mother liquors yielded a small quantity of dark oil which reacted with 3 ml. of 100% hydrazine hydrate in 2 ml. of ethanol. The mixture solidified on cooling. After repeated recrystallization from hot ethanol, *ca.* 1.0 g. of fluorenone was isolated as the hydrazone (m. p. 148–149°; mixed m. p. 148–149°).

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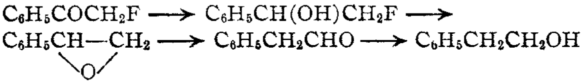
Reduction of Phenacyl Fluoride with Aluminum Isopropoxide[1]

BY WILLIAM E. TRUCE AND B. H. SACK

The original purpose of this investigation was to prepare ω-fluorostyrene by reduction of phenacyl fluoride with aluminum isopropoxide, followed by dehydration of the resulting fluorohydrin.

Phenacyl fluoride was prepared by acylating benzene with fluoroacetyl chloride[2] in the presence of aluminum chloride. After this portion of the work had been completed our attention was called to the publication of similar results.[3] However, the authors did not report the yield of phenacyl fluoride obtained nor that phenacyl chloride was an important by-product.

Phenacyl fluoride was treated with aluminum isopropoxide and isopropyl alcohol according to the procedure given for the reduction of benzophenone.[4] The product contained no fluorine. On the basis of previous results where halogen-free carbinols and ethers were obtained as reduction products of certain α-bromoketones,[4] 2-phenyl-1-ethanol was considered as a possible reduction product of phenacyl fluoride. The failure of the α-naphthylurethan of this alcohol to alter the melting point of the same derivative of an authentic sample of 2-phenyl-1-ethanol led to the conclusion that the reduction product was 2-phenyl-1-ethanol. It may have been formed by the following sequence of reactions[4]



$$C_6H_5COCH_2F \longrightarrow C_6H_5CH(OH)CH_2F \longrightarrow C_6H_5\underbrace{CH{-}CH_2}_{O} \longrightarrow C_6H_5CH_2CHO \longrightarrow C_6H_5CH_2CH_2OH$$

Experimental

Preparation of Phenacyl Fluoride.—Into a mixture of 117 g. (1.50 moles) of benzene, 198 g. (1.50 moles) of technical anhydrous aluminum chloride, and 300 ml. of carbon disulfide, surrounded by ice-water, was added 114 g. (1.32 moles) of fluoroacetyl chloride (b. p. 71° (755 mm.), $n^{27}{}_{\mathrm{D}}$ 1.3835). The addition was carried out dropwise with stirring over a period of five hours. The reaction mixture was allowed to warm up to room temperature and stirred for an additional four hours. The contents were poured into a mixture of ice and hydrochloric acid and then extracted twice with ether. This solution was treated with Drierite, the ether removed, and a vacuum rectification was carried out through a two-foot, helix-packed column. The yield of phenacyl fluoride was 46%, b. p. 94–95° (12 mm.), m. p. 27–28°.

Anal. Calcd. for C_8H_7FO: F, 13.77. Found: F, 13.78, 13.82; Cl, trace.

Phenacyl benzoate was prepared by refluxing a mixture of 1.0 g. of sodium benzoate, 5 cc. of water, 5 cc. of ethyl alcohol and 1.0 g. of phenacyl fluoride, for six hours. After chilling overnight an oil precipitated and after standing several days a small crop of long needles formed. These were recrystallized from 95% ethyl alcohol; m. p. 117–118° (lit. value 117–117.5°).[5]

The residue from the distillation of phenacyl fluoride amounted to 34 g. On recrystallization from methyl alcohol it melted at 56–57° and did not depress the melting point an authentic sample of phenacyl chloride.

Reduction of Phenacyl Fluoride.—Thirty-two grams (0.23 mole) of phenacyl fluoride was added to a mixture of 47 g. (0.23 mole) of aluminum isopropoxide in 235 cc. of isopropyl alcohol (distilled from calcium oxide) in a flask connected to a Hahn partial condenser. The solution was refluxed at such a rate that four to eight drops were distilled per minute. After thirteen hours the distillate showed a negative acetone test when treated with 2,4-dinitrophenylhydrazine reagent. The excess isopropyl alcohol was removed under reduced pressure. The residue was allowed to cool and was then hydrolyzed with cold, dilute hydrochloric acid (80 cc. of concd. acid and 400 cc. of water). The organic material was extracted with ether and, after removal of the ether, it was distilled, the material boiling at 97–102° (8 mm.) being collected; weight 16.3 g., $n^{26.8}{}_{\mathrm{D}}$ 1.5238, $d^{20}{}_4$ 1.024. The α-naphthyl urethan, prepared according to directions given by Shriner and Fuson,[6] melted at 116–117°. It did not depress the melting point of the α-naphthyl urethan of an authentic sample of 2-phenyl-1-ethanol.

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[1] Abstracted from the M.S. thesis of B. H. Sack.

[2] Truce, THIS JOURNAL, **70**, 2828 (1948).

[3] Gryszkiewicz-Trochimowski, Sporzynski and Wnuk, *Rec. trav. chim.*, **66**, 419 (1947).

[4] Wilds, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, Chap. 5.

[5] Zincke, *Ann.*, **216**, 308 (1882).

[6] Shriner and Fuson, "Identification of Organic Compounds," 3rd edition, John Wiley and Sons, New York, N. Y., 1940, p. 163.

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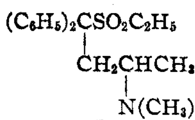
The Resolution of Ethyl 1,1-Diphenyl-3-dimethylaminobutyl Sulfone

BY B. F. TULLAR, W. WETTERAU AND S. ARCHER

In a previous paper[1] it was reported that the sulfone, I, exhibited strong analgesic action. For pharmacological reasons it became desirable to resolve this compound into its optical antipodes.



$$\begin{array}{l}(C_6H_5)_2CSO_2C_2H_5\\ \quad\quad\; |\\ \quad\quad CH_2CHCH_3\\ \quad\quad\quad\quad\;\; |\\ \quad\quad\quad\quad N(CH_3)_2\end{array}$$

I

The yield of ethyl benzohydryl sulfone was somewhat improved by using benzohydryl bromide rather than the chloride as the starting material. The sulfone was alkylated with dimethylaminoisopropyl chloride and sodium hydride rather than sodium amide as the condensing agent. The yield of pure I was 45% and about 29% of

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[1] Klenk, Suter and Archer, THIS JOURNAL, **70**, 3846 (1948).

TABLE I

PROPERTIES OF THE OPTICALLY ACTIVE BASE AS SALTS

Compound	Formula	M. p., °C. (cor.)	$[\alpha]_D$ 27°	Analyses					
				Calcd.			Found		
				C	H	N	C	H	N
d-Base	$C_{20}H_{27}NO_2S$	110–110.6	−10 (2% A)[a] 0 (2% E)[b] +33.8 (5% HCl)[c]	69.70	7.88	4.06	70.11	7.86	3.98
l-Base		110–110.8	+12 (2% A)[a] 0 (2% E)[b] −31.6 (5% HCl)[c]				70.11	7.67	3.98
d-Base HCl	$C_{20}H_{27}NO_2S \cdot HCl$	196.8–198	+34.6 (1.5% H_2O)	62.86	7.39	3.66	62.64	7.39	3.60
l-Base HCl		196–197	−32.6 (1.5% H_2O) −36.4 (5% H_2O)				63.20	7.65	3.61
d-Base *d*-Tartrate	$C_{20}H_{27}NO_2S \cdot C_4H_6O_6$	166–169	+45 (2%, 50% *M*)[d]			2.82			2.95
l-Base *d*-Tartrate		171–172.5	−22.5 (2%, 50% *M*)						2.76

[a] A = Acetone. [b] E = U.S.P. ethanol. [c] Five per cent. solution in aqueous hydrochloric acid. [d] Fifty per cent. aqueous methanol.

unreacted ethyl benzohydryl sulfone was recovered from the neutral fraction.

Resolution was accomplished by taking advantage of the difference in solubility of the diastereomeric *d*-bitartrates in aqueous acetone. A levorotatory salt separated first; this yielded a crystalline base which was dextrorotatory in acetone. A two per cent. solution of the base in U.S.P. ethanol did not give any measureable rotation. On the other hand, the hydrochloride was levorotatory in aqueous solution. For convenience, the sulfone which yielded levorotatory salts was designated as the *l*-base. The isomeric sulfone was obtained from the filtrates of the *l*-bitartrate after treatment with ammonia followed by dilution. It was of interest to note that the active bases and hydrochlorides melted lower than the corresponding racemic substances. Pharmacologically, the levorotatory hydrochloride was about twenty times more active than the *d*-form.

Experimental

***dl*-Ethyl 1,1-Diphenyl-3-dimethylaminobutyl Sulfone.**—A mixture of 332 g. of ethyl benzohydryl sulfone and 38.3 g. of sodium hydride in 1280 ml. of dry benzene was heated and stirred for twenty-six hours. Then 180 g. of dimethylaminoisopropyl chloride was added dropwise in one hour. After heating for an additional five hours the mixture was cooled and 30 ml. of ethanol added to destroy the excess sodium hydride. The suspension was washed with two 500-ml. portions of water and then shaken with 600 ml. of 2.5 *N* hydrochloric acid. The hydrochloride of the base separated immediately. The benzene layer was decanted and washed with 200 ml. of 10% hydrochloric acid. The acid fractions were combined and cooled to 5°. The salt was collected and washed with 100 ml. of 6 *N* hydrochloric acid. The combined acid filtrates yielded 19 g. of crude I after being made alkaline with sodium hydroxide solution.

The main crop of salt was dissolved in 2 liters of water and 600 ml. of ethanol, filtered and made basic with 35% sodium hydroxide. The suspension was cooled in ice with stirring for one half hour and then filtered. The base was collected and combined with the crop obtained above; yield, 236 g. or 54% of the theoretical. On recrystallization from ethanol there was obtained 196 g. (45%) of I, suitable for use in the resolution. The analytical sample was obtained after two more crystallizations from ethanol; m. p. 150.5–151.8° (cor.).

Anal. Calcd. for $C_{20}H_{27}NSO_2$: N, 4.06. Found: N, 4.06.

Concentration of the benzene fraction gave 97 g. (29%) of ethyl benzohydryl sulfone which had not reacted.

1-Ethyl 1,1-Diphenyl-3-dimethylaminobutyl Sulfone Bitartrate.—A solution of 196 g. of I in 3 liters of acetone was added to a solution of 88 g. of *d*-tartaric acid in an equal volume of water and then cooled to 5° for twenty-four hours. The crystals that separated were washed with 200 ml. of cold 50% acetone and then with pure acetone. After drying at 50° there was obtained 119 g. (79%) of the salt, m. p. 169–171°, as a dihydrate.

The filtrates were made basic with 75 ml. of concentrated ammonium hydroxide, stirred at 10° for one-half hour and then filtered. The solid, which was the racemic base, amounted to 50 g. It was resolved as above and an additional 21 g. of *l*-bitartrate was obtained. The recovery of racemic base was 22 g. This second crop yielded an additional 6 g. of levo salt. The combined fractions of practically pure *l*-bitartrate weighed 146 g. or 96% of the theoretical. It was dissolved in 1200 ml. of 50% acetone containing 3.0 g. of *d*-tartaric acid and cooled. The solid was collected and dried at 50° to give 136 g. of pure dihydrate which was converted to the anhydrous form by drying at 85° for fifteen hours.

Addition of ammonia to the filtrate from the above crystallization caused 4.7 g. of *dl*-base, m. p. 145–148°, to separate.

The **base** was prepared by dissolving 191 g. of the pure *l*-bitartrate in 1800 ml. of 50% acetone and making the solution alkaline with concentrated ammonium hydroxide. After cooling to 5° the solid was collected and dried, wt. 120 g. It was recrystallized from 95% ethanol.

The ***l*-hydrochloride** was prepared by dissolving at 80°, 115 g. of the base in 250 ml. of water containing 35 ml. of concentrated hydrochloric acid and cooling to 5°. The salt was filtered and dried to constant weight at 70°; wt. 118 g. It was recrystallized from 700 ml. of acetone to give 100 g. of pure ***l*-hydrochloride**.

***d*-Ethyl *l,l*-Diphenyl-3-dimethylaminobutyl Sulfone Hydrochloride.**—The combined ammoniacal filtrates from which all the racemic base had been removed were diluted to 16 liters and allowed to cool after crystallization had started. The solid that separated weighed 60 g. and melted at 106–110°. After recrystallization from 140 ml. of 95% ethanol the pure isomeric base was obtained.

Twenty grams was dissolved in 40 ml. of water containing 6 ml. of hydrochloric acid and cooled. The ***d*-hydrochloride** was collected and dried, wt. 21 g. After recrystallization from acetone the pure salt amounted to 15 g.

The ***d*-bitartrate** was prepared in 50% acetone from equimolar quantities of the base and *d*-tartaric acid. From 5.3 g. of base there was obtained 4.5 g. of pure bi-tartrate.

The properties of all the compounds are listed in Table I.

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