96129-52-1; **6a**, 96129-53-2; **6b**, 96129-54-3; **7a**, 96129-55-4; **7b**, 77130-01-9; **8**, 96150-65-1; **10**, 96129-57-6; **11**, 96150-66-2; trichloroacetaldehyde, 75-87-6; tribromoacetaldehyde, 115-17-3; 2-methyl-3,3-dibromopropenoic acid, 1578-22-9.

Application of the Swern Oxidation to the Manipulation of Highly Reactive Carbonyl Compounds†,[1]

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In the course of synthetic studies toward the polyether ionophore antibiotics, we encountered several aldehydes and ketones which were inductively destabilized by strongly electronegative substituents toward hydration and decomposition.[3] Here we report that the direct addition of nucleophilic reagents to crude Swern oxidation[4] mixtures can circumvent the deleterious side reactions characteristic of highly reactive carbonyl compounds.

The Swern oxidation is anhydrous, proceeds rapidly at low temperature, and produces relatively innocuous byproducts: carbon monoxide, carbon dioxide, dimethyl sulfide, and triethylamine hydrochloride.[5] Thus, while other oxidation methods led to the formation of an intractable 2-ketofuranoside hydrate,[6] Swern oxidation of the alcohol **1** (Scheme I) in THF gave the ketone **2** nearly quantitatively, and addition of 5 equiv of methylmagnesium bromide provide the branched-chain carbohydrate[7] **3** as a single diastereomer in 85% yield.

The aldehyde **5** was also prone to hydration and decomposition and could not be isolated in good yield, even in an impure state. In this case, addition of methyl (triphenylphosphoranylidene)acetate to the crude Swern oxidation mixture provided a remarkable 98% yield of the unsaturated esters **6**.

Aliphatic α-keto aldehydes are another class of hyperreactive carbonyl compounds, and, as a consequence of their propensity toward hydration, polymerization, and air oxidation,[8] they have seen little use in organic synthesis.[9,10] Addition of methyl (triphenylphosphoranylidene)acetate to the crude Swern oxidation of 1,2-octanediol quenched the bright yellow color characteristic of hexylglyoxal[10] instantaneously at −78 °C, and the Wittig condensation product **9**[11] was isolated in 90% yield. This constitutes a simple new method for the synthesis[12] of the γ-oxygenated crotonates found in several natural products.[13]

As an even more demanding test of this protocol, we selected the hitherto unknown parent acylsilane, (trimethylsilyl)formaldehyde. In this instance, Swern oxidation of (trimethylsilyl)methanol[14] was carried out entirely at −78 °C, and the addition of trimethylamine was followed 5 min later by the addition of ethyl 2-(triphenylphosphoranylidene)propionate. The solution was then allowed to warm to room temperature, and the novel silicon compound **12** was isolated by chromatography in 54% yield.[15] Since the addition of the Wittig reagent to a crude reaction mixture which had been allowed to warm to 0 °C produced no condensation product, we infer that polymerization occurs quite rapidly. However, the low-temperature viability of monomeric (trimethylsilyl)formaldehyde suggests new possibilities for the incorporation of silicon into organic molecules.[16,17]

† Contribution No. 7086.

Experimental Section

Melting points are uncorrected. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 90 MHz. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.0 ppm) as an internal standard. Data are reported as follows: chemical shift (multiplicity, integrated intensity, coupling constants, assigment). Optical rotations were measured in 1-dm cells of 1-mL capacity. Chloroform, when used as a solvent for optical rotations, was filtered through neutral alumina (activity I) immediately prior to use. Analytical thin-layer chromatography (TLC) was conducted on 2.5 × 10 cm precoated TLC plates: layer thickness 0.25 cm. Silica gel columns for chromatography utilized 70–230-mesh ASTM. Reaction solvents and liquid reagents were purified by distillation or drying shortly before use. All other reactants and solvents were reagent grade unless described otherwise. Reaction were run under an argon atmosphere arranged with a mercury bubbler so that the system could be alternatively evacuated and filled with argon and left under a positive pressure. Reported temperatures were measured externally. Syringes and reaction flasks were dried at least 12 h in an oven (120–140 °C) and cooled in a desiccator over anhydrous $CaSO_4$ prior to use. If feasible, reaction flasks were also flame-dried in vacuo.

Allyl 3,5-*O*-(1-Methylethylidene)-2-*C*-methyl-D-lyxofuranoside (3). To a stirred solution of 67 μL (0.77 mmol) of oxalyl chloride in 2.0 mL of THF at −78 °C was added 57 μL (0.81 mmol) of dimethyl sulfoxide. The solution was allowed to warm to −35 °C for 3 min and was then recooled to −78 °C. A solution of 169 mg (0.734 mmol) of the alcohol **1** in 1.0 mL of THF was then added to the reaction mixture. The resulting solution was allowed to warm to −35 °C and after 15 min was treated with 0.51 mL (3.7 mmol) of triethylamine. The reaction mixture was allowed to warm briefly to room temperature and was then recooled to

(1) Grateful acknowledgement is made for support of this investigation by NIH (HL-23167). No reprints available.

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(3) (a) Gold, H. In "Methoden der Organischen Chemie" (Houben-Weyl); Muller, E., Ed.; Georg Thieme Verlag: Stuttgart, 1976; Vol. 7/2b, pp 1930–1931. (b) Bayer, O., ref 3a, 1954; Vol. 7/1, pp 413–417.

(4) Omura, K.; Swern, D. *Tetrahedron* **1978**, 1651–1660.

(5) Mancuso, A. J.; Brownfain, D. S.; Swern, D. *J. Org. Chem.* **1979**, *44*, 4148–4150.

(6) Collins, P. M.; Hurford, J. R.; Overend, W. G. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2163–2177. See also: Tam, T. F.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1980**, 556. Anderson, R. C.; Fraser-Reid, B. *Tetrahedron Lett.* **1978**, 3233–3236.

(7) Grisebach, H. *Adv. Carbohydr. Chem. Biochem.* **1978**, *35*, 81. Grisebach, H.; Schmid, R. *Agnew, Chem., Int. Ed. Engl.* **1972**, *11*, 159.

(8) Blaise, E. E. *Ct. R. Hebd. Seances Acad. Sci.* **1922**, *175*, 1216–1218. Royals, E. E.; Robinson, A. G., III. *J. Am. Chem. Soc.* **1956**, *78*, 4161–4164. Tiffany, B. D.; Wright, J. B.; Moffet, R. B.; Heinzelman, R. V.; Strube, R. E.; Aspergren, B. D.; Lincoln, E. H.; White, J. L. *J. Am. Chem. Soc.* **1957**, *79*, 1682–1687. Rubin, M.; Paist, W. D.; Elderfield, R. C. *J. Org. Chem.* **1941**, *6*, 260–269. Verhe, R.; Courtheyn, D.; De Kimpe, N.; De Buyck, L.; Schamp, N. *Synthesis* **1982**, 667–670. Kuchar, M. *Collect. Czech. Chem. Commun.* **1968**, *33*, 880–893.

(9) Lipshutz, B. H.; Morey, M. C. *J. Org. Chem.* **1983**, *48*, 3745–3750.

(10) Rosowsky, A.; Chen, K. K. N. *J. Org. Chem.* **1973**, *38*, 2073–2077.

(11) Bestmann, H. J.; Seng, F.; Schulz, H. *Chem. Ber.* **1963**, *96*, 465–469.

(12) Bartlett, P. A. *J. Am. Chem. Soc.* **1976**, *98*, 3305–3312. Greene, A. E.; Le Drian, C.; Grabbe, P. *J. Org. Chem.* 1980, *45*, 2713–2715. Bohm, I.; Schulz, R.; Reissig, H.-U. *Tetrahedron Lett.* **1982**, *23*, 2013–2016. Asaoka, M.; Abe, M.; Mukuta, T.; Takei, H. *Chem. Lett.* **1982**, 215–219. Asaoka, M.; Mukuta, T.; Takei, H. Tetrahedron *Lett.* 1981, *22*, 735–738, and references therein.

(13) Reviews: Nicolau, K. C. *Tetrahedron* **1977**, *33*, 683. Back, T. G. *Ibid.* **1977**, *33*, 3041. Masamune, S.; Bates, G. S.; Corcoran, J. W. *Agnew. Chem., Int. Ed. Engl.* **1977**, *16*, 585. Masamune, S. *Aldrichimica Acta* **1978**, *11*, 23.

(14) Ambasht, S.; Chiu, S.; Peterson, P. E.; Queen, J. *Synthesis* **1980**, 318–320.

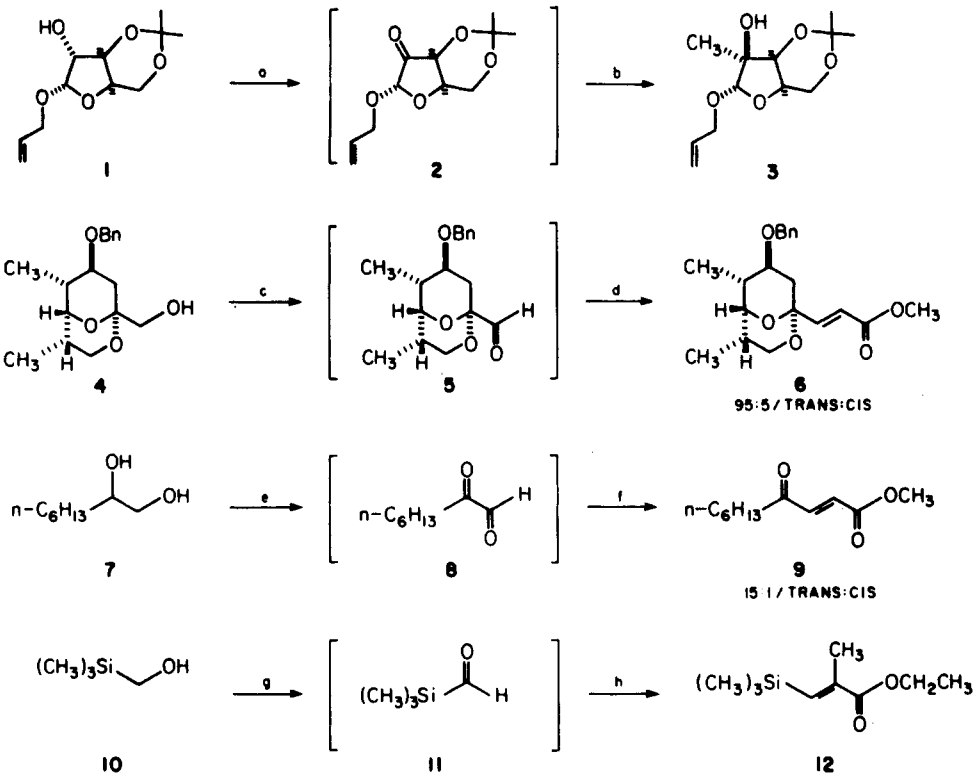
(15) The vinyl proton of **12** appears at 6.82 ppm, indicating that it is cis to the carbethoxy group. Compare: Cunico, R. F.; Lee, H. M.; Herbach, J. *J. Organomet. Chem.* **1973**, *52*, C7-10.

(16) Carter, M. J.; Fleming, I.; Percival, A. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2415–2434. Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595–4597.

(17) Colvin, E. "Silicon in Organic Synthesis"; Butterworths: London, 1981.

0022-3263/85/1950-2198$01.50/0

Scheme I[a]



[a] (a) $(COCl)_2$, Me_2SO, THF, −78 °C to −35 °C, 15 min; TEA, −35 °C to 20 °C; (b) MeMgBr, Et_2O, −78 °C to −50 °C, 1 h; (c) $(COCl)_2$, Me_2SO, CH_2Cl_2, −60 °C, 15 min, TEA, −60 °C to 0 °C; (d) $(Ph)_3PCHCO_2Me$, 0 °C to 20 °C, 10 min; (e) $(COCl)_2$, Me_2SO, CH_2Cl_2, −78 °C, 20 min; TEA, −78 °C, 10 min; (f) $(Ph)_3PCHCO_2Me$, −78 °C to 20 °C; (g) $(COCl)_2$, Me_2SO, CH_2Cl_2, −78 °C, 15 min; TEA, −78 °C, 5 min; (h) $(Ph)_3PCH(Me)CO_2Et$, −78 °C to 20 °C.

−78 °C. An ethereal solution of methylmagnesium bromide (1.31 mL, 3.67 mmol) was then added dropwise to the vigorously stirred reaction mixture. The temperature of the solution was allowed to warm to −50 °C over 1 h, was recooled to −78 °C, and was then cautiously treated with 0.5 mL of ethanol and then 1.0 mL of a saturated aqueous solution of NH_4Cl buffered to pH 8 with concentrated aqueous ammonia. The warmed reaction mixture was then poured into 75 mL of the above buffer and extracted with two 150-mL portion of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 12 g of silica gel with 1:1 ether/petroleum ether afforded 153 mg (85%) of the alcohol **3** as a colorless oil: R_f 0.28 (silica gel, 4:6 ether/petroleum ether); evaporative distillation 100 °C (0.005 mmHg); $[\alpha]^{22}_D$ +105° (*c* 1.80, $CHCl_3$); IR ($CHCl_3$) 3550, 3000, 2920, 1450, 1385, 1375, 1165, 1050, 1010, 840 cm^{-1}; ^1H NMR ($CDCl_3$) 1.30, 1.42, 1.42 (3 s, 9 H, 3 CH_3C), 3.27 (s, 1 H, OH), 2.63–4.40 (m, 6 H), 4.93 (s, 1 H, OCHO). Anal. Calcd for $C_{12}H_{20}O_5$: C, 59.00; H, 8.25. Found: C, 58.95; H, 8.19.

Methyl 3-[(5*R*)-4(*S*),6(*R*)-Dimethyl-7(*S*)-(benzyloxy)-2,9-dioxabicyclo[3.3.1]non-1-yl]-*cis*- and -*trans*-propenoate (6). To a stirred solution of 42 μL (0.49 mmol) of oxalyl chloride in 4.0 mL of dichloromethane at −60 °C was added 69 μL (0.97 mmol) of dimethyl sulfoxide. After 10 min, a solution of 118 mg (0.404 mmol) of the alcohol **4** in 3 mL of dichloromethane was added to the reaction mixture. After 15 min, the reaction mixture was treated with 0.28 mL (2.0 mmol) of triethylamine and then allowed to warm to 0 °C. Methyl (triphenylphosphoranylidene)acetate (405 mg, 1.21 mol) was then added, and, after 10 min at room temperature, the reaction mixture was poured into 40 mL of saturated aqueous NaCl and extracted with two 100-mL portions of dichloromethane. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 25 g of silica gel with 1:1 ether/petroleum ether afforded 138 mg (99%) of a 95:5 trans:cis mixture (^1H NMR) of α,β-unsaturated esters as a colorless oil: R_f 0.67 (trans), 0.63 (cis) (silica gel, ether). The trans isomer had the following physical properties: evaporative distillation 165–170 °C (0.005 mmHg); $[\alpha]^{21}_D$ +92.9° (*c* 1.47, $CHCl_3$); IR ($CHCl_3$) 3000, 2950, 2885, 1715, 1430, 1305, 1275, 1125, 1070, 1000, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90, 1.15 (2 d, 6 H, *J* = 7 Hz, 2 CH_3CH), 1.75 (dd, 1 H, *J* = 14 Hz, *J'* = 9 Hz, CC*H*HCH), 2.42 (dd, 1 H, *J* = 14 Hz, *J'* = 6 Hz CCH*H*CH), 3.70 (s, 3 H, OCH_3), 4.43, 4.65 (2 d, 2 H, *J* = 12 Hz, $C_6H_5CH_2$), 6.10, 6.77 (2 d, 2 H, *J* = 16 Hz, CH=CH), 7.31 (s, 5 H, C_6H_5). Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.56. Found: C, 69.29; H, 7.50. ^1H NMR (cis isomer, $CDCl_3$) δ 0.88, 1.14 (2 d, 6 H, *J* = 7 Hz, 2 CH_3CH), 3.37 (s, 3 H, OCH_3), 5.83 (s, 2 H, CH=CH), 7.32 (s, 5 H, C_6H_5).

Methyl (*E*)- and (*Z*)-4-Oxo-2-decenoate (9). To a stirred solution of 192 μL (2.20 mmol) of oxalyl chloride in 8 mL of dichloromethane at −78 °C was added 184 μL (2.60 mmol) of dimethyl sulfoxide. After 10 min, a solution of 146 mg (1.00 mmol) of 1,2-octanediol in 2 mL of dichloromethane was added over 3 min to the reaction mixture. After 20 min, 0.84 mL (6.0 mmol) of triethylamine was added, and after 10 min at −78 °C, a solution of 501 mg (1.50 mmol) of methyl (triphenylphosphoranylidene)acetate in 2.0 mL of dichloromethane was added to the reaction mixture over 3 min. The reaction mixture was allowed to warm to room temperature, was poured into 50 mL of 50% saturated aqueous NaCl, and was then extracted with 100 mL of ether. The organic phase was dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 15 g of silica gel with 1:9 ether/petroleum ether afforded first 167 mg (84%) of the olefin **9** as a low melting white solid: mp 43–45 °C (lit.[15] mp 48–49 °C); R_f 0.33 (silica gel, 2:8 ether/petroleum ether); IR ($CHCl_3$) 2960, 2940, 2860, 1720, 1700, 1630, 1460, 1435, 1305, 1180, 980, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (br t, 3 H, *J* = 6 Hz, CH_3CH_2), 1.25 (br s, 6 H), 1.40–1.80 (br m, 2 H), 2.57 (t, 2 H, *J* = Hz, $CH_2CH_2C(O)$), 3.80 (s, 3 H, OCH_3), 6.62, 7.05 (2 d, 2 H, *J* = 17 Hz, CH=CH). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.45; H, 9.04. There was then eluted 11 mg (5.5%) of the cis isomer as a colorless oil: R_f 0.20 (silica gel, 2; 8 ether/petroleum ether); evaporative distillation 85 °C (0.5 mmHg); IR ($CHCl_3$) 2960, 2940, 2860, 1725, 1700, 1630, 1460, 1440, 1390, 1230, 1130, 1085, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (br t, 3 H, *J* = 6 Hz, CH_3CH_2), 1.30 (br s, 6 H), 1.40–1.80 (br m, 2 H), 2.63 (t, 2 H, *J* = 6 Hz, $CH_2CH_2C(O)$), 3.70 (s, 3 H, OCH_3), 6.00, 6.47 (2 d, 2 H, *J* = 12 Hz, CH=CH). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.38; H, 9.03.

Ethyl (*E*)-3-(Trimethylsilyl)methacrylate (12). To a stirred solution of 131 μL (1.50 mmol) of oxalyl chloride in 8.0 mL of dichloromethane at −78 °C was added 121 μL (1.70 mmol) of dimethyl sulfoxide. After 10 min, a solution of 104 mg (1.00 mmol) of (trimethylsilyl)methanol in 2 mL of dichloromethane was added over 4 min to the reaction mixture. After 15 min, 0.52 mL (3.7 mmol) of triethylamine was added over 1 min. After 5 min at −78 °C, a solution of 690 mg (1.9 mmol) of ethyl 2-(triphenylphosphoranylidene)propionate was added over 3 min. The reaction mixture was then allowed to warm to room temperature, was diluted with 70 mL of ether, and was then washed with 40 mL of water and then 40 mL of saturated aqueous NaCl. The organic phase was dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 10 g of silica gel with 3:97 ether/petroleum ether afforded 101 mg (54%) of the olefin **12** as a colorless oil: R_f 0.33 (silica gel, 5:95 ether/petroleum ether); IR ($CHCl_3$) 3000, 2960, 1700, 1610, 1370, 1330, 1320, 1210, 1100, 860, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.17 (s, 9 H, $(CH_3)_3Si$), 1.30 (t, 3 H, J = 7 Hz, CH_3CH_2), 2.00 (s, 3 H, CH_3C), 4.17 (q, 2 H, J = 7 Hz, CH_3CH_2), 6.82 (s, 1 H, CH=C); mass spectrum; m/e (relative intensity, composition) 171 (100, $C_8H_{15}O_2Si$), 143 (46, $C_7H_{15}OSi$), 113 (5, $C_6H_{13}Si$), 75 (38, $C_3H_7O_2$), 73 (32, $C_3H_5O_2$, C_3H_9Si).

Registry No. 1, 96150-76-4; **3**, 96150-78-6; **4**, 96056-09-6; *trans*-**6**, 96056-10-9; *cis*-**6**, 96149-11-0; **7**, 1117-86-8; *trans*-**9**, 96245-80-6; *cis*-**9**, 96245-81-7; **10**, 3219-63-4; **12**, 96245-82-8; oxalyl chloride, 79-37-8; methylmagnesium bromide, 75-16-1; methyl (triphenylphosphoranylidene)acetate, 2605-67-6; ethyl 2-(triphenylphosphoranylidene)propionate, 5717-37-3.

A New Approach to the Preparation of *N*-Carboxy α-Amino Acid Anhydrides

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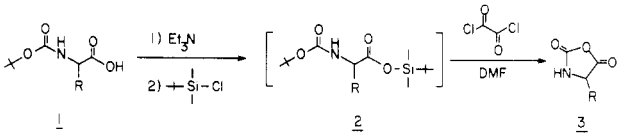
N-Carboxy α-amino acid anhydrides (NCA's) would appear to be reagents of considerable utility in peptide synthesis, since their preparation achieves both amino-group protection and carboxylate activation in a single step. While the NCA's have been used routinely in prepartion of homopolymers of high molecular weight and in random copolymerizations,[1] this strategy has found only limited application in the stepwise synthesis of polypeptides.[2] Dipeptide formation, by condensation of one amino acid with the NCA of a second, is a facile process,[3] but there are difficulties in controlling the amide bond-forming reaction when the NCA technology is applied to heteropolymers.[4] An additional problem is attributable to the fact that the *N*-carboxy anhydrides themselves are accessible by less-than-straightforward routes. These often involve harsh reaction conditions, long reaction times with poor yields and—not inconsequentially—the use of severely toxic reagents.

Scheme I



N-Carboxy anhydrides have been prepared most frequently by treatment of an amino acid with large excesses of phosgene at elevated temperatures,[5] an obviously hazardous method. Goodman and co-workers[6] introduced a technique for monitoring NCA formation by infrared spectroscopy, which allows the use of standardized phosgene solutions. While this approach reduces the quantity of phosgene typically specified in the older literature, the amounts required are by no means stoichiometric. In an attempt to avoid the use of phosgene altogether, Oya and his colleagues[7] have prepared NCA's using trichloromethyl chloroformate, the socalled phosgene dimer. But this method is not wholly satisfactory; the NCA of alanine, for example, is obtained only after extensive workup and then in only about 60% yield. Moreover, trichloromethyl chloroformate is not widely available commercially.

Alternative procedures for preparation of the *N*-carboxy anhydrides include reaction of the N^{α}-protected amino acids with PBr_3.[8] In fact, the NCA's of glutamine and asparagine can be prepared only by treatment with PBr_3; the phosgene methods gives dehydration to the corresponding cyano derivatives.[2b,8] Generally, methods involving the use of the phosphoro halides suffer from the need for very long reaction times, extensive product purification and, frequently, very poor yields.

We have been involved in the preparation of antibacterial peptides,[9] which occasions a general interest in synthetic methods allowing for the facile introduction of β-haloalanyl residues into peptides. In this connection, we have discovered that the *N*-carboxy anhydrides of several α-amino acids (**3**), including β-chloro-L-alanine (Table I), can be formed by reaction of an *N*-*tert*-butoxycarbonyl (BOC) amino acid (**1**) with *tert*-butyldimethylsilyl chloride and subsequent treatment of the resulting silyl ester (**2**) with oxalyl chloride in the presence of dimethylformamide (DMF) (Scheme I). The sequence **1** → **3** is an adaptation of the method for preparation of carboxylic acid chlorides (and esters) developed by Wissner and Grudzinskas.[10]

In a typical reaction, an *N*-BOC amino acid is dissolved in ethyl acetate and is then treated with 1 equiv each of triethylamine and *tert*-butyldimethylsilyl chloride. Ad-

(1) Hasimoto, Y.; Imanishi, Y. *Biopolymers* **1981** *20*, 488; **1981**, *20*, 507. Oya, M.; Takahishi, T. *J. Polym. Sci. Polym. Chem. Ed.* **1982**, *20*, 529. Atreyi, M.; Rao, V. R.; Kumar, S. *Biopolymers* **1983**, *22*, 747.

(2) (a) Rudinger, J.; Sorm, F. *Collect. Czech. Chem. Commun.* **1951**, *16*, 214. Honzl, J.; Rudinger, *J. Ibid.* **1955**, *20*, 1190. Wilchek, M.; Patchornik, A. *J. Org. Chem.* **1963**, *28*, 1874. Hirschman, R.; Strachan, R. G.; Schwam, H.; Schoenewaldt, E. F.; Joshua, H.; Barkemeyer, B.; Veber, D. F.; Paleveda, W. J.; Jacob, T. A.; Beesly, T. E.; Denkewalter, R. G. *J. Org. Chem.* **1967**, *32*, 3415. Iwakura, Y.; Uno, k.; Oya, M.; Katakai, R. *Biopolymers* **1970**, *9*, 1419. (b) Hirschmann, R.; Schwam, H.; Strachan, R. G.; Schoenewaldt, E. F.; Barkemeyer, H.; Miller, S. M.; Conn, J. B.; Garsky, V.; Veber, D. F.; Denkewalter, R. G. *J. Am. Chem. Soc.* **1971**, *93*, 2746.

(3) Bailey, J. L. *J. Chem. Soc.* **1950**, 3471. Grovestine, E. M.; Langlois, J. R.; Williams, R. E. *Can. J. Chem.* **1972**, *51*, 1284. Wies, R.; Pfaender, P. *Liebigs Ann. Chem.* **1979**, *1269*. Halstrom, J.; Brunfeldt, K.; Kovacs, K. *Acta. Chem. Scand., Ser. B* **1979**, *B33*, 685. Kircher, K.; Berndt, H.; Zahn, H. *Liebigs Ann. Chem.* **1980**, 275.

(4) Bartlett, P. D.; Jones, R. H. *J. Am. Chem. Soc.* **1957**, 79, 2153. Bartlett, P. D.; Dittmer, D. C. *Ibid.* **1957**, *79*, 2159. Brenner, M.; Hofer, W. *Helv. Chim. Acta* **1961**, *44*, 1798. Grant, N. H.; Alburn, H. E. *J. Am. Chem. Soc.* **1964**, *86*, 3870.

(5) Fuchs, R. *Chem. Ber.* **1922**, *55*, 2943. Levy, A. L. *Nature (London)* **1950**, *165*, 152. Farthing, A. C.; Reynolds, R. J. *Ibid.* **1950**, *165*, 647. Farthing, A. C. *J. Chem. Soc.* **1950**, 3213. Patchornik, A.; Sila, M.; Katchalski, E. *J. Am. Chem. Soc.* **1954**, *76*, 299.

(6) Fuller, W. D.; Verlander, M. S.; Goodman, M. *Biopolymers* **1976**, *15*, 1869.

(7) Oya, M.; Katakai, R.; Nakai, H. *Chem. Lett.* **1973**, 1143.

(8) Leuchs, H. *Chem. Ber.* **1906**, *39*, 857. Ben-Ishai, D.; Katchalski, E. *J. Am. Chem. Soc.* **1952**, *74*, 3688. Berger, A.; Kurtz, J.; Katchalski, E. *J. Am. Chem. Soc.* **1954**, *76*, 2522.

(9) Cheung, K.-S.; Dudek, E.; Wasserman, S.; Lerner, S. A.; Johnston, M. *J. Med. Chem.* **1983**, *26*, 1733.

(10) Wissner, A.; Grudzinskas, C. V. *J. Org. Chem.* **1978**, *43*, 3972.

0022-3263/85/1950-2200$01.50/0