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THE REDUCTION OF AMIDES AND SILYL ESTERS WITH TRICHLOROSILANE-t-AMINES *

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Summary

It is demonstrated that the trichlorosilane-t-amine combination is capable of reducing aromatic tertiary amides. As is customary in such reductions, the carbonyl moiety of the amide grouping is replaced by the elements of $H\cdots SiCl_3$. The intermediates in these reductions have been identified and characterized. A one-pot, two step synthesis has been developed for reducing aromatic tertiary amides to the corresponding benzylamines. Unexpectedly, aromatic esters proved resistant to reduction by trichlorosilane-t-amine, despite the fact that aromatic acids are readily reduced. On the other hand, silicon esters reduce with remarkable ease. The reason for the dramatic differences in rate of reduction of these carbonyl derivatives is not understood.

Introduction

In a review article [2] we mentioned that trichlorosilane-t-amine combinations are capable of reducing aromatic tertiary amides. No experimental details of this reaction were published. Hence, we wish to give full details of these amide reductions and to describe the intermediates in the reaction which have now been isolated and characterized in several cases.

When *N,N*-dimethylbenzamide was treated with trichlorosilane and tri-n-propylamine, both IR and NMR spectra disclosed that the product was α-(*N,N*-dimethyl)benzyltrichlorosilane (eq. 1). It was clear that this reductive silylation had proceeded in complete accord with other carbonyl [3] compounds such that the oxygen of the carbonyl moiety $(-\overset{\overset{\displaystyle O}{\|}}{C}-)$ had been replaced by the ele-

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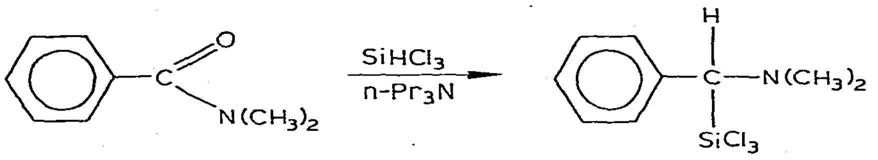
[*] This paper is dedicated to Professor Eugene G. Rochow on the occasion of his 70th birthday.

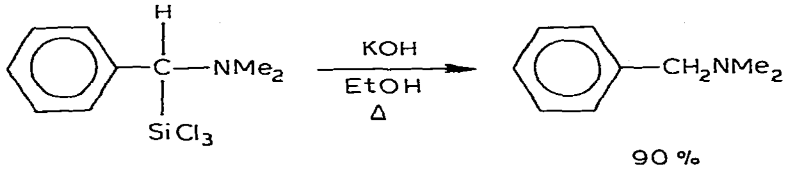
[**] Abstracted in part from the theses submitted by G.S.L. [1a] and E.C.M. [1b] in partial fulfillment of the requirements for the Ph. D. degree [1a].



(1)

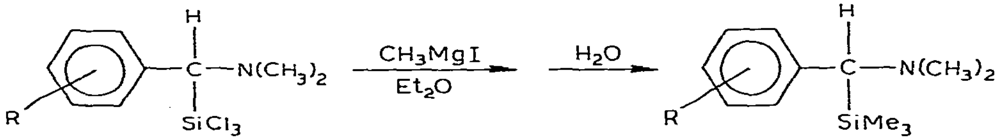
(I)

ments of H···SiCl$_3$. Compound I was extremely sensitive to atmospheric moisture as might be expected. Further evidence for its structure could be deduced from the fact that it was cleaved by alcoholic potassium hydroxide to *N,N*-dimethylbenzylamine in 90% yield (eq. 2). This opened the way for a



(2)

conversion of aromatic amides to benzylamines in a one-pot two step sequence (see Table 2). In the case of other ring substituted benzamides, the intermediates corresponding to compounds I were difficult to isolate in a pure enough form to obtain satisfactory elemental analyses, although the IR and NMR spectra of these materials strongly suggested we were dealing with compounds akin to I (see Table 1). Furthermore, treatment of these latter intermediates with alcoholic base led to the isolation and characterization of the corresponding benzylamines which provided additional proof for their structure. Finally, the intermediates were treated with methylmagnesium iodide to replace the active halogens on silicon with methyl groups. The methylated compounds were sufficiently stable to permit purification and to allow for elemental analysis (eq. 3).



(3)

In order to ascertain whether primary and secondary amides would undergo

TABLE 1

PROTON NMR SPECTRA [a] OF PRODUCTS FROM REDUCTIVE SILYLATION OF VARIOUS AMIDES

Amide	Reductive silylation product [b]	^{1}H NMR(δ, ppm) [c]
$C_6H_5CONMe_2$	$C_6H_5CHSiCl_3N(CH_3)_2$	2.4(s, 6 H); 3.46(s, 1 H); 7.25(s, 5 H)
p-$ClC_6H_4CONMe_2$	p-$ClC_6H_4CHSiCl_3N(CH_3)_2$	2.38(s, 6 H); 3.45(s, 1 H); 7.31(s, 4 H)
p-$CH_3C_6H_4CONMe_2$	p-$CH_3C_6H_4CHSiCl_3N(CH_3)_2$	2.32(2s, 9 H); 3.38(s, 1 H); 7.15(m, 4 H)
p-$CH_3OC_6H_4CONMe_2$	p-$CH_3OC_6H_4CHSiCl_3N(CH_3)_2$	2.33(s, 6 H); 3.43(s, 1 H); 3.72(s, 3 H); 7.07(m, 4 H)

[a] CDCl$_3$ solution with TMS internal standard (60 MHz); s, singlet; d, doublet; m, multiplet. [b] The IR spectra of all these compounds showed no carbonyl absorption. [c] Single numbers represent center of resonance.

TABLE 2

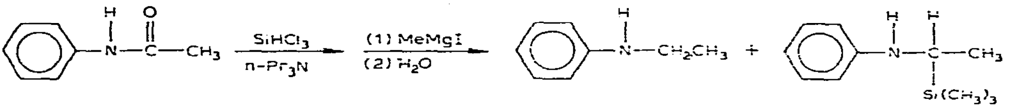
REDUCTIVE SILYLATION OF AROMATIC AMIDES TO BENZYLAMINES IN A TWO-STEP SEQUENCE

$$ArCONMe_2 \xrightarrow[R_3N]{SiHCl_3} ArCHSiCl_3NMe_2 \xrightarrow{OH^-} ArCH_2NMe_2$$

Starting tertiary Amide	Benzylamine product (yield (%))[a]
$C_6H_5CONMe_2$	$C_6H_5CH_2NMe_2$ (60)
p-$CH_3OC_6H_4CONMe_2$	p-$CH_3OC_6H_4CH_2NMe_2$ (55)
$p ClC_6H_4CONMe_2$	p-$ClC_6H_4CH_2NMe_2$ (53)
p-$CH_3C_6H_4CONMe_2$	p-$CH_3C_6H_4CH_2NMe_2$ (50)

[a] Yields given in parentheses are the composite of the two-step reaction.

the same type of reaction, acetanilide was submitted to the same reaction sequence. Methylation of the intermediate with methylmagnesium iodide gave rather low yields of two products, *N*-ethylaniline and *N*-(α-trimethylsilylethyl)-aniline (eq. 4). The source of the *N*-ethylaniline was not established with certainty. However, when compound II was subjected to base treatment, *N*-ethylaniline was formed. This might suggest that during the methylation process (eq. 4), the *N*-ethylaniline somehow arose from II.



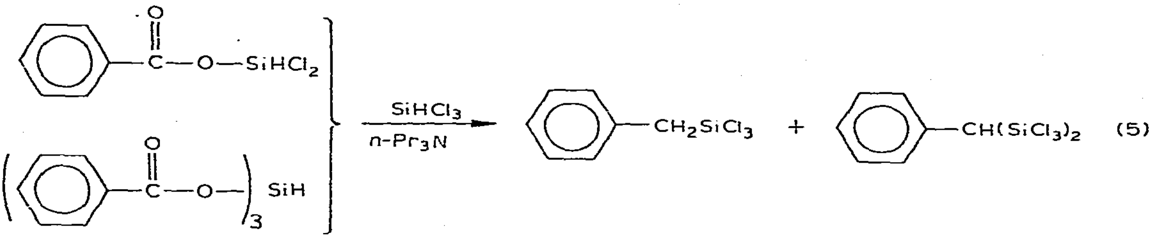
(4)

(II)

Benzamide did not seem to react in the usual way with trichlorosilane and tri-n-propylamine in that no recognizable products could be isolated. With regard to tertiary aliphatic amides, *N*,*N*-dimethylacetamide gave intermediates which analyzed correctly for the products obtained after treatment with the methyl Grignard reagent, albeit in low yields. When this material was treated with base, however, no amine product could be identified. On the basis of these results, one must conclude that tertiary aromatic amides undergo reductive silylation more successfully than do secondary or primary amides and that the reaction with aliphatic amides is of dubious value.

Earlier [4] we had shown that the carboxyl group of an aromatic acid could be reduced to a methyl group in a two step sequence involving trichlorosilane and t-amines. This result would imply that simple aromatic esters like ethyl benzoate should undergo a similar type of reduction, since ester groups are routinely easier to reduce than their corresponding acid. In this instance this did not prove to be the case. Repeated efforts to reduce ethyl benzoate under a variety of conditions failed completely and the ester could be recovered almost quantitatively in every instance.

In the procedure [5] devised for the reduction of aromatic acids, the first step involved adding the acid to trichlorosilane (in acetonitrile) and heating for about one hour before the tertiary amine was added. During this heating period, hydrogen chloride gas was evolved. On the basis of this observation, it



seemed that the entity undergoing reduction was a silicon ester rather than the acid itself. To test this, both benzoxydichlorosilane and tribenzoxysilane were synthesized and each subjected to the reductive silylation procedure. In both case good yields of benzyltrichlorosilane and 1,1-bis(trichlorosilyl)toluene were realized. It is clear, then, that while ordinary esters do not reduce under these conditions, silicon esters are readily reduced. The reason for this dichotomy is not immediately apparent but obviously has its foundation in the mechanism by which these reductive silylations proceed.

Experimental section

All experiments involving the use of trichlorosilane were conducted under dry nitrogen and all glassware was dried by a Bunsen flame prior to use. The solvents were previously dried over calcium sulfate or molecular sieves. All boiling points and melting points are uncorrected.

Elemental analyses were performed in the Purdue Microanalytical Laboratory by Dr. C.S. Yeh and her associates. Sample purification was by GC using an F and M Model 500 chromatograph. The proton NMR spectra were determined on a Varian A-60-A Spectrometer. The IR spectra were obtained on a Perkin—Elmer 127 Spectrophotometer.

Reductive silylation of various N,N-dimethyl substituted amides

N,N-Dimethylbenzamide. Trichlorosilane (65.3 g, 480 mmol, Dow Corning) was added over a 2 h period to a solution of *N,N*-dimethylbenzamide (30 g, 200 mmol) and tri-n-propylamine (34.4 g, 240 mmol, Aldrich). The mixture was heated for 6 h at 115°C, then cooled and combined with 150 ml of n-pentane. The precipitate which formed was filtered, washed with pentane and dried in vacuo to give 31 g of tri-n-propylammonium chloride (170 mmol, m.p. 135°C, lit [6] 137°C). The filtrate was distilled yielding 33 g of a slightly green liquid boiling at 99—100°C (2.7 mmHg). Analysis by GC showed this to be pure α-(*N,N*-dimethylamino)benzyltrichlorosilane (64% yield); the IR and NMR spectra were in agreement with this assignment. Anal.: Found: C, 40.21; H, 4.36; Cl, 39.44; N, 5.49; Si, 10.61. Calcd. for $C_9H_{12}Cl_3NSi$: C, 40.20; H, 4.46; Cl, 39.00; N, 5.21; Si, 10.00%.

A solution of 50 ml of 80% anhydrous ethanol containing 12 g of potassium hydroxide (270 mmol) was cooled in an ice bath and then treated slowly with 5.4 g (20 mmol) of α-(*N,N*-dimethylamino)benzyltrichlorosilane. The mixture was stirred at room temperature for 4 h. It was combined with 50 ml of water and extracted three times with 100 ml portions of ether. The ether extracts were combined and dried over anhydrous $MgSO_4$. The dried solution was concentrated to 2.5 g. Analysis by GC (10 ft Carbowax column at 150°C) showed this to be pure *N*,*N*-dimethylbenzylamine [7] (90%). Its IR spectrum was identical to Sadtler [8] spectrum No. 4718 for *N*,*N*-dimethylbenzylamine.

N,N-Dimethyl-p-chlorobenzamide. A solution of *N*,*N*-dimethyl-*p*-chlorobenzamide (18.3 g, 100 mmol) and trichlorosilane (40.7 g, 300 mmol) in 20 ml of benzene was treated slowly with tri-n-propylamine (17.2 g, 120 mmol). The mixture was then heated for 24 h at 70°C, cooled and treated with 300 ml of pentane. The work-up that followed was identical to that described for *N*,*N*-dimethylbenzamide. The filtrate was distilled to give 10 g of a yellow liquid boiling at 201—205°C at 0.5 mmHg. Analysis by GC was unsuccessful. IR spectra showed no carbonyl band and the NMR spectrum (Table 1) was in agreement with the structure of α-(*N*,*N*-dimethylamino)-*p*-chlorobenzyltrichlorosilane.

N,N-Dimethyl-p-methoxybenzamide. A solution of *N*,*N*-dimethyl-*p*-methoxybenzamide (18.3 g, 100 mmol) and trichlorosilane (40.7 g, 300 mmol) in 20 ml of benzene was treated slowly with tri-n-propylamine (17.2 g, 120 mmol). It was then heated for 12 h at 75°C. The work-up was similar to that described above. The filtrate, after distillation, gave 12 g of liquid boiling at 160°C at 0.7 mmHg. Analysis by GC was unsuccessful but the IR spectra showed no carbonyl band and the NMR spectrum (Table 1) was in agreement with the structure of α-(*N*,*N*-dimethylamino)-*p*-methoxybenzyltrichlorosilane.

Reductive silylation of amides followed by immediate treatment with methylmagnesium iodide

N,N-Dimethyl-p-methoxybenzamide. A solution of 18.3 g of *N*,*N*-dimethyl-*p*-methoxybenzamide (100 mmol) and 40.7 g of trichlorosilane (300 mmol, Dow Corning) in 20 ml of benzene was treated slowly with 17.2 g of tri-n-propylamine (120 mmol, Aldrich) and heated for 12 h at 75°C. The mixture was cooled and combined with 30 ml of pentane. The precipitate which resulted was filtered and the filtrate was concentrated by solvent removal until about 20 g of residue remained. The latter was added to 20 ml of absolute ether and treated slowly with 250 ml, 0.8 *M* (200 mmol) of methylmagnesium iodide in ether. After refluxing for 12 h, the resulting mixture was hydrolyzed with saturated ammonium chloride solution followed by the usual work-up. Distillation gave 8 g of liquid boiling at 115°C/6 mmHg. Analysis by GC (10 ft, 20% Carbowax column at 225°C) showed this to be 95% pure α-(*N*,*N*-dimethylamino)-*p*-methoxybenzyltrimethylsilane (35% yield based on starting amide); NMR spectrum (CCl_4 without TMS): δ 0.05 (s, 9 H), 2.28 (s, 6 H), 3.80 (s, 3 H), 6.95 (m, 4 H). Anal.: Found: C, 65.76; H, 9.72; N, 6.21; Si, 11.61. Calcd. for $C_{13}H_{23}NOSi$: C, 65.79; H, 9.79; N, 5.90; Si, 11.80%.

N,N-Dimethylacetamide. A solution of 17.4 g of *N*,*N*-dimethylacetamide (200 mmol), 81 g of trichlorosilane (600 mmol) in 20 ml of benzene was treated slowly with 34.4 g of tri-n-propylamine (240 mmol). The temperature rose spontaneously to 60°C after which the mixture was heated for 1 h at this temperature. It was then cooled and combined with 600 ml of pentane. The precipitate of tri-n-propylammonium chloride (37 g, 210 mmol) was filtered and the filtrate distilled to give 10 g of liquid boiling at 40—50°C/5—10 mmHg. Analysis by GC was not possible, however, the IR spectra of the material showed no carbonyl band. Its NMR spectrum: δ 1.3 (d, 3 H); 2.42 (s, 6 H); 2.90 (q, 1 H) was in agreement with the possible structure of 1-(*N*,*N*-dimethylamino)ethyltrichlorosilane.

To 10 g of the above material was added 50 ml of absolute ether followed by the slow dropwise addition of 500 ml (0.8 *M*, 400 mmol) of methylmagnesium iodide in ether. After the vigorous exothermic effects had ceased, the mixture was refluxed for 12 h. It was then hydrolyzed in the ususal way with saturated ammonium chloride solution. After the usual treatment, the remaining liquid was distilled to give 8 g of material boiling at 30° C/8 mmHg. Analysis by GC (10 ft. 20% Carbowax at 75° C) indicated a mixture of 50% tri-n-propylamine and 50% 1-(*N*,*N*-dimethylamino)ethyltrimethylsilane (14% based on starting amide). NMR spectrum of the latter: δ 1.30 (d, 3 H); 2.41 (s, 6 H); 2.83 (q, 1 H). Anal.: Found: C, 58.23; H, 13.04; N, 9.98; Si, 19.20. Calcd. for $C_7H_{19}NSi$: C, 57.85; H, 13.21; N, 9.65; Si, 19.28%.

Acetanilide. A solution of 13.5 g of acetanilide (100 mmol, Mallinckrodt) and 40.5 g of trichlorosilane (300 mmol) in 20 ml of benzene was treated slowly with 15.7 g of tri-n-propylamine (110 mmol) while the reaction flask was kept in an ice bath. The mixture was refluxed for 14 h at 70° C. It was then cooled and combined with 200 ml of pentane. The resulting precipitate was filtered and the filtrate concentrated by solvent removal until there was about 20 g of residue remaining. This was combined with 20 ml of dry ether and then treated slowly with 250 ml (0.8 *M*, 200 mmol) of methylmagnesium iodide. This mixture was refluxed for 12 h, then combined with saturated ammonium chloride solution and worked up in the customary fashion. Distillation resulted in 5 g of liquid boiling at 75—100° C/6 mmHg. Analysis by GC (10 ft., 20% Carbowax column) showed this to be 37% *N*-ethylaniline [9] (16% yield) and 63% *N*-(α-trimethylsilylethyl)aniline (12% yield). The NMR of the latter was in agreement with the assigned structure: δ 0.01 (s, 9 H); 1.9 (d, 3 H); 2.95 (m, 2 H); 6.72 (m, 5 H). Anal.: Found: C, 68.25; H, 10.00; N, 7.53; Si, 14.31. Calcd. for $C_{11}H_{19}NSi$: C, 68.33; H, 9.91; N, 7.25; Si, 14.50%.

Benzamide. A solution of 24 g of benzamide (200 mmol) and 28.6 g tri-n-propylamine (200 mmol) in 20 ml of benzene was treated slowly with 81 g of trichlorosilane (600 mmol). The mixture was stirred and refluxed for 1.5 h (60° C). It was then poured into 500 ml of ether. The solution was worked up in the usual fashion but distillation gave no identifiable products.

Attempted reduction of ethyl benzoate. Ethyl benzoate (15.0 g, 0.1 mol), 80.7 g (60 ml, 0.6 mol) of trichlorosilane in 30 ml of acetonitrile was cooled to 0° C and 43.0 g (0.3 mol) of tri-n-propylamine was added dropwise. The mixture was refluxed for 12 h in a dry 300 ml, three neck flask, equipped with a reflux condenser and a magnetic stirrer. It was then cooled and poured into 1 l of 50% ether in pentane, whereupon a white precipitate formed. This was filtered and the solvent flash distilled. The residue was distilled under vacuum giving 14.8 g (98% recovery) of ethyl benzoate.

In another attempt, ethyl benzoate (7.9 g, 53 mmol), trichlorosilane (13 ml, 130 mmol) and acetonitrile (25 ml) were combined. Tri-n-propylamine (8.6 g, 60 mmol) was added at room temperature. The mixture was transferred to a dry, 150 ml stainless steel bomb by means of a dry syringe. The bomb was sealed and heated at 110° C for 18 h. After a work-up similar to that above, 7.8 g (99% recovery) of ethyl benzoate was realized.

Benzoxydichlorosilane. A mixture of benzoic acid (200 mmol, Mallinckrodt) and 203 g of trichlorosilane (1.49 mol, Union Carbide) was stirred and heated at 40° C for 55 min. During this time period, gas evolved vigorously and benzoic acid gradually dissolved in the solution. The resulting clear solution was distilled to give 31 g benzoxydichlorosilane (70%) boiling at 77—78° C/1.3 mmHg. The IR and NMR spectra of this compound were in agreement with the structural assignments. Anal.: Found: C, 38.28; H, 2.65; Cl, 31.92; Si, 12.65. Calc. for $C_7H_5Cl_2O_2Si$: C, 38.01; H, 2.78; Cl, 32.11, Si, 12.62%.

Reductive silylation of benzoxydichlorosilane. A solution of 5 g benzoxydichlorosilane (22.6 mmol) and 20 g of trichlorosilane (150 mmol) in 20 ml of acetonitrile was refluxed for 10 min (40° C). The mixture was then treated over a 15 min period with 7.15 g of tri-n-propylamine (50 mmol) and refluxed for an additional 16 h (50° C). It was then cooled and 600 ml of anhydrous ether added to precipitate 9.0 g of tri-n-propylammonium chloride. The filtrate was distilled to give 2.5 g of liquid boiling at 90—120° C/4.0 mmHg. Analysis by GC (10 ft., QF-1 at 175° C) showed this to be a mixture of benzyltrichlorosilane (64%) and 1,1-bistrichlorosilyltoluene (36%). Their IR spectra matched those of authentic samples [10]. The combined yield of these products was 43%.

Tribenzoxysilane. A solution of 24.4 g of benzoic acid (200 mmol, Mallinckrodt) in 50 ml of benzene was treated slowly with 27.1 g of trichlorosilane (200 mmol). The mixture was stirred and heated at 40° C for 2 h during which time there was vigorous gas evolution. The reaction flask was then immersed in a water bath and the solvent was slowly removed over a 12 h period under vacuum. There remained 26 g (100% yield) of a white solid whose IR and NMR spectra were in agreement with the structure of tribenzoxysilane. Anal.: Found: C, 63.89; H, 4.38; Si, 6.99. Calcd. for $C_{21}H_{16}O_6Si$: C, 64.17; H, 4.12; Si, 7.13%.

Reductive silylation of tribenzoxysilane. A solution of 10 g (25.6 mmol) of tribenzoxysilane and 28.6 g (200 mmol) of tri-n-propylamine in 30 ml of acetonitrile was treated slowly with 54 g of trichlorosilane and then refluxed for 16 h (60° C). The mixture was cooled and combined with 500 ml of ether. The tri-n-propylammonium chloride which precipitated (35 g, 200 mmol) was filtered. The dried filtrate was distilled, giving 9.5 g of liquid boiling at 80—120° C/5—10 mmHg. Analysis by GC (10 ft. QF-1 column at 175° C) showed this to be 88% benzyltrichlorosilane and 12% 1,1-bis(trichlorosilyl)toluene. The IR spectra of these materials matched those of authentic samples [10]. The combined yield of these two products was 53%.

Reductive silylation of amides to amines in a two-step sequence. A solution of 9.1 g of *N,N*-dimethyl-*p*-methylbenzamide (61 mmol) and 24.8 g of trichlorosilane (180 mmol, Dow Corning) in 20 ml of benzene was treated slowly with 10.5 g tri-n-propylamine (72 mmol, Aldrich). The mixture was refluxed for 24 h (75° C), cooled, and then carefully mixed with a solution of 55 g of potassium hydroxide (1 mol) in 250 ml of 80% ethanol. This was stirred at room temperature for 12 h after which it was extracted with 500 ml of ether. After the usual work-up, distillation gave 4.5 g of pure *p*-methyl-*N,N*-dimethylbenzylamine (50%) boiling at 197—198° C/760 mmHg (lit. [11] 196—197° C). The IR and NMR spectra were in agreement with the structural assignments.

The above directions are typical for all reactions listed in Table 2.

Acknowledgments

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