

Although these studies are limited, one can conclude from Table III that the *l*-base, either as the hydrochloride or as the bitartrate, has about twice the nicotolytic activity of the *d*-base in the form of its corresponding salt.

TABLE I

SUMMARY OF PHYSICAL PROPERTIES OF RACEMIC AND OPTICALLY ACTIVE N-(2-DIETHYLAMINOPROPYL)-PHENOTHIAZINE AND ITS SALTS

Salt	M.p., °C.	$[\alpha]^{25D}$ ^a
<i>dl</i> -Bitartrate	135-138	ca. +7 to +8 ^{ob}
<i>d</i> -Bitartrate	156-158 ^c	-4.6 ^{ob}
<i>l</i> -Bitartrate dihydrate	93-95 ^d	+19 ^{oe}
<i>dl</i> -Base	Oil ^{f,g}
<i>d</i> -Base	Oil	+16.7 ^{oh}
<i>l</i> -Base	Oil	-16.7 ^{oh}
<i>dl</i> -Hydrochloride	220-225 ^g
<i>d</i> -Hydrochloride	203-210 ^{h,i}	+1 ^{ok}
<i>l</i> -Hydrochloride	203-210 ^{i,l}	-1 ^{ok}

^a All rotations observed in a one decimeter tube. ^b 8% in distilled water. ^c *Anal.* Calcd. for C₁₉H₂₄N₂S·C₄H₈O₆: C, 59.72; H, 6.54. Found: C, 59.53; H, 6.38. ^d *Anal.* Calcd. for C₁₉H₂₄N₂S·C₄H₈O₆·2H₂O: C, 55.42; H, 6.82. Found: C, 55.49; H, 6.65. ^e 1% in distilled water. ^f Solidified on standing at room temperature. ^g Prepared and analyzed by P. Charpentier and R. Ducrot, *Compt. rend.*, 232, 415 (1951). ^h 4% in ethanol. ⁱ Could be raised to 206-210° by repeated recrystallizations from isopropyl alcohol. ^j *Anal.* Calcd. for C₁₉H₂₄N₂S·HCl: N, 8.04; Cl, 10.16. Found: N, 8.02; Cl, 9.94. ^k 6% in ethanol. ^l *Anal.* Calcd. for C₁₉H₂₄N₂S·HCl: N, 8.04; Cl, 10.16. Found: N, 7.78; Cl, 9.92.

TABLE II

SUMMARY OF INTRAVENOUS LD₅₀ DETERMINATIONS IN MICE OF RACEMIC AND OPTICALLY ACTIVE N-(2-DIETHYLAMINOPROPYL)-PHENOTHIAZINE SALTS

Salt	LD ₅₀ (mg./kg.) ^a		Limits of error, %
	Salt	Calcd. as free base	
<i>dl</i> -Base hydrochloride	36	32	95-105
<i>d</i> -Base hydrochloride	36	32	90-111
<i>l</i> -Base hydrochloride	35.5	32	88-114
<i>d</i> -Base <i>d</i> -bitartrate	62	42	93-108
<i>l</i> -Base <i>d</i> -bitartrate	54.5	34	93-108

^a All solutions were made in physiological saline and were injected at the same rate (0.4 cc./20 g. mouse/10 sec.) by the same worker.

TABLE III

PROTECTION AGAINST NICOTINE-INDUCED TREMORS IN THE RABBIT BY INTRAVENOUS RACEMIC AND OPTICALLY ACTIVE N-(2-DIETHYLAMINOPROPYL)-PHENOTHIAZINE SALTS

Salt	Dose, mg./kg.		No. of animals, protected/no. injected
	Salt	Calcd. as free base	
None	0	0	0/37
<i>dl</i> -Base hydrochloride	2.5	2.24	4/10
	5.0	4.47	9/10
<i>d</i> -Base hydrochloride	2.5	2.24	3/5
	5.0	4.47	5/5
<i>l</i> -Base hydrochloride	1.25	1.12	2/10
	2.5	2.24	5/5
	5.0	4.47	4/5
<i>d</i> -Base <i>d</i> -bitartrate	2.5	1.68	1/5
	5.0	3.37	5/5
<i>l</i> -Base <i>d</i> -bitartrate	1.79	1.12	4/10
	2.5	1.56	5/5
	5.0	3.13	5/5

We wish to acknowledge the technical assistance of Mr. Heino A. Luts. Microanalyses were carried out by or under the supervision of Dr. F. A. Buehler.

Experimental⁷

dl-N-(2-Diethylaminopropyl)-phenothiazine.—The base was prepared from the corresponding purified hydrochloride, obtained essentially by the procedure of Charpentier,⁴ by dissolving the latter in water, basifying the aqueous solution and extracting the resultant oil with ether. Removal of the ether gave the base in quantitative yield.

Resolution of *dl*-N-(2-Diethylaminopropyl)-phenothiazine.—The racemic base (25.0 g., 0.08 mole) and *d*-tartaric acid (12.0 g., 0.08 mole) were dissolved in 300 ml. of warm (50°) *n*-propanol and the solution was allowed to cool slowly. Crystallization was induced by scratching. After remaining 1.5 hours at room temperature the crystals were filtered off and dried *in vacuo*. There was obtained about 13 g. (70%) of partially resolved *d*-base *d*-bitartrate, $[\alpha]^{25D} +1^\circ$, m.p. 149-151°. The impure *d*-base *d*-bitartrate was purified by three recrystallizations from *n*-propanol. There was obtained 5.9 g. (45%) of pure material, $[\alpha]^{25D} -4.6^\circ$.

The filtrate from which the impure *d*-base *d*-bitartrate had been removed was allowed to stand for 24-36 hours more at room temperature (25-30°), and deposited crystals that were rich in *l*-base *d*-bitartrate. The crystals were filtered off and dried; they weighed 12 to 15 g. (65-80%) and had $[\alpha]^{25D} +14$ to $+16^\circ$. This material could not be purified by recrystallization from *n*-propanol but it was found that the sparingly soluble *l*-base *d*-bitartrate dihydrate could be readily obtained by several recrystallizations of the crude material from water. The pure *l*-base *d*-bitartrate dihydrate obtained from the crude material by recrystallization from three parts of water weighed about 5.4 g. (40%), $[\alpha]^{25D} +19^\circ$, m.p. 93-95°.

d- and *l*-N-(2-Diethylaminopropyl)-phenothiazine.—Each pure *d*-bitartrate was dissolved in water and the solution was made alkaline with sodium hydroxide and extracted with ether. The ether extract was dried over anhydrous potassium carbonate and the ether removed *in vacuo* leaving the optically active bases as oils. The *d*-bitartrate having $[\alpha]^{25D} -4.6^\circ$ gave a base having $[\alpha]^{25D} +16.7^\circ$ and the *d*-bitartrate having $[\alpha]^{25D} +19^\circ$ gave a base having $[\alpha]^{25D} -16.7^\circ$.

***d*- and *l*-N-(2-Diethylaminopropyl)-phenothiazine Hydrochloride.**—The optically active bases were dissolved in ether (5% solution) and dry hydrogen chloride passed in until no more precipitate formed. The precipitates were filtered, washed with ether and dried *in vacuo*. The *d*- and *l*-hydrochlorides, $[\alpha]^{25D} +1$ and -1° , respectively, m.p. 203-210°, were obtained in quantitative yield. Samples of these hydrochlorides were converted back to the free bases in the usual manner; these bases had $[\alpha]^{25D} +16.7$ and -16.7° , respectively.

(7) Melting points are uncorrected.

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The Preparation of Some Trialkyltin-lithium Compounds

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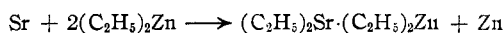
RECEIVED NOVEMBER 20, 1952

In a previous publication¹ from this Laboratory the preparation of triphenyltin-lithium from stannous chloride and three equivalents of phenyl-lithium was described. In order to ascertain if aromatic groups bonded to the tin atom were necessary for the formation of complexes of this type and investigate the possibility of preparing alkylorganotin compounds by means of similar

(1) H. Gilman and S. D. Rosenberg, *THIS JOURNAL*, **74**, 531 (1952). See also G. Wittig, F. J. Meyer and G. Lange, *Ann.*, **571**, 167 (1951); G. Wittig, *Angew. Chem.*, **62**, 231 (1950).

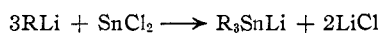
complexes, reactions have been carried out between stannous chloride and some alkyl lithium compounds, and the results are reported herein.

In 1858, Wanklyn² tried unsuccessfully to prepare ethylsodium by the reaction of diethylzinc with sodium metal. Much later, Hein³ showed that ethylsodium and diethylzinc form a stable complex metal alkyl, triethylzinc-sodium. Hein demonstrated that ethylsodium, a non-conductor, will conduct an electric current when diethylzinc is used as solvent, and that on electrolysis sodium ion migrates to the cathode and triethylzinc complex ion migrates to the anode. These findings support the idea that, in attempting to prepare ethylsodium from diethylzinc and sodium, Wanklyn² had actually prepared the first reported complex metal alkyl, triethylzinc-sodium. More recently, it has been reported⁴ that an attempt to prepare diethylstrontium by the action of strontium metal on diethylzinc actually resulted in the preparation of a complex involving one molecule of diethylstrontium and one molecule of diethylzinc.



Schlesinger and Brown⁵ reported the preparation of trimethylethylboronlithium, and Hurd⁶ described tetramethylaluminum-lithium, tetramethylboron-lithium and tetramethylzinc-dilithium. In each case the complex metal alkyl was formed by treating the methylorganometallic compound with an ether solution of the appropriate alkyl lithium compound.

It was found in this Laboratory that it is not necessary to prepare the dialkyltin compound separately, and then treat it with the alkyl lithium compound to form the complex metal alkyl. As before,¹ tri-*n*-butyltin-lithium was prepared directly by treating finely ground, anhydrous stannous chloride with three equivalents of *n*-butyllithium in the cold. Similarly, triethyltin-lithium was



prepared by treating stannous chloride with ethyl-lithium. In the addition of *n*-butyllithium to stannous chloride, Color Test I⁷ became positive⁸ when exactly two equivalents of RLi had been added, but color test II,⁹ for very reactive organometallic compounds, remained negative until exactly three equivalents of RLi had been added. The Color Test results were not quite the same in the formation of triethyltin-lithium. As before, Color Test I became positive at the two-equivalents point,⁸ but Color Test II became positive when 2.5 equivalents of ethyllithium had been added. This

(2) J. A. Wanklyn, *Ann.*, **107**, 125 (1858); **111**, 284 (1859); **140**, 211 (1866).

(3) F. Hein, *Z. Elektrochem.*, **28**, 469 (1922); *Z. anorg. Chem.*, **141**, 161 (1924); **158**, 159 (1926); *Z. physik. Chem.*, **151A**, 24 (1930).

(4) H. Gilman, R. N. Meals, G. O'Donnell and L. Woods, *THIS JOURNAL*, **65**, 268 (1943).

(5) H. I. Schlesinger and H. C. Brown, *ibid.*, **62**, 3429 (1940); see also A. E. Finholt, A. C. Bond and H. I. Schlesinger, *ibid.*, **69**, 1199 (1947).

(6) D. T. Hurd, *J. Org. Chem.*, **13**, 711 (1948).

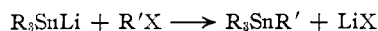
(7) H. Gilman and F. Schulze, *THIS JOURNAL*, **47**, 2002 (1925).

(8) Color Test I at this point was not the usual dark green color but was reminiscent of the blue of Michler hydrol. In contrast with this, triphenyltin-lithium does not give a positive Color Test I.

(9) H. Gilman and J. Swiss, *THIS JOURNAL*, **62**, 1847 (1940).

latter result is similar to that obtained in the preparation of triphenyllead-lithium from lead chloride and three equivalents of phenyllithium.¹⁰

Tri-*n*-butyltin-lithium has been treated with *n*-butyl iodide and iodobenzene to form tetra-*n*-butyltin and tri-*n*-butylphenyltin, respectively; triethyltin-lithium and ethyl bromide gave tetraethyltin in good yield.



Experimental

Tri-*n*-butyltin-lithium.—To a well-stirred suspension of 8.54 g. (0.045 mole) of finely ground, anhydrous stannous chloride in 100 ml. of ether maintained at -10° , was added, dropwise, 0.135 mole (3 equivalents) of *n*-butyllithium in 150 ml. of ether. When one equivalent (0.045 mole, 50 ml.) had been added, the reaction mixture was orange-colored; with two equivalents (0.09 mole, 100 ml.) the color was deep red; with three equivalents (0.135 mole, 150 ml.) the color was deep brown. Color Test I⁷ was negative until two equivalents (100 ml.) of *n*-butyllithium were added; Color Test II⁹ was negative until three equivalents (150 ml.) were added.

Tetra-*n*-butyltin.—To 0.045 mole of tri-*n*-butyltin-lithium was added 9.1 g. (0.0495, 10% excess 0.045, mole) of *n*-butyl iodide. The deep brown color of the reaction mixture immediately changed to bright yellow. The mixture was refluxed for 3 hours and hydrolyzed by pouring it into a saturated ammonium chloride solution. The layers were separated, and the ether layer dried over sodium sulfate. The ether was removed by distillation from a water-bath leaving about 15 ml. of a water-like liquid. The liquid was distilled under reduced pressure to yield 8.2 g. (52.5%) of tetra-*n*-butyltin, b.p. 127° (1.7 mm.),¹¹ n_{D}^{20} 1.4727.¹² The compound gave a positive qualitative test for tin.¹³

Run 2.—This run was carried out exactly as the first. The yield of tetra-*n*-butyltin was 7.0 g. (44.9%), b.p. 130° (2.0 mm.), n_{D}^{20} 1.4729.

Tri-*n*-butylphenyltin.—To 0.10 mole of tri-*n*-butyltin-lithium was added 20.4 g. (0.10 mole) of iodobenzene in 30 ml. of ether. The reaction mixture was refluxed for 24 hours and hydrolyzed as above. Removal of the ether yielded a water-like liquid which was distilled under reduced pressure. Two fractions were collected: Fraction I distilled at $70-87^\circ$ (0.1 mm.), weighed 10.0 g., n_{D}^{20} 1.4780. Fraction II distilled at $94-110^\circ$ (0.1 mm.), weighed 15.4 g., n_{D}^{20} 1.5094. Fraction II was redistilled under reduced pressure to yield a forerun distilling at $108-136^\circ$ (0.6 mm.) and 10.1 g. (27.6%) of tri-*n*-butylphenyltin, b.p. 139° (0.6 mm.), n_{D}^{20} 1.5155. The forerun was combined with Fraction I which was then redistilled under reduced pressure to yield 7.2 g. (27.8%) of tetra-*n*-butyltin, b.p. 109° (0.5 mm.), n_{D}^{20} 1.4731.¹² Both compounds gave a positive qualitative test for tin.¹³

Anal. Calcd. for $\text{C}_{18}\text{H}_{32}\text{Sn}$: Sn, 32.33. Found: Sn, 32.37.

Triethyltin-lithium.—To a well-stirred suspension of 8.54 g. (0.045 mole) of finely ground, anhydrous stannous chloride in 100 ml. of ether maintained at -10° , was added dropwise 0.135 mole (3 equivalents) of ethyllithium in 162 ml. of ether. When one equivalent (0.045 mole, 54 ml.) had been added, the reaction mixture was deep orange-colored; with two equivalents (0.09 mole, 108 ml.) the color was very deep red; with three equivalents (0.135 mole, 162 ml.) the color was very deep red. Color Test I was negative until two equivalents (108 ml.) of ethyllithium were added; Color Test II was negative until 2.5 equivalents (135 ml.) were added.

Ethyl Bromide; Tetraethyltin.—To 0.045 mole of triethyltin-lithium was added 10.0 g. (0.09 mole, 100% excess 0.045 mole) of ethyl bromide. The very deep red color of the reaction mixture immediately changed to dark gray.

(10) H. Gilman, L. Summers and R. W. Leeper, *J. Org. Chem.*, **17**, 630 (1952).

(11) All boiling points are uncorrected.

(12) W. J. Jones and co-workers, *J. Chem. Soc.*, 39 (1935), report n_{D}^{20} 1.4730 for tetra-*n*-butyltin.

(13) H. Gilman and T. N. Goreau, *J. Org. Chem.*, **17**, 1470 (1952).

The mixture was stirred overnight and hydrolyzed. Removal of the ether yielded a water-like liquid which was distilled to yield 7.3 g. (68.6%) of tetraethyltin, b.p. 178.5°, n_{D}^{20} 1.4691.¹⁴ The compound gave a positive qualitative test for tin.¹³

Run 2.—This run was carried out exactly as the first. The yield of tetraethyltin was 7.7 g. (72.6%), b.p. 177°, n_{D}^{20} 1.4691.

(14) L. L. Gershbein and V. N. Ipatieff, *THIS JOURNAL*, **74**, 1540 (1952), report n_{D}^{20} 1.4693 for tetraethyltin.

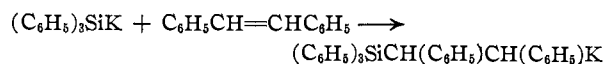
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Formation of Tetraphenylsilane from Reactions Involving Triphenylsilylpotassium

BY HENRY GILMAN AND T. C. WU

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It has been shown that triphenylsilylpotassium adds to unsaturated linkages such as the carbon-carbon double bond of *trans*-stilbene.¹ Studies



of the extension of the addition reaction to the acetylenic linkage showed that good yields of tetraphenylsilane were obtained. Thus, the reaction of triphenylsilylpotassium with phenylacetylene gave tetraphenylsilane as the major product.² Similarly, toluene reacts with triphenylsilylpotassium to give tetraphenylsilane in a lower yield. The high yield of tetraphenylsilane from the phenylacetylene reaction suggested the possible significance of the acidic hydrogen although we observed tetraphenylsilane was also formed from reactions involving triphenylsilylpotassium and some other compounds.³ We have examined the reactions of triphenylsilylpotassium with phenylcarbinols and obtained high yields of tetraphenylsilane in all cases. It was interesting to observe that triphenylsilanol also gave a high yield of tetraphenylsilane. Whether tetraphenylsilane was formed by disproportionation in these reactions is not known. The course of these reactions is being examined with compounds containing other functional groups as well as compounds containing substituted aryl groups, like the *m*-tolyl group.

Incidental to the studies of the reaction of triphenylsilylpotassium with triphenylcarbinol we observed that triphenylcarbinol does not depress the melting point of triphenylsilanol. The similarities between these two compounds rendered the separation of a mixture of them very difficult. It has been found that by treating a mixture of triphenylcarbinol and triphenylsilanol with formic acid the carbinol was reduced to triphenylmethane,⁴ whereas the silanol was converted into hexaphenyldisiloxane.⁵

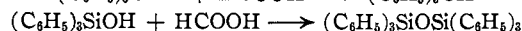
(1) H. Gilman and T. C. Wu, *THIS JOURNAL*, **75**, 234 (1953).

(2) From one reaction between phenylacetylene and triphenylsilylpotassium, followed by carbonation, there was isolated phenylpropionic acid as well as tetraphenylsilane.

(3) For example, reaction of triphenylsilylpotassium with diphenyl sulfoxide also gives tetraphenylsilane.

(4) A. Kovache, *Ann. chim.*, **10**, 184 (1918).

(5) Unpublished studies by H. W. Melvin.



The resulting hydrocarbon and the silicon compound were separated by recrystallization.

Experimental⁶

Reaction of Triphenylsilylpotassium with Phenylacetylene.—A triphenylsilylpotassium suspension in ether prepared from 5.2 g. (0.01 mole) of hexaphenyldisilane followed by amalgamation according to the recent directions⁷ was added rapidly to 1 g. (0.01 mole) of phenylacetylene dissolved in 20 ml. of ether. There was a slight heating effect accompanied by a slight change in color during the addition. The reaction mixture was stirred at room temperature for 30 hours. At the end of this period Color Test I⁸ was still positive. Water was added to the reaction mixture and the latter was stirred and filtered. There was obtained 3.5 g. of light gray solid melting at 230°. This solid was extracted with benzene and filtered hot in order to remove a trace of gray residue. The filtrate yielded 2.8 g. (83%) of colorless shining crystals melting at 233–235°; a mixed melting point with an authentic sample of tetraphenylsilane showed no depression. The ether solution of the hydrolyzed mixture was separated, dried over sodium sulfate, and distilled. The oily solid residue was recrystallized from a mixed solvent of benzene and petroleum ether (b.p. 60–70°) to give 0.5 g. of triphenylsilanol (mixed m.p.) melting at 149–151°.

In another experiment involving the same quantities of reactants the phenylacetylene was added to the triphenylsilylpotassium suspension. After 22 hours of stirring at room temperature the reaction mixture was carbonated with Dry Ice-ether slurry. Following the attainment of room temperature the carbonation mixture was hydrolyzed with dilute hydrochloric acid. There was separated 3.1 g. of light gray solid melting from 228–234°. This was recrystallized twice from benzene to yield 1.6 g. (48%) of tetraphenylsilane. Some impure tetraphenylsilane was recovered from the mother liquor. The ethereal solution from the hydrolysis mixture was extracted with dilute alkali. Some white solid was separated upon the acidification of the alkaline extract. This was dissolved in ether from which 0.8 g. of light brown solid residue was obtained by evaporation. This solid was recrystallized from benzene to give colorless shining prisms melting at 134–136°; a mixed melting point with phenylpropionic acid showed no depression. The purified acid weighed 0.5 g. (34%).

Reaction of Triphenylsilylpotassium with Toluene.—One and eight-tenths grams (0.01 mole) of toluene in 30 ml. of ether was added to 0.02 mole of a triphenylsilylpotassium suspension in ether without amalgamation over a period of 5 minutes. No appreciable amount of heat was evolved while the reaction mixture became very dark brown during the period of addition. The resulting mixture was stirred at room temperature for 24 hours. The black mixture thus formed was hydrolyzed with water and filtered by suction. There was collected 1.6 g. of solid melting to a turbid mass at 190°. This was recrystallized from benzene. The first crop separated as a fine white powder melting from 325–340°. Evaporation of the mother liquor to a small volume yielded 0.7 g. of colorless crystals melting from 225–230°. One recrystallization from benzene gave 0.5 g. (15%) of tetraphenylsilane (mixed m.p.) melting at 233–235°. Evaporation of the ethereal solution from the hydrolysis mixture resulted in a glue-like residue. Attempts to purify it by crystallization and by chromatographic separation were unsuccessful.

Reaction of Triphenylsilylpotassium with Triphenylcarbinol.—A triphenylsilylpotassium suspension was prepared by cleaving 5.2 g. (0.01 mole) of hexaphenyldisilane with sodium-potassium alloy in ether. The excess alloy was removed by amalgamation and the triphenylsilylpotassium

(6) All melting points are uncorrected.

(7) H. Gilman and T. C. Wu, *J. Org. Chem.*, in press; H. Gilman and T. C. Wu, *THIS JOURNAL*, **73**, 4031 (1951); H. Gilman, T. C. Wu, H. A. Hartzfeld, G. A. Guter, A. G. Smith, J. J. Goodman and S. H. Eidt, *ibid.*, **74**, 561 (1952).

(8) H. Gilman and F. Schulze, *ibid.*, **47**, 2002 (1925).

(9) The percentage yield was calculated on the assumption that from an initial mole of hexaphenyldisilane there is obtained 1 mole of tetraphenylsilane.