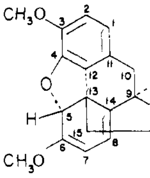
A STANDARD OF ABSOLUTE CONFIGURATION FOR OPTICALLY ACTIVE BIPHENYLS[1]

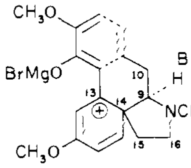
Sir:

The establishment of the absolute configuration of D-tartaric acid by the anomalous diffraction technique[2] provides the basis for the unique assignment of stereochemistry to any center of carbon atom asymmetry. Heretofore, no basis has existed for such assignments in the case of substances possessing axial asymmetry, *e.g.*, optically active biphenyls. We should like to point out that the configuration of the biphenyl system in phenyldihydrothebaine (III) can be related *operationally*[3] to the configuration of thebaine (I). Consequently, since the absolute configuration of the morphine thebaine group of alkaloids is now known,[5] the absolute configurations of the axially asymmetric systems in III, and in a series of its derivatives of the general formula IV, are established.

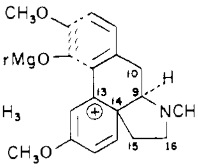
Thebaine (I) is converted by phenylmagnesium bromide to a mixture of two phenyldihydrothebaines (III) which differ only in the configuration at the asymmetric carbon atom.[6]



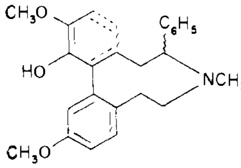
I



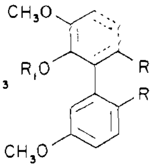
IIa



IIb



III



IV

Regardless of the details of the mechanism of this reaction, C.13 must become trigonal at or near the transition state for the migration of C.15 from C.13 to C.14. The two rings of the potential biphenyl system then approach coaxiality. This sets up two diastereomeric transition states,[7] and the configuration of the biphenyl becomes fixed when the reacting system chooses to employ one of them in thermodynamic preference to the other. For convenience, we discuss the choice between the metastable intermediates IIa and IIb, although the argument applies with at least equal force to the transition states. Models reveal that IIa is much more stable than IIb. In IIa, the angle between the plane defined by C.15–C.14–C.9 and that defined by C.14–C.9–*N* is close to 0°. In IIb, however, this angle is close to 60°. Thus if IIb were the intermediate, the five-atom ring (C.15, C.14, C.9, N, C.16) would have to be severely puckered. Even when the resultant release of non-bonded interaction is taken into consideration, an interplanar angle of 60° would be intolerable[8] when the system has available the Baeyer-strain-free alternative IIa. The biphenyl system of phenyldihydrothebaine therefore has the absolute configuration shown in III, and the simpler bicyclic derivatives (*e.g.*, the methines, isomethines, phenyltetrahydrothebaimine and the nitrogen-free degradation products[6]) all have the absolute configuration IV. The series provides a standard of absolute configuration for optically active biphenyls.

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[1] The support of this work by a grant from the National Science Foundation is gratefully acknowledged.

[2] J. M. Bijvoet, A. F. Peerdeman and A. J. van Bommel, *Nature*, **168**, 271 (1951).

[3] We recognize that because of the difference in symmetry orders between the asymmetric frames[4] (bisphenoid *vs.* regular tetrahedron), there is, in general, no *conceptual* way of relating an axially asymmetric configuration to that of a centrally asymmetric one.

[4] R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia*, **12**, 81 (1956).

[5] (a) K. W. Bentley and H. M. E. Cardwell, *J. Chem. Soc.*, 3252 (1955); (b) J. Kalvoda, P. Buchsacher and O. Jeger, *Helv. Chim. Acta*, **38**, 1847 (1955).

[6] (a) M. Freund, *Ber.*, **38**, 3234 (1905). (b) L. Small, L. J. Sargent and J. A. Bralley, *J. Org. Chem.*, **12**, 1839 (1947). (c) R. Robinson, *Nature*, **160**, 815 (1947). (d) K. W. Bentley and R. Robinson, *J. Chem. Soc.*, 947 (1952).

[7] *Cf.* J. A. Berson and E. Brown, THIS JOURNAL, **77**, 450 (1955).

[8] Compare the interplanar angle of 17° in the pyrrolidine ring of hydroxyproline [J. Donohue and K. N. Trueblood, *Acta Cryst.*, **5**, 419 (1952)].

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INTERACTION OF DEUTERIUM WITH OLEFINS AND ALKANES ON CHROMIUM OXIDE GEL

Sir:

The background data for current interest in the mechanism of olefin hydrogenation are largely confined to platinum and nickel catalysts. It seemed important to investigate as different a catalyst as possible. Chromium oxide gel[1] was chosen because much is known about its behavior in other catalytic reactions. In reactions between hydrocarbons and deuterium we find that it yields products which are isotopically much simpler than those obtained with metallic catalysts. These reactions are of both mechanistic and preparative interest.

After dehydration above 400°, the gel[2] acquires hydrogenating activity at low temperatures. Table I presents isotopic distribution patterns of products of experiments with 2:1 mixtures of deuterium and hydrocarbon at space rates of about 1 cc. of liquid hydrocarbon per cc. of catalyst per hour. At 42°, the hexane from 1-hexene is largely hexane-d_2. Even at −78°, similar hydrogenation on nickel–kieselguhr gives broad distribution of exchanged species.[3]

At −20°, 1-butene yields butane-d_2 nearly exclusively. Cyclopentene behaves similarly at 27°. Mass spectrometric fragmentation patterns indicate that the butane is nearly all butane-1, 2-d_2. The hexane prepared at 42° is mainly 1,2-d_2 with smaller amounts of other dideuterohexanes, principally 2,3-d_2.

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[1] W. A. Lazier and J. V. Vaughen, THIS JOURNAL, **54**, 3080 (1932).

[2] Prepared by the urea method, R. L. Burwell, Jr., *ibid.*, **59**, 1609 (1937).

[3] C. D. Wagner, J. N. Wilson, J. W. Otvos and D. P. Stevenson, *J. Chem. Phys.*, **20**, 338 (1952).

TABLE I

ISOTOPIC DISTRIBUTION PATTERNS

Number of D atoms	Addition to 1-hexene 42°	150°	Exchange with hexane 201°	350°
0	0.6%	1.9%	95.6%	73.3
1	4.9	15.4	4.2	17.6
2	89.5	53.6	0.2	2.7
3	4.3	19.7		0.82
4	0.7	5.8		.72
5		1.7		.80
6		0.8		.89
7		.5		.84
8		.3		.69
9		.2		.57
10				.42
11				.29
12				.22
13				.10
14				.02

At 150°, however, the distribution pattern is broader (Table I) and somewhat resembles patterns observed with nickel catalysts. Intermediate temperatures yield intermediate patterns.

At 0°, ethylene gives ethane-d_2, but, at $-78°$, reaction is incomplete and the product is ethane-d_2 and undeuterated ethylene.

Table I presents distribution patterns for isotopic exchange between hexane and deuterium. Correction for multiple adsorption shows that only a single deuterium atom is exchanged upon adsorption of hexane. The multiple exchange of low intensity at the higher temperature probably results from dehydrogenation to hexenes followed by rehydrogenation. Metallic catalysts give quite different patterns characterized by extensive multiple exchange.[4,5,6]

Acknowledgment.—This investigation is supported by the Petroleum Research Fund of the American Chemical Society. Mr. S. Meyerson of the Standard Oil Company (Indiana) assisted us with mass spectroscopy.

(4) S. O. Thompson, J. Turkevich and A. P. Irsa, THIS JOURNAL, **73**, 5213 (1951).

(5) R. L. Burwell, Jr., and W. S. Briggs, *ibid.*, **74**, 5096 (1952); H. C. Rowlinson, R. L. Burwell, Jr., and R. H. Tuxworth, *J. Phys. Chem.*, **59**, 225 (1955).

(6) C. Kemball, *Proc. Roy. Soc. (London)*, **223A**, 361 (1954).

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FRACTIONAL DIALYSIS WITH CELLOPHANE MEMBRANES

Sir:

Preliminary data[1] concerned with fractional dialysis with cellophane indicated the possibility of unexpected selectivities for the separation of mixtures of dialyzable solutes. Further study has confirmed this indication and shown that considerable improvement in selectivity, adaptability and interpretability is possible particularly with solutes of larger molecular size which scarcely pass through the membrane.

A simple modification of the cell reported for fractionation purposes[1] adapts it for analytical work with 5–10 mg. of substance. In this the inside glass tube nearly displaces all the volume in the sac[2] and leaves only space for a thin film of solution. Stirring with nitrogen is now not required and a faster rate of dialysis is obtained by the resulting increase in the membrane area with respect to the inside solution volume. The outside solution can be replaced by fresh solvent at arbitrary intervals and analyzed for determination of the escape rate.

Under these conditions the escape rate expressed as decrease in precentage of the original remaining in the sac with time should be independent of the amount taken provided a single solute is present which behaves ideally. A plot of the logarithm of the percentage against time should give a straight line. This has been found to hold experimentally with many solutes. Thus in Fig. 1, curve 1 gives the escape rate of bacitracin A (solvent is 0.1 N acetic acid), curve 2 that of aspartic acid.

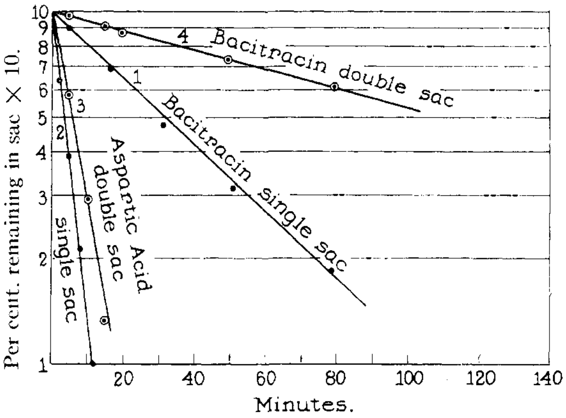

Fig. 1.

For the separation of mixtures greatly improved selectivity can be obtained by choice of solvent, the particular size of tubing, treatment of the membrane, etc. As an example curves 1 and 2 are escape rates respectively of aspartic acid and bacitracin A (mol. wt. 1421) through single membranes of Visking 18/32 seamless cellulose tubing while 3 and 4 are those found for double membranes (one sac inside the other).

That the improved selectivity holds for a mixture is shown by comparison of Figs. 1 and 2. In Fig. 2 a mixture of 10 mg. each of bacitracin and aspartic acid was studied. Curve 1 is a weight curve. Curve 2 is an optical density curve (255 mμ) referring only to bacitracin. Curve 3, that of aspartic acid, can be calculated from the values in 1 and 2.

The significance of this general approach for studying homogeneity with respect to size and/or shape (and perhaps charge) under extremely mild conditions is self evident. Comparison with similar solutes of known size gives a good estimation of size for the unknown.

Although different sizes of Visking have shown great variation in selectivity and permeability

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(1) L. C. Craig and T. P. King, THIS JOURNAL, **77**, 6620 (1955).

(2) W. H. Seegars, *J. Lab. Clin. Med.*, **28**, 897 (1942).