Chromatography—L-3-Chloroalanine, because of its lability, must be applied to the TLC chromatogram as a fresh aqueous solution of the hydrochloride (1%) and dried immediately with a stream of warm air. The chromatogram was developed with Solvent System A, and the location of material was visualized by spraying with 1% ninhydrin in 1-butanol followed by heating at 80° until the pink spot of chloroalanine was clearly visible (about 7 min); R_f 0.31.

Comparative chromatography of L-lysine and the two isosteres, L-4-thialysine (I) and L-4-selenalysine (VIII) was carried out with their hydrochlorides. The highly polar nature of these amino acid hydrochlorides requires equally polar solvents for chromatographic separation, and Solvent Systems B and C were found to be satisfactory. The values for the hydrochloride of L-lysine, L-4-thialysine, and L-4-selenalysine were R_f 0.47, 0.75, and 0.78 in Solvent System B and R_f 0.37, 0.75, and 0.76 in Solvent System C, respectively. These results show the greater polarity of L-lysine compared to its sulfur and selenium analogs as well as the close similarity between the two hetero analogs.

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New Compounds: Synthesis of *O*-(2,3,4,5,6-Pentafluorobenzyl)hydroxylamine Hydrochloride

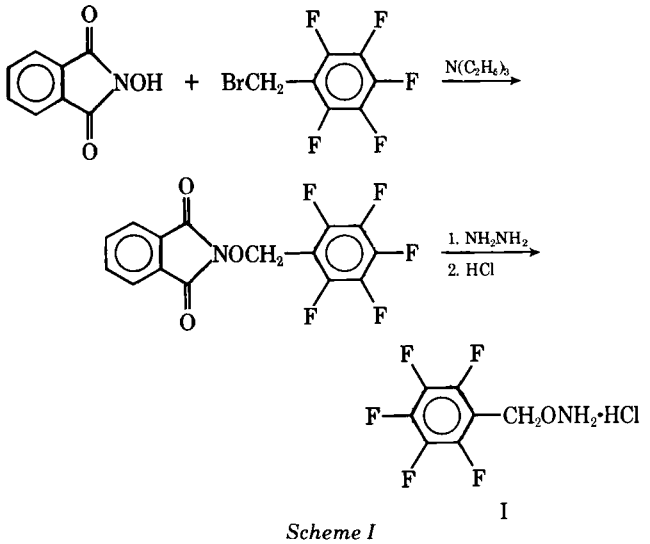
GILBERT A. YOUNGDALE

Abstract □ Reaction of 2,3,4,5,6-pentafluorobenzyl bromide with *N*-hydroxyphthalimide produced *N*-(2,3,4,5,6-pentafluorobenzyloxy)phthalimide which, after hydrazinolysis and treatment with hydrogen chloride, yielded *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine hydrochloride. The latter compound was used to derivatize keto steroids for their analysis by electron-capture GLC.

Keyphrases □ *O*-(2,3,4,5,6-Pentafluorobenzyl)hydroxylamine hydrochloride—GLC derivatization reagent, synthesized from pentafluorobenzyl bromide □ GLC derivatization reagent—synthesis of *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine hydrochloride

A recent article (1) described the use of *O*-(2,3,4,5,6-pentafluorobenzyl)hydroxylamine hydrochloride (I) to derivatize keto steroids for their analysis by electron-capture GLC. The synthesis of I is reported in this article.

Synthesis of I was achieved following the general method of McKay *et al.* (2). Reaction of 2,3,4,5,6-pentafluorobenzyl bromide with *N*-hydroxyphthalimide produced *N*-(2,3,4,5,6-pentafluorobenzyloxy)-phthalimide which, after hydrazinolysis and treatment with anhydrous hydrogen chloride, yielded I (Scheme I).



I

Scheme I

EXPERIMENTAL[1]

***N*-(2,3,4,5,6-Pentafluorobenzyloxy)phthalimide**—A mixture of 25 g (0.0957 mole) of 2,3,4,5,6-pentafluorobenzyl bromide, 15.6 g (0.0957 mole) of *N*-hydroxyphthalimide, 10.1 g (0.1 mole) of triethylamine, and 150 ml of dimethylformamide was stirred at room temperature for 19 hr and then on a steam bath for 2 hr. The majority of the solvent was removed under reduced pressure.

A solution of the residual material in methylene chloride was washed with 10% sodium carbonate solution and dried over anhydrous magnesium sulfate. The solvent was evaporated. Crystallization of the residue from acetone–hexane gave 27.4 g (83%) of buff crystals, mp 140–142°. An analytical sample was prepared by recrystallizing a portion from acetone–hexane, and buff crystals, mp 141–143°, were obtained.

Anal.—Calc. for $C_{15}H_6F_5NO_3$: C, 52.49; H, 1.76; F, 27.68. Found: C, 52.63; H, 1.76; F, 27.99.

***O*-(2,3,4,5,6-Pentafluorobenzyl)hydroxylamine Hydrochloride**—Fifteen grams (0.295 mole) of hydrazine hydrate was added to a suspension of 51.5 g (0.15 mole) of *N*-(2,3,4,5,6-pentafluorobenzyloxy)phthalimide in 87 ml of dimethylformamide and 870 ml of methanol at 60°. The mixture was stirred at ambient temperature for 3 hr and was then acidified to pH 2 by the addition of 2 *N* hydrochloric acid. The phthalylhydrazide was removed by filtration, and the filtrate was evaporated to dryness. The residue was treated with 200 ml of 2 *N* sodium hydroxide solution and extracted with ether (3 × 100 ml).

The combined ether extracts were dried over anhydrous magnesium sulfate, and anhydrous hydrogen chloride was bubbled through the ether solution. The solid which separated was collected by filtration, giving 31.1 g. Crystallization from ethanol gave 21.2 g, and an additional 5.1 g was obtained by concentrating the filtrate. The combined solids were recrystallized from ethanol, giving 20.4 g of white plates, mp 215° (sublimes[2]). An additional 4.2 g of white plates, mp 215° (sublimes[2]), was obtained by concentrating the filtrate. The total yield was 24.6 g (66%).

Anal.—Calc. for $C_7H_4F_5NO{\cdot}HCl$: C, 33.68; H, 2.02; Cl, 14.21; F, 38.06. Found: C, 33.77; H, 2.24; Cl, 14.29; F, 37.38.

[1] Melting points (Thomas Hoover apparatus) are corrected. The IR spectra were recorded on a Perkin-Elmer 241 spectrophotometer. NMR spectra were taken on a Varian A60 instrument. Mass spectra were recorded on a Consolidated Electrodynamics Corp. 21-110B mass spectrometer. The compounds were subjected to IR, NMR, and mass spectrometry, and the results were consistent with structures assigned.

[2] Drying the compound under high vacuum at elevated temperature will result in loss by sublimation.

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New Compounds: Derivatives of Methyl 2-Aminoacetyl-4,5-dimethoxyphenylacetate

P. CATSOULACOS

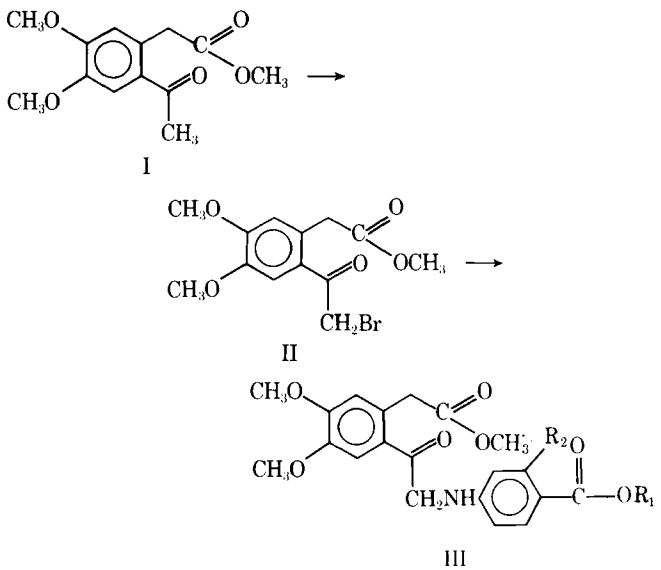
Abstract □ Methyl 2-bromoacetyl-4,5-dimethoxyphenylacetate was prepared by reacting cupric bromide with methyl 2-acetyl-4,5-dimethoxyphenylacetate. Aminoacetyl derivatives formed on condensation of substituted *p*-aminobenzoic esters with the bromoacetyl derivative. Some prepared compounds were tested for local anesthetic and anti-inflammatory activities.

Keyphrases □ 2-Aminoacetyl-4,5-dimethoxyphenylacetate derivatives—synthesized, evaluated for local anesthetic and anti-inflammatory activity □ Anesthetics, local, potential—derivatives of 2-aminoacetyl-4,5-dimethoxyphenylacetate synthesized, evaluated □ Anti-inflammatory agents, potential—derivatives of 2-aminoacetyl-4,5-dimethoxyphenylacetate synthesized, evaluated

In view of the importance of the local anaesthetic activity of α-aminoketone derivatives (1–3), it was decided to condense methyl 2-bromoacetyl-4,5-dimethoxyphenylacetate with esters of *p*-aminobenzoic acid and *p*-aminosalicylic acid.

DISCUSSION

Methyl 2-acetyl-4,5-dimethoxyphenylacetate (I) (4) was halogenated with cupric bromide (5) to give the corresponding bromoacetyl derivative (II) in a 50% yield. Treatment of II with methyl and ethyl esters of *p*-aminobenzoic and *p*-aminosalicylic acid produced the aminoacetyl compounds (III) in good yields (Scheme I).



Scheme I