secondary > tertiary alcohol. This reactivity trend follows the relative basicity order of the respective alkoxide anions.

Steric hindrance of reagents and adsorption of the heavier compounds on the bed are determining factors in the process, and their total effect clearly appears when one compares the data within Tables I and II. Both an increase of molecular dimension of the primary alcohol and the steric hindrance at the carbonyl group of the ester cause a decrease of conversion.[6] However, conversion increases if the starting ester is high boiling, therefore remaining longer on the bed (cf. EtOAc with AmOAc).[7]

The nature of the leaving alkoxide group is also important. Thus, the reaction between *t*-BuOAc and *n*-BuOH over 400 g of K_2CO_3 containing 5% by weight of Carbowax 6000 only yielded 5% of transesterification product, showing that no alkyl scission occurs and that this process is also controlled by the basicity of the leaving group.

The application of GL-PTC to the transesterification reactions allows the reaction to be carried out in a continuous way and in the absence of solvents. On coupling a catalytic and a distillation column, one could produce pure ester and alcohol with the continuous recycling of the not converted compounds. At the end of the process the expensive 18-crown-6 can be easily recovered, extracting the bed in a Soxhlet apparatus with diethyl ether.

Experimental Section

General Methods. ^1H NMR spectra were recorded on a Hitachi-Perkin Elmer R-24 60-MHz spectrometer. GLC analyses were performed on a Varian 1400 instrument equipped with a CDS 111L integrator and a column of 5% SE-30 on Varaport. A double-jacketed glass column (750 mL in volume, 60 cm in length) thermostated with a Lauda MGW ultrathermostat and an FMI lab pump, Type RRP, were used. Organic and inorganic reagents were ACS reagent grade.

Preparation of the Catalytic Bed. The catalyst (Carbowax 6000 or 18-crown-6, 5% by weight with respect to the base) was dissolved in methanol, potassium carbonate was added, and the suspension was evaporated to remove the solvent. The solid mass obtained was oven-dried at 130 °C for 3 h.

Typical Procedure of Transesterification under GL-PTC Conditions: Reaction between Ethyl Acetate and 1-Butanol. A 1:2 molar solution of ethyl acetate and 1-butanol (1.0:1.9 v/v) was passed at a flow rate (liquid) of 60 mL/h through the column thermostated at 170 °C and containing 400 g of K_2CO_3 coated with Carbowax 6000 (5% by weight). The cooled reaction mixture was analyzed by GLC (temperature 100 °C) and by ^1H NMR. All the products were confirmed by comparison with authentic samples. The conversion reported in Table I (42%) was constant after 25 mL of reagent mixture was passed through the column. No byproduct was detected in any of the cases examined.

Acknowledgment. This work was supported by the Ministero della Pubblica Istruzione.

Registry No. Ethyl acetate, 141-78-6; *n*-amyl acetate, 628-63-7; methyl benzoate, 93-58-3; methanol, 67-56-1; *n*-propanol, 71-23-8; *n*-butanol, 71-36-3; isobutyl alcohol, 78-83-1; *sec*-butyl alcohol, 78-92-2; *tert*-butyl alcohol, 75-65-0; 1-pentanol, 71-41-0; ethanol, 64-17-5; 1-octanol, 111-87-5; Carbowax 6000, 25322-68-3; 18-crown-6, 17455-13-9.

(6) The reaction between ethyl valerianate and *n*-butanol, under the here-reported conditions, yielded only 9% conversion into *n*-butyl valerianate (400 g of bed constituted of K_2CO_3 coated with 18-crown-6, 5% by weight).

(7) When the difference between the boiling points of the leaving alcohol and of the produced ester is great, conversions corresponding or higher than those at the equilibrium point are obtained (Table II and III). This fact, necessarily linked with the partial pressure of the products in the reactor, alows one to foresee that higher or 100% conversions could be reached by a one-step process, controlling the pressure during the reaction.

Active Metals from Potassium-Graphite. Zinc-Graphite-Promoted Synthesis of β-Hydroxy Esters, Homoallylic Alcohols, and α-Methylene-γ-butyrolactones

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Within the area of metal-catalyzed or -promoted organic reactions, an increasing interest is addressed to the use of highly active forms of zerovalent metals.[1] They include thin films, supported or unsupported small particles, blacks, sponges, colloids, and even ligand-stabilized clusters,[2] which represent the boundary between homogeneous and heterogeneous catalysis.

We have recently reported a new method for the preparation of highly reactive metals by the potassium–graphite (C_8K) reduction of the corresponding metal halides (MX_n) in ethereal solvents according to eq 1.[3-6] Nickel-,[4] palla-

$$nC_8K + MX_n \rightarrow C_{8n}M + nKX \quad (1)$$

dium-,[5] and iron–graphite[6] obtained by this procedure were found to be useful catalysts or reagents in organic chemistry.

We now report the use of zinc–graphite (Zn-Gr)[7] in the preparation of Reformatsky reagents and allylic zinc bromides.

The Reformatsky reaction,[8] because of its simplicity and the ready availability of the requisite reagents, is still one of the best routes to β-hydroxy esters. Several improvements[9-15] have been reported in recent years to overcome the drawbacks (variable yields, side reactions, etc.) associated with the original Reformatsky reaction.

We have carried out several experiments exploiting Zn-Gr in Reformatsky reactions and in homoallylic alcohols syntheses (Table I). Optimized conditions require the preparation of Zn-Gr in tetrahydrofuran (THF) under argon, followed by addition of the bromo derivative and carbonyl compound at 0 °C in the case of α-bromo esters and at 20 °C in the case of allylic bromides. We believe that the excellent yields obtained, comparable and in some instance superior to those reported by the previously quoted procedures,[9-15] are due to the high activity of Zn-Gr which allows a quantitative formation of organozinc derivative. Side reactions (self-condensation of the α-bromo ester or carbonyl compound and elimination or retro-

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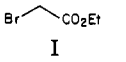
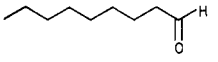
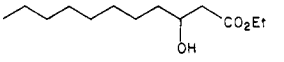
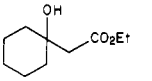
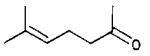
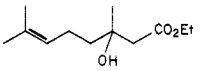
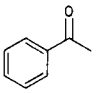
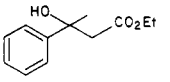
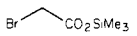
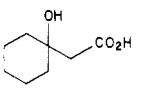
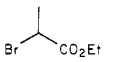
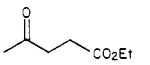
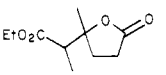
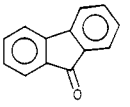
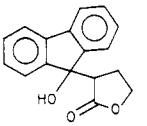
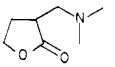
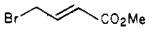
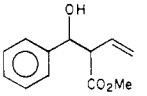
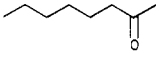
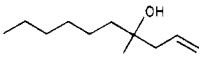
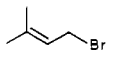
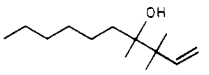
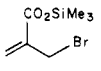
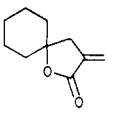
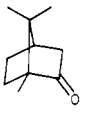
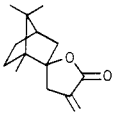
Table I. Condensation of Organozinc Derivatives with Carbonyl Compounds[a]

entry	bromo deriv	carbonyl compd	product[b]	yield,[c] %
1	 I			90
2	I			88
3	I			87
4	I			89
5				75
6				86[d]
7	 II			88
8[e]	II	$CH_2=N^+Me_2\ I^-$		55[f]
9				85[g]
10[e]				94
11[e]				94
12[e]	 III			90
13[e]	III			65[h]

[a] Unless otherwise stated the reactions were carried out at 0 °C, on a 10-mmol scale of carbonyl compound with a molar ratio of Zn-Gr/bromo derivative/carbonyl compound of 15/12/10. [b] Satisfactory analytical data (±0.4% for C and H) were obtained for all new compounds listed in the table. [c] Yields refer to pure compounds isolated by silica gel column chromatography with hexane-ether mixtures as the eluent. [d] See ref 22. [e] The reactions were carried out at 20 ± 2 °C. [f] The reaction mixture was quenched at 0 °C with 10% aqueous HCl (10 mL) and extracted with CH_2Cl_2. The organic phase contained α-methylene-γ-butyrolactone (7%) and γ-butyrolactone (25%). The β-amino lactone was recovered by adding an excess of $NaHCO_3$ to the acidic aqueous phase and extracting with CH_2Cl_2. [g] The erythro/threo isomer ratio was 45/55 as determined after chromatographic separation on a silica gel column (hexane-ether, 95/5). [h] Two epimers at the spiranic center in a 5/1 ratio were separated by gas chromatography.

aldolization of the intermediate β-bromo zinc oxy ester) are almost completely suppressed when working at 0 °C. Among the various experiments performed on α-bromo esters, we wish to emphasize a construction of the geranic acid skeleton (entry 3), the convenient use of trimethylsilyl esters owing to their facile and mild hydrolysis (entry 5), and the regiospecific α-adduct formation when γ-bromocrotonate is used (entry 9).[16] Moreover, α-substituted γ-lactones are easily accessible on starting from α-bromo-γ-butyrolactone (entry 7), as shown by its reaction with the Eschenmoser's salt (entry 8); the resulting amino lactone is precursor of α-methylene-γ-butyrolactone (tulipalin A),[17] an allergenic agent isolated from the tulip bulbs,[18] which represents the simplest member of a family of naturally occurring sesquiterpenes[19] with citotoxic an-

(16) The same behavior has been previously reported by Nozaki et al.[15a,c] and by: Bellasoued, M.; Dardoize, F.; Frangin, Y.; Gaudemar, M. *J. Organomet. Chem.* **1981**, *219*, C1. On the contrary, the condensation at −70 °C between methyl crotonate metalated with lithium diisopropylamide and benzaldehyde is not regiospecific: Dugger, R. W.; Heathcock, C. H. *J. Org. Chem.* **1980**, *45*, 1181.

(17) The β-amino lactone is quantitatively converted into α-methylene-γ-butyrolactone by treatment with CH_3I in methanol at 25 °C, followed by stirring with 5% aqueous $NaHCO_3$: Harmon, A. D.; Hutchinson, C. R. *Tetrahedron Lett.* **1973**, 1293.

(18) (a) Brongersma-Oosterhoff, U. W. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 705. (b) Bergman, B. H. H.; Beijersbergen, J. C. M.; Overeem, J. C.; Sijpesteijn, A. K. *Ibid.* **1967**, *86*, 709.

tineoplastic activity related to the presence of the five-membered α-methylene lactone moiety.[20]

As concerns allylic zinc bromides, besides verification of the almost quantitative attack on carbonyl compounds (entry 10) which takes place with complete allylic rearrangement (entry 11)[21] we have improved the route to γ-substituted α-methylene-γ-butyrolactones which starts from α-(bromomethyl)acrylic esters (entries 12, 13).[22,23] We replaced methyl or ethyl α-(bromomethyl)acrylate with the more accessible trimethylsilyl ester,[24] and we limited losses of product for concomitant polymerization reactions by performing the reaction at 20 °C (on the contrary temperatures ≥50 °C are reported in the literature). In comparison, spiro lactones deriving from cyclohexanone and norcamphor were previously synthesized in 37% and 29% yields,[23e] respectively.

Experimental Section

General Methods. ^1H nuclear magnetic resonance (NMR) spectra were measured with a Perkin-Elmer R12B instrument (60 MHz) by using tetramethylsilane as the internal standard and $CDCl_3$ as the solvent. Chemical shifts are reported as δ values. Infrared (IR) spectra were recorded on a Perkin-Elmer 710B spectrophotometer, and the absorptions are given in reciprocal centimeters. Mass spectra (MS) were taken on a double-focusing Varian MAT 112S instrument at an ionizing voltage of 70 eV. Analytical gas chromatography was performed on a Carlo Erba Fractovap 4160 apparatus with a 15-m capillary column coated with OV1 (film thickness 0.1–0.15 μm). Column chromatography separations were performed on silica gel (Merck, 70–230 mesh). Tetrahydrofuran (THF) was distilled from $LiAlH_4$ immediately before use. Melting points are uncorrected.

Preparation of Zinc–Graphite (Zn-Gr). Graphite powder (Roth, 3.1 g) is poured in a 100-mL two-necked flask and heated under argon at about 150 °C. Freshly cleaned potassium (Carlo Erba; 1.2 g, 30.7 mmol) is added in pieces; when the potassium melts, the mixture is vigorously stirred with a Teflon-covered magnetic stirring bar, and heating is stopped. Potassium–graphite (C_8K)[25] so prepared is a bronze-colored powder (pyrophoric). C_8K is covered with THF (30 mL) and solid anhydrous $ZnCl_2$ (Ventron; 2.05 g, 15 mmol) is added. A very exothermic reaction takes place, causing the solvent to reflux vigorously. When the temperature subsides, the reaction mixture is stirred at 70 °C (external oil bath) for an additional 30 min.

Synthesis of Ethyl 3-Hydroxyundecanoate (Entry 1). General Procedure. To the freshly prepared slurry of Zn-Gr (15 mmol) in THF (30 mL), cooled with an ice-bath, one-tenth of the total amount of ethyl bromoacetate (0.2 g, 1.2 mmol) is added, followed by the dropwise addition of a THF (5 mL) solution of the remaining bromo ester (1.8 g, 10.8 mmol) and nonanal (1.42 g, 10 mmol). The reaction mixture is stirred at 0 °C and monitored by gas chromatography. When the nonanal disappears (2 h), the reaction is quenched with 10% aqueous H_2SO_4. Graphite is filtered off, the organic phase is separated, and the aqueous phase is extracted with CH_2Cl_2. The combined organic extracts are dried over anhydrous $MgSO_4$, the solvent is stripped off under vacuum, and the crude product is chromatographed on a silica gel column (hexane–ether, 95/5), affording 2.05 g (90%) of the title compound as a colorless oil: IR 3450, 1735; NMR 3.6–4.3 (m, 3 H), 3.35 (s, 1 H, OH), 2.35 (m, 2 H), 1.1–1.6 (17 H), 0.9 (t, 3 H); MS, *m/e* (relative intensity) 141 ($C_9H_{17}O^+$, 5), 117 (100), 89 (22), 88 (30), 71 (65).

Ethyl 1-hydroxycyclohexaneacetate (entry 2): IR 3450, 1725; NMR 4.2 (q, 2 H), 3.3 (s, 1 H, OH), 2.45 (s, 2 H), 1.1–1.9 (10 H), 1.25 (t, 3 H); MS, *m/e* (relative intensity) 186 (M^+, 2), 168 ($M^+ - H_2O$, 2), 143 (30), 130 (100), 99 (27), 97 (25), 81 (25).

Ethyl 3,7-dimethyl-3-hydroxy-6-octenoate (entry 3): IR 3500, 1725, 1030; NMR 5.1 (m, 1 H), 4.2 (q, 2 H), 3.5 (s, 1 H, OH), 2.5 (s, 2 H), 1.7 (s, 3 H), 1.65 (s, 3 H), 1.9–2.3 (m, 2 H), 1.2–1.6 (5 H), 1.25 (s, 3 H); MS, *m/e* (relative intensity) 196 ($M^+ - H_2O$, 15), 122 (33), 109 (65), 107 (42), 85 (30), 69 (65), 43 (100).

Ethyl 3-phenyl-3-hydroxybutanoate (entry 4): IR 3500, 1725, 765, 700; NMR 7.2–7.7 (m, 5 H), 4.4 (s, 1 H, OH), 4.1 (q, 2 H), 3.0 (d, 1 H, J = 16 Hz), 2.8 (d, 1 H, J = 16 Hz), 1.55 (s, 3 H), 1.15 (t, 3 H); MS, *m/e* (relative intensity) 192 ($M^+ - H - CH_3$, 13), 121 (47), 105 (39), 77 (21), 51 (11), 43 (100), 29 (16).

1-Hydroxycyclohexaneacetic acid (entry 5): mp 61–62 °C (hexane); IR 3420, 1710; NMR 7.5 (s, 2 H, 2 OH), 2.55 (s, 2 H), 1.3–1.9 (10 H).

Ethyl α,2-dimethyl-5-oxotetrahydrofuran-2-acetate (entry 6): IR 1775, 1730; NMR 4.2 (q, 2 H), 1.7–3.0 (m, 5 H), 1.1–1.55 (9 H, 3 CH_3); MS *m/e* (relative intensity) 185 ($M^+ - CH_3$, 2), 99 (100), 83 (9), 71 (15), 56 (10), 55 (13), 43 (55), 29 (62).

9-Hydroxy-9-(tetrahydro-2-oxo-3-furyl)fluorene (entry 7): mp 148–149 °C (hexane/$CHCl_3$, 1/1); IR 3475, 1740; NMR 7.1–7.7 (m, 8 H), 5.05 (s, 1 H, OH), 3.8–4.3 (m, 2 H), 3.6 (t, 1 H, J = 9 Hz), 1.0–2.0 (m, 2 H); MS, *m/e* (relative intensity) 266 (M^+, 7), 181 (100), 180 (58), 153 (21), 152 (60), 151 (24), 150 (13), 76 (16).

3-[(Dimethylamino)methyl]dihydro-2(3*H*)-furanone (entry 8): mp (of hydrochloride) 186–187 °C (lit.[17] mp 190 °C); IR 2820, 2770, 1760, 1455, 1370, 1170, 1030; NMR 4.4 (m, 2 H), 2.2–3.1 (m, 5 H), 2.3 (s, 6 H); MS, *m/e* (relative intensity) 143 (M^+, 1), 142 (2), 84 (4), 71 (5), 58 (100), 44 (14), 42 (16).

Ethyl 2-Ethenyl-3-hydroxy-3-phenylpropanoate (entry 9). Column chromatography on silica gel (hexane–ether, 95/5) afforded analytical samples of erythro and threo isomers. Erythro isomer (first eluted): IR 3540, 1730; NMR 7.45 (s, 5 H), 5.7–6.3 (m, 1 H), 5.0–5.4 (m, 3 H), 3.6 (s, 3 H), 3.4 (dd, 1 H, J = 6, 9 Hz), 3.2 (s, 1 H, OH); MS, *m/e* (relative intensity) 206 (M^+, 2), 107 (55), 106 (65), 105 (65), 100 (100), 79 (32), 77 (88), 69 (50), 59 (50), 51 (40), 41 (55), 39 (43), 31 (55). Threo isomer: mp 80–81 °C (hexane); IR 3440, 1710; NMR 7.45 (s, 5 H), 5.5–6.1 (m, 1 H), 4.8–5.4 (m, 3 H), 3.75 (s, 3 H), 3.55 (dd, 1 H, J = 8.5, 17.5 Hz), 3.0 (m, 1 H, OH).

4-Methyl-1-decen-4-ol (entry 10): IR 3390, 3070, 1640, 1000, 910; NMR (CCl_4) 4.8–6.35 (m, 3 H), 2.15 (d, 2 H), 1.8 (s, 1 H, OH), 1.3 (m, 10 H), 1.1 (s, 3 H), 0.9 (t, 3 H); MS, *m/e* (relative intensity) 129 ($M^+ - C_3H_5$, 43), 85 (23), 69 (55), 43 (100).

3,3,4-Trimethyl-1-decen-4-ol (entry 11): IR 3490, 3080, 1635, 1010, 910; NMR (CCl_4) 4.6–6.3 (m, 4 H, 3 H after D_2O exchange), 1.35 (m, 10 H), 0.8–1.15 (12 H, 4 CH_3); MS *m/e*, (relative intensity) 129 ($M^+ - C_5H_9$, 40), 70 (36), 69 (60), 55 (33), 43 (100), 41 (39).

3-Methylene-1-oxaspiro[4.5]decan-2-one (entry 12): mp 30–31 °C (ether); IR 3095, 1760, 1665, 1105, 1065, 960, 935, 820; NMR 6.25 (t, 1 H, J = 2.7 Hz), 5.65 (t, 1 H, J = 2.7 Hz), 2.75 (t, 2 H, J = 3.0 Hz), 1.65 (m, 10 H); MS, *m/e* (relative intensity) 166 (M^+, 57), 123 (100), 110 (50), 68 (80), 55 (35).

4′,5′-Dihydro-4′-methylene-1,7,7-trimethylspiro[bicyclo-[2.2.1]heptane-2,2′(5′*H*)-furan]-5′-one (entry 13): mp 82–83 °C (hexane); IR 1755, 1665, 1040, 970, 930, 910; NMR 6.3 (t, 1 H, J = 2.9 Hz), 5.7 (t, 1 H, J = 2.9 Hz), 2.7–3.1 (m, 1 H), 2.1–2.55 (m, 1 H), 1.0–2.0 (m, 7 H), 1.1 (s, 3 H), 0.9 (s, 3 H), 0.85 (s, 3 H); MS, *m/e* (relative intensity) 220 (M^+, 3), 205 (6), 137 (30), 110 (40), 95 (100), 41 (30).

(19) "Steroids, Terpenes and Alkaloids"; Korte, F.; Goto, M., Eds.; Georg Thieme Verlag: Stuttgart, 1978; Chapter 2 (part 3 of the series "Natural Products"). Concerning methods for the synthesis of α-methylene lactones see: (a) Grieco, P. A. *Synthesis* **1975**, 67. (b) Newaz, S. S. *Aldrichim. Acta* **1977**, *10*, 64.

(20) Kuphan, S. M.; Fessler, D. C.; Eakin, M. A.; Giacobbe, T. J. *Science (Washington, D.C.)* **1970**, *168*, 376.

(21) Ruppert, J. F.; White, J. D. *J. Org. Chem.* **1976**, *41*, 550.

(22) When γ-bromo zinc oxy esters are formed as intermediates, a spontaneous lactonization occurs.

(23) (a) Ohler, E.; Reininger, K.; Schmidt, V. *Angew. Chem. Int. Ed. Engl.* **1970**, *9*, 457. (b) Rosowsky, A.; Papathanasopoulos, N.; Lazarus, H.; Foley, G. E.; Modest, E. J. *J. Med. Chem.* **1974**, *17*, 672. (c) Lee, K. H.; Ibuka, T.; Kim, S. H.; Vestal, B. R.; Hall, I. H.; Huang, E. S. *Ibid.* **1975**, *18*, 812. (d) Howie, G. A.; Stamos, I. K; Cassady, J. M. *Ibid.* **1976**, *19*, 309. (e) Schlewer, G.; Stampf, J. L.; Benezra, C. *Ibid.* **1980**, *23*, 1031. (f) Heindel, N. D.; Minatelli, J. A. *J. Pharm. Sci.* **1981**, *70*, 84.

(24) α-(Bromomethyl)acrylic acid (Aldrich) is converted into the sodium salt (NaH, THF, 0 °C) and silylated (Me_3SiCl, 0 °C, 2 h) in 85% yield; bp 85 °C (0.2 mmHg); IR 1725, 1630 cm^{-1}; NMR ($CDCl_3$) δ 6.3 (s, 1 H), 6.0 (s, 1 H), 4.15 (s, 2 H), 0.3 (s, 9 H). The acid-catalyzed esterification of α-(bromomethyl)acrylic acid with ethanol requires a prolonged reflux with continuous azeotropic distillation of water and gave us poor yields for partial polymerization. For an alternative approach to the ethyl ester see: Villieras, J.; Rambaud, M. *Synthesis* **1982**, 924.

(25) The X-ray diffraction pattern recorded with a Debye–Scherrer camera corresponds to the first stage of intercalation of potassium in graphite: Rudorff, W.; Schulze, E. *Z. Anorg. Allg. Chem.* **1954**, *227*, 156.

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Registry No. Gr-xZn, 69704-06-9; Gr, 7782-42-5; K, 7440-09-7; C_8K, 12081-88-8; $ZnCl_2$, 7646-85-7; ethyl bromoacetate, 105-36-2; trumethylsily bromoacetate, 18291-80-0; ethyl α-bromopropanoate, 535-11-5; α-bromo-γ-butyrolactone, 5061-21-2; methyl 4-bromocrotonate, 1117-71-1; allyl bromide, 106-95-6; 1-bromo-3-methyl-2-butene, 870-63-3; trimethylsilyl α-(bromomethyl)-acrylate, 87070-51-7; nonanal, 124-19-6; cyclohexanone, 108-94-1; 6-methyl-5-hepten-2-one, 110-93-0; acetophenone, 98-86-2; ethyl 4-oxovalerate, 539-88-8; fluorenone, 486-25-9; Eschenmoser's salt, 33797-51-2; benzaldehyde, 100-52-7; 2-octanone, 111-13-7; camphor, 464-49-3; ethyl 3-hydroxyundecanoate, 87070-52-8; ethyl 1-hydroxycyclohexaneacetate, 5326-50-1; ethyl 3,7-dimethyl-3-hydroxy-6-octenoate, 54211-39-1; ethyl 3-phenyl-3-hydroxybutanoate, 2293-60-9; 1-hydroxycyclohexaneacetic acid, 14399-63-4; ethyl α,2-dimethyl-5-oxotetrahydrofuran-2-acetate, 87070-53-9; 9-hydroxy-9-(tetrahydro-2-oxo-3-furyl)fluorene, 87070-54-0; 3-[(dimethylamino)methyl]dihydro-2(3*H*)-furanone, 42023-17-6; 3-[(dimethylamino)methyl]dihydro-2(3*H*)-furanone hydrochloride, 87070-55-1; ethyl *erythro*-2-ethenyl-3-hydroxy-3-phenylpropanoate, 65203-03-4; ethyl *threo*-2-ethenyl-3-hydroxy-3-phenylpropanoate, 65203-02-3; 4-methyl-1-decen-4-ol, 38564-33-9; 3,3,4-trimethyl-1-decen-4-ol, 74120-67-5; 3-methylene-1-oxaspiro[4.5]decan-2-one, 52978-85-5; dihydro-4′-methylene-1,7,7-trimethylspiro[bicyclo[2.2.1]heptane-2,2′(5′*H*)-furan]-5′-one (isomer 1), 87070-56-2; dihydro-4′-methylene-1,7,7-trimethylspiro[bicyclo[2.2.1]heptane-2,2′(5′*H*)-furan]-5′-one (isomer 2), 87099-34-1.

Cleavage of Silicon–Nitrogen Bonds by Acid Chlorides: An Unusual Synthetic Route to Amides

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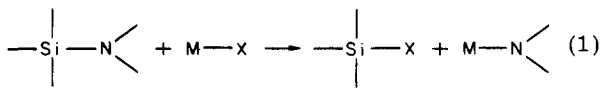
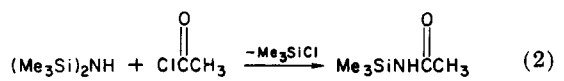
It has long been known that a wide variety of covalent halides react with silylamines under mild conditions to cleave the silicon–nitrogen bond (eq 1).



(1)

This reaction has been extensively used in organometallic synthesis;[1] however, the C–Cl bond of alkyl and aryl chlorides is generally inert toward silylamines. Early exceptions were observed by Anderson[2] and by Pump and Wannagat,[3] who converted an acid halide into a silyl-substituted amide by this method (eq 2).



(2)

This reaction should in theory be useful for the preparation of amides that retain silicon in their structures as well as those that do not; however, it does not appear that a detailed study of its utility has ever been reported. We have therefore determined the generality of this reaction and explored some of its possible synthetic applications; herein are reported our results.

(1) See references in Lappert, M. F.; Power, P. P.; Sanger, A. R.; Srivastava, R. C. "Metal and Metalloid Amides: Synthesis, Structures, and Physical and Chemical Properties"; Wiley: New York, 1980.
(2) Anderson, H. H. *J. Am. Chem. Soc.* **1952**, *74*, 1421.
(3) Pump, J.; Wannagat, U. *Monatsh. Chem.* **1962**, *93*, 352.

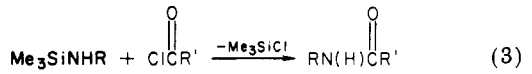
Table I. Products from the Reactions of Silylamines with Monoacid Chlorides ($R_1R_2NC(=O)R_3$)

R_1	R_2	R_3	yield,[a] %
Et	H	Me	71
Et	H	Et	68
Et	H	Ph	74
i-Pr	H	Me	82
i-Pr	H	Et	78
i-Pr	H	Ph	86
t-Bu	H	Me	90
t-Bu	H	Et	72
t-Bu	H	Ph	64
Ph	H	Me	61
Ph	H	Et	74
Ph	H	Ph	75
Et	Et	Me	67
Et	Et	Et	71
Et	Et	Ph	67

[a] Isolated yields of purified products; reported values represent an average of two or more trials.

Results and Discussion

Generality of the Reaction. To determine whether this reaction is a general one, and to evaluate the effect of varying the substituents of the silylamines, a series of reactions was performed in which N-substituted acetamides, propionamides, and benzamides were produced (eq 3).



(3)

R = Et, *i*-Pr, *t*-Bu, Ph, Me_3Si; R′ = Me, Et, Ph

It was found in each case that the reaction proceeded smoothly at or near room temperature to form the amide, usually as a crystalline precipitate from hexane or diethyl ether solvent. Those cases where R = Me_3Si were exceptional, as these silyl amides have somewhat higher solubilities in nonpolar solvents; this, coupled with their sensitivity toward hydrolysis, decreased the isolated yields unless special precautions (i.e., in-line filtration and removal of solvent under N_2) were taken.

The presence of bulky substituents on the nitrogen atom diminished the reaction rate; this is consistent with previous suggestions[3,4] that the mechanism is probably a simple nucleophilic displacement at the carbonyl carbon. It was also not surprising that the poorest nucleophiles, (trimethylsilyl)aniline and bis(trimethylsilyl)amine, often required some heating to allow the reaction to proceed at a reasonable rate. There were no significant differences in reactivity among acetyl, propionyl, and benzoyl chlorides.

The sterically hindered tertiary amine Me_3SiNEt_2 was used to convert monoacid chlorides to the corresponding *N,N*-diethyl amides in moderate yields (typically 60–70% after purification). The reaction conditions and observations generally paralleled those involving alkyl(trimethylsilyl)amines, indicating that both secondary and tertiary amides are readily synthesized by this process.

The individual results of these reactions are summarized in Table I.

Reactions of Diacid Chlorides with Alkyl(trimethylsilyl)amines. A. Formation of Diamides. As an extension of the above, it was found that mixing a 2:1 or greater molar ratio of diethyl(trimethylsilyl)amine with various diacid chlorides in an inert solvent results in the

(4) Gasparini, J. P.; Gassend, R.; Maire, J. C.; Elguero, J. *J. Organomet. Chem.* **1980**, *188*, 141.

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