Alkyl 1-Chloroalkyl Carbonates: Reagents for the Synthesis of Carbamates and Protection of Amino Groups

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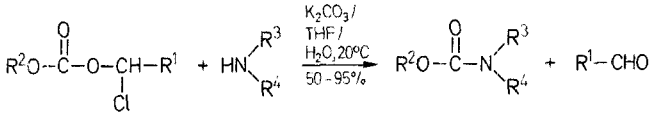
The synthesis of 1-chloroalkyl carbonates and their reaction with various type of amines are described. This reaction is useful for the synthesis of carbamate pesticides and for the protection of various amino groups, including amino acids.

As part of our program concerning the synthetic potential of 1-chloroalkyl carbonochloridates[1,2], we were interested in the development of 1-chloroalkyl carbonates as reagents for organic synthesis. These carbonates are known to react with nucleophiles to effect chlorine displacement, and this property has been widely used in the modification of antibiotics[3]. We have already described the use of 1,2,2,2-tetrachloroethyl *t*-butyl carbonate as a reagent for the synthesis of

Boc-amino acids[4]. We now give a complete description of our efforts in the design of new economical reagents for the synthesis of carbamates.

Carbamates have considerable importance as intermediates in organic synthesis and as final products for industrial and agricultural uses. A wide number of methods already have been described for their synthesis[5], the most important ones being the reaction of an amine with a carbonochloridate and the reaction of an alcohol with the required isocyanate. However, many carbonochloridates are unstable and the use of isocyanates is sometimes dangerous due to their well-known toxicity. This led to the design of numerous reagents to overcome this difficulty[5], most of them having been used in peptide synthesis.

We have discovered that 1-chloroalkyl carbonates (**1a–k**) readily react with primary and secondary amines to give the corresponding carbamates, aldehydes, and hydrogen chloride.



R^1 = CH_3, CCl_3

R^2 = alkyl, aryl

Aldehydes have rarely been used as leaving groups and this can be a severe limitation in the use of this reaction since the aldehyde formed can react with the starting amine to lead to a considerable decrease in the yield of the expected carbamate. We found, however, that this difficulty can be simply overcome if the respective structures of the carbonate and the amine are correctly chosen and if the reaction conditions are adapted to minimize this side reaction.

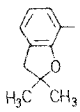
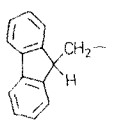
1-Chloroalkyl carbonates **1a–k** are easily obtained by the reaction of the desired alcohol with 1-chloroalkyl carbonochloridates in the presence of pyridine. Tertiary amines are not satisfactory bases because they are dealkylated by the carbonochloridate[2]. In some cases (e.g. 1-chloroethyl alkyl carbonates), no added base is necessary and the carbonates can be obtained by heating gently a mixture of the carbonochloridate and the alcohol under controlled vaccum to remove the released hydrogen chloride[3]. Since the presence of pyridine can lead to decomposition of the starting carbonochloridate, it is recommended to add the base slowly to the mixture of the reactants.

1-Chloroethyl alkyl carbonates are generally stable products which can be easily distilled without appreciable decomposition whereas 1,2,2,2-tetrachloroethyl carbonates are generally crystalline products stable for months at room temperature. However, they have been found to be very sensitive to nucleophilic impurities, e.g., by moisture or chloride contents. Hence, to secure a good stability, care must be taken to avoid any contamination in the handling of the products. Also, it has not been possible to isolate 1,2,2,2-tetrachloroethyl benzyl carbonate due to its rapid decomposition during the isolation procedure. Spectral and physical properties of these carbonates are given in Table 1.

1-Chloroethyl carbonates are ambident electrophiles that can react both at the carbonyl or at C-α with displacement of the chlorine. This property has been used with some success in the synthesis of antibiotics, pharmaceutical or agricultural products[3,6]. In these cases, carboxylates[3] or dithiophosphates[6] act as soft nucleophiles and reaction occurs at the softer electrophilic site.

We have observed that amines attack at the carbonyl and that 1-chloroethyl alkyl carbonates are less reactive than 1,2,2,2-tetrachloroethyl alkyl carbonates (**2m** in Table 2).

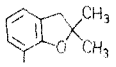
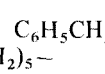
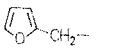
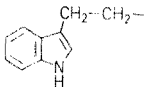
Table 1. 1-Chloroalkyl Carbonates (**1a–k**) prepared

	R^1	R^2	Yield [%]	m.p. [°C] or b.p. [°C]/torr	Molecular Formula[a] or Lit. Data	^{1}H-N.M.R. ($CDCl_3$/TMS_{int}) δ [ppm]
a	CH_3	C_2H_5	97	b.p. 67/22	b.p. 160°/760[1] b.p. 67°/22[1]	1.3 (t); 1.8 (d); 4.25 (t); 6.4 (q)
b	CH_3	t-C_4H_9	90	b.p. 88/20	$C_7H_{13}ClO_3$ (180.6)	1.5 (s); 1.8 (d); 6.4 (q)
c	CH_3	2-furyl	88	b.p. 95/0.2	$C_8H_9ClO_4$ (204.6)	1.8 (d); 5.2 (s); 6.3–6.6 (m); 7.5 (m)
d	CH_3	$C_6H_5CH_2$	94	b.p. 100/0.5	$C_{10}H_{11}ClO_3$ (214.6)	1.8 (d); 5.2 (s); 6.4 (q); 7.3 (s)
e	CH_3	C_6H_5	94	b.p. 117/0.5	$C_9H_9ClO_3$ (200.6)	1.7 (d); 6.4 (q); 7.0–7.3 (m)
f	CH_3		84	b.p. 127/0.5	$C_{13}H_{15}ClO_4$ (270.7)	1.5 (s); 1.9 (d); 3.05 (s); 6.5 (q); 6.9–7.1 (m)
g	CH_3	C_2H_5S[b]	80	b.p. 78/20	$C_5H_9ClO_2S$ (168.6)	1.3 (t); 1.7 (d); 2.8 (q); 6.5 (q)
h	CCl_3	t-C_4H_9	87	m.p. 68–70	$C_7H_{10}C_{14}O_3$ (283.98)	1.5 (s); 6.7 (s)
i	CCl_3		98	m.p. 98–100	$C_{17}H_{11}C_{14}O_3$ (405.1)	4.3–4.6 (m); 6.7 (s); 7.2–8.0 (m)
j	CCl_3	CCl_3CH_2—	67	b.p. 108/0.05 36	$C_5H_3Cl_7O_3$ (359.3)	4.85 (s); 6.7 (s)
k	CCl_3	$(CH_3)_3Si$—CH_2—CH_2—	83	b.p. 94/0.05	$C_8H_{14}Cl_4O_3Si$ (328.1)	0.1 (s); 1.1 (t); 4.35 (t); 6.7 (s)

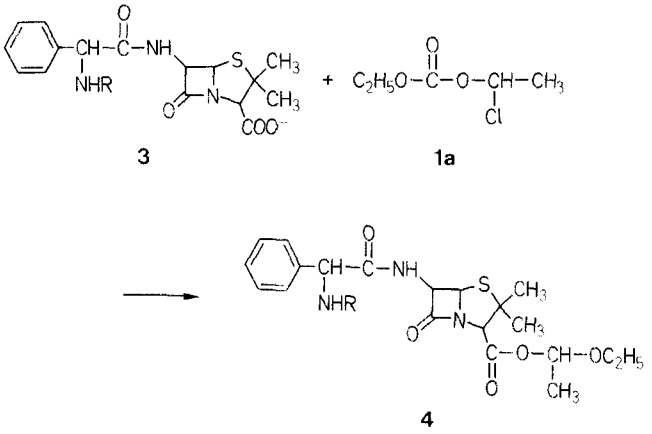
[a] The microanalyses showed the following maximum deviations from the calculated values: C ±0.39, H ±0.33, Cl ±0.4. Exception: **1h**, Cl +1.13.

[b] $R^2O = C_2H_5S$

Table 2. Carbamates (**2a–o**) prepared

2	R^2	R^3	R^4	Reagent	Yield [%]	m.p. [°C] or b.p. [°C]/torr	
						found	reported
a	C_2H_5	$-(CH_2)_5-$		**1a**	88	b.p. 95°/18	b.p. 52°/3[11]
b	C_6H_5	$-(CH_2)_5-$		**1e**	80	m.p. 81°	m.p. 83°[12]
c	SC_2H_5[a]	$-(CH_2)_6-$		**1g**	70	b.p. 141°/13	b.p. 137°/10[13]
d		H	CH_3	**1f**	79	m.p. 148°	m.p. 150°[14]
e	$C_6H_5CH_2$	H	$C_6H_5CH_2$	**1d**	84	b.p. 175°/0.1 m.p. 64°	m.p. 64°[15]
f	$C_6H_5CH_2$	CH_3	$C_6H_5CH_2$	**1d**	87	b.p. 165°/1	b.p. 173°/2[16]
g	$C_6H_5CH_2$	$-(CH_2)_5-$		**1d**	97	b.p. 128°/0.5	b.p. 137°/1[17]
h	$C_6H_5CH_2$	$-(CH_2)_2-O-(CH_2)_2$		**1d**	84	b.p. 140°/1 m.p. 49.5°	m.p. 50°[18]
i	$C_6H_5CH_2$			**1d**	88	m.p. 75–76°	m.p. 77°[20]
j	$C_6H_5CH_2$	H	$HO-CH_2-CH_2-$	**1d**	74	b.p. 170°/0.5 m.p. 62–63°	m.p. 62°[28]
k	C_2H_5	H	$C_2H_5OOC-CH_2-$	**1a**	54	b.p. 102°/0.6	b.p. 135°/16[21]
l		H	$C_2H_5OOC-CH_2-$	**1c**	66	b.p. 144°/0.3	b.p. 184°/16[22]
m	t-C_4H_9	H	$C_6H_5CH_2$	**1b**	58	m.p. 53°	m.p. 53–54°[15]
				1h	91	m.p. 53°	m.p. 53–54°[15]
n	t-C_4H_9			**1b**	50	m.p. 44–47°	m.p. 45–47.5°[19]
				1h	86	m.p. 44–47°	m.p. 45–47.5°[19]
o	$(CH_3)_3Si-CH_2-CH_2-$	H		**1k**	92	m.p. 69–70°	m.p. 69.5–70.5°[15]

[a] $R^2O = SC_2H_5$



3 **1a**

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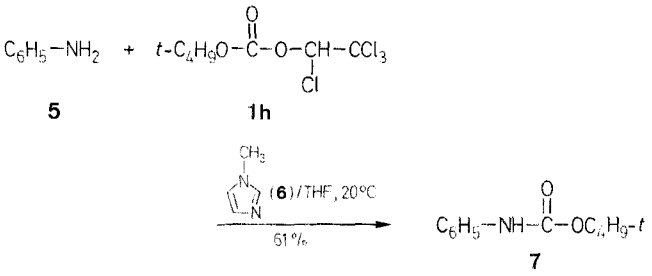
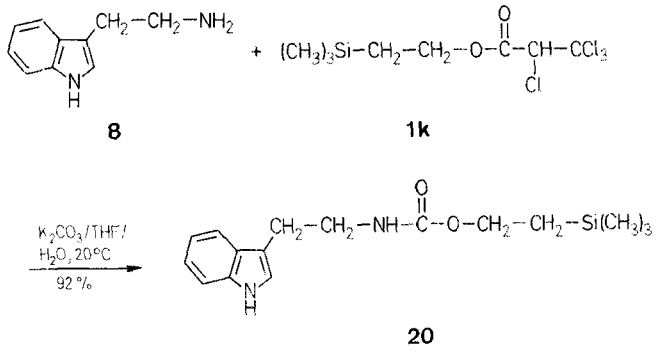
The reaction is generally run in tetrahydrofuran or dioxane in the presence of an added base to trap the released hydrogen chloride. Due to the fact that the aldehyde by-product can react with the starting amine to give Schiff bases or aminals, it is important to note that this side reaction can be considerably reduced or even eliminated by the proper choice of either the carbonate or the amine. Indeed, the reaction of amines with 1-chloroalkyl carbonates is generally more rapid than the formation of Schiff bases and the yields are satisfactory. If a more reactive carbonate needs to be used, this can be accomplished by replacing the 1-chloroethyl moiety by the more reactive 1,2,2,2-tetrachloroethyl group. Also, the formation of Schiff bases can be slowed down by running the reaction in an aqueous medium. In this case, formation of the aldehyde hydrate competes with the formation of an aminal. This is particularly true with 1,2,2,2-tetrachloroethyl carbonates where chloral hydrate is generally the sole by-product. However, the use of 1,2,2,2-tetrachloroethyl carbonates is not always necessary, particularly if the other part of the carbonate is sufficiently electron-withdrawing, as is the case with benzyl carbonates (**2e–j** in Table 2). It is worthy of note that chloral and chloral hydrate, unlike acetaldehyde, is not capable of aldol side reactions and hence the reaction medium would be free of colored by-products. This property is particularly important if the products are to be isolated by simple crystallization.

The reaction has been performed with various type of amines (Table 2) using different kinds of 1-chloroalkyl carbonates. Although we have not as yet investigated in details the limitations imposed on the reaction by the presence of other functional groups, weakly basic groups such as the hydroxyl group were found to cause no interference (**2j** in Table 2). Nevertheless, the reaction is quite general, except with weakly nucleophilic amines, such as aniline. We have made some attempts to catalyze this reaction with conventional acylation catalysts such as DMAP or *N*-methylimidazole. However, we have noticed in parallel experiments that the catalyst is rapidly poisoned by the released aldehyde. Despite this, it has been possible to obtain *N*-*t*-butyloxycarbonylaniline (**7**) in 61% yield when using one equivalent of *N*-methylimidazole in tetrahydrofuran for 3 hours at room temperature. In this case, *N*-methylimidazole acts both as an auxiliary base and as the catalyst. However, the yield is to some extent lowered by the relative ease of formation and stability of Schiff bases.



Imidazole reacts with **1b** to give a 50% yield of its *t*-butyloxycarbonyl derivative **2n** whereas reaction with **1d** gives 86% of the Boc-imidazolide under the same conditions (20°C, 1 h; **2n** in Table 2). Pyrroles and indoles are not acylated under standard conditions which made possible the amino protection of tryptamine **(8)** as its 2-(trimethylsilyl)-ethyl carbamate with a yield of 92%.



The application of the above method to the synthesis of the insecticide carbamates Carbofuran **(2d)** and Aldicarbe **(12)** was briefly examined. Carbofuran was readily obtained in 79% yield from 2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl 1-chloroethyl carbonate **(1f)** which itself is obtained in 89% yield from the corresponding phenol. The synthesis of Aldicarbe was less successful. Indeed, it has not been possible to obtain the 1-chloroalkyl carbonate of 2-methyl-2-methylthio-propanal oxime in pure form. This is probably due to the relative ease with which this carbonate reacts with the sodium salt of the oxime to form a symmetrical carbonate. Nevertheless, the crude mixture was reacted with methylamine to afford a 63% yield of Aldicarbe together with ~ 7% of the starting oxime **10**. Unfortunately, this, is far from being competitive with the known methyl isocyanate route.

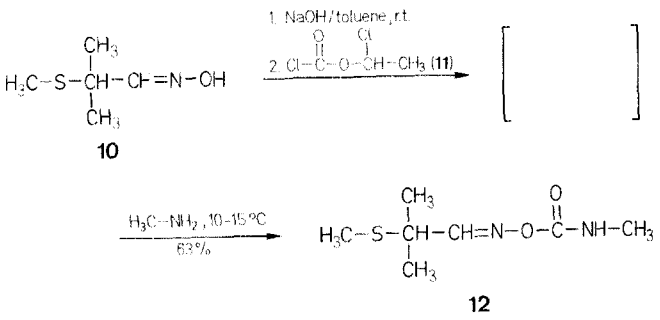


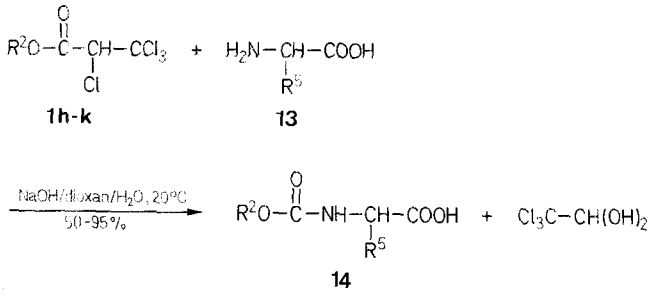
Table 3. *N*-Protected L-Amino Acids **(14)**

Product	Reagent/Method	Yield [%]	m.p. [°C]; $[\alpha]_D^{20}$	Lit. Data[8,23–26] m.p. [°C]; $[\alpha]_D^{20}$
Boc—Ala—OH	**1h**/A	90	80–81°; −24, c = 2.1 (AcOH)	83–84°; −22.4, c = 2.1 (AcOH)
Boc—Asp—OH	**1h**/A	60	117–119°; −5, c = 1.0 (methanol)	118–119°; −6.2, c = 1.0 (methanol)
Boc—Gly—OH	**1h**/B pH 9.0[a]	84	87–88	88.5–89°
Boc—Ile—OH	**1h**/B pH 9.5	71	66°; +3.3, c = 1 (AcOH)	66–68°; +3.0 c = 2 (AcOH)
Boc—Leu—OH, H_2O	**1h**/B pH 9.75	95	75°; −27, c = 1 (AcOH)[b]	78–81; −30 (AcOH)[b]
Boc—Met—OH, DCHA	**1h**/B pH 9.7	75	137–138°; +16.8, c = 1 (DMF)[b]	138–139; +17.3, c = 1 (DMF)[b]
Boc—Pro—OH	**1h**/A	91	132–133°; −60, c = 2 (AcOH)	136–137°; −60.2, c = 2 (AcOH)
Boc—Phe—OH	**1h**/A	79	85–87°; +28, c = 1.5 (ethanol)	85–87°; +24.7, c = 1.5 (ethanol)
Boc—Ser—OH, DCHA	**1h**/A	78	139–140°; +8, c = 2.8 (methanol)	142–144°; +13, c = 3 (methanol)
Boc—Ser (OBzl)—OH	**1h**/B pH 9.5	74	58–61°; +21.2, c = 2 (ethanol)	60–62°; +20.4, c = 2 (ethanol)
Boc—Thr(OBzl)—OH	**1h**/B pH 9.0	76	114°; +16.3, c = 1 (methanol)	115–116°; +15.8, c = 1 (methanol)
Boc—Trp—OH	**1h**/B pH 8.3	74	135–139°; −21.2, c = 1 (AcOH)[b]	135–137°; −21.5, c = 1 (AcOH)[b]
Boc—Tyr—OH, DCHA	**1h**/A	82	206°	215–217°
Boc—Val—OH	**1h**/B pH 9.2	80	78°; −6.0, c = 1 (AcOH)	77–79°; −5.8, c = 1 (AcOH)
Fmoc—Phe—OH	**1i**/C	75	178–179°; −40.1, c = 0.1 (DMF)	178–179°; −41.7, c = 0.1 (DMF)
Fmoc—Pro—OH	**1i**/C	83	112–113°; −32.9, c = 1 (DMF)	116–117°; −33.2, c = 1 (DMF)
Troc—Asp—OH	**1j**/A	47	144–145°; −32.8, c = 3 (DMF)	146–147°; −31.9, c = 4 (DMF)
Troc—Phe—OH	**1j**/A	84	128–129°; −30.8, c = 3 (DMF)	126–127°; −29.9, c = 3 (DMF)
Troc—Ser—OH	**1j**/A	82	111–113°; +11.3, c = 0.9 (ethyl acetate)	115°; +11.7 (ethyl acetate)
Tmseoc—Phe—OH, DCHA	**1k**/C	78	111–112°; +34.1, c = 1 (ethanol)	$C_{27}H_{46}N_2O_4Si$ (490.5)

[a] Solvent: acetone/water.

[b] $[\alpha]_{578}^{20}$.

The reaction with amino acids **(13)** has been thoroughly investigated with particular attention given to the synthesis of *t*-butoxycarbonyl (Boc), 9-fluorenyloxycarbonyl (Fmoc), 2,2,2-trichloroethoxycarbonyl (Troc), and 2-(trimethylsilyl)-ethoxycarbonyl (Tmseoc) amino acids.



1h-k **13**

14

For this purpose, we used the readily accessible 1,2,2,2,-tetrachloroethyl carbonates, which are more reactive and give cleaner reactions. Due to the instability of the corresponding tetrachloroethyl carbonate, benzyloxycarbonylation is best effected by using 1-chloroethyl benzyl carbonate **(1d)**, but this reaction is not recommended because of the resulting color of the reaction medium that would be difficult to eliminate in the purification procedure. The reaction of the carbonates **1h–k** is generally carried out by employing equivalent amounts of the reagent and the amino acid dissolved in aqueous dioxane in the presence of at least two equivalents of triethylamine. The reaction mixture can also be stabilized at a constant pH by the controlled addition of sodium hydroxide. In this case, two equivalents of sodium hydroxide are generally required, the first being used for the neutralization of the released hydrogen chloride while the second contributes to the degradation of chloral to chloroform and sodium formate[7] depending on the reaction conditions. The purification procedure includes washing with ether or hexane to remove any unreacted reagent, followed by acidification and extraction of the protected amino acid with ethyl acetate or *t*-butyl methyl ether. The by-products, chloral hydrate and sodium formate, remain in the aqueous phase. Evaporation of the solvent affords the protected amino acid in pure form. Further crystallization is done in the conventional manner. In this way, a variety of amino acids were protected in satisfactory yields without racemization (Table 3). Reagents **1h–k** gave preferential amino protection rather than hydroxy protection with tyrosine or serine as it was expected from mechanistic considerations. Reagents **1h** and **1i** were effective for the protection of serine, which is not possible when using the corresponding carbonochloridate[8]. Boc-tryptophane was in some cases contaminated by traces of β-carboline, from the assumed formylation-cyclization of tryptophane with the sodium formate obtained from the base degradation of chloral. Also the α-protection of ε-benzyloxycarbonyllysine could be effected without prior purification of the ε-Z intermediate. In none of the protections investigated could be detect any trace of dipeptide by-products nor could we observe any sign of racemization.

We think that the reagents described in this paper are promising for the protection of amino groups. Generally, they give satisfactory yields and can be advantageneously compared with already known reagents, e.g., succinimidyl 9-fluorenylmethyl carbonate[8], di-*t*-butyl dicarbonate[9], or 2-butoxycarbonyloxyimino-2-phenylacetonitrile[10]. Moreover, they are prepared from simple and economical reagents and should contribute to reduce the price of amino protection on an industrial scale.

IR absorption spectra were recorded on a Beckman Acculab 4 Spectrometer, ^{1}H-NMR spectra on a Varian EM 360 A spectrometer, and optical rotation with a Perkin-Elmer Model P-141 instrument.

1,2,2,2-Tetrachloroethyl Carbonochloridate (Hood!)[1]:
Liquid phosgene (109 g, 1.1 mol) is added at 0 °C into a three-necked flask containing benzyl tributylammonium chloride (15.5 g, 0.05 mol) and equipped with a dropping funnel and a dry ice condenser to trap refluxing phosgene. Chloral (anhydrous) (147.5 g, 1.0 mol) is added slowly to the stirred mixture. After 1 h at 0 °C, ^{1}H-NMR examination of the crude mixture shows no remaining chloral. Excess phosgene is then removed by aspiration. The crude material so obtained (quantitative yield by NMR) can be used in the next step. However, distillation at low temperature (40–47 °C/4 torr) affords the pure product; yield: 173.5 g (70%).

IR (neat): $\nu = 1795\ cm^{-1}$.

^{1}H-NMR ($CDCl_3/TMS_{int}$): $\delta = 6.66$ ppm (s).

1-Chloroalkyl Carbonates (1a–k); General Procedure:
The 1-chloroalkyl carbonochloridate[1] (0.55 mol) and the required alcohol (0.5 mol) are dissolved in dichloromethane (600 ml) and cooled to 0 °C. Pyridine (0.55 mol) is then added dropwise while maintaining the temperature below 15 °C. The mixture is then stirred at room temperature until no alcohol remains in the solution as indicated by GLC or TLC analysis (generally 4–5 h). The resulting mixture is then washed with 1 normal hydrochloric acid (100 ml) then with a saturated solution of potassium carbonate (100 ml) twice with water (2 × 100 ml). The organic phase is dried with magnesium sulfate and the solvent is evaporated under reduced pressure. The resulting carbonate is then distilled in vacuo or crystallized from hexane (Table 1).

Reaction of 1-Chloroalkyl Carbonates (1) with Amines: General Procedures:
A solution of the required carbonate **1a–k** (0.1 mol) in tetrahydrofuran (20 ml) is added dropwise to a solution of the amine (0.1 mol) in tetrahydrofuran (60 ml) mixed with a 5 molar solution of potassium carbonate (40 ml) while maintaining the temperature at 5–10 °C. The mixture is then stirred at room temperature until GLC (or TLC) analysis indicates that the amine has been consumed or that there is no more reaction. The organic phase is separated, washed with a saturated solution of sodium chloride (40 ml), dried with magnesium sulfate, and concentrated under reduced pressure. The resulting carbamate is distilled under reduced pressure or crystallized from a suitable solvent (Table 2).

***N*-(*t*-Butoxycarbonyl)-aniline (7):**
Aniline (2.8 g, 0.03 mol) and 1-methylimidazole (2.5 g, 0.03 mol) are dissolved in tetrahydrofuran (30 ml). The solution is stirred at room temperature and *t*-butyl 1,2,2,2-tetrachloroethyl carbonate (**1h**; 8.5 g, 0.03 mol) is added in one portion. The mixture is stirred at room temperature for 3 h. Ethyl acetate (50 ml) is added and the organic solution is washed with cold 0.1 normal hydrochloric acid (2 × 10 ml) and with a saturated solution of sodium chloride (2 × 10 ml). The organic phase is dried with magnesium sulfate, concentrated in vacuo, and the product crystallized from petroleum ether; yield: 2.85 g (61%) of pure product; m.p. 133–134 °C (Lit.[27], m.p. 136 °C).

2-Methyl-2-(methylthio)-propanal *O*-(Methylaminocarbonyl)-oxime (12, Aldicarb):
2-Methyl-2-(methylthio)-propanal oxime (**10**; 6.65 g) is added to a mixture of 10 normal sodium hydroxide (5 ml) and of toluene (50 ml). The mixture is stirred a few minutes at room temperature and water is distilled azeotropically. The resulting suspension is cooled in an ice bath and 1-chloroethyl carbonochloridate (7.15 g) is added dropwise. The mixture is then stirred at 10–15 °C for 1 h and 40% aqueous methylamine (10 ml) is added dropwise. Stirring is continued for 1 h and the organic phase is washed with ice water

(10 ml), dried with magnesium sulfate, and the solvent evaporated to leave 8.7 g of a brown solid which is chromatographed with ethyl acetate/hexane (2/8) to give pure **12**; yield: 6.0 g (63%); m.p. 98–100°C (Ref.[14], m.p. 98–100°C); recovery of the starting oxime: 0.5 g (7.5%).

N-(*t*-Butyloxycarbonyl)-L-amino acids; General Procedures:

Method A: The amino acid (0.02 mol) is dissolved in dioxane/water (2/1; 60 ml) containing triethylamine (0.06 mol). 1,2,2,2-tetrachloroethyl *t*-butyl carbonate (**1h**; 5.7 g, 20 mmol) is added and the mixture is stirred at room temperature for 6 h. Water (50 ml) is then added and the resulting solution washed with *t*-butyl methyl ether (20 ml). The aqueous phase is acidified to pH 3 with dilute hydrochloric acid and extracted with ethyl acetate (3 × 40 ml). The combined organic phases are dried with magnesium sulfate and evaporated under reduced pressure. The residue is crystallized from ethyl acetate/petroleum ether (Table 3).

Method B: The amino acid (0.02 mol) is dissolved in dioxane/water (2/1; 60 ml) and the pH is carefully adjusted to 9.5 by the addition of 4 normal sodium hydroxide. 1,2,2,2-tetrachloroethyl *t*-butyl carbonate (**1h**; 0.022 mol) dissolved in dioxane (10 ml) is added all at once and the pH is stabilized to 9.5 by the controlled addition of aqueous 4 normal sodium hydroxide. The reaction is stopped when the sodium hydroxide uptake is over and when TLC shows no more free amino acid remaining in solution. Water (50 ml) is then added and the resulting solution washed with 20 ml of *t*-butyl methyl ether. The aqueous phase is acidified to pH 3 with dilute hydrochloric acid and extracted with *t*-butyl methyl ether (3 × 40 ml). The combined organic phases are dried with magnesium sulfate and evaporated under reduced pressure. The residue is crystallized from ethyl acetate/petroleum ether (Table 3).

N-(9-Fluorenylmethoxycarbonyl)-L-amino Acids (Fmoc-Amino Acids); General Procedure:

Method C: The amino acid (0.005 mol) is dissolved in 30% aqueous dioxane (12 ml) containing triethylamine (0.01 mol) and cooled to 0°C. 1,2,2,2-tetrachloroethyl 9-fluorenylmethyl carbonate (**1i**; 0.005 mol) dissolved in dioxane (4 ml) is added in one portion. The mixture is stirred at 0°C for 2 h, water (20 ml) is then added, and the resulting solution is washed with 20 ml of *t*-butyl methyl ether (20 ml). The aqueous phase is acidified to pH 2–3 with dilute hydrochloric acid and extracted with ethyl acetate (3 × 40 ml). The combined organic phases are dried with magnesium sulfate and evaporated under reduced pressure. The residue is crystallized from ethyl acetate/petroleum ether (Table 3).

N-(2,2,2-Trichloroethoxycarbonyl)-L-amino Acids; General Procedure:

The amino acid is treated with 1,2,2,2-tetrachloroethyl 2,2,2-trichloroethyl carbonate **1j** as described in method A (Table 3).

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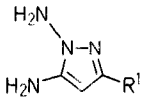
Errata and Addenda 1986

I. Ganboa, C. Palomo *Synthesis* **1986**, 52. The ^{1}H-NMR data for compounds **2d** and **2e** in the Table (p. 53) should be, respectively: 8.13 (d, 2 H_{arom}); 7.46 (d, 2 H_{arom}); 7.3 (s, 5 H_{arom}); 5.73 (m, 1 H, C–H); 5.26 (s, 2H, CH_2–$C_6H_4NO_2$); 4.9 (m, 1H, C–H); 3.7 (m, 2H, CH_2–CO–NH); 3.3 (m, 2H, S–CH_2); 2.13 (s, 3H, CH_3). 7.33 (s, 5 H_{arom}); 7.3 (s, 5 H_{arom}); 5.76 (m, 1 H, C–H); 5.2 (s, 2H, C_6H_5–CH_2); 4.9 (m, 1 H, C–H); 3.63 (s, 2 H, CH_2–CO–NH); 3.3 (m, 2H, S–CH_2); 2.13 (s, 3 H, CH_3).

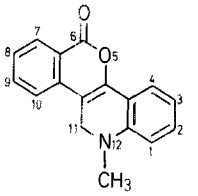
The ^{1}H-NMR data for compound **6** (p. 54) should be:
^{1}H-NMR ($CDCl_3$/TMS_{int}): δ = 8.03 (d, 2 H_{arom}); 7.43 (d, 2 H_{arom}); 5.65 (s, 1 H, CH); 5.23 (s, 2 H, CH_2); 4.5 (s, 1 H, NH); 1.53, 1.35 ppm (2 s, 6 H, 2 CH_3).

K. Tanaka, H. Yoda, K. Inoue, A. Kaji *Synthesis* **1986**, 66. The $[\alpha]_D^{25}$ value for compound **2e** in Table 1 (p. 67) should be:
$-28.2°$ (1.80).

D. R. Sliskovic, M. Siegel, Y. Lin *Synthesis* **1986**, 71. The structures for compounds **6a, b** (p. 73) should be:

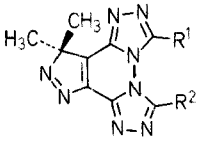


O. Meth-Cohn *Synthesis* **1986**, 76. The correct numbering for compounds **8** and **10** (p. 76) is as illustrated below for compound **10**:



10

B. Furlan, B. Stanovnik, M. Tišler *Synthesis* **1986**, 78. The double-bond arrangement of compounds **3, 6,** and **7** (pp. 78, 79) should be:

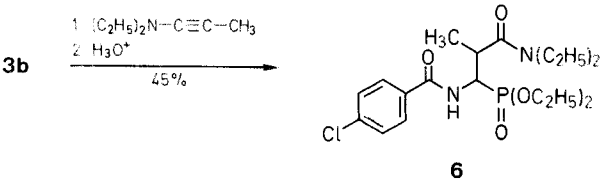


N. Petragnani, H. M. C. Ferraz, G. V. J. Silva *Synthesis* **1986**, 157. The authors wish to include the following pertinent references:
R. M. Adlington, A. G. M. Barret *Tetrahedron* **1981**, *37*, 3935.
R. M. Adlington, A. G. M. Barret *J. Chem. Soc. Perkin Trans. I* **1981**, 2848.
R. M. Adlington, A. G. M. Barret *J. Chem. Soc. Chem. Commun.* **1981**, 65.
R. M. Adlington, A. G. M. Barret *J. Chem. Soc. Chem. Commun.* **1979**, 1122.

A. J. Fatiadi *Synthesis* **1986**, 249. The heading for the first experimental procedure on p. 268 should be:
2,6-Diphenyl-4-(2,3,3-tricyanoallylidene)pyran (201)[354]:

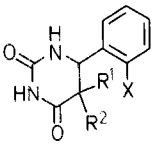
D. P. Matthews, J. P. Whitten, J. R. McCarthy *Synthesis* **1986**, 336. The headings for the first and last experimental procedures should be, respectively:
***N*^{1},*N*^{3}-Bis(2,2-dimethoxyethyl)oxaldiamidine Dihydrochloride (2):**
2-(2-Imidazolyl)-4-methoxy-4,5-dihydroimidazole (5):

T. Schrader, R. Kober, W. Steglich *Synthesis* **1986**, 372. The last equation in the formula scheme (p. 372) should be:

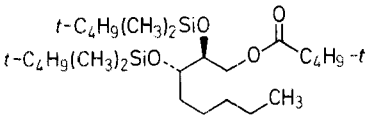


6

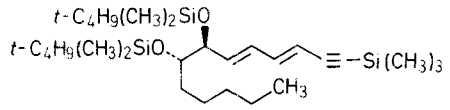
D. N. Dhar, K. S. K. Murthy *Synthesis* **1986**, 437. The heading for Table 2 (p. 440) should be:
4-Aryl-2(1*H*)-quinazolines **(13)** and 4-Aryl-1*H*-2,1,3-benzothiadiazine 2,2-Dioxides **(14)**
The names of compounds **13a** and **14a** in the experimental procedure on the same page should be corrected accordingly.
For compounds **60** and **61** (p. 445) R^3 = H, SO_2Cl.
The product in the lower, left reaction scheme on p. 446 should be:



K. C. Nicolaou, S. E. Webber *Synthesis* **1986**, 453. The structures of compounds **8** (p. 454) and **16** (p. 455) should be:



8

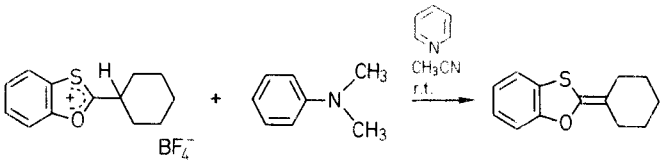


16

E. Dalcanale, M. Foà *Synthesis* **1986**, 492. In the reaction scheme, products **4** and **5** are obtained in 33 and 8%, respectively, a ratio of 80:20.

W. G. Dauben, J. M. Gerdes, G. C. Look *Synthesis* **1986**, 532. In the experimental procedure headings (p. 534), the names of compounds 3, 5, 7, and 9 should read:
(3,3-Ethylenedioxybutyl)triphenylphosphonium Bromide (3)
6-*t*-Butyldimethylsiloxy-3,7-dimethyl-1,6-octadiene (5)
5-[1,1-Bis(ethoxycarbonyl)ethyl]bicyclo[3.3.0]octan-2-one (7)
2,2-Ethylenedioxy-1,3,3-trimethylbicyclo[2.2.1]heptane (9).

S. Cadamuro, I. Degani, R. Fochi, A. Gatti, V. Regondi *Synthesis* **1986**, 544. Formula Scheme **B** should be:



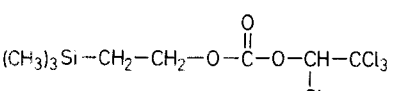
1c **2** **5**

H. M. R. Hoffmann, K. Giesel, R. Lies, Z. M. Ismail *Synthesis* **1986**, 548. The heading for the last experimental procedure (p. 551) should be:
Cycloadditions; 4-Oxatricyclo[7.2.1.0^{3,8}]dodeca-3,10-dien-2-one (11e):

Abstract 7330, *Synthesis* **1986**, 599. The structure of compound **7** should be: CH_2=C(R^6)R^7.

Abstract 7333, *Synthesis* **1986**, 600. Line 2 of the text should read: dimenthyl succinate **(1)** with lithium 2,2,6,6-tetramethylpiperidide reacts...

G. Barcelo, J. P. Senet, G. Sennyey, J. Bensoam, A. Loffet *Synthesis* **1986**, 627. The structure of compound **1k** (p. 630) should be:



D. Achet, D. Rocrelle, I. Murengezi, M. Delmas, A. Gaset *Synthesis* **1986**, 642. The last word of the title should be: **Sulfate**