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Stereoisomeric 2,3-Butanediamines, 3-Amino-2-butanols and 2,3-Dimethylethyleneimines; Stereochemistry of the Opening and Closing of the Imine Ring¹

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The configurations of the following compounds have been established; the *meso*-, D- and L-2,3-butanediamines, *meso*-, D- and L-2,3-dimethylethyleneimines (2,3-dimethylaziridines), and the D- and L-*erythro*- and D- and L-*threo*-3-amino-2-butanols. It has been shown that one Walden inversion is associated with a number of ring openings and closing, *viz.* (1) opening of the oxide ring of 2,3-epoxybutane with ammonia; (2) opening of the imine ring of 2,3-dimethylethyleneimine with ammonia; (3) opening of the same ring with water, and (4) closing of the same ring. The reduction of dimethylglyoxime can be accomplished with Raney aluminum-nickel alloy and aqueous base to yield a mixture of DL- and *meso*-2,3-butanediamine along with some 3-amino-2-butanol.

The stereochemistry of aliphatic amino alcohols is of growing importance.³ Any relationships between optical activity and configuration that can be established for the simplest amino alcohol of two asymmetric carbon atoms, namely, 3-amino-2-butanol, may prove useful in other cases. It is known from much earlier work, in particular the studies of Levene and co-workers,⁴ that the size of a normal aliphatic radical is of minor importance in determining the sign and magnitude of rotation of the methylcarbinols.

Relationships between the optical activity and configuration of the isomeric 3-amino-2-butanols have been developed from the simple premise that the mechanism of each of the following ring opening operations involves a single Walden inversion: (1) 2,3-epoxybutane with ammonia and (2) 2,3-dimethylethyleneimine (2,3-dimethylaziridine) with water. These two reactions are strictly analogous to two other ring-opening operations that are accompanied by a single Walden inversion. They are: (3) 2,3-epoxybutane with water^{5a} and (4) 2,3-dimethylethyleneimine with ammonia.^{5b} Thus the reactants of (1) and (2) are the same as those of (3) and (4), the only difference being in the way they are paired.⁶

(1) Presented before the XIIth International Congress of Pure and Applied Chemistry, New York, N. Y., September 11, 1951.

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(3) Interest in the structure of sphingosine has led to studies on aliphatic amino alcohols, *cf.* C. Niemann, A. A. Benson and J. E. Mead, *J. Org. Chem.*, **8**, 397 (1943).

(4) K. Freudenberg, "Stereochemie," F. Deuticke, Leipzig, 1933, p. 695.

(5) (a) C. E. Wilson and H. J. Lucas, *THIS JOURNAL*, **58**, 2396 (1936). (b) The proof of this is established by the present work.

(6) The premise of a single Walden inversion accompanying a ring opening with ammonia is in conformity with the known stereochemical results of still other ring openings of the oxide ring of 2,3-epoxybutane. A single inversion accompanies its reaction with hydrogen bromide, (a) S. Winstein and H. J. Lucas, *ibid.*, **61**, 1576, 2845 (1939); with hydrogen chloride, (b) H. J. Lucas and C. W. Gould, Jr., *ibid.*, **63**, 2541 (1941); (c) H. J. Lucas and H. K. Garner, *ibid.*, **70**, 990 (1948); and hydrogen iodide, (d) H. J. Lucas and H. S. Garner, *ibid.*, **72**, 2145 (1950). Other oxides of acyclic olefins act similarly, for example, a Walden inversion accompanies the reaction of stilbene oxides with hydrogen chloride, hydrogen bromide or hydrogen iodide; (e) D. Reulos, *Compt. rend.*, **216**, 774 (1943); D. Reulos and C. Collin, *ibid.*, **218**, 795 (1944). In some cases the results are not so clear cut, probably owing to neighboring group participation. Thus, although *cis*-epoxysuccinic acid hydrates with 100% Walden inversion, the *trans*-isomer reacts with only 60% inversion; (f) R. Kuhn and F. Abel, *Ber.*, **58**, 919 (1925).

A single Walden inversion accompanies the opening of the oxide ring

The series of reactions investigated and the stereochemical relationships of the compounds involved therein are shown in Figs. 1 and 2.

meso-2,3-Epoxybutane to D- and L-2,3-Butanediamines.—The DL-*threo* amino alcohol, II, Fig. 1, obtained from the *meso*-oxide,^{5a} I, was resolved with tartaric and malic acids. The less soluble tartrate gave the (–)-amino alcohol, IIa, and the less solu-

of cyclohexene oxide with water; (g) C. van Loon, Thesis, Delft, 1919; J. Boeseken and J. van Giffen, *Rec. trav. chim.*, **39**, 184 (1920). An inversion is indicated also in the reaction with hydrogen chloride; (h) P. D. Bartlett, *THIS JOURNAL*, **67**, 224 (1935) and with hydrogen bromide; (i) S. Winstein, *ibid.*, **64**, 2792 (1942). Other oxides of cyclic hydrocarbons likewise give *trans*-glycols with water; (j) J. Boeseken, *Ber.*, **56**, 2409 (1923); M. Godchot and M. Mousseron, *Compt. rend.*, **198**, 837 (1934).

The opening of the oxide ring of cyclohexene oxide by ammonia has been shown to be a *trans*-opening, for the product is *trans*-2-amino-cyclohexanol; (k) G. E. McCasland, R. K. Clarke, Jr., and H. E. Carter, *THIS JOURNAL*, **71**, 638 (1949); *cf.* S. Winstein and R. Boschan, *ibid.*, **72**, 4669 (1950). An odd number of inversions is thus involved. Since the stereochemical results of similar openings of different oxide rings usually are similar it would be logical to expect a *trans*-opening of 2,3-epoxybutane with ammonia.

A *trans*-opening of the imine ring of 2,3-dimethylethyleneimine with water receives support from the reaction of *cis*- and *trans*-2,3-diphenylethyleneimines with water to give 2-amino-1,2-diphenylethanol, the former giving mainly the lower melting (127–128°) isomer, the latter mainly the higher melting (161–163°) isomer; (l) A. Weissberger and H. Bach, *Ber.*, **64**, 1095 (1932); **65**, 633 (1933). On the basis of melting points of the inactive forms; (m) E. Erlenmeyer, Jr., *ibid.*, **32**, 2378 (1899), and magnitudes of rotation of optically active forms; (n) J. Read and I. G. M. Campbell, *J. Chem. Soc.*, 2377 (1930), it is reasonable to assign the *threo*-configuration to the lower melting and the *erythro*-configuration to the higher melting form. Thus a *trans*-opening of the imine ring of 2,3-diphenylethyleneimine is a reasonable assumption. A similar conclusion in regard to configurations has been made by others: (o) R. E. Lutz, J. A. Freck and R. S. Murphey, *THIS JOURNAL*, **70**, 2019 (1948); and (p) J. Weijlard, K. Pfister, 3rd., E. F. Swanezy, C. A. Robinson and M. Tishler, *ibid.*, **73**, 1216 (1951).

The formation of *cis*-2,3-diphenylethylene oxide from a quaternary ammonium salt derived from the active form of (–)-*threo*-2-amino-1,2-diphenylethanol confirms the above assignment of configuration on the basis of a *trans*-closing of the epoxide ring, although Read and Campbell put the opposite interpretation on the reaction. It has been shown that the opening of the ring of 2,3-epoxybutane with dimethylamine and its closing by the elimination of trimethylamine and water from the quaternary ammonium base of the amino alcohol produced by the ring opening involve similar stereochemical changes.^{6a} Since opening of the oxide ring by dimethylamine is strictly analogous to its opening by ammonia, and since ammonia is here considered to open the ring *trans*, closing of the oxide ring from the corresponding amino alcohol is therefore also *trans*. Thus the *threo*-configuration of the lower melting 2-amino-1,2-diphenylethanol is consistent with a *trans*-opening of the imine ring with ammonia and a *trans*-closing of the oxide ring from the quaternary ammonium base of the lower melting isomer.

A *trans*-opening of the ring of 2,3-epoxybutane with alcohols has been established, (q) G. K. Helmkamp and H. J. Lucas, *ibid.*, **74**, 951 (1949).

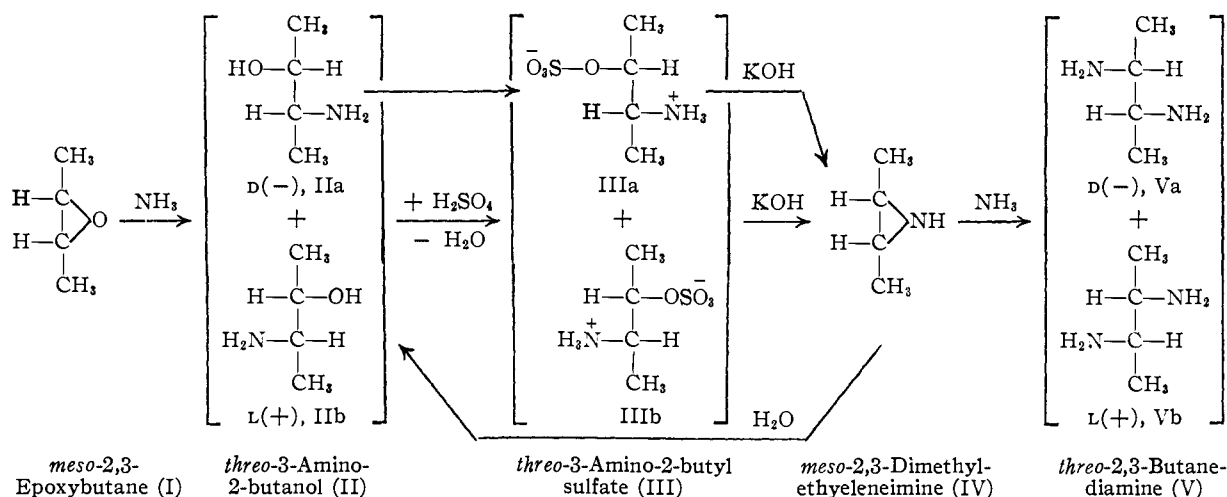


Fig. 1.—Configurational relationships of compounds from *meso*-2,3-epoxybutane.

ble malate gave the (+)-amino alcohol, IIb.⁷ An optically inactive imine, IV, was obtained from the inactive amino alcohol, II, and one of the active isomers, IIa, by way of the respective acid sulfate, III and IIIa, according to the methods used in other cases,⁸ and applied to 3-amino-2-butanol.⁹ This imine, the higher boiling isomer, was thus shown to have the *cis*- (or *meso*) configuration. If one inversion accompanies the opening of the epoxide ring with ammonia, then one inversion accompanies the closing of the imine ring.¹⁰ The diamine, V, resulting from the imine by the action of ammonia and ammonium chloride, according to the procedure of Clapp,¹¹ was resolved with tartaric acid into (-)- and (+)-2,3-butanediamines, Va and Vb, respectively. This diamine, the lower boiling and lower melting inactive diamine, was thus shown to have the DL or *threo*-configuration. This result proves that an odd number of inversions accompanies the opening of the imine ring with ammonia. In the absence of evidence to the contrary it is justifiable to say that the number is one.

The assignment of the *threo*-configuration to the DL-amino alcohol, II, arising from the *meso*-oxide, I, on the premise that ammonia opens the oxide ring with one inversion is strengthened by other results. One of these is the observation that this same amino alcohol is formed from *cis*-2,3-dimethylethyleneimine (IV) by the action of water. Thus *trans*-opening of the imine ring by water is a necessary corollary to *trans*-opening of the oxide ring by ammonia. Other evidence, described later, is based on the physical properties of the inactive forms of the 3-amino-2-butanols and the magnitude of rotation of optically active forms. These show that the *threo*-configuration should be assigned to

(7) The *threo*-configuration is assigned on the premise that one inversion accompanies the ring opening. Assignment of configuration to each of the two antipodes, although not described until later, is indicated on the figure, for convenience.

(8) (a) H. Wenker, *THIS JOURNAL*, **57**, 2328 (1935); (b) T. L. Cairns, *ibid.*, **63**, 871 (1941).

(9) G. D. Jones, *J. Org. Chem.*, **9**, 491 (1944).

(10) A *trans*-closing of an imine ring has been reported in the case of cyclohexeneimine by P. E. Fanta and O. E. Paris, Philadelphia Meeting of the American Chemical Society, April 9 to 13, 1950. A similar result is indicated in the work of Weissberger and Bach.⁴¹

(11) L. B. Clapp, *THIS JOURNAL*, **70**, 184 (1948).

II. Thus the stereochemical results of Fig. 1 are consistent with *trans*-opening and *trans*-closing of the oxide and imine rings.

D(+)-2,3-Epoxybutane to *meso*-2,3-Butanediamine.—Starting with *d*(+)-2,3-epoxybutane^{6c} (VI, Fig. 2), more definite assignments of configuration can be made. On the premise that the oxide

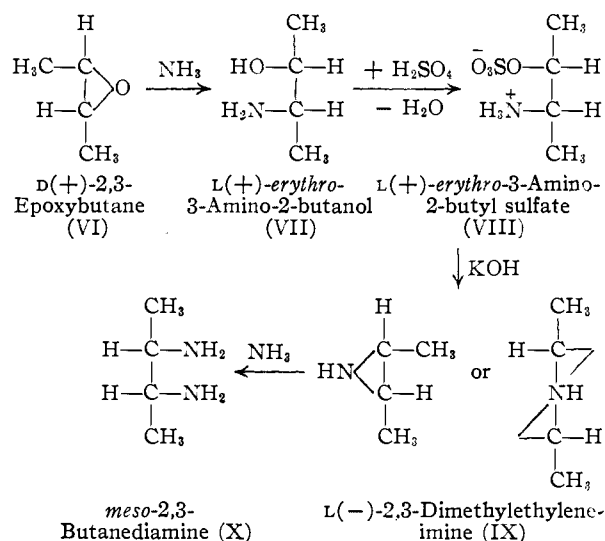


Fig. 2.—Configurational relationships of compounds from *d*(+)-2,3-epoxybutane.

ring is opened by ammonia with one inversion, the product must be *L*(+)-*erythro*-3-amino-2-butanol (VII). It is shown later that physical data, in particular the sign and magnitude of rotation of this amino alcohol and its derivatives, indicate quite conclusively that it has the *L-erythro* configuration. There is thus a *trans*-opening of the oxide ring by ammonia. The conversion of VII, through the acid sulfate, VIII, to an imine, IX, possessing optical activity, shows again that the closing of the imine ring takes place with one inversion, because the imine is a *trans*- not a *cis*-compound. Moreover, this imine is *L*(-)-2,3-dimethylethyleneimine (IX) because each asymmetric carbon atom is inverted once, C-3 when the oxide ring is opened by ammonia to yield *L*(+)-

erythro-3-amino-2-butanol,¹² C-2 when the imine ring is closed.

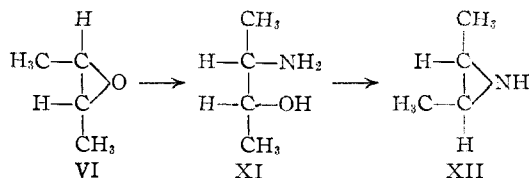
The formation of *meso*-2,3-butanediamine (X), by the action of ammonia on the active imine, IX, again proves that one inversion accompanies this ring opening. Thus the stereochemical results of Fig. 2 also are consistent with *trans*-opening and *trans*-closing of oxide and imine rings.

Configurations and Rotations.—On the basis of the assigned configurations of imines, diamines and amino alcohols, and taking into account also the configurations of the corresponding oxides^{5a,6c} and glycols,^{5a,13} a completely consistent body of relationships between configurations and the signs and magnitudes of rotation exists. First and of major importance is the relation of imine to oxide: $[\alpha]^{25}_D$ of D(+)-2,3-epoxybutane (VI) is $+59^\circ$, and of the L-imine, IX, is -102° . Thus these two ring systems produce rotations in the same direction. Because of this, and also because the imine ring produces a much higher rotation than the oxide ring, it is reasonable to expect the amino group to produce in 2,3-disubstituted butanes, optical activity of the same sign as the hydroxyl group and to a considerably greater extent.

Configurations have been assigned to the active *threo*-3-amino-2-butanols and active 2,3-butanediamines on the principle that the amino group in 2,3-disubstituted butanes produces optical activity of the same sign as the hydroxyl group. Thus the levorotatory isomers, IIa and Va, respectively, are assigned the D-configuration because D-2,3-butanediol is levorotatory,¹³ and the dextrorotatory isomers, IIb and Vb, respectively, are assigned the L-configuration.

The following relationships among optically active 2,3-disubstituted butanes are logical deductions from the relative rotations of the oxide, VI, and the imine, IX: (1) an active diamine should have a higher rotation than an active glycol; (2) an active *threo*-amino alcohol should have a rotation between those of the diamine and the glycol; (3) an active *erythro*-amino alcohol should have a much lower rotation than an active *threo*-isomer; (4) the sign of rotation of D-*erythro*-3-amino-2-butanol, like that of the D-glycol,¹³ should be negative because the rotation due to the asymmetric carbon atom holding the amino group should outweigh that due to the one holding the hydroxyl group.

(12) Another possible name for this amino alcohol is D(+)-*erythro*-2-amino-3-hydroxybutane or D(+)-*erythro*- α,β -dimethylethanolamine, (XI). In this case C-2 would be inverted when the oxide ring of VI is opened and C-3 would be inverted when the imine ring is closed, yielding XII. The over-all stereochemical result is the same in either case, for XII is seen to be identical with IX. The naming of the amino al-



cohol as VII is preferred to that as XI, because then the hydroxyl group is kept in the 2-position and the compound is named as a derivative of an alcohol. At the same time attention is called to the inversion of configuration.

(13) S. A. Morell and A. H. Anenheider, *THIS JOURNAL*, **66**, 792 (1944)

Observed rotations of the pure compounds (Table I) are as follows: (1) an active diamine, Va, Vb, has 29° , whereas the glycol has 13° ; (2) an active *threo*-amino alcohol, IIa, IIb, has 17° , whereas the diamine has 29° and glycol, 13° ; (3) active *erythro*-amino alcohol, VII, has 0.85° , whereas the *threo*-isomer has 17° ; (4) L-*erythro*-3-amino-2-butanol is positive. Thus all of the relationships of the preceding paragraph are found to hold.¹⁴ Moreover the rotations of derivatives, in particular those of the di-*p*-toluenesulfonyl derivatives, show similar relationships, as pointed out later.

Such striking agreements between predictions and observations lend strong support to the premise on which the predictions are made and strengthen the assignment of configurations made on this basis. In addition, the correlation of physical constants among glycols, diamines and amino alcohols, as pointed out later, is further substantiation of the configurations of the inactive 3-amino-2-butanols. All this is entirely consistent with the stereochemical results of other investigators.^{6,10}

Physical Constants.—All of the amino compounds are very hygroscopic. The anhydrous diamines and amino alcohols fume on exposure to air; spattering occurs when they are mixed with water. It was difficult to prepare anhydrous samples; the best way is decomposition of the dry hydrochloride with methanolic sodium methoxide. The most anhydrous products still contained 1 to 3% water, as determined by titration to a methyl orange end-point with hydrochloric acid.

In Table I are listed physical constants of the compounds shown in Figs. 1 and 2. Only the highest values for melting points and boiling points are tabulated. In order to make comparisons among the various physical constants it was necessary that the physical states be similar. Since *erythro*-3-amino-2-butanol (VII) is a solid at room temperature, it was necessary to cool this carefully so that it would remain a supercooled liquid while the measurements were being made. The same thing was done with *meso*-2,3-butanediol. Other data on glycols and oxides are taken from earlier work and are included for comparison purposes.

Configurational Purity.—It is believed that the various compounds were configurationally pure, for in no instance was there any indication of the presence of any stereoisomer in amounts other than less than 1%. For example, the crude L-*erythro*-3-amino-2-butanol (VII) from D(+)-2,3-epoxybutane (VI) melted above 45° ; the pure compound melts at 49.3° . The crude imines, IV and IX, when fractionally distilled came over in a narrow temperature range, although their boiling points differ by eight degrees. Resolution of DL-2,3-butanediamine (V) with (+)-tartaric acid gave no evidence of the presence of *meso*-2,3-butanediamine (X) the acid tartrate of which is less soluble

(14) Another interesting relationship is the ratio of rotations between nitrogen and similar oxygen compounds. Rotation of active oxide is 58% that of active imine, and that of glycol, 45% that of diamine. The rotations of the oxide and imine in heptane are close to the values for the pure liquids.

TABLE I
 CONSTANTS OF SOME 2,3-DISUBSTITUTED BUTANES

		M.p., °C.	B.p., °C. (cor.)	Mm.	d_{25}^4	n_D^{25}	α_D^{25}	$[\alpha]^{25D}$
3-Amino-2-butanol	DL- <i>threo</i> , II ^a	18-20	69-70	20	0.9299	1.4445		
	D(-)- <i>threo</i> , IIa	15-16	70.6-71.3	20	.9289	1.4450	-15.84°	-17.05°
	L(+)- <i>threo</i> , IIb	7-11			.9274	1.4448	+15.69	+16.91
	L(+)- <i>erythro</i> , VII	49.2-49.3			.9378 ^b	1.4488 ^b	+0.80	+0.85
	DL- <i>erythro</i> ^c	43.0-44.8	75.0-75.5	20	.9447 ^b	1.4480 ^b		
2,3-Dimethylethyl- eneimine	<i>meso</i> , IV ^d	-9 to -6	82.5-82.9	747	.8171	1.4172	+0.22°	
	L(-), IX ^f	-26 to -23	74.5-74.8	746	.7880	1.4070	-80.37	-102.0
2,3-Diaminobutane	DL, V	-22 to -21	57-58	60	.8499	1.4408		
	L(+), Vb		58-59	60		1.4462	+25.18	+29.48
	<i>meso</i> , X	-24 to -22	59-60	60	.8564	1.4420		
2,3-Epoxybutane	<i>meso</i> , I ^{6a}		59.7 ± 0.05	742	.8226	1.3802		
	DL ^{6a}		53.5 ± 0.05	742	.8010	1.3705		
	D(+), VI ^{6a}		53.5-53.7	745	.7998	1.3705	+47.23	+59.05
2,3-Butanediol	DL ^{5a}	7.6	176.7	742				
	D(-) ^g	19.7	77.5-77.6	10	.9869	1.4308	-13.0	-13.19
	<i>meso</i> ^{5a}	34.4	181.7	742	1.0003	1.4367		

^a Previous values,⁹ b.p. 85-105° (185 mm.), n_D^{25} 1.4425. ^b Supercooled liquid. ^c Previous values,⁹ b.p. 116-119° (185 mm.), n_D^{25} 1.4445. ^d Previous values for the *trans* (?): b.p. 75-76°, n_D^{25} 1.4070, d_{25}^{25} 0.7887, and b.p. 76-77° (185 mm.), n_D^{25} 1.4105. ^e One product from L(+)-*threo*-3-amino-2-butanol. ^f Previous values for the DL: b.p. 65-76° (185 mm.), n_D^{25} 1.4074. ^g A. C. Neish, *Can. J. Research*, 23B, 10 (1945).

 TABLE II
 DI-*p*-TOLUENESULFONYL AND DIBENZENESULFONYL DERIVATIVES

		M.p., °C. (cor.)	$[\alpha]^{25D}$ in butanone	Analyses, %							
				Carbon		Hydrogen		Nitrogen		Sulfur	
				Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
3- <i>p</i> -Toluenesulfon- amido- <i>p</i> -toluene- sulfonoxybutane	DL- <i>threo</i>	125.7-126.7		54.26	54.20	5.85	5.78	3.52	3.44	16.11	15.94
	D(+)- <i>threo</i>	140.1-141.0	+42.5°	54.26	54.35	5.85	5.85	3.52	3.47	16.11	16.01
	DL- <i>erythro</i>	94.5-96.3		54.26	54.47	5.85	5.80	3.52	3.47	16.11	16.01
	L(-)- <i>erythro</i>	104.2-105.2	-7.14	54.26	54.36	5.85	5.99	3.52	3.46	16.11	16.36
2,3-Di- <i>p</i> -toluene sulfonamido- butane	DL- <i>threo</i>	179.3-180.7		54.52	54.61	6.10	6.18	7.07	6.99	16.17	15.98
	L(-)- <i>threo</i>	201.1-202.8	-70.3	54.52	54.90	6.10	6.12	7.07	7.02	16.17	16.09
	<i>meso</i>	168.5-169.0		54.52	54.31	6.10	5.96	7.07	7.04	16.17	16.52
3-Chloro-2- <i>p</i> - toluenesulfon- amidobutane	DL- <i>threo</i> ^a	100.5-101.5		50.47	50.43	6.16	6.12	5.37	5.50	13.55°	13.48°
	L- <i>erythro</i> ^b	96.3-96.7	-23.6	50.47	50.59	6.16	6.23	5.37	5.30	13.55°	13.44°
3-Chloro-2-benzene- sulfonamidobutane	DL- <i>threo</i> ^a	120.6-121.7		48.48	48.50	5.70	5.68	5.66	5.61	14.51°	14.30°
	L- <i>erythro</i> ^b	54.2-54.8	-24.8	48.48	48.51	5.70	5.76	5.66	5.68	14.51°	14.34°

^a From the *meso*-imine. ^b From the L-imine. ^c Chlorine, %.

 TABLE III
 DIACETYL DERIVATIVES

		M.p., °C. (cor.)	$[\alpha]^{25D}$ in butanone	Analyses, %					
				Carbon		Hydrogen		Nitrogen	
				Calcd.	Found	Calcd.	Found	Calcd.	Found
3-Acetamido-2-acetoxybutane	DL- <i>threo</i>	73.4-74.4		55.47	55.53	8.73	8.69	8.09	8.02
	D(+)- <i>threo</i>	59.3-60.5	+35.0°	55.47	55.52	8.73	8.70	8.09	8.01
	DL- <i>erythro</i>	51.0-52.4		55.47	55.55	8.73	8.79	8.09	7.99
	L(-)- <i>erythro</i>	62.3-63.3	-33.0	55.47	55.63	8.73	8.80	8.09	7.95
2,3-Diacetamidobutane	DL- <i>threo</i>	178.6-178.9		55.78	55.80	9.37	9.30	16.27	16.22
	L(-)- <i>threo</i>	199.3-199.7	-56.8	55.78	55.92	9.37	9.33	16.27	16.18
	<i>meso</i>	277.9-280.0 ^a		55.78	55.79	9.37	9.32	16.27	16.19

^a Sealed tube.

than that of the D-isomer. The best evidence was the low rotation of the *cis*-imine, IV, from L(+)-*threo*-3-amino-2-butanol. One quarter per cent. of active *trans*-imine would account for the observed rotation of the *meso*-imine.

Deductions from Physical Data.—It is noted from Table I that the *meso*-isomers of 2,3-butanediol and 2,3-butanediamine have higher melting points, boiling points, densities and refractive indices than DL or active isomers. Also, one of the

3-amino-2-butanols has a higher melting point, boiling point, density and refractive index than the other. The higher melting solid therefore should be the *erythro*-isomer. This is the configuration arrived at on the premise that ring openings are attended with one Walden inversion. It is seen, therefore, that there are two independent lines of evidence substantiating configurations arrived at on this premise, to wit: (1) physical data and (2) the consistent relationship existing

among configurations and the signs and magnitudes of rotation. The logical conclusion is drawn from the experimental evidence herein presented that the configurations are well established.

The configurations of the active amino alcohols and diamines are believed to be sufficiently certain to warrant their being used as reference compounds for other optically active nitrogen compounds of unknown configuration. Also, the relationships in regard to signs and magnitudes of rotations should hold with normal symmetrical homologs of 3-amino-2-butanol.

Rotations of Derivatives.—The rotation of *L*-2,3-di-*p*-toluenesulfonamidobutane is -70.3° compared to $+37.2^\circ$ for *D*(+)-2,3-di-*p*-toluenesulfonybutane.¹⁵ This illustrates again the greater rotation of amine derivatives, compared to analogous alcohol derivatives. The rotation of the ditosyl derivative of *D*(-)-*threo*-3-amino-2-butanol, $[\alpha]^{25}_D + 42.5^\circ$, being intermediate between those of the corresponding diamine derivative, $+70^\circ$, and glycol derivative, $+37.2^\circ$, and the rotation of the corresponding *L*-*erythro* derivative, $[\alpha]^{25}_D - 7.14^\circ$, being much less than that of the *D*-*threo*-derivative, $+42.5^\circ$, reaffirm the deductions drawn earlier, on the basis of the magnitude of rotation, in relation to the configurations of the 3-amino-2-butanols. Similarly, in the diacetyl derivatives, the rotation of the one from *D*-*threo*-3-amino-2-butanol, $+35^\circ$, is intermediate between $+56.8^\circ$ (corresponding to -56.8° for the *L*-diamine derivative) and $+13.7^\circ$ for the glycol derivative.^{6c,15}

The sign of rotation of derivatives of *L*-*erythro*-3-amino-2-butanol should be negative, and this is true of both the ditosyl and diacetyl derivatives. The magnitude of rotation of an *erythro*-diacyl derivative should be much lower than that of the *threo*-isomer. This is true of the ditosyl but not of the diacetyl compound, which has a rotation almost equal to that of the *threo*-isomer. It is possible that the high rotation of *L*(-)-*erythro*-3-acetamido-2-acetoxybutane may be due to a cyclic structure, *i.e.*, one characteristic of an oxazolidine. Except for one compound, therefore, the signs and relative magnitudes of rotation of ditosyl and diacetyl derivatives of isomers of 2,3-butanediol, 2,3-butanediamine and 3-amino-2-butanol are confirming evidence of the configurations assigned.

Reduction of Dimethylglyoxime.—The reduction of dimethylglyoxime to 2,3-butanediamine has been accomplished with hydrogen¹⁶ and that of diacetyldimethylglyoxime with sodium and alcohol.¹⁷ These reductions, and also the reduction of 3-nitro-2-butanol with hydrogen,^{9,18} were found to be less satisfactory than the reduction of dimethylglyoxime with Raney aluminum-nickel alloy and aqueous sodium hydroxide, a reagent that has been used by Schwenk and co-workers for other

reductions,¹⁹ but not for that of oximes. The reduction of dimethylglyoxime with Raney aluminum-nickel alloy is a convenient source of 2,3-butanediamine and 3-amino-2-butanol, which are obtained in yields of 40 and 25%, respectively. They are easily separated from each other by distillation; the diamine distills first.

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Experimental²⁰

***meso*- and *D*(+)-2,3-Epoxybutanes.**—These were prepared from *meso*- and *D*(-)-2,3-butanediol, respectively, by methods previously described^{6b,c} except that a somewhat longer time, about 3 weeks, was allowed for the reaction of hydrochloric acid with the butanediol diacetates. The oxides were not carefully purified since the amino alcohols prepared from them were easily purified by crystallization of their salts. The yields of oxides from glycols were 80–90%, and their properties agreed closely with those previously described^{6b,6c}; *meso*, b.p. 59.7–60.0° (747 mm.), n^{25}_D 1.3800; *D*, b.p. 53.2–53.6° (748 mm.), n^{25}_D 1.3704, $\alpha^{25}_D + 46.73$ (undiluted).

***DL*-*threo*- and *L*(+)-*erythro*-3-Amino-2-butanols.**—The reaction of 2,3-epoxybutane with aqueous ammonia has been previously reported^{9,21} to give only a fair yield of 3-amino-2-butanol mainly because the oxide reacts with the resulting amino alcohol. This difficulty can be avoided by using a large excess of ammonia. To 2 liters (*ca.* 30 moles) of concentrated aqueous ammonia were added 72 g. (1 mole) of 2,3-epoxybutane. The mixture was allowed to stand at room temperature for 10 days in an ordinary screw-cap acid bottle. It was found advisable to cool the ammonia to 10–15° beforehand in order to avoid rapid evolution of gas on mixing. Reasonable but smaller yields were obtained with a reaction time as short as 4 days. After 10 days the excess ammonia and most of the water were removed by distillation at atmospheric pressure through a 15-cm. packed column, until the flask temperature reached 105°. The remaining water was then removed at reduced pressure, using a 60-cm. column packed with Raschig rings. The *DL*-*threo*-amino alcohol, obtained from the *meso*-oxide, was purified by distillation through this column; yield 68 g., 76%, b.p. 69–70° at 20 mm.

Distillation of the *L*-*erythro*-amino alcohol, obtained from the *D*-oxide, was inconvenient because of its high melting point. It was freed from water by distillation at 20 mm. up to 72°, the residue at this point having a melting point above 45°; yield 62 g., 70%. Crystallization from 100 ml. of isopropyl ether gave 46 g., 74% yield on the crystallization and 52% on the initial 1 mole of oxide. Because of its strong affinity for water the solid was washed finally with dry benzene and then dried in a vacuum desiccator; m.p. 49.3°, $\alpha^{25}_D + 0.80^\circ$; $[\alpha]^{25}_D + 0.85^\circ$.

Resolution of *DL*-*threo*-3-Amino-2-butanol.—Solutions of 10.4 g. (0.117 mole) of the amino alcohol and 26.6 g. (0.117 mole) of (+)-tartaric acid were combined to give a solution of *DL*-*threo*-3-amino-2-butanol acid tartrate. The solvent was ethanol containing 5% methanol and 5% water by volume. Four recrystallizations gave a salt having a constant solubility of 0.3 g. per 100 ml. Another lot of 4.9 g. of the same solubility was obtained by reworking the mother liquors. The yield of salt was 21.0 g., 96%. Treatment with aqueous sodium hydroxide yielded the free base which was recovered by distillation; b.p. 69–70° (20 mm.),

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(20) Microanalyses by A. Elek. Physical data not given in the experimental section are listed in tables.

(21) V. S. Batalin and P. G. Ugryumov, *Sintet. Kauchuk*, No. 6, 8, (1936); *see C. A.*, **80**, 6701 (1936).

$\alpha^{25}_D - 15.51^\circ$ (undiluted), neut. equiv.: calcd. 44.5, found 45.5. A sample of this material was again converted to its acid tartrate and crystallized from the same solvent: solubility 0.32 g. per 100 ml. The recovered base had $\alpha^{25}_D - 15.84^\circ$ (undiluted), neut. equiv., 45.2.

The other form of the amino alcohol, recovered from the mother liquors by similar procedures, showed a lower rotation of opposite sign: $\alpha^{25}_D + 13.75^\circ$, neut. equiv., 45.5. With an equivalent amount of (-)-malic acid it gave a salt that was recrystallized twice from absolute ethanol. The recovered base had $\alpha^{25}_D + 15.69^\circ$, neut. equiv., 45.4.

meso- and L-2,3-Dimethylethyleneimines.—A solution of 32 g. (0.36 mole) of 3-amino-2-butanol was neutralized to a methyl orange end-point with a measured volume of 50% aqueous sulfuric acid, and then an equal volume of the acid was added in excess. This solution was evaporated on a steam-bath at 15–20 mm. until a solid lump remained (8 hours). This was then ground in a mortar and subjected to the same conditions of evaporation until constant weight was obtained (16 hours). Completion of the reaction was shown by the loss in weight, corresponding to the loss of one mole of water, and by the neutrality of the residue to methyl orange. The yield of 3-amino-2-butyl hydrogen sulfate (as the inner salt) was probably nearly quantitative. The rotation of only one sulfate was taken, that from L(+)-*erythro*-3-amino-2-butanol; $[\alpha]^{25}_D + 3.6^\circ$ ($c = 0.05$, $\alpha = +0.18^\circ$, water).

A 3-necked, 1-l. flask was fitted with a broad-bladed stirrer, an exit line leading to a condenser, and a vertical, 10-mm. tube for introduction of the solid aminobutyl hydrogen sulfate. During the reaction a slow current of air, just sufficient to prevent condensation in the tube, was drawn through the system. A solution of 95 g. (1.4 moles) of potassium hydroxide in 125 ml. of water was placed in the flask, heated to about 90° , and 64 g. (0.36 mole) of the solid sulfate was added in small portions. The imine distilled from the mixture almost as rapidly as the sulfate was added. After the addition was complete the heating was increased and a total of about 50 ml. was taken over.

The distillate from the reaction mixture was redistilled through a 60-cm. column of glass helices and the products were collected at temperatures a degree or two above their proper boiling points since the fractionation was not sufficient to remove the last traces of water. These crude products were dissolved in *n*-butyl ether, allowed to stand over solid potassium hydroxide, and again recovered by distillation through the same apparatus.

The *meso*-imine was obtained from the inactive *threo*-amino alcohol in 63% yield; b.p. $82.5\text{--}82.9^\circ$ (747 mm.), m.p. -9.3 to -6.2° ; neut. equiv., calcd. 71.1, found 71.9. The L-imine was obtained from the L-*erythro*-amino alcohol in 58% yield; b.p. $74.5\text{--}74.8^\circ$ (746 mm.), m.p. -26 to -23° , neut. equiv., calcd. 71.1, found 71.8; $\alpha^{25}_D - 80.37^\circ$, $[\alpha]^{25}_D - 102.0^\circ$.

The above procedure represents an improvement of those heretofore reported.^{8,9} However, the following method was found to be more convenient and to give a higher yield in the conversion of L(+)-*erythro*-3-amino-2-butyl hydrogen sulfate to the L-imine. To a cooled solution of 18 g. (0.127 mole) of the solid sulfate in 50 ml. of water was added slowly, with further cooling, a cold solution of 25 g. (0.45 mole) of potassium hydroxide in 25 ml. of water. The mixture was then placed in a distilling apparatus and warmed slowly. At about 80° a white precipitate of potassium sulfate appeared. Distillation began at 85° and was continued to 100° . The imine was salted out of the distillate with potassium hydroxide and dried over potassium hydroxide. Distillation gave 7.96 g., 95% yield, of L(-)-2,3-dimethylethyleneimine, b.p. $74.7\text{--}75.7^\circ$ (746 mm.), $n^{25}_D 1.4076$, $[\alpha]^{25}_D - 103.8^\circ$ ($c = 0.2218$, $\alpha = -2.29^\circ$, *n*-heptane).

meso-2,3-Dimethylethyleneimine from L(+)-*threo*-3-Amino-2-butanol.—The preparation was carried out by the improved method. From 4.45 g. (0.05 mole) of amino alcohol was obtained 1.57 g., 48% yield, of imine. The crude dry product weighed 2.14 g. and was fractionated in a semi-micro apparatus. The first fraction of 0.46 g., b.p. $83.3\text{--}84.2^\circ$ (746 mm.), had $n^{25}_D 1.4188$, $\alpha^{25}_D + 0.35^\circ$ (undiluted); the second, 1.11 g., b.p. $84.2\text{--}84.4^\circ$ (746 mm.), had $n^{25}_D 1.4177$, $\alpha^{25}_D + 0.16^\circ$ (undiluted). The average rotation of $+0.22^\circ$ indicates a contamination by active imine to the extent of about 0.2%.

meso- and DL-2,3-Butanediamines, by Ammoniation of Imines.—Preliminary experiments showed that no appreciable reaction occurred between ammonia and an imine

when a solution of the imine and ammonium chloride in liquid ammonia was refluxed at -33° for 48 hours. The reaction was therefore carried out in a bomb at a higher temperature. A monel metal lined bomb containing 8.3 g. (0.12 mole) of imine, 15 g. (0.28 mole) of ammonium chloride, and 130 ml. (ca. 6 moles) of liquid ammonia was closed and heated to $50\text{--}55^\circ$ for 110 hours. The excess ammonia was evaporated to give the diamine, probably as the monohydrochloride. The residue was treated with excess aqueous sodium hydroxide, and distilled to dryness. Hydrochloric acid was added to the distillate and the diamine was recovered from the aqueous distillate as the dihydrochloride. The residue was dried thoroughly by warming under vacuum, and decomposed with excess sodium methylate in methanol. After the methanol was separated by distillation, although a complete separation was difficult, the diamines were distilled at reduced pressure. *meso*-2,3-Butanediamine was obtained from L(-)-2,3-dimethylethyleneimine; b.p. $59\text{--}60^\circ$ (60 mm.), m.p. -22 to -21.1° . DL-2,3-Butanediamine was obtained from *meso*-2,3-dimethylethyleneimine; b.p. $57\text{--}58^\circ$ (60 mm.), m.p. -23.5 to -21.6° . The yield was 2.5 g., 23%, with both isomers.

Subsequent to the above-described experiments, the method of Clapp¹¹ became available and was found to be an improvement, mainly because of convenience. For reaction vessels war surplus stainless steel oxygen ball-out cylinders having a capacity of 320 ml. were used. The *meso*-imine and ammonium chloride were placed in the cylinder which was then cooled in Dry Ice and evacuated. The ammonia was introduced by connecting to an ordinary ammonia tank and keeping the small cylinder in Dry Ice. About half an hour was required to introduce 100 g. per cylinder. The reaction was carried out with 20.1 g. (0.29 mole) of *meso*-2,3-dimethylethyleneimine, 1.59 g. (0.06 mole) of ammonium chloride, and approximately 210 g. (12 mole) of ammonia, divided between two cylinders. Heating was at 100° for 56 hours. The bombs were cooled and opened. The slightly rust-colored reaction mixture (in this respect stainless steel is much better than monel metal, which gave very dark reaction mixtures containing much solid material) was poured into a cold flask and allowed to evaporate through a condenser kept at -10° to prevent escape of unreacted imine. The remaining material was distilled rapidly at 60 mm. and then fractionated. About 5 g. (25%) of imine, b.p. $83\text{--}86^\circ$, 2.2 g. of an intermediate fraction, and 8.5 g., 30% yield, of DL-diamine boiling at $58.8\text{--}61.8^\circ$ (60 mm.) were obtained. The material remaining in the pot, about 2 g., was probably mostly polymer. The yield could probably have been improved slightly by decomposing the solid residue from the first distillation with base.

Resolution of DL-2,3-Butanediamine.—The acid tartrate of the DL-diamine was prepared by mixing absolute ethanol solutions of 2.5 g. (0.028 mole) of diamine and 8.4 g. (0.056 mole) of (+)-tartaric acid. From the total volume of 100 ml. of absolute ethanol solution 10.4 g. of salt precipitated. Four recrystallizations from a solvent containing 2 volumes of ethanol to 1 of water gave a product having a constant solubility of 0.6 g./100 ml. More material having the same solubility was obtained by reworking the mother liquors, in all, 3.8 g., 70% yield. Because of its low solubility in anhydrous solvents this salt could not be decomposed with sodium methylate. It was treated with aqueous sodium hydroxide, the diamine was distilled, converted to the dihydrochloride, dried, and recovered as in the original diamine preparations; yield 0.4 g., 32%, b.p. $57\text{--}59^\circ$ (60 mm.), $n^{25}_D 1.4311$, $\alpha^{25}_D + 14.98^\circ$. Titration indicated about 70% diamine.

Modification of the procedure led to better resolution, a more active product and better recovery. To a warm solution of 20.47 g. (0.1364 mole) of (+)-tartaric acid in 450 ml. of absolute ethanol and 250 ml. of water were added 6.0 g. (0.068 mole) of DL-2,3-butanediamine dissolved in 50 ml. of absolute ethanol. After standing overnight the mixture was filtered and the rosette-shaped crystals dried in vacuum over calcium chloride. The dry weight was 14.80 g. so that the solubility in this solvent (ethanol-water 2:1) was 1.55 g./100 ml. A 5% aqueous solution had $\alpha^{25}_D + 0.95^\circ$. After five recrystallizations from the same solvent, 6.85 g. of material was obtained having a constant solubility of 0.40 g./10 ml. and $\alpha^{25}_D + 0.89^\circ$ for a 5% aqueous solution. By reworking the mother liquors another 3.0 g. of material having the same solubility was obtained; yield 9.85 g., 74%.

As a further check on the completeness of resolution of the acid tartrate, 0.02 g. was dissolved in a few drops of warm water and several pellet potassium hydroxide were added with gentle cooling. The diamine separated as a separate layer and was dissolved by adding dry benzene and stirring gently; the aqueous layer was not extracted with benzene. The benzene solution was filtered and had $\alpha^{25D} +0.82^\circ$, $[\alpha]^{25D} +28.8^\circ$. The concentration of diamine (0.0284 g./ml.) was determined by passing dry hydrogen chloride into 1.00 ml. of the benzene solution and weighing the precipitated dihydrochloride (0.0520 g.).

One gram of the acid tartrate salt was then recrystallized from 20 ml. of the same solvent and the same measurement was repeated on the recrystallized material. The solution of the diamine (0.0266 g./ml.) in benzene had $\alpha^{25D} +0.78^\circ$, $[\alpha]^{25D} +29.3^\circ$ (wt. of dihydrochloride from 1 ml. of solution, 0.0486 g.).

The recovery of the active diamine from the acid tartrate salt was carried out in the same way. The benzene solution was first distilled through a small Vigreux column to remove the benzene-water azeotrope. The last of the benzene was removed at 120 mm. and finally at 60 mm. through a small semi-micro column, and the diamine was distilled through the same column at the latter pressure. From 4 g. of salt was obtained about 0.35 g., 40% yield, of diamine, b.p. 57–58°, n^{25D} 1.4462, $\alpha^{25D} +25.18^\circ$, $[\alpha]^{25D} +29.48^\circ$. The high refractive index may have been due to the presence of some benzene, because of the small amount of material.

The tartrate salt of the enantiomorph, obtained by evaporation of the combined mother liquors, was decomposed with base. The diamine had $\alpha^{25D} -11.43^\circ$. Further resolution was attempted by preparation of the acid salt with (–)-malic acid. This material proved to be very gummy and only a small portion of it could be induced to crystallize.

Attempted Resolution of meso-2,3-Butanediamine.—The other diamine isomer, obtained in the series of reactions starting with D-2,3-butanediol, was converted by the same procedure into a less soluble acid tartrate. Successive crystallizations of this salt from water showed constant solubility, 8 g./100 ml., and therefore no tendency to separate into isomeric forms.

3-*p*-Toluenesulfonamido-2-*p*-toluenesulfonybutanes.—To a solution of 0.89 g. (0.10 mole) of DL-*threo*-3-amino-2-butanol in 6 ml. of pyridine was added slowly, with cooling and shaking, 4.00 g. (0.020 mole) of *p*-toluenesulfonyl chloride. After about an hour the solution was filled with crystals of pyridine hydrochloride and was allowed to stand overnight. The solution was neutralized with 10 ml. of 6 *N* hydrochloric acid, the resulting yellow precipitate removed by filtration and the aqueous solution extracted with benzene. The DL-*threo*-3-*p*-toluenesulfonamido-2-*p*-toluenesulfonybutane was recrystallized from benzene-ligroin, giving after one recrystallization 2.88 g., 72% yield, of nearly-white needles. Six recrystallizations were required for constant melting point. The D(+)-*threo*-isomer, from D(–)-*threo*-3-amino-2-butanol had $[\alpha]^{25D} +42.5^\circ$ ($c = 0.0792$, $\alpha = +3.37^\circ$, butanone). The L(–)-*erythro* isomer from L(+)-*erythro*-3-amino-2-butanol had $[\alpha]^{25D} -7.14^\circ$ ($c = 0.0560$, $\alpha = -0.40^\circ$, butanone).

3-Acetamido-2-acetoxybutanes.—To a solution of 0.45 g. (0.0050 mole) of DL-*threo*-3-amino-2-butanol in 1.2 ml. of pyridine was added dropwise, with cooling, 1.53 g. (0.015 mole) of acetic anhydride. After standing overnight the mixture was placed in a vacuum desiccator over sulfuric acid and potassium hydroxide. After about ten days 0.82 g., 94% yield, of DL-*threo*-3-acetamido-2-acetoxybutane remained as dry white needles. Constant melting point was reached after two recrystallizations from benzene-ligroin. The D(–)-*threo*-isomer from D(–)-*threo*-3-amino-2-butanol had $[\alpha]^{25D} +35.0^\circ$ ($c = 0.0503$, $\alpha = +1.76^\circ$, butanone). The L(–)-*erythro*-isomer, from L(+)-*erythro*-3-amino-2-butanol had $[\alpha]^{25D} -33.0^\circ$ ($c = 0.0500$, $\alpha = -1.65^\circ$, butanone).

3-Chloro-2-*p*-toluenesulfonamidobutanes.—To a cooled solution of 0.35 g. (0.005 mole) of L(–)-2,3-dimethylethyleneimine in 3 ml. of pyridine was added dropwise 1.0 g. (0.005 mole) of *p*-toluenesulfonyl chloride dissolved in 2 ml. of pyridine. After standing for three days the solution was evaporated in vacuum to 3 ml. and 10 ml. of benzene was added. The two phase mixture was shaken with 25 ml. of 1 *N* hydrochloric acid which was then extracted after separation with another 10 ml. of benzene. Vacuum evaporation of the dried benzene extracts gave 0.30 g., 21% yield,

of D-*erythro*-3-chloro-2-*p*-toluenesulfonamidobutane, crystallizing as white needles in rosette patterns. Three recrystallizations from isopropyl ether were required to reach constant melting point; $[\alpha]^{25D} -23.6^\circ$ ($c = 0.0500$, $\alpha = -1.18^\circ$, butanone). The DL-*threo*-isomer was prepared similarly from meso-2,3-dimethylethyleneimine.

3-Chloro-2-benzenesulfonamidobutanes.—The reaction was carried out in exactly the same way as with the tosyl derivative except that the reaction mixture was allowed to stand a week before working up. The crystals were similar to those of the tosyl derivative but smaller. Yield of D-*erythro*-3-chloro-2-benzenesulfonamidobutane from L-imine was 0.22 g., 18%; $[\alpha]^{25D} -24.8^\circ$ ($c = 0.0400$, $\alpha = -0.99^\circ$, butanone). It was found to be too soluble in isopropyl ether and so was recrystallized from heptane. Constant melting point was reached after three recrystallizations. The DL-*threo*-isomer was prepared similarly from the meso-imine.

2,3-Di-*p*-toluenesulfonamidobutanes.—The reaction was carried out as for the amino alcohols, using 0.44 g. (0.005 mole) of diamine. The original product from the meso-diamine was quite yellow, but two crystallizations from isopropyl ether gave 0.74 g., 37% yield of meso-2,3-di-*p*-toluenesulfonamidobutane, colorless crystals. Four more recrystallizations were required to reach constant melting point. The DL-isomer was obtained similarly from the DL-diamine, and the L(–)-isomer from the L(+)-diamine; $[\alpha]^{25D} -70.3^\circ$ ($c = 0.0298$, $\alpha = -2.09^\circ$, butanone).

2,3-Diacetamidobutanes.—To a cooled solution of 0.44 g. (0.005 mole) of meso-2,3-butanediamine in 2 ml. of pyridine was added dropwise 1.53 g. (0.015 mole) of acetic anhydride. A white precipitate appeared as the anhydride was added. The whole was placed in a vacuum desiccator over sulfuric acid and potassium hydroxide and the liquid allowed to evaporate. The resulting meso-2,3-diacetamidobutane, 0.86 g., 100% yield, crystallized in needles. The material was recrystallized from acetone, although the temperature coefficient of solubility was not completely satisfactory. A constant melting point was obtained after four recrystallizations. The L(–)-2,3-diacetamidobutane prepared from L(+)-2,3-butanediamine had $[\alpha]^{25D} -56.8^\circ$ ($c = 0.0095$, $\alpha = -0.54^\circ$, butanone).

Hydration of meso-2,3-Dimethylethyleneimine and Identification of the Product.—To 50 ml. of 1 *N* sulfuric acid was added 1.42 g. (0.02 mole) of meso-1,2-dimethylethyleneimine. After 20 days standing at room temperature some imine odor could still be detected. The solution was made basic with 30% sodium hydroxide solution and distilled to dryness. The distillate was distilled through a semi-micro column. A first cut, approximately 0.5 ml., b.p. 90–97°, was probably unreacted imine. The remaining material was distilled to dryness at 80 mm. and the distillate titrated with hydrochloric acid to a methyl red end-point. It required 0.00991 mole (9.20 ml. of 1.078 *N* HCl) of acid, indicating an approximate 50% yield of amino alcohol. The solution was evaporated almost to dryness, care being taken to avoid excessive heating. The resulting yellow sirup was dried in vacuum over sulfuric acid. This crude hydrochloride was dissolved in about 5 ml. of methanol and a solution of 0.23 g. (0.01 mole) of sodium in methanol was added. The precipitate of sodium chloride was removed by filtration and the solution distilled through a semi-micro column. The last fraction, about 0.5 ml., had b.p. ca. 70° (20 mm.) and n^{25D} 1.4441.

A small amount of this material was converted to the ditosyl derivative, and recrystallized three times from benzene-ligroin: m.p. 126.1–126.9°, mixed melting point of 126.2–127.0° with the ditosyl derivative, m.p. 125.7–126.7°, from DL-*threo*-3-amino-2-butanol, the ammonation product of meso-2,3-epoxybutane. The product was thus reasonably pure *threo*-isomer. Had any *erythro*-isomer been present it would have been concentrated in the last fraction since its boiling point is slightly higher.

Reduction of Dimethylglyoxime.—To a solution of 116 g. (1 mole) of dimethylglyoxime and 371 g. (9 moles) of sodium hydroxide in 3 liters of water, heated to about 50° and contained in a three-necked 3-liter flask fitted with a sealed, broad-bladed stirrer, a thermometer, and an exit line to dispose of hydrogen and ammonia, were added 248 g. (50% excess) of Raney aluminum-nickel alloy in 2-g. portions and at such a rate that the temperature was maintained between 48 and 52°. Ninety minutes were required.

The reaction mixture stood overnight and the residual

nickel was removed by suction filtration. The liquid was distilled quickly without fractionation until all but a trace of volatile base had been removed. The distillate, 2 liters, was made just acid to methyl orange with hydrochloric acid and evaporated to dryness. The last traces of water were removed by azeotropic distillation with isopropyl alcohol. The dry salt was decomposed with a solution of 34 g. (1.48 moles) of sodium in 350 ml. of methanol. This quantity of sodium was equivalent to the base present in the distillate from the reaction mixture as determined by titration. The mixture was flash distilled to give a solution of the organic bases in anhydrous methanol. This was distilled under reduced pressure through a 60-cm. ring-packed column.

There were two main fractions: (1) 40 to 45° at 30 mm.; (2) 70 to 74° at 20 mm. The first was diamine, weight 40 g., yield 41%, purity 92%, determined by titration with hydrochloric acid to a methyl orange end-point; the second was amino alcohol, weight 21 g., yield 25% (on a 100% basis), purity, 102% by titration. The two amines were separated by crystallization but no further investigation of the amino alcohol mixture was made.

Separation of *meso*- and *DL*-2,3-Diaminobutane.—A part of the diamine from the reduction of dimethylglyoxime was neutralized in aqueous solution with hydrochloric acid. The solution was evaporated to dryness to yield 13.2 g. of the dihydrochloride, equivalent to 7.7 g. of diamine. Fractional crystallization from methanol and aqueous methanol

gave 3.7 g. of dihydrochloride having a constant solubility of 0.9 g. per 100 ml. of methanol at 22°. The more soluble solid from the mother liquors had a solubility of 7 g. per 100 ml. Comparison with the approximate solubilities of the dihydrochlorides of the diamines from the reactions of the imines with ammonia showed that the less soluble solid is the salt of the *meso*- and the more soluble, that of the *DL*-isomer.

Reduction of 3-Nitro-2-butanol.—Hydrogenation with a platinum oxide catalyst but at a lower pressure (48 to 6 pounds) than described by Johnson and Degering,²² who, however, used a Raney nickel catalyst, was carried out in batches. In a typical run, to 17.9 g. (0.15 mole) of 3-nitro-2-butanol in 100 ml. of ethanol 0.225 g. of catalyst was added and hydrogen introduced up to 48 pounds pressure. After 22 hours the pressure had dropped to 6 pounds. The combined reaction mixture from a total of 143.2 g. (1.20 moles) of 3-nitro-2-butanol was found to contain, by titration, 0.72 mole of basic material. By a process of extraction, and distillation at 20 mm., 22.8 g., 21% yield of product, distilling at 64–70°, mostly at the higher temperature, was obtained. This corresponds to *DL*-*threo*-3-amino-2-butanol, b.p. 70° (20 mm.); the *erythro*-isomer boils at 75.5° (20 mm.).

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Stereochemistry of the Reaction of 2,3-Epoxybutane with Alcohols

By G. K. HELMKAMP AND H. J. LUCAS

The *trans*-opening of the oxide ring of 2,3-epoxybutane by methyl and ethyl alcohols shows that a Walden inversion accompanies each of the reactions. Enantiomorphous 2-methoxy-3-ethoxybutanes have been prepared from *D*(+)-2,3-epoxybutane merely by changing the order of reagents in the steps: oxide to monoether to diether. Comparing *erythro*- and *threo*-ethers of 2,3-butanediol, refractive indices and densities are higher for *erythro*-isomers if hydrogen bonding is possible, otherwise *threo*-isomers have the higher values. Anomalous relationships have been observed among rotations of optically active *erythro*- and *threo*-ethers.

The reaction of 2,3-epoxybutane with a number of compounds, for example, water,¹ acetic acid,² hydrohalic acids^{3,4,5} and ammonia,⁶ has been shown to proceed with a *trans*-opening of the ring. The assumption of a *trans*-opening with methanol has been made by Winstein and Henderson,⁷ in their study of the participation of the methoxy group in reactions at an adjacent carbon atom. These authors believe that a *trans*-opening of the oxide ring accompanies also the reaction of cyclohexene oxide with methanol.^{7,8}

In the present work it has been found that methyl and ethyl alcohols cause *trans*-openings of the oxide ring of *D*(+)-2,3-epoxybutane (I) Fig. 1. This has been established by converting the monoethers that result from the ring openings, *viz.*, *L*(+)-*erythro*-3-methoxy-2-butanol (II) and *L*(+)-*erythro*-3-ethoxy-2-butanol (III) into the corresponding symmetrical diethers

by a Williamson synthesis which is expected not to cause any stereochemical change. These diethers

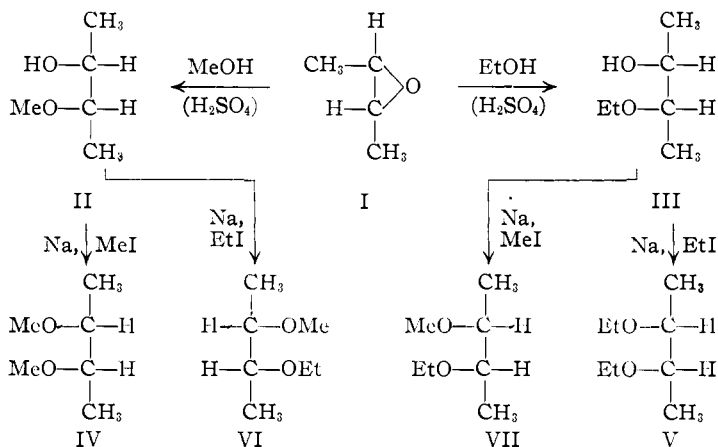


Fig. 1.—Proof of *trans*-opening of the epoxide ring with alcohols.

lack optical activity and thus have the *meso*-(*erythro*)-configuration; they are, respectively, *meso*-dimethoxybutane (IV) and *meso*-diethoxybutane (V). Since the oxide has the *threo*-configuration,⁹ the ring openings take place with a single Walden inversion. The conclusion that the inactive diethers have the *meso*-configuration is strengthened by the preparation of diastereomeric diethers (also monoethers)

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