[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Studies in Stereochemistry. XXIV. The Preparation and Determination of Configuration of the Isomers of 2-Amino-3-phenylbutane, and the Steric Course of the Amine Oxide Pyrolysis Reaction in this System

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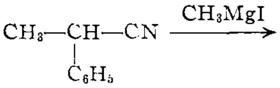
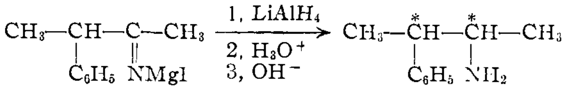
Three of the four stereoisomers of 2-amino-3-phenylbutane have been prepared in an essentially optically pure state, and their configurations have been determined by the ammonolysis of the stereoisomers of 3-phenyl-2-butyl *p*-toluenesulfonate. A novel synthesis of primary amines carrying secondary alkyl groups is reported. The Leuckart reaction is found to follow the rule of steric control of asymmetric induction in the synthesis of the system at hand. Pyrolysis of the oxides of the diastereomeric 2-(N,N-dimethylamino)-3-phenylbutane gave mixtures of *cis*- and *trans*-2-phenyl-2-butene and 3-phenyl-1-butene, the conjugated olefin resulting from *cis*-elimination markedly predominating over the other two isomers.

This investigation was undertaken for three reasons: (1) to prepare and determine the configurations of the four stereoisomers of 2-amino-3-phenylbutane (I) as a preliminary to a study of the solvolytic deammonation reaction with nitrous acid; (2) to determine if the rule of steric control of asymmetric induction[1] applies to the Leuckart reaction; (3) to determine the stereochemical course of the elimination reaction occurring when amine oxides are pyrolyzed.[2] The results of the solvolytic deamination reaction will be reported in a future publication. The synthesis of mixtures of diastereoisomers through the Leuckart reaction represents the first case in which the rule of steric control of asymmetric induction has been tested in a reaction not involving a metal-containing reagent. Although the amine–oxide elimination reaction (discovered by Cope, *et al.*[2a]) by its very nature has been judged to belong to the class of pyrolytic elimination reactions that assume a *cis*-steric course,[2a,b] the stereochemistry of the reaction has not been determined in a system that allows a differentiation to be made between the two possibilities.[3]

Synthesis and Resolution of the Isomers of 2-Amino-3-phenylbutane (I).—Three syntheses of the diastereomeric mixtures of 2-amino-3-phenylbutane (I) were employed: the catalytic reductive amination reaction of 3-phenyl-2-butanone[4]; the chemical reductive amination (Leuckart reaction)[5] of the same ketone; and the novel reaction sequence outlined in the formulation.[6]



$$\underset{\displaystyle C_6H_5}{CH_3—\overset{|}{CH}}—CN \xrightarrow{CH_3MgI}$$



$$CH_3—\underset{C_6H_5}{CH}—\underset{NMgI}{\overset{\|}{C}}—CH_3 \xrightarrow[\substack{2,\ H_3O^+\\ 3,\ OH^-}]{1,\ LiAlH_4} CH_3—\underset{C_6H_5}{\overset{*}{C}H}—\underset{NH_2}{\overset{*}{C}H}—CH_3$$

I

Of these, only the Leuckart reaction gave satisfactory yields. The two racemates of amine I were separated through fractional crystallization of the benzoate salt to give the *threo*-racemate, and of the hydrochloride to give the *erythro*-racemate[7] (see Table I for physical constants and analyses). This separation was aided greatly by fractional distillation of the mixture of racemates with an efficient column, the *threo* boiling about 0.5–1.0° below the *erythro* isomer at 100 mm. pressure. These salts were converted to the free amines, samples of which were converted to the sharp-melting benzamides (see Table I) in high yields.

The *threo* isomer (I) was resolved into its optical antipodes through fractional crystallization of the amine salt of *l*-malic acid on the one hand, and of the amine salt of *d*-tartaric acid on the other, (−)-*threo*-I being obtained from the former and (+)-*threo*-I from the latter salt. That these amines are essentially optically pure is indicated by the relative magnitudes of their rotations, and those of their benzamides (see Table I). The *erythro*-racemate (I) was resolved through fractional crystallization of the amine salt of *d*-tartaric acid to give upon conversion to the free base, (+)-*erythro*-I, a sample of which was converted to its (+)-benzamide. Although (−)-*erythro*-I was not prepared in an optically pure form, its benzamide (−) was obtained from a different source (see next section). The relative magnitudes of the rotations of the two *erythro*-benzamides attest to their optical purity. Table I reports the physical constants and analyses of the above substances.

Determination of Configuration of the Isomeric 2-Amino-3-phenylbutanes (I).—Since the configurations of the stereomers of 3-phenyl-2-butanol have been related to (−)-tartaric acid[8] (whose absolute configuration has been determined[9]), the configurations of the isomers of 2-amino-3-phenylbutane are established through the interconversions that are formulated.

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(1) (a) D. J. Cram and F. A. Abd Elhafez, THIS JOURNAL, **74**, 5828 (1952); (b) D. J. Cram and J. D. Knight, *ibid.*, **74**, 5835 (1952); (c) D. J. Cram, F. A. Abd Elhafez and H. Weingarten, *ibid.*, **75**, 2293 (1953); (d) D. J. Cram and F. D. Greene, *ibid.*, **75**, 6005 (1953); (e) D. J. Cram and J. Allinger, *ibid.*, **76**, 4516 (1954).

(2) (a) A. C. Cope, T. T. Foster and P. H. Towle, *ibid.*, **71**, 3939 (1949); (b) D. J. Cram, *ibid.*, **74**, 2137 (1952); (c) A. C. Cope, R. A. Pike and C. Spencer, *ibid.*, **75**, 3212 (1953); (d) A. C. Cope, Meeting American Chemical Society, Chicago, Ill., Sept., 1953, pp. 11F of Abstracts.

(3) Cope, *et al.*, (ref. 2c) observed that N,N-dimethylcycloöctylamine oxide when pyrolyzed gave *cis*-cycloöctene. Although this experiment demonstrated a high degree of stereospecificity for the reaction, either *cis*- or *trans*-olefin could have arisen from a *cis*-elimination.

(4) L. Haskelberg, THIS JOURNAL, **70**, 2811 (1948).

(5) C. M. Suter and A. W. Weston, *ibid.*, 2811 (1948).

(6) (a) D. J. Cram, Abs. of the 13th Nat. Org. Sym. of the Amer. Chem. Soc., June, 1953; (b) A. Pohland and H. R. Sullivan, THIS JOURNAL, **75**, 5898 (1953).

(7) These configurational assignments will be justified in a later section.

(8) (a) D. J. Cram, THIS JOURNAL, **71**, 3863, 3883 (1949); (b) **74**, 2149 (1952).

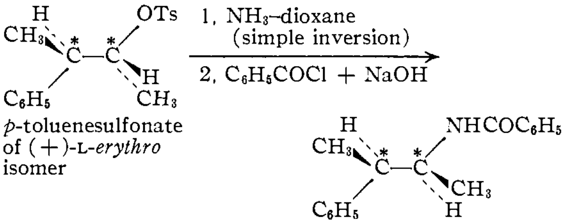
(9) J. M. Bijvoet, A. F. Peerdeman and A. J. van Bommel, *Nature*, **168**, 271 (1951).

TABLE I

PHYSICAL PROPERTIES AND ANALYSES OF ISOMERS OF 2-AMINO-3-PHENYLBUTANE AND DERIVATIVES

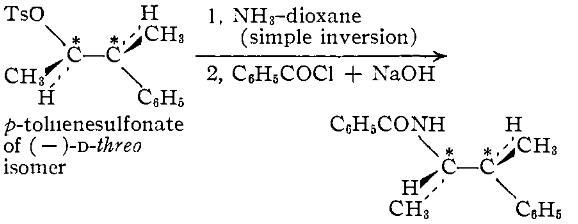
$CH_3\text{—}\overset{\overset{C_6H_5}{\vert}}{CH}\text{—}\overset{\vert}{CH}\text{—}CH_3$	°C. or n^{25}D	$[\alpha]^{24-25}$D	Molecular formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
L-(+)-*threo*-Amine[a]	1.5143	+41.23[b]	$C_{10}H_{15}N$	80.48	80.35	10.14	10.42
D-(−)-*threo*-Amine[a]	1.5143	−42.29[b]	$C_{10}H_{15}N$	80.48	80.23	10.14	10.33
L-(+)-*erythro*-Amine[a]	1.5159	+ 9.01[b]	$C_{10}H_{15}N$	80.48	80.58	10.14	10.38
(±)-*threo*-Benzamide	111.1–111.8	......	$C_{17}H_{19}NO$	80.59	80.41	7.56	7.57
(±)-*erythro*-Benzamide	117.0–117.3	......	$C_{17}H_{19}NO$	80.59	80.34	7.56	7.54
L-(−)-*threo*-Benzamide	141.2–141.5	−19.5[c]	$C_{17}H_{19}NO$	80.59	80.51	7.56	7.63
D-(+)-*threo*-Benzamide	141.2–141.5	+19.4[c]	$C_{17}H_{19}NO$	80.59	80.78	7.56	7.79
L(+)-*erythro*-Benzamide	138.4–138.8	+41.0[c,d]	$C_{17}H_{19}NO$	80.59	80.51	7.56	7.57
D-(−)-*erythro*-Benzamide	138.5–139	−39.8[c]	$C_{17}H_{19}NO$	80.59	80.60	7.56	7.75
(±)-*erythro*-Amine-HCl	217.0–217.3	......	$C_{10}H_{16}NCl$	64.66	64.64	8.68	8.71
(±)-*threo*-Amine-benzoate	120.3–120.8	......	$C_{17}H_{21}O_2N$	75.23	75.34	7.82	7.87
(±)-*threo*-Dimethylamine	1.5027	......	$C_{12}H_{19}N$	81.28	81.23	10.82	10.90
(±)-*erythro*-Dimethylamine	1.4988	......	$C_{12}H_{19}N$	81.23	81.14	10.82	10.80

[a] For (±)-*threo*-amine, n^{25}D 1.5142; for (±)-*erythro*-amine, n^{25}D 1.5160. [b] $\alpha^{24-25}_{\text{obsd.}}$D, l = 1 dm., neat. [c] C 10% $CHCl_3$. [d] With C 2% $CHCl_3$, $[\alpha]^{24}$D +46.6.°



p-toluenesulfonate of (+)-L-*erythro* isomer

(−)-benzamide of L-*threo*-I
$[\alpha]^{24}$D −19.3° (c 10% $CHCl_3$)
m.p. 141–141.5°

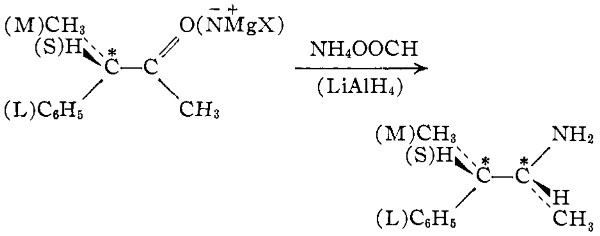


p-toluenesulfonate of (−)-D-*threo* isomer

(−)-benzamide of D-*erythro*-I
$[\alpha]^{24}$D −46.4° (c 3% $CHCl_3$)
−39.8° (c 10% $CHCl_3$)
m.p. 138.5–139°

That essentially optically pure benzamides (and hence the amines from which the amides were made) were obtained is demonstrated by the relationships between their rotations and melting points and those reported in Table I for the same compounds prepared by direct resolution. The fact that optically pure amines were produced in these substitution reactions strongly supports the thesis that the reactions occurred with simple inversion (bimolecular reaction involving ammonia and sulfonate ester). Had phenyl participation in the ammonolysis reactions played a role in the mechanism (as happens in acetolysis[8a,10] of the same compound), the *threo-p*-toluenesulfonate would have given racemic *threo*-amine (I). The relatively greater nucleophilic character of ammonia as compared to acetic acid must account for the difference in mechanism of the reactions of these sulfonate esters with the two types of solvents. The identity of each isomeric benzamide was confirmed by: (1) suitable mixed melting point determinations between the same compounds prepared by different routes; (2) preparation of racemic compounds by mixing equal amounts of an isomer prepared by one route with its enantiomer prepared by the other, and determination of the melting point of this racemate and its mixed melting point with the appropriate nonresolved racemate (see Experimental).

The Rule of Steric Control of Asymmetric Induction as Applied to the Synthesis of the 2-Amino-3-phenylbutane System.—The two syntheses of the 2-amino-3-phenylbutane system (Leuckart reaction and action of lithium aluminum hydride on the imine–magnesium salt) allow two new tests of the rule of steric control of asymmetric induction to be made since the products are kinetically controlled, and the asymmetric carbons of the starting materials carry three groups that differ considerably in bulk. Thus this rule would predict that the *threo* should predominate over the *erythro* isomer in the two syntheses in question (see formulation). The compositions of the amine mixtures I prepared in these two reactions were determined roughly through infrared analysis (see Experimental), the ratio of *threo*/*erythro* isomer being about 2 for the Leuckart reaction, and about 1.9 for the lithium aluminum hydride reduction of the imine salt. The above value of the ratio for the Leuckart product was consistent with the data obtained from the fractional distillation of this material (see Experimental).



threo isomer

The Leuckart reaction represents the first case in which the stereochemical course of the reaction is that predicted by this rule and in which the reagent adding to the carbonyl group does not involve a metal capable of coördinating with the carbonyl function. On the other hand, the imine salt reduction with lithium aluminum hydride is analo-

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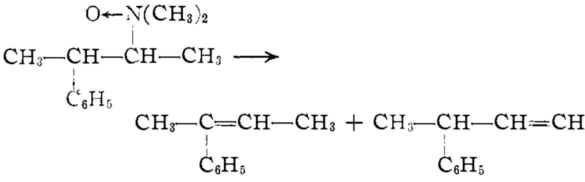
(10) D. J. Cram, THIS JOURNAL, **74**, 2129 (1952).

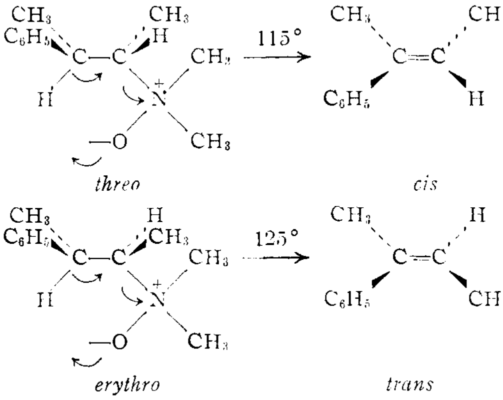
gous to the reduction of the corresponding ketone with the same reagent, and the stereochemical results are very similar.[1a]

The Stereochemical Direction of the Amine Oxide Elimination Reaction.—The *threo* and *erythro* racemates of I were converted to the corresponding N,N-dimethylamine oxides, and these substances were submitted to the pyrolytic elimination reaction.[2a] In both transformations, three olefinic products were obtained, *cis*-2-phenyl-2-butene, *trans*-2-phenyl-2-butene and 3-phenyl-1-butene, the composition of each mixture being established through the infrared analysis scheme developed earlier[11] (see Experimental for details). The formulations summarize the results obtained, the two sets of numbers representing two analyses of each mixture (different wave lengths were employed). Each diastereomer produced the same amount of unconjugated olefin, which made up only 7% of the total olefin obtained. In the *threo* series, *cis*- predominated over *trans*-2-phenyl-2-butene by a factor of from 400 to 900, whereas in the *erythro* series, *trans*-predominated over *cis*-olefin by a factor of from 20 to 40. These results make it clear that the Cope transformation belongs to the family of pyrolytic elimination reactions which assume a predominantly *cis* steric course.[12] The results indicate a more stereospecific course as well as a greater tendency for conjugated olefin to form than in the Chugaev reaction in the same system.[12b] In the latter reaction, about 40% of the olefinic product was unconjugated olefin, the ratio of *cis* to *trans* elimination being 3/1 in the *threo* and 9/1 in the *erythro* series. Although kinetic measurements were not made, for both the Chugaev and amine oxide transformations the *threo* underwent reaction more readily than the *erythro* isomer. This observation correlates with the greater steric repulsions associated with eclipsing a phenyl–methyl and methyl–hydrogen in going to *trans*-2-phenyl-2-butene as compared to eclipsing phenyl–hydrogen and methyl–methyl in going to *cis*-2-phenyl-2-butene. Furthermore, in the amine oxide reaction, the *threo* system that goes to the more thermodynamically stable *cis*-olefin is markedly the more stereospecific of the transformations of the two diastereomers, these results contrasting with those obtained in the Chugaev reaction (see above). This last fact, coupled with the greater tendency of the amine oxide reaction to give conjugated olefin, suggests that the transition state involves more double-bond character in the amine oxide than in the Chugaev reaction.



$$CH_3-\underset{\underset{C_6H_5}{|}}{CH}-\overset{\overset{O\leftarrow N(CH_3)_2}{|}}{CH}-CH_3 \longrightarrow CH_3-\underset{\underset{C_6H_5}{|}}{C}=CH-CH_3 + CH_3-\underset{\underset{C_6H_5}{|}}{CH}-CH=CH_2$$

		% *cis*	% *trans*	% unconjugated
threo	⟶	94(93)	0.1(0.2)	7(7)
erythro	⟶	4(2)	89(90)	7(8)



Experimental

2-Amino-3-phenylbutane (I) by the Leuckart Reaction.[13]—From 176 g. of 90% aqueous formic acid, 100 ml. of ice-water, 210 g. of ammonium hydroxide (d_4 0.90) and 102 g. of racemic 3-phenyl-2-butanone[8a] ($n^{25}D$ 1.5066) was obtained crude product which was distilled at 33 mm. to give 83 g. of 2-amino-3-phenylbutane, b.p. 115–119°, $n^{25}D$ 1.5149. This mixture was submitted directly to infrared analysis (see later section). This material was subjected to fractional distillation through an efficient column (70 plates at highest efficiency) to give the following fractions (100 mm.): first fraction, 50.5 g., b.p. 145.0–146.0°, $n^{25}D$ 1.5137–1.5147; second fraction, 23.4 g., b.p. 146.0–146.6°, $n^{25}D$ 1.5147–1.5161. A total of 0.6 g. of forerun and 4.5 g. of material held in the column was discarded.

Separation of the Racemates of 2-Amino-3-phenylbutane (I).—To 41.4 g. of benzoic acid dissolved in 200 ml. of ethyl acetate was added 50.5 g. of 2-amino-3-phenylbutane (first cut from above distillation). The crystalline material that separated was recrystallized twice from ethyl acetate to give 46.9 g. of *d,l-threo*-N-(3-phenyl-2-butyl)-ammonium benzoate, m.p. 120.3–120.8°.

The ethyl acetate filtrates were combined, the solvent was evaporated through a short column, and the oily residue was suspended in 100 ml. of water. An excess of 5 *N* aqueous sodium hydroxide was added, and the mixture was extracted with ether. The ether extracts were combined, washed with 0.1 *N* aqueous sodium hydroxide, dried with potassium carbonate and the ether was evaporated through a short column. Distillation of the colorless residue gave 16.7 g. of distillate (2-amino-3-phenylbutane), $n^{25}D$ 1.5148, and 21.3 g. of a white solid residue, m.p. 87–107°. A small sample of this solid was recrystallized eight times from chloroform–pentane to give what is probably either *threo*- or *erythro*-3-phenyl-2-acetamidobutane (formed by amide-ester interchange with solvent), m.p. 146.2–146.5°.

Anal. Calcd. for $C_{12}H_{17}ON$: C, 75.33; H, 8.97. Found: C, 75.49; H, 9.06.

The bulk of the above solid was heated under gentle reflux for five weeks with 200 ml. of 12 *N* hydrochloric acid. The solution was made strongly basic with 10 *N* aqueous sodium hydroxide, and the amine was extracted with ether. Evaporation of the ether and distillation of the residue provided 14.4 g. of 2-amino-3-phenylbutane, $n^{25}D$ 1.5147. The recovered amine in these experiments was again submitted to careful fractional distillation and the cycle repeated.

To 250 ml. of dry toluene was added 23.4 g. of racemic 2-amino-3-phenylbutane (fraction 2 of the original fractional distillation, predominantly *erythro* material), and dry hydrogen chloride gas was bubbled into the resulting solution for 2 hours. The mixture was then stirred at room temperature

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[11] D. J. Cram, THIS JOURNAL, **74**, 2137 (1952).

[12] For the Chugaev reaction, see (a) W. Hückel, W. Tappe and G. Legutke, *Ann.*, **543**, 191 (1940); (b) D. J. Cram, THIS JOURNAL, **71**, 3883 (1949) and ref. 1a; (c) D. H. R. Barton, *J. Chem. Soc.*, 2174 (1949); (d) D. H. R. Barton and W. J. Rosenfelder, *ibid.*, 2459 (1949); (e) D. H. R. Barton, A. J. Head and R. J. Williams, *ibid.*, 453 (1952), and 1715 (1953); (f) E. R. Alexander and A. Mudrak, THIS JOURNAL, **72**, 1810, 3194 (1950), and **73**, 59 (1951). For the ester pyrolysis reaction see ref. 12d, 12f; (g) R. T. Arnold, G. G. Smith and R. M. Dodson, *J. Org. Chem.*, **15**, 1256 (1950); (h) N. L. McNivan and J. Read, *J. Chem. Soc.*, 2067 (1952). For halide pyrolyses, see ref. 12e.

[13] This preparation simulates that of F. S. Crossley and M. L. Moore, *J. Org. Chem.*, **9**, 529 (1944).

for 18 hours, the solid that separated was collected and recrystallized from a 70% benzene-25% chloroform-5% methanol solution to give 9.7 g. of first crop of hydrochloride of *d,l-erythro*-I, m.p. 218.1–218.5°. A second crop of 7.9 g. of salt was obtained from the filtrates, m.p. 218.0–218.5°.

The solvent of the filtrates was evaporated through a short column, the oily residue was dissolved in water and an excess of 5 *N* aqueous sodium hydroxide was added. The resulting mixture was extracted with ether, the ether layer was washed with dilute alkali, dried with potassium carbonate and evaporated through a short column. Distillation of the residue gave 9.1 g. of recovered amine ($n^{25}\mathrm{D}$ 1.5149) which was again submitted to careful fractional distillation, and the cycle was repeated.

Conversion of Various Amine Salts to the Respective Amines.—The procedure will be illustrated by the conversion of *d,l-threo*-N-(3-phenyl-2-butyl)-ammonium benzoate (m.p. 120.3–120.8°) to *d,l-threo*-2-amino-3-phenylbutane. To 180 g. of the amine salt dissolved in 1 l. of water was added 100 ml. of 10 *N* sodium hydroxide solution. The resulting mixture was extracted with ether, the ether solution was washed with 0.1 *N* aqueous sodium hydroxide and dried with anhydrous potassium carbonate. The solvent was evaporated through a short column, and the residue was distilled through a short-path still at 30 mm. of pressure to give 98.2 g. of colorless *d,l-threo*-I, $n^{25}\mathrm{D}$ 1.5142. In the conversions of various salts to amines the yields ranged from 95–98%.

Conversion of Various Amines to Their Respective Benzamides.—A mixture of 2.0 g. of amine, 10 ml. of 8 *N* aqueous sodium hydroxide, 10 ml. of water and 2.0 g. of benzoyl chloride was shaken for 5 minutes and cooled to 0°. The solid that separated was collected, washed with water, dried and recrystallized from chloroform–pentane to give the benzamide derivative in from 95–98% yield (see Table I for physical properties).

Preparation of 2-Amino-3-phenylbutane by the Reductive Amination Reaction.[14]—To 350 ml. of absolute ethanol containing 17% by weight of dry ammonia was added 130 g. of 3-phenyl-2-butanone[8a] ($n^{25}\mathrm{D}$ 1.5067, b.p. 144–145° (94 mm.)) and 47 g. of recently prepared Raney nickel catalyst, together with about 50 ml. of absolute ethanol. The mixture was placed in a high-pressure hydrogenation bomb, hydrogen was introduced to a pressure of 500 p.s.i., and the bomb was rocked for 24 hours. The hydrogen pressure was then increased to 1000 p.s.i. and kept there until hydrogen uptake ceased. The mixture was then filtered, and the filtrate was warmed to 50° for 1 hour to remove some of the excess ammonia. The ethanolic solution was poured into 2 l. of water, the resulting mixture being extracted with ether. The ether layer was extracted with excess 1 *N* hydrochloric acid, dried and the ether was evaporated. The residue was flash-distilled to give 70 g. of 3-phenyl-2-butanol,[8a] b.p. 129–135° (19 mm.).

The hydrochloric acid extract was made basic with excess 18 *N* aqueous sodium hydroxide, and the resulting mixture was extracted with ether. The ether layer was washed with 0.1 *N* aqueous sodium hydroxide and dried with potassium carbonate. The ether was evaporated through a short column, and the residue was distilled at 20 mm. (b.p. 102–105°) to give 47 g. of 2-amino-3-phenylbutane, $n^{25}\mathrm{D}$ 1.5153. Attempts to isolate either the benzoic acid or hydrochloric acid salts of the *threo*- and *erythro*-amine (I) demonstrated the material to be a mixture of racemates in which neither isomer markedly predominated.

Preparation of 2-Amino-3-phenylbutane from α-Phenylpropionitrile.—To a Grignard reagent (prepared from 24 g. of magnesium and excess gaseous methyl bromide in 300 ml. of dry ether) was added 50 g. of α-phenylpropionitrile[15] ($n^{25}\mathrm{D}$ 1.5094), and the resulting mixture was held at reflux temperature under a positive pressure of pure nitrogen for 144 hours. Lithium aluminum hydride (14.5 g.) was then added in portions over a period of 6 hours. The resulting mixture was heated at reflux for 20 hours, the excess hydride and Grignard reagents were decomposed with ethyl acetate, and excess 6 *N* hydrochloric acid was added to decompose the complexes. The ether was evaporated, and the resulting mixture was steam-distilled until the distillate contained only one phase, 14.76 g. of colorless neutral oil ($n^{25}\mathrm{D}$ 1.5200) being obtained in the usual way from the distillate. The reaction mixture was then made strongly basic with 10% aqueous sodium hydroxide and again subjected to steam-distillation until no more organic material distilled. The distillate was extracted with ether, the ether layer was dried over potassium carbonate and the solvent was evaporated through a short column. Flash-distillation of the residue at 20 mm. gave 11.74 g. of the amine (I) as a colorless oil, $n^{25}\mathrm{D}$ 1.5187. Fractional distillation through an efficient column gave material, b.p. 140.7–141.4° (84 mm.), $n^{25}\mathrm{D}$ 1.5155. This material was employed in the following infrared analysis for the diastereomers of 2-amino-3-phenylbutane.

Infrared Analysis of Diastereomeric 2-Amino-3-phenylbutanes (I).—Determination of the infrared spectra of the two pure racemates of I revealed four wave lengths suitable for analyzing mixtures of these two substances (see Table II). The optical densities of the diastereomeric mixtures of I from the Leuckart and lithium aluminum hydride–imine reactions were then determined at these wave lengths, along with those of the pure isomers and known mixtures of the pure isomers. The compositions of the unknown mixtures were then calculated by solving two independent sets of simultaneous equations in two unknowns, and correcting the values obtained for deviations from Beer's law. The magnitude of these deviations was revealed by comparing the calculated and known values of the synthetic mixtures of diastereomers. Table II records the relevant data.

TABLE II

INFRARED ANALYSIS OF DIASTEREOMERIC 2-AMINO-3-PHENYLBUTANE[a]

Composition of amine being analyzed, % *threo*	*erythro*	Optical density[b] at λ in μ (slit width in mm.) 7.49 (0.700)	8.60 (0.937)	8.82 (0.997)	9.04 (1.05)
100	0	0.550	0.336	0.855	0.352
0	100	.375	.675	.423	.733
66.0	34.0	.498	.472	.771	.509
35.4	64.6	.450	.564	.589	.612
Amine from Leuckart		.499	.450	.709	.490
Amine from imine		.471	.420	.638	.479

[a] Beckman infrared spectrophotometer, IR2T, NaCl prism and cells. [b] Liquid films, 0.10 mm. thick.

Resolution of Racemic *threo*-2-Amino-3-phenylbutane (I).—To 98.2 g. of pure *threo*-I ($n^{25}\mathrm{D}$ 1.5142, prepared from 180 g. of benzoate salt, m.p. 120–121°) was added a solution of 44.6 g. of *l*-malic acid in 300 ml. of 95% ethanol. Four recrystallizations of the salt that separated from ethanol gave 17.53 g. of small white plates (double malate salt), $[\alpha]^{25}\mathrm{D}$ −30.6° (H_2O, *c* 1%). This salt was converted to D-(−)-*threo*-I (see Table I) by the usual procedure (see above). A small sample of this amine was converted to the D-(+)-*threo*-benzamide (see Table I) by the usual procedure (see above).

The amine from the filtrates was recovered and distilled to give 73.3 g. of partially resolved L-(+)-*threo*-I, $\alpha^{24}\mathrm{D}$ +6.42° (*l* = 1 dm., neat).

This amine, 21.65 g., was mixed with 21.82 g. of *d*-tartaric acid, and the resulting salt was crystallized and recrystallized nine times from 95% ethanol to give 1.18 g. of this acid salt. This material was converted to L-(+)-*threo*-I (see Table I) by the usual procedure (see above). A sample of this material was converted to the L-(−)-*threo*-benzamide (see Table I) by the usual procedure (see above).

Resolution of Racemic *erythro*-2-Amino-3-phenylbutane (I).—To 15.3 g. of *d*-tartaric acid dissolved in 300 ml. of water was added 15.2 g. of *d,l-erythro*-I ($n^{25}\mathrm{D}$ 1.5160, prepared by hydrolysis of 19.0 g. of the hydrochloride salt, m.p. 217.0–217.3°). The mixture was heated until it became homogeneous, and was then cooled slowly to room temperature. Three recrystallizations of the resulting solid from water provided pure material (12.42 g. of white needles). In other runs as many as ten recrystallizations were necessary. The progress of the purification was followed by conversions of small samples of the salt to the corresponding benzamide in almost quantitative yield, the melting point and rotation of this derivative providing good

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(14) Preparation patterned after that of L. Haskelberg, ref. 4.

(15) Prepared by dehydration of hydratropaldoxime, Ph.D. Thesis of C. E. Burr presented to Department of Chemistry of U.C.L.A., 1952.

criteria for the optical purity of the salt. The acid tartrate salt of the amine was converted in the usual way (see above) to L-(+)-*erythro*-I (see Table I), a small sample of which was converted to L-(+)-*erythro*-benzamide (see Table I) in the usual way (see above procedure). Attempts to prepare D-(−)-*erythro*-I in an optically pure state using a variety of salts of the amine enriched in this enantiomer failed. The benzamide of this isomer was prepared by another route (see next section).

Determination of the Configurations of the Isomeric 2-Amino-3-phenylbutanes (I).—The following procedure was employed for converting L-*erythro*-3-phenyl-2-butyl *p*-toluenesulfonate into L-*threo*-2-benzamido-3-phenylbutane on one hand, and D-*threo*-3-phenyl-2-butyl *p*-toluenesulfonate into D-*erythro*-2-benzamide-3-phenylbutane on the other. The procedure for the former conversion is illustrated. To a thick-walled tube containing 10 ml. of purified dioxane in which was dissolved 1.9 g. of *p*-toluenesulfonate ester (m.p. 36–37°, $[\alpha]^{24}\mathrm{D}$ −17.4°, C_6H_6, *c* 5%) was added (−78°) 10 ml. of liquid ammonia. The tube was sealed and allowed to warm to room temperature. The resulting solution was heated at 40° for 24 hours and at 75° for 24 hours. The tube was cooled to −78°, opened and allowed to slowly warm to room temperature (the ammonia evaporated). The solution was shaken with a mixture of water and pure pentane, the pentane layer was washed with water and extracted with aqueous 0.1 *N* hydrochloric acid. The extracts were washed with pentane, made strongly basic with sodium hydroxide solution and extracted with pure pentane. The pentane layer was dried, the solvent was evaporated through a short column, and the residual oil was shaken immediately with 1 g. of benzoyl chloride and 2 ml. of 10 *N* sodium hydroxide solution. The solid that separated was collected, washed with water, dried and recrystallized twice from ether to give 0.155 g. of fine white needles of L-(−)-*threo*-benzamide, m.p. 141–141.5°, $[\alpha]^{24}\mathrm{D}$ −19.3° (*c* 10%, $CHCl_3$). Only a trace of material was found in the filtrates from the crystallizations.

The m.p. of this benzamide was undepressed by admixture with the same material prepared by resolving racemic *threo*-I through the acid tartrate salt with subsequent conversion of the optically pure amine to its benzamide (see above). A mixture of 9 mg. of this benzamide and 9 mg. of the enantiomorphic benzamide (prepared by resolution of *threo*-I through the *l*-malate salt with subsequent conversion to the amide) was recrystallized from chloroform–pentane to give racemic material, m.p. 111.1–111.8°, undepressed by admixture with benzamide prepared from the *threo*-benzoate salt.

From 1.70 g. of D-*threo*-3-phenyl-2-butyl *p*-toluenesulfonate (m.p. 62–63° $[\alpha]^{25}\mathrm{D}$ −16.89°, *c* 5%, C_6H_6) was obtained 0.420 g. of D-*erythro*-2-benzamido-3-phenylbutane as fine white needles, m.p. 138.5–139° (ether), $[\alpha]^{24}\mathrm{D}$ −46.4° (*c* 3%, $CHCl_3$), $[\alpha]^{24}\mathrm{D}$ −39.8 (*c* 10%, $CHCl_3$). This material depressed the melting point of the above L-(−)-*threo*-benzamide to 103–122°. A mixture of 5 mg. of this material and 5 mg. of L-*erythro*-2-benzamido-3-phenylbutane (prepared by resolution of *erythro*-I through the acid tartrate salt with subsequent conversion of the active amine to the benzamide) was recrystallized once from ether to give racemic *erythro*-I-benzamide, m.p. 117.5–118.2°, undepressed by admixture with material prepared from the hydrochloride salt of I.

Preparation of *threo*- and *erythro*-2-(N,N-Dimethylamino)-3-phenylbutane.—The procedure[16] is illustrated with the *erythro* isomer. To 2.38 g. of racemic *erythro*-2-amino-3-phenylbutane ($n^{25}\mathrm{D}$ 1.5160) was added 12 ml. of 90% formic acid and 12 ml. of 35% aqueous formaldehyde. The resulting solution was heated at 95° for 12 hours and then heated at gentle reflux for 4 hours. The solution was made strongly basic with 6 *N* potassium hydroxide, and the mixture was extracted with pure pentane. The pentane layer was washed with 1 *N* aqueous potassium hydroxide, and extracted with excess 1 *N* hydrochloric acid solution. The extracts were washed with pure pentane, made strongly basic with 6 *N* aqueous potassium hydroxide, and the resulting mixture was extracted with pure pentane. The extracts were dried over potassium carbonate, the solvent was evaporated through a short column and the residual oil was distilled at 35 mm. to give a colorless oil which was again distilled (26 mm.) to give 2.82 g. of the tertiary amine (*erythro* isomer), $n^{25}\mathrm{D}$ 1.4988.

From 7.0 g. of racemic-*threo*-N-(3-phenyl-2-butyl)-ammonium benzoate (m.p. 120–121°) was obtained *threo*-I, which was converted to its dimethyl derivative by the above procedure, 3.38 g. of product ($n^{25}\mathrm{D}$ 1.5027) being obtained.

Preparation and Pyrolysis of the Amine Oxides of *threo*- and *erythro*-2-(N,N-Dimethylamino)-3-phenylbutane.—The procedure is an adaptation of those recorded in ref. 2, and will be illustrated as applied to the *threo* isomer. To 50 ml. of 30% hydrogen peroxide was added 15.00 g. of racemic *threo*-2-(N,N-dimethylamino)-3-phenylbutane, and the resulting mixture was stirred at room temperature until it became homogeneous (77 hours). The excess hydrogen peroxide was decomposed with an extract of catalase (prepared from avocado fruit), the solution was filtered and lyophilized at 1 mm. The resulting sirup was heated at 2 mm. at 110–115° (bath temperature) until the decomposition was complete (20 minutes), the mixture of olefins and dimethylhydroxylamine that distilled being collected in a trap held at −78°. This distillate was shaken with a mixture of water and pure pentane, and the pentane layer was washed with water, with dilute hydrochloric acid and with dilute aqueous sodium hydroxide. The pentane layer was dried, the solvent was evaporated through a short column and the residue was twice flash-distilled at 20 mm. to give 5.90 g. of colorless olefinic mixture, $n^{25}\mathrm{D}$ 1.5372. This material was submitted directly to infrared analysis (see next section).

By the same procedure, from 2.24 g. of *erythro*-2-(N,N-dimethylamino)-phenylbutane was obtained 0.60 g. of olefinic mixture, $n^{25}\mathrm{D}$ 1.5192. The temperature of the pyrolysis had to be raised to 120–125° before the reaction proceeded at a convenient rate (10 minutes for completion).

Infrared Analysis of Olefinic Mixtures from Amine Oxide Pyrolyses.—This analysis is patterned after that developed previously for mixtures of 2-phenyl-1-butene, *cis*- and *trans*-2-phenyl-2-butene and 3-phenyl-1-butene,[11] although in the present case only the last three olefins were present, and the analyses were simplified accordingly. The four most suitable wave lengths for analysis of the three components were utilized, and are recorded in Table III. The optical densities of the three pure olefins and of the two unknown mixtures were determined. Calculations (based on Beer's law) were then made of the compositions of the unknown mixtures. From the results, synthetic mixtures of the three olefins were prepared whose compositions approximate those of the unknown mixtures. The optical densities of the pure

TABLE III

INFRARED ANALYSIS OF MIXTURES OF *cis*-2-PHENYL-2-BUTENE (II), *trans*-2-PHENYL-2-BUTENE (III) AND 3-PHENYL-1-BUTENE (IV)[a]

% Compn. of olefinic mixture II[c]	III[d]	IV[e]	Optical density[b] at λ in μ (slit width in mm.) 9.97 (1.06)	10.88 (1.30)	12.02 (1.64)	12.16 (1.71)
100	0	0	0.198	0.162	0.459	0.114
0	100	0	.076	0.362	.391	.676
0	0	100	.588	1.40	.52	.050
unknown from *erythro*-oxide[f]			.123	0.449	.365	.630
4.0	89.4	6.7[g]	.121	0.433	.366	.625
h			9.97[i] (0.664)[j]	10.88[i] (0.815)[j]	11.98[i] (1.07)[j]	12.16[i] (1.12)[j]
100	0	0	0.200	0.132	0.500	0.104
0	100	0	.074	0.361	.242	.655
0	0	100	.569	1.42	.051	.044
unknown from *threo*-oxide[k]			.227	0.240	.472	.103
93.5	0.4	6.1[l]	.222	.223	.470	.103

[a] Beckman infrared spectrophotometer, IR2T, NaCl prism and cells. [b] Liquid films, 0.03 mm. thick. [c] $n^{25}\mathrm{D}$ 1.5402. [d] $n^{25}\mathrm{D}$ 1.5193. [e] $n^{25}\mathrm{D}$ 1.5055. [f] $n^{25}\mathrm{D}$ 1.5192. [g] Known mixture, $n^{25}\mathrm{D}$ 1.5193. [h] Mixtures were analyzed at different times and at slightly different wave lengths and slit widths. [i] λ in μ. [j] Slit widths in mm. [k] $n^{25}\mathrm{D}$ 1.5372. [l] Known mixture, $n^{25}\mathrm{D}$ 1.5371.

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(16) Procedure is adapted from that recorded by M. L. Moore, "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 307.

components, of the known and unknown mixtures were again taken, and the compositions of the known and unknown mixtures calculated by solving two sets of three simultaneous equations in three unknowns. The two equations based on the optical densities at $\lambda = 11.98$ and 12.16 μ were used in each set of solutions, the optical densities at 9.97 μ being used in one set of solutions and at 10.88 μ in the other. The compositions of the unknown mixtures were then corrected to those of the known mixtures for deviations from Beer's law. The pertinent data are set forth in Table III.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Stereoisomeric 1,2-Bis-(arylmercapto)-ethenes and Corresponding Sulfones[1]

BY WILLIAM E. TRUCE AND ROBERT J. MCMANIMIE

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The stereoisomeric 1,2-bis-(phenylmercapto)-ethenes and 1,2-bis-(*p*-tolylmercapto)-ethenes were prepared and related to the corresponding *cis*- and *trans*-sulfones by a mild non-isomerizing oxidation. In the phenyl series, assignment of *cis* and *trans* structures on the basis of the isomers' solubilities and melting points is consistent for the sulfides and sulfones. However, in the *p*-tolyl series the sulfides exhibit anomalous melting point and solubility behavior, in that the low melting, more soluble isomer is related structurally to the high melting, more insoluble sulfone. Infrared spectra and dipole moments of the 1,2-bis-(*p*-tolylmercapto)-ethenes and 1,2-bis-(*p*-tolylsulfonyl)-ethenes, respectively, confirm the empirical assignments of structure.

In an earlier paper[2] the geometrical isomers of 1,2-bis-(*p*-tolylsulfonyl)-ethene were assigned *cis* and *trans* structures by the empirical criteria that a *trans* isomer is usually the higher melting, more insoluble and less thermally-labile form.[3] Both isomers were prepared by the action, at reflux temperature, of 30% hydrogen peroxide and glacial acetic acid on the single known[4] 1,2-bis-(*p*-tolylmercapto)-ethene. In the present work the isomeric 1,2-bis-(*p*-tolylmercapto)-ethene was prepared by a partial thermal isomerization of the known isomer, and both compounds were oxidized under conditions such that each sulfide was related structurally to one of the isomeric 1,2-bis-(*p*-tolylsulfonyl)-ethenes (Fig. 1). It will be noted that the low melting (and more soluble) sulfide II is related structurally to the high melting (and more insoluble) sulfone IV. These results cast some doubt on the empirical assignments of *cis* and *trans* structures to the sulfones, for assignment of structures to the sulfides on the same basis would result in a "*cis*" sulfide being related geometrically to a "*trans*" sulfone. However, with the 1,2-bis-(phenylmercapto)-ethenes and the corresponding sulfones (Fig. 1), a regular relationship exists in that the higher melting and more insoluble sulfide VI is related to the more insoluble and higher melting sulfone VIII.

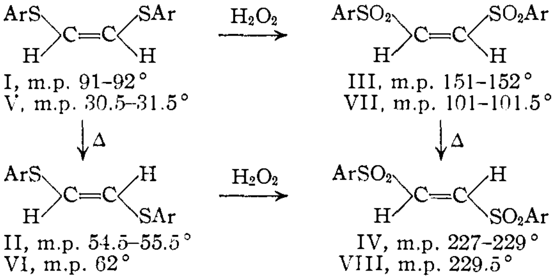

Fig. 1.—Relationships among the 1,2-bis-(arylmercapto)-ethenes and the corresponding sulfones. Ar is *p*-tolyl for I, II, III, IV and phenyl for V, VI, VII, VIII.

Conclusive confirmation of the original structure assignments for *cis*- and *trans*-1,2-bis-(*p*-tolysulfonyl)-ethenes and the corresponding sulfides are the dipole moments and infrared spectra, respectively, of these compounds. The lower melting sulfone has the higher dipole moment, indicative of a *cis* configuration. Furthermore, the lower melting sulfide (corresponding to the higher melting sulfone) has an absorption band at 10.88 μ. Although the *trans*-double bond absorption occurs in straight chain olefins at 10.36 μ, this shift (0.5 μ) is not infrequent when certain polar groups are held by the double bond.[5]

Chemical methods of verifying the assignments of the *cis* and *trans* structures shown in Fig. 1 were attempted. Although the results were inconclusive, they are of some interest. Since the elimination of hydrogen chloride occurs much more readily from *cis*-dichloroethylene than from *trans*-dichloroethylene,[6] it was thought that a similar difference might exist for the reaction of the 1,2-bis-(*p*-tolysulfonyl)-ethenes with base. It had been reported that the 1,2-bis-(*p*-tolysulfonyl)-ethene melting at 149–150° was stable to base,[4] which indicated that the low melting, more soluble isomer might be the *trans* form. However, both isomers react with base; the low melting isomer appears to react faster. But this result is not necessarily consistent with the empirical assignment of configuration, since the initial step in the reaction was probably a nucleophilic addition to the olefinic bond, and since the poor solubility of the sulfones resulted in heterogeneous reaction mixtures. To obviate the first of these complications, the adducts of the 1,2-bis-(*p*-tolylsulfonyl)-ethenes with cyclopentadiene were considered. Since the Diels–Alder reaction proceeds by a "*cis*" addition, the arrangements in space of the sulfonyl groups should be essentially retained in the adducts. If the original structure assignments

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[1] Presented at the Kansas City Meeting of the American Chemical Society, March 24, 1954.

[2] W. E. Truce and R. J. McManimie, THIS JOURNAL, **75**, 1672 (1953).

[3] (a) H. Gilman, "Organic Chemistry," Vol. I, 2nd Edition, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 449–453; (b) L. Crombie, *Quarterly Revs.*, **6**, 101 (1952).

[4] E. Fromm and E. Seibert, *Ber.*, **55B**, 1014 (1922).

[5] J. D. Stroupe, Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy, March, 1952.

[6] S. I. Miller and R. M. Noyes, THIS JOURNAL, **74**, 629 (1952).