When 117 mg. of these crystals in 10 ml. of ethanol containing a drop of hydrochloric acid and 50 mg. of prereduced Adam's catalyst was subjected to hydrogenation at room temperature and atmospheric pressure, there was absorbed 99% of the theoretical amount of hydrogen for 4 moles. Isolation of the product as its picrate derivative gave yellow crystals, m.p. 226°, either alone or mixed with an authentic sample of indolizidine picrate.[14]

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Trimethylsilyl Derivatives of Hydroxy Aromatic Acids

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Received September 27, 1956

Organic chemists have used a number of groups or radicals to protect hydroxyl groups in organic compounds from degradation during distillations, hydrolyses, oxidations, reductions, *etc.* Examples of such protecting groups are illustrated by the use of the methyl or acetyl group to protect the hydroxyl groups of carbohydrates during reaction studies involving the acetal or ketal linkages. In contrast to the ease with which such protecting groups are placed in a carbohydrate, the removal of these groups, especially the methyl group, is difficult. In fact, the reaction conditions required for the removal of these protecting groups may often destroy the compounds during the removal reactions.

The trimethylsilyl group has been used as a protecting group for the hydroxyl groups in the methylolphenols,[2] allyloxy-2,4,6-trimethylolbenzene,[3] and the polyols[4] during separations by distillations. The trimethylsilyl derivatives are thermally stable, *i.e.* they can be distilled without decomposition, and have the added advantage of having either the same or a lower boiling point than that of the original hydroxylic compound. The trimethylsilyl group can be removed very easily by hydrolysis at room temperature to give a mixture of the desired compound and hexamethyldisiloxane. The hexamethyldisiloxane and the excess water can be separated by filtration in the case of solid products or can be removed by evaporation at room temperature at a low pressure.

During a recent study of the carbonation of phenol it became necessary to devise a method for the separation of salicylic, 4-hydroxybenzoic, and 4-hydroxyisophthalic acid mixtures. Previously this was accomplished by use of selective solvents. It was desirable to effect this separation by a distillation if possible, but it is known that these acids will decarboxylate if heated at elevated temperatures. The previous experience with trimethylsilyl derivatives in separating thermally unstable compounds indicated that the trimethylsilyl derivatives of these acids would be distillable and would be stable during distillation operations.

The trimethylsilyl derivatives of these acids were prepared by the method outlined by Martin.[2] It is of interest to note that while only one derivative was isolated from 4-hydroxybenzoic acid and 4-hydroxyisophthalic acid, salicylic acid always gave two. Salicylic acid gave 2-trimethylsiloxybenzoic acid and trimethylsilyl 2-trimethylsiloxybenzoate, while 4-hydroxybenzoic acid gave trimethylsilyl 4-trimethylsiloxybenzoate and 4-hydroxyisophthalic acid gave bistrimethylsilyl 4-trimethylsiloxyisophthalate.

In addition to making it possible to separate the phenol carbonation mixture by distillation, these trimethylsilyl derivatives now make it possible to detect and determine the various components of the phenol carbonation mixture. Previously, the analysis of these carbonation mixtures was effected by the determination of the neutral equivalent or by ultraviolet spectroscopy.[5]

The detection and determination of these compounds is aided by several characteristic infrared absorption bands. These bands are tabulated in Table I.

TABLE I

CHARACTERISTIC INFRARED ABSORPTION BANDS

Compound	Absorption Maxima, μ.
2-Trimethylsiloxybenzoic acid	3.18, 5.98, 8.75, 9.15, 9.68, 12.36
Trimethylsilyl 2-trimethylsiloxybenzoate	5.85, 8.66, 8.87, 9.30, 9.63, 10.87
Trimethylsilyl 4-trimethylsiloxybenzoate	5.84, 8.60, 8.94, 9.10, 9.87
Bistrimethylsilyl 4-trimethylsiloxyisophthalate	5.85, 8.74, 8.97, 9.30, 10.67

EXPERIMENTAL

Trimethylsilyl derivatives of salicylic acid. Trimethyl, chlorosilane, 50 g., was added dropwise with stirring to a mixture of 20 g. of salicylic acid in 300 ml. of anhydrous pyridine. The mixture was stirred for an additional 3 hr. at room temperature and filtered in the absence of moisture to free the product of the solid pyridine hydrochloride. The pyridine was stripped from the filtrate and the residue that remained was distilled in the Podbielniak spinning-band column giving 2-trimethylsiloxybenzoic acid, b.p. 62°C. at

(1) Present address: Locomotive & Car Equipment Department, General Electric Co., Erie, Pa.

(2) R. W. Martin, *J. Am. Chem. Soc.*, **74**, 3024 (1952).

(3) C. A. Burkhard, J. V. Schmitz, and R. E. Burnett, *J. Am. Chem. Soc.*, **75**, 5957 (1953).

(4) M. M. Sprung and L. S. Nelson, *J. Org. Chem.* **20**, 1750 (1955).

(5) O. Baine, G. F. Adamson, J. W. Barton, J. L. Fitch, D. R. Swayampati, and H. Jeskey, *J. Org. Chem.* **19**, 510 (1954).

0.95 mm., n_D^{20} 1.5004, and trimethylsilyl 2-trimethylsiloxybenzoate, b.p. 77.5°C. at 1.1 mm., n_D^{20} 1.4788.

Anal. Calcd. for $C_{10}H_{14}O_3Si$: Si, 13.34; sapon. equiv., 210. Found: Si, 13.4; sapon. equiv., 211.

Anal. Calcd. for $C_{13}H_{22}O_3Si_2$: Si, 19.87; sapon. equiv., 282. Found: Si, 19.5; sapon, equiv., 280.

The absorption band at 3.18 μ in the infrared spectrum of the monosubstituted derivative indicated the presence of a free rather than a combined carboxyl group, thus permitting an assignment of the above structure to this derivative.

Trimethylsilyl 4-trimethylsiloxybenzoate. 4-Hydroxybenzoic acid, in contrast to salicylic acid, gave only one derivative, trimethylsilyl 4-trimethylsiloxybenzoate, when it was allowed to react with trimethylchlorosilane under the same conditions used for salicylic acid. The trimethylsilyl 4-trimethylsiloxybenzoate was a water clear liquid, b.p. 82°C. at 0.85 mm., n_D^{20} 1.4838.

Anal. Calcd. for $C_{13}H_{22}O_3Si_2$: Si, 19.87; sapon. equiv., 282. Found: Si, 19.7; sapon. equiv., 274.

Bistrimethylsilyl 4-trimethylsiloxyisophthalate. Bistrimethylsilyl 4-trimethylsiloxyisophthalate was obtained as a viscous water clear liquid by the further distillation of the residue which resulted from the distillation of the trimethylsilylation of the dried carbonation products of phenol in dry pyridine. The preliminary distillation removed the two trimethylsilyl derivatives of salicylic acid. The distillation of the residue gave bistrimethylsilyl 4-trimethylsiloxyisophthalate, b.p. 148–150°C. at 1 mm., n_D^{20} 1.4801.

Anal. Calcd. for $C_{17}H_{30}O_5Si_2$: Si, 21.12; sapon. equiv., 199. Found: Si, 21.0; sapon. equiv., 202.

The structure of this organosilicon derivative was established by hydrolysis giving 4-hydroxyisophthalic acid, m.p. 303°C. (uncorrected), 312° (corrected).

Anal. Calcd. for $C_8H_6O_5$: neutral equiv., 91. Found: neutral equiv., 95.

Acknowledgment. The author wishes to thank Dr. E. L. Simons, Mrs. M. DeVito, Miss M. O. Fragomeni, Mr. C. A. Hirt and Miss B. N. Fey for analytical data.

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Structures Related to Morphine. VII.[1] Piperidine Derivatives and Examples of Failure in Knoevenagel Reaction

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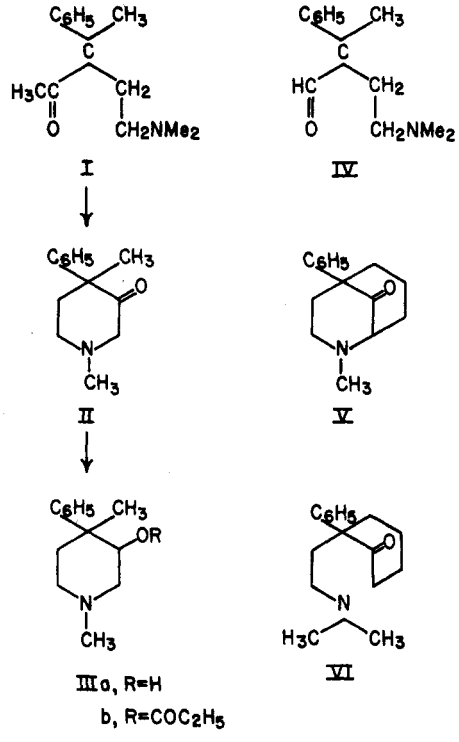
Received September 10, 1956

This note deals principally with the synthesis of α- and β-*dl*-1,4-dimethyl-4-phenyl-3-propionoxypiperidine (IIIb), isomers of *alpha-* and *beta*-prodine[2] in which the positions of the C-methyl and propionoxy groups are reversed. The IIIb diastereoisomers were prepared by the hydrogenation (platinum oxide) of 1,4-dimethyl-4-phenyl-3-piperidone (II)[3] followed by treatment of the resultant alcohol hydrochloride mixture (IIIa) with propionic anhydride in pyridine. A satisfactory separation of the acylated mixture into the IIIb α- and β-racemates could be effected by fractional crystallization. Although a practicable separation of the IIIa hydrochloride mixture was not achieved (chromatographic purification was not attempted), the predominant IIIa racemate[4] was readily obtained pure and in good yield, by conversion of the hydrochloride mixture to the free bases in aqueous ammonium hydroxide.



The results reported in this paper are, in fact, a by-product of another project aimed at the synthesis of 2,5,9-trimethyl-6,7-benzomorphan,[5] a compound which was desired for its potential as an analgesic agent. The sequence of reactions planned for the preparation of this substance (which has now been prepared by another method) involved, at an early stage, the Knoevenagel reaction with 5-dimethylamino-3-methyl-3-phenyl-2-pentanone (I). However, neither I nor its hydrochloride (both of which showed strong carbonyl absorption in the infrared) could be induced to react with either methyl cyanoacetate or malononitrile by

(1) Paper VI, E. L. May, *J. Org. Chem.*, **21**, 899 (1956).

(2) *Alpha*-prodine and *beta*-prodine are international, nonproprietary names for α-*dl*-1,3-dimethyl-4-phenyl-4-propionoxypiperidine and the β-diastereoisomer, respectively, two potent analgesic agents; *cf.* A. Ziering and J. Lee, *J. Org. Chem.*, **12**, 911 (1947) and O. J. Braenden, N. B. Eddy, and Halbach, *Bull. World Health Organization*, **13**, 937(1955).

(3) F. F. Blicke and J. Krapcho, *J. Am. Chem. Soc.*, **74**, 4001 (1952).

(4) This predominant form has been designated as the α-alcohol. Although its configuration has not been established, one might expect the hydroxy to form more readily in a position *trans* (equatorial-equatorial) to the bulkiest (phenyl) adjacent group. The lesser isomer is designated as β.

(5) The corresponding *2,5-dimethyl* analog, E. L. May and J. G. Murphy, *J. Org. Chem.*, **20**, 257 (1955), was moderately effective.