Dimethyl (*S*)-2-((Phenylmethoxy)methoxy)pentanedioate (9). A solution of (*S*)-α-butyrolactone-α-carboxylic acid (5.22 g, 0.0401 mol) and 4 drops of concentrated HCl in 50 mL of dry methanol was heated to reflux overnight. The mixture was cooled to 0 °C, and solid $NaHCO_3$ was added. The solution was filtered, concentrated in vacuo, then taken up in 50 mL of methylene chloride, and dried. Filtration followed by concentration in vacuo gave 7.06 g (100%) of the desired diester. This material was immediately dissolved in 80 mL of methylene chloride and treated with diisopropylethylamine (11.4 g, 88.2 mmol) and chloromethyl benzyl ether (12.6 g, 80.2 mmol). After stirring at room temperature for 48 h, aqueous workup and ether extraction followed by MPLC chromatography (silica gel, 25% EtOAc/hexanes) gave 10.2 g (86%) of the protected diester as a colorless oil: $[\alpha]_D$ -38.6° (*c* 3.94, $CHCl_3$); R_f 0.41 (35% EtOAc/hexanes); 300-MHz ^1H NMR ($CDCl_3$) δ 7.33 (m, 5 H), 4.81 (dd, *J* = 1.2 Hz, 2 H), 4.63 (s, 2 H), 4.26 (dd, *J* = 7.6, 4.9 Hz, 1 H), 3.70 (s, 3 H), 3.66 (s, 3 H), 2.48 (dt, *J* = 3.7, 2.9 Hz, 2 H), 2.12 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 173.1, 172.4, 137.4, 128.4, 127.8, 127.7, 94.3, 74.4, 70.1, 29.5, 27.8; IR (neat, cm^{-1}) 3050, 2900, 1740, 1730. Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.92; H, 6.77.

Methyl (*S*)-5-Oxo-4-((phenylmethoxy)methoxy)pentanoate (10). A solution of the protected diester (1.27 g, 4.29 mmol) and magnesium bromide etherate (1.22 g, 4.72 mmol) in 25 mL of methylene chloride was stirred at room temperature for 30 min and then cooled to -95 °C. Diisobutylaluminum hydride (3.1 mL of a 1.5 M solution in toluene, 4.72 mmol) was then added dropwise via syringe pump (one drop every 8-10 s) in such a manner as to allow the solution to run down the side arm of the flask and be thoroughly cooled to -95 °C before entry into the reaction mixture. After addition was complete, 3 mL of anhydrous methanol was added in the same manner, and the reaction mixture was then allowed to warm to room temperature. Saturated aqueous Rochelle salts (10 mL) was added, the solution was stirred for 2 h, and the layers were separated. The aqueous layer was extracted with 2 × 10 mL portions of methylene chloride, and the combined organic layers were dried over sodium sulfate. Concentration in vacuo followed by MPLC chromatography (silica gel, 25% EtOAc/hexanes) gave 0.868 g (76%) of the aldehyde as a colorless oil: $[\alpha]_D$ -50.6° (*c* 1.5, $CHCl_3$); R_f 0.28 (35% EtOAc/hexanes); 300-MHz ^1H NMR ($CDCl_3$) δ 9.75 (d, *J* = 1.1 Hz, 1 H), 7.32 (m, 5 H), 4.80 (d, *J* = 2.0 Hz, 2 H), 4.63 (d, *J* = 2.9, 2 H), 4.25 (dd, *J* = 7.1, 5.1 Hz, 1 H), 3.70 (s, 3 H), 2.59 (m, 2 H), 2.12 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 201.1, 172.4, 137.4, 127.8, 94.3, 74.4, 70.3, 52.1, 34.4, 25.2; IR (neat, cm^{-1}) 2945, 2900, 1740, 1730, 1360. Anal. Calcd for $C_{14}H_{18}O_5$: C 63.10; H 6.81. Found: C, 62.89; H, 6.79.

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Registry No. 1, 129151-77-5; 4, 82130-73-2; 7, 129151-78-6; 8, 129151-79-7; 9, 129151-80-0; 10, 129151-81-1; $Bu_3SnCH_2CH=CH_2$, 24850-33-7; (*S*)-$MeO_2CCH_2CH_2CH(OH)CO_2Me$, 55094-97-8; (*S*)-$MeO_2CCH_2CH(OH)CO_2Me$, 617-55-0; (*S*)-α-butyrolactone-α-carboxylic acid, 21461-84-7.

N-Alkylation of Trifluoroacetamide with 2-Bromo Carboxylic Esters under PTC Conditions: A New Procedure for the Synthesis of α-Amino Acids

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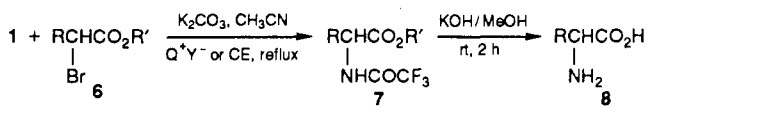
Mono- and bis-N-alkylations of trifluoroacetamide (1) are useful procedures for the synthesis of primary and secondary amines, respectively.[1-3] The intermediate mono- and bis-N-substituted trifluoroacetamides 2 and 3 are either hydrolyzed or reduced by $NaBH_4$ under very mild reaction conditions[4] to the corresponding primary or secondary amines 4 and 5, in almost quantitative yields.[1-3,5,7]

The alkylation reaction is accomplished under homogeneous conditions using the preformed sodium[1] or potassium[2] salt of 1, or better still under solid-liquid phase-transfer catalysis (SL-PTC) conditions starting from 1 and anhydrous potassium carbonate.[8]

Here we report that the SL-PTC procedure can be used for the selective mono-N-alkylation of 1 by alkyl 2-bromo carboxylic esters 6, affording the corresponding *N*-(trifluoroacetyl)-2-amino esters 7. Since, as discussed above,[4] 7 is easily and quantitatively hydrolyzed to 8, the procedure described here represents a new way of synthesis of natural and unnatural α-amino acids 8 (Scheme I).

Scheme I



R = H, alkyl, aryl; R' = Me, Et; Q^+Y^- = $C_6H_5CH_2N^+Et_3Cl^-$, $Bu_4N^+Br^-$, $Bu_4N^+Cl^-$, $hexyl_4N^+Cl^-$, $Bu_4P^+Br^-$; CE = dicyclohexano-18-crown-6.

Table I. *N*-(Trifluoroacetyl)-2-amino Carboxylic Esters 7a-k, 10, Prepared under SL-PTC Conditions[a] at 80 °C from 2-Bromo Carboxylic Esters 6, $RCHBrCO_2R'$

	6					
entry		R	R'	time, h	products	yield,[b] %
1	a	H	Et	0.5	7a	65
2	b	Me	Et	2	7b	72
3	c	$Me(CH_2)_9$	Et	3.5	7c	75
4	d	Ph	Et	0.3	7d	70
5	e	C_6H_4Me-2	Me	0.3	7e	81
6	f	C_6H_4OMe-3	Me	0.3	7f	70
7	g	C_6H_4F-4	Me	0.3	7g	–[c]
8	h	C_6H_4Cl-4	Me	0.3	7h	–[c]
9	i	C_6H_4Br-4	Me	0.3	7i	–[c]
10	j	$PhCH_2$	Et	48[d]	7j	16
					9	60
11	k	$Br(CH_2)_4$	Me[e]	20	7k	11
					10	52

[a] 6 (20 mmol), TEBA (2 mmol), 1 (40 mmol), K_2CO_3 (40 mmol) in CH_3CN (40 mL), at 80 °C. [b] Isolated yields. [c] Not isolated. The crude of N-alkylation was hydrolyzed (see Table II, entries 7-9). [d] At 25 °C. [e] 80 mmol of 1 and K_2CO_3 were used.

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(4) Owing to the very easy removal of trifluoroacetyl group, trifluoroacetylation of amines and amino acids is a useful method for the reversible protection of amino group,[5,6] and the monoalkylation of 1 can be considered an interesting alternative to the classical Gabriel synthesis of primary amines.[1-3]
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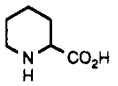
Table II. α-Amino Acids 8, 11, Prepared by Hydrolysis of *N*-(Trifluoroacetyl)-2-amino Carboxylic Esters 7, 10[a]

entry	starting ester	α-amino acid	yield, %
1	**7a**	**8a**, NH_2CH_2COOH	96[b]
2	**7b**	**8b**, $MeCH(NH_2)COOH$	99[b]
3	**7c**	**8c**, $Me(CH_2)_9CH(NH_2)COOH$	100
4	**7d**	**8d**, $PhCH(NH_2)COOH$	91
5	**7e**	**8e**, $2\text{-}MeC_6H_4CH(NH_2)COOH$	90
6	**7f**	**8f**, $3\text{-}MeOC_6H_4CH(NH_2)COOH$	91
7	**7g**	**8g**, $4\text{-}FC_6H_4CH(NH_2)COOH$	72[c]
8	**7h**	**8h**, $4\text{-}ClC_6H_4CH(NH_2)COOH$	70[c]
9	**7i**	**8i**, $4\text{-}BrC_6H_4CH(NH_2)COOH$	68[c]
10	**7j**	**8j**, $PhCH_2CH(NH_2)COOH$	100[b]
11	**10**	**11**, 	97[b]

[a] **7**, **10** (5 mmol) in MeOH (2.5 mL) and 20% aqueous KOH (2.4 mL) at room temperature for 2 h. [b] As hydrochloride. [c] Overall yield referred to the 2-bromo ester **6** after hydrolysis of the crude of N-alkylation.

Results and Discussion

The alkylation reaction (Scheme I) was carried out by stirring, at 80 °C, a heterogeneous mixture of solid anhydrous potassium carbonate (2 mol) and an acetonitrile solution of trifluoroacetamide (**1**) (1.1–2 mol), 2-bromo carboxylic ester **6** (1 mol), and a PTC catalyst (0.1 mol) until the complete disappearance of **6** (GLC and/or TLC analyses) (Table I).

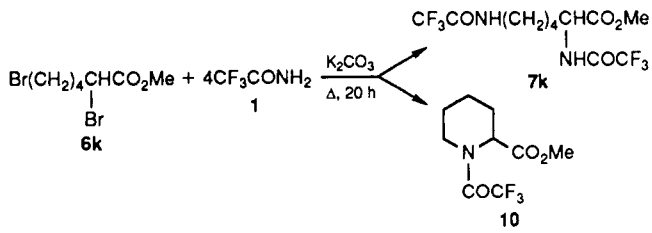
The *N*-(trifluoroacetyl)-2-amino carboxylic esters **7** were isolated as pure compounds in 65–81% yields (Table I) or directly converted into α-amino acids **8** by treating the crude reaction mixture with methanolic potassium hydroxide at room temperature for 2 h. As expected,[1-7] the yields of this second step were very high (90–100%) (Table II).

The best results in the alkylation reactions were obtained using 1.1–2 mol of trifluoroacetamide (**1**) per mole of the alkylating agent; higher excess of **1** did not improve the yields.

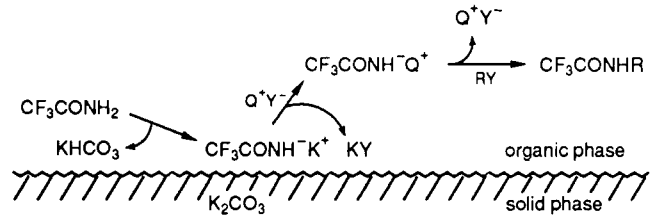
Lipophilic quaternary onium salts as well as crown ethers were found to be effective PTC agents. Of those examined (Scheme I), benzyltriethylammonium chloride (TEBA) was the most efficient. As generally found for reactions performed under liquid–liquid PTC conditions,[11] the reaction rates increased by increasing the amount of the catalyst; without the catalyst the reaction times were much longer (~10 times) and the yields of **7** were lower. Anhydrous conditions which avoided hydrolytic side reactions gave the best results.

The reflux temperature of CH_3CN (i.e. 80–81 °C) represented an optimal compromise in order to have almost quantitative conversions (≥97%) and the highest yields in relatively short reaction times. Ethyl bromoacetate (**6a**) and its higher homologues **6a,c** as well as (bromoaryl)acetic esters **6d–i** were successfully used as alkylating agents (Table I). In contrast to previous results found for common secondary alkyl bromides,[1,3] no elimination reactions were observed in the case of 2-bromo esters **6b,c**. The latter process predominated in reaction of ethyl 2-bromo-3-phenylpropanoate (**6j**), the ethyl *trans*-cinnamate (**9**) (60%) being obtained together with minor amounts

Scheme II



Scheme III



(16%) of ethyl *N*-(trifluoroacetyl)-2-amino-3-phenylpropanoate (**7j**).

The alkylation is subject to steric retardation, i.e. the ethyl 2-bromo-2-methylpropanoate (**6l**) was recovered unchanged from the reaction mixture after 72 h. In an attempt to prepare methyl *N,N'*-bis(trifluoroacetyl)lysinate (**7k**), methyl 2,6-dibromohexanoate (**6k**) was heated at 80 °C for 20 h with **1** (4 mol/mol of bromo derivative), but this afforded only the methyl *N*-(trifluoroacetyl)-2-piperidinecarboxylate (**10**) (52%) and minor amounts of **7k** (11%)[12] (Scheme II). These results clearly indicate that the intramolecular bis-alkylation is the favored process.

The reactions of **6b–j** afforded negligible amounts of dialkylated products, in agreement with previous reports.[1,3] In the case of bromoacetate **6a**, ≤6% of dialkylated product was found.

As shown in Table I, (bromoaryl)acetates **6d–i** were the most reactive, while ethyl bromoacetate (**6a**) reacted faster than higher homologues **6b,c**. Unsatisfactory yields of **7** were obtained by using 2-chloro derivatives as alkylating agents.

The data show that SL-PTC is a versatile and powerful tool in organic synthesis, especially suitable when anhydrous conditions are required[11] and that anhydrous potassium carbonate represents an effective nonnucleophilic reagent for promoting base-catalyzed reactions.[3,11c,d,14-22]

In an attempt to give a mechanistic rationale of the N-alkylation of **1**, the following experimental facts should be considered: (i) no detectable amounts of potassium

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carbonate were found in CH_3CN at 80 °C, in agreement with the literature.[2,3] The addition of a PTC agent to the SL system did not result in any significant extraction of the carbonate anion into the organic phase, in accordance with preceding reports;[17,23] (ii) when an acetonitrile solution of trifluoroacetamide (1) was stirred over K_2CO_3, acid/base titrations showed the presence of basic species (6% molar equiv per mol of 1), which increased when the PTC catalyst was added to the heterogeneous system (see the Experimental Section). ^{19}F NMR measurements carried out under the above conditions showed the actual presence of azaanion salt (see the Experimental Section). On the basis of these results the alkylation reaction likely involves the following steps.

Trifluoroacetamide (1) reacts with solid K_2CO_3 at the phase boundary[11,17b] and affords the potassium salt of 1,[24] which is transferred, in part, into the bulk of the organic phase where the alkylation reaction occurs. The strong catalytic effect of the PTC agent can be ascribed to the increased solubility of the anion reagent[11,17b] and to a higher reactivity of the $CF_3CONH^-Q^+$ species with respect to that of $CF_3CONH^-K^+$.[11a,b,26]

Experimental Section

Starting 2-bromo carboxylic esters were either commercially available or previously described in the literature. Commercial trifluoroacetamide was recrystallized from $CHCl_3$ before use, mp 71–72 °C. Analar grade CH_3CN was dried over 3-Å molecular sieves and used without further purification. K_2CO_3 was carefully dried by heating at 140 °C under vacuum (0.05 mm) for 6 h and stored in a dessicator. ^1H and ^{13}C NMR spectra were recorded at 80 or 20 MHz using TMS (in $CDCl_3$) or DSS (in D_2O) as internal standards. ^{19}F NMR spectra were performed at 282 MHz, and chemical shifts are reported upfield from $CFCl_3$ as external standard. Melting points are uncorrected. Potentiometric titrations were carried out with a Metrohm titroprocessor E 636 using a glass electrode. 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, polyethylene glycol, 0.25 μm thickness). Silica gel 60 (70–230 mesh) was used for column chromatography. TLC was performed on Merck silica gel 60 F 254 precoated plates. Amberlite IRA 93 was used to prepare the amino acids **8b,j** from the corresponding hydrochlorides.

General Procedure for the Alkylation of CF_3CONH_2 (1) with 2-Bromo Carboxylic Esters 6. Solid K_2CO_3 (40 mmol) was added to a solution of CF_3CONH_2 (1) (4.52 g, 40 mmol)), TEBA (0.46 g, 2 mmol), and the 2-bromo ester **6** (20 mmol) in CH_3CN (40 mL) at room temperature. The mixture was refluxed under vigorous magnetic stirring until complete disappearance of the substrate **6** (TLC and/or GLC analysis). After cooling, the crude was filtered on Celite, the solvent was evaporated, and the product was purified by column chromatography. Starting material, reaction time, chromatographic eluant, yield, and physical and spectroscopic data of reaction products are as follows.

Ethyl *N*-(trifluoroacetyl)-2-aminoacetate (7a): ethyl 2-bromoacetate (**6a**); 30 min; mixture of petroleum ether and AcOEt (2:1); **7a**, 2.59 g, 65%; mp 49–50 °C (lit.[27] mp 51.5 °C); IR (Nujol) 3320, 1740, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (t, 3 H, J = 5 Hz), 4.15–4.35 (m, 4 H), 7.12 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.96, 41.35, 62.19, 115.67 (q, J_{CF} = 287 Hz), 157.37 (q, J_{CF} = 38 Hz), 168.25.

Ethyl *N*-(trifluoroacetyl)-2-aminopropanoate (7b): ethyl 2-bromopropanoate (**6b**); 2 h; mixture of petroleum ether and Et_2O (2:1); **7b**, 3.09 g; 72%; mp 34–35 °C; IR (Nujol) 3310, 1740, 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20–1.52 (m, 6 H), 4.28 (q, 2 H, J = 7 Hz), 4.58 (q, 1 H, J = 7 Hz), 7.42 (br s, 1 H). Anal. Calcd for $C_7H_{10}F_3NO_3$: C, 39.44; H, 4.73; N, 6.57. Found: C, 39.41; H, 4.78; N, 6.51.

Ethyl *N*-(trifluoroacetyl)-2-aminododecanoate (7c): ethyl 2-bromododecanoate (**6c**); 3.5 h; mixture of petroleum ether and Et_2O (9:1); **7c**, 5.10 g, 75%; mp 54–55 °C; IR (Nujol) 3320, 1740, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.65–2.00 (m, 24 H), 4.28 (q, 2 H, J = 7 Hz), 4.58 (q, 1 H, J = 7 Hz), 7.42 (br s, 1 H). Anal. Calcd for $C_{16}H_{28}F_3NO_3$: C, 56.62; H, 8.31; N, 4.13. Found: C, 56.59; H, 8.37; N, 4.12.

Ethyl *N*-(trifluoroacetyl)-2-amino-2-phenylacetate (7d): ethyl 2-bromo-2-phenylacetate (**6d**); 20 min; mixture of petroleum ether and AcOEt (4:1); **7d**, 3.85 g, 70%; mp 69 °C; IR (Nujol) 3325, 1735, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (t, 3 H, J = 8 Hz), 4.05–4.37 (m, 2 H), 5.53 (d, 1 H, J = 8 Hz), 7.35 (s, 5 H), 7.40 (br s, 1 H). Anal. Calcd for $C_{12}H_{12}F_3NO_3$: C, 52.36; H, 4.40; N, 5.09. Found: C, 52.30; H, 4.43; N, 5.06.

Methyl *N*-(trifluoroacetyl)-2-amino-2-(2-methylphenyl)-acetate (7e): methyl 2-bromo-2-(2-methylphenyl)acetate (**6e**); 20 min; mixture of petroleum ether and AcOEt (4:1); **7e**, 4.16 g, 76%; mp 106 °C; IR (Nujol) 3340, 1745, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.50 (s, 3 H), 3.74 (s, 3 H), 5.76 (d, 1 H, J = 8 Hz), 7.20 (s, 4 H), 7.35 (br s, 1 H). Anal. Calcd for $C_{12}H_{12}F_3NO_3$: C, 52.36; H, 4.40; N, 5.09. Found: C, 52.38; H, 4.43; N, 5.04.

Methyl *N*-(trifluoroacetyl)-2-amino-2-(3-methoxyphenyl)acetate (7f): methyl 2-bromo-2-(3-methoxyphenyl)-acetate (**6f**); 20 min; mixture of petroleum ether and AcOEt (9:1); **7f**, 4.09 g, 70%; mp 68–70 °C; IR (Nujol) 3320, 1740, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.75 (s, 3 H), 3.80 (s, 3 H), 5.44 (d, 1 H, J = 7 Hz), 6.80–7.50 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 52.80, 54.82, 56.35, 113.12, 114.15, 115.15 (q, J_{CF} = 287 Hz), 119.19, 129.99, 135.88, 156.27 (q, J_{CF} = 38 Hz), 159.92, 169.71. Anal. Calcd for $C_{12}H_{12}F_3NO_4$: C, 49.49; H, 4.15; N, 4.81. Found: C, 49.45; H, 4.18; N, 4.77.

Ethyl *N*-(trifluoroacetyl)-2-amino-3-phenylpropanoate (7j): ethyl 2-bromo-3-phenylpropanoate (**6j**); 48 h at 25 °C; mixture of petroleum ether and Et_2O (6:1); **7j**, 0.89 g, 16%, together with *trans*-ethyl cinnamate (**9**), 2.13 g, 60%; ^1H NMR, IR, and GLC characteristics of **9** are identical with an authentic sample; **7j**, mp 57–58 °C; IR (Nujol) 3320, 1740, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (t, 3 H, J = 7 Hz), 3.16 (d, 2 H, J = 6 Hz), 4.20 (q, 2 H, J = 7 Hz), 4.85 (dt, 1 H, J = 6, 7 Hz), 6.82 (br s, 1 H), 7.00–7.63 (m, 5 H). Anal. Calcd for $C_{13}H_{14}F_3NO_3$: C, 53.97; H, 4.89; N, 4.84. Found: C, 53.78; H, 4.77; N, 4.74.

Methyl 1-(Trifluoroacetyl)-2-piperidinecarboxylate (10). General procedure was followed with **6k**, using 80 mmol of CF_3CONH_2 and K_2CO_3 at reflux for 20 h. The main product isolated after column chromatography (petroleum ether and Et_2O, 5:1) is **10** (2.52 g, 52%) together with a minor amount (0.77 g, 11%) of methyl *N*,*N*'-(trifluoroacetyl)-2,6-diaminohexanoate (**7k**). The latter was not isolated as pure compound but detected by GLC and ^1H NMR. Product **10** has n^{27}_D 1.4291; IR (neat) 3320, 1740, 1695 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85–2.50 (m, 7 H), 3.85 (s, 3 H), 4.35–4.70 (m, 2 H), 5.25 (br s, 1 H). Anal. Calcd for $C_9H_{12}F_3NO_3$: C, 45.18; H, 5.07; N, 5.86. Found: C, 45.27; H, 5.01; N, 5.73.

General Method for the Hydrolysis of *N*-(Trifluoroacetyl)-2-amino Carboxylic Esters. Synthesis of the Corresponding α-Amino Acids. A mixture of **7a–j** or **10** (20 mmol), aqueous 20% KOH (30 mL, 40 mmol), and MeOH (30 mL) was stirred at room temperature for 2 h. After evaporation of MeOH, the crude was acidified with 10% HCl to the specific isoelectric pH in the cases of the α-amino acids **8c–i** isolated as such. The compounds **8a,b,j**, **11** are isolated as hydrochlorides, by acidifying the crude to pH 2 (see Table II). On cooling, the α-amino acids or their hydrochlorides crystallized and were filtered and washed thrice with H_2O (5 mL) and dried in an oven (80 °C) overnight. Yield and physical and spectroscopic data of the products of hydrolysis are reported.

Glycine hydrochloride (8a): 2.12 g, 96%; mp 180 °C dec (lit.[14] mp 185 °C dec); IR (Nujol) 3200, 2100, 1730, 1625, 1590 cm^{-1}; ^1H NMR (D_2O) δ 3.45 (s).

Alanine hydrochloride (8b): 2.49 g, 99%; IR (Nujol) 3180, 2100, 1730, 1610, 1590 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.60 (d, 3 H, J = 9), 4.00 (q, 1 H, J = 9). Free alanine (**8b**) was obtained from the hydrochloride via exchange with a basic polymeric resin and

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had mp 290 °C (lit.[28] mp 295 °C).

2-Aminododecanoic acid (8c): 4.30 g, 100%; mp 260 °C dec. (lit.[28] mp 263 °C dec); IR (Nujol) 3300, 2100, 1610, 1585 cm^{-1}; ^1H NMR (DMSO-d_6 + DCl) δ 0.50–1.90 (m, 21 H), 3.90–3.96 (m, 1 H).

Phenylglycine (8d): 2.75 g, 91%; mp 263–265 °C dec (lit.[28] mp 256 °C, subl); IR (Nujol) 3100, 2100, 1660, 1630, 1590 cm^{-1}; ^1H NMR (DMSO-d_6 + DCl) δ 5.30 (s, 1 H), 7.55 (s, 5 H).

2-(2-Methylphenyl)glycine (8e): 2.97 g, 90%; mp 234–238 °C dec; IR (Nujol) 3200, 2080, 1630, 1570 cm^{-1}; ^1H NMR (DMSO-d_6 + DCl) δ 2.55 (s, 3 H), 5.52 (s, 1 H), 7.30–7.60 (m, 4 H). Anal. Calcd for $C_9H_{11}NO_2$: C, 65.43; H, 6.72; N, 8.48. Found: C, 65.36; H, 6.81; N, 8.51.

2-(3-Methoxyphenyl)glycine (8f): 3.30 g, 91%; mp 215 °C dec (lit.[29] mp 220–222 °C dec); IR (Nujol) 3200, 2060, 1605, 1585 cm^{-1}; ^1H NMR (DMSO-d_6 + DCl) δ 3.90 (s, 3 H), 5.18 (s, 1 H), 7.00–7.55 (m, 4 H).

Phenylalanine hydrochloride (8j): 4.01 g, 100%; IR (Nujol) 3230, 2200, 1730, 1595 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.05–3.20 (m, 2 H), 3.80–4.15 (m, 1 H), 7.10–7.25 (m, 5 H). Free **8j** was obtained with a basic resin and had mp 280 °C (lit.[28] mp 284–288 °C).

2-Piperidinecarboxylic acid hydrochloride (11): 3.21 g, 97%; mp 255 °C (lit.[30] mp 259–261 °C); IR (Nujol) 3480, 2110, 1730, 1585 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.10–2.60 (m, 6 H), 2.90–3.50 (m, 2 H), 4.15–4.45 (m, 1 H).

The alkylation products of CF_3CONH_2 (1) with 2-bromo carboxylic esters **6g–i** were not isolated, but the crude of reaction, after filtration and evaporation of the solvent, was directly hydrolized following the general procedure described above. The yield and physical and spectroscopic data are the following:

2-(4-Fluorophenyl)glycine (8g): 2.44 g, 72% (yield based on the starting 2-bromo ester **6g**); mp 270–272 °C dec (lit.[31] mp 271–273 °C); IR (Nujol) 3080, 2100, 1620, 1580, 1115 cm^{-1}; ^1H NMR (DMSO-d_6 + DCl) δ 5.28 (s, 1 H), 7.25–7.80 (m, 4 H).

2-(4-Chlorophenyl)glycine (8h): 2.46 g, 70% (overall yield): mp 272–274 °C, dec (lit.[31] mp 270–272 °C dec); IR (Nujol) 3060, 2100, 1620, 1580 cm^{-1}; ^1H NMR (DMSO-d_6 + DCl) δ 5.33 (s, 1 H), 7.45–7.66 (m, 4 H).

2-(4-Bromophenyl)glycine (8i): 3.11 g, 68% (overall yield); mp 262–264 °C (lit.[32] mp 265 °C subl); IR (Nujol) 3080, 2100, 1630, 1590 cm^{-1}; ^1H NMR (DMSO-d_6 + DCl) δ 5.25 (s, 1 H), 7.40–7.80 (m, 4 H).

Extractability of Carbonate Ion in the Organic Phase. Anhydrous potassium carbonate (6.90 g, 50 mmol) and CH_3CN (50 mL) were magnetically stirred at 80 °C for 20 min both in the absence and presence of benzyltriethylammonium chloride (TEBA, 1.14 g, 5 mmol). The stirring was stopped, and aliquots (5 mL) of the organic phase were withdrawn and titrated with 0.01 N HCl (potentiometric titration). No basic species were detected in either case.

Extractability of Trifluoroacetamide Anion as Potassium or Quaternary Ammonium Salt in the Organic Phase. An acetonitrile solution (50 mL) of CF_3CONH_2 (1) (5.65 g, 50 mmol) was stirred over anhydrous K_2CO_3 (6.90 g, 50 mmol) at 80 °C for 20 min. The acid titration of aliquots (5 mL) of organic phase showed the presence of basic species (0.06 mol/mol of starting 1). When the above run was performed in the presence of TEBA (1.14 g, 5 mmol) the basic species reached 0.10 mol/mol of 1.

^{19}F NMR Measurements. The ^{19}F NMR spectrum of a CD_3CN solution of trifluoroacetamide (1) showed a singlet at ca. −65 ppm. The ^{19}F NMR spectrum of an equimolar solution of 1 and preformed CF_3CONHK[2] in CD_3CN showed two singlets at ca. −65 and −64 ppm, the latter can be assigned to fluorine of the CF_3CONH^-. When a CD_3CN (5 mL) solution of 1 (0.57 g, 5 mmol) was stirred over anhydrous K_2CO_3 (0.69 g, 5 mmol) for 20 min at 80 °C, ^{19}F NMR analysis showed, together with the signal of 1, the presence of the singlet at ca. −64 ppm. From the integrals of the two signals 0.06 mol of CF_3CONH^-/mol of 1 was evaluated, in agreement with the results obtained by potentiometric titrations. In a similar run, but carried out in the presence of TEBA (0.11 g, 0.5 mmol), the amount of CF_3CONH^- reached 0.10 mol/mol of 1, as previously found by acid titrations.

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Registry No. 1, 354-38-1; **6a**, 105-36-2; **6b**, 41978-69-2; **6c**, 129592-86-5; **6d**, 2216-90-2; **6e**, 129592-87-6; **6f**, 86215-57-8; **6g**, 129592-88-7; **6h**, 129592-89-8; **6i**, 129592-90-1; **6j**, 129592-91-2; **6k**, 70288-66-3; **7a**, 367-62-4; **7b**, 26629-29-8; **7c**, 129592-92-3; **7d**, 129592-93-4; **7e**, 129592-94-5; **7f**, 129592-95-6; **7j**, 16417-60-0; **7k**, 129592-97-8; **8a**·HCl, 6000-43-7; **8b**·HCl, 25616-13-1; **8b** (free base), 302-72-7; **8c**, 35237-37-7; **8d**, 2835-06-5; **8e**, 129592-98-9; **8f**, 7314-43-4; **8g**, 7292-73-1; **8h**, 7292-70-8; **8i**, 129592-99-0; **8j**·HCl, 27172-85-6; **8j** (free base), 150-30-1; **9**, 4192-77-2; **10**, 129592-96-7; 11·HCl, 5107-10-8.

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A New and Efficient Method for the Resolution of 2,2'-Dihydroxy-1,1'-binaphthyl

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In the past few years, much attention has been focused on the studies of the chirality recognition properties of chiral crown ether hosts containing the binaphthol unit.[1] Also, the application of binaphthyl-containing chiral catalysts or reagents in asymmetric synthesis has proven fruitful.[2] Consequently, the preparation of optically active binaphthol is of current interest. Its conventional large-scale preparation relies on the optical resolution of its cyclic phosphoric ester using cinchonine as a resolving agent.[3] By this method, the overall resolved yield is only moderate (41% for (+)-*R*-1; 52% for (−)-*S*-1), and the enantiomeric purity of the product is even less satisfactory (96.6% for (+)-*R*-1).[1] Cinchonine is expensive and often recovered in contaminated from. Recently, a method for preparing (−)-*S*-1 by the coupling of the *S*-(+)-amphetamine-copper(II) complex of β-naphthol has been reported.[4] It is attractive owing to its simplicity, but the amine is expensive and is needed in large quantity (1:8 mol ratio). An efficient method of optical resolution by enantioselective complex formation using specially prepared tartaric amide has also been described recently.[5] Jacques's[6] and Truesdale's[7] work improved Cram's procedure by preparing a purer BNP acid and resolving it with cinchonine. The enantiomeric acids were methylated to the esters, which were reduced by Red-Al (Aldrich). The enantiomeric purity of each resulting binaphthol was higher, but the procedure is composed of a number of preparative steps, each entailing separations and purifications. This resulted in a lower overall yield (34% for (*R*)-(+)-2,2'-dihydroxy-1,1'-binaphthyl and 39% for the *S*-(−) enantiomer) than Cram's procedure.

We now report a new and more efficient method for this enantiomeric resolution via the formation of the phos-

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