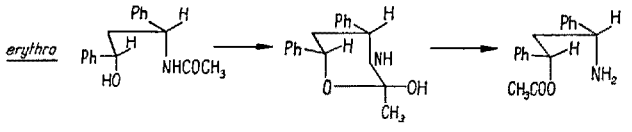
Transformations Involving 6-Ring Transitional Intermediates

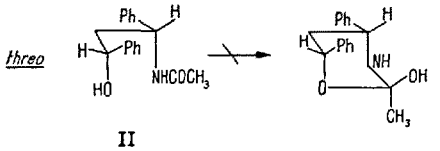
The importance of non-bonded interactions in the transition state of transformations involving substituted 1,2-ethanolamines has been extensively demonstrated[1].

Recently STÜHMER and FREY[2] have applied these considerations in the assignment of configuration to the isomeric 1,3-diphenyl-3-amino 1-propanols. These authors observed that only the β-isomer in the form of its N-acetyl derivative undergoes N $\rightarrow$ O acyl migration under acidic conditions whereas the α-isomer on successive treatment with phosphorous pentachloride and water is converted irreversibly to the β-isomer[3]. On the basis of these observations and in analogy with the established specificity of these transformations in the case of the *nor*-ephedrines and the 1,2-diphenyl-ethanolamines (l.c.), the α-isomer was assigned the *erythro* (mesoid) and the β-isomer the *threo* (racemoid) configuration.

A consideration of the probable transitional intermediates arising in the transformations of 1,3-propanolamine systems suggests the opposite configurational assignment from that proposed by STÜHMER and FREY. Thus, in contrast to the 5-membered ring transitional intermediates formed in the reactions of 1,2-ethanolamines, the corresponding intermediates arising from the internal transformations of 1,3-propanolamines should be 6-ring in character and consequently subject to steric factors encountered in cyclohexane derivatives[4]. Considered from this point of view, the β-isomer of 1,3-diphenyl-3-amino-1-propanol should posses the *erythro* (mesoid) configuration (I) since the chair form of the 6-ring transition state for acyl migration bears the phenyl groups di-equatorially disposed in contrast to a polar-equatorial arrangement of these same groups required by the α-isomer. The irreversible conversion of

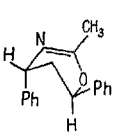


I

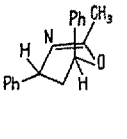


II

the α-isomer $\rightarrow$ β-isomer should correspondingly require the formation, with inversion at C–OH, of a 6-ring oxazine as a transitional intermediate. The oxazine derived from the *erythro*-form (I) could exist in two possible conformations, III*a* and III*b*, both of which possess unfavorable phenyl-hydrogen interactions.

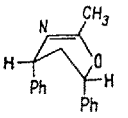


III*a*

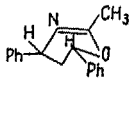


III*b*

The oxazine derived from the *threo* form (II), however, can give rise to either an unfavorable conformation IV*a* having phenyl-phenyl interaction or a second conformation IV*b* in which all nonbonded interactions are minimized.



IV*a*



IV*b*

These same considerations likewise provide a satisfactory explanation for the selective formation of a tribenzoyl derivative with the *erythro*-form of 1,3-dihydroxy-2-aminoöctadecane in contrast to the *threo*-form which only gives a dibenzoyl derivative as recently reported[1]. Only in the case of the *erythro* isomer could an initially formed N, O_1-dibenzoyl derivative give rise to a 6-ring transitional intermediate favorable to $O_1 \rightarrow O_3$ acyl migration.

N. L. WENDLER

Merck & Co., Inc., Rahway, New Jersey, June 16, 1953.

Zusammenfassung

Dem β-Isomer des 1,3-Diphenyl-3-amino-1-propanols, welches in der Literatur als Threo-Verbindung formuliert ist, wird die mesoide Erythro-Konfiguration zugewiesen. Diese Zuweisung erfolgt auf Grund der vorauszusehenden grösseren Stabilität des bei der N$\rightarrow$O-Azylwanderung intermediär auftretenden 6-gliedrigen Ringes.

Die einseitige Umwandlung des α-Isomers des 1,3-Diphenyl-3-amino-1-propanols in die β-Form durch Phosphorpentachlorid und nachfolgende Hydrolyse wird durch die günstigere Konformation des aus der Threo-Form erhältlichen Oxazins erklärt.

[1] H. E. CARTER, D. SHAPIRO, and J. B. HARRISON, J. Amer. Chem. Soc. *75*, 1007 (1953).

Diabetogene Wirkung des 2,3,4-Triketo-Tetrahydropyridins

Im Rahmen unserer Arbeiten über Polyoxoverbindungen prüften wir die diabetogene Wirkung von OSTS Pyromekazon[1], das nach den Untersuchungen von PERATONER[2] die Struktur des 2,3,4-Triketo-tetrahydro-

[1] P. I. POLLAK and D. Y. CURTIN, J. Amer. Chem. Soc. *72*, 961 (1950). – L. H. WELSH, *ibid.* *71*, 3500 (1949). – V. BRUCKNER, G. FODOR, J. KISS, and J. KOVACS, J. Chem. Soc. *1948*, 885. – J. ATTENBURROW, D. F. ELLIOT, and G. F. PENNY, J. Chem. Soc. *1948*, 310. – J. WEIJLARD, K. PFISTER 3rd, E. F. SWANEZY, C. A. ROBINSON, and M. TISHLER, J. Amer. Chem. Soc. *73*, 1216 (1951).

[2] W. STÜHMER and H. FREY, Arch. Pharm. *286/58*, 8, 26 (1953).

[3] W. STÜHMER and W. HEINRICH, Chem. Ber. *84*, 224 (1951).

[4] D. H. R. BARTON, Exper. *6*, 315 (1950).

[1] H. OST, J. pr. [2] *23*, 442 (1881); *27*, 260 (1883).

[2] A. PERATONER, R. A. L. [5] *11*, I., 333 (1902); G. *41*, II., 628, 660 (1911).