the combined mother liquors on silica gel separated an additional 92.5 mg. (total yield, 958.5 mg. or 56%) of the acetamido ketone **5b**, m.p. 148–152°, as well as small quantities (total 56 mg.) of fractions whose thin layer chromatographs[11] indicated the presence of **5b, 5c**, and a third component, possibly **6b**. The R_f value of this third minor component corresponded to the R_f value for the minor unidentified component present in the reaction mixture from the oxime tosylate **1b**. However, as in the previous case, we were unable to obtain a pure sample of this minor component.

Butyllithium-Induced Rearrangement of Methylnaphthyl Phenyl Sulfones[1,2]

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A series of new isomeric sulfones, namely 2-methyl-1-naphthyl phenyl, 1-methyl-2-naphthyl phenyl, 8-methyl-1-naphthyl phenyl, and 3-methyl-2-naphthyl phenyl sulfones, has been synthesized. On treatment with *n*-butyllithium, three of these sulfones rearranged to the corresponding benzylnaphthalenesulfinic acids. The 2,3-substituted sulfone, on similar treatment, gave a low yield of an unstable product.

It has been shown[3a-c] that *o*-methyldiphenyl sulfones, when treated in ether solution with *n*-butyllithium, rearrange to *o*-benzylbenzenesulfinic acids. This study was successfully extended to substituted-phenyl mesityl sulfones and qualitative effects of different substituents on the migrating phenyl ring were noted.[4] The subsequent transformations of the sulfinic acids to sulfonic acids, diarylmethanes, and chloromercuridiarylmethanes also have been demonstrated.[3a,b,4]

This investigation concerns extension of the reaction to naphthyl phenyl sulfones. Unpublished results indicated difficulties when the naphthyl group is the migrating entity in such *n*-butyllithium–induced rearrangements.[5] In view of this, it was of interest to know whether the rearrangement would occur if the methyl group involved was a substituent on the naphthalene ring. Rearrangement studies were carried out on 2-methyl-1-naphthyl phenyl, 1-methyl-2-naphthyl phenyl, 3-methyl-2-naphthyl phenyl, and 8-methyl-1-naphthyl phenyl sulfones. The sulfones were prepared from the corresponding sulfides by hydrogen peroxide oxidation and characterized by physical constants such as melting point and infrared spectrum. 2-Methyl-1-naphthyl phenyl and 8-methyl-1-naphthyl phenyl sulfides were obtained from cuprous benzenethiolate and the suitably substituted aromatic bromide by the method of Adams, Reifschneider, and Nair.[6] In our hands, this method provided significantly increased yields over those obtained from reaction of benzenesulfenyl chloride with naphthyllithium or naphthylmagnesium bromide reagents.[3b,7] The condensation of benzenethiol and the appropriate naphthol in the presence of *p*-toluenesulfonic acid, according to the procedure of Furman and co-workers,[8] provided the sulfide precursors of the other sulfones investigated.

The Experimental section describes the technique for the rearrangement studies and the methods used to obtain derivatives of the sulfinic acids. The propensity to rearrange (see Table I) was estimated from the yields of crude acids[9] and the time required to attain these yields. On this basis, the following qualitative order was observed: 2-methyl-1-naphthyl phenyl > 1-methyl-2-naphthyl phenyl > 8-methyl-1-naphthyl phenyl > 3-methyl-2-naphthyl phenyl sulfone. McClement and Smiles have reported that the base-induced rearrangements of 3-chloro-2-hydroxy-5,6-dimethyl-2′-nitrodiphenyl sulfones and 2-hydroxy-1-naphthyl 2-nitrophenyl sulfone are unusually facile.[10] A similar effect was observed in the analogous *n*-butyllithium-induced rearrangements of aryl sulfones which possess two *o*-methyl groups in the same ring, that is, dimesityl, mesityl phenyl, and phenyl 2,6-xylyl sulfones.[3a,b] The ease with which 2-methyl-1-naphthyl phenyl sulfone rearranges is consistent with the steric acceleration effect proposed by Bunnett and Zahler[11] and supported by Bunnett and Okamoto.[12] There is evidence that the *peri*-hydrogen of naphthalene would provide less steric acceleration for the rearrangement than would an *o*-methyl grouping[13]; this may account in part for the less than quantitative yield of sulfinic acid from this sulfone.

The resistance of 3-methyl-2-naphthyl phenyl sulfone to rearrange may be related to a diminished stabilization of the metalated intermediate by the arylsulfonyl group. This would result in slower metalation of the side chain; hence, nuclear metalation of either ring might predominate under these circumstances.[14]

Similarly, in 8-methyl-1-naphthyl phenyl sulfone, stabilization of the organolithium intermediate may be lowered because the phenylsulfonyl group is more distal; experiments using this isomer produced only a small amount of rearrangement. In addition, the steric requirements for rearrangement should be different in the 1,8-substituted sulfone as compared to those present in other *o*-methyldiaryl sulfones studied, because re-

(1) Abstracted from the Ph.D. thesis of D. C. Hampton.

(2) Paper V in the series "Rearrangements of Aryl Sulfones."

(3) (a) W. E. Truce, W. J. Ray, Jr., C. L. Norman, and D. B. Eickemeyer, *J. Am. Chem. Soc.*, **80**, 3625 (1958); (b) W. E. Truce and W. J. Ray, Jr., *ibid.*, **81**, 481 (1959); (c) **81**, 484 (1959).

(4) W. E. Truce and M. M. Guy, *J. Org. Chem.*, **26**, 4331 (1961).

(5) D. E. Hoiness, M.S. thesis, Purdue University (1960). Mesityl 1-naphthyl sulfone and mesityl 2-naphthyl sulfone did not give isolable sulfinic acid when treated with *n*-butyllithium.

(6) R. Adams, W. Reifschneider, and M. D. Nair, *Croatica Chem. Acta*, **29**, 277 (1957).

(7) H. Lecher, F. Holschneider, K. Koberle, W. Speer, and P. Stocklin, *Ber.*, **58**, 409 (1925).

(8) F. M. Furman, J. H. Thelin, D. W. Hein, and W. B. Hardy, *J. Am. Chem. Soc.*, **82**, 1450 (1960).

(9) The sulfinic acids formed were somewhat unstable; it was necessary to avoid heating or exposing these compounds to air for any period of time.

(10) C. S. McClement and S. Smiles, *J. Chem. Soc.*, 1016 (1937).

(11) J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 369 (1951).

(12) J. F. Bunnett and T. Okamoto, *J. Am. Chem. Soc.*, **78**, 5363 (1956).

(13) R. Adams and L. O. Binder, *ibid.*, **63**, 2773 (1941).

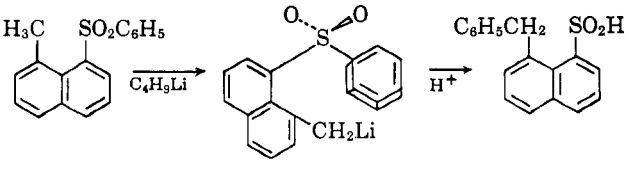
(14) W. E. Truce and M. F. Amos, *ibid.*, **62**, 2327 (1940).

TABLE I

CHARACTERISTIC RESULTS ON REARRANGEMENT OF NAPHTHYL PHENYL SULFONES

Sulfone	Sulfone, moles	n-C_4H_9Li,[a] moles	Reaction time, hr.	Crude recovered, sulfone, %	Crude acid, %	Neut. equiv. Calcd.	Neut. equiv. Found	Chloromercuriarylmethane, m.p.
2-Methyl-1-naphthyl phenyl	0.007	0.008[b]	18	15[c]	89[d]	282	286	147.5–148.0[e]
1-Methyl-2-naphthyl phenyl	.007	.008[f]	20	60[c]	41[g]	282	282	207–208[h]
3-Methyl-2-naphthyl phenyl	.011	.013	48[i]	66[c]	13[j]			
8-Methyl-1-naphthyl phenyl	.007	.009	18	46[k]	24			227.5–229.0[l]

[a] Commercial n-butyllithium in heptane solution (Lithium Corp. of America), which had been analyzed, was employed in these experiments. [b] An experiment in which n-butyllithium prepared by the authors was used afforded 90% yield of crude acid. [c] Mixture melting point of a recrystallized sample with original sulfone was not depressed. [d] Purification of the crude acid provided a colorless solid, m.p. 102–103° dec. [e] *Anal.* Calcd. for $C_{17}H_{13}ClHg$: C, 45.04; H, 2.89; Cl, 7.82. Found: C, 45.00; H, 2.70; Cl, 7.62. [f] An experiment in which n-butyllithium prepared in the laboratory was utilized furnished 45% yield of crude acid. [g] Purification of the crude acid produced a solid whose melting point was determined using a bath preheated to 100°. The melting point of this acid was 116.0–118.5° dec. [h] *Anal.* Calcd. for $C_{17}H_{13}ClHg$: C, 45.04; H, 2.89; Cl, 7.82. Found: C, 44.92; H, 3.03; Cl, 8.00. The S-benzylthiuronium sulfinate of the sulfinic acid showed m.p. 182.5–183.5° dec. [i] An experiment having a reaction time of 18 hr. provided 15% unstable crude sulfinic acid, which was isolated as a resinous material. [j] The acid produced in this experiment showed the expected bands for a sulfinic acid in its infrared spectrum, *viz.*, 3.92 μ, 2550 cm.$^{-1}$, and 9.15 μ, 1090 cm.$^{-1}$. This acid product was very unstable and readily decomposed to a base-insoluble material, which was assumed to be the corresponding thiosulfonate for reason of its infrared spectrum. When purification by precipitation using ferric chloride was attempted, the yield on the basis of the ferric sulfinic formed was 2% of theory. [k] An unidentified yellow oil was isolated from the crude neutral product by chromatography. The infrared spectrum of this material did not possess absorption bands in the regions characteristic of the $-SO_2-$ grouping. [l] *Anal.* Calcd. for $C_{17}H_{13}ClHg$: C, 45.04; H, 2.89. Found: C, 45.21; H, 2.88.



arrangement *via* a six-membered transition state would be necessary in this case[15] (see above).

Although the other sulfinic acids formed in this work were easily purified solids, the products resulting from 3-methyl-2-naphthyl phenyl and 8-methyl-1-naphthyl phenyl sulfone were isolated as resinous materials and only the acid from the 1,8-isomer gave a chloromercuri derivative. The acid from the rearrangement of 3-methyl-2-naphthyl phenyl sulfone was very unstable and decomposed rapidly during purification and drying. Impure sulfinic acids could be isolated and purified through their insoluble ferric salts[16] and regenerated by washing the salts with dilute ammonia. Only a trace of ferric sulfinate was formed when purification of the unstable acid from 3-methyl-2-naphthyl phenyl sulfone was attempted.

The benzylnaphthalenesulfinic acids were characterized by their infrared spectra and their chloromercurinaphthylphenylmethane derivatives. The formation of 8-chloromercuri-1-naphthylphenylmethane occurred only when the reaction mixture was continuously heated, possibly a consequence of a steric effect by the adjacent *peri*-substituent.

The sulfinic acid from the rearrangement of 2-methyl-1-naphthyl phenyl sulfone was selected as a model compound for structure proof. The chloromercuri derivative from this acid did not depress the melting point of the chloromercuri compound obtained from the reaction of mercuric chloride with the Grignard reagent from 2-benzyl-1-bromonaphthalene.

Experimental[17]

Preparation of Methylnaphthyl Phenyl Sulfides and Their Sulfones. A. Using the Reaction of Cuprous Benzenethiolate and Substituted Bromonaphthalenes.—Freshly prepared cuprous benzenethiolate and a suitably substituted bromonaphthalene were dissolved in a mixture of quinoline and dry pyridine and refluxed for 16–24 hr. longer than was necessary to obtain homogeneity of the reaction mixture.[6] The reflux temperatures were somewhat lower than the temperatures reported by Adams and co-workers,[6] but the yields were not affected. The liquid sulfides were purified by distillation under reduced pressure. A solution of the sulfide in glacial acetic acid was treated with a 50–100% excess of 30% hydrogen peroxide solution and, after stirring for 1 hr. at room temperature, the reaction mixture was refluxed for 0.5 hr. and poured onto crushed ice. The crude sulfone separated as a gum or a solid and was isolated, washed with water, and recrystallized from 95% ethanol.

B. Using the Condensation of Benzenethiol and Substituted Naphthols.—Using the method of Furman, *et al.*,[8] a mixture of an appropriately substituted naphthol and benzenethiol, together with *p*-toluenesulfonic acid catalyst and a small amount of toluene was heated at 110° with stirring under nitrogen for 24 hr. The crude sulfides were isolated as described[8] and purified by vacuum distillation. Unchanged naphthol was recovered by treating the combined basic and water washings with a small amount of hydrogen peroxide, filtering the precipitated solid disulfide and acidifying the basic solution to precipitate the naphthol in relatively pure state. The sulfones were prepared by hydrogen peroxide oxidation of the sulfides as described earlier.

2-Methyl-1-naphthyl Phenyl Sulfide and Sulfone.—Eastman 2-methylnaphthalene (142 g., 1.0 mole) was brominated according to the method of Adams and Binder[13] to afford 1-bromo-2-methylnaphthalene in 66–78% yield ($n^{25}D$ 1.6477, b.p. 103.5–106.0° at 0.9 mm., lit.[13] b.p. 152–156° at 14 mm.). Crude cuprous benzenethiolate (76.3 g., 0.44 mole), when condensed with 88.4 g. (0.40 mole) of 1-bromo-2-methylnaphthalene, in 225 ml. of quinoline and 30 ml. of dry pyridine, gave a yellow liquid, 2-methyl-1-naphthyl phenyl sulfide (91.1 g., 91% yield, b.p. 163–165° at 0.7 mm., $n^{23}D$ 1.6800). Oxidation of this oil provided 2-methyl-1-naphthyl phenyl sulfone (m.p. 105.0–106.5°, yield 68%).

Anal. Calcd. for $C_{17}H_{14}O_2S$: C, 72.32; H, 5.00. Found: C, 72.19; H, 4.84.

Phenyl disulfide, prepared by hydrogen peroxide oxidation of a basic solution of benzenethiol, was treated with an equimolar quantity of chlorine dissolved in carbon tetrachloride. The resulting benzenesulfenyl chloride was obtained in 82% yield (b.p. 42.7–44.3° at 1 mm., lit.[7] b.p. 58–60° at 3 mm.).

The reaction of 75.4 g. (0.34 mole) of 1-bromo-2-methylnaphthalene with 9.8 g. (0.71 g.-atom) of finely cut lithium wire in dry ether afforded the corresponding aryllithium compound. Benzenesulfenyl chloride (42.7 g., 0.30 mole) in an equal volume of ether was added to the organometallic solution[3b] and 27.2 g.

(15) W. J. Evans and S. Smiles, *J. Chem. Soc.*, 329 (1936). Other sulfones that undergo Smiles rearrangement and require six-membered transition states have been reported.

(16) S. Krishna and H. Singh, *J. Am. Chem. Soc.*, **50**, 729 (1928).

(17) Melting and boiling points are uncorrected.

(37% yield) of 2-methyl-1-naphthylphenyl sulfide (b.p. 169–175° at 0.9 mm.) was isolated and oxidized to the sulfone.

1-Methyl-2-naphthyl Phenyl Sulfide and Sulfone.—Following the directions of Russell and Lockhart,[18] 200 g. (1.4 moles) of 2-naphthol was transformed by the Reimer–Tiemann reaction to 2-hydroxy-1-naphthaldehyde (74.3 g., 32% yield after two recrystallizations from 95% ethanol, m.p. 79.5–82.0°, lit.[18] m.p. 79–80°). Reduction of 2-hydroxy-1-naphthaldehyde using a modification of the method of Buu-Hoï and Lavit[19] provided 1-methyl-2-naphthol. An ethylene glycol solution of the hydrazone of 2-hydroxy-1-naphthaldehyde was treated with potassium hydroxide, heated to reflux, and the aqueous distillate collected until the distilling temperature reached 185°. The reaction mixture was heated at a pot temperature of 200–220° until nitrogen evolution was no longer detected. The solution was poured onto crushed ice, diluted with water, acidified, and the precipitated product was extracted using benzene. After removing the solvent, the crude dry product was recrystallized from a solution of benzene and 65–67° petroleum ether, affording 72–81% of 1-methyl-2-naphthol (m.p. 108.5–110.0°, lit.[19] m.p. 110–111°).

In a typical condensation reaction, 79.2 g. (0.5 mole) of 1-methyl-2-naphthol, 55 g. (0.5 mole) of benzenethiol, 27.2 g. (0.13 mole) of *p*-toluenesulfonic acid, and 25 ml. of toluene were heated with stirring at 110° for 45 hr. and the crude sulfide isolated and purified by distillation. 1-Methyl-2-naphthyl phenyl sulfide was obtained in 50% conversion (63.2 g., b.p. 178.5–187.0° at 0.6 mm., m.p. 34–35°, $n^{23}D$ 1.6886). Unchanged 1-methyl-2-naphthol (11.3 g.) was recovered from the basic aqueous washings as previously described; hence, a 59% yield for the reaction. By means of hydrogen peroxide oxidation, 1-methyl-2-naphthyl phenyl sulfone (24.9 g., m.p. 142.0–143.5°), was formed in 70% yield.

Anal. Calcd. for $C_{17}H_{14}O_2S$: C, 72.32; H, 5.00. Found: C, 72.42; H, 5.18.

3-Methyl-2-naphthyl Phenyl Sulfide and Sulfone.—Esterification of Eastman technical grade 3-hydroxy-2-naphthoic acid in methanol formed methyl 3-hydroxy-2-naphthoate (187.7 g., m.p. 73.5–74.5°, lit.[20] m.p. 73–74°) in 81–86% yield. Using lithium aluminum hydride, the ester was reduced to 3-hydroxymethyl-2-naphthol according to the procedure of Miller and coworkers.[20] After several recrystallizations from methanol, 3-hydroxymethyl-2-naphthol (32% yield, m.p. 188.5–189.5°, lit.[20] m.p. 189.5–190.5°) was furnished.[21]

Hydrogenation at high pressure using copper chromite catalyst[20] converted 3-hydroxymethyl-2-naphthol to 3-methyl-2-naphthol (13% yield, m.p. 155–161°, lit.[20] m.p. 156–157°), using chromatography for purification. In another preparation of this compound, a solution of 4.0 g. (0.02 mole) of 3-hydroxymethyl-2-naphthol in absolute alcohol was shaken at room temperature under 3 atm. hydrogen with 2.0 g. of 5% palladium-on-charcoal catalyst for 18 hr. After filtering, the solvent was removed and the crude product was extracted with benzene. The benzene solution was concentrated and chromatographed, giving 0.75 g. of 3-methyl-2-naphthol (23% yield, m.p. 157–160°).[22] Acid-catalyzed condensation of 3-methyl-2-naphthol with benzenethiol produced 3-methyl-2-naphthyl phenyl sulfide. The crude sulfide was oxidized to 3-methyl-2-naphthyl phenyl sulfone (m.p. 159.0–162.5°) in 49–68% yield over-all from 3-methyl-2-naphthol. Recrystallization gave an analytical sample having a m.p. 163.0–164.0°.

Anal. Calcd. for $C_{17}H_{14}O_2S$: C, 72.32; H, 5.00; S, 11.36. Found: C, 72.46; H, 4.99; S, 11.62.

8-Methyl-1-naphthyl Phenyl Sulfide and Sulfone.—Diazotization of freshly purified 1,8-diaminonaphthalene (K and K Laboratories, Inc., technical grade redistilled, b.p. 148.0–151.5° at 7 mm., m.p. 64.5–66.0°) provided 1,8-azaminonaphthalene[23] as described by Fieser and Seligman.[24] Using a modification[25] of the method of these workers, 1,8-azaminonaphthalene was added to a hot solution–suspension of electrolytic copper powder in 48% hydrobromic acid at 100–110° and an 11% yield of 8-bromo-1-naphthylamine (m.p. 84–89°, lit.[23] m.p. 87–88°)[26] was realized.

Upon diazotization and treatment with potassium iodide solution,[24] 1-bromo-8-iodonaphthalene (b.p. 154–168° at 0.7 mm., m.p. 96.5–99.5°, lit.[25] m.p. 97–99°) was supplied in 77% of the theoretical amount. Methyl sulfate in dry benzene and the Grignard reagent of this aromatic halide reacted to produce 1-bromo-8-methylnaphthalene, which was purified by distillation (b.p. 115–130° at 1.1 mm., lit.[25] b.p. 132° at 4 mm.) and recrystallization from methanol in 33% yield. On condensation with cuprous benzenethiolate, 1-bromo-8-methylnaphthalene was transformed to 8-methyl-1-naphthyl phenyl sulfide. Upon oxidation of the crude sulfide, 8-methyl-1-naphthyl phenyl sulfone (m.p. 112–115°, 63% based on 1-bromo-8-methylnaphthalene) was isolated by chromatography. The melting point for a recrystallized analytical sample was 113.5–114.5°.

Anal. Calcd. for $C_{17}H_{14}O_2S$: C, 72.32; H, 5.00; S, 11.36. Found: C, 72.27; H, 4.94; S, 11.08.

General Procedure Followed in the *n*-Butyllithium-Induced Rearrangement of the Sulfones.—The apparatus used in these experiments was a standard taper three-neck flask equipped with condenser, drying tube, 60-ml. vapor by-pass addition funnel, magnetic or mechanical stirrer, and heating mantle. The glassware was thoroughly dried in an oven, assembled immediately, and permitted to cool in a stream of high purity nitrogen gas. The rearrangements were carried out in a nitrogen atmosphere with a minimum of exposure during the addition of the reactants and solvent. The solvent used in these experiments was freshly opened Mallinckrodt anhydrous ether. Commercially available *n*-butyllithium reagent in heptane solution was used throughout most of the experiments; rearrangement yields of sulfinic acids from experiments using commercial *n*-butyllithium were nearly identical with those obtained when *n*-butyllithium prepared fresh in the laboratory was employed. In all cases, the reagent was analyzed before use by the titration method of Jones and Gilman.[27] Although the commercial *n*-butyllithium contained noticeable suspended material in the yellow solution, the analyses of this product showed its *n*-butyllithium normality was nearly constant[28] throughout the experiments. The correct volume of reagent was removed from the original container under nitrogen and transferred to the addition funnel containing 30 ml. of anhydrous ether using a carefully dried 20-ml. hypodermic syringe. The diluted *n*-butyllithium was added dropwise at room temperature to an ether solution of the sulfone and, when the addition was completed, the reaction mixture was refluxed and stirred for the time indicated. Unless color changes and precipitation were observed, the reaction period was extended to a minimum of 17–18 hr.

The reaction was hydrolyzed by the addition of water in a large enough amount to remove the water-soluble lithium salt of the acid. The ether layer was separated and washed with water several times before it was dried over anhydrous magnesium sulfate. After removal of the solvent, the neutral material was carefully dried and infrared analysis showed that it contained predominantly unreacted sulfone in most circumstances. Using recrystallization and chromatography, the recovered sulfone was isolated and thereupon identified by mixture melting point and superposability of its infrared spectrum with that of the original sulfone.[29]

Acidification to pH 1 using hydrochloric acid precipitated the sulfinic acid as a gummy solid from the aqueous layer and washings. The acid product was extracted with ether, the solution

(18) A. Russell and L. B. Lockhart, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 463.

(19) N. P. Buu-Hoï and D. Lavit, *J. Chem. Soc.*, 2776 (1955).

(20) L. E. Miller, W. W. Hanneman, W. L. St. John, and R. R. Smeby, *J. Am. Chem. Soc.*, **76**, 296 (1954).

(21) Extensive purification which was necessary because of the impurity of the crude naphthol lowered the yields significantly from those reported.[20]

(22) The benzene-insoluble material from this reaction was unchanged 3-hydroxymethyl-2-naphthol in relatively pure condition.

(23) R. E. Damschroder and W. D. Peterson, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 106. The method for preparing benzotriazole described by R. E. Damschroder and W. D. Peterson was also adapted for synthesis of 1,8-azaminonaphthalene.

(24) L. F. Fieser and A. M. Seligman, *J. Am. Chem. Soc.*, **61**, 136 (1939).

(25) L. H. Klemm, J. W. Sprague, and E. Y. K. Mak, *J. Org. Chem.*, **22**, 161 (1957).

(26) The yield of 8-bromo-1-naphthylamine was nearly the same when the azimino compound was combined with analytical copper strips dissolved in hot hydrobromic acid (12%)[24] or with cuprous bromide dissolved in hot hydrobromic acid (18%). In all cases our yields were somewhat lower than those reported previously.[24,25]

(27) R. G. Jones and H. Gilman, "Organic Reactions," Coll. Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 339.

(28) Concentration of the reagent was 2.02–1.95 *N*, from titration, and approximately 70% of the total base was *n*-butyllithium.

(29) For the neutral product from the rearrangement of 8-methyl-1-naphthyl phenyl sulfone, infrared spectrum was the only criterion used.

dried over magnesium sulfate in the refrigerator, the solvent evaporated, and the residue dried thoroughly over phosphorus pentoxide at 1–2 mm.[30] For further purification the crude sulfinic acid was dissolved in ether and extracted with 5% sodium bicarbonate solution. The basic solution was treated with charcoal, acidified, and the precipitated acid either filtered or removed by ether extraction.

The ferric sulfinates of the acids also were employed for isolation and purification of the products. An excess of 3% ferric chloride solution was added to an aqueous solution of the sodium salt of the acid and the pH adjusted to 1 using hydrochloric acid.[16] The ferric sulfinate was collected by vacuum filtration, washed repeatedly with acid solution followed by water, and dried. The original acid could be recovered by treating the ferric sulfinate with dilute ammonium hydroxide and filtering the ferric hydroxide precipitate. Yields of unstable acids could be determined by the quantitative formation of the ferric sulfinate.[16]

Chloromercurinaphthylphenylmethanes were prepared conveniently from the sulfinic acids.[3b] 8-Benzyl-1-naphthalenesulfinic acid formed a chloromercuri compound only when heated for 2 hr. at 70–80°.

1-Chloromercuri-2-naphthylphenylmethane.—*N*-Bromosuccinimide treatment[31] of 1-bromo-2-methylnaphthalene formed 1-bromo-2-bromomethylnaphthalene (m.p. 103.5–106.5°, lit.[31] m.p. 103.5–105.5°) in 60% of the theoretical quantity. 1-Bromo-2-naphthaldehyde (m.p. 117.5–119.5°, lit.[32] m.p. 119–120°) was prepared[32] from this dibromide in 22% yield. Following the procedure of Evans,[33] 1-bromo-2-naphthaldehyde was treated with phenylmagnesium bromide and the resulting carbinol directly reduced with phosphorus and iodine to 2-benzyl-1-bromonaphthalene (b.p. 200–204° at 1.0 mm., m.p. 40.5–42.0°, lit.[33] m.p. 39–40°) in 39% yield. Mercuric chloride and the Grignard from 2-benzyl-1-bromonaphthalene provided 39% yield of 1-chloromercuri-2-naphthylphenylmethane, m.p. 147.0–148.5°. Mixture melting point of this compound and the chloromercuri derivative of 2-benzyl-1-naphthalene sulfinic acid was not depressed and the infrared spectra of the two compounds were identical.

Acknowledgment.—The authors are indebted to Phillips Petroleum Company and the National Cancer Institute, National Institutes of Health (grant CY-4536), for financial support of this project.

(30) Some of the sulfinic acid products were especially labile to heat and air; they slowly decomposed during the isolation and drying process forming base-insoluble residue.

(31) M. S. Newman and A. S. Kosak, *J. Org. Chem.*, **14**, 375 (1949).

(32) D. M. Hall and E. E. Turner, *J. Chem. Soc.*, 1242 (1955).

(33) E. A. Evans, *ibid.*, 2790 (1957).

The Synthesis and Resolution of Methylleucines

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β-Methylleucine and N,β-dimethylleucine were synthesized from 2,3-dimethylbutyraldehyde by a Strecker procedure. Separation of the diastereomeric N,β-dimethylleucines was accomplished by fractional crystallization. The N-acetyl-β-methylleucines were separated and one racemate was resolved by acylase. In addition to 2,3-dimethylbutyraldehyde, 2,3-dimethylbutyraldol and a dimeric ether were produced by the rearrangement of 2,3-dimethyl-1,2-butanediol.

During the elucidation of the structure of the peptide antibiotic Etamycin, N,β-dimethylleucine (I) was discovered.[2] This new amino acid is of biogenetic interest since the corresponding aldehyde, derived from hypochlorite degradation of the amino acid, is structurally and stereochemically identical to the aldehyde obtained from the ozonization of the ergosterol side chain.[2]

In this communication, the synthesis of the β-methylleucines (II),[3] the separation of the diastereomeric N-acetyl derivatives and the resolution of one isomer are reported. Also, the formation and separation of the diastereomeric N,β-dimethylleucines are described. The β-methylleucines represent promising intermediates for the synthesis of the four stereoisomeric N,β-dimethylleucines.

β-Methylleucine was synthesized in 66% over-all yield from 2,3-dimethylbutyraldehyde (III) by a modified Strecker procedure. The amino acid mixture was precipitated fractionally from water–acetone to remove the excess ammonium chloride. Although no attempt was made to separate the diasteroisomers, it is probable that some fractionation was achieved as indicated by changes in crystalline form, in the infrared spectra, and in the solubility of the various fractions.

Since the diastereomeric amino acids were not separated quantitatively, it was not established whether the isomers were formed in relatively equal quantities. However, treatment of the acetyl derivatives with excess acetic anhydride would be expected to equalize any unfavorable ratio by racemization at the α-center of the intermediate azlactone.[4] This facile isomerization and the amenability of the acetylamino acids to resolution by acylase indicates the advantages of approaching the N,β-dimethylleucines from the β-methylleucines.

N-Acetyl-β-methylleucine (IV) was obtained in 92% yield by the reaction of excess acetic anhydride with II. One diastereoisomer (IV–isomer I) was purified by fractional recrystallization[5] from water and from acetone. Purification of the second isomer (IV–isomer II) was accomplished by repeated precipitation from acetone–benzene or by very slow deposition from acetone.[6]

(1) Aided by a contract from the Office of Naval Research, Biochemistry Branch.

(2) J. C. Sheehan, H. G. Zachau, and W. B. Lawson, *J. Am. Chem. Soc.*, **80**, 3349 (1958).

(3) The synthesis of the ureido derivative of this amino acid by an alternate route has been reported by P. E. Gagnon, P. A. Boivin, and H. M. Craig, *Can. J. Chem.*, **29**, 70 (1951).

(4) J. P. Greenstein, S. M. Birnbaum, and L. Levintow, *Biochem. Prep.*, **3**, 84 (1953).

(5) Unless the amino acids are in a high state of purity the acylated derivatives are difficult to crystallize.

(6) The solvents employed were identical to those used for the separation of the acetyl isoleucines reported by W. A. H. Huffman and A. W. Ingersoll, *J. Am. Chem. Soc.*, **73**, 3366 (1951). Greenstein, Birnbaum, and Levintow[4] have described the preferential precipitation of N-acetylalloisoleucine and the subsequent purification of the acylamino acid by recrystallization from acetic acid–water. This latter procedure was not applicable to the N-acetyl-β-methylleucines since the isopropyl group confers increased solubility. Once crystallization was induced, the entire acetylation product solidified and no preferential deposition was obtained.