Silylations with Bis(trimethylsilyl)acetamide, a Highly Reactive Silyl Donor

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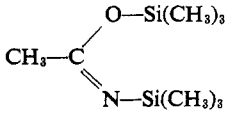
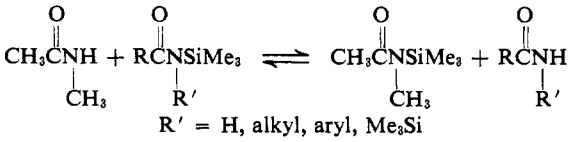
Abstract: Silyl–proton exchange reactions with bis(trimethylsilyl)acetamide proceed rapidly and quantitatively under mild conditions. The preparative silylation of amides, ureas, and amino acids, as well as hindered phenols, carboxylic acids, and enols, is described. Examples of silylation as a protective measure and a means of preparing reactive intermediates are included.

The quantitative conversion of organic compounds to stable, easily separated and identified derivatives has long been the crux of analytical procedures in organic and biological chemistry. With the advent of gas chromatography, the general character of desirable derivatives has changed from high-melting solids to volatile liquids and this, in turn, has required the development of new reagents and techniques. In the case of hydrogen-bonded materials such as carboxylic acids, alcohols, amines, and amides, one of the more useful methods has been silylation.[1] In general, silylation has had the advantage of producing readily volatile products even from such intractable materials as carbohydrates,[2-6] amino acids,[7,8] peptides,[9] steroids,[10] flavonoid compounds,[11] bile,[12] and Krebs cycle acids;[13] however, the available methods for the preparation of silyl derivatives often are not completely satisfactory.[14] It has now been found that bis(trimethylsilyl)acetamide (BSA) is a silylating agent superior, in many respects, to the presently used methods.

Bis(trimethylsilyl)acetamide (I) was first described by Birkofer, Ritter, and Giessler;[15] the N-silyl-silylimidate structure proposed by Pump and Rochow is based on its pmr spectrum.[16]



Our studies on silyl–proton exchange reactions of silyl-substituted amides and ureas[17,18] have shown that silyl groups on nitrogen adjacent to carbonyl in general show greatly enhanced mobilities as compared with silylamines, a fact which was preparatively utilized in our laboratory[18] as well as by Birkofer, Ritter, and Bentz who employed trimethylsilylacetamide for the silylation of glucose.[19] An investigation of correlations between structure and donor strength of silylamides[20] included several bis(silyl-substituted) amides. The scale of silyl donor strength which was established by measurement of exchange equilibria shows bis(trimethylsilyl)acetamide (by a factor of about 50) more powerful than any of the monosilyl-substituted amides that were investigated. The reactivity increase can be expected since the second silyl group will claim its share of the available π electrons and thus weaken the $d\pi$–$p\pi$ overlap between silicon and nitrogen.



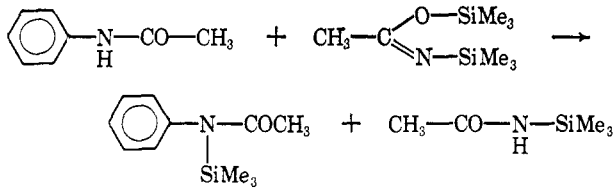
Silyl–proton transfer between silylamides and acceptor molecules is an equilibrium process. Silylations of "good" acceptors—alcohols, amines, carboxylic acids—can be carried out with monosilylamides since the rapidly established equilibria lie far on the product side. However, displacement of protons from other amides is bound to be incomplete when monosilylamides are used as silyl donors; it is here where the thermodynamically greater silylating strength of disilylamides is of special significance. We found that bis(trimethylsilyl)acetamide will silylate amides, ureas, and dipeptides; the reactions are fast at low or moderate temperatures, no acids or bases are involved, and no difficult to remove by-products are formed. Pmr or vpc was used to establish that the conversions are practically quantitative for a number of representative compounds.

(1) The term "silylation" is used here in the sense of replacement of protons by triorganosilyl and specifically trimethylsilyl groups.
(2) M. M. Sprung and L. S. Nelson, *J. Org. Chem.*, **20**, 1750 (1955).
(3) E. V. Hedgley and W. G. Overend, *Chem. Ind.* (London), 378 (1960).
(4) F. A. Henglein, G. Abelsnes, H. Heneka, K. Lienhard, P. Nakhre, and K. Scheinost, *Makromol. Chem.*, **24**, 1 (1957).
(5) R. J. Ferrier and M. F. Singleton, *Tetrahedron*, **18**, 1143 (1962).
(6) C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wels, *J. Am. Chem. Soc.*, **85**, 2497 (1963).
(7) L. Birkofer and A. Ritter, *Chem. Ber.*, **93**, 424 (1960).
(8) K. Rühlmann, *ibid.*, **94**, 1876 (1961).
(9) L. Birkofer, A. Ritter, and P. Neuhausen, *Ann.*, **659**, 190 (1692).
(10) T. Luukainen, W. J. A. VandenHeuvel, and E. C. Horning, *Biochim. Biophys. Acta*, **62**, 153 (1962).
(11) A. C. Waiss, Jr., R. E. Lundin, and D. J. Stern, *Tetrahedron Letters*, **10**, 573 (1964).
(12) M. Makita and W. W. Wells, *Anal. Biochem.*, **5**, 523 (1963).
(13) Z. Horii, M. Makita, and Y. Tamura, *Chem. Ind.* (London), 1494 (1965).
(14) The silylating agents in general use are hexamethyldisilazane, trimethylsilylalkylamines, or a mixture of trimethylsilylamine and trimethylchlorosilane. Silylations with hexamethyldisilazane or silylamines require prolonged heating and continuous removal of ammonia or amine. The chlorosilane–silazane mixture, while more reactive, has the disadvantage of producing amine hydrochlorides which often are difficult to separate from the desired product.
(15) L. Birkofer, A. Ritter, and W. Giessler, *Angew. Chem.*, **75**, 93 (1963).
(16) J. Pump and E. G. Rochow, *Ber.*, **97**, 627 (1964).
(17) J. F. Klebe, J. B. Bush, Jr., and J. E. Lyons, *J. Am. Chem. Soc.*, **86**, 4400 (1964).
(18) J. F. Klebe, *ibid.*, **86**, 3399 (1964).
(19) L. Birkofer, A. Ritter, and F. Bentz, *Chem. Ber.*, **97**, 2196 (1964).
(20) J. F. Klebe and J. B. Bush, Jr., presented at the International Symposium on Organosilicon Chemistry, Prague, 1965.

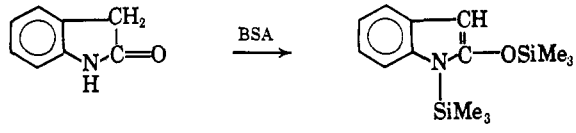
Both silyl groups can be exchanged in cases where the position of equilibrium favors the transfer, as with alcoholic or carboxylic hydroxyl groups or amines; the separation from acetamide is then carried out by extraction with a hydrocarbon solvent or by distillation. However, even with easily silylated materials we found it often more convenient to use a full equivalent of bis(trimethylsilyl)acetamide per exchangeable proton. The monosilylacetamide thus formed has a boiling point of 45–47° (0.2 mm) and can easily be removed under a good vacuum whenever the vapor pressure of the silylated product is sufficiently low. No separation is usually required for vapor phase chromatographic analyses; both mono- and disilyl-substituted acetamide give sharp peaks with relatively low retention times on most nonpolar columns.

In the following part of this paper, examples of the various silylations with bis(trimethylsilyl)acetamide (BSA) that were carried out in our laboratory are shown. All products are listed in Table I.

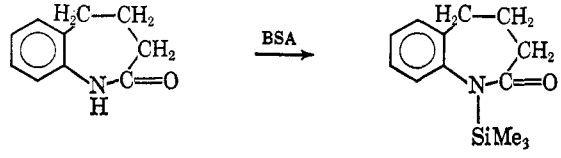
A. Amides. Various silyl-substituted anilides and other aromatic silylamides were needed for a study of their silyl donor properties.[20] The starting materials were heated with a slight excess of BSA in acetonitrile solvent at 70–80° for 10 to 30 min until clear solutions were obtained at which point the silylations were found to be complete in all cases. Quantitative conversion



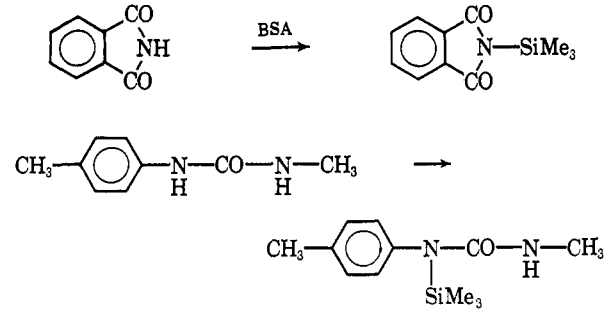
was also achieved at room temperature in longer periods of time; limited solubility of the amides in convenient, low-boiling solvents determines the relatively low rates of reaction. Oxindole was converted into the bissilyl derivative; no monosilyloxindole could



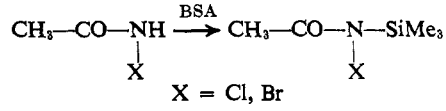
be isolated. The silylation of the enolic hydroxyl group is aided by the formation of the conjugated double bond; homodihydrocarbostyril forms only a



monosilyl derivative. Two compounds of related structure, phthalimide and *p*-tolylmethylurea, were also readily converted into the silyl derivatives. The fact that only one of the two nitrogen-bound protons in the urea is displaced by a silyl group is plausible since the lone electron pairs on the nitrogen atoms are integrated in the π system of the urea group; the disilyl-substituted urea should thus be on an energy level close to that of BSA. Diketopiperazine as an example of a dipeptide was somewhat more difficult to



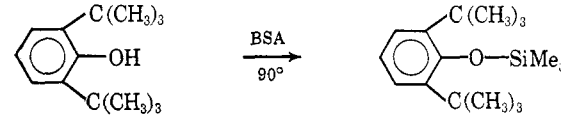
silylate due to its low solubility in nonhydroxylic solvents. A suspension of the dipeptide in a mixture of equal volumes of BSA (slight excess) and acetonitrile had to be heated to 80° for 4 hr in order to complete the silylation; in dimethylformamide the reaction was completed at 30° within about the same period of time. Birkofer and Dickopp[21] recently silylated N-chloro- and N-bromoacetamide with BSA.



B. Amino Acids. Amino acids can be silylated with silylamines or hexamethyldisilazane.[7,8] We were interested in a fast, convenient method of silylating mixtures of amino acids on a small scale for vapor phase chromatographic analysis. Mixtures of 10 to 50 mg of amino acids or their hydrochlorides with a slight excess of BSA and about twice the volume of acetonitrile were placed in screw-cap vials and heated near the boiling point of the mixture. Clear solutions were obtained with 22 amino acids[22] or mixtures thereof within 10 to 30 min. Vpc analysis on an SE-30 silicone gum column gave sharp, single peaks for all amino acids except arginine, which showed indication of decomposition on the column; silylated glycine and alanine could not be separated from trimethylsilylacetamide on the column used.

Trimethylsilylated threonine and tryptophan which had not been described in the literature were prepared on a larger scale by the same procedure and isolated in pure form by distillation.

C. Phenols. Trimethylsilyl aryl ethers have been prepared with trimethylsilylchlorosilane or hexamethyldisilazane.[23,24] Phenolic hydroxyl groups are rapidly silylated with BSA at room temperature, even with relatively bulky groups such as 2,6-diphenylphenol in adjacent positions. The highly hindered 2,6-di-*t*-butylphenol can be silylated quantitatively by refluxing with BSA in acetonitrile for 15 hr, as shown by vpc.



In a control experiment, 2,6-di-*t*-butylphenol was refluxed with trimethylchlorosilane and triethylamine for

(21) L. Birkofer and H. Dickopp, *Tetrahedron Letters*, **45**, 4007 (1965).
(22) Glycine, alanine, valine, leucine, isoleucine, serine, threonine, sarcosine, lysine, proline, cystine, histidine, phenylalanine, methionine, hydroxylproline, tryptophan, hydroxytryptophan, tyrosine, diiodotyrosine, arginine, glutaric acid, aspartic acid.
(23) M. Langer, P. Pantages, and I. Wendler, *Chem. Ind.* (London), 1664 (1958).
(24) R. I. Ismail, *Z. Naturforsch*, **18b**, 582 (1963).

Table I. Products of Silylation with BSA

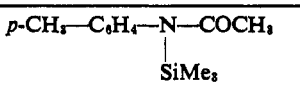
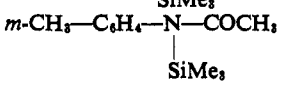
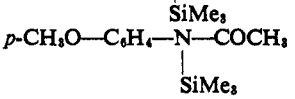
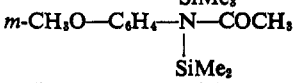
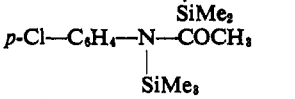
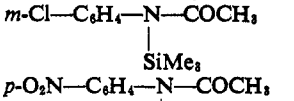
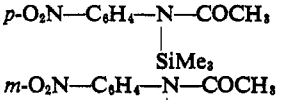
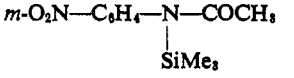
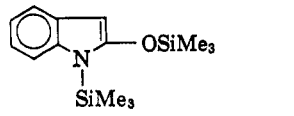
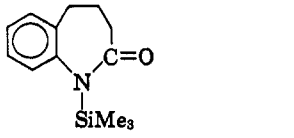
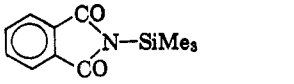
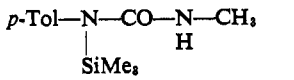
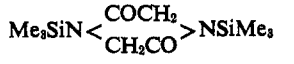
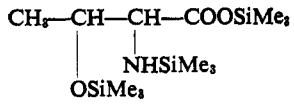
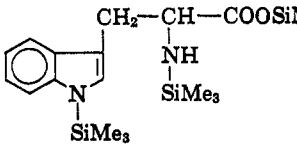
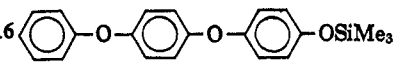
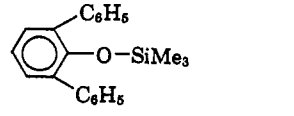
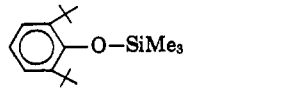
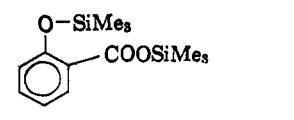
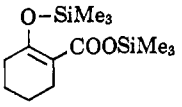
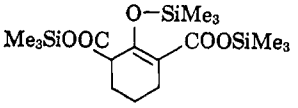
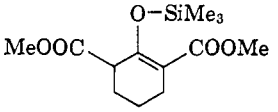
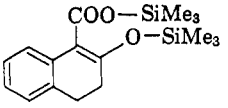
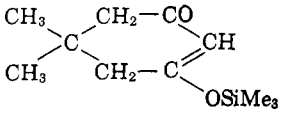
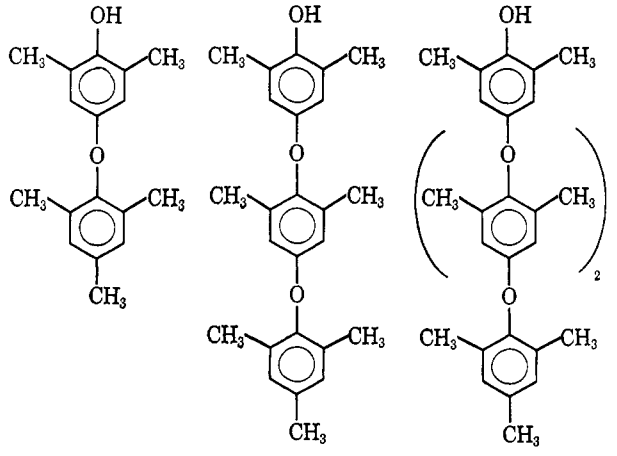
No.	Compound Formula	Conditions of silylation	Bp (mm) or mp, °C	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found	Si, % Calcd	Si, % Found
1		in CH_3CN, 5 min at 80°	50–53 (0.2)	65.1	65.4	8.6	8.9	6.3	6.6	...	...
2		in CH_3CN, 30 min at 30°	53–55 (0.2)	65.1	64.9	8.6	8.9	6.3	6.5	12.7	12.5
3		in CH_3CN, 15 min at 30°	75–76 (0.2)	60.7	60.9	8.0	8.0	5.9	6.0	11.8	12.0
4		in CH_3CN, 10 min at 80°	69–70 (0.3)	60.7	60.3	8.1	7.9	5.9	6.0	11.8	11.8
5		in CH_3CN, 5 min at 80°	61–63 (0.2)	54.6	54.7	6.7	6.7	Cl 14.7	Cl 14.8	11.6	11.4
6		in CH_3CN, 15 min at 30°	64–66 (0.2)	54.6	54.3	6.7	6.6	...	...	...	...
7		in CH_3CN, 5 min at 80°	88–90 (0.2)	52.4	52.3	6.4	6.2	11.1	11.0	11.1	10.7
8		in CH_3CN, 10 min at 80°	85–88 (0.2)	52.4	52.8	6.4	6.3	11.1	10.9	11.1	11.5
9		in CH_3CN, 1 hr at 30°	98–100 (0.2)	60.6	60.5	8.3	8.2	5.0	4.8	20.2	20.0
10		in CH_3CN, 1 hr at 80°	60–61 (0.1)	67.0	66.9	8.2	7.9	6.0	6.1	...	...
11		in CH_3CN, 15 hr at room temp	68–69	60.2	60.6	6.0	6.3	6.4	6.6	...	...
12		in CH_3CN, 15 min at 30°	79–81	60.9	60.9	8.5	8.7	11.8	12.1	...	...
13		in CH_3CN, 4 hr at 80°	94–95	46.4	46.7	8.6	8.8	10.8	10.7	21.7	21.7
14		in CH_3CN, at 30°	60–62 (0.2)	46.6	46.6	9.6	9.7	4.2	4.3	25.2	25.0
15		in CH_3CN, 2 hr at 30°	140–142 (0.2)	57.1	56.7	8.6	8.5	...	...	...	...
16		in benzene, 5 min at 30–40° (exothermic reaction)	...	...	...	...	...	...	...	8.1	8.1
17		in $HCCl_3$, 30 min at 30°	107–108	79.2	79.5	7.0	7.0	...	...	...	...
18		in CH_3CN, 15 hr at 90°	106–108	73.3	73.6	10.9	10.9	...	...	...	...
19		in $CHCl_3$, 10 min at 30°		...	...	...	...	...	...	...	...

Table I (*Continued*)

No.	Compound Formula	Conditions of silylation	Bp (mm) or mp, °C	C, % Calcd	C, % Found	H, % Calcd	H, % Found	N, % Calcd	N, % Found	Si, % Calcd	Si, % Found
20		in Et_2O, 10 min at 30°		54.4	55.2	9.1	8.9	...	...	...	...
21		in Et_2O, 10 min at 30°	The compounds were isolated in small quantities by vpc (2-ft SE-30 silicone gum column)	50.7	50.3	8.5	8.1	...	...	...	...
22		in Et_2O, 10 min at 30°		54.5	54.1	7.7	7.7	...	...	...	...
23		in Et_2O, 10 min at 30°		61.0	60.4	7.8	7.7	...	...	...	...
24		in benzene, 15 hr at 30°	56–58	62.26	62.28	9.47	9.04	...	...	...	...

5 days; after this time, less than 10% of the phenol was converted into the trimethylsilyl ether. The silyl ether can be refluxed in aqueous ethanol for several hours without appreciable hydrolysis.

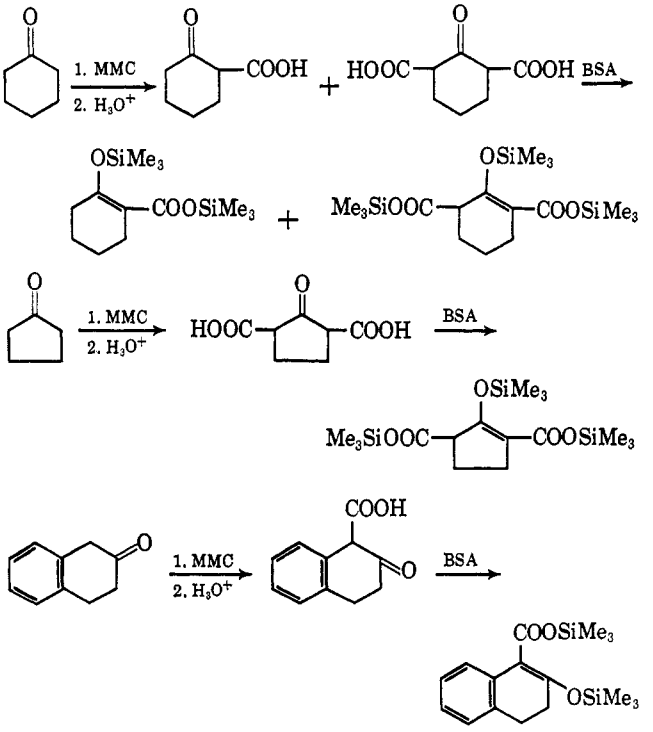
The application of BSA as a fast-reacting quenching agent for compounds with reactive protons is illustrated in the following example. Studies on the mechanism of the oxidative coupling of phenols in our laboratory[25] required the preparation of di-, tri- and tetrameric coupling products of the following structure. The



I II III

synthesis is based on a redistribution reaction between mesitol and poly(2,6-dimethylphenyl oxide) which is to be represented in Scheme I. An attempt to separate the low oligomers from higher molecular weight material by distillation would shift the equilibrium toward mesitol, yielding mainly starting material. Addition of BSA leads to the rapid silylation of all hydroxyl groups, thus freezing the equilibrium. The various components can now be separated by distillation and later reverted to the parent phenols.

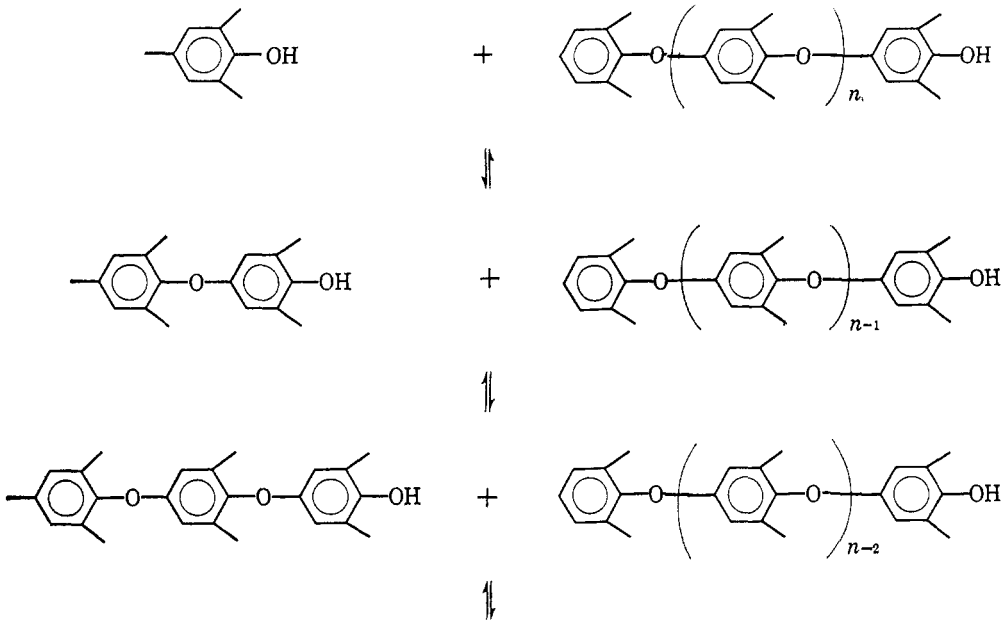
D. Carboxylic Acids and Enols. A study of carboxylation of cyclic ketones with magnesium methyl carbonate[26,27] led to a number of β-keto acids which could not be analyzed by vapor phase chromatography due to their facile decomposition at elevated temperatures. Addition of BSA to the ether extract of the



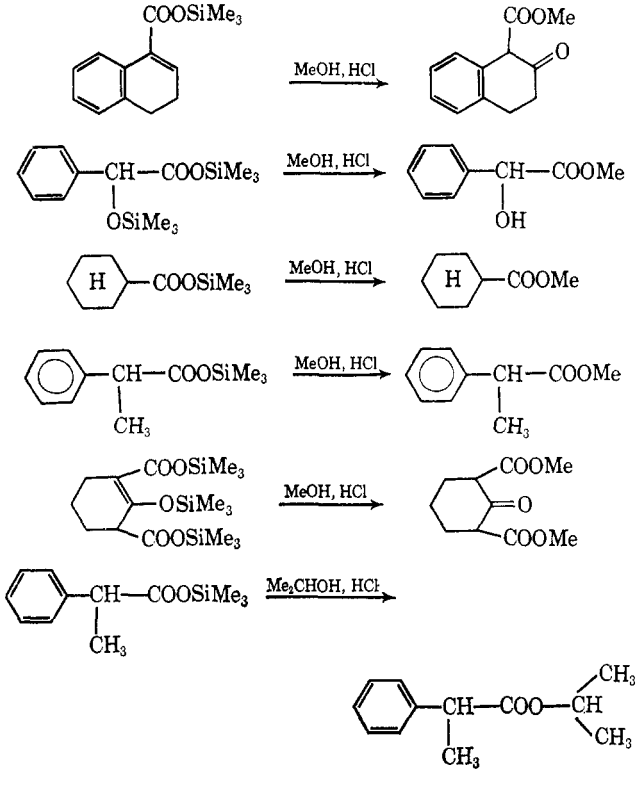
(25) Abstracts of the Winter Meeting of the American Chemical Society, Polymer Division, Phoenix, Ariz., Jan 1966: G. D. Cooper, A. R. Gilbert, and H. Finkbeiner, Paper E35; D. A. Bolon, Paper E36; D. M. White, Paper E37.

(26) M. Stiles, *J. Am. Chem. Soc.*, **81**, 2598 (1959).
(27) H. Finkbeiner, *ibid.*, **87**, 4588 (1965).

Scheme I



reaction mixture after the carboxylation reaction was complete led immediately to the silylated products which could be distilled or analyzed by vpc. Hydrolysis or alcoholysis in neutral medium leads to the parent β-keto acid. However, when the cleavage of the Si–O ester and ether bonds was carried out in an anhydrous methanolic solution of hydrochloric acid, the methyl ester of the corresponding acid was obtained. The reaction was found general for the silyl esters of all acids investigated; the formation of the methyl esters was complete within a few minutes at room temperature. When the silyl ester of hydrotropic acid was cleaved in isopropyl alcohol–HCl, isopropyl hydrotropate was formed with the same ease. The procedure appears to constitute a convenient and rapid method of esterification. Starting with the carboxylic acid, silylation and formation of the ester may be completed within 15 min at room temperature.



Experimental Section

1. *Bis(trimethylsilyl)acetamide.* To a mixture of 295 g (5 moles) of acetamide and 2700 ml of triethylamine in a 12-l. flask fitted with stirrer, reflux condenser, and addition funnel is added with stirring 1460 g (1745 ml, 13.3 moles) of trimethylchlorosilane. Atmospheric moisture is kept out by means of Drierite-filled tubes. The conversion to monosilylacetamide is exothermic; replacement of the second proton requires refluxing The amount of Et_3N used here is a minimum; less solvent results in too thick reaction mixtures. Addition of toluene as a second solvent was found to lead to the formation of mostly monosilylacetamide.

After the addition of chlorosilane is complete, the mixture is refluxed gently for 8 to 15 hr (too vigorous boiling leads to excessive sublimation of $Et_3N \cdot HCl$ and clogging of the condenser). After 8 hr of refluxing, vpc showed 90% conversion to the disilylacetamide (2-ft silicone rubber SE-30 column, 50° isothermal). The mixture was filtered under a blanket of dry nitrogen; the filter cake was washed several times with Et_3N (total amount about 500 ml). The filtrate was then concentrated. The temperature should not be allowed to exceed about 100° during the distillation; a decrease in yield of product in one particular run was probably caused by thermal decomposition due to excessive heating during the stripping. The remaining dark liquid was fractionated on a spinning-band column; $CH_3CON(SiMe_3)_2$, bp 71–73° (35 mm), was obtained in about 80% yield. The principal by-product is $CH_3CONHSiMe_3$, bp 105–107° (35 mm) (solid at room temperature).

2. Silylations with BSA. A. Determination of Extent of Conversion. Vpc retention times of a number of representative compounds of Table I and of their precursors—whenever these were stable under vpc conditions or gave well-defined decomposition products—were measured. The time was recorded after which no starting material was left in the silylation mixture. The data are shown in Table II.

The silylation of oxindole and of N-*p*-tolyl-N′-methylurea (**9** and **12**, Table I) was followed by pmr. Oxindole shows a singlet at 3.45 ppm in pyridine (13%) due to the methylene group. This signal had disappeared 5 min (at 40°) after the addition of 2 equiv of BSA and a new signal due to the vinyl proton of compound **9** had appeared at 5.62 ppm. The tolylmethyl signal of the urea appearing at 2.24 ppm (4% in $HCCl_3$) gave way to the corresponding signal at 2.33 ppm of the silylated material (**12**) within 1 min at 30° after addition of 1 equiv of BSA. The position of the N-methyl doublet remained essentially unchanged.

The extent of silyl transfer could not be determined by vpc or nmr with the amino acids **14** and **15** and with glycine anhydride

Table II

Compd no[a]	Retention time,[b] min	Retention time[b] of precursor, min	Conditions of silylation	Conversion complete after
1	8.6	4.7	20% in pyridine, 25°, 20% excess BSA	3 min
4	10.8	7.0	20% in pyridine, 25°, 20% excess BSA	3 min
7	15.4	10.0	10% in pyridine, 25°, 20% excess BSA	5 min
10	10.5	7.1	20% in pyridine, 25°, 20% excess BSA	22 hr (30 min, 66% conv) (5 hr, 94% conv)
11	8.7	7.7	20% in pyridine, 25°, 20% excess BSA	2 min
17	14.2	14.9	5% in chloroform, 30°, 25% excess BSA	5 min
21	12.5	3.8[d]	5% in ether, 25°, 50% excess BSA	3 min
24	9.7[c]	11.3[c]	20% in pyridine, 25°, 20% excess BSA	3 min

[a] See Table I. [b] Silicone gum column (2 ft), temperature programming 100–300°, 7.5°/min temperature rise. [c] Temperature programming 50–300°, 7.5°/min temperature rise. [d] Cyclohexanone from decarboxylation.

(13) due to lack of solubility of the starting materials in a suitable solvent for silylation. The fact that nonvolatile distillation residues were not observed at the end of these silylations and only a single product was observed in each case allows the conclusion that the reactions were essentially quantitative after the reaction times indicated in Table I.

B. Preparations. Silylations were carried out in benzene, carbon tetrachloride, chloroform, acetone, acetonitrile, pyridine, or dimethylformamide. The solvents were generally used in amounts up to three times that of the combined weight of substrate and BSA; the starting materials went into solution as the silylations progressed. Standard procedures for the drying of the solvents were applied; small amounts of water can be tolerated in the solvent used for the silylation if excess BSA is applied. Carefully dried benzene and hexane were used for recrystallization of silylated products. All operations were carried out in a dry atmosphere. The following preparation is representative for the procedure generally used.

3. N-Trimethylsilyl-*p*-nitroacetanilide. A mixture of 18 g of *p*-nitroacetanilide, 25 g of BSA, and about 30 ml of acetonitrile was placed in a flask fitted with reflux condenser and heated on a steam bath; air moisture was kept out by means of a "Drierite" tube. A clear solution was obtained after 5 min. The solvent and $CH_3CONHSiMe_3$ were removed *in vacuo;* the monosilylamide sublimed rapidly at 0.2 mm and 50° bath temperature. The dark yellow residue was distilled in a small distillation apparatus without separation column, bp 88–90° (0.2 mm). Very little forerun and residue were obtained. The yellow distillate solidified on cooling; it was recrystallized from dry hexane, mp 64–67°.

4. Carboxylation of Ketones. The procedure for carboxylation of ketones was essentially that described previously.[26,27] A 50-ml portion of 2 *M* magnesium methyl carbonate[28] was heated to 90°, 0.05 mole of ketone was added, and the temperature was maintained for an additional 2 hr. The β-keto acid was isolated by pouring the reaction mixture, with vigorous stirring, into a slurry of 100 g of ice and 30 ml of concentrated hydrochloric acid. If the β-keto acid was a solid it was filtered off and dried under vacuum; otherwise it was extracted with several portions of ether. After drying and removing the ether, the subsequent steps were identical in either case.

5. Silylation of Carboxylic Acids. A slurry of 10.0 mmoles of the carboxylic acid in 5 ml of ether was vigorously swirled as 2 ml of bis(trimethylsilyl)acetamide (3 ml in the case of β-keto acids) was slowly added. Samples were chromatographed as soon as solution was complete and showed quantitative conversion to the trimethylsilyl derivatives.

6. Esterification of Trimethylsilyl Carboxylate. An ether solution of the trimethylsilyl carboxylate was added to anhydrous methanolic hydrogen chloride at 5°. In general, the best results were obtained using a 10–20-fold excess of hydrogen chloride. In a typical example, 1.0 mmole of the trimethylsilyl derivative of benzoylacetic acid in 1 ml of ether was added to 10-ml portions of methanolic hydrogen chloride containing 20, 10, 5, and 2 mmoles of hydrogen chloride. After standing for 10 min at 5° the solutions were poured into 20 ml of water and the ester extracted with ether. Ester yields of 86%, 76%, 69%, and 15% were obtained, respectively. For acids other than the β-keto acids the excess of hydrogen chloride did not seem to be as critical.

7. Equilibration of Mesitol with Poly(2,6-dimethylphenylene Oxide). The Synthesis of Aryloxyxylenols I, II, and III. Mesitol (111 g, 0.82 mole) and 3,3′,5,5′-tetramethyl-4,4′-diphenoquinone (6.0 g, 0.025 mole) were added in small portions at 10-min intervals over a 2-hr period[29] to a solution of poly(2,6-dimethylphenylene oxide) (100 g, $[\eta]^{30}$ ($CHCl_3$) 0.27 dl/g) in 500 ml of benzene at reflux. After an additional 4 hr, the reaction mixture was cooled to 25° and extracted with 10% sodium hydroxide (to remove most of the mesitol and the reduced diphenoquinone) and with 5% aqueous hydrochloric acid (to convert the phenol salts to free phenols), dried over $MgSO_4$, and filtered.

BSA (100 g, 90% pure,[30] 0.44 mole) was added to the benzene solution and the solution was heated at reflux for 1 hr. The solution was distilled at reduced pressure and the higher boiling fractions were redistilled to yield the data given in Table III.

Table III

Trimethylsilyl ether of	Bp, °C (mm)	Weight, g	Purity, %
Compound I	120 (0.01)	25	>95
Compound II	180 (0.01)	18	>95
Compound III	230 (0.01)	15	>90

The trimethylsilyl ether of compound I (13.7 g, 0.042 mole) was dissolved in 140 ml of methanol containing 4 drops of concentrated hydrochloric acid at 25°. Water was added to the cloud point and the solution was gradually cooled to 5°. The crystalline product, after filtration, washing with aqueous methanol, and drying, weighed 8.5 g, mp 133–135°. From the filtrate an additional amount was recovered (1.6 g), total yield 10.1 g (95%). *Anal.* Calcd for $C_{17}H_{20}O_2$: C, 79.7; H, 7.9; mol wt, 256. Found: C, 79.9; H, 8.1; mol wt, 246. The pmr spectrum in DCl_3 has peaks at 125 and 130 cps (six *o*-methyl H's for each peak), 138 cps (three *p*-methyl H's), 255 cps (one hydroxyl H), 385 and 415 cps (two aromatic H's for each peak).

The trimethylsilyl ether of compound II (12.0 g, 0.027 mole) was hydrolyzed by the procedure described above. The first crop of crystals weighed 8.7 g, mp 141–144°, and a second crop weighed 0.7 g; total yield of II was 9.4 g (93%). *Anal.* Calcd for $C_{25}H_{28}O_3$: C, 79.8; H, 7.4; mol wt, 376. Found: C, 79.9; H, 7.6; mol wt, 381. The pmr spectrum in DCl_3 has peaks at 123, 128, and 130 cps (six *o*-methyl H's for each peak), 139 cps (three *p*-methyl H's), 256 cps(one hydroxyl H), 386, 390, and 415 (two aromatic H's for each peak).

Hydrolysis of the trimethylsilyl ether of compound III did not yield a crystalline product. The trimethylsilyl ether was redistilled and a pmr measurement was made in DCl_3. Peaks occurred at 12 cps (nine trimethylsilyl H's), 122 and 125 cps (24 *o*-methyl H's), 137 cps (three *p*-methyl H's), 375 cps (two aromatic H's), 384 (four aromatic H's), and 409 cps (two aromatic H's). All pmr spectra were recorded on a Varian A-60 spectrometer.

(28) H. Finkbeiner and G. W. Wagner, *J. Org. Chem.*, **28**, 215 (1963).

(29) The slow addition of mesitol and diphenoquinone minimizes side reactions which are extensive at higher concentration.

(30) The minor component is trimethylsilylacetamide.