of the product were identical to that of authentic 4-*tert*-butylcyclohexanone (mp 47–50 °C). Similarly, 9-fluorenone, cyclododecanone, and camphor were isolated and confirmed.

Acknowledgment. We thank the University of Kentucky for ^{13}C NMR analyses. This research was supported by a grant from the National Science Foundation (CHE-8700848).

Registry No. 1, 85282-84-4; cyclopentanol, 96-41-3; cyclohexanol, 108-93-0; 2-pentanol, 6032-29-7; 4-methyl-2-pentanol, 108-11-2; 2-octanol, 123-96-6; 3-pentanol, 584-02-1; 2,4-dimethyl-3-pentanol, 600-36-2; 2-*tert*-butylcyclohexanol, 13491-79-7; 4-*tert*-butylcyclohexanol, 98-52-2; menthol, 89-78-1; borneol, 507-70-0; cyclododecanol, 1724-39-6; *sec*-phenethyl alcohol, 98-85-1; 9-fluorenol, 1689-64-1; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; 2-pentanone, 107-87-9; 4-methyl-2-pentanone, 108-10-1; 2-octanone, 111-13-7; 3-pentanone, 96-22-0; 2,4-dimethyl-3-pentanone, 565-80-0; 2-*tert*-butylcyclohexanone, 1728-46-7; 4-*tert*-butylcyclohexanone, 98-53-3; menthone, 89-80-5; camphor, 76-22-2; cyclododecanone, 830-13-7; acetophenone, 98-86-2; 9-fluorenone, 486-25-9; pyridinium trifluoroacetate, 464-05-1; pyridinium 3-nitrobenzenesulfonate, 84752-61-4; pyridinium *p*-toluenesulfonate, 24057-28-1; pyridinium chloride, 628-13-7.

Synthesis of 2-Amino Acids via Selective Mono-N-alkylation of Trichloroacetamide by 2-Bromo Carboxylic Esters under Solid–Liquid Phase-Transfer Catalysis Conditions

Domenico Albanese, Dario Landini,* and Michele Penso*

Centro CNR and Dipartimento di Chimica Organica e Industriale dell'Università, via Golgi 19, I-20133 Milano, Italy

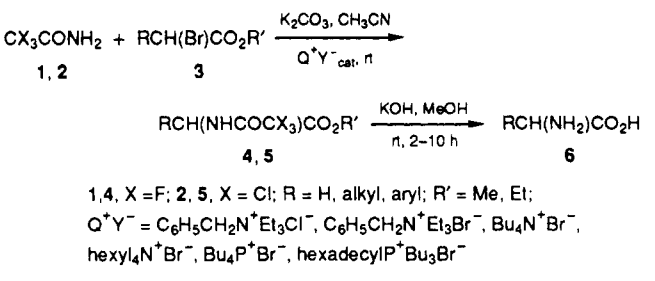
Received May 2, 1991 (Revised Manuscript Received November 12, 1991)

In a previous paper[1] we described a new procedure for the synthesis of 2-amino acids **6** via N-alkylation of trifluoroacetamide (**1**) with 2-bromo carboxylic esters **3** under solid–liquid phase-transfer catalysis (SL-PTC) conditions, followed by hydrolysis of the intermediate *N*-(trifluoroacetyl)-2-amino esters **4** (Scheme I). The use of an excess of trifluoroacetamide (**1**), which cannot be recovered at the end of the reaction, and its relatively high cost are severe limitations to the scale up of this process. Here we report that these drawbacks can be overcome by using the cheaper trichloroacetamide (**2**) instead of **1**. In fact **2** is selectively mono-N-alkylated by alkyl 2-bromo carboxylic esters **3** under SL-PTC conditions in the presence of anhydrous K_2CO_3, giving the corresponding *N*-(trichloroacetyl)-2-amino carboxylic esters **5**. Like trifluoro derivatives **4**, trichloroacetamides **5** are easily and quantitatively converted to 2-amino acids **6**.[2] Moreover the excess of **2** used in the process can be recovered from the reaction mixture and reused.

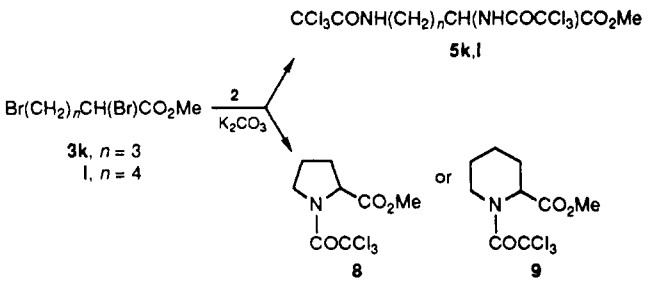
Results and Discussion

The alkylation reaction (Scheme I) was easily accomplished by stirring, at room temperature, an acetonitrile solution of trichloroacetamide (**2**) (3–4 mol), 2-bromo carboxylic ester **3** (1 mol), and a PTC catalyst (0.1 mol) over solid anhydrous potassium carbonate (4 mol). *N*-(trichloroacetyl)-2-amino carboxylic esters **5** were isolated in 51–95% yield and hydrolyzed in nearly quantitative yield to amino acids **6** with methanolic–aqueous potassium hydroxide at room temperature (see Table I).[2]

Scheme I



Scheme II



The best yields of **5** were obtained using 3–4 mol of **2** per mole of **3** and by working at room temperature under anhydrous conditions. Attempts to reduce reaction times for the less reactive bromo esters **3b–f,j–m** by working at higher temperature failed, because of the side decomposition of trichloroacetamide (**2**) (e.g. in the case of ester **3b**, at 80 °C 100% conversion was reached after 5 h, but **5b** was isolated in 54% yield, only). Benzyltriethylammonium chloride (TEBA) was again[1] the most efficient PTC agent. In the absence of the catalyst the reaction was much slower and the yields of **5** were poorer.

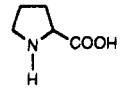
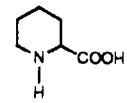
As shown in the table, the process works quite well using ethyl 2-bromoacetate (**3a**) and its higher homologues (**3b–e**) as alkylating agents; using 2-chloro derivatives resulted in unsatisfactory yields of **5**. Ethyl 2-bromo-2-phenylacetate (**3i**) afforded only traces of the corresponding trichloroacetamido ester **5i** together with a mixture of byproducts.

As found for **1**,[1] elimination reactions were observed only in the case of ethyl 2-bromo-3-phenylpropanoate (**3j**), the ethyl *trans*-cinnamate (**7**) (31%) being obtained together with comparable amounts (24%) of ethyl *N*-(trichloroacetyl)-2-amino-3-phenylpropanoate (**5j**). Steric requirements probably account for the very long reaction time (18 days) and poor yield (51%) found in the reaction of methyl 2-bromo-4-methylpentanoate (**3f**). Accordingly, ethyl 2-bromo-2-methylpropanoate (**3h**) and ethyl 2-bromo-3-methylbutanoate (**3g**) were recovered unchanged after the same reaction time. The methyl esters of 2,5-dibromopentanoic acid (**3k**) and 2,6-dibromohexanoic acid (**3l**) reacted with **2**, affording after 24 h 75% of methyl *N*-(trichloroacetyl)-2-pyrrolidinecarboxylate (**8**) and 60% of methyl *N*-(trichloroacetyl)-2-piperidinecarboxylate (**9**), respectively, together with small amounts of the *N,N'*-bis(trichloroacetyl)-α,ω-diamino carboxylic esters **5k** and **5l** (Scheme II).[3] In the case of methyl 5-bromopentanoate (**3m**), the same conditions led to 75% conversion after 20

(1) Landini, D.; Penso, M. *J. Org. Chem.* **1991**, *56*, 420.
(2) Greene, T. W. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1981; pp 254–255 and references therein.
(3) The same results were previously found for the reaction of **3l** with **1**[1] or 2,6-dihalohexanoic acids with ammonia.[4]
(4) (a) Effenberger, F.; Dranz, K. *Angew. Chem., Int. Ed. Engl.* **1979**, *12*, 474. (b) Effenberger, F.; Dranz, K.; Foster, S.; Muller, W. *Chem. Ber.* **1981**, *114*, 173.

0022-3263/92/1957-1603$03.00/0

Table I. *N*-(Trichloroacetyl)-2-amino Carboxylic Esters 5a–f,j,m, 8, 9 Prepared[a] and the Corresponding Amino Acids 6a–f,j,m, 10, 11 from Hydrolysis[b]

	3, 5		*N*-(trichloroacetyl)-2-amino esters 5, 8, 9			
	R	R′	time, h	yield, %[c]	amino acids 6, 10, 11	yield, %[c]
a	H	Et	15	59[d]	NH_2CH_2COOH	95[e]
b	Me	Et	40	79[f]	$CH_3CH(NH_2)COOH$	100[e]
c	Et	Et	72	95	$CH_3CH_2CH(NH_2)COOH$	95[e]
d	n-C_6H_{13}	Et	48	86	$CH_3(CH_2)_5CH(NH_2)COOH$	92
e	n-$C_{14}H_{29}$	Me	160	62[g]	$CH_3(CH_2)_{13}CH(NH_2)COOH$	90
f	Me_2CHCH_2	Me	18d	51	$Me_2CHCH_2CH(NH_2)COOH$	90[e]
g	Me_2CH	Et	18d[h]	–	–	–
h	–	–[i]	18d[h]	–	–	–
i	Ph	Et	12	–[j]	–	–
j	$PhCH_2$	Et	40	24[k]	$PhCH_2CH(NH_2)COOH$	100[e]
k	$Br(CH_2)_3$	Me	24	75[l]	 (10)	100
l	$Br(CH_2)_4$	Me	24	60[m]	 (11)	97[e]
m	–	–[n]	20d	68[o]	$NH_2CH_2(CH_2)_2CH_2COOH$	100[e]

[a] 3 (10 mmol), TEBA (1 mmol), 2 (40 mmol), K_2CO_3 (40 mmol) in CH_3CN (20 mL), at rt. [b] 5, 8, 9 (5 mmol) in MeOH (2.5 mL) and 20% aqueous KOH (2.4 mL) at rt overnight. [c] Isolated yields. [d] When the reaction was conducted at 80 °C, 75% of 5a was isolated after 1 h. [e] Isolated as hydrochloride. [f] At 80 °C, after 5 h, 5b was isolated in 54% yield. [g] The conversion of 3e was not complete. [h] Starting material was recovered unchanged. [i] $Me_2C(Br)COOEt$ (3h). [j] GLC and ^1H NMR analyses of the crude reaction mixture showed the presence of traces of the expected *N*-(trichloroacetyl)-2-amino ester 5i, together with unidentified byproducts. [k] Ethyl cinnamate (7) (31%), was isolated. [l] Product 8. [m] Product 9. [n] $Br(CH_2)_4COOMe$ (3m). [o] Partial conversion of the substrate (75%).

days, and methyl *N*-(trichloroacetyl)-5-aminopentanoate (5m) was isolated in 68% yield. Moreover no detectable amounts of dialkylated products were isolated in the reactions of 3a–f,j,m.[5] These results show that bis-N-alkylation became the preferred process only in the case of substrates which can give intramolecular cyclization, such as 3k,l.

On the reasonable assumption that under SL-PTC conditions common steps are involved in the alkylation of both trifluoroacetamide (1) and trichloroacetamide (2) by 2-bromo carboxylic esters 3, the mechanistic rationale should be the same as that already discussed in the former case.[1]

Experimental Section

Starting 2-bromo carboxylic esters 3a–c,m are commercially available, whereas 3d,e,g–k were prepared by standard procedures from the corresponding carboxylic acids and are known compounds. The syntheses of the new compounds 3f,l are described below. Commercial trichloroacetamide (2) was recrystallized from $CHCl_3$, mp 143 °C. Analar grade CH_3CN was dried over 0.3-nm molecular sieves and used as such. K_2CO_3 was carefully dried by heating at 140 °C under vacuum (0.05 mm) for 6 h. ^1H NMR spectra were recorded at 80 MHz in $CDCl_3$ using TMS as internal standard. Melting points are uncorrected. GLC analyses were obtained with an Alltech RSL-150 column (10 m × 0.35 mm, polydimethylsiloxane, 0.25-μm thickness) or Superox II column (10 m × 0.35 mm, poly(ethylene)glycol), 0.25-μm thickness). Amberlite IRA-93 was used to prepare the amino acids 6b,f,j from the corresponding hydrochlorides.

Methyl 2,6-Dibromohexanoate (3l). To a mixture of ε-caprolactone (11.08 mL, 0.1 mol) and PBr_3 (0.05 mL) heated at 100 °C was added Br_2 (5.41 mL, 0.105 mol) dropwise, keeping the reaction temperature at 120 °C by the rate of bromine addition. The heating was continued until hydrogen bromide evolution ceased. Then the crude was cooled with an ice bath, diluted with anhydrous MeOH (100 mL), saturated with hydrogen chloride, and stirred at rt for 20 h. After this time the solvent was distilled, and the residue was extracted with Et_2O. The ether layer was dried over $MgSO_4$ and stripped, and the crude was distilled under reduced pressure. 3l: 24.19 g, 84%; bp 120–127 °C (20 Torr); n^{20}_D 1.5011; IR (neat) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.35–2.40 (m, 6 H), 3.40 (t, 2 H, J = 8 Hz), 3.80 (s, 3 H), 4.23 (t, 1 H, J = 6 Hz). Anal. Calcd for $C_7H_{12}Br_2O_2$: C, 29.19; H, 4.21. Found: C, 29.48; H, 4.36.

Methyl 2-Bromo-4-methylpentanoate (3f). To 4-methylpentanoic acid (5.81 g, 50 mmol) was added $SOCl_2$ (4 mL, 55 mmol) dropwise, keeping the reaction temperature below 30 °C by cooling. After the addition the temperature was slowly increased to 80 °C, the mixture was refluxed for 1 h, and Br_2 (2.7 mL, 52.5 mmol) was added dropwise. The heating was continued for 12 h, and then the reaction mixture was cooled to rt, diluted with anhydrous MeOH (10 mL), and stirred overnight. After evaporation of the solvent, water (10 mL) was added. The organic layer was washed with 10% aqueous $NaHSO_3$ and water, dried over $MgSO_4$, and distilled under reduced pressure. 3f: 8.16 g, 78%; bp 100–110 °C (40 Torr); n^{22}_D 1.4559; IR (neat) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75–1.20 (m, 6 H), 1.65–2.10 (m, 3 H), 3.85 (s, 3 H), 4.20 (t, 1 H, J = 12 Hz). Anal. Calcd for $C_7H_{13}BrO_2$: C, 40.20; H, 6.28. Found: C, 39.98; H, 6.28.

General Method for the Alkylation of CCl_3CONH_2 (2) with Bromo Carboxylic Esters 3. Solid anhydrous K_2CO_3 (5.53 g, 40 mmol) was added to a solution of CCl_3CONH_2 (2) (6.50 g, 40 mmol), TEBA (0.23 g, 1 mmol), and the bromo ester 3 (10 mmol) in CH_3CN (20 mL). The mixture was stirred at rt until no starting ester 3 was detectable (TLC and/or GLC analysis), and then the crude product was filtered on Celite, stripped, diluted with $CHCl_3$ (10 mL), and left to stand at –20 °C overnight. Most of unreacted 2 (>80%) crystallized and was filtered off. The residual was stripped and purified by flash chromatography. Starting material, reaction time, chromatographic eluant, yield, and physical and spectroscopic data of reaction products are as follows.

Ethyl *N*-(trichloroacetyl)-2-aminoacetate (5a): ethyl 2-bromoacetate (3a); 15 h; petroleum ether and Et_2O (1.5:1). 5a: 1.47 g, 59%; mp 28–30 °C; IR (neat) 3350, 1750, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, 3 H, J = 6 Hz), 4.10–4.45 (m, 4 H), 7.55 (br s, 1 H). Anal. Calcd for $C_6H_8Cl_3NO_3$: C, 29.00; H, 3.25; N, 5.64. Found: C, 29.32; H, 3.17; N, 5.73.

Ethyl *N*-(trichloroacetyl)-2-aminopropanoate (5b): ethyl 2-bromopropanoate (3b): 40 h; petroleum ether and Et_2O (4:1). 5b: 2.08 g, 79%; mp 41 °C; IR (neat) 3480, 1735, 1705 cm^{-1}; ^1H

(5) Similar results were previously reported for the alkylation of 1.[1,6,7]
(6) Harland, P. A.; Hodge, P.; Maughan, W.; Wildsmith, E. *Synthesis* 1984, 941.
(7) Landini, D.; Penso, M. *Synth. Commun.* 1988, *18*, 791.

NMR ($CDCl_3$) δ 1.20–1.65 (m, 6 H), 4.20–4.65 (m, 3 H), 7.33 (br s, 1 H). Anal. Calcd for $C_7H_{10}Cl_3NO_3$: C, 32.02; H, 3.85; N, 5.34. Found: C, 32.02; H, 3.88; N, 5.43.

Ethyl *N*-(trichloroacetyl)-2-aminobutanoate (5c): ethyl 2-bromobutanoate (**3c**); 72 h, petroleum ether and Et_2O (2:1). **5c**: 2.63 g, 95%; mp 45–47 °C; IR (Nujol) 3300, 1740, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85–1.50 (m, 6 H), 1.65–2.25 (m, 2 H), 4.10–4.70 (m, 3 H), 7.30 (br s, 1 H). Anal. Calcd for $C_8H_{12}Cl_3NO_3$: C, 34.74; H, 4.38; N, 5.07. Found: C, 34.79; H, 4.30; N, 5.03.

Ethyl *N*-(trichloroacetyl)-2-aminooctanoate (5d): ethyl 2-bromooctanoate (**3d**); 48 h; petroleum ether and Et_2O (12:1). **5d**: 2.86 g, 86%; n^{20}_D 1.4700; IR (neat) 3350, 1740, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.63–1.60 (m, 14 H), 1.70–2.20 (m, 2 H), 4.10–4.75 (m, 3 H), 7.25 (br s, 1 H). Anal. Calcd for $C_{14}H_{20}Cl_3NO_3$: C, 43.32; H, 6.07; N, 4.21. Found: C, 43.46; H, 6.18; N, 4.23.

Methyl *N*-(trichloroacetyl)-2-aminohexadecanoate (5e): methyl 2-bromohexadecanoate (**3e**); 160 h; petroleum ether and CH_2Cl_2 (4:1). **5e**: 2.67 g, 62%; mp 39 °C; IR (nujol) 3320, 1760, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.50–1.60 (m, 27 H), 1.65–2.25 (m, 2 H), 3.85 (s, 3 H), 4.30–4.60 (m, 1 H), 7.15 (br s, 1 H). Anal. Calcd for $C_{19}H_{34}Cl_3NO_3$: C, 52.96; H, 7.97; N, 3.25. Found: C, 52.88; H, 7.87; N, 3.25.

Methyl *N*-(trichloroacetyl)-2-amino-4-methylpentanoate (5f): methyl 2-bromo-4-methylpentanoate (**3f**); 18 d; petroleum ether and Et_2O (3:1). **5f**: 1.48 g, 51%; mp 64–65 °C; IR (Nujol) 3275, 1755, 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85–1.25 (m, 7 H), 1.60–2.00 (m, 2 H), 3.85 (s, 3 H), 4.40–4.85 (m, 1 H), 7.15 (br s, 1 H). Anal. Calcd for $C_9H_{13}Cl_3NO_3$: C, 37.20; H, 4.87; N, 4.82. Found: C, 36.98; H, 4.94; N, 4.88.

Ethyl *N*-(trichloroacetyl)-2-amino-3-phenylpropanoate (5j): ethyl 2-bromo-3-phenylpropanoate (**3j**); 40 h; petroleum ether and Et_2O (5:1). **5j**: 0.81 g, 24%; mp 61 °C; IR (Nujol) 3320, 1760, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (t, 3 H, J = 9 Hz), 3.20 (d, 2 H, J = 16 Hz), 4.20 (q, 2 H, J = 11 Hz), 4.60–4.95 (m, 1 H), 7.18 (m, 6 H). Anal. Calcd for $C_{13}H_{14}Cl_3NO_3$: C, 46.11; H, 4.18; N, 4.14. Found: C, 46.40; H, 4.24; N, 4.10. *trans*-Ethyl cinnamate (**7**): 0.55 g, 31%.

Methyl 1-(trichloroacetyl)-2-pyrrolidinecarboxylate (8): methyl 2,5-dibromopentanoate (**3k**); 24 h; petroleum ether and Et_2O (1:1). **8**: 2.06 g, 75%; n^{20}_D 1.5115; IR (neat) 1745, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.90–2.50 (m, 4 H), 3.80 (s, 3 H), 3.90–4.25 (m, 2 H), 4.40–4.65 (m, 1 H). Anal. Calcd for $C_8H_{10}Cl_3NO_3$: C, 35.00; H, 3.68; N, 5.10. Found: C, 35.02; H, 3.60; N, 5.07.

Methyl 1-(trichloroacetyl)-2-piperidinecarboxylate (9): methyl 1,6-dibromohexanoate (**3l**); 24 h; petroleum ether and Et_2O (2:1). **9**: 1.70 g, 59%; n^{20}_D 1.5120; IR (neat) 1740, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85–2.10 (m, 4 H), 2.20–2.50 (m, 3 H), 3.85 (s, 3 H), 4.35–4.65 (m, 2 H), 5.10–5.40 (m, 1 H). Anal. Calcd for $C_9H_{12}Cl_3NO_3$: C, 37.46; H, 4.20; N, 4.85. Found: C, 37.38; H, 4.22; N, 4.88.

Methyl *N*-(trichloroacetyl)-5-aminopentanoate (5m): methyl 5-bromopentanoate (**3m**); 20 d; petroleum ether and Et_2O (3:1). **5m**: 1.88 g, 68%; mp 23–25 °C; IR (neat) 3320, 1740, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50–1.90 (m, 4 H), 2.25–2.50 (m, 3 H), 3.25–3.55 (m, 2 H), 4.75 (s, 3 H), 7.05 (br s, 1 H). Anal. Calcd for $C_8H_{12}Cl_3NO_3$: C, 34.74; H, 4.38; N, 5.07. Found: C, 34.66; H, 4.30; N, 5.12.

General Method for the Hydrolysis of *N*-(Trichloroacetyl)-2-amino Carboxylic Esters 5. Preparation of the Corresponding Amino Acids 6. A mixture of **5a–f,j,m** and **8,9** (5 mmol), aqueous 20% KOH (2.4 mL, 10 mmol), and MeOH (8.5 mL) was stirred overnight at rt. After the previously described workup,[1] amino acids **6d,e** and **10** were isolated as such, while products **6a–c,f,j,m** and **11** were obtained as hydrochlorides (Table I). Yields and physical data of the products of hydrolysis are reported.

Glycine hydrochloride (6a): 0.53 g, 95%; mp 180 °C dec (lit.[8] mp 185 °C dec).

Alanine hydrochloride (6b): 0.63 g, 100%. Free alanine **6b** was obtained from the hydrochloride via exchange with a basic polymeric resin and had mp 290 °C (lit.[8] mp 295 °C).

2-Aminobutanoic acid hydrochloride (6c): 0.66 g, 95%; mp 177 °C (lit.[8] mp 179–180 °C).

2-Aminooctanoic acid (6d): 0.73 g, 92%; mp 264 °C (lit.[8] mp 270 °C).

2-Aminohexadecanoic acid (6e): 1.22 g, 90%; mp 85 °C (lit.[8] mp 86–87 °C).

2-Amino-4-methylpentanoic acid hydrochloride (6f): 0.75 g, 90%. Free **6f**, obtained in the usual manner, had mp 288 °C (lit.[8] mp 293–295 °C).

2-Amino-3-phenylpropanoic acid hydrochloride (6j): 1.01 g, 100%. Free **6j** had mp 280 °C (lit.[8] mp 284–288 °C).

2-Pyrrolidinecarboxylic acid (10): 0.58 g, 100%; mp 200 °C (lit.[8] mp 203–205 °C).

2-Piperidinecarboxylic acid hydrochloride (11): 0.80 g, 97%; mp 255 °C (lit.[9] mp 259–261 °C).

5-Aminopentanoic acid hydrochloride (6m): 0.77 g, 100%; mp 93 °C (lit.[10] mp 92–94 °C).

Acknowledgment. The present work was supported by a grant from the Progetto Finalizzato Chimica Fine II of the CNR Roma.

Registry No. **2**, 594-65-0; **3a**, 105-36-2; **3b**, 41978-69-2; **3c**, 66025-42-1; **3d**, 138286-76-7; **3e**, 115401-57-5; **3f**, 70288-63-0; **3g**, 84984-05-4; **3h**, 600-00-0; **3i**, 2216-90-2; **3j**, 129592-91-2; **3k**, 138286-77-8; **3l**, 70288-66-3; **3m**, 5454-83-1; **5a**, 116963-47-4; **5b**, 138286-78-9; **5c**, 138286-79-0; **5d**, 138286-80-3; **5e**, 138286-81-4; **5f**, 138286-82-5; **5j**, 138286-83-6; **5m**, 138286-84-7; **6a**, 6000-43-7; **6b**, 25616-13-1; **6c**, 40522-79-0; **6d**, 644-90-6; **6e**, 98320-69-5; **6f**, 2508-63-6; **6j**, 27172-85-6; **6m**, 627-95-2; **7**, 4192-77-2; **8**, 138286-85-8; **9**, 138286-86-9; **10**, 609-36-9; **11**, 5107-10-8; $Me_2CHCH_2CH_2COOH$, 646-07-1; ε-caprolactone, 502-44-3.

(8) *Dictionary of Organic Compounds*; Chapman & Hall: London, 1982.

(9) Stevens, C. M.; Ellman, P. B. *J. Biol. Chem.* **1950**, *182*, 75.

(10) Schniepp, L. E.; Marvel, C. S. *J. Am. Chem. Soc.* **1935**, *57*, 1557.

Lipase-Catalyzed Enantioselective Transesterification of *O*-Trityl 1,2-Diols. Practical Synthesis of (*R*)-Tritylglycidol

Mahn-Joo Kim* and Yoon Kyung Choi

Department of Chemistry and Center for Biofunctional Molecules, Pohang Institute of Science and Technology, P.O. Box 125, Pohang 790-600, Korea

Received July 25, 1991 (Revised Manuscript Received November 21, 1991)

Glycidol and its derivatives are versatile C_3 synthons in organic synthesis.[1] Their optically active forms are especially useful in the asymmetric synthesis of β-blockers[2] and lipids.[3] Although several procedures[4] are currently available for their enantioselective synthesis (for example, Sharpless epoxidation of allylic alcohols[4b] and lipase-catalyzed hydrolysis of glycidyl esters[4c]), few of them provide high optical purity (>98% ee). We herein report a short efficient chemoenzymatic synthesis of optically pure (*R*)-tritylglycidol (**4**, >98% ee) whose optical purity results from lipase PS (LPS)-catalyzed enantioselective transesterification of an intermediate, 3-chloro-1-*O*-trityl-1,2-propanediol (**2a**).

(1) (a) Kleeman, A.; Wagner, R. *Glycidol: Properties, Reactions, Applications*; Huethig: Heidelberg, 1981. (b) Jurczak, J.; Pikul, S.; Bauer, T. *Tetrahedron* **1986**, *42*, 447–88.

(2) Kloosterman, M.; Elfernik, V. H. M.; Lersel, J. V.; Roskam, J.-H.; Meijer, E. M.; Hulshof, L. A.; Sheldon, R. A. *Trends Biotechnol.* **1988**, *6*, 251–55 and therein references.

(3) (a) Guividalsky, P. N.; Bittman, R. *J. Am. Chem. Soc.* **1989**, *111*, 3077–79.

(4) (a) Baldwin, J. J.; Raab, A. W.; Mensler, K.; Arison, B. H.; McClure, D. E. *J. Org. Chem.* **1978**, *43*, 4876–78. (b) Gao, Y.; Hansen, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–80. (c) Ladner, W. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1984**, *106*, 7250–51. (d) Grandjean, D.; Pale, P.; Chuche, J. *Tetrahedron Lett.* **1991**, *32*, 3043–46.

0022-3263/92/1957-1605$03.00/0