

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF TORONTO]

The Resolution of 2,3-Diphenylbutane

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In connection with studies in this Laboratory on the so-called "pseudoracemic" type of enantiomeric mixture, symmetrical diphenylbutane seemed to be of interest. Although preliminary examination indicated that it belonged to this category of enantiomer which shows no melting point depression on admixture, a detailed study has shown that inactive diphenylbutane forms a racemic compound.

The liquid diastereomer of *s*-diphenylbutane was first actually isolated and described in detail by Lepin¹ by coupling of Grignardized 1-bromo-1-phenylethane; his sample melted at +8°. Ott² later obtained the compound in low enantiomeric purity by a Wurtz reaction with partially resolved 1-chloro-1-phenylethane. Although some racemization occurred (*meso*-diphenylbutane was produced as well), this worker obtained the *levo* hydrocarbon from *dextro* α -phenylethyl chloride. The latter was produced from *dextro* phenylethyl alcohol. If one assumes with McKenzie and Clough³ that no inversion occurs when *dextro* rotatory phenylethyl chloride is formed from *dextro* rotatory phenylethyl alcohol, then an extrapolation of Marker's empirical rules⁴ indicates that this Wurtz reaction occurs without inversion. If on this basis *dextro* α -phenylethanol is considered the *d*-enantiomer, then *dextro* diphenylbutane must possess the *ll*-configuration. This convention will be used in the present report.

One may expect less racemization during a reaction involving tetrahedral apex replacement (direct substitution) than during one involving tetrahedral base replacement (inversion substitution). This is significant to the present report since if, in Ott's Wurtz reaction, racemization did not occur during the coupling reaction, it may then have been caused by a side reaction, rearrangement of *dd, ll*-diphenylbutane to *dl, ld*-diphenylbutane. Actually Lepin reported that *dd, ll*-diphenylbutane was isomerized, to the *meso* diastereomer during long heating.

The low yields and low optical purity do not recommend Ott's method as a source of enantiomeric diphenylbutanes. The diastereomeric 2,3-diphenylbutanes were therefore prepared from disodium diphenylethane and dimethyl sulfate^{5,6} and were rigorously purified before use. Racemic diphenylbutane contains no polar functional group, so that direct resolution would not be possible unless it might be accomplished by formation

of a coordinative compound. Attempts to form isomeric choleic acids with desoxycholic acid^{7,8} were unsuccessful. We turned therefore to the *dd, ll-p, p'*-dinitrodiphenylbutane reported previously,^{5,6} and catalytically reduced this racemate to the diamine. The *meso*-dinitrodiphenylbutane was also reduced; as might have been expected, the latter diamine was not resolvable. The *dd, ll-p, p'*-diaminodiphenylbutane, on the other hand, was resolved conveniently because the *dd(-)*-diamine formed an insoluble salt with α -bromocamphor- π -sulfonic acid, whereas the salt of camphorsulfonic acid with *ll(+)* enantiomeric diamine was less soluble than the corresponding salt of the *dd(-)* enantiomer. About twenty fractional crystallizations in each series yielded salts from which were obtained *ll(+)* diamine with specific rotation of +105° and *dd(-)* diamine with rotation of -110°, both in methanol. Both enantiomers melted at 43.5-46°. Since the *dd, ll*-mixture melted at 75-78°, it was evident that the latter was a true racemic compound. The melting point ranges are probably owing to contamination with the *meso* diamine. This could not be proved because of the difficulty in purification of the diamines. Crystallization was not feasible because the amines precipitated as oils which crystallized only after several months. Distillation seemed not to remove the *meso* isomer; the high distillation temperature of 245° did not seem to increase its quantity because of racemization.

The removal of the amino groups was effected by reduction of the corresponding diazonium salts with hypophosphorous acid. Both of the enantiomeric hydrocarbons obtained in this manner were contaminated with the high-melting *meso*-diphenylbutane. Since the *dd, ll*-racemic diphenylbutane was pure according to its time-temperature cooling curve, and since the corresponding *dd, ll-p, p'*-dinitrodiphenylbutane melted sharply after it had been freed from a contaminant which was probably the *ortho* isomer, it is believed that interconversion of *dd, ll* and *dl, ld*-diastereomers occurred during catalytic reduction. Such an isomerization would account for the melting point ranges found for the diamines.

The enantiomeric diphenylbutanes could be freed from most of the *meso* diastereomer by distillation. The specific rotation of the *dd*-isomer was -94° while that of the *ll*-1,2-diphenylbutane was +98.8° in absolute ethanol. The respective melting points of these two enantiomers were 21.4 and 20.4°. Since these melting points are higher than that of *dd, ll*-2,3-diphenylbutane

(1) A. E. Lepin, *J. Russ. Phys.-Chem. Soc.*, **44**, 1190 (1912).
(2) E. Ott, *Ber.*, **61**, 2124 (1928).
(3) A. McKenzie and G. W. Clough, *J. Chem. Soc.*, **103**, 687 (1913).
(4) R. E. Marker, *This Journal*, **58**, 976 (1936).
(5) G. F. Wright, *ibid.*, **61**, 2106 (1939). (6) G. S. Myers, H. H. Richmond and G. F. Wright, *ibid.*, **67**, 710 (1947).

(7) J. H. Adriani, *Z. physik. Chem.*, **33**, 453 (1900).
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(11.6°), this compound must not be "pseudoracemic" but, rather, a true racemic compound. The existence of this racemic compound is confirmed by the melting point-composition diagram shown in Fig. 1.

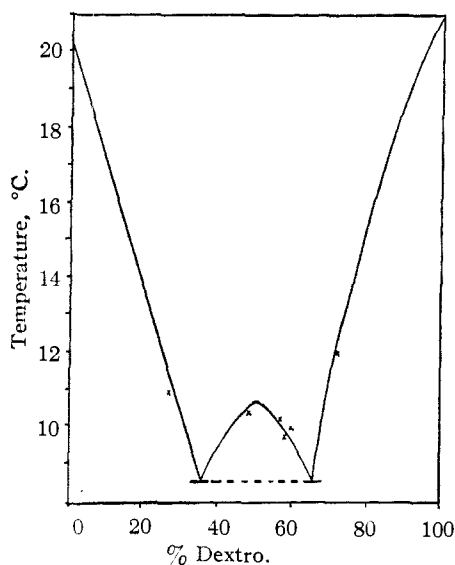


Fig. 1.—Melt curve of levo and dextro diphenylbutane.

Examination of the X-ray diffraction patterns characteristic of *ll* and *dd, ll* 2,3-diphenylbutanes reveals differences in lattice organization expected between the enantiomer and the associated racemic compound. The pattern characteristic of *meso*-2,3-diphenylbutane has also been examined, and included in Table I. Although visually-estimated relative line intensities have been included, it is suggested that they may not be too reliable. Since both the *ll* and *dd, ll* samples were liquids which had to be frozen on a Pyrex fiber, there exists the possibility that preferred orientation would alter these intensities in a manner not characteristic of the lattice arrangement of the substances.

Experimental⁹

The diphenylbutanes required for this work were prepared and separated crudely by the method reported earlier.¹ The *dd, ll* isomer melted at 2–6° and was therefore not pure. Twenty crystallizations from ethanol at –80° gave an 18% recovery of pure *dd, ll*-2,3-diphenylbutane, the time-temperature cooling curve of which showed temperature invariance at +11.6° over a fifteen-minute period.

Repeated crystallization of *meso*-diphenylbutane from boiling 95% ethanol raised the melting point to 125.5°.

Nitration of *meso*-Diphenylbutane.—The procedure previously outlined⁸ was followed to give a 61% yield of *meso-p, p'*-dinitrodiphenylbutane, m. p. 245°, but crystallization from benzene increased this melting point to 256°, or higher than the 249°, previously reported. The filtrate from which the crude *para* derivative was obtained yielded additional material melting at 130–139°, after neutralization of the acetic acid. This material (35% of theoretical of diphenylbutanes) was crystallized twice from

(9) All melting points have been corrected against known standards.

TABLE I
INTERPLANAR SPACINGS (*d*) IN DIPHENYLBUTANE

<i>d, ll</i> <i>meso</i>		<i>d, ll</i> <i>dd</i>		<i>d, ll</i>	
<i>d, Å.</i>	Rel. int.	<i>d, Å.</i>	Rel. int.	<i>d, Å.</i>	Rel. int.
8.8	0.1	8.6	0.4	8.1	0.4
		8.0	0.6	6.9	.05
				6.4	.4
5.9	0.1	5.9	1.0	5.9	.05
				5.5	.05
5.1	1.0	5.0	1.0	5.0	1.0
4.94	0.2				
4.54	.3				
4.40	.1				
4.24	.4	4.24	0.4		
4.13	.05	4.13	1.0	4.15	0.5
				4.03	.2
		3.98	0.4		
3.81	.1	3.79	.8	3.88	.4
				3.70	.4
3.55	.1	3.69	.3	3.50	.3
3.43	.3			3.41	.2
3.37	.4	3.37	.2		
3.21	.2			3.25	.05
3.04	.2	3.12	.1	3.08	.05
2.96	.3	2.94	.1	2.97	.2
				2.92	.05
		2.78	.05	2.81	.1
2.70	.1			2.72	.05
2.65	.05	2.63 ^a	.05		
2.58	.05			2.58	.05
2.55	.1	2.46	.1	2.50	.1
2.42	.1				
2.34	.1	2.36	.05		
2.13	.1	2.30	.05		
		2.27	.1	2.26	.05
				2.16	.05
2.06	.1	2.05	.1	2.05	.2
1.93	.1	1.89	.1	2.00	.1

^a This is the mean of what appears to be an unresolved doublet.

ethanol, dioxane-water and benzene to melt at 163.5°. The compound gave the analysis expected for a dinitrobutane.

Anal. Calcd. for C₁₆H₁₆N₂O₄: C, 64.0; H, 5.37. Found: C, 64.1; H, 5.54.

This compound is probably the *o, p'*-dinitro-2,3-diphenylbutane corresponding to *meso-p, p'*-dinitro-2,3-diphenylbutane. Chromic acid oxidation yielded a mixture of two acids which were separated into one melting poorly at 138° (m. p. *o*-nitrobenzoic acid 147°) and another melting at 240° (m. p. *p*-nitrobenzoic acid, 242°).

Nitration of *dd, ll*-Diphenylbutane.—The yield of *dd, ll-p, p'*-dinitro-2,3-diphenylbutane was increased to 59% of pure compound by following directions⁸ previously outlined. No solid isomer could be obtained from the remaining oil from the crystallization and the neutralized reaction liquors, although this oil (40% yield as diphenylbutane) probably contained the *ortho* isomer.

***meso-p, p'*-Diamino-2,3-diphenylbutane.**—A suspension of 5.3 g. (0.0176 mole) of *meso*-dinitrodiphenylbutane in 150 cc. of glacial acetic acid was catalytically reduced using

50 mg. of Adams platinum oxide catalyst over twenty hours until 6 molar equiv. of hydrogen was taken up. Filtration removed 1.4 g. (26%) of unchanged nitro compound. Neutralization of the filtrate with alkali precipitated 2.8 g. of the diamine, m. p. 168°, or 66% of theoretical. This was crystallized from 60 cc. of petroleum ether (b. p. 60–70°) (m. p. 171°) and then from ethanol to melt at 173°.

Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.9; H, 8.39. Found: C, 80.0; H, 8.64.

dd, ll-p, p'-Diamino-2,3-diphenylbutane.—A solution of 4.8 g. (0.015 mole) of *dd, ll*-dinitrodiphenylbutane in 100 cc. absolute ethanol was catalytically reduced using 70 mg. of Adams catalyst. After thirty minutes 0.8 mole of hydrogen had been taken up. After filtration of the catalyst, the filtrate was distilled, finally at 8 mm., to yield 3.2 g. or 88% of the theoretical amount. This oil crystallized completely after several months and melted at 75–78°.

Anal. Calcd. for $C_{16}H_{20}N_2$: C, 79.9; H, 8.39. Found: C, 79.8; H, 8.20.

dd(-)-p, p'-Diamino-2,3-diphenylbutane.—To a solution of 20.5 g. (0.086 mole) of *dd, ll*-diamine in 14.6 ml. (0.17 mole) of concentrated hydrochloric acid and 150 cc. of water was added 56.0 g. (0.17 mole) of ammonium α -bromocamphor- π -sulfonate.¹⁰ The solution was boiled, filtered and allowed to cool very slowly. Since the precipitate tended to be an oil if cooling was too rapid, a seed was added when it was available. The specific rotation of the first crystal crop was +60° in methanol. Twenty fractional crystallizations from water separated this into 10 g. of pure salt with specific rotation of +34.9° and the remainder in fractions $[\alpha]^{25}_D$ +40 to +85°. The 10-g. portion was dissolved in water, ammonia was added and the precipitate allowed to crystallize over one week. This yielded 6.0 g. of diamine, m. p. 42–43°. This was distilled at 245° (10 mm.) with nitrogen in the anti-bumping gas inlet. The distillate crystallized slowly over twelve months, $[\alpha]^{25}_D$ -110° in methanol.

A solution of 6.0 g. (0.025 mole) of this diamine in 400 cc. of ether was treated with an excess of hydrogen chloride. The hydrochloride, precipitated quantitatively, weighed 7.88 g., $[\alpha]^{25}_D$ -85.2°.

ll-(+)-p, p'-Diamino-2,3-diphenylbutane.—The resolution of the *dd, ll*-diamine with camphorsulfonic acid (Reychler's acid, m. p. 196°) was extremely unsatisfactory and erratic, we believe because diastereomeric salts of the *dd, ll* B.d A type were co-precipitated with the *ll* B.d A type which was sought. The partially resolved *ll* (+) amine which was recovered from the more soluble salt fractions remaining after the isolation of *dd*-diaminodiphenylbutane α -bromocamphor- π -sulfonate was more amenable to resolution. These combined fractions were converted by addition of ammonia to amine $[\alpha]^{25}_D$ +39.0 (methanol). A boiling solution of 13.6 g. (0.0567 mole) of this amine with 25.6 g. (0.134 mole) of Reychler's acid in 90 cc. water was cooled to yield a camphorsulfonate $[\alpha]^{25}_D$ +54.5 (methanol). This was fractionally crystallized five times to yield a final crop of salt $[\alpha]^{25}_D$ +73°, m. p. 230–235°. The amine recovered from the solution of this salt in dilute ammonia weighed 0.95 g. (14% re-

covery), $[\alpha]^{25}_D$ +106°, m. p. 43.5–46°. The hydrochloride, precipitated quantitatively from ether, would not melt up to 300°.

Neither the *dd* nor the *ll* amines were analyzed, but identification was effected by fusion of equal parts of each. The oil thus formed solidified after some hours to melt at 73–74°. A mixed melting point with the *dd, ll* racemic compound was not lowered.

dd(-)-2,3-Diphenylbutane.—A solution of 7.88 g. (0.025 mole) of *dd(-)-p, p'*-diamino-2,3-diphenylbutane dihydrochloride in 6.4 ml. (0.075 mole) of concentrated hydrochloric acid and 250 cc. of water was stirred at 0–2° while 3.45 g. (0.05 mole) of 10% aqueous sodium nitrite was added over one hour. To this solution was added 66 g. (0.75 mole) of sodium hypophosphite and 75 cc. of concentrated hydrochloric acid. After one week (negative diazonium test) at 0°, the reaction mixture was steam distilled and the distillate extracted with ether. This ether solution, washed with acid and then alkali, and dried with sodium sulfate, was distilled, first at 146° (10 mm.) to yield 3.72 g., m. p. 20°, or 71% of theoretical. Redistillation of this product at 76° (0.002 mm.) raised the melting point to 21.4°. The rotation, $[\alpha]^{25}_D$, was -94.9° (ethanol).

Anal. Calcd. for $C_{16}H_{18}$: C, 91.4; H, 8.6. Found: C, 91.0; H, 8.8.

Alternative reductions of the diazonium salt with formaldehyde or ethanol gave much lower yields of about 10%.

ll(+)-2,3-Diphenylbutane.—The diazotization and reduction was repeated with the *ll* (+) diaminodiphenylbutane to give an identical yield of material melting at 20.4°, $[\alpha]^{25}_D$ +98.8° and with elemental carbon and hydrogen values of 91.3 and 9.0, respectively. The residue remaining after each distillation of either enantiomer contained a detectable amount of *meso*-diphenylbutane, so that there is no assurance that the rotations observed are the highest ones attainable. This is undoubtedly true with respect to the melting points. The melting point of a 1:1 mixture of these *dd* and *ll* enantiomers was 10.9° while the *dd, ll*-racemic compound from which they were prepared melted sharply at 11.6°.

X-Ray Diffraction.—All patterns were determined with a "Norelco" powder camera of 11.46 cm. diameter using copper radiation with a nickel filter and a pinhole 0.25 mm. in diameter. The camera was modified so that a dry air stream passed through a trap chilled with Dry Ice-acetone mixture and thence by rubber tubing to a point directly opposite the sample so that this cold air stream (ca. 1 liter per minute) flowed over the sample, originally as liquid which wetted the outside of an etched glass thread drawn out of Pyrex No. 707. The film was paper-wrapped so that visual observation could be made of the frozen state of the specimen.

Summary

Resolution of pure *dd, ll*-2,3-diphenylbutane into *dd* and *ll* enantiomers demonstrates that the *dd, ll*-mixture crystallizes as a racemic compound melting lower than the optical antipodes.

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