by thick layer preparative chromatography (benzene/ethyl acetate 1/1, silica gel) and gave 52 mg (49%) of colorless crystalline Praziquantel (1): mp 132-133 °C, mixed mp 133-137 °C. The ^{1}H NMR and IR spectra of the product were identical with those of an authentic sample of Praziquantel (mp 137-138 °C).

Pyrolysis of the methoxy- and acetoxymethylamides in various solvents (toluene, xylene, and dichloro- and dibromobenzene, etc.) gave varying amounts of decomposition, the main component isolable being amide **6**, but no trace of Praziquantel.

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Registry No. 1, 55268-74-1; **2**, 6809-91-2; **3**, 1005-19-2; **4**, 93255-04-0; **5**, 93255-05-1; **6**, 93255-06-2; **7**, 93255-07-3; **8**, 93255-08-4; chloroacetamide, 79-07-2; cyclohexanecarboxylic acid, 98-89-5; glycinamide hydrochloride, 1668-10-6; paraformaldehyde, 30525-89-4; acetic anhydride, 108-24-7.

Mild Deprotection of Carbapenem Esters with Aluminum Trichloride

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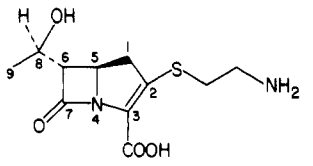
Since the isolation of the potent carbapenem antibiotic thienamycin **1** (Chart I) many similar antibiotics have been discovered and synthesized.[1] One crucial step in the synthesis of carbapenems is the final deprotection step of the C-3 ester function because *tert*-butyl, benzyl, and benzhydryl esters, which have been used as efficient protective groups in cephalosporin synthesis, have been found to be unsuitable in the synthesis of carbapenems which are very unstable to acid conditions.

Two representative methods in this area have been the deprotection of the *p*-nitrobenzyl (PNB) ester group by catalytic reduction[2] and the cleavage of the allyl ester group by the action of palladium(0).[3,4] However, these procedures have been used restrictively because the PNB ester group is sensitive to reduction and base-mediated transformations and the allyl ester group is sensitive to reduction and oxidation. Accordingly, a new deprotection method was needed for the carbapenem synthesis.

Here we describe the mild deprotection of benzhydryl (Bh) and *p*-methoxybenzyl (PMB) esters using aluminum trichloride in anisole.[5] PMB esters were expected to regenerate the carboxylic acid under milder conditions because of electronic factors. Although the reaction conditions appear to be drastic, the reaction can be carried out under completely nonacidic conditions, as illustrated by the effective synthesis of 1-oxacephems, which are believed to be more fragile than cephalosporins.

Chart I



1

First, we examined the deprotection of Bh esters of (±)-PS-5 **2a** and its analogue **2b** (Table I). Deprotection with aluminum trichloride in anisole diluted with cosolvent at −50 °C was carried out in a few minutes and the reaction mixture was quenched with aqueous sodium bicarbonate solution with cooling at −50 °C. After the temperature had been raised to 0 °C, passing the aqueous phase through an HP-20 (registered name) column gave the desired products **3a,b** in good yields. As expected, deprotection of the PMB ester of (±)-NS-5 **2c** proceeded smoothly and gave the zwitterionic product, i.e., (±)-NS-5 **3c** in 53.6% yield. In the same manner, several carbapenems containing optically active compounds **3g-l** were obtained in satisfactory yields.

The present mild deprotection with aluminum trichloride in anisole makes it possible to employ Bh and PMB esters as protecting groups in carbapenem chemistry. Moreover, it is an inexpensive and safe method for large-scale experiments.

Details of the chemical transformations leading to the substrates[7] for deprotection and the biological results of carbapenems will be published elsewhere.

Experimental Section

General Methods. All reactions were carried out under anhydrous conditions in a nitrogen atmosphere with anhydrous solvents dried over 4-Å molecular sieves. Melting points were determined on a Yanagimoto apparatus and were not corrected. Infrared (IR) spectra were recorded on a Hitachi 215 spectrometer. Proton nuclear magnetic resonance (^{1}H NMR) spectra were measured on a Varian T60-A or EM-390 spectrometer with tetramethylsilane or sodium 2,2-dimethyl-2-silapentane-5-sulfonate (in D_2O) as an internal reference. Ultraviolet (UV) spectra were recorded on a Hitachi 323 spectrometer. For column chromatography, silica gel (Merck silica gel 60) or Merck's Lobar column was used.

Sodium Salt of (±)-PS-5 3a (General Procedure for Compounds 3b-l). A stirred solution of **2a** (46.4 mg, 0.1 mmol) in

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(2) (a) See ref 1. (b) Johnston, D. B. R.; Schmitt, S. M.; Bouffard, F. A.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 313.

(3) McCombie, S. W.; Ganguly, A. K.; Girijavallabhan, V. M.; Jefferey, P. D.; Lin, S.; Pinto, P. *Tetrahedron Lett.* **1981**, *22*, 3489.

(4) The other protecting groups are utilized. (a) Photolysis of *o*-nitrobenzyl esters; Cama, L. D.; Christensen, B. G. *J. Am. Chem. Soc.* **1978**, *100*, 8006. (b) Electrochemical cleavage of *p*-(methoxycarbonyl)-benzyl esters: Corbett, D. F.; Eglington, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1083. (c) Ferres, H. *Med. Actual.* **1983**, *19*, (9) 499.

(5) Tsuji, T.; Kataoka, T.; Yoshioka, M.; Sendo, Y.; Nishitani, Y.; Hirai, S.; Maeda, T.; Nagata, W. *Tetrahedron Lett.* **1979**, 2793.

(6) The stereochemistry at the C-8 position of compounds **2i-l** was confirmed by inspection of their ^{1}H NMR spectra and comparison with those reported: (a) Bouffard, F. A.; Johnston, D. B. R.; Christensen, B. G. *J. Org. Chem.* **1980**, *45*, 1130. (b) Bouffard. F. A.; Christensen, B. G. *J. Org. Chem.* **1981**, *46*, 2208. (c) Crugnola, A.; Longo, A.; Casabuona, F.; Lombardi, P. *Tetrahedron Lett.* **1982**, *23*, 2777. (d) Martel, A.; Collerette, J.; Banville, J.; Daris, J.-P.; Lapointe, P.; Belleau, B.; Ménard, M. *Can. J. Chem.* **1983**, *61*, 613. (e) Corbett, D. F.; Coulton, S.; Southgate, R. *J. Chem. Soc., Perkin Trans. 1* **1982**, 3011.

(7) Substrates **2e,f** and **2i-l** are new compounds. All were prepared by application of the methods described in the following literature: (a) Kametani, T.; Honda, T.; Nakayama, A.; Sasakai, Y.; Mochizuki, T.; Fukumoto, K. *J. Chem. Soc., Perkins Trans. 1* **1981**, 2228. (b) Karady, S.; Amato, J. S.; Reamer, R. A.; Weinstock, L. M. *J. Am. Chem. Soc.* **1981**, *103*, 6765. (c) Salzmann, T. N.; Ratcliffe, R. W.; Christensen, B. G.; Bouffard, F. A. *J. Am. Chem. Soc.* **1980**, *102*, 6161. (d) Ikota, N.; Shibata, H.; Koga, K.; *Heterocycles* **1980**, *14*, (8), 1077. (e) Brooks, D. W.; Lu, L. D.-L.; Masamune, S. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 72. (f) Ratcliffe, R. W.; Salzmann, T. N.; Christensen, B. G. *Tetrahedron Lett.* **1980**, *21*, 31. (g) Sletzinger, M.; Liu, T.; Reamer, R. A.; Shinkai, I. *Tetrahedron Lett.* **1980**, *21*, 4221. (h) Reider, P. J.; Grabowski, E. J. J. *Tetrahedron Lett.* **1982**, *23*, 2293. (i) Shinkai, I.; Liu, T.; Reamer, R. A.; Sletzinger, M. *Tetrahedron Lett.* **1982**, *23*, 4899.

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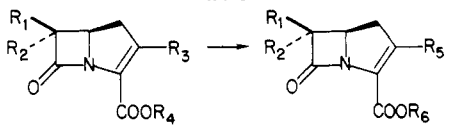
Table I



	substrate					product				
	R_1	R_2	R_3	R_4		R_1	R_2	R_5	R_6	yield, %
2a	H	Et	SCH_2CH_2NHAc	Bh	**3a**	H	Et	SCH_2CH_2NHAc	Na	56.3
2b	Me	Me	SCH_2CH_2NHAc	Bh	**3b**	Me	Me	SCH_2CH_2NHAc	Na	56.3
2c	H	Et	$SCH_2CH_2NHCO_2PMB$	PMB	**3c**	H	Et	$SCH_2CH_2NH_2$	H	53.6
2d	Et	H	$SCH_2CH_2NHCO_2PMB$	PMB	**3d**	Et	H	$SCH_2CH_2NH_2$	H	54.0
2e	H	Et	CH_2CO_2Et	PMB	**3e**	H	Et	CH_2CO_2Et	Na	64.0
2f	H	Et	CH_2CO_2Bh	PMB	**3f**	H	Et	CH_2CO_2Na	Na	82.0
2g	H	$Me_2C(OH)$	SCH_2CH_2NHAc	PMB	**3g**	H	$Me_2C(OH)$	SCH_2CH_2NHAc	Na	47.6
2h	H	$Me_2C(OH)$	$SCH_2CH_2NHCO_2PMB$	PMB	**3h**	H	$Me_2C(OH)$	$SCH_2CH_2NH_2$	H	56.7
2i	H	$MeOCH_2CH(OH)$[a]	SCH_2CH_2NHAc	PMB	**3i**	H	$MeOCH_2CH(OH)$[a]	SCH_2CH_2NHAc	Na	60.0
2j	H	$MeOCH_2CH(OH)$[a]	$SCH_2CH_2NHCO_2PMB$	PMB	**3j**	H	$MeOCH_2CH(OH)$[a]	$SCH_2CH_2NH_2$	H	36.9
2k	H	$MeOCH_2CO(OH)$[b]	SCH_2CH_2NHAc	PMB	**3k**	H	$MeOCH_2CH(OH)$[b]	SCH_2CH_2NHAc	Na	29.0
2l	H	$MeOCH_2CH(OH)$[b]	$SCH_2CH_2NHCO_2PMB$	PMB	**3l**	H	$MeOCH_2CH(OH)$[b]	$SCH_2CH_2NH_2$	H	24.0

[a] 8*S* isomer. [b] 8*R* isomer: see ref 6.

a mixture of anisole (0.8 mL) and CH_2Cl_2 (0.2 mL) was cooled to −50 °C and treated with aluminum trichloride (33.3 mg, 0.25 mmol). The reaction mixture was stirred for 30 min at −50 °C, quenched with aqueous 5% sodium bicarbonate solution (3 mL) at the same temperature, and partitioned between ethyl acetate and water. The resulting inorganic precipitates were removed by filtration and the filtrate was separated. The aqueous phase was passed through an HP-20 (30 mL) column, with elution with deionized water followed by freeze–drying, and gave 18.0 mg (56.3%) of **3a** as a pale yellow powder: mp 135–142 °C dec; identical in all respects (UV, IR, ^1H NMR, HPLC) except for biological activity (half of (+)-PS-5) with natural PS-5.

Compound **3b** (56.3%): pale yellow powder; mp 150 °C dec; IR (KBr) 1753, 1655, 1596, 1553; UV λ_{max} (H_2O) 300 nm (ϵ 8600). Anal. Calcd for $C_{13}H_{17}N_2O_4SNa\cdot H_2O$: C, 46.14; H, 5.67; N, 8.28. Found: C, 46.31; H, 6.00; N, 8.07. Compound **3c** (53.6%): mp 140 °C dec; IR (KBr) 1766, 1570 cm^{-1}; UV λ_{max} (H_2O) 297 nm (ϵ 6800). Anal. Calcd for $C_{11}H_{16}N_2O_3S\cdot 0.7H_2O$: C, 49.12; H, 6.53; N, 10.42. Found: C, 49.01; H, 6.43; N, 10.18. **3d** (54.0%): mp 140 °C dec; IR (KBr) 1773, 1595 cm^{-1}; UV λ_{max} (H_2O) 294 nm (ϵ 6800). Anal. Calcd for $C_{11}H_{16}N_2O_3S$: C, 51.53; H, 6.30; N, 10.93. Found: C, 51.11; H, 6.08; N, 10.92. **3e** (64.0%): mp 120 °C dec; IR (KBr) 1760, 1737, 1605 cm^{-1}; ^1H NMR (D_2O) δ 0.93 (s, 3 H), 1.20 (t, J = 7 Hz, 3 H), 1.73 (m, 2 H), 2.60–3.10 (m, 3 H), 3.60–4.26 (m, 3 H), 4.13 (q, J = 7 Hz, 2 H); UV λ_{max} (H_2O) 273 nm (ϵ 3200). **3f** (82.0%): mp 200 °C dec; IR (KBr) 1753, 1587 cm^{-1}; UV λ_{max} 270 nm (ϵ 2700). 6-Epicarpetimycin derivative **3g** (47.6%): colorless powder; IR (KBr) 3400, 1750, 1640, 1586, 1552, 1394 cm^{-1}; UV λ_{max} (H_2O) 302 nm (ϵ 8800); ^1H NMR (D_2O–Me_4Si as an external reference) δ 1.76 (s, 3 H), 1.81 (s, 3 H), 2.44 (s, 3 H), 3.30–3.90 (m, 6 H), 3.87 (d, J = 2.7 Hz, 1 H), 4.64 (td, J = 9, 2.7 Hz, 1 H). Anal. Calcd for $C_{14}H_{19}N_2O_5SNa\cdot 1.4H_2O$: C, 44.77; H, 5.85; N, 7.46. Found: C, 44.81; H, 5.64; N, 7.79. Compound **3h** (56.7%): pale yellow powder; IR (KBr) 3385, 1755, 1580, 1387 cm^{-1}; UV λ_{max} (H_2O) 298 nm (ϵ 6800); ^1H NMR [D_2O–Me_4Si (external)] δ 1.76 (s, 3 H), 1.81 (s, 3 H), 3.20–3.80 (m, 6 H), 3.91 (d, J = 2.8 Hz, 1 H), 4.67 (td, J = 9, 2.8 Hz, 1 H). Anal. Calcd for $C_{12}H_{18}N_2O_4S\cdot 1.5H_2O$: C, 45.99; H, 6.75; N, 8.94. Found: C, 46.13; H, 6.51; N, 8.85.

9-Methoxythienamycin derivative **3i** (60%): pale yellow powder; IR (KBr) 1750, 1655, 1590 cm^{-1}; UV λ_{max} (H_2O) 301 nm (ϵ 4800); ^1H NMR (D_2O) δ 1.98 (s, 3 H), 2.88, 2.98 (AB qd, J = 14, 7 Hz, 2 H), 3.10, 3.24 (AB qd, J = 17, 10, 8 Hz, 2 H), 3.39 (s, 3 H), 3.30–3.64 (m, 5 H), 4.10–4.32 (m, 2 H). Compound **3j** (36%): pale yellow powder; IR (Nujol) 1753, 1575 cm^{-1}; UV λ_{max} (H_2O) 299 nm (ϵ 6100); ^1H NMR (D_2O) δ 2.90–3.32 (m, 6 H), 3.40 (s, 3 H), 3.52, 3.60 (AB qd, J = 10, 6, 4, Hz, 2 H), 3.54 (m, 1 H), 4.16–4.34 (m, 2 H). Compound **3k** (29%): pale yellow powder, mp 130 °C dec; IR (KBr) 1755, 1660, 1610 cm^{-1}; UV λ_{max} (H_2O) 301 nm (ϵ 3900); ^1H NMR (D_2O) δ 1.98 (s, 3 H), 2.88, 2.97, (AB qd, J = 14, 8, 6 Hz, 2 H), 3.11, 3.25 (AB qd, J = 17, 9 Hz, 2 H), 3.30–3.70 (m, 5 H), 3.40 (s, 3 H), 4.10–4.32 (m, 2 H). Compound **3l** (24%): pale yellow powder; IR (KBr) 1755, 1583 cm^{-1}; UV λ_{max} (H_2O) 299 nm (ϵ 4600); ^1H NMR (D_2O) δ 2.86–3.65 (m, 9 H), 3.40 (s, 3 H), 4.10–4.30 (m, 2 H).

Registry No. (±)-**2a**, 93451-21-9; (±)-**2b**, 93349-51-0; (±)-**2c**, 93349-52-1; (±)-**2d**, 93349-53-2; (±)-**2e**, 93451-22-0; (±)-**2f**, 93349-54-3; **2g**, 93349-55-4; **2h**, 93349-56-5; **2i**, 93349-57-6; **2j**, 93349-58-7; **2k**, 93451-23-1; **2l**, 93451-24-2; (±)-**3a**, 77058-07-2; (±)-**3b**, 93451-25-3; (±)-**3c**, 93451-26-4; (±)-**3d**, 93451-27-5; (±)-**3e**, 93451-28-6; (±)-**3f**, 93451-29-7; **3g**, 82744-14-7; **3h**, 92936-51-1; **3i**, 93349-59-8; **3j**, 93349-60-1; **3b**, 93451-30-0; **3e**, 93451-31-1; $AlCl_3$, 7446-70-0.

Vicarious Substitution of Hydrogen with Carbanions of Dithioacetals of Aldehydes[1]

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In previous papers[2,3] we have shown that carbanions having leaving groups X at the carbanion centers react with aromatic nitro compounds, replacing the hydrogen ortho or para to the nitro group with the carbanion moiety. The reaction, termed vicarious nucleophilic substitution of hydrogen (VNS), proceeds via the formation of σ complexes followed by base-induced β-elimination of HX.[4]

We have shown that PhS, MeS, and $Me_2NC(S)S$ substituents are efficient leaving groups in the reaction; thus nitriles and esters containing these substituents in the α-position are suitable starting materials for this process.[3] These substituents not only are good leaving groups but also stabilize carbanions efficiently. $(PhS)_3CH$ has been recently shown to react with some nitroarenes in the presence of base to form dithioacetals of *p*-nitrobenzaldehyde derivatives.[5]

The valuable properties of PhS or other similar groups—namely, stabilization of carbanions, ability to depart in the β-elimination process, and resistance toward direct nucleophilic substitution (S_N2) can also be exploited for direct introduction of α-(RS)alkyl substituents into nitroaromatic rings via VNS with dithioacetals of aldehydes. These possibilities might not have been anticipated

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