that was added to acetone. The precipitate was filtered off. Evaporation of the solvent under reduced pressure gave crude containing (1-bromo-2-hydroxypropyl)phosphonic acid (8) and tartaric acid: $^1$H NMR ($D_2O$) 1.34 (dd, 3 H, $J_{H-CH_3}$ = 6, $J_{P-CH_3}$ = 1.2), 3.98 (dd, 1 H, $J_{H-H}$ = 3.6, $J_{P-H}$ = 11.5), 4.20 (ddq, 1 H, $J_{H-H}$ = 3.6, $J_{CH_3-H}$ = 6, $J_{P-H}$ = 9.3), and 4.75 (singlet of tartaric acid).

The crude 8, thus obtained, was dissolved in methanol (50 mL) and the solution was added dropwise at 40 °C under nitrogen to a solution of sodium methoxide in methanol (5.55 M, ca. 15 mL), in such a way as to maintain the pH at 12.5–13. At complete conversion of 8, the reaction mixture was cooled to ambient temperature and filtered. The pH of the solution was brought to pH 9–10 with methanesulfonic acid. The mixture was concentrated under reduced pressure to half volume and filtered. Evaporation of the solvent under reduced pressure gave a residue (3.38 g) containing 63% w/w of **1b** (2.13 g, 11.7 mmol) as determined by HPLC. The residue was dissolved in methanol (18 mL) and added, under stirring at ambient temperature, to 2-propanol (90 mL). Methanesulfonic acid (2.5 g, 26 mmol) was added to the suspension at 15 °C. The mixture was kept at 15 °C for 15 min and filtered. The solution was added at 15 °C to a solution of sodium methoxide in methanol (5.55 M, 4.32 mL) and kept at 15 °C for 2 h. The precipitate was filtered and dried at 50 °C under reduced pressure to yield (1*R*,2*S*)-(epoxypropyl)phosphonic acid, disodium salt (**1b**) (1.91 g, 10.5 mmol): HPLC assay 101.2%; Karl Fisher 2%; $[\alpha]^{20}_{365}$ −19.0° (*c* 10, water); $^1$H NMR ($D_2O$) 1.50 (d, 3 H, $J$ = 6), 2.83 (dd, 1 H, $J$ = 5.4, $J_{P-H}$ = 18), 3.27 (ddq, 1 H, $J_{CH_3-H}$ = 6, $J_{H-H}$ = 5.4).

A sample of **1b**, thus obtained, was dissolved in methanol, added to 2 equiv of methanesulfonic acid, and treated with an ethereal solution of diazomethane. Evaporation of the solvent under reduced pressure gave enantiomerically pure dimethyl ester of **1a** as determined by $^1$H NMR analysis ($CDCl_3$) with the optically active shift reagent Eu(tfc)$_3$.

**Registry No.** 1 (m = m′ = Me), 25460-63-3; (1*R*,2*S*)-**1b**, 26016-99-9; (1*S*,2*R*)-**1b**, 26017-01-6; **2b**, 25522-46-7; **3a**, 13171-64-7; **3b**, 63126-52-3; **3d**, 102197-56-8; **3e**, 118894-34-1; **3g**, 118894-35-2; **3i**, 108321-43-3; **4a**, 116653-95-3; **4b**, 116653-96-4; **4d**, 118894-36-3; **4e**, 118894-37-4; **4g**, 118894-38-5; **4i**, 118894-39-6; **5a**, 118894-40-9; **5b**, 118894-41-0; **5c**, 118920-32-4; **5d**, 118894-42-1; **5e**, 116654-11-6; **5f**, 118920-33-5; **5g**, 118894-43-2; **5h**, 118920-34-6; **5i**, 118919-65-6; **6a**, 118894-44-3; **6b**, 119007-46-4; **6d**, 118894-45-4; **6e**, 116698-37-4; **6g**, 118894-46-5; **6i**, 118894-47-6; **7a**, 119008-38-7; **7b**, 119008-39-8; **7d**, 119007-47-5; **7e**, 116698-38-5; **7g**, 119007-48-6; **7i**, 119007-49-7; **8**, 119007-50-0; 8 (dimethyl ester), 119007-51-1.

## Silylcupration-Mediated Synthesis of 2-Substituted Allylamines

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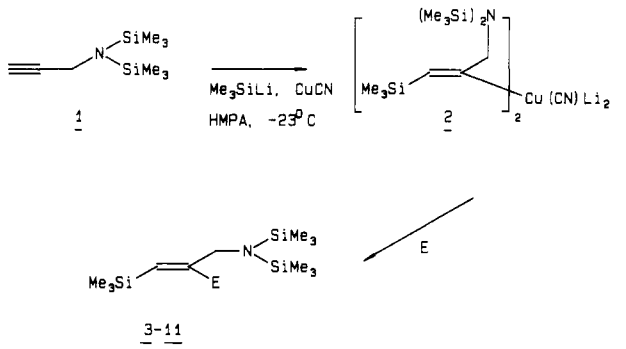
In many instances, the presence in organosilicon compounds of a nitrogen functionality separated from the silicon atom by two or three carbon atoms confers to the molecule various kinds of biological activity.[1]

**Scheme I**




As part of our current interest[2] in the search for new biologically active organosilicon compounds, we thought it worthwhile to focus our attention on the development of new methods for the synthesis of molecules bearing a SiC≡CCN skeleton.

We report in this paper a new simple one-step procedure for the synthesis of a wide series of 1-silylallylic amines substituted at position 2 from the readily available[3] precursor *N*,*N*-bis(trimethylsilyl)propargylamine (1) by means of a silylcupration followed by in situ reaction with electrophiles, according to Scheme I.

One of the most important aspects of the reaction in Scheme I turns out to be the inversion of regioselectivity in the addition of the reagents to the C≡C bond with respect to that previously reported by Corriu et al.[3] for the carbocupration of 1, which allowed functionalization of the allylic framework only at position 3. The regiochemistry in Scheme I on the other hand fits well with the previous findings of Fleming[4] and does not appear to be affected by replacement of the commonly used $PhMe_2Si$ group with a $Me_3Si$ moiety. Also worth mentioning is the fact that both equivalents of $Me_3Si$ were consumed (see Experimental Section) in the 1,2 addition process, in agreement with the formation of **2** from a $(Me_3Si)_2Cu(CN)Li_2$ mixed organocuprate.[5]

These features prompted us to envisage our reaction as a good entry into the not easily accessible class of 2-substituted allylic amines[6] and the results with a series of electrophiles are summarized in Table I.

In the case of $I_2$ (entry 2) and of alkyl halides (entries 3–5), the alkenylcuprate reacts easily, while with less reactive electrophiles (entries 6–8) transmetalation into the zinc species is necessary in order to obtain coupling using Pd(0) catalysis.[7] Otherwise reaction with carbon dioxide was performed in the presence of $P(OEt)_3$ as catalyst.[8]

In all cases the final products, isolated in satisfactory to good yields and fully characterized by GC-MS and $^1$H NMR analyses, showed a stereochemistry coming from syn attack by the trimethylsilyl group and copper to the triple bond, which was maintained in the subsequent coupling step. The coupling constant of 18.6 Hz observed for the

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(2) Ricci, A.; Taddei, M.; Rapi, G.; Seconi, G.; Dembech, P.; Omodei-Salè, A. It. Pat. 48262A87.

(3) Corriu, R. J. P.; Huynh, V.; Iqbal, J.; Moreau, J. J. E. *J. Organomet. Chem.* **1984**, *276*, C61.

(4) Fleming, I.; Newton, T. W. *J. Chem. Soc., Perkin Trans. I* **1984**, 1805 and references therein.

(5) Lipshutz, B. H. *Synthesis* **1987**, 325.

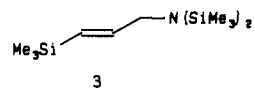
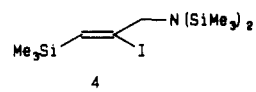
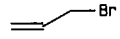
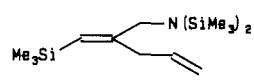
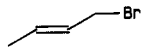
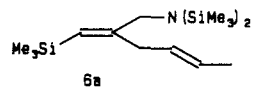
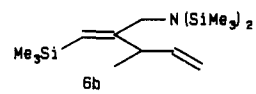
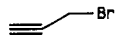
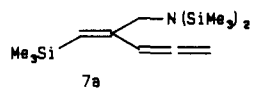
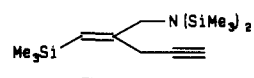
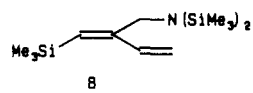
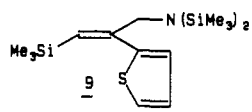
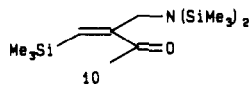
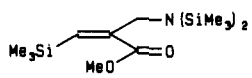
(6) (a) Cheikh, R. B.; Chaabouni, R.; Laurent, A.; Mison, P.; Nafti, A. *Synthesis* **1983**, 685. (b) Bargar, T. M.; McCowan, J. R.; McCarthy, J. R.; Wagner, E. R. *J. Org. Chem.* **1987**, *52*, 678.

(7) (a) Jabri, N.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1983**, *24*, 5081. (b) Jabri, N.; Alexakis, A.; Normant, J. F. *Bull. Soc. Chim. Fr.* **1983**, *II*, 321.

(8) Alexakis, A.; Cahiez, G.; Normant, J. F. *Tetrahedron* **1980**, *36*, 1961.

0022-3263/89/1954-1473$01.50/0 

**Table I. 2-Substituted Allylamines from Coupling of 2 with Electrophiles**

| entry | electrophile | obtained product | yield, % |
|---|---|---|---|
| 1 | $H_2O$ |  **3** | 92[a] |
| 2 | $I_2$ |  **4** | 93[b] |
| 3 |  |  **5** | 85[b] |
| 4 |  |  **6a**  **6b** | 75[b,c] |
| 5 |  |  **7a**  **7b** | 95[b,c] |
| 6 |  |  **8** | 76[b] |
| 7 |  |  **9** | 58[b] |
| 8 |  |  **10** | 81[b] |
| 9 | $CO_2$ |  **11** | 83[a,d] |

[a] Isolated yields. [b] Gas chromatographic yields. [c] Total yield (**6a**/**6b** 4/1, **7a**/**7b** 6/1). [d] After esterification with $Me_2SO_4$.

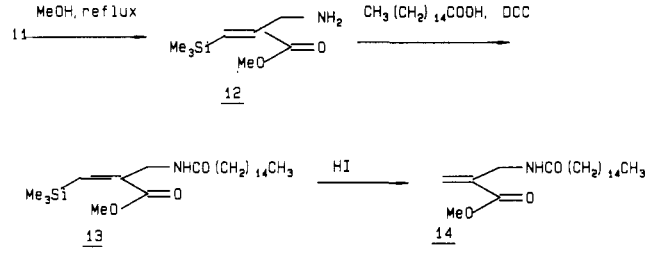
vinylic protons in compound **3**, accessible by quenching with water of the copper intermediate **2** or through deiodination with *n*-BuLi and water treatment of **4**, was in fact in perfect agreement with the *J* value found[9] for (*E*)-1-(trimethylsilyl)hex-1-ene.

Desilylation of reaction products to give the primary allylic amines is exemplified by **3a** and **12** (see Experimental Section) and was performed without any difficulty, according to the usual procedures.

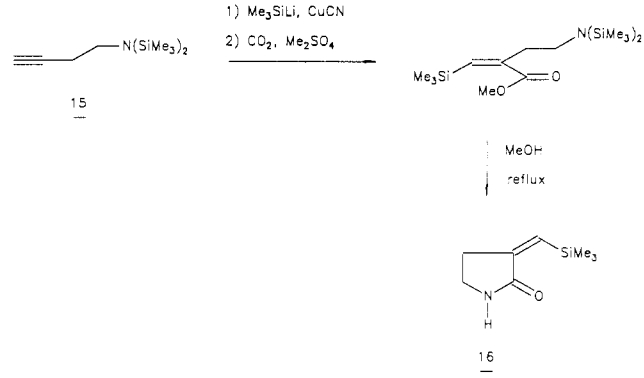
2-Substituted allylamines[10] and (aminoalkyl)trimethylsilanes[11] have recently received a great deal of attention as enzyme inhibitors: compounds in Table I therefore appear of high interest from this point of view as such or as precursors, through desilylation or reduction, of the previously mentioned classes of compounds.

(Silylallyl)-*N*,*N*-bis(trimethylsilyl)amines **3**–**11** behave as versatile building blocks, on which further structural transformations can be performed via Si—N, C=C, or C—Si bond functionalization: thus for example, from the compound **11** containing the amino acid α-methylene-β-alanine structure, after exposure of the primary amino functionality followed by acylation with palmitic acid and removal of the vinylic silicon (Scheme II) compound **14**,

**Scheme II**



**Scheme III**



identical[12] with a natural product found in the Red Sea sponge *Fasciospongia cavernosa*, can be easily synthesized.

(9) Mille, R. B.; McGarvey, G. *J. Org. Chem.* **1978**, *43*, 4424.
(10) (a) McDonald, I. A.; Lacoste, J. M.; Bey, P.; Palfreyman, M. G.; Zreika, M. *J. Med. Chem.* **1985**, *28*, 186. (b) Bargar, T. M.; Broersma, R. J.; Creemer, L. C.; McCarthy, J. R. *Ibid.* **1986**, *29*, 315.
(11) Silverman, R. B.; Banik, G. M. *J. Am. Chem. Soc.* **1987**, *109*, 2219.

The possibility of placing a carbomethoxy group in position 2, as in **11**, finally opens new synthetic perspectives for the synthesis of α-methylene lactams: (*Z*)-3-[(Trimethylsilyl)methylene]pyrrolidin-2-one was in fact obtained (Scheme III), thus suggesting an alternative route to α-methylene-γ-lactams with respect to that very recently reported in the literature.[13]

Due to the inherent interest in α-methylene-β-lactams[14] as biologically active species and as useful synthetic intermediates, the synthesis of these compounds through the above reported procedure is currently being investigated.

## Experimental Section

$^1$NMR spectra were recorded on a Varian VXR-300 instrument; chemical shifts are given with respect to TMS. IR spectra were recorded on a Perkin-Elmer 283 spectrophotometer. Mass spectra were obtained on a HP5970-HP5790 selective ion detector equipped with a high performance dimethylsilicone fluid capillary 25-m column. GC analyses were performed with a Perkin-Elmer 8500 gas chromatograph equipped with a 30-m Supercovax 10 capillary column; *n*-dodecane was used as internal standard.

Tetrakis(triphenylphosphine)palladium(0) was prepared as described by Cotton[15] and stored under nitrogen. $ZnBr_2$ was melted under vacuum and stored under nitrogen.

(Trimethylsilyl)lithium was prepared according to the published procedure of Hudrlik.[16]

All reactions were carried out under inert atmosphere and in anhydrous solvents.

***N*,*N*-Bis(trimethylsilyl)propargylamine (1)** was prepared according to the general route outlined by Corriu.[3] Hexamethyldisilazane (25 mL, 120 mmol) was dissolved in ether, and after cooling to 0 °C, 72 mL (115 mmol) of *n*-BuLi in hexane was added dropwise. The reaction mixture was allowed to reach room temperature and after 30 min 3.8 mL (50 mmol) of propargyl bromide in 20 mL of THF was added. After 3 h the solution was quenched with a 0.1 M NaOH solution, and the ethereal layer was separated, washed with water, and dried over $Na_2SO_4$. After solvent removal 6.96 g (70%) of **1** was obtained by distillation (bp 67 °C, 14 mmHg): $^1$H NMR ($CDCl_3$) δ 0.05 (s, 18 H), 2.15 (t, 1 H $J$ = 3.1 Hz), 3.65 (d, 2 H, $J$ = 3.1 Hz); IR (film) 3315, 2960, 1255 cm$^{-1}$; MS *m*/*e* 199 (11), 184 (100), 86 (91), 73 (93).

**Silylcupration Procedure.** To a solution of (trimethylsilyl)lithium (1.50 mmol) in THF was added 70 mg (0.8 mmol) of CuCN at −23 °C. After stirring for 20 min, 300 mg (1.50 mmol) of **1** was added with a syringe and the temperature held at −23 °C for 30 min.

***(E)*-*N*,*N*,3-Tris(trimethylsilyl)-2-propen-1-amine (3).** The vinylcopper reagent was quenched with $NH_4Cl/NH_4OH$ solution at low temperature and added with ether. The organic layer was separated, washed three times with a saturated NaCl solution, and dried over $Na_2SO_4$. After evaporating the solvent and bulb-to-bulb distillation, 380 mg (92%) of compound **3** was obtained as a colorless oil (bp 80 °C, 10 mmHg): $^1$H NMR ($CDCl_3$) δ 0.02 (s, 9 H), 0.05 (s, 18 H), 3.44 (dd, 2 H, $J$ = 4.1 Hz, $J$ = 1.8 Hz), 5.72 (dt, 1 H, $J$ = 18.6 Hz, $J$ = 1.8 Hz), 5.94 (dt, 1 H, $J$ = 18.6 Hz, $J$ = 4.1 Hz); IR (film) 2960, 1620, 1250 cm$^{-1}$; MS *m*/*e* 273 (4), 258 (8), 200 (25), 174 (89), 73 (100). Anal. Calcd for $C_{12}H_{31}NSi_3$: C, 52.67; H, 11.42; N, 5.12. Found: C, 52.50; H, 11.35; N, 5.01.

***(E)*-3-(Trimethylsilyl)-2-propen-1-amine (3a).** A total of 200 mg (0.77 mmol) of **3** was refluxed in MeOH for 2 h. After evaporating the solvent in vacuo, bulb-to-bulb distillation afforded 80 mg (80%) of **3a** (bp 75 °C, 55 mmHg): $^1$H NMR ($CDCl_3$) δ 0.12 (s, 9 H), 1.63 (bs, 1 H), 3.38 (bd, 2 H, $J$ = 4.5 Hz), 5.79 (dt, 1 H, $J$ = 18.9 Hz, $J$ = 1.5 Hz), 6.19 (dt, 1 H, $J$ = 18.9 Hz, $J$ = 4.5 Hz); IR (film) 3490, 3320, 2960, 1250 cm$^{-1}$; MS *m*/*e* 129 (1), 114 (32), 73 (100), 56 (48). Anal. Calcd for $C_6H_{15}NSi$: C, 55.74; H, 11.70; N, 10.83. Found: C, 55.60; H, 11.58; N, 10.71.

***(Z)*-*N*,*N*,3-Tris(trimethylsilyl)-2-iodo-2-propen-1-amine (4).** The vinylcopper reagent was added at −23 °C with a solution of 380 mg (1.5 mmol) of $I_2$ in 2 mL of THF. The reaction mixture was allowed to reach room temperature overnight. After the workup bulb-to-bulb distillation afforded compound **4** as a dark yellow oil (bp 90 °C, 60 mmHg): $^1$H NMR ($CDCl_3$) δ 0.09 (s, 18 H), 0.20 (s, 9 H), 3.68 (d, 2 H, $J$ = 1 .8 Hz), 6.82 (t, 1 H, $J$ = 1.8 Hz); IR (film) 2960, 1610, 1250, 1020, 830 cm$^{-1}$; MS *m*/*e* 384 (1), 174 (100), 73 (86).

**General Procedure for the Reaction with Alkyl Halides** (entries 3–5). The appropriate alkyl halide (1.5 mmol) was added at −23 °C to the solution of the vinylcopper reagent and then the reaction mixture was let up to room temperature overnight. After hydrolytic workup and bulb-to-bulb distillation products **5** (bp 100 °C, 5 mmHg), **6a** (bp 135 °C, 4 mmHg), and **7a** (bp 95 °C, 20 mmHg) were obtained as colorless liquids. **5**: $^1$H NMR ($CDCl_3$) δ 0.01 (s, 18 H), 0.08 (s, 9 H), 2.77 (d, 2 H, $J$ = 6.6 Hz), 3.26 (d, 2 H, $J$ = 1.8 Hz), 4.95 (dd, 1 H, $J$ = 1.5, $J$ = 9.9 Hz), 5.01 (dd, 1 H, $J$ = 17.0 Hz, $J$ = 1.5 Hz), 5.56 (t, 1 H, $J$ = 1.8 Hz), 5.66 (m, 1 H, $J$ = 9, 9 Hz, $J$ = 6.6 Hz, $J$ = 17.0 Hz); IR (film) 2970, 1615, 1250 cm$^{-1}$; MS *m*/*e* 313 (2), 298 (2), 174 (100), 73 (91). **6a**: $^1$H NMR δ 0.12 (s, 9 H), 0.14 (s, 18 H), 1.13 (d, 3 H, $J$ = 7.2 Hz), 3.20 (d, 2 H, $J$ = 1.8 Hz), 3.32 (dd, 2 H, $J$ = 1.2 Hz, $J$ = 3.2 Hz), 5.02 (dt, 1 H, $J$ = 13.8 Hz, $J$ = 3.2 Hz), 5.46 (t, 1 H, $J$ = 1.8 Hz), 5.84 (m, 1 H); IR ($CCl_4$) 2960, 2900, 1620, 1250 cm$^{-1}$; MS *m*/*e* 327 (1), 174 (100), 73 (69). **7a**: $^1$H NMR ($CDCl_3$) δ 0.07 (s, 18 H), 0.15 (s, 9 H), 3.47 (bs, 2 H), 4.97 (bd, 2 H, $J$ = 6.9 Hz), 5.74 (bs, 1 H), 6.15 (t, 1 H, $J$ = 6.9 Hz); IR (film) 2955, 1940, 1600, 1250, 890, 830 cm$^{-1}$; MS *m*/*e* 311 (4), 296 (2), 238 (16), 174 (74), 73 (100).

**General Procedure for Reactions with Vinyl Bromide, Iodothiophene, and Acetyl Chloride** (entries 6–8). To the solution of the vinylcopper reagent cooled at −40 °C was added 180 mg (0.8 mmol) of $ZnBr_2$ in 5 mL of THF dropwise, and then the solution was stirred for 30 min at −23 °C. $Pd(PPh_3)_4$ (80 mg, 0.07 mmol) was dissolved in 5 mL of THF together with 1.5 mmol of the appropriate electrophile and then added at −40 °C. The reaction mixture was allowed to warm to room temperature overnight and then hydrolyzed. After the usual workup and bulb-to-bulb distillation compounds **8** (bp 100 °C, 10 mmHg), **9** (bp 85 °C, 0.01 mmHg), and **10** (bp 75 °C, 2 mmHg) were obtained. **8**: $^1$H NMR ($CDCl_3$) δ 0.06 (s, 18 H), 0.14 (s, 9 H), 3.59 (d, 2 H, $J$ = 1.8 Hz), 5.06 (d, 1 H, $J$ = 11.1 Hz), 5.21 (d, 1 H, $J$ = 17.8 Hz), 5.92 (t, 1 H, $J$ = 1.8 Hz), 6.66 (dd, 1 H, $J$ = 11.1 Hz, $J$ = 17.8 Hz); IR (film) 2960, 1600, 1250 cm$^{-1}$; MS *m*/*e* 299 (1), 284 (4), 174 (100), 73 (19). **9**: $^1$H NMR ($CDCl_3$) δ −0.06 (s, 9 H), 0.11 (s, 18 H), 3.60 (d, 2 H, $J$ = 1.8 Hz), 5.98 (t, 1 H, $J$ = 1.8 Hz), 6.84 (dd, 1 H, $J$ = 1.2 Hz, $J$ = 3.4 Hz), 6.97 (dd, 1 H, $J$ = 3.4 Hz, $J$ = 5.1 Hz), 7.23 (dd, 1 H, $J$ = 1.2 Hz, $J$ = 5.1 Hz); IR ($CCl_4$) 2960, 1615, 1250, 900, 860, 840 cm$^{-1}$; MS *m*/*e* 355 (1), 340 (3), 174 (100), 73 (16). **10**: $^1$H NMR ($CDCl_3$) δ 0.04 (s, 18 H), 0.09 (s, 9 H), 2.21 (s, 3 H), 3.64 (d, 2 H, $J$ = 1.8 Hz), 6.11 (t, 1 H, $J$ = 1.8 Hz); IR (film) 2960, 2890, 1690, 1250 cm$^{-1}$; MS *m*/*e* 315 (1), 300 (14), 174 (100), 73 (50).

***(Z)*-*N*,*N*,3-Tris(trimethylsilyl)-2-carbomethoxy-2-propen-1-amine (11).** The solution of the vinylcopper reagent was cooled to −40 °C and 15 mg (0.1 mmol) of triethyl phosphite was added. A carbon dioxide stream (from $CO_2$ sublimation) was bubbled, after drying on a $CaCl_2$ column, into the reaction mixture, which was then allowed to reach room temperature overnight. Dimethyl sulfate (190 mg, 1.5 mmol) was added at room temperature and allowed to react for 2 h and the reaction hydrolyzed with an $NH_4Cl/NH_4OH$ solution; after the usual workup and bulb-to-bulb distillation 410 mg (83%) of **11** (bp 125 °C, 1 mm Hg) was obtained as a pale yellow liquid: $^1$H NMR ($CDCl_3$) δ 0.07 (s, 18 H), 0.13 (s, 9 H), 3.67 (d, 2 H, $J$ = 2.1 Hz), 3.75 (s, 3 H), 6.47 (t, 1 H, $J$ = 2.1 Hz); IR (film) 2960, 1730, 1250, 835 cm$^{-1}$; MS *m*/*e* 316 (37), 190 (26), 174 (100), 73 (29). Anal. Calcd for $C_{14}H_{33}NO_2Si_3$: C, 50.70; H, 10.03; N, 4.22. Found: C, 50.73; H, 10.01; N, 4.20.

***(Z)*-3-(Trimethylsilyl)-2-carbomethoxy-2-propen-1-amine (12).** **11** (200 mg, 0.6 mmol) was refluxed in MeOH for 2 h. After evaporating the solvent in vacuo bulb-to-bulb distillation afforded 102 mg (91%) of compound **12** (bp 74 °C, 1 mmHg): $^1$H NMR ($CDCl_3$) 0.17 (s, 9 H), 1.42 (bs, 2 H), 3.52 (bd, 2 H, $J$ = 1.8 Hz),

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3.78 (s, 3 H), 6.31 (t, 1 H, $J$ = 1.8 Hz); IR (film) 3390, 3330, 2960, 2900, 1730, 1610, 1250 cm$^{-1}$; MS $m/e$ 187 (1), 172 (100), 156 (21), 89 (51), 73 (29). Anal. Calcd for $C_8H_{17}NO_2Si$: C, 51.30; H, 9.15; N, 7.48. Found: C, 51.45; H, 9.02; N, 7.51.

**Methyl (*Z*)-3-(Trimethylsilyl)-2-[(palmitoylamino)-methyl]propenoate (13).** **12** (100 mg, 0.5 mmol) dissolved in 1 mL of $CH_2Cl_2$ was cooled to 0 °C and added with a solution of 112 mg (0.05 mmol) of DCC in 1 mL of $CH_2Cl_2$ and 140 mg (0.5 mmol) of palmitic acid in 7 mL of $CH_2Cl_2$. The reaction mixture was kept overnight at room temperature and then filtered. After column chromatography (30 g of $SiO_2$, 230–400 mesh, eluent MeOH) 120 mg (53%) of **13** was isolated (mp 62–64 °C): $^1$H NMR ($C_6D_6$) $\delta$ 0.23 (s, 9 H), 0.92 (t, 3 H, $J$ = 6.6 Hz), 1.31 (bm, 26 H), 3.31 (s, 3 H), 4.12 (dd, 2 H, $J$ = 1.5 Hz, $J$ = 6.3 Hz), 5.06 (bt, 1 H, $J$ = 6.3 Hz), 6.35 (t, 1 H, $J$ = 1.5 Hz); IR ($CCl_4$) 3470, 2930, 2860, 1730, 1685, 1500, 1250 cm$^{-1}$; MS $m/e$ 425 (2), 410 (74), 366 (20), 352 (67), 214 (25), 172 (100), 156 (74), 73 (29).

**Palmitoylamide of β-Alanine Methyl Ester (14).** Compound **12** was refluxed in toluene and hydroiodic acid following the procedure described by Utimoto et al.[17] Compound **14**, isolated by column chromatography (20 g of $SiO_2$, 230–400 mesh, eluent MeOH) shows spectral properties that are in good agreement with those described by Kashmann.[12]

**(*Z*)-3-[(Trimethylsilyl)methylene]pyrrolidin-2-one (16).** To a solution of (trimethylsilyl)lithium (1.50 mmol) in THF was added 70 mg (0.8 mmol) of CuCN at −23 °C. After stirring for 20 min, 320 mg (1.50 mmol) of *N*,*N*-bis(trimethylsilyl)-3-butynamine (**15**)[18] was added dropwise and kept at −23 °C for 30 min. After cooling at −40 °C and adding 15 mg (0.1 mmol) of triethyl phosphite a carbon dioxide stream (from $CO_2$ sublimation) was bubbled into the reaction mixture and then allowed to reach room temperature overnight. Dimethyl sulfate (190 mg, 1.5 mmol) was added at room temperature and then allowed to react for 2 h. After the usual workup and evaporation of the solvent, the crude residue was refluxed in MeOH for 2 h, affording, after column chromatography (20 g of $SiO_2$, 230–400 mesh, eluent EtOAc/*n*-hexane 2/1), 140 mg (55%) of **16**: $^1$H NMR ($CDCl_3$) $\delta$ 0.18 (s, 9 H), 2.85 (td, 2 H, $J$ = 6.9 Hz, $J$ = 2.4 Hz), 3.42 (bt, 2 H, $J$ = 6.9 Hz), 6.03 (t, 1 H, $J$ = 2.4 Hz), 6.12 (bs, 1 H); IR ($CHCl_3$) 3440, 2980, 2960, 1700, 1245 cm$^{-1}$; MS $m/e$ 154 (100).

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## Poly(ethylene glycol)s and Their Dimethyl Ethers as Catalysts for the Reaction of Aryl Halides with Diphenylamine in the Presence of Potassium Hydroxide

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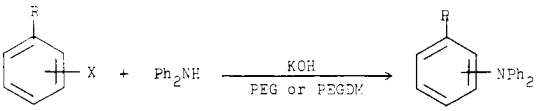
Since poly(ethylene glycol)s (PEG) and their ethers are more accessible than crown ethers or cryptands and more stable to strong alkali than onium salts at high temperature, they have been widely used as phase transfer agents (PTA) for reactions under strongly alkaline conditions.[1-12] However, there are few examples[8] of the reaction of an alkali-generated organic anion with an unactivated aryl halide in the presence of PEG or PEG ethers.

We here report on the phase-transfer reaction of unactivated aryl halides with diphenylamine ($Ph_2NH$) using KOH as base and PEG or PEG dimethyl ethers (PEGDM) as PTA. Recently, Gokel et al.[13] and Neumann et al.[10] have reported that one molecule of a PEG derivative can transport only one cation at a time under phase-transfer conditions. However, our kinetic and UV spectral studies have led to a different conclusion.




### Results and Discussion

The reaction of PhCl or PhBr with $Ph_2NH$ was carried out under various conditions in the presence of PEG-3000 as PTA (Table I). The reaction with PhCl produced only small amounts of $Ph_3N$, whereas the reaction with PhBr gave substantial yields of $Ph_3N$ when KOH was used as base. Since the reaction was very slow with 65% aqueous KOH, 85% KOH was used. All of the additives tried had either no effect or a negative effect on the yield of $Ph_3N$. Addition of $PdCl_2$ gave substantial yields of biphenyl and benzene, and $CuCl_2$ gave a poor material balance of PhBr.

Neumann and Sasson[8] have reported that in the reaction of an aryl halide with alkoxide the molecular weight of PEG had significant influence on the activity. At a constant weight of PEG, higher molecular weight resulted in higher catalytic activity, and a plateau was reached at PEG-6000. Although we observed the same trend for PEG, even the low molecular weight PEGDM-400 was as efficient as PEG-6000 (Figure 1).

Accordingly, we carried out reactions of $Ph_2NH$ with various aryl halides in the presence of PEGDM-400, continuously removing the water formed in the reaction to prevent reduction of the KOH concentration (Table II). In reactions with aryl bromides, complete conversion of $Ph_2NH$ was observed after relatively short times, whereas reactions with aryl chlorides were considerably slower. It is well known that the cine-substitution reaction can occur in reactions of amide anions with aryl halides.[14] Our reactions gave mixtures of isomeric triphenylamine derivatives. In the reaction with *o*-dichlorobenzene, nucleophilic addition to the aryne should occur predominantly at the meta position to form the stable intermediate.

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