absolute ethanol with two equivalents of sodium ethoxide and two equivalents of urea.

Reaction of the *n*-butyl derivative (52) with thiourea yielded a sodium bicarbonate-soluble compound (m.p. 152–153°) which was possibly 5-*n*-butyl-2-thiobarbituric acid resulting from loss of 2,3-dihydrothiophene 1,1-dioxide from the molecule.

*Anal.* Calcd. for $C_8H_{12}N_2O_2S$: C, 47.98; H, 6.04; N, 13.99. Found: C, 47.98; H, 6.09; N, 14.25.

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# Some 2,5,8-Trimethyl-5,10-dihydrophenazasiline Derivatives

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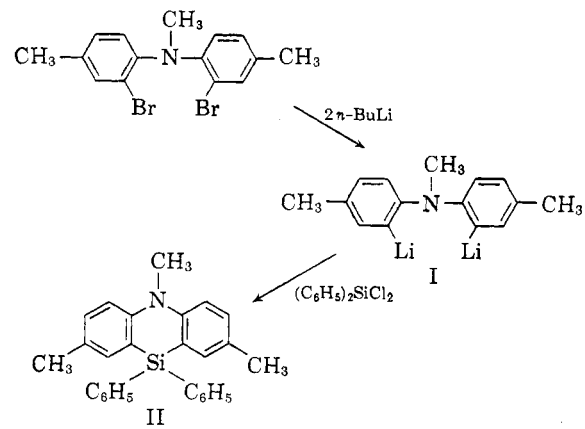
Bromination of *N*-methyldi-*p*-tolylamine gave *N*-methyl-2,2′-dibromodi-*p*-tolylamine in good yield. From the reaction of *N*-methyl-2,2′-dilithiodi-*p*-tolylamine and the appropriate halosilane, 2,5,8-trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline, 2,5,8-trimethyl-10,10-dibenzyl-5,10-dihydrophenazasiline, 2,5,8,10,10-pentamethyl-5,10-dihydrophenazasiline, and 2,2′,5,5′,8,8′-hexamethyl-10,10′-spirobi[5,10-dihydrophenazasiline] were prepared. Reactions of the dilithium compound with *sym*-tetraphenyldisilane and with triphenylchlorosilane are also described.

The applicability and versatility of the cyclization reactions involving N-substituted 2,2′-dilithiodiarylamine derivatives and the appropriate halosilanes for the synthesis of 5,10-dihydrophenazasiline compounds have been previously demonstrated.[1,2] However, these procedures suffer because the required 2,2′-dibromodiarylamines are difficult to prepare and because N-alkylation has been accomplished only by reacting the corresponding N-lithio intermediates with alkyl sulfates in refluxing tetrahydrofuran.[1,2] The general interest in these nitrogen-containing heterocyclic silanes has prompted a search for simplified methods for their preparation. In a recent communication,[3] preliminary work was reported describing the synthesis of 5,10-dihydrophenazasiline compounds from di-*p*-tolylamine derivatives. This is a more thorough description of that work and includes several extensions.

Treatment of a glacial acetic acid solution of N-methyldi-*p*-tolylamine with two molar equivalents of bromine gave N-methyl-2,2′-dibromodi-*p*-tolylamine in a 61% yield. This same compound was also prepared from the known 2,2′-dibromodi-*p*-tolylamine[2,4] by reaction first with methyllithium and then with dimethyl sulfate in refluxing tetrahydrofuran. Subsequently, *N*-methyl-2,2′-dibromodi-*p*-tolylamine was converted to N-methyl-2,2′-dilithiodi-*p*-tolylamine (I) by halogen-metal interconversion with *n*-butyllithium and then to 2,5,8-trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline (II) by treatment with diphenyldichlorosilane.

In an effort to obtain the dilithium compound I without the use of *n*-butyllithium, an ethereal




solution of N-methyl-2,2′-dibromodi-*p*-tolylamine was allowed to react with lithium metal. Treatment of this reaction mixture with diphenyldichlorosilane gave the 2,5,8-trimethylphenazasiline, compound II, but in a lower yield than that obtained above. Therefore, the method involving halogen-metal interconversion is preferred.

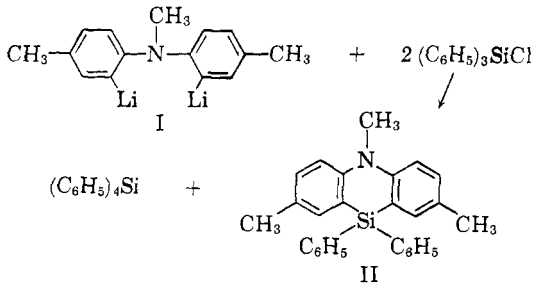
When two molar equivalents of N-methyl-2,2′-dilithiodi-*p*-tolylamine (I) were caused to react with silicon tetrachloride, 2,2′,5,5′,8,8′-hexamethyl-10,10′-spirobi[5,10-dihydrophenazasiline] was obtained in good yield. Likewise, treatment of the dilithium compound I with dimethyldichlorosilane and with dibenzyldichlorosilane gave 2,5,8,-10,10-pentamethyl-5,10-dihydrophenazasiline and 2,5,8-trimethyl-10,10-dibenzyl-5,10-dihydrophenazasiline, respectively.

In an attempt to prepare a seven-membered heterocyclic system, N-methyl-2,2′-dilithiodi-*p*-tolylamine (I) was allowed to react with *sym*-tetraphenyldisilane. However, scission of the silicon-silicon bond occurred and the only isolable product was 2,5,8-trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline (II). Similar cleavages of

(1) H. Gilman and E. A. Zuech, *Chem. Ind.* (London), 1227, (1958); *J. Am. Chem. Soc.*, **82**, 2522 (1960).
(2) H. Gilman and E. A. Zuech, *J. Org. Chem.*, **26**, 3481 (1961).
(3) H. Gilman and E. A. Zuech, *ibid.*, **24**, 1394 (1959).
(4) H. Gilman and E. A. Zuech, *ibid.*, **26**, 2013 (1961).

silicon-silicon bonds by organometallic reagents have been demonstrated previously.[5]

The reaction of N-methyl-2,2′-dilithiodi-*p*-tolylamine (I) with triphenylchlorosilane unexpectedly gave nearly equimolar amounts of 2,5,8-trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline (II) and tetraphenylsilane. Thus, it appears that one anion of the dilithium compound first displaces the chlorine; then, the second anion cleaves a silicon-phenyl linkage to give the silicon heterocycle II and phenyllithium which, in turn, couples with triphenylchlorosilane to give tetraphenylsilane. Similar cleavage-cyclization reactions have




been observed in the dibenzosilole[6] and silacyclopentane[7] systems. It should be noted from the latter study[7] that this abnormal cyclization seems to occur preferably when a five-membered cyclic silane is formed. However, in this case, the six-membered phenazasiline compound was formed in a yield comparable to those from the other investigations.

## Experimental

All reactions involving organometallic compounds were carried out in an atmosphere of dry, oxygen-free nitrogen, and all melting and boiling points are uncorrected. In accordance with the procedure of Weitz and Schwechten,[8] di-*p*-tolylamine was treated with dimethyl sulfate to give N-methyldi-*p*-tolylamine in a 52% yield. Employing the modification of Gibson and Vining,[9] the N-methyl compound was obtained in a 74% yield.

**N-Methyl-2,2′-dibromodi-*p*-tolylamine.**—The reaction of 31 g. (0.147 mole) of N-methyldi-*p*-tolylamine and 59 g. (0.37 mole) of bromine under the conditions previously employed for the bromination of di-*p*-tolylamine[2] afforded a 77% yield of colorless needles, m.p. 102–104° (ethanol).

*Anal.* Calcd. for $C_{15}H_{15}Br_2N$: Br, 43.30; N, 3.80. Found: Br, 43.26, 43.06; N, 4.04, 3.86.

N-Methyl-2,2′-dibromodi-*p*-tolylamine was also prepared in 89% yield by treatment of 2,2′-dibromodi-*p*-tolylamine with methyllithium followed by dimethyl sulfate.[2]

**2,5,8-Trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline. (A) By Halogen-Metal Interconversion.**—A solution of 7.38 g. (0.02 mole) of N-methyl-2,2′-dibromodi-*p*-tolylamine in 100 ml. of ether, cooled in an ice bath, was treated with 0.04 mole of *n*-butyllithium. After stirring for 45 min., Color Test II[10] was negative and 5.06 g. (0.02 mole) of diphenyldichlorosilane in 50 ml. of ether was added. The reaction mixture was stirred at room temperature for 18 hr., but Color Test I[11] remained positive. Toluene (50 ml.) was added and the ether removed by distillation. The toluene suspension was then refluxed for 4 hr., before the color test was negative. The reaction mixture was hydrolyzed, ether was added, and the organic layer separated. After drying with anhydrous calcium sulfate, the organic layer was evaporated, and the resulting solid was taken up in petroleum ether (b.p. 60–70°) to give 5.2 g. of pale yellow solid, m.p. 158–167°. After two recrystallizations from petroleum ether, there was obtained 3.87 g. (50%) of colorless crystals, m.p. 163–165°. Another recrystallization did not change the melting point.

*Anal.* Calcd. for $C_{27}H_{25}NSi$: C, 82.81; H, 6.44; N, 3.58; Si, 7.19. Found: C, 82.93, 83.13; H, 6.13, 6.18; N, 3.49, 3.43; Si, 7.30, 7.08.

**(B) By Direct Preparation.**—Ten milliliters of a solution of 5.55 g. (0.015 mole) of N-methyl-2,2′-dibromodi-*p*-tolylamine in 75 ml. of ether was added to 1.4 g. (0.2 g.-atom) of lithium in 10 ml. of ether. After adding three drops of methyl iodide, the reaction started and the rest of the dibromo compound was added at such a rate as to maintain a gentle reflux. The reaction mixture was stirred at room temperature for 45 min., and filtered through a previously dried glass wool plug. Acid titration of an aliquot indicated the presence of 0.022 mole of organolithium reagent. Assuming this to be all in the form of the dilithium compound, the yield was 73%.

The above solution was added to 3.03 g. (0.012 mole) of diphenyldichlorosilane in 25 ml. of ether and stirred for 18 hr. at room temperature. Color Test I[11] was negative, and the reaction mixture was hydrolyzed. The aqueous solution was separated, extracted with ether, and discarded. After drying and evaporating the combined organic layer, the residue was taken up in petroleum ether (b.p. 60–70°) to give a pale yellow solid, m.p. 145–158°. After two recrystallizations from petroleum ether, there was obtained 2.19 g. (37%, based on the N-methyl compound) of colorless crystals, m.p. 162–165°. An additional recrystallization raised the melting point to 163–165°. A mixed melting point determination with an authentic sample of 2,5,8-trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline was not depressed.

**2,2′,5,5′,8,8′-Hexamethyl-10,10′-spirobi[5,10-dihydrophenazasiline].**—A solution of 11.1 g. (0.03 mole) of N-methyl-2,2′-dibromodi-*p*-tolylamine in 150 ml. of ether, cooled in an ice bath, was treated with 0.06 mole of *n*-butyllithium. After stirring for 45 min., the solution was transferred to a dropping funnel and added to 2.55 g. (0.015 mole) of silicon tetrachloride in 100 ml. of ether. After hydrolysis and the usual work-up, the residue was taken up in ethyl acetate to give 3.85 g. of large colorless crystals, m.p. 228–232°. This material was recrystallized twice from ethyl acetate and then twice from cyclohexane to give 2.32 g. (35%) of colorless crystals, m.p. 230–233°.

*Anal.* Calcd. for $C_{30}H_{30}N_2Si$: C, 80.67; H, 6.77; Si, 6.29. Found: C, 80.74, 80.70; H, 6.70, 6.56; Si, 6.32, 6.24.

**2,5,8,10,10-Pentamethyl-5,10-dihydrophenazasiline.**—A solution of 3.9 g. (0.03 mole) of dimethyldichlorosilane in 50 ml. of ether was added to an ethereal solution containing 0.03 mole of N-methyl-2,2′-dilithiodi-*p*-tolylamine, prepared from 0.03 mole of N-methyl-2,2′-dibromodi-*p*-tolylamine and 0.06 mole of *n*-butyllithium. Work-up gave 3.77 g. (47%) of colorless crystals, m.p. 115–118°. The analytical sample melted at 117.5–119° (absolute ethanol).

*Anal.* Calcd. for $C_{17}H_{21}NSi$: C, 76.34; H, 7.86; N, 5.24. Found: C, 76.60, 76.42; H, 7.69, 7.76; N, 5.30, 5.20.

**2,5,8-Trimethyl-10,10-dibenzyl-5,10-dihydrophenaza-**

(5) For a discussion of the scission of silicon-silicon bonds, see H. Gilman and G. D. Lichtenwalter, *ibid.*, **24**, 1588 (1959).

(6) H. Gilman and R. D. Gorsich, *J. Am. Chem. Soc.*, **80**, 3243 (1958).

(7) D. Wittenberg and H. Gilman, *ibid.*, **80**, 2677 (1958).

(8) E. Weitz and H. W. Schwechten, *Ber.*, **60**, 550 (1927).

(9) C. S. Gibson and D. C. Vining, *J. Chem. Soc.*, **123**, 831 (1923).

(10) H. Gilman and J. Swiss, *J. Am. Chem. Soc.*, **62**, 1847 (1940).

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

**siline.**—An ethereal solution containing 0.015 mole of N-methyl-2,2′-dilithiodi-*p*-tolylamine was treated with 4.55 g. (0.015 mole) of dibenzyldichlorosilane[12] in 50 ml. of ether. After the customary reaction procedures and work-up, recrystallization from petroleum ether (b.p. 60–70°) gave 2.67 g. (43%) of colorless crystals, m.p. 123–125°. An additional recrystallization raised the melting point to 124–125.5°.

*Anal.* Calcd. for $C_{29}H_{29}NSi$: Si, 6.69. Found: Si, 6.87, 6.82.

**Reaction of N-Methyl-2,2′-dilithiodi-*p*-tolylamine and *sym*-Tetraphenyldisilane.**—N-Methyl-2,2′-dilithiodi-*p*-tolylamine, prepared from 5.75 g. (0.015 mole) of N-methyl-2,2′-dibromodi-*p*-tolylamine and 0.03 mole of *n*-butyllithium, was added to 5.55 g. (0.015 mole) of *sym*-tetraphenyldisilane[13] in 100 ml. of ether, and the reaction mixture stirred at room temperature for 24 hr. Toluene was added, the ether removed by distillation, and the resulting solution refluxed for 12 hr. before Color Test I[11] was negative. After hydrolysis and the usual work-up, the reaction products were chromatographed over alumina with petroleum ether (b.p. 60–70°). The first fractions gave only traces of oils; however, further elution with the same solvent gave a colorless solid which was recrystallized from petroleum ether to give 3.38 g. (58%) of colorless crystals, m.p. 160–165°. An additional recrystallization raised the melting point to 163–165°. This material was identified as 2,5,8-trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline by mixed melting point and by comparison of the infrared spectra. Elution with other solvents gave oils which could not be further purified or identified.

**Reaction of N-Methyl-2,2′-dilithiodi-*p*-tolylamine and Triphenylchlorosilane.**—An ethereal solution containing 0.03 mole of N-methyl-2,2′-dilithiodi-*p*-tolylamine, prepared by halogen-metal interconversion as described above, was treated with 17.7 g. (0.06 mole) of triphenylchlorosilane in 150 ml. of ether. The reaction mixture was stirred 24 hr. at room temperature, 50 ml. of toluene was added, and then the ether removed by distillation. After heating the toluene suspension at reflux for 4 hr., Color Test I[11] was negative. The reaction mixture was hydrolyzed with water, ether was added, and the resulting solid material was removed by filtration. After washing with ether, the solid was recrystallized from a 1:1 mixture of benzene and petroleum ether (b.p. 60–70°) to give 5.36 g. of colorless needles, m.p. 236–240°. A portion was recrystallized from ethyl acetate to give needles, m.p. 237.5–239°, which was identified as tetraphenylsilane by mixed melting point and by comparison of the infrared spectra.

The combined organic layer and ether washings were dried and evaporated. The residue was chromatographed over alumina. Elution with petroleum ether (b.p. 60–70°), followed by three recrystallizations from absolute ethanol, gave 1.09 g. (6%) of *n*-butyltriphenylsilane, m.p. 86–88°, identified by mixed melting point. Further elution with petroleum ether gave a colorless solid, which was recrystallized two times from ethyl acetate to give 0.28 g. of tetraphenylsilane, m.p. 235–238°.

After continued elution with petroleum ether and then with cyclohexane, there was obtained a colorless solid, which resisted purification by recrystallization. This solid material was subsequently rechromatographed over alumina. Using petroleum ether as the eluent, there was obtained a trace of solid which was recrystallized from ethyl acetate to give 0.17 g. of tetraphenylsilane. This is a total yield of 5.81 g. (58%, based on one half of the silicon). Further elution with petroleum ether and then with cyclohexane gave a colorless solid. This material was recrystallized three times from petroleum ether to give 4.93 g. (42%) of colorless crystals, m.p. 161–165°. A portion was recrystallized from the same solvent raising the melting point to 163–165°. The material was identified as 2,5,8-trimethyl-10,10-diphenyl-5,10-dihydrophenazasiline by mixed melting point and by comparison of the infrared spectra.

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(13) H. Gilman and W. Steudel, *Chem. Ind.* (London), 1094 (1959).

# Potential Antiradiation Agents. II. Selenium Analogs of 2-Aminoethylisothiouronium Hydrobromide and Related Compounds[1–3]

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The selenium analogs of 2-aminoethylisothiouronium salts, 2-aminothiazoline, and 2-thioethylguanidine have been prepared.

In view of the considerable effectiveness of aminoethyl mercaptan (cysteamine) and of 2-aminoethylisothiouronium salts (AET) in protecting animals against the effects of ionizing radiation,[4] efforts have been made to prepare even more active analogs of these compounds.

This problem can be approached in several ways: (1) through attachment of the 2-mercaptoethylamino grouping to molecules potentially capable of carrying it to sites where protection is needed;

(1) This work was supported, in part, by a contract (DA-49-193-MD-2106) from the U.S. Army Medical Research and Development Command, Office of the Surgeon General.
(2) Part of this material was presented before the Medicinal Chemistry Section of the American Chemical Society Meeting, Washington, D.C., March, 1962, 28-N.
(3) S. H. Chu and H. G. Mautner, *J. Org. Chem.*, **26**, 4998 (1961); Part I of this series.
(4) For a review of this field the reader is referred to A. Pihl and L. Eldjarn, *Pharmacol. Rev.*, **10**, 437 (1958).