A solution of 36.6 ml. (0.2 mole) of the fluorosilane and 63.5 ml. (0.5 mole) of trimethylchlorosilane was refluxed for three hours under a small fractionating column, equipped with a Dry Ice trap. Only traces of trimethylfluorosilane, b. p. 17°, were obtained. The addition of 1 g. of aluminum chloride still yielded only small amounts of product. However, when the temperature of the reaction mixture was raised by distilling about 75% of the trimethylchlorosilane, appreciable quantities of trimethylfluorosilane began to condense in the trap. The distilled trimethylchlorosilane was returned to the reaction mixture flask in small portions, keeping the take-off temperature below 30°. Distillation at reduced pressure yielded two compounds: A, b. p. 71–72° (50 mm.), 9.6 g.; B, b. p. 95–96° (50 mm.), 18.7 g. Fraction A is $F\mathbf{D}CH_2\mathbf{D}Cl$, 26% yield.

Anal. Calcd. for $C_5H_{14}Si_2FCl$: Cl, 19.20. Found: Cl, 19.0, 18.9.

Fraction B is $Cl\mathbf{D}CH_2\mathbf{D}Cl$, 47% yield, $n^{20}\text{D}$ 1.4480, $d^{20}{}_4$ 1.016, *MR*D (calcd.) 53.10, (fd.) 53.01.

Anal. Calcd. for $C_5H_{14}Si_2Cl_2$: Cl, 35.22. Found: Cl, 35.14.

The mixed chlorofluorosilane disproportionates into the dichloro and the difluoro-silane when distilled at atmospheric pressure.

Discussion

Of the silmethylene–siloxane compounds isolated in the above experiments, only $\mathbf{MOD}CH_2\mathbf{D}CH_2\mathbf{DOM}$ and $(\mathbf{MOD}CH_2\mathbf{D})_2O$ could have been formed as direct products of the synthetic method employed. The compound, $\mathbf{MOD}CH_2\mathbf{DOM}$, must have resulted from siloxane rearrangements either during the course of the Grignard reaction or during the hydrolysis of the products thereof. To explain the presence of $\mathbf{MOD}CH_2\mathbf{M}$, it is necessary to assume that the Grignard reagent, $\mathbf{MOD}CH_2MgCl$, reacted with Si–O bonds present in the reaction mixture,[11] possibly according to the equation

$$\mathbf{MOD}CH_2MgCl + \mathbf{MOD}CH_2Cl \longrightarrow \mathbf{MOD}CH_2\mathbf{M} + ClMgO\mathbf{D}CH_2Cl$$

An analysis of the physical properties of the silmethylenesiloxanes prepared in this Laboratory and the compounds prepared by Sommer, *et al.*,[4] shows that the substitution of a methylene group for an oxygen atom between two silicons results in the following changes in the physical properties of the lower members of the series: (1) an increase in the boiling point of 20–30°, (2) a lowering of the density by about 0.01 g./cc., and (3) an increase in the refractive index by 0.02–0.03. The introduction of a second silmethylene group has a somewhat smaller effect.

Chemically, the disilmethylene group is shown to be quite stable. During the course of this work, compounds containing this grouping have been subjected to treatment with cold concentrated sulfuric acid, gaseous, anhydrous hydrogen fluoride and aqueous, boiling potassium hydroxide with no apparent deleterious effects. They are somewhat susceptible to oxygen at elevated temperatures; one of the oxidation products is formaldehyde. Their thermal stability is, however, quite good in the absence of oxygen.

The investigation of other derivatives and of higher members of this interesting series of compounds is being continued.

Acknowledgment.—The author wishes to express his thanks to Dr. R. O. Sauer for his advice and interest in this work and to Mr. L. B. Bronk and Miss M. L. Caldwell for the analyses reported herein.

Summary

1. Organosilicon compounds, containing di- and tri-silmethylene linkages, have been prepared; and their chemical and physical properties have been investigated.

2. The use of hydrogen fluoride and concentrated sulfuric acid to convert complex siloxanes to fluorosilanes has led to the synthesis of two new organofluorosilanes.

3. Organofluorosilanes have been shown to undergo "halogen interchange" with trimethylchlorosilane.

SCHENECTADY, NEW YORK RECEIVED DECEMBER 31, 1947

[CONTRIBUTION FROM THE CHEMISTRY LABORATORIES OF WASHINGTON SQUARE COLLEGE OF NEW YORK UNIVERSITY]

Nitrogen Analogs of Hexestrol.[1] The Synthesis of N,N′-Dimethyl-α,α′-bis-(4-hydroxyphenyl)-ethylenediamine and Derivatives

BY JOSEPH B. NIEDERL AND MARTIN I. DEXTER[2]

Intramolecular synchronization of molecular groupings possessing *a priori* divergent physiological properties, were extended to the hexestrol series. It was surmised that by replacing carbon atoms in the aliphatic portion of the hexestrol structure by nitrogen, compounds exhibiting interesting pressor action, or estrogenic activity, or both, might result. In the present paper account is given of the first of these types of compounds, namely, the N,N-dimethyl-α,α′-bis-(4-hydroxyphenyl)-ethylenediamine, a compound which incorporates the physiologically active phenylethylamine grouping into the hexestrol structure. The synthesis of this compound, from anisaldehyde as the starting material, involved the Decker and Becker[3] methylation procedure of the intermediate di-anisal derivative of the substituted ethylenediamine, in addition to conventional

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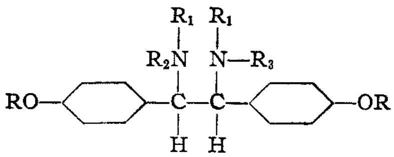
[1] Presented before the Division of Organic Chemistry of the American Chemical Society, Chicago, Ill., April 19–23, 1948.

[2] This paper has been abstracted from a portion of the thesis presented by Martin I. Dexter to the faculty of the Graduate School of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[3] Fischer and Prause, *J. prakt. Chem.*, [2] **77**, 130 (1908).

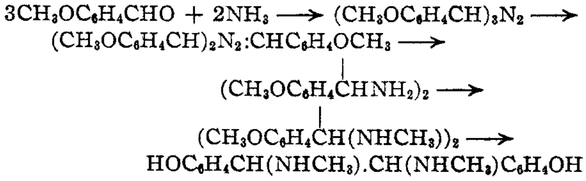
TABLE I



R	R₁	R₂	R₃	Procedure	Dec. pt.,[a] °C.	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
CH_3	CH_3	H	H	B	145[b]	$C_{18}H_{24}N_2O_2$	9.33	9.38
		Hydrochloride		H	273	$C_{18}H_{26}O_2N_2Cl_2$	7.52	7.41
		Hydriodide		H	260	$C_{18}H_{26}O_2N_2I_2$	5.03	5.05
CH_3	CH_3	$COCH_3$	$COCH_3$	J, P	218[b]	$C_{22}H_{28}O_4N_2$	7.29	7.17
CH_3	CH_3	NO	NO	D	238	$C_{18}H_{22}O_4N_4$	15.64	15.72
H	CH_3	H	H	F	183	$C_{16}H_{20}O_2N_2$	10.29	10.02
		Hydrochloride		G	269	$C_{16}H_{22}O_2N_2Cl_2$	8.13	7.84
		Hydrobromide		E	272	$C_{16}H_{22}O_2N_2Br_2$	6.49	6.50
		Hydriodide		G	278	$C_{16}H_{22}O_2N_2I_2$	5.30	5.30
H	CH_3	$COCH_3$	$COCH_3$	O	331	$C_{20}H_{24}O_4N_2$	7.87	7.89
$COCH_3$	CH_3	$COCH_3$	$COCH_3$	N	257[b]	$C_{24}H_{28}O_6N_2$	6.36	6.25
CH_3	Dianisal			3	180[b]			
	Methiodide			A	230	$C_{34}H_{38}O_4N_2I_2$	3.53	3.35
CH_3	H	$COCH_2Cl$	$COCH_2Cl$	K	286	$C_{20}H_{22}O_4N_2Cl_2$	6.60	6.58
CH_3	H	$SO_2C_6H_5$	$SO_2C_6H_5$	L	280	$C_{28}H_{28}O_6N_2S_2$	5.07	4.96
H	H	H	H	F	205	$C_{14}H_{16}O_2N_2$	11.47	11.52
		Hydrochloride		G	306	$C_{14}H_{18}O_2N_2Cl_2$	8.86	8.74
		Hydrobromide		E	323	$C_{14}H_{18}O_2N_2Br_2$	6.90	6.64
		Hydriodide		G	301	$C_{14}H_{18}O_2N_2I_2$	5.60	5.50
$COCH_3$	H	$COCH_3$	$COCH_3$	M	350	$C_{22}H_{24}O_6N_2$	6.79	6.71
CH_3	H	CH_3	H	C	94[b]	$C_{17}H_{22}O_2N_2$	9.76	9.57
CH_3	$COCH_3$	CH_3	H	I	250[b]	$C_{21}H_{24}O_4N_2$	7.57	7.32
H	H	CH_3	H					
		Hydriodide		E	259	$C_{15}H_{20}O_2N_2I_2$	5.44	5.31

[a] The thermometer readings are all uncorrected. The decomposition points in this series of compounds are very dependent on the rate of heating. The capillary containing the compound was inserted into the melting point bath 10° below the decomposition point. The rate of heating was 20° per minute. [b] Melting point.

procedures. The entire synthesis may be schematically illustrated as given



$$3CH_3OC_6H_4CHO + 2NH_3 \longrightarrow (CH_3OC_6H_4CH)_3N_2 \longrightarrow (CH_3OC_6H_4CH)_2N_2{:}CHC_6H_4OCH_3 \longrightarrow (CH_3OC_6H_4CHNH_2)_2 \longrightarrow (CH_3OC_6H_4CH(NHCH_3))_2 \longrightarrow HOC_6H_4CH(NHCH_3).CH(NHCH_3)C_6H_4OH$$

Experimental

A. N,N'-Dianisal-α,α'-bis-(4-methoxyphenyl)-ethylenediamine Dimethiodide.—Two grams of N,N'-dianisal-α,α'-bis-(4-methoxyphenyl)-ethylenediamine[3] was sealed in a glass tube with 7 g. of methyl iodide and heated for ten hours in a boiling water-bath. After cooling, the tube was opened, and the crystalline product was filtered and washed with alcohol. The yield was 2.27 g.

B. N,N'-Dimethyl-α,α'-bis-(4-methoxyphenyl)-ethylenediamine.—A suspension of 2.27 g. of the above quaternary ammonium salt in 25 cc. of water was boiled in a beaker on a hot-plate. The volume was kept constant by the addition of water. After thirty minutes, the solution was cooled and extracted with ether. The aqueous phase was then made strongly alkaline with sodium hydroxide. The crystalline base was filtered and air-dried. The dry material was dissolved in toluene and clarified with charcoal. Upon removal of the solvent by vacuum distillation, 1.3 g. of the base was obtained. The product was crystallized from toluene–petroleum ether without change in melting point.

C. N-Methyl-α,α'-bis-(4-methoxyphenyl)-ethylenediamine.—The mother liquor from the crystalline quaternary ammonium salt was combined with the alcoholic wash liquors and hydrolyzed as above. The yield was 0.120 g. after crystallization from toluene–petroleum ether.

D. N,N'-Dimethyl-N,N'-dinitroso-α,α'-bis-(4-methoxyphenyl)-ethylenediamine.—A solution of 0.100 g. of N,N'-dimethyl-α,α'-bis-(4-methoxyphenyl)-ethylenediamine in water was prepared with the aid of an excess of dilute sulfuric acid. Upon the addition of sodium nitrite solution, the dinitroso derivative precipitated. The product was filtered, washed with water and crystallized from acetone–water mixture. The yield was 0.100 g.

E. Dimethylation from the Phenolic Ethers.—A suspension of 0.200 g. of the methyl ether was refluxed with 5 cc. of 48% hydrobromic acid for four hours. After cooling, the hydrobromide was filtered from the solution. The product was purified by dissolving in 10 cc. of warm water, clarifying with charcoal and precipitating by the addition of 4 cc. of 48% hydrobromic acid. The crystals were washed with alcohol followed by ether. Hydriodic acid was used instead of hydrobromic acid for the preparation of N-methyl-α,α'-bis-(4-hydroxyphenyl)-ethylenediamine dihydriodide. The yields were over 90%.

F. Free Base of the Aminophenols.—The bases of the aminophenols were obtained from their salts by dissolving them in water and adding sufficient aqueous ammonia to make the solution alkaline to phenolphthalein. The crystalline bases were filtered and washed with water and alcohol.

G. Salts of Aminophenols.—The salts were obtained by treating the free bases with an excess of aqueous halogen acid. They were purified by dissolving in warm water and precipitated by the addition of more acid. The salts were filtered and washed with alcohol followed by ether.

H. Salts of the Amines of Phenolic Ethers.—The free amines were dissolved in alcohol, and the halogen salts were precipitated by the addition of an aqueous solution of the appropriate acid. The salts, after filtration, were washed with alcohol followed by ether.

I. **N-Methyl-N,N′-diacetyl-α,α′-bis-(4-methoxyphenyl)-ethylenediamine.**—This product was prepared by refluxing 0.050 g. of the amine with 1 cc. of acetic anhydride for one hour. After cooling, the crystalline precipitate was filtered and washed with ether. The yield was 0.050 g.

J. **N,N′-Dimethyl-N,N′-diacetyl-α,α′-bis-(4-methoxyphenyl)-ethylenediamine.**—A solution of 0.050 g. of the amine was refluxed in 1 cc. of acetic anhydride for one hour. The solvent was removed by distillation *in vacuo*, and the residue was crystallized from toluene–petroleum ether. The yield was 0.055 g.

K. **N,N′-Dichloroacetyl-α,α′-bis-(4-methoxyphenyl)-ethylenediamine.**—A mixture of 0.091 g. of α,α′-bis-(4-methoxyphenyl)-ethylenediamine, 0.114 g. of chloroacetic anhydride and 10 cc. of toluene was refluxed for two hours. The yield was 0.124 g.

L. **N,N′-Dibenzenesulfonyl-α,α′-bis-(4-methoxyphenyl)-ethylenediamine.**—Benzenesulfonyl chloride (0.14 g.), α,α′-bis-(4-methoxyphenyl)-ethylenediamine[3] (0.091 g.) and 0.5 cc. of pyridine was heated on a steam-bath for two hours. After diluting the reaction mixture with water, the product was filtered and washed with alcohol and ether. The yield was 0.161 g. The product was insoluble in dilute sodium hydroxide.

M. **N,N′-Diacetyl-α,α′-bis-(4-acetoxyphenyl)-ethylenediamine.**—A mixture of 0.150 g. of α,α′-bis-(4-hydroxyphenyl)-ethylenediamine, 15 cc. of acetic anhydride and 1 cc. of pyridine was refluxed for two hours. After cooling, the tetra-acetyl derivative was filtered and washed with ether. The yield was 0.184 g. Recrystallization from glacial acetic acid did not change the decomposition point.

N. **N,N′-Dimethyl-N,N′-diacetyl-α,α′-bis-(4-acetoxyphenyl)-ethylenediamine.**—N,N′-Dimethyl-α,α′-bis-(4-hydroxyphenyl)-ethylenediamine (0.140 g.) was refluxed with 35 cc. of acetic anhydride for one hour and fifteen minutes, during which time the solids dissolved completely. The solution was then concentrated *in vacuo* and the residue crystallized from toluene–petroleum ether. The yield was 0.180 g.

O. **N,N′-Dimethyl-N,N′-diacetyl-α,α′-bis-(4-hydroxyphenyl)-ethylenediamine.**—A suspension of 0.200 g. of N,N′-dimethyl-N,N′-diacetyl-α,α′-bis-(4-acetoxyphenyl)-ethylenediamine in 5 cc. of 1 *N* sodium hydroxide was warmed until solution of the solids was complete. The phenol was then precipitated by bubbling carbon dioxide into the alkaline solution. The crystalline phenol was then filtered and washed with water and alcohol. The yield was 0.160 g.

P. **N,N′-Dimethyl-N,N′-diacetyl-α,α′-bis-(4-methoxyphenyl)-ethylenediamine.**—A solution of the above phenol (0.06 g.) was dissolved in an excess of 10% sodium hydroxide and shaken with a few drops of methyl sulfate. The crude methyl ether was then filtered and crystallized from alcohol–water solution. The yield was 0.050 g., m. p. 218–219°. This melting point was identical with that obtained from the acetylation of N,N′-dimethyl-α,α′-bis-(4-methoxyphenyl)-ethylenediamine. The mixed melting point showed no depression. This would indicate the structure of the methyl ether remained intact save for the removal of the methyl groups during hydrolysis with hydrobromic acid.

Physiology.—The hydrochlorides of N,N′-dimethyl-α,α′-bis-(4-hydroxyphenyl)-ethylenediamine (I) and its methyl ether (II) were tested for estrogenic activity and effect on blood pressure. (I) and (II) were inactive as estrogens up to 100 γ doses. Compounds (I), (II) and ephedrine sulfate (III) were tested for effect on blood pressure by intravenous administration to dogs. The table shows some of the results:

	I	II	III
Dose[a]	4	4	0.25
B. pr.[b]	122	122	122
B. pr.[c]	−2, 13	−22, 6	18
t[d]	0.25, 8.0	0.50, 3.0	10.0

[a] In mg. per kgm. [b] Blood pressure before injection in mm. [c] Change in blood pressure in mm. [d] Duration of change in minutes.

Acknowledgment.—The authors desire to express their appreciation to Dr. F. E. Stirn, Dr. B. K. Harned and Mr. Robert Vessey of the Lederle Laboratories, Pearl River, N. Y., for the physiological results.

Summary

A series of derivatives of α,α′-bis-(4-hydroxyphenyl)-ethylenediamine has been prepared and characterized.

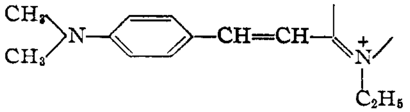
NEW YORK, N. Y. RECEIVED MARCH 15, 1948

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

Bridge Substituted Hemicyanines

BY NORMAN PICUS[1] AND PAUL E. SPOERRI

One of the important types of cyanine dyes used as photographic sensitizers is the hemicyanines or *p*-dimethylaminostyryl[2] type of dye (I). Many compounds of this type have been prepared by the condensation of *p*-dimethylaminobenzaldehyde with quaternary salts of α-methyl-N-heterocyclics.[3] Hemicyanines containing longer methylidyne bridges have been prepared by the condensation of the respective aldehyde and heterocyclic salt.[4] The reaction of a heterocyclic salt



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[1] From a thesis submitted in partial fulfillment of the requirements for the degree of M.S. in Chemistry.

[2] Although the term, hemicyanine, was not originated to include the *p*-dimethylaminostyryl type of dye, C. E. K. Mees in "The Theory of the Photographic Process," The Macmillan Co., New York, N. Y., 1946, p. 1034, indicates that this term may well be used to include this general type of dyestuff.

[3] L. G. S. Brooker and co-workers, THIS JOURNAL, **67**, 1875 (1945).

[4] W. König and O. Treichel, *J. prakt. Chem.*, **102**, 63 (1921).