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WADC TECHNICAL REPORT 59-151
PART I

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RESEARCH ON SYNTHESIS OF CHEMICAL INTERMEDIATES FOR HIGH TEMPERATURE FLUIDS AND POLYMERS

D58

Robert E. Jones
John D. Garber
Samuel A. Robinson
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George Gal

Merck Sharp & Dohme Research Laboratories

SEPTEMBER 1959

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WRIGHT AIR DEVELOPMENT CENTER

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NOTICES

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SEPTEMBER 1959

Materials Laboratory
Contract No. AF 33(616)-5329
Project No. 1428

WRIGHT AIR DEVELOPMENT CENTER
AIR RESEARCH AND DEVELOPMENT COMMAND
UNITED STATES AIR FORCE
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

400 – October 1959 – 8-257

FOREWORD

This report was prepared by the Merck Sharp & Dohme Research Laboratories under USAF Contract No. AF 33(616)-5329. This contract was initiated under Project No. 1428, "Secondary Power Components and Materials", Task No. 73313, "Hydraulic Fluids". The work was administered under the direction of the Materials Laboratory, Directorate of Laboratories, Wright Air Development Center, with Mr. George Moore acting as project engineer.

This report covers work conducted from July 1, 1957 to March 1, 1959.

This work was carried on in the Merck Sharp & Dohme Research Laboratories under the direction of Dr. Karl Pfister III, Executive Director of Developmental Research.

ABSTRACT

This report covers the preparation of a wide variety of chemical intermediates required for the preparation of high temperature fluids and polymers. The intermediates prepared include organosilanes, chlorotriazines, haloalkanes, amino and nitroaryl ethers, an ester, a phosphonitrilic halide and a tetra substituted urea. The experimental procedures used were adapted from published research on related materials. Reaction conditions and analysis of desired products are given.

PUBLICATION REVIEW

This report has been reviewed and is approved.

FOR THE COMMANDER:

A. M. Lovelace

A. M. LOVELACE
Chief, Polymer Branch
Non-Metallic Materials Division

TABLE OF CONTENTS

Dimethyl-α,α'-dimethylenepimelate(1)

A. Tetramethylpentanecarboxylate

Dimethyl malonate was redistilled (178 - 182°C./760 mm.; 80% recovery; n_D^{25} 1.4127) and 990 g. (7.50 moles) was added to a solution of 1.5 moles freshly cut sodium metal in 700 ml. anhydrous methanol. The sodium addition was done with good agitation at 5 - 15°C. This addition was accomplished in 1 1/2 - 2 hrs. and was followed by heating under reflux for 2 1/2 hours.

With reflux continuing very gently, 0.75 moles of distilled 1,3-dibromopropane (163 - 168°C./760 mm.; n_D^{25} 1.5180) was added over a period of 6 hours. This addition time was somewhat critical. A suspension of sodium bromide appeared after about one-half of the dibromopropane had been added. The reflux was continued for 16 hours after dibromopropane addition was completed.

The solvent (methanol) was removed on a water aspirator and steam bath, and the residue was washed with 300 ml. of water containing 25 drops of concentrated sulfuric acid and with 100 ml. of saturated sodium chloride solution. The organic layer was dried over magnesium sulfate.

The residue was fractionally distilled under vacuum as follows:

Cut	Pressure	Vapor	Remarks
1	24 mm.	35 - 80°C.	Two layers. The lower layer being crude dimethyl malonate.
2	24 mm.	85 - 95°C.	Recovered dimethyl malonate; n_D^{25} 1.4140
3	0.15 mm.	60 - 130°C.	Intermediate material.
4	0.15 mm.	130 - 160°C.	White solid product; m.p. 41 - 42°C. Yield: 63 - 67%

Manuscript released by authors 29 May 1959 for publication as a WADC Technical Report.

B. Dimethyl-α,α'-dicarboxypimelate

Two and eighteen hundredths moles of above tetramethyl ester was heated under reflux for 5 1/2 hrs. in a solution of 4.36 moles of potassium hydroxide in 2620 ml. of anhydrous methanol. The solvent was removed under vacuum and the residue was dissolved in 4700 ml. of water; this solution was extracted with 725 ml. of ether to remove unhydrolyzed tetramethyl ester.

The aqueous layer was placed in a suitable 3-necked flask fitted with a stirrer and two addition funnels and cooled (while stirring) to -5 to 0°C. Then, with rather slow agitation, 373 ml. of concentrated hydrochloric acid and 1300 ml. of ether were added simultaneously. The layers were separated, the aqueous layer extracted with 3 x 650 ml. of ether, the ether extract was dried over sodium sulfate, and the ether was removed under vacuum.

Yield: ~ 100%

M.P.: 100 - 112°C. (Further purification not necessary)

C. Dimethyl-α,α'-dimethylenepimelate

The above dimethyl-α,α'-dicarboxypimelate was dissolved in 3 1/2 volumes of water and, at 5-10°C., gaseous dimethylamine was bubbled in until the pH was 9-10. Then, 1.15 weight ratio (based on the weight of dicarboxypimelate) of 37% formaldehyde solution was added in about 1/2 - 1 hour. The resulting solution was heated under gentle reflux (complete solution at about 87°C.) for 4 hrs. and cooled to room temperature. It was then extracted with 1.95 volumes of petroleum naphtha (30 - 60°C., b.p.; volume ratio figured on weight of starting diester-diacid). The petroleum naphtha solution was chilled at -10°C. overnight.

The product was filtered and washed with a small amount of cold petroleum naphtha, and was dried.

Yield: 30%

M.P.: 32 - 33°C.

Table of Results

Product	Yield	B.P. and/or M.P.	Analysis		
				Calc.	Found
Tetra-ester	65%	160 - 170°C./.2 mm. m.p. 41 - 42°C.	C:	51.35	51.78
			H:	6.59	6.46
			I.R. Ester carbonyl at 5.7 - 5.8 μ		
Tetra-ester	63.3%	130 - 160°C./.15 mm. m.p. 41 - 42°C.	C:	51.35	51.47
			H:	6.59	6.37
			I.R. Ester carbonyl at 5.7 5.8 μ		
Tetra-ester	77.5%	120 - 160°C./.15 mm. m.p. 41 - 42°C.	--		
Tetra-ester	81.5%	130 - 160°C./.2 mm.	--		
Diester-diacid	107% (crude)	--	C:	47.9	48.11
			H:	5.84	5.90
			I.R. Ester carbonyl		
Diester-diacid	100%	--	--		
Diester-diacid	94.5%	--	--		
Diester-diacid	100%	--	--		
Dimethyl-α,α'-dimethylene-pimelate	30.5%	m.p. 32 - 33°C.	C:	62.2	61.52
			H:	7.61	7.42
			I.R. Ester carbonyl at 5.79 - 5.85 μ; C = C at 6.04 μ No-OH		
Dimethylene-pimelate	29.5%	m.p. 31 - 32.2°C.	C:	62.2	62.05
			H:	7.61	7.53

Table of Results

Product	Yield	B.P. and/or M.P.	Analysis		
				Calc.	Found
Dimethylene-pimelate	27.3%	m.p. 31 - 32.3°C.	C:	62.2	62.63
			H:	7.61	7.24
Dimethylene-pimelate	29.5%	m.p. 31 - 32°C.	--		
Dimethylene-pimelate	--	--	C:	62.2	61.85
			H:	7.61	7.40
			I.R. -COOR, C = C, No -OH		

Tridodecyl-Bromo-Silane(2)

A. Tridodecyl-magnesium bromide

One hundred forty-five grams (6.05 M.) of magnesium turnings was suspended in 375 ml. of anhydrous ethyl ether in a 5-liter, 3-necked round-bottom flask, fitted with a Hershberg stirrer, a long condenser, a nitrogen inlet tube, and an addition funnel. The system was flushed with dry nitrogen and to the magnesium was slowly added (over 3 1/2 hrs.), 1386 g. (5.56 M.) n-dodecyl bromide in 2600 ml. of ether. At this rate, the ether refluxed gently. A few crystals of iodine were added to get the reaction started, and the agitation was maintained at a vigorous rate. The dark, opaque, solution was aged for two hrs.

B. Tridodecyl-silane

To this Grignard reagent was added slowly, 1.45 M., 196.9 g. of trichloro-silane (very exothermic). After completion of this addition, the light grey reaction mixture was held under gentle reflux overnight.

The reaction mixture was poured into shaved ice with stirring and neutralized with about 450 ml. of 2.5N hydrochloric acid. The layers were separated, the ether layer was dried over sodium sulfate, and the solvent removed.

Yield: 110 - 125% by weight (crude).

C. Tridodecyl Bromosilane

The crude tridodecyl silane was dissolved in 0.3 volume of dry carbon tetrachloride and cooled to -5 to 0°C. With excellent agitation and intermittent cooling, (236.5 g., 1.48 M.) bromine was added at a rate so as to maintain the temperature at -5 to 0°C. After the addition was completed, the reaction mixture was heated on a steam bath for about one hour, after which the solvent was removed, leaving the crude product.

Yield: 127%

n_D^{25} : 1.4588

d : 0.905

The distillation of this bromo-silane compound should be done under conditions which allow a dry atmosphere to be "bled" into distillation apparatus whenever the vacuum is to be vented to change receivers, etc. Otherwise, the product comes out light yellow, whereas it should be colorless. Furthermore, the "break" between the product cut and the preceeding tetracontane cut should not be made before the vapor temperature reaches 244°C. at 0.035 mm.

A sample distillation is as follows:

Cut	Pressure	Vapor	Remarks
1	0.025 mm.	27-40°C.	Colorless liquid n_D^{25}: 1.4205 d : 0.75 g./ml. By analysis this is n-dodecane. About 13% of charge.
2	0.025 mm.	160-171°C.	7.5% of charge of a mixture of solid and liquid. Filtered under nitrogen: Solid: 20% of cut; m.p. 44-45°C. Filtrate: 80% of cut; n_D^{25}: 1.4662; d : 0.915 g./ml.
3	0.025 mm.	220-240°C.	67% of charge; light yellow liquid. n_D^{25}: 1.4677 d : 0.914 g./ml. MR (obs): 186.96 MR(calc): 189.95

Cuts 3 and the filtrate from cut 2 were combined and redistilled.

Cut	Pressure	Vapor	Remarks
1	0.035 mm.	< 240°C.	27% of this charge of light yellow liquid.
2 Final product for delivery	0.035 mm.	244-248°C.	n_D^{25}: 1.4681 d : 0.916 MR (obs): 186.7 MR(calc): 184.95

	Calc.	Found	I.R.: No Si-H or Si-OH bands
C:	70.3	71.02	
H:	12.28	12.47	
Br:	13.01	12.97	

Two series of runs were made as described here, and 930 g. of product was delivered.

1,1,1-Trifluoro-3-bromopropane(3)

A. 1,1-Difluoro-1,3-dibromopropane

A 3.3-liter autoclave in an isolated area was used for these reactions. It was mounted on a rocker with heating device, thermocouples, pressure gauge, a line for pressurizing with ethylene, and a vent. The unit was fitted for operation by remote control through a steel wall.

In representative runs, 1450 g. (6.9 M.) of dibromodifluoromethane (Freon-12 B_2) was charged into the bomb along with 22.5 g. of benzoyl peroxide. The bomb was then closed, and the system was pressurized with ethylene to 400 - 500 p.s.i. with shaking, shaking was continued, and the contents slowly heated to 78 - 82°; this usually required 30 - 40 minutes. In all runs but one, after holding at this temperature and shaking for 5 -10 min., there was a rapid "flash" of pressure from about 750 - 800 p.s.i. to 1125 - 1250 p.s.i. A concurrent sharp rise in temperature from 82° to 115°C. within two minutes was observed. (The rapid pressure increase took place in only a few seconds.) After the above vigorous spot in the reaction, the temperature returned to 80 - 82° and the bomb was shaken at this temperature for 3 - 4 hours.

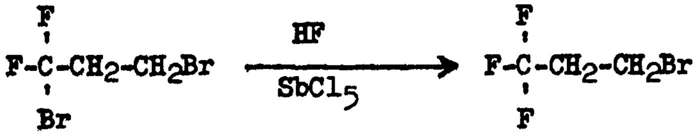
In the one exceptional run noted above, where the rapid pressure-temperature "flash" was not noted, the pressure of the ethylene tank only allowed pressurization to 320 p.s.i. (at room temperature). This system, on heating (with shaking) to 78°C., increased in pressure to 570 p.s.i. and then slowly dropped to 250 p.s.i. This run, while not rechecked, probably represents a better way to operate in that: a) the lack of pressure "flash" seems safer and b) the distilled product was obtained in 41.4% yield, in contrast to the lower yields on other runs.

In general, the batch from the autoclave was stirred for 1 hr. at 5 - 10°C. with 10% (by volume) of 10% NaOH. Peroxide tests were then negative. The layers were separated and the organic layer was washed with saturated sodium chloride solution, dried over Na_2SO_4, filtered, and washed with cold Freon-12 B_2. The organic layer was distilled at atmospheric pressure to recover Freon-12 B_2 (27 - 30°C. b.p.) until no more came over; the pressure was gradually reduced to 86 mm. and an intermediate cut taken (< 60°C. vapor), followed by the product cut 60 - 65°C. at 86 mm. (Distillation through a 16" Vigreux column.)

Autoclave Run	Charge Freon-12 B_2	Recov. Freon-12 B_2	Product* Wt.	Product* %	n_D^{25}	d
1	950 g.		93.9 g.	8.7	1.4480	2.01
2	950 g.	500 g.	77.7 g.	15.4	1.4485	
3 & 4	1900 g.	1140 g.	213.5 g.	25.0	1.4482	
5 & 6	2900 g.	1961 g.	483 g.	45.0	1.4482	
7 & 8	2900 g.	1914 g.	474.0 g.	42.4	1.4490	
9	1450 g.	457 g.	645 g.	57.5	1.4470	

* Corrected for recovered Freon.

B. 1,1,1-Trifluoro-3-bromopropane



$$CF_2Br\text{-}CH_2\text{-}CH_2Br \xrightarrow[SbCl_5]{HF} CF_3\text{-}CH_2\text{-}CH_2Br$$

One thousand and sixty grams of 1,1-difluoro-1,3-dibromopropane (4.45 M.), 380 ml. of anhydrous HF (346 g.; 17.3 M.), and 27 ml. of $SbCl_5$ were mixed in the bomb (3.3 liter).

Note: The difluoro-dibromopropane was well chilled in dry-ice/acetone, and the HF and $SbCl_5$ were well chilled in an ice bath previous to mixing. This kept HF and $SbCl_5$ fumes at a minimum during charging.

The bomb was heated during rocking at 150°C. for 15 hours. At the end of this time, it was well-cooled with ice water and slowly vented (HF fumes!). The bomb was opened (Caution!), and the batch was poured over 4 - 5 kg. of shaved ice and neutralized to pH 8 - 9 with a solution of 700 g. of NaOH in 2500 ml. of water (previously cooled 0-5°C.).

The layers were separated.

The organic layer was steam-distilled (vapors 59 - 100°C.) and the distillate dried over Na_2SO_4 and filtered.

Yield: 601.0 g. colorless liquid.

$$\left.\begin{array}{ll} n_D^{25}: & 1.4203 \\ d: & 1.89\text{ g./ml.} \end{array}\right\} \begin{array}{ll} \text{MR (obs):} & 0.1337 \\ \text{MR(calc):} & 0.1427 \end{array}$$

The aqueous layer was steam-distilled (vapors 97 - 101°C.)

Yield: 56.3 g. light yellow liquid.

$$\left.\begin{array}{ll} n_D^{25}: & 1.4230 \\ d: & 1.88\text{ g./ml.} \end{array}\right\} \text{MR (obs):}\ 0.136$$

The combined organic material was distilled through a 12-plate glass-bead packed column (24" x 3/4") fitted with a variable reflux head at atmospheric pressure.

Cut	Pot	Vapor	Refl. ratio	Remarks
-			total	--
1	89 - 90°C.	60 - 62°C.	8/1	5.5 g. colorless liq. n_D^{25}: 1.3538
2*	90 - 96°C.	62 - 64°C.	8/1	53.0 g. colorless liq. n_D^{25}: 1.3603
3*	96-126°C.	64 - 66°C.	5/1	121.0 g. colorless liq. n_D^{25}: 1.3610
4	126°C.	66-122°C.	8/1	20.6 g. colorless liq.
5	125 - 130°C.	123 - 128°C.	6/1	361.0 g. colorless liq. n_D^{25}: 1.4468

Cuts 2 and 3: 174.0 g. 1,1,1-trifluoro-3-bromopropane (22.1% yield)
(or 35.1% conversion)

Cut 5: recovered starting material.

* A previous run (952 g. charge) had yielded 93.9 g. of distilled product and these combined products were delivered.

1,1,2,2-Tetrahydroperfluorononyliodide(4)

A. Preparation of Silver Salt of Perfluorooctanoic Acid

$$\begin{array}{ccccc} 2xCF_3(CF_2)_6\cdot COOH & + & Ag_2O & \xrightarrow{\text{Acetone}} & 2CF_3(CF_2)_6\cdot COOAg + H_2O \\ 2 \text{ x } 414.08 & & 231.76 & & 2 \text{ x } 520.8 \end{array}$$

Eleven hundred and sixty-seven grams (2.82 mol) of pentadecafluorooctanoic acid (Matheson, Coleman and Bell Division) was dissolved in 3000 ml. acetone and 338.2 g. (1.46 mole) 3.5% excess) Ag_2O (Merck) was added portion-wise into the acid solution during a period of 1.5 hrs. (temp. 20 - 38°C.). After the addition of Ag_2O, the mixture was stirred for two hours at room temperature. Then 15 g. Norit was added to the solution, stirred 20 minutes and filtered by suction; washed the cake with 2 x 100 ml. acetone and evaporated the colorless solution in vacuo (5 mm./25-30° bath temp.). Dehydrated the white crystalline residue azeotropically with 3 x 1000 ml. petroleum ether, and dried the product to constant weight in vacuo: Yield: 1458 g. (99.5%). Theor.: 1465 g.

B. Preparation of Perfluoroheptyliodide

$$\begin{array}{ccccc} CF_3(CF_2)_6\cdot COOAg & + & I_2 & \longrightarrow & CF_3(CF_2)_6\cdot COOI + AgI \\ 500.8 & & 254 & & \end{array}$$

$$\begin{tikzcd} CF_3(CF_2)_6\cdot COOI \arrow[r, "\Delta"'] & CF_3(CF_2)_6\ COO + I \arrow[d, "\Delta"] \\ & CF_3\cdot(CF_2)_6\cdot I + CO \\ & 496 \end{tikzcd}$$

Seven hundred and ten grams (1.36 mol) of finely powdered dried silver perfluorooctanoate was mixed with 685 g. (2.7 mol) finely powdered iodine in a 5-l. three-necked pyrex flask. The flask was connected with air condenser and this with two dry-ice traps. The mixture was heated slowly (~1 hr.) to 80 - 90°C. The CO_2 evaluation was finished after 3 - 4 hrs. at this temperature. Evacuated the apparatus and distilled the product in vacuo (4 mm., reaction mixture temp. 80-100°C.).

The product solidified in the dry-ice trap. Warmed the trap to 0 - 5°C. and filtered the crude product from iodine by suction. Crude yield = 584 g. (86.2%). Theor. 677.2 g.

The violet colored product was shaken with $\sim$10 ml. Hg in a brown bottle and the colorless liquid was filtered and then fractionated using a helix-packed distillation column with outside electrical heating mantle (20° long and 1.2" ∅; column efficiency $\sim$20 plates). B.p. 80°/115 mm. n_D^{25} 1.3292. Yield: 498.2 g. (73.6%). Theor. 677.2 g.

C. Preparation of 1,1,2,2-Tetrahydroperfluorononyliodide

$$\underset{496}{CF_3(CF_2)_6I} + \underset{28}{CH_2 = CH_2} \xrightarrow[\text{pressure}]{\Delta} \underset{524}{CF_3(CF_2)_6CH_2 \cdot CH_2I}$$

One thousand, three hundred and thirteen grams (2.64 mol) of perfluoroheptyliodide was charged into a 3300 ml. glass-lined steel autoclave. Bomb was flushed with N_2 three times and then N_2 evacuated and ethylene was pressured to 400 p.s.i. (73.9 g. $CH_2 = CH_2$; 2.64 mol). The autoclave was rocked and heated at 200°C. for 4.5 hours. The bomb was thoroughly cooled, vented and the solid product was dissolved in 1200 ml. absolute ethanol. After cooling to -10° the crystalline product was filtered, washed with 2 x 100 ml. absolute ethanol (-10°C.) and dried in desiccator over H_2SO_4. The yellowish product became colorless after 30 minutes exposure to the air. Yield: 970 g. (70.3%); m.p. 47.0 - 47.2°C. (sintered 46.0 - 46.2°C.).

Anal. Calcd.: C, 20.63; H, 0.77.

Found: C, 20.30; H, 0.93.

Comments

The alcoholic mother liquor was not worked up. In previous batches in which the product was isolated by fractional distillation (b_{35} 97°) only unreacted perfluoroheptyliodide was recovered. Separation of the product from unreacted heptyliodide by alcohol crystallization is simpler and gives a better product. Formation of an undecyltelomer in the last step as claimed in the WADC Technical Report 56-590 could not be confirmed. The physical constants for the product as given in this report appear to be in error. However, the physical constants of our product agree with those given in the supplemental report.

A total of 1250 g. of product was delivered.

Approximately 100 - 200 g. of perfluoroheptyliodide could be recovered from the ethanolic crystallization mother liquor if so desired.

N-Hexadecyltriphenylurea(5)

A. Preparation of N-phenyl-n-hexadecylamine

$$\underset{352.18}{CH_3(CH_2)_{14}CH_2I} \quad + \quad \underset{2 \times 91.06}{2C_6H_5NH_2} \quad \longrightarrow$$

$$\longrightarrow \quad \underset{317.53}{CH_3(CH_2)_{14}CH_2NH \cdot C_6H_5} \quad + \quad C_6H_5NH_2 \cdot HI$$

Eighteen hundred and sixty-one grams (20 moles) of aniline and 1760.9 g. (5 moles) cetyliodide (Columbia Chemicals Co., Inc.) are placed in a 5-liter, 3-necked flask fitted with thermometer, stirrer and reflux condenser. The reaction mixture is stirred and heated to 60 - 65°C. The reaction is exothermic and heat is turned off at about 65°C. and the temperature allowed to climb to 90 - 95°C. After two hours, heating is continued for six additional hours at about 95°C. Aniline hydroiodide separates as fine crystals. After cooling to room temperature, the mixture is poured into 10 liters of ice-cold water. The solid waxy material is filtered and washed with 15 liters ice-cold water.

The crude, wet product is transferred to a 12-liter separatory funnel and dissolved in the funnel with 2-liters of water and 6-liters of petroleum ether. After separation of the aqueous layer, the organic phase is washed with 2 x 2000 ml. water, 3 x 2000 ml. 10% acetic acid, 2000 ml. water, 2000 ml. (2%) $NaHCO_3$ solution and again with 2000 ml. water. After drying over anhydrous magnesium sulfate, the petroleum ether solution is decolorized with 50 g. Norit.

Yield = 1483 g. (93%); m.p. 38 - 41°C.(1) The product is pure enough for preparation of n-hexadecyltriphenylurea.

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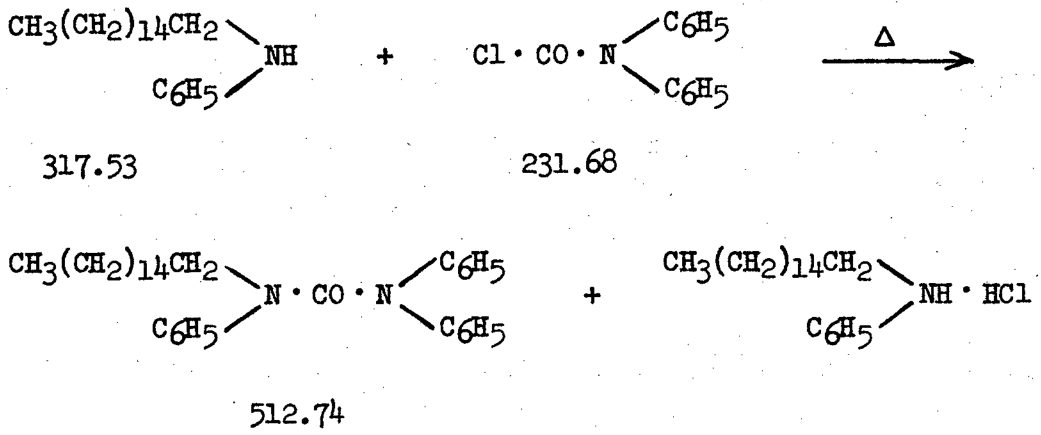
(1) - Literature (J. Chem. Soc. 1937, p. 1119-25) reports m.p. 41-3°.

B. Preparation of n-Hexadecyltriphenylurea



Eight hundred and eighty-five grams (3.82 moles) of diphenylcarbamoylchloride (Eastman Organic Chemicals), 2440 g. (7.64 moles) N-phenyl-n-hexadecylamine are placed in a 10-liter, 3-necked flask, equipped with a thermometer, stirrer, reflux condenser and N_2 inlet. The reaction mixture is heated at 150-155°C. for 8 hrs. with stirring in a nitrogen atmosphere. The mixture is then cooled to 80°C. and poured in 12 liters petroleum ether (b.p. 30 - 60°) with good agitation. After cooling at room temperature, the separated N-phenyl-n-hexadecylamine hydrochloride is filtered by suction. The amine salt is washed with 5 liters of petroleum ether(1) and the petroleum ether solution washed with 2 x 2000 ml. 5% NaOH solution, then water until free of alkali. After drying over anhydrous $MgSO_4$, the solvent is removed under reduced pressure. The viscous, brown-colored residue (2010 g.) is fractionally distilled in vacuo, using a 2-inch long Vigreux column.

B.p. 264°C./0.20 mm. Yield = 1510 g. (77%) based on diphenylcarbamoylchloride.

Found: n_D^{25} = 1.5418 (est. 1.5418)

$\lambda_{max.}^{EtOH}$: 2620, E% 292

Anal. calcd. for $C_{35}H_{48}N_2O$: C, 81.99; H, 9.43; N, 5.46.

Found: C, 82.08; H, 9.15; N, 5.57.

I.R. spectrum as an oil film shows: C = O at 5.96 μ, ϕ at 3.26, 6.22 and 6.65 μ. No absorption is present in 3 μ region. Spectrum is consistent with above structure.

---

(1) 1.3 kg. crude N-phenyl-n-hexadecylamine hydrochloride was recovered.

5-Ethyl-10,10-diphenylphenazasiline(6)

Summary

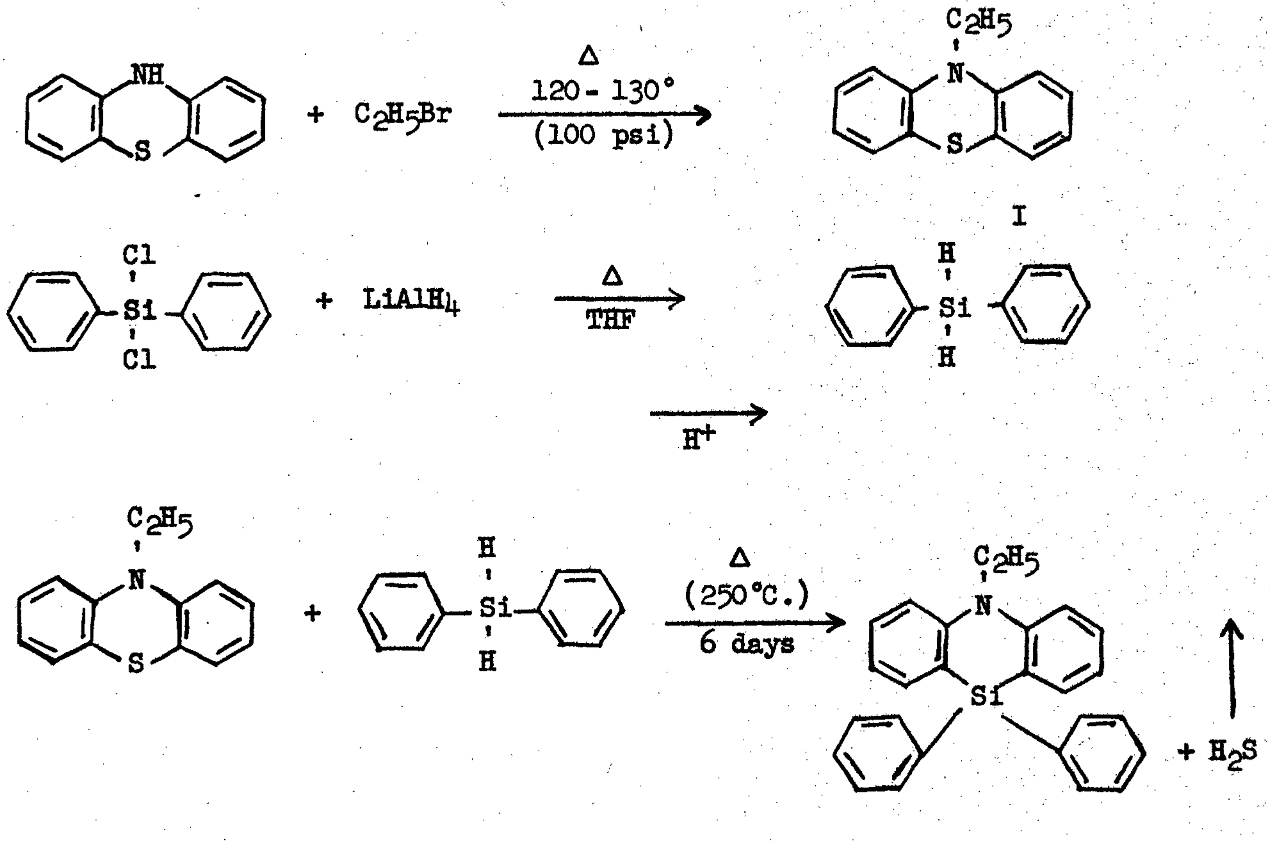
Using a very sketchy process, recorded as a communication by Gilman and Wittenberg [J. Am. Chem. Soc., 79, 6339 (1957)], and with experimental details provided by a telephone conversation with Dr. Wittenberg, we have prepared and delivered one pound of this material using Pilot Plant and laboratory scale equipment.

N-ethylphenothiazine and diphenylsilane (the starting materials) were prepared by literature processes with little difficulty.

Several difficulties were met on the final step (6-day reflux of equimolar quantities of N-ethylphenothiazine and diphenylsilane). These difficulties were, in brief: control of the reflux of increasing amounts of volatile materials during the six-day heating period--particularly on large-scale runs; thorough removal of unreacted N-ethylphenothiazine from the final crude reaction mixture prior to chromatography; the proper preparation of chromatogram "feed", and finally, selection of product cuts and final product purification of 5-10-10.

Once the above trouble spots were recognized, and solved, the synthesis proceeded in a routine manner, affording on the last (4.2 M) run, an isolated yield of 8%, where Gilman reported 6.6 - 7.2%. By far the most costly lesson was the one on reflux control of the final (6 day) reflux. Here, twin 18-mole runs, in 12-liter flasks were lost due to a combination of overheating and inadequate reflux capacity.

Reactions



I

III

Process

A. <u>N-ethylation of phenothiazine</u> [J. Am. Chem. Soc. 66, 1215 (1944)], originally Berenthesen method: Ann. 230, 88 (1885).

A mixture of 100 g. (0.5 mole) of crude phenothiazine, 200 cc. of absolute ethanol, and 80 g. (0.75 mole) of ethyl bromide was heated at 120 - 130°C. for 15 hours in a steel bomb. (The maximum pressure achieved during heating was about 100 psi.) The yield of N-ethylphenothiazine (m.p. 101 - 103°) was 60 g. (56%) after recrystallization from (7.5 volumes) hot ethanol.

Sixteen kilograms of phenothiazine was ethylated by this method in the Pilot Plant. The crude yield was 85% and the recrystallized yield was 65%. This recrystallized material was used for nearly all runs made on this project.

B. Diphenylsilane (WADC T.R. 53-426-Pt.V, page 40)

Nine and three-quarters grams (0.257 M.) of $LiAlH_4$ was stirred in 200 cc. of purified tetrahydrofuran (THF). To this cooled slurry was added 127 g. (0.50 M.) of dichlorodiphenylsilane in 40 cc. of THF for about 30 minutes (slightly more time is required on large batches).

The mixture was then heated under gentle reflux for one hour, cooled slightly and ethyl acetate added to decompose the excess $LiAlH_4$. The batch was then acidified (following cooling to 20 - 25°C.) by slowly pouring into an iced, well-agitated, dilute HCl solution.

Extraction of the batch was aided by adding 100 cc. of ethyl ether and separating the layers. The aqueous layer (gray) was given an extra (50 - 75 cc.) ether extraction, and the combined ether layers given one wash with 100 cc. of a saturated salt brine. The ether layer was then separated and dried over Na_2SO_4, filtered and concentrated. The product was distilled under vacuum (133 - 136°/17 mm.) and weighed 82 g. (89%) $n_D^{20} = 1.5797$.

Several runs of this type were made on a 1 kg. scale with yields of 85-90%. A run made in the Pilot Plant on about 10 kg. gave only a 75% distilled yield, apparently due to loss of dichlorodiphenylsilane through reaction with moisture in the air.

C. 5-Ethyl-10,10-diphenylphenazasiline

The first part of this preparation consists in 6-day reflux of equimolar portions of A and B. As mentioned earlier, two 18-mole runs (3320 g. diphenylsilane and 4090 g. N-ethylphenothiazine) were set up for reflux simultaneously and were lost on the second and third days of reflux. The loss was clearly shown by workup of aliquots, and was due to thermal damage of overheating and, apparently, entrainment of diphenylsilane out of the mixture. This loss due to entrainment in the escaping H_2S stream becomes increasingly severe as the batch size increases.

For production of one pound, following the above incident, a series of 6 x 4.2 mole runs was run, for it was known that a 2-3 ft. spiral air condenser would give the required total reflux on this scale batch. The best run on 4.2 mole scale is described:

In a 3-liter, one-necked flask with 45/50 joint, was placed 954.0 g. (4.2 mole) of N-ethylphenothiazine (m.p. 101-103°) and 773 g. (4.2 mole) of diphenylsilane. The mixture was a moist solid in the flask. Several boiling chips were added to the batch (which was placed in an electric heating mantle) and an adapter placed on the flask. To this was fitted a 30-inch condenser with a jacket and a spiral in the middle part of the condensing tube. Heat was applied to the mantle (85 - 90 volts) and over about one hour, slow reflux started. Air was run through both the spiral and the jacket of the condenser at such a rate that the temperature of the exhaust air was not more than 45-50°C. The refluxing vapor was 135 - 165°C.

During the first several hours of reflux, evolution of H_2S was noted, and an increase in volatility of the boiling mass was noted (temperature of batch 240 - 260°C.). This was watched carefully, for it was usually necessary to reduce the power of the heater by about 5 volts on the second day of reflux. Near the end of reflux, an increase of heat was often used to maintain even boiling. The reflux was continued for six days, and on all successful runs, they were checked at least every 8-9 hours in order to adjust the heating rate, if necessary. As a safety margin, it was attempted to allow 1/3 - 1/2 the length of the condenser surface unwet by condensate. (This is important, for on all "lost" runs, condensate was spilling out the top of the condenser when checked, and surprisingly little of this loss can be tolerated.) Obviously, a more efficient method of condensation would be a steel condenser with a slow flow of water in it--glass condensers were not used with water in the laboratory due to the high ΔT, and the violent effects if water should flow into (260°C.) batch. The metal condenser with water is recommended for larger-scale work.

At the end of the 6-day reflux period, the heat is cut off, and the batch allowed to cool to 50 - 100°C.--this usually occurs over 3-4 hrs. standing in the mantle. The batch is weighed, and on good batches, should show only 50-100 g. loss from the charged weight--mostly due to H_2S. Fresh boiling chips were added, and all material which was volatile below 200°C. at 1.5 - 2.0 mm. was removed from the batch. The weight of volatile material removed in this manner was 300 - 480 g., and was a mixture of benzene, phenylsilanes, N-ethylcarbazole and, mainly, N-ethylphenothiazine. It is very important to remove as much N-ethylphenothiazine as possible (b.p. 175 -180°/1.5 mm.) for on the chromatogram, it moves very close to the product, and when mixtures are obtained, they require special purification as will be seen.

The "stripped" batch usually weighed 1180 - 1250 g. and, while still hot, was poured into a 3-gal. stainless steel bucket. The glassy crude (dark green, stench!) was kept in the hood, and allowed to cool below 40°C. To it was added 3 liters of ethyl ether, and, with about 15 - 20 minutes of sustained stirring with a steel bar, it was completely in solution. In a 5-gallon Pyrex bottle was placed 12 liters of Skellysolve "B" and an air agitator was inserted. The ether solution of batch was poured slowly (3 - 5 min.) into the rapidly stirred Skellysolve "B". In most cases, only a very small amount of tarry material (30 - 60 g.)--of extremely foul odor--was deposited on the walls of the bottle. After stirring and standing for a few minutes, the ether-Skellysolve

"B"-batch system was filtered through glass wool into a 12-liter flask from which most of the solvent was stripped (10 in. vacuum). Near the end of the concentration, when the batch began to separate, two 3-liter portions of Skellysolve "B" were added, and then concentrated off as a "flush". (It is important that all ethyl ether be removed since it upsets the operation of the chromatogram.) At the end of the "flush", 6 liters of fresh Skellysolve "B" is added, and the entire feed brought into homogeneous solution by warming to 40 - 60°C. with slight agitation. The feed was held at this point for placing on the column.

A column for the above feed had been prepared previously in an inverted 12-gallon carboy with the bottom cut off. The column was mounted on a wooden stand, and, with acetone in the column, 53 lb. of acid-washed alumina was sprinkled in over a base of screen, glass head, glass wool and an inch of sand. On top of the well-settled alumina bed was placed another 1-2 inches of sand, and the column was displaced with 10 gallons of Skellysolve "B".

To feed, the solvent on the column was run off to "bed" level, and the hot (50 - 60°C.) batch (in Skellysolve "B") was poured onto the sand. The column was allowed to run, and drop to "bed" level, after which it was continuously eluted with Skellysolve "B" for about 35 gallons. [During the first part of the development, any lumps which may have formed due to cooling (and precipitation) of the feed on top of the column, were pulverized with a spatula.]

The cuts were taken as follows, and, cut (1) (largely a column displacement) was held aside until cut (2) was concentrated and, in all cases, discarded. Size, composition, and disposal of the various product cuts are indicated in the table. All cuts were concentrated in vacuum in the laboratory.

In order to convert the crude oils to crystalline material, an equal volume of cyclohexane was added, following concentration, the batch was transferred to a smaller flask, and allowed to crystallize overnight in the refrigerator.

Cut No.	Solvent	Volume	Crystalline Wt.	Composition
1	Skelly "B"	5 gal.	x	6 g. x
2	"	2 1/2 gal.	15 g.	6 g. tetraphenylsilane + 3 - 4 g. 5-10-10
3	"	"	65 g.	N-ethylphenothiazine + 5-10-10
4	"	"	45.1 g.	5-10-10
5	"	"	20 g.	"
6	"	5 gal.	17 g.	"
7	"	"	6 g.	"
8	"	"	x	
9	"	"	x	
10	Ethyl ether	"		
11	" "	"		
Total:			168 g.	Recrystallized wt. 126 g. (8%) (m.p. 122 - 123°C.)

The isolation of the maximum amount of 5-10-10 from a series of column cuts must be carefully done. Cut (2) yields tetraphenylsilane which is insoluble in cyclohexane and can be removed by immediate filtration (m.p. usually 220 - 230°C. vs. m.p. 234 - 237° for pure material). The mother liquor may be crystallized overnight in the refrigerator for 3-4 g. of 5-10-10, but it, too, is contaminated with N-ethylphenothiazine in many cases. Thus, it is more efficient to merely mix this with all combined "crude mother liquors" for further purification. The crude from cut (3) usually melts low (80 -100°C.) and this indicates contamination with N-ethylphenothiazine. This can be clearly resolved by ultraviolet examination: 5-10-10 has the following unique U.V. curve (in isooctane); λmax. 3374, E% 145; λmax. 3270, E% 148; λmax. 3030, E% 226; λmax. 2855, E% 372; λmax. 2270, E% 1179. Cut (3) is often 40-50% N-ethylphenothiazine. The mixed cut is put in a large-necked, distillation unit, under 0.150 mm. vacuum, and with careful heating, all N-ethylphenothiazine removed by distillation (b.p. 0.150 mm. = ca. 175°C.). At the end of the distillation, the calculated weight (U.V.) of 5-10-10 is usually obtained upon crystallizing from one volume of cyclohexane, as before. The other product cuts (4-5-6-7, etc.) usually melt over 115-116°C. and are by U.V. over 85% pure. All such material is recrystallized from 25-30 volumes of boiling ethanol (2 BA) and on chilling overnight, filtering and washing, yields 85-90% recovery. This material usually melts 121-124°C. and is very pure.

The crude mother liquors were all combined and, after removal of solvent, (100-120 g. residue) were subjected to the same distillation as used in mixtures like cut (3). After this "stripping", the weight was 60-66 g. and was dissolved in 2 volumes of hot cyclohexane, decolorized with 6-6.5 g. of Nuchar C-1000N, filtered and allowed to crystallize. This operation afforded 20-22 g. of additional high-quality material which, after recrystallization yielded 15-17 g. of pure material.

An additional 6 g. of product was obtainable by concentration, "stripping", and crystallization of the 2 BA mother liquors from recrystallization mother liquors. (2 BA is absolute ethanol.)

Thus, the 126 g. (8%) of recrystallized yield reported in the Table, was obtained from a combination of these sources. It is apparent that much of the final purification difficulty was due to incomplete removal of N-ethylphenothiazine during the initial "stripping" operation. The large quantity of unwanted (polar) material seems to hold the 50-80 g. of troublesome N-ethylphenothiazine until its separation (with product) on the chromatograph column.

The one pound delivery was made up of a series of the above operations. All material was finally blended on a melting point basis, pulverized, and 455 g. delivered with the following characteristics:

M.p. 121.2-124°C.

U.V. (as reported in text)

I.R. "OK in all respects"

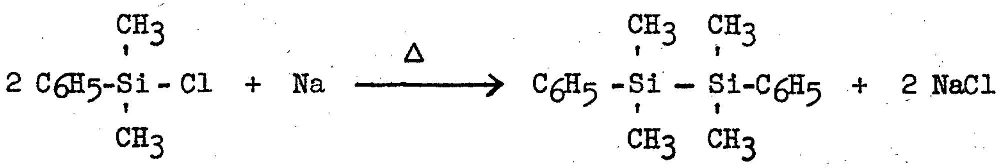
Anal. Calcd. for $C_{26}H_{23}MSi$: C, 83.0%; H, 6.14%; N, 3.72%; Si, 7.44%.

Found: C, 83.24%, H, 6.17%; N, 3.70%; Si, 7.36%.

Solubility Analysis: 99.3% ± 0.3%.

Note: Since this preparation was completed, Professor Gilman has published his experimental procedure for this compound [J. Am. Chem. Soc., 80, 5421 (1958)]. In comparison, it will be noted that, for operational simplicity, we did not carry out the distillation at 10 microns prior to chromatography. This, no doubt, explains the presence of troublesome amounts of N-ethylphenothiazine in some of our runs.

1,2-Diphenyl-1,1,2,2-Tetramethyl Disilane(7)



$$2\ C_6H_5-\overset{CH_3}{\underset{CH_3}{Si}}-Cl + Na \xrightarrow{\Delta} C_6H_5-\overset{CH_3}{\underset{CH_3}{Si}}-\overset{CH_3}{\underset{CH_3}{Si}}-C_6H_5 + 2\ NaCl$$

One hundred and twenty-eight grams (0.75 M.) of freshly distilled (193 - 196°C./760 mm.; 0.755 M.) phenyldimethyl-chlorosilane was dissolved in 244 ml. of dry xylene in a 1000 ml. round-bottom flask fitted with condenser and paddle-bladed stirrer. Forty-two and six-tenths grams of metallic sodium was added (1.85 M.), and this mixture was heated, with no stirring, until the sodium melted, then agitation was started at a moderate rate. The mixture was heated under reflux with stirring for 25 hours. The reaction mixture soon (in about 1-2 hours) became dark blue.

After cooling to room temperature, the mixture was filtered through a Supercel precoat, and the cake was washed three or four times with xylene. (Cake saved for disposal - caution, contains sodium!)

The solvent was stripped by distillation at atmospheric pressure. (The vapor temperature holds at 136 - 137°C.; then raises to a maximum of 155°C. after which it drips back to 125°C. At this point, solvent stripping was terminated.)

The pale straw, liquid, residue (100 g.) was distilled:

Cut	Pressure	Vapor	Remarks
1	7 mm.	60-147°C.	4.0 g. colorless liquid
2	7 mm.	147-152°C.	73.5 g. colorless liquid, which solidifies easily; hence air condenser used which could be heated with steam if necessary. (m.p. 34 - 35.5°C.)

Calcd.	Found
C: 71.05	71.88
H: 8.15	8.68

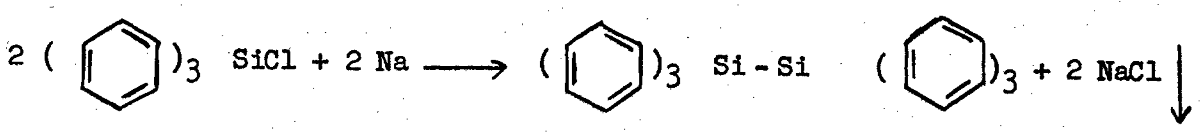
Cut 2 (above) redistilled:

Cut	Pressure	Vapor	Remarks
A	7 mm.	< 150°C.	2.5 g. cloudy liquid
B	7 mm.	150-152°C.	63.9 g. colorless liquid, which solidifies. m.p. 35 - 36°C. (n_D^{25}: 1.5598: supercooled) (Yield: 63.2% overall)

Calcd.	Found
C: 71.05	71.25
H: 8.15	8.27
Si: 20.75	20.85; 20.56

Four runs, as described, were made to complete the delivery of 1221 g.

Hexaphenyl Disilane(8)



Eight hundred grams (2.7 M.) of technical grade triphenylchlorosilane was dissolved in 2500 ml. xylene, warmed slightly to overcome the slight cooling on dissolving, and slurried 15 minutes with 40 g. of Nuchar C 1000 N. This removed the dark green color and produced a lemon-yellow colored solution on filtration. The cake was washed with 800 ml. of xylene.

This was heated under reflux, with good stirring for three hours (stirrer should reach almost to the bottom of the flask), after addition of 112 g. metallic sodium. During this time a deep blue color forms rapidly and the sodium forms very small globules of molten metal; hence the agitation is critical to prevent agglomeration of this molten metal.

The reaction mixture was cooled to room temperature and filtered. The cake was washed with 3 displacement washes of xylene. The cake was sucked until no more xylene came through the funnel. This cake was then added, with good cooling and agitation and in portions to 5000 ml. of 95% ethanol. After all the cake was added, the slurry was stirred for 30 min. to make certain all the sodium was decomposed. When this was complete, then 20,000 ml. of water was added with stirring. This slurry was filtered, after 15 min. stirring, and washed well with water. (These must be slurry washes, for the product is not wet by water.) The cake was vacuum-dried at 100 - 120°C.

Yield:	557 g. white plates (80%).
M.P.:	360°C.
Note 1:	Literature yields (Gilman and Dunn, Journ. Am. Chem. Soc., 73, 5077 [1951]) are about 85% on smaller scale.
2:	This material can be recrystallized from dimethylformamide (44 volumes) in 90% recovery, however, no improvement in melting point, but analysis and appearance are noticeably better.

Phosphonitrilic Dichloride (Trimer)(9)

A mixture of 650 g. of ammonium chloride and 6500 cc. of (symmetrical) tetrachloroethane was distilled, with stirring, until no more water came over with the solvent. A total of 1500 cc. of the solvent was removed in this operation. Over a 3-hr. period, the batch was allowed to cool to 45°C., at which time 2000 g. of phosphorus pentachloride was added rapidly, with stirring. With continued stirring, the mixture was heated to 131°C., but not over 135°, with a slow stream of dry nitrogen over the surface. The batch was held at 131°C. for 25 hrs. under the above conditions, cooled to room temperature and the unreacted ammonium chloride removed by filtration. The solvent was removed by distillation under aspirator vacuum, and the organic residue finally dried under oil pump vacuum.

The residue, a crystalline mass at this point, was taken up in 300 cc. of hot benzene and, on standing overnight, was a heavy crystalline slurry. The crude crystalline material was removed by filtration, dried, and combined with the product from another run this size and another half this size. The combined crudes weighed 852 g., and melted 88 - 109°C. A second crop of 100 g. was obtained from the (1 liter) benzene mother liquors.

The above product was submitted to vacuum distillation at 3.5 - 4.5 mm. (N_2 atmosphere) and a product cut of 686 g. was obtained, boiling at 107 - 114°C. This product was combined with 85 g. from second crops, and recrystallized from boiling Skellysolve C. The yield was 665 g., m.p. 106 - 111°C. Again, the product was dissolved in petroleum benzin, at room temperature, and filtered. The filtrate was concentrated to two liters, and the product crystallized. Weight 472 g., m.p. 112 - 114°C., 2nd crop 36 g., m.p. 113 - 114°C.

This product was delivered. The I.R. spectrum showed only a trace of tetramer, and the analysis was:

Anal. calcd. for $N_3P_3Cl_6$: N, 12.07.

Found: N, 12.24.

3-Nitro-diphenyl Ether(10)

One hundred and seventy-six grams of 85% potassium hydroxide (150 g., 2.78 M. of 100% KOH) was dissolved in 1359 g. (14.4 M.) of Merck U.S.P. phenol. To this solution was added 13.59 g. of copper powder (Fisher, electrolytic dust) and 545 g. of m-bromonitrobenzene (2.78 M.). The mixture was heated at 150°C. (with stirring) for 3 hrs. and then the temperature was raised to 180°C. for an additional 30 min. (a 5-liter flask was used to allow plenty of room for foaming). The slurry was cooled, after the above heating cycle, and poured into 1600 cc. of 30% aqueous sodium hydroxide solution in an ice bath. When the quenched slurry had cooled to about 15°C., it was extracted with 3 x 600 cc. of ether. The combined ether extracts were washed with 2 x 500 cc. of saturated sodium chloride solution, dried over sodium sulfate and filtered. The solvent was removed, using a water aspirator, and the oily residue combined with that from a similar run (6.2 M. scale). The combined crude oils weighed 1885 g. (98.9%). The oil was distilled under vacuum: a forerun was taken to 138°C., at 0.30 mm., which weighed 480 g. (n_D^{25} = 1.5820). The product cut (138 - 140°/0.30 mm.) weighed 1173 g., n_D^{25} = 1.6002 (63%).

3-Aminodiphenyl Ether(11)

The above 1173 g. (5.47 M.) of 3-nitrodiphenyl ether was dissolved in 7400 cc. of absolute ethanol and with 11.4 g. of PtO_2 catalyst, was hydrogenated at 40 p.s.i. at room temperature. Hydrogenation proceeded rapidly and was complete after 3 hrs., the temperature held constant during the reduction, and external cooling was not necessary.

After hydrogenation was complete, the catalyst was removed by filtration. The solvent was removed using the water aspirator and the residue weighed 1020 g. This crude amine was dissolved in 3 liters of 2.5 N. hydrochloric acid and the solution was extracted with ether (3 x 800 cc.) to remove neutral impurities. Then, the aqueous layer was treated with 2 g. of tartaric acid and 2 g. of sodium bisulfite along with 50 g. of Norit. After stirring this mixture for 1 hr. with nitrogen bubbling (to entrain out ether, and to exclude air), the solids are removed by filtration. After filtration, the slightly yellow solution was made alkaline (to pH 10) with concentrated ammonium hydroxide. The precipitated oil was extracted into three 1-liter portions of ether, the ether layer washed with 3 x 500 cc. of water, and dried over sodium sulfate. The filtrate from sodium sulfate drying was evaporated to an orange-yellow oil which was purified by distillation. The product cut boiled 128 - 130°C. at 0.25 - 0.30 mm. and weighed 722 g. (71.5%). The refractive index was 1.6206 (n_D^{25}). (Lit. value, 1.6204) m.p. 37.8 - 38.2°. This material had an ultraviolet spectrum as follows (in methanol), $\lambda_{max.}$ 2880, E% 144; $\lambda_{max.}$ 2790, E% 139; $\lambda_{max.}$ 2720, E% 124.

Anal. Calcd. for $C_{12}H_{11}NO$: C, 77.81; H, 5.99; N, 7.56.

Found: C, 77.40; H, 5.93; N, 8.00.

Diphenyl Silane(12)

Ninety grams of $LiAlH_4$ (2.52 M.) was suspended in 1800 ml. of tetrahydrofuran (THF), in a 5-liter, round-bottom, 3-necked flask fitted with an air stirrer, condenser, nitrogen inlet and an addition funnel. Then, with a slow nitrogen flow 1140 g. of dichlorophenylsilane (4.6 M.) was slowly added in 370 ml. THF at a rate to maintain reflux with ice bath with slow agitation. (The addition time is approximately 1 1/4 hrs.)

Reflux (external heating) is continued 1 hr. after addition is complete.

The batch is cooled to room temperature and 240 ml. of ethyl acetate is added to quench excess lithium aluminum hydride.

The batch is poured slowly and with cooling ($<$40°C.) into 1200 ml. 2.5 N HCl. Stirring is continued for 15 min. and 1000 ml. of ether is added. After additional stirring, the layers are separated and the aqueous layer is extracted with 200 ml. of ether. The combined ether layers are washed with 2 x 200 cc. of saturated salt solution, the extract dried over sodium sulfate, and after filtration the solvent is removed in vacuum. The product is collected at 88 - 92°C. at 0.4 mm., and the yield is 89%. $n_D^{25} = 1.5782$.

Anal. calcd. for $C_{12}H_{12}Si$: Si, 15.04.

Found: Si, 15.23.

Two runs of this size were made and the products were combined for distillation.

4,4'-Diaminodiphenyl Ether(13)

Five hundred grams of Eastman Kodak Co. practical grade 4,4'-diaminodiphenyl ether (m.p. 180 - 185°C.) was purchased. This (very dark colored) crude product was purified as follows:

The crude diamine (500 g.) was dissolved in a solution of 500 cc. of concentrated hydrochloric acid in 10 l. of water. To this acidic solution was added 5 g. of tartaric acid, 10 g. of sodium bisulfite and 50 g. of Norit. After stirring for one hour, the solids were removed from the above mixture by filtration. The color of the filtrate was a dark red, therefore the charcoal treatment was repeated twice more, using 50 g. quantities of carbon. After the third filtration, the filtrate was light yellow and the diamine was precipitated by addition of concentrated ammonia to pH 9.5. A snow white solid precipitated which was removed by filtration (nitrogen atmosphere at all times), washed and dried in vacuum. (Caution: the product is sensitive to both air and light.) The yield was 467 g. (93%), m.p. 190.5 - 191.5°C.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 71.97; H, 6.04; N, 14.00.

Found: C, 72.00; H, 5.92; N, 14.25.

Preparation of 2-Phenyl-4,6-Dichloro-s-Triazine(14)

Phenylmagnesium bromide solution was prepared from 340.5 g. (14 atoms) of magnesium and 2198 g. (14 M.) of bromobenzene in 5100 ml. of absolute ether. (Apparatus: 12-liter, three-necked flask equipped with stirrer, thermometer, dropping funnel and condenser.)

Addition of the ethereal bromobenzene solution required 4 hours. The induction period was 40 minutes at 15°C. The reaction mixture was cooled in an ice bath during the addition of bromobenzene. After the complete addition of bromobenzene, the reaction mixture was heated at 35-40°C. until all the magnesium was dissolved, then cooled to room temperature.

Condensation of cyanuric chloride with phenylmagnesium bromide

Apparatus: 2 x 12 liter three-necked flasks, with reflux condenser, thermometer, stirrer and dropping funnel. Fourteen moles of phenylmagnesium bromide ethereal solution was added to a solution of 1622 g. (17.6 M.) of cyanuric chloride in 10 liters of benzene (two 12-liter flasks). Addition time, 5 to 5 1/2 hrs., the temperature during the addition was held at 12 to 15°C.

The mixtures were allowed to stand overnight and then were heated under reflux (65-68°C.) for three hours. The precipitated MgClBr was filtered through a sintered glass funnel and washed with 3 x 1.5 liters ether (each batch). The combined filtrates and washes were evaporated *in vacuo* (ca. 20 mm.). The residue was 220 g.

The crude product was distilled from a 5-liter three-necked flask by means of a 7-inch column which was heated by electrical tape.

3250 g. crude product (three batches) gave 2100 g. (74%) distilled product. B.p. 155-174°C., 2.25-5.00 mm. The distilled product was crystallized from 5.2 liters of Skellysolve C. Yield = 1807.5 g.; m.p. = 120-120.5°C. (overall yield = 53.5%).

Analysis:

	Calcd. ($C_9H_5Cl_2N_3$)	Found
C	48.02	48.30
H	2.22	2.10
N	18.56	18.44

U.V. (in isooctane):

$\lambda_{max.}$	E%
2740	1056
2270	265
2240	271

Preparation of 2,4-Dichloro-6-Methyl-s-Triazine(15)

A methylmagnesium bromide solution was prepared from 505 g. of magnesium (21 atoms) and 2000 g. of methylbromide (21 M.) in 5800 ml. of anhydrous ether. (12-liter flask, three-necked, equipped with a stirrer, dry ice cooled reflux condenser, dropping funnel and a thermometer.)

The addition of the ethereal CH_3Br solution required 4 hours. The induction period was 35 minutes at 21°C. The reaction mixture was cooled in an ice bath during the addition of the CH_3Br. After the complete addition of CH_3Br, the reaction mixture was heated at 35 - 40°C. until all magnesium was dissolved, then cooled to room temperature. (The total volume of methylmagnesium bromide solution was 6550 ml. [21 M.].)

Condensation of Cyanuric chloride with CH_3MgBr:

Mol ratio: $CH_3MgBr : (CNCl)_3 = 1.5 : 1$

$= 21 : 14$

(Apparatus: 2 x 12 liter three-necked flask, with reflux condenser, thermometer, dropping funnel.)

Twenty-one moles of CH_3MgBr (ethereal solution) was added to a solution of 2582 g. (14 M.) of cyanuric chloride in 12 liters of benzene (two runs!). The addition time was 6-6 1/2 hours and the temperature during the addition was held at 13 - 18°C. using a cooling bath.

After the complete addition of Grignard reagent, the mixture was heated to 40°C. for 1 hr. and then allowed to stand overnight. The mixture was heated again to 60 - 65°C. for 3 hours. After cooling to room temperature, the precipitated MgClBr was filtered off by means of a filterstick, and was washed with 3 x 1.5 liters of benzene. The combined benzene solution was concentrated in vacuo. The orange-yellow crystalline residue was redissolved in 16 liters of benzene (in 3 portions) and filtered by means of a filterstick.

After evaporation of the benzene solution in vacuo, the crude methyl-dichloro-s-triazine was distilled at 125 - 130°C. and 95 - 100 mm. vacuum, using a 7-inch electrically heated column. The yield of distilled product was 1950 g. (84.5%).

Two crystallizations from Skellysolve C, using 1-2 liters each time, gave 1485 g. (65%) of pure product melting at 98.2 - 98.8°C. (lit. 98.6°).

<u>Anal</u>. Calcd. for $C_4H_3N_3Cl_2$ (163.99): C, 29.30; H, 1.84.

Found: C, 29.53; H, 2.07.

The structure is further confirmed by the I.R. spectrum.

The compound is a lachrymator, and should be protected from air and moisture.

In view of the ease of hydrolysis, suction filtration on the crystallization step must be avoided. Instead, removal of mother liquor was done by means of a filterstick and final drying of the product was carried out in a rotating vacuum evaporator.

2-Chloro-4,6-Diphenoxy-s-Triazine(16)

To a suspension of 418 g. cyanuric chloride (2.25 M.) in 1690 ml. acetone in the 5-liter round-bottom flask (fitted with an air motor and agitator, condenser, thermometer, and addition funnel) was added a solution of 482 g. of an 88% aqueous solution of phenol ("Phenol Liquified - Merck") and 180 g. of sodium hydroxide (4.50 M.) in 1630 ml. of water. This addition was done with stirring at 10 - 15°C. Following completion of addition, the slurry was aged with stirring at 25°C. for 1 hour. The product was filtered and washed well with water and was vacuum dried at room temperature.

Yield: 581 g. off-white solid (86.6%)

M.p. : 113 - 115°C., (Lit. m.p. 124 - 126°C.)

The product was recrystallized from 2400 ml. of Skellysolve C. Insoluble filtered off and filtrate iced.

Recovery: 464 g. white plates (80% recovery = 69.3% overall)

M.p. : 118 - 119°C.

(Two runs were made using this scale.)

Anal. Calcd. for $C_{15}H_{10}N_3O_2Cl$: C, 60.15; H, 3.36; N, 14.02; Cl, 11.83.

Found: C, 60.01; H, 3.24; N, 14.00; Cl, 11.68.

Note 1.: Commercial sodium phenate can be used, but the moisture content and purity must be determined by acid titration against phenolphthalein.

2.: During recrystallization of this material, it is necessary to attain a vigorous, rolling boil to ensure maximum solubility.

2-Chloro-4,6-Dimethoxy-s-Triazine(17)

To a mixture of 1800 g. of methanol (2280 ml.) and 200 ml. of water was added a mixture of 743 g. (4.0 M.) cyanuric chloride and 671 g. (2.0 moles) of sodium bicarbonate in a 5-liter round-bottom flask fitted with an agitator, condenser, and thermometer. The temperature was allowed to rise to 33 - 35°C. where it was held by means of an ice bath (raised and lowered when necessary) until all the carbon dioxide had apparently been evolved. The temperature was raised to reflux (below 64°C., but above 60°C.) for 30 minutes. The (moderately heavy) slurry was cooled to room temperature where it became very heavy. The batch was diluted with 2000 ml. of water and aged 15-20 minutes before filtering. The cake was washed well with water to a negative halide test. The product was vacuum dried at room temperature in a desiccator.

Yield: 500 g. white solid (71.1%)

M.p. : 69 - 73°C. (Lit. m.p. 74 - 76°C.)

The product was recrystallized from 525 ml. of Skellysolve C after filtering from a slight amount of insolubles.

Recovery: 442 g. white crystals (93% recovery = 66.1% yield)

M.p. : 78 - 79°C.

Anal. Calcd. for $C_5H_6ClN_3$: C, 34.2; H, 3.45; N, 23.95; Cl, 20.20.

Found: C, 34.36; H, 3.20; N, 23.46; Cl, 20.19.

Note: If the reflux temperature gets above 65°C., an exothermic reaction sets in which is impossible to control, and one obtains a mixture of trimethoxy-s-triazine and cyanuric acid instead of the desired dimethoxy triazine.

Trimethoxy-s-triazine: white solid, m.p. 134 - 139°C.
Ref: Dudley, J.A.C.S., 73, 2984 (1951).

This mixture can be split into about 75% cyanuric acid insoluble in 2-3 volumes hot Skellysolve C and the trimethoxy-S-triazine which crystallizes from the Skellysolve C solution upon chilling in an ice bath.

1,1,2,2-Tetraphenyl-1,2-dimethyl-disilane(18)

Nine hundred grams (3.86 M.) of previously distilled diphenylmethyl-chlorsilane (106 - 110°C. at 0.8 mm. Hg) was dissolved in 1800 ml. of dry toluene. To this, 120 g. (5.23 M.) of freshly cut up sodium was added in the 5-liter, three-necked, round-bottom flask fitted with an agitator, reflux condenser plus drying tube, and gas inlet. This mixture was heated until blue spots appeared on the sodium, and vigorous stirring is then commenced, and the heating continued to reflux. The reflux with stirring is continued for 48 hours. (This time can be noncontinuous, however; and, in the interest of safety, run only on the daytime shift. An inert atmosphere of nitrogen was provided in this case--particularly during the "off" periods.)

This dark blue suspension was cooled to room temperature and centrifuged. (See Note 1.) The decanted liquors plus washes (see Note 2) are stirred with 75-100 g. of Nuchar C 1000-N and filtered through Supercel with a Supercel admix. The cake was washed well with toluene, and these washes combined with the filtrate for concentration to a semi-solid residue.

Residue: 747 g.

This residue was dissolved in 700 ml. of refluxing benzene, and 1400 ml. of absolute alcohol added at reflux and the suspension was chilled in ice overnight.

Recovery: 344 g. white crystals

M.p. : 142 - 143°C.

This was combined with other batches at this point for a crystallization from benzene-ethanol.

Anal. Calcd. for $C_{26}H_{26}Si_2$: C, 79.2; H, 6.65; Si, 14.26.

Found: C, 78.8; H, 6.55; Si, 14.02.

2-Chloro-4,6-Diphenyl-s-Triazine(19)

Eight hundred and nine milliliters of bromo-benzene (1203 g. = 7.68 M.) in 1800 ml. anhydrous ether was added slowly (see Note 1) to a stirred mixture of 184 g. of magnesium turnings (7.68 M.; Grignard quality). The metal was suspended in 720 ml. of anhydrous ether in a 6-liter, three-necked, round-bottom flask fitted with an agitator, reflux condenser plus drying tube, gas inlet tube, addition funnel, and thermometer. This addition was carried out at slow reflux with a very slow nitrogen (H.P. dry) stream passing through the apparatus. The addition time was 4-6 hours. The dark suspension was refluxed one and one-half hours after completion of the addition.

The above solution was added slowly with good cooling (salt/ice bath) and good stirring to 446 g. of cyanuric chloride (2.4 M.) in 2900 ml. of anhydrous benzene in a 12-liter, three-necked, round-bottom flask fitted with an agitator, reflux condenser plus drying tube, thermometer, gas inlet, and addition funnel. The addition was carried out at 10 -15°C. and under an inert atmosphere (H.P. nitrogen, dry). About 2-3 hrs. were required for this addition. The resulting suspension was heated under reflux for 2 hrs. after completion of the addition. The suspension was cooled to room temperature and filtered through a 10-inch Buchner funnel and the cake washed well with benzene and ether. (See Note 2.)

The filtrate plus cake washes was then concentrated to a residue of about 1300 to 1400 g.

This residue was then heated under reflux for at least one hour with 3360 ml. of Skellysolve C, filtered rapidly through a preheated Buchner funnel (10-inch diameter) and the cake washed with hot Skellysolve C. The filtrate plus washes was iced. (The cake was saved. See Note 3.)

Yield: 155 g. (24.1%)

M.p. : 139- 142°C.

This first crop was combined with other first crops and recrystallized from eight volumes of Skellysolve C after filtering off a small amount of insolubles.

Recovery: 824 g.

M.p. : 133- 135°C.

This was combined with the second crops for a final crystallization from eight volumes of Skellysolve C.

Recovery: 933 g.

M.p. : 133 - 135°C.

Anal. Calcd. for $C_{15}H_{10}ClN_3$: C, 67.4; H, 3.70; N, 15.72.

Found: C, 69.8; H, 3.93; N, 14.63.

This crop was distilled from a five-liter, round-bottom flask with a 45/50 standard taper joint with 4 cm. diameter tubing as a condenser to the receiver. This condenser was as short as possible and wrapped, full-length, with heating tape. The distillation pot was heated at 290°C. with vacuum of 0.8 mm. mercury. The vapor temperature was 188 - 193°C.

Yield: 850 g.

M.p. : 136 - 137°C.

Anal. Found: C, 68.03; H, 3.66; H, 15.82

Note 1.: This Grignard reagent formation presents the customary induction period requiring great caution in not getting too much (about 50 ml. of bromo-benzene solution is the limit) of the halide mixed with the magnesium before reaction sets in.

2.: These magnesium salts can be disposed of by slowly adding to a large volume of well agitated water in a pail. This minimizes the heat of reaction.

3.: This cake is refluxed with two volumes of Skellysolve C, filtered, and the filtrate iced to afford the second crops.

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