TABLE I

	B. p. 765 mm., °C.	$n^{25}D$	d^{25}_4	$\alpha^{22}D$	$HgCl_2$ complex M. p.	Mixed m. p.
Compound A	187–189	1.4888	0.8830	0.00°	61–63°[a]	61.5–65°[d]
$(CH_3CH{=}CHCH_2)_2S$	186–187[b]	1.4938	0.8873	0.00°	63–65°[c]	

[a] Preliminary sintering at 60.5°. [b] At 766 mm. [c] Preliminary sintering at 62°. [d] Preliminary sintering at 61°.

150°. The failure to achieve complete purification can be attributed to the presence of complexes from isomeric or related sulfides, difficult to remove, as well as to the somewhat unstable character of the complex.

The action (evident within one, and apparently complete after three days) of methyl iodide upon A at 25° yielded crystals of trimethylsulfonium iodide, which after separation from the adhering red oil, were recrystallized from ethanol. The feather-like crystals dissociated to gaseous products at 202–203°—a characteristic of trimethyl sulfonium iodide.[12]

Dicrotyl Sulfide.—This compound,[13] after careful fractionation (b. p. 81° (17 mm.)) gave, with aqueous chloramine-T, *p*-toluenesulfonamide instead of a sulfilimine.[14] With 20% ethanolic mercuric chloride, it yielded an addition compound, as clusters of thin plates which, after recrystallization from warm ethanol, sintered at 62°, melted at 63–65°, became opaque at about 95°, and decomposed at 145–150°, thus paralleling the behavior of the same compound obtained from A of the skunk scent.

(12) Steinkopf and Müller give 203–207°, *Ber.*, **56**, 1926 (1923).

(13) Prepared according to Charon, *Ann. chim.*, [7] **17**, 197 (1899).

(14) Davies and Oxford, *J. Chem. Soc.*, 224 (1931).

Summary

1. No large ring alcohols or ketones of the musk or civet type are present in the scent of the common skunk.

2. Dicrotyl sulfide has been identified as present in the scent.

NEW HAVEN, CONN. RECEIVED NOVEMBER 13, 1944

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF RICHMOND]

Phenylacetates, Diphenylacetates and Phenylalkylacetates of β-Methyl-β-monoalkylaminopropanols[1,2]

BY J. STANTON PIERCE, WALTER W. HADEN AND ROBERT D. GANO

In this Laboratory we have synthesized various aromatic acid esters of β-monoalkylaminoalkanols[3,4,5] in a study of local anesthetics. This paper deals with the synthesis of phenylacetates, phenylalkylacetates and diphenylacetates of β-methyl-β-monoalkylaminopropanols. These alkamine esters are being examined for antispasmodic properties. Several β-monoalkylaminoethyl and β-monoalkylaminobutyl diphenylacetates were prepared but as the hydrochlorides of most of these substances were obtained as oils, these products are not included in this paper.

The β-methyl-β-monoalkylaminopropanols used in this work were prepared by methods previously described.[3,4] The phenylalkylacetic acids were made from phenylacetonitrile by alkylation and hydrolysis. The chlorides from these acids were reacted with the dry hydrochlorides of the amino alcohols. The esters thus formed were purified by modifications of methods previously described.[3,4,5]

Pharmacological tests on these compounds are being carried out by Dr. Charles C. Haskell. The results will be reported elsewhere.

(1) Acknowledgment is made to Dr. E. Emmet Reid, Research Advisor to the Chemistry Department of the University of Richmond, for his advice in this work.

(2) This research was made possible by a grant from Chas. C. Haskell and Co., Inc., Richmond, Va.

(3) J. Stanton Pierce, J. M. Salsbury and J. M. Fredericksen, THIS JOURNAL, **64**, 1691–1694 (1942).

(4) J. Stanton Pierce, J. M. Salsbury, Walter W. Haden and L. H. Willis, *ibid.*, **64**, 2884–2885 (1942).

(5) J. Stanton Pierce, Robert D. Gano and J. M. Lukeman, *ibid.*, not yet published.

Experimental

Phenylethylacetic Acid.[6]—Phenylacetonitrile was alkylated by heating with equimolar quantities of ethyl iodide and sodium hydroxide under reflux at 100, 130 and 165° for approximately two hours at each temperature. The phenylethylacetonitrile formed by this reaction, after the unethylated phenylacetonitrile was removed by treatment with benzaldehyde, was hydrolyzed by heating for forty hours at 155° in a sealed tube with 6 *N* hydrochloric acid, yielding phenylethylacetic acid, boiling at 155–160° at 15 mm.; yield 24%.

Diphenylacetyl Chloride.[7]—In a typical run, 42.5 g. (0.2 mole) of diphenylacetic acid and 95 g. (0.8 mole) of thionyl chloride were heated on an oil-bath at 100° for one and a half hours. The excess thionyl chloride was removed *in vacuo*, several 10-ml. portions of dry benzene being added to remove the last traces. The diphenylacetyl chloride was divided into aliquot portions for reaction with amino alcohol hydrochlorides.

Phenylethylacetyl Chloride.—A mixture of 23.7 g. (0.145 mole) of phenylethylacetic acid and 71 g. (0.6 mole) of thionyl chloride was heated under reflux at 112° for three hours. The excess thionyl chloride was removed *in vacuo* and the phenylethylacetyl chloride, 25 g. (94%), was collected at 112–115° at 15 mm.

Alkamine Ester Hydrochlorides.—β-Methyl-β-monoalkylaminopropyl aryl acetate hydrochlorides were prepared by ester formation between amino alcohol hydrochlorides and acid chlorides by methods described previously.[3,4] In a typical run of 0.05 mole each of β-methyl-β-*n*-amylaminopropanol hydrochloride and diphenylacetyl chloride, the ester was purified as follows: The thick oil remaining in the flask was dissolved in 35 ml. of warm alcohol and the solution poured into 400 ml. of 0.5 *N* sodium hydroxide solution. The oil which separated was dissolved in 100 ml. of isopropyl ether. This solution was washed with 400 ml. of 0.5 *N* sodium hydroxide solution and extracted with 400 ml. of 0.5 *N* hydrochloric acid

(6) K. Neure, *Ann.*, **250**, 151 (1889).

(7) F. Klingemann, *ibid.*, **275**, 81 (1893).

TABLE I[a]

ALKAMINE ESTER HYDROCHLORIDES, $C_6H_5CH(A)COOCH_2C(CH_3)_2NH(B)\cdot HCl$

A	B	Molecular formula	M. p., °C. (uncor.)	Cl analyses, % Calcd.	Found
C_6H_5	*n*-C_3H_7	$C_{21}H_{28}O_2NCl$	158–159	9.80	9.78
C_6H_5	*n*-C_4H_9	$C_{22}H_{30}O_2NCl$	173–174	9.43	9.44
C_6H_5	*n*-C_5H_{11}	$C_{23}H_{32}O_2NCl$	117–118	9.09	9.07
C_6H_5	*n*-C_6H_{13}	$C_{24}H_{34}O_2NCl$	100–101	8.78	8.75
C_6H_5	*i*-C_4H_9	$C_{23}H_{30}O_2NCl$	156–157	9.43	9.44
C_6H_5	*i*-C_5H_{11}	$C_{23}H_{32}O_2NCl$	141–142	9.09	9.12
H	*n*-C_3H_7	$C_{15}H_{24}O_2NCl$	112–113	12.41	12.61
H	*n*-C_4H_9	$C_{16}H_{26}O_2NCl$	126–127	11.83	12.00
C_2H_5	*n*-C_3H_7	$C_{17}H_{28}O_2NCl$	115–116	11.30	11.46
C_2H_5	*n*-C_4H_9	$C_{18}H_{30}O_2NCl$	109–110	10.81	10.96
C_2H_5	*n*-C_5H_{11}	$C_{20}H_{34}O_2NCl$	108–109	9.96	10.21

[a] This table contains only the amino alcohol ester hydrochlorides which were readily purified by recrystallization.

A heavy red oil sank from the ether to the bottom of the aqueous layer. A sample of this oil, on being seeded with crystals of a previous preparation of the hydrochloride of β-methyl-β-mono-*n*-amylaminopropyl diphenylacetate, crystallized within a few minutes. The remainder of the oil and the aqueous layer were made basic with sodium hydroxide solution and extracted with isopropyl ether. Dry hydrogen chloride was passed into the isopropyl ether solution, precipitating a heavy oil, which crystallized within a few minutes, on being seeded. The product, β-methyl-β-mono-*n*-amylaminopropyl diphenylacetate hydrochloride, was purified by recrystallization from acetone and anhydrous ether.

Summary

A series of hydrochlorides of β-methyl-β-monoalkylaminopropyl phenylacetates, diphenylacetates and phenylalkylacetates is described.

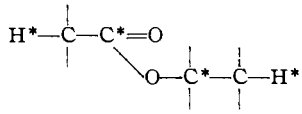
RICHMOND, VA. RECEIVED SEPTEMBER 12, 1944

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

β-Elimination and Other Types of Reaction with Certain β-Phenylethyl Esters and Potassium Amide in Liquid Ammonia

BY CHARLES R. HAUSER, JOSEPH C. SHIVERS AND PHILIP S. SKELL

Although the carbonyl carbon or α-hydrogen in the acyl portion of carboxylic esters generally enters into reaction with bases, the α-carbon or β-hydrogen in the alkoxy portion is also capable of reacting. These four vulnerable positions of esters are indicated by asterisks in the following general formula.



Reactions involving the alkoxy portion of esters would be analogous to those exhibited by alkyl halides. Actually several substitutions at the α-carbon, in which the carboxylate group of the ester is replaced by the attacking base, have been observed.[1] β-Elimination, which involves the removal of the β-hydrogen as a proton accompanied by the release of the carboxylate ion to form an olefin,[2] has apparently not been observed with esters of simple aliphatic alcohols, although olefins are produced on pyrolysis of certain of these esters.[3] With esters of alcohols having sufficiently activated β-hydrogens, however, β-elimination is readily effected by bases. β-Nitroethyl acetate, for example, forms nitroethylene even in the presence of bicarbonate.[4]

$$CH_3COO{-}CH_2CH_2NO_2 \longrightarrow CH_3COOH + CH_2{=}CHNO_2$$

In the present investigation β-elimination has been realized with certain β-phenylalkyl esters and potassium amide in liquid ammonia.

Although β-phenylethyl benzoate exhibits with potassium amide the carbonyl carbon reaction to form benzamide and β-phenylethyl alcohol, β-phenylethyl mesitoate in which the carbonyl group is hindered undergoes mainly β-elimination to form styrene and mesitoic acid.[5]

$$C_6H_5CO_2CH_2CH_2C_6H_5 \xrightarrow{^-NH_2} C_6H_5CONH_2 + C_6H_5CH_2CH_2OH$$

$$Mes\text{-}CO_2CH_2CH_2C_6H_5 \xrightarrow{^-NH_2} Mes\text{-}COOH + C_6H_5CH{=}CH_2$$

(1) These include the reaction of methyl benzoate with sodium methoxide to form dimethyl ether [Adickes, *Ber.*, **66**, 1904 (1933); Magnani and McElvain, THIS JOURNAL, **60**, 813 (1938)], the reaction of dimethyl, diethyl or dibutyl phthalate with sodium phenoxide to form the corresponding alkyl phenyl ether [King and Wright, *J. Chem. Soc.*, 1168 (1939)], the reaction of methyl benzoate or acetate with trimethylamine to form the tetramethylammonium ion [Willstätter and Kahn, *Ber.*, **35**, 2757 (1902); Hammett and Pfluger, THIS JOURNAL, **55**, 4079 (1933)], the alkylation of mono-substituted malonic esters with diethyl carbonate to form di-substituted malonic esters [Wallingford and Jones, *ibid.*, **64**, 578 (1942)] and the so-called abnormal acetoacetic ester reaction of benzyl or allyl acetate in the presence of sodium to form the ester of β-phenylpropionic or allylacetic acid [Tseou and Wang, *J. Chinese Chem. Soc.*, **5**, 224 (1937); Bacon, *Am. Chem. J.*, **33**, 68 (1905)]. In the latter reaction the ester anion is assumed to be formed as in the ordinary acetoacetic ester reaction, but, instead of being acylated, it is alkylated by unchanged ester molecules.

(2) The elimination reaction to form nitriles instead of olefins is common with esters of aldoximes, for example, aldoxime acetates, especially the anti isomers, the reaction being effected by tertiary amines or alkali: see Hauser and Jordan, THIS JOURNAL, **57**, 2450 (1935); Vermillion and Hauser, *ibid.*, **63**, 1227 (1941); Vermillion and Hauser, *J. Org. Chem.*, **6**, 510 (1941).

(3) See Hurd "Pyrolysis of Carbon Compounds," Chemical Catalog Co., New York, N. Y., 1929, pp. 529–531; Norris and Rigby, THIS JOURNAL, **54**, 2097 (1932).

(4) Schmidt and Rutz, *Ber.*, **61**, 2142 (1928); Hass and Riley, *Chem. Rev.*, **32**, 408, 411 (1943).

(5) β-Elimination was realized also with β-phenyl-*n*-butyl mesitoate (b. p. 176° at 3 mm.) but with this ester, in which the β-hydrogen is somewhat deactivated by the β-ethyl group, the carbonyl carbon reaction predominated. With excess potassium amide in liquid ammonia, the products were mesitamide (61%), mesitoic acid (20%) and an unsaturated neutral substance which appeared to be the olefin