kinetics only over the initial stages of the decomposition. This is because the vinylidene dichloride produced partially inhibits the reaction. The velocity constant falls off at initial pressures below 70 mm., but increases only slowly at initial pressures above this. In the 70 to 80 mm. range it can be represented by $10^{12.53}\ e^{-47,900/RT}$ sec.$^{-1}$ in the empty reactor. The radical chain mode of decomposition is completely suppressed by small additions of propylene and is decreased by packing.

All the facts with regard to the radical chain mechanism can be explained quantitatively in terms of a chain termination process involving CH_2CCl_3 and Cl, which occurs either in the gas phase or on the walls of the reactor.

The radical chain mechanism exhibits well defined induction periods which, in the empty reactor, can be represented by the equation $I = 10^{-14.4}e^{50,000/RT}$ sec. These are independent of initial pressure and only slightly dependent on packing. The unimolecular mechanism does not show induction periods.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Meta Rearrangement in the Reaction of Triphenyl-(*p*-bromophenyl)-silane with Lithium Dimethylamide

BY HENRY GILMAN AND H. W. MELVIN, JR.

In earlier communications it has been reported that *o*- and *p*-haloanisoles and related types undergo rearrangement reactions with metal amides in liquid ammonia and with lithium dialkylamides in ether to yield *m*-amino- and *m*-dialkylaminoanisoles, respectively.[1] It has also been ob-

$$p\text{-}BrC_6H_4OCH_3 + LiN(C_2H_5)_2 \longrightarrow m\text{-}(C_2H_5)_2NC_6H_4OCH_3 + LiBr$$

served that α-halonaphthalenes form β-dialkylaminonaphthalenes in their reaction with lithium dialkylamides in ether,[2] and β-aminonaphthalene is obtained when these halogen compounds are treated with metal amides in liquid ammonia.[3] When sulfur-containing compounds were investigated, *o*-halophenyl methyl sulfides and *o*-bromophenyl methyl sulfone were found to react with metal amides in liquid ammonia to yield *m*-amino derivatives.[4]

During the course of our investigations of organosilicon compounds, triphenyl-(*p*-bromophenyl)-silane was treated with lithium dimethylamide in ether, and in a benzene–ether mixture. The compound obtained was triphenyl-(*m*-dimethylaminophenyl)-silane.

$$(C_6H_5)_3SiC_6H_4Br\text{-}p + LiN(CH_3)_2 \longrightarrow (C_6H_5)_3SiC_6H_4N(CH_3)_2\text{-}m + LiBr$$

The product of this rearrangement reaction was identified through its synthesis in accordance with the scheme

$$(C_6H_5)_3SiCl + m\text{-}(CH_3)_2NC_6H_4Li \longrightarrow (C_6H_5)_3SiC_6H_4N(CH_3)_2\text{-}m + LiCl$$

(1) Gilman and Kyle, THIS JOURNAL, **70**, 3945 (1948). Earlier references may be traced from this citation.

(2) Gilman, Crounse, Massie, Benkeser and Spatz, *ibid.*, **67**, 2106 (1945).

(3) Urner and Bergstrom, *ibid.*, **67**, 2108 (1945).

(4) Martin, Doctoral Dissertation, Iowa State College, 1945.

Experimental

Triphenyl-(*p*-bromophenyl)-silane.—*p*-Bromophenyllithium[5] was prepared in ether by treating 13 g. (0.055 mole) of 1,4-dibromobenzene with 0.05 mole of *n*-butyllithium.[6] Color Test II-A[7] was negative immediately upon the conclusion of the addition of *n*-butyllithium. Then, 13.3 g. (0.045 mole) of triphenylchlorosilane dissolved in ether was added at such a rate as to maintain a gentle reflux, and a precipitate was promptly formed. After refluxing the mixture for one hour, it was hydrolyzed with 1:3 hydrochloric acid and most of the solid product settled at the ether–water interface. This material was collected on a filter. After the ether layer was separated and dried, the solvent was removed by distillation and a small quantity of solid remained. The total product was dissolved in the minimum volume of hot benzene and 95% ethanol was added until the hot solution began to assume a cloudy appearance. After cooling the solution, the solid that precipitated was collected on a filter and dried in a vacuum desiccator over sulfuric acid. The yield of triphenyl-(*p*-bromophenyl)-silane, melting at 167–168°, was 14.5 g. (78%, based on the quantity of triphenylchlorosilane used).

Anal. Calcd. for $C_{24}H_{19}BrSi$: Br, 19.3; Si, 6.7. Found: Br, 19.2; Si, 6.7.

In two other preparations, the yields were 73 and 77%, respectively.

Triphenyl-(*p*-bromophenyl)-silane and Lithium Dimethylamide.—Lithium dimethylamide was prepared by passing dimethylamine through an ether solution containing 0.03 mole of *n*-butyllithium against a pressure of 2–3 cm. of mercury.[2] Color Test II-A[7] was negative at the end of the reaction and Color Test IV[8] was positive.

To the suspension of lithium dimethylamide was added 10 g. (0.024 mole) of solid triphenyl-(*p*-bromophenyl)-silane and the mixture was refluxed for thirty-six hours. The usual procedure was followed in working up the reaction, and a viscous oil which could not be resolved by crystallization was obtained. This material was then suspended in ether, in which some of the product was sol-

(5) Gilman, Langham and Moore, THIS JOURNAL, **62**, 2327 (1940).

(6) *n*-Butyllithium was prepared in accordance with the recent directions of Gilman, Beel, Brannen, Bullock, Dunn and Miller, *ibid.*, **71**, 1499 (1949). The titer was determined by the double-titration method of Gilman and Haubein, *ibid.*, **66**, 1515 (1944).

(7) Gilman and Swiss, *ibid.*, **62**, 1847 (1940).

(8) Gilman and Woods, *ibid.*, **65**, 33 (1943).

uble, and the suspension treated with anhydrous hydrogen chloride. The precipitate was extracted with petroleum ether (b. p. 77–115°) and the insoluble portion was recrystallized from 95% ethanol. From the ethanolic solution was obtained 1.4 g. (14%) of a solid, the hydrochloride of triphenyl-(*m*-dimethylaminophenyl)-silane, which melted with decomposition at 210–211°. The quantity of unreacted triphenyl-(*p*-bromophenyl)-silane (mixed m. p.) recovered from the petroleum ether was 4.2 g. (42%). A viscous oil was also obtained. In a second experiment conducted in refluxing ether for thirty-eight hours, the yield of the hydrochloride was 1.5 g. (15%). The quantity of starting silane recovered was 4.1 g. (41%), and a viscous oil was obtained.

On the basis of the quantities of triphenyl-(*p*-bromophenyl)-silane entering into the reaction, the yields of the hydrochloride of triphenyl-(*m*-dimethylaminophenyl)-silane were 24.5 and 25.8%, respectively.

In each of two other experiments using the same quantities of starting materials as mentioned above, most of the ether was removed by distillation and replaced by 100 ml. of pure benzene, and the suspension refluxed for approximately forty hours. From the first run the products obtained were 3 g. (30%) of the hydrochloride, 4 g. (40% recovery) of triphenyl-(*p*-bromophenyl)-silane, and a viscous oil; and from the second run the products were 3.2 g. (32%) of hydrochloride, 4.1 g. (41% recovery) of triphenyl-(*p*-bromophenyl)-silane, and an oil. A mixed melting point determination of the hydrochlorides formed in each experiment showed no depression.

In these latter reactions, the yields of the hydrochloride of triphenyl-(*m*-dimethylaminophenyl)-silane, based on the amount of triphenyl-(*p*-bromophenyl)-silane reacting, were 50 and 55%, respectively.

Anal. Calcd. for $C_{26}H_{26}NClSi$: N, 3.4; Cl, 8.5; Si, 6.7. Found: N, 3.3; Cl, 8.6; Si, 6.6.

The oils formed in these reactions have not as yet been identified. Possibly these non-crystallizable liquids which decompose to a glass in attempts to distil them might contain some of the normal condensation product: triphenyl-(*p*-dimethylaminophenyl)-silane hydrochloride.

Triphenyl-(*m*-dimethylaminophenyl)-silane.—To 9.4 g. (0.034 mole) of triphenylchlorosilane dissolved in 50 ml. of ether was added 0.0375 mole of *m*-dimethylaminophenyllithium (prepared from 0.043 mole of *m*-bromodimethylaniline and 0.09 g. atom of lithium in 87% yield). Color Test I[9] was negative during the addition, and became positive only after an excess of the organolithium compound had been added. This indicates prompt reaction. The mixture was hydrolyzed and worked up in the customary manner. The yield of crude product, melting at 90–95°, was 11 g. (85%). The product was recrystallized from petroleum ether (b. p. 77–115°) to a constant melting point of 95–96°. The yield of pure triphenyl-(*m*-dimethylaminophenyl)-silane was 7.5 g. (58%).

Anal. Calcd. for $C_{26}H_{25}NSi$: N, 3.7; Si, 7.4. Found: N, 3.7; Si, 7.3.

Identification of the Product of Amination.—A portion of the amination product was dissolved in ethanol and gently heated with a solution of 10% sodium hydroxide dissolved in 50% ethanol. The precipitated free base was recrystallized from ethanol and melted at 94–95°. A mixture of this compound and authentic triphenyl-(*m*-dimethylaminophenyl)-silane (m. p. 95–96°) melted at 95–96°.

An ethereal solution of authentic triphenyl-(*m*-dimethylaminophenyl)-silane was treated with anhydrous hydrogen chloride, and the precipitate that formed was recrystallized from 95% ethanol. The melting point of this hydrochloride was 210–211° dec. The melting point of a mixture of this hydrochloride with that of the amination product was 210–211° dec.

Each free base formed a picrate melting with decomposition at 203–205°, and a mixed melting point showed no depression.

Anal. Calcd. for $C_{32}H_{28}O_7N_4Si$: N, 9.36; Si, 4.68. Found: N, 9.4; Si, 4.4.

The authors wish to thank Dr. S. V. Sunthankar for the *m*-bromodimethylaniline used in this study.

Summary

It has been shown that triphenyl-(*p*-bromophenyl)-silane undergoes a rearrangement reaction with lithium dimethylamide to form triphenyl-(*m*-dimethylaminophenyl)-silane.

The authentic specimen of triphenyl-(*m*-dimethylaminophenyl)-silane was prepared by interaction of triphenylchlorosilane and *m*-dimethylaminophenyllithium.

(9) Gilman and Schulze, *ibid.*, **47**, 2002 (1925).

AMES, IOWA RECEIVED JULY 21, 1949

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Naphthoquinone Antimalarials. XXIV. A New Synthesis of Lapinone

BY GEORGE FAWAZ[1] AND LOUIS F. FIESER

Preceding papers of this series have described investigations leading to the discovery of a drug, coded as M-2350, of promise as a curative antimalarial. We now propose the name lapinone, in recognition of the fact that the original clue came from observation of weak antimalarial activity of naphthoquinones resulting from Samuel C. Hooker's studies in the lapachol series. In an initial clinical trial conducted at the American University, Beirut, Lebanon, nine patients with primary vivax malaria treated with 2 g. of lapinone per day for four days (intravenous injection in gelatin solution[2]). All patients were promptly relieved of fever and parasites; two had relapses two and three weeks after treatment; one was free of symptoms for ten months and then either relapsed or was reinfected; and the other six have been without relapse for periods of thirteen to fifteen months after treatment.

Lapinone was originally synthesized by one of us (G.F.)[3] by a Grignard reaction on the hydroquinone triacetate I and subsequent air oxidation. These reactions proceeded well, as did the preparation of I from ethyl ω-(3-hydroxy-1,4-naphthoquinonyl-2)-nonanoate, but the latter substance was available in only very low yield by peroxide alkylation of hydroxynaphthoquinone.[4] The present investigation was thus aimed

(1) On leave of absence in 1945–1946 from the Department of Biochemistry, American University, Beirut, Lebanon; present address; Department of Pharmacology, American University.

(2) Fieser, Leffler and co-workers, THIS JOURNAL, **70**, 3155 (1948), see Note Added to Proof.

(3) Fieser, Leffler and co-workers, *ibid.*, **70**, 3210 (1948).

(4) Fieser and Turner, *ibid.*, **69**, 2338 (1947).