roughly the translational entropy of water. The enthalpy change is also large, but favors the reverse reaction, and hence the balance gives a relatively small free-energy change.

### Experimental Section

*cis*- and *trans*-4-*t*-Butyl-1-methylcyclohexanol.—A mixture of the alcohols was prepared by the addition of methyl Grignard to 4-*t*-butylcyclohexanone.[13] A 3.0-g sample of the mixture was dissolved in hexane and chromatographed on 150 g of Merck chromatographic grade alumina. The column was developed with a hexane–benzene mixture (100 to 100%) and each fraction collected was 150 ml. Totally, 80 fractions were collected and the elution was effected with benzene. The first eluate (fractions 30 to 51) contained the *trans*-1-methyl-4-*t*-butylcyclohexanol: yield 1.2 g (40%); mp 69–70° from hexane (lit.[13] mp 71°). The second eluate (fractions 64 to 76) contained *cis*-1-methyl-4-*t*-butylcyclohexanol: yield 1.0 g (33%); mp 91–92° from petroleum ether (bp 30–60°) (lit.[13] mp 97.9°).

Equilibration of the *cis* and *trans* Isomers of 1-Methyl-4-*t*-butylcyclohexanol.—A 0.5-g sample of *trans*-enriched (1.8:1) 1-methyl-4-*t*-butylcyclohexanol was dissolved in 6 ml of dioxane containing 4 ml of 1.75 *M* aqueous perchloric acid.[14] The equilibration was carried out at 75°. Aliquots of reaction mixture were removed after 18 and 36 hr and were worked up and analyzed immediately by vpc using a column of Dow polyglycol E-20,000 on base-washed firebrick at 130° and 11 psi of helium pressure. The equilibration reaction was quenched with a large amount of ice and water and the mixture was extracted with ether. The ether layer was thoroughly washed with water and then dried over magnesium sulfate. After removal of the solvent, the liquid remaining was analyzed. The retention times of *trans*- and *cis*-1-methyl-4-*t*-butylcyclohexanol were 17 min and 24 min, respectively. The retention time of 1-methyl-4-*t*-butylcyclohexane was 3 min. The ratio of the isomeric alcohols was taken as equal to the ratio of the peak areas, as determined by the product of the band height and the half-band width. Each sample was analyzed at least four times. The equilibrium mixture contained 59% *trans* and 41% *cis* alcohol at 75°.

The equilibration data at 58 and 93° were also obtained in a similar manner and the values of $\Delta H°$ and $\Delta S°$ for the reaction *cis*-4-*t*-butyl-1-methylcyclohexanol $\rightleftharpoons$ *trans*-4-*t*-butyl-1-methylcyclohexanol were determined from the slope and intercept of a line drawn by the method of least squares through points obtained from a plot of ln $K$ against $1/T$. The values along with the probable errors (estimated by statistical methods) are $\Delta H° = -0.14 \pm 0.06$ kcal/mol and $\Delta S° = 0.3 \pm 0.18$ cal/deg mol.

The equilibrations were carried out in homogeneous solution, but in a few cases an oil suspension (olefin) appeared on the surface. In such a case, care was taken in the process of quenching so as not to get oil into the aliquot being removed.

The gas phase analysis indicated that during the prolonged heating of the reaction mixture, some undesired products were beginning to form which made the analysis inaccurate. The amount of decomposition product became significant if the period of heating was longer than twice that which was needed for equilibration. If the heating was continued beyond this time, the total percentge of alcohol decreased with respect to the increased amount of the side products, and, in addition, the ratio of the alcohols changed. The retention times for these side products were 20 and 29 min. No attempt was made to identify them, but they are believed to be ethers of *cis*- and *trans*-4-*t*-butyl-1-methylcyclohexanol with glycols which arose from decomposition of the dioxane. The results are summarized in Table I.

The temperature variation of the equilibrium between olefin (from dehydration) and *trans*-4-*t*-butyl-1-methylcyclohexanol was also measured. The vpc peak corresponding to 4-*t*-butyl-1-methylcyclohexene was collected, and the structure of the compound was assigned from the nmr (chloroform solvent) spectrum which showed a multiplet at $\tau$ 4.5 (1 H), a singlet at 8.35 (3 H) and 9.2 (9 H), and multiplets at 8.15 (4 H) and 9.0 (3 H).

In Tables I and II, the data for the calculation of entropy and enthalpy of isomerization of 4-*t*-butyl-1-methylcyclohexanol and the interconversion of *trans*-4-*t*-butyl-1-methylcyclohexanol $\rightleftharpoons$ 4-*t*-butyl-1-methylcyclohexene are tabulated.

(13) W. J. Houlihan, *J. Org. Chem.*, **27**, 3860 (1962).

(14) C. A. Bunton, K. Khaleeluddin, and D. W. Whittaker, *Tetrahedron Lett.*, 1825 (1963).

**Registry No.**—1-Methylcyclohexanol, 590-67-0; *trans*-4-*t*-butyl-1-methylcyclohexanol, 16980-55-5; *cis*-4-*t*-butyl-1-methylcyclohexanol, 16980-56-6; 4-*t*-butyl-1-methylcyclohexene, 3419-74-7.

## Synthesis of (*R*)-3-Methylpentanoic Acid

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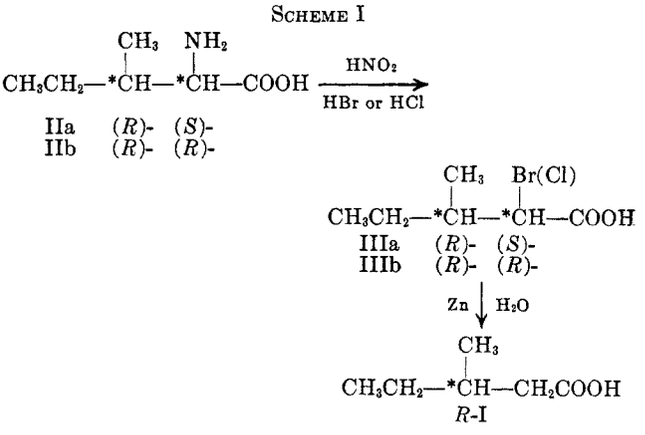
In the course of our study of optically active imidazole-containing polymers,[1] we found it necessary to obtain (*R*)-3-methylpentanoic acid (*R*-I) and (*S*)-3-methylpentanoic acid (*S*-I) in high optical purity in order to prepare the corresponding enantiomeric pair of substrate esters. While *S*-I could be readily prepared from the commercially available (*S*)-2-methylbutyl alcohol,[2] *R*-I was difficult to obtain because *R* isomers are not usually naturally occurring. All attempts to resolve racemic 3-methylpentanoic acid utilizing alkaloids failed. Moreover, there have been no reports in the literature describing the preparation of *R*-I or of (*R*)-2-methylbutyl alcohol in high optical purity or in workable quantity. (*R*)-2-Methylbutyric acid, prepared by Markwald[3] in 1896, can be reduced[4] to (*R*)-2-methylbutyl alcohol which can then be converted into *R*-I. However, the low optical purity (61%) of the acid ruled out the possibility of utilizing it in our work.

In the present investigation, however, we found that *R*-I could be obtained in good optical purity (92%) and in reasonable quantity from optically active isoleucines (IIa or IIb) *via* diazotization[5] in concentrated acids (HCl or HBr) at ~5° and subsequent reductive dehalogenation of the resulting $\alpha$-halo acids (IIIa or IIIb) by zinc in neutral water (Scheme I).

Scheme I




This synthesis would give the desired acid *R*-I from both D-isoleucine (IIb) and L-alloisoleucine (IIa),

(1) C. G. Overberger and I. Cho, *J. Polym. Sci., Part A-1*, in press.

(2) K. B. Wiberg and T. W. Hutton, *J. Amer. Chem. Soc.*, **78**, 1640 (1956).

(3) O. Schütz and W. Markwald, *Ber.*, **29**, 52 (1896).

(4) D. S. Noyce and D. B. Denney, *J. Amer. Chem. Soc.*, **72**, 5743 (1950).

(5) For a review of the diazotization of amino acids, see A. Neuberger, *Advan. Protein Chem.*, **4**, 333 (1948).

IIa and IIb being prepared by Greenstein's procedure.[6] However, this procedure affords IIa more easily than IIb. It is also interesting to note that under identical diazotization conditions, the yield of the resulting α-bromo acids was higher when prepared from alloisoleucine (50%) than isoleucine (35%). This effect may reflect the steric requirements[7] governing the diazotization of amino acids.

A zinc–acetic acid system has been used in many instances to dehalogenate reductively not only α-halo ketones[8] but also α-halo acids. In 1859, Ulrich[9] reduced α-chloropropionic acid to propionic acid with zinc in hydrochloric acid. Paal[10] reported a successful conversion of α-chlorobutyric acid into butyric acid by hydrogenation in the presence of Pd.

$$R{-}\underset{\displaystyle X}{\underset{|}{CH}}{-}COOH \xrightarrow{Zn\ (H_2O)} R{-}CH_2{-}COOH$$

R = $CH_3$, Bz, *sec*-butyl
X = Cl, Br

Compound *R*-I obtained from IIa ($[\alpha]^{25}D$ +40.0°, 4.5 *N* HCl) exhibited rotation $\alpha^{25}D$ −7.5° (neat, 1 dm). This rotation corresponds to an optical purity of 92%, based on optically pure *S*-I.[11] It is not certain during which step 4% racemization occurred.

When an asymmetric, acyclic, alkylcarboxylic acid does not occur naturally in optically active form, the classical resolution of the asymmetric acid ultilizing alkaloids is often unsuccessful, or, if successful, an extensive purification of the diastereomers by many recrystallizations is usually required.[12] We report the present synthesis as an alternative route for the preparation of optically active, acyclic, alkyl carboxylic acids when the classical alkaloid resolution fails.

### Experimental Section

**α-Bromo Acids (IIIa and IV).**—According to the procedure reported previously,[1] IIIa was prepared in 50% yield from IIa and IV in 35% yield from isoleucine. Nmr spectra showed the α proton as a doublet at 4.20 ppm ($J$ = 6.0 cps) for IIIa and at 4.10 ppm ($J$ = 8.0 cps) for IV.

**General Procedure for the Reductive Dehalogenation of α-Halo Acids.**—To a dispersion of 15 g (0.25 g-atom) of zinc dust in 500 ml of distilled water was added 0.05 mol of α-halo acid. The resulting mixture was stirred overnight, and, during this time, zinc hydroxide precipitated. When the acid was insoluble in water, the mixture was allowed to reflux for the same time period. The reaction mixture was then acidified with dilute hydrochloric acid and the product acid was extracted with ether. After the ether extract was dried over anhydrous sodium sulfate, distillation afforded dehalogenated acid in almost quantitative yield.

**(*R*)-3-Methylpentanoic Acid (*R*-I).**—Employing the above procedures, 13 g (0.1 mol) of L-alloisoleucine[6] ($[\alpha]^{25}D$ +40.0°, *c* 1.70 in 4.5 *N* HCl) gave *R*-I {$[\alpha]^{25}D$ −7.5° (neat, 1 dm)} in 50% over-all yield.

(6) J. P. Greenstein, S. M. Birnbaum, and L. Levintow, *Biochem. Prep.*, **3**, 84 (1951).

(7) Assuming that the α-propiolactone intermediate proposed by Neuberger[5] is correct, the attack of nucleophile $Br^-$ would be more hindered in the case of isoleucine.

(8) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, p 56.

(9) C. Ulrich, *Ann.*, **109**, 268 (1859).

(10) C. Paal and H. Schiedewitz, *Ber.*, **62**, 1935 (1929).

(11) L. Lardicci and L. Conti, *Ann. Chim.* (Rome), **51**, 823 (1961).

(12) For examples, see ref 4; W. von E. Doering and K. B. Wiberg, *J. Amer. Chem. Soc.*, **72**, 2608 (1950); S. Stallberg-Stenhagen, *Ark. Kemi*, **A23**, 14 (1946); J. Cason and R. A. Coad, *J. Amer. Chem. Soc.*, **72**, 4695 (1950).

**Registry No.**—*R*-I, 16958-25-1.

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## A New Synthesis of 11H-Indeno[2,1-*a*]phenanthrenes

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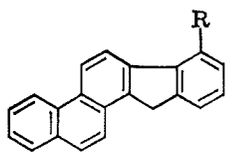
The incentive for the synthesis of 11H-indeno[2,1-*a*]phenanthrene (**1**) and its alkyl derivatives stems from a desire to prepare materials of known structure for comparison with certain complex dehydrogenation products. Steroids in particular furnish an array of dehydrogenation products,[2] among which indenophenanthrenes have been recognized.[3-8] The structures of several of these pentacyclic dehydrogenation products are unknown;[2] the compounds presumably arise from unknown or unrecognized transformations.




**1**, R = H
**2**, R = $CH_3$

All previous syntheses[7-12] of substituted 11H-indeno[2,1-*a*]phenanthrenes have a common characteristic. A partially aliphatic precursor with the same skeletal features as the desired compound is first synthesized, and then this precursor is aromatized by dehydrogenation. Since the syntheses produce the comparison samples by dehydrogenation methods which may promote obscure transformations, the conclusions based on comparisons with these samples lack logical rigor. While the results and conclusions of earlier workers may not eventually prove to be invalid, they certainly warrant reinvestigation.

Obviously, a synthesis of 11H-indeno[2,1-*a*]phenanthrenes which does not include dehydrogenation would be highly desirable. This objective has been

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(2) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd ed, Reinhold Publishing Corp., New York, N. Y., 1949, pp 147–156.

(3) W. O. Godtfredsen and S. Vangedal, *Tetrahedron*, **18**, 1029 (1962).

(4) H. Dannenberg and H.-G. Neumann, *Ann.*, **646**, 148 (1961); *Ber.*, **94**, 3085 (1961).

(5) D. J. Cram and N. L. Allinger, *J. Amer. Chem. Soc.*, **78**, 5275 (1956).

(6) W. R. Nes and E. Mosettig, *ibid.*, **76**, 3182 (1954).

(7) J. W. Cook, C. L. Hewett, W. V. Mayneord, and E. Roe, *J. Chem. Soc.*, 1727 (1934).

(8) W. E. Bachmann, J. W. Cook, C. L. Hewett, and J. Iball, *ibid.*, 54 (1936).

(9) D. Nasipuri and D. N. Roy, *ibid.*, 3361 (1961).

(10) E. Buchta and H. Krätzer, *Ber.*, **95**, 1820 (1962).

(11) B. B. Datta and J C. Bardhan, *J. Chem. Soc.*, 3974 (1962).

(12) S. Uyeo, T. Mizutani, A. Yoshitake, and A. Ito, *Yakugaku Zasshi*, **84**, 458 (1964); *Chem. Abstr.*, **61**, 4286 (1964).