positive Cotton effect centered at the long-wavelength absorption (442–450 nm). The same relationship exists between the *R* and *S* chirality of C-1′ of purine nucleosides and *C*-nucleosides

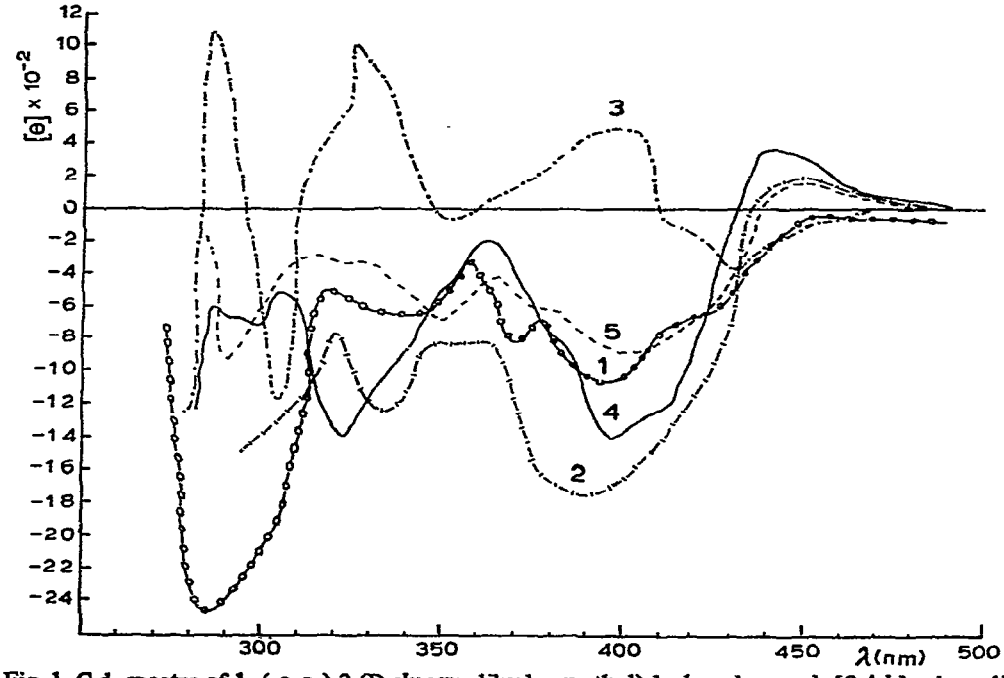


Fig. 1. C.d. spectra of 1, (-o-o-) 3-(D-*glycero*-dihydroxyethyl)-1-phenylpyrazolo[3,4-*b*]quinoxaline; 2, (- - -) 3-(L-*glycero*-dihydroxyethyl)-1-phenylpyrazolo[3,4-*b*]quinoxaline; 3, (- · - · -) 3-(D-*erythro*-glycerol-1-yl)-1-phenylpyrazolo[3,4-*b*]quinoxaline; 4, (——) 1-phenyl-3-(D-*arabino*-tetritol-1-yl)-pyrazolo[3,4-*b*]quinoxaline; and 5, (- - - -) 1-phenyl-3-(D-*lyxo*-tetritol-1-yl)-pyrazolo[3,4-*b*]quinoxaline.

and the sign of their Cotton effect. An explanation of this has recently been proposed[7]. A negative Cotton effect indicates *S* chirality at C-1′. Centers of asymmetry other than C-1′ affect only the intensity of the band. Compound **4**, having the *arabino* configuration, has the highest amplitude at the long-wavelength region. Circular dichroism can thus be used to determine the absolute stereochemistry at C-4 of a sugar by converting it into its 1-phenylpyrazolo[3,4-*b*]quinoxaline derivative and recording the c.d. spectrum. The method has been used recently to reveal inversion in the configuration of C-1′ in the *C*-nucleoside analog[8] prepared by the dehydrative cyclization of **4**. Circular dichroism spectra of solutions (c = 0.4–0.6 mg/ml) in 1,4-dioxane were recorded with a Cary 60 spectropolarimeter at a dynode voltage $\leqslant$ 0.75 kV.

ACKNOWLEDGMENTS

The author thanks Dr. U. Hornemann for making available the facilities for this work, and M. McDonough for help in obtaining the spectral measurements.

REFERENCES

1 N. K. Richtmyer and C. S. Hudson, *J. Am. Chem. Soc.*, 64 (1942) 1612–1615.
2 H. El Khadem, *J. Org. Chem.*, 28 (1963) 2478.
3 J. A. Mills, *Aust. J. Chem.*, 17 (1964) 277–280.
4 H. El Khadem and Z.M. El Shafei, *Tetrahedron Lett.*, (1963) 1887–1889.
5 W. S. Chilton and R. C. Krahn, *J. Am. Chem. Soc.*, 89 (1967) 4129–4132.
6 G. G. Lyle and M. J. Piazza, *J. Org. Chem.*, 33 (1968) 2478–2484.
7 H. S. El Khadem, *Carbohydr. Res.*, 59 (1977) 11–18.
8 M. A. E. Sallam, *Carbohydr. Res.*, in press.