A Synthesis of a New Type of Alkoxycarbonylating Reagents from 1,1-Bis[6-(trifluoromethyl)benzotriazolyl] Carbonate (BTBC) and Their Reactions[1]

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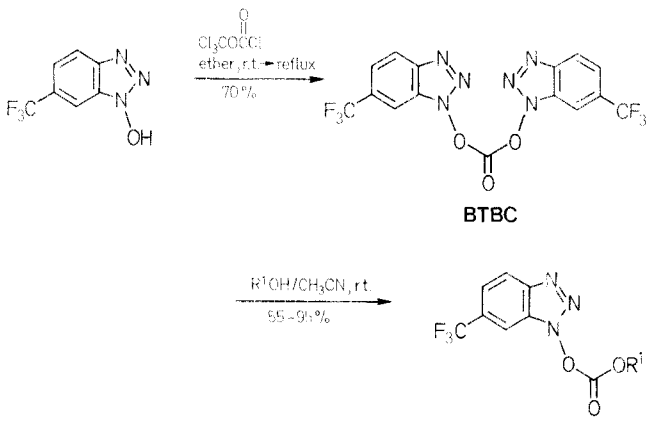
1,1'-Bis[6-(trifluoromethyl)benzotriazolyl] carbonate (BTBC) was prepared from 1-hydroxy-6-trifluoromethylbenzotriazole and trichloromethyl chloroformate (trichloromethyl carbonochloridate). The reaction of BTBC and alcohols afforded the corresponding active carbonates which were converted into the corresponding carbamates and carbonates.

Several alkoxycarbonylating reagents for amino groups having heterocyclic leaving groups such as *N*-hydroxyimide have been reported.[2-4] Recently, we also have reported on the utility and versatility of carbonates and oxalates containing an electron withdrawing group such as *N*-hydroxyimide and benzotriazole derivatives as reagents for various transformations.[2] Surprisingly, however, the alkoxycarbonylating reagents for alcohols are scanty, with the exception of alkoxycarbonyl chloride.

Recently we found that 1-alkoxy[6-(trifluoromethyl)benzotriazolyl] carbonates **1a–f** easily derived from 1,1-bis[6-(trifluoromethyl)benzotriazolyl] carbonate (BTBC) show high acylating reactivity towards alcohols as well as amino groups. In this paper, we wish to report on the preparation and reactions of novel alkoxycarbonylating agents **1a–g** (Scheme A).

BTBC was easily prepared from 6-trifluoromethyl-1-hydroxybenzotriazole and trichloromethyl chloroformate in dry ether and was easily purified by washing with dry ether and can be stored for several months in a freezer.

BTBC was allowed to react with primary alcohols in acetonitrile at room temperature to give stable but active carbonates **1a–f**.

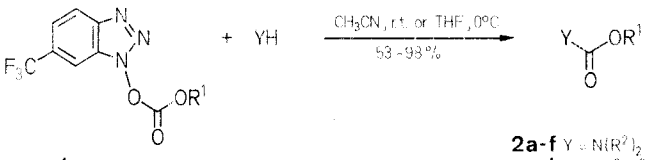


Scheme A

The carbonates could be easily purified by washing with 4% sodium bicarbonate solution and by crystallization of crude products. The structure was confirmed by MS as well as ^{1}H-NMR-spectra (Table 1). *t*-Butyl alcohol and *p*-anisyl alcohol failed to react with BTBC.

The utility of the reagents **1a–f** was demonstrated in the preparation of carbamates **2a–f** of carbonates **2g–l**. Thus, as anticipated, the reactive carbonates **1a–g** were attacked by the hydroxy group of primary alcohol under the same conditions.

Thus, the active carbonates **1a–f** were treated with amines and alcohols to give the carbamates **2a–f** or carbonates **2g–l**, respectively. The syntheses of carbamates **2a–f** and carbonates **2g–l** were carried out in acetonitrile at room temperature, or in tetrahydrofuran at 0 °C, respectivity (Scheme **B**). The alkoxycarbonylation of 2-pyrrolidinemethanol afforded only the *N*-alkoxycarbonylated compound **2b**. In the case of alkoxycarbonylation of alcohols, the reaction was carried out in the presence of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (Table 2).



Carbamates **2a–f** and carbonates **2g–l** were readily formed by the nucleophilic attack of amino or hydroxy groups of amines and alcohols on the carbonyl group of active carbonates **1** because of the presence of electron withdrawing trifluoromethylbenzotriazolyl group.

In summary, we were able to show that as excepted, the esterification with 6-trifluoromethylbenzotriazole esters gave rise to desired products in higher yield than active esters bearing benzotriazole or chlorobenzotriazole. The higher reactivity of the 6-trifluoromethylbenzotriazole ester must be associated with the strong electron withdrawing effect of 6-trifluoromethyl group.

1,1'-Bis[6-(trifluoromethyl)benzotriazolyl] Carbonate (BTBC):
To a stirred solution of 1-hydroxy-6-trifluoromethylbenzotriazole[2] (20.3 g, 0.1 mol) in dry ether (700 ml) is added trichloromethylchloroformate (5.34 g, 0.025 mol) at room temperature. After 10 min, a further quantity of trichloromethyl chloroformate (5.34 g, 0.025 mol) is added to the mixture, refluxed gently for 1 h, and the precipitate formed is collected and washed with dry ether. Almost pure crystals of BTBC are obtained; yield: 15.1 g (70%); m.p. 138–143 °C.

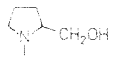
$C_{15}H_6F_6N_6O_3$	calc.	C 41.65	H 1.28	N 19.44
(432.2)	found	41.67	1.46	19.40

Table 1. Active Carbonates **1a–f** Prepared

Product	R^1	Yield (%)	m.p. (°C) (solvent)	Molecular Formula[a]	IR (KBr) $\nu_{C=O}$ (cm^{-1})	^{1}H-NMR (Solvent/TMS) δ (ppm)	MS (m/z M^+)
1a	$C_6H_5CH_2$	55	153–155	$C_{15}H_{10}F_3N_3O_3$	1750	$CDCl_3$: 5.50 (s, 2H, $C_6H_5CH_2$); 7.34 (s, 5H, C_6H_5); 7.67–8.00 (m, 3H$_{arom}$)	337
1b	Cl_3CCH_2	56	164–165 ($CHCl_3$/ether)	$C_{10}H_5Cl_3F_3N_3O_3$ (378.5)	1760	$CDCl_3$: 5.09 (s, 2H, CH_2); 7.80–8.40 (m, 3H$_{arom}$)	378.5
1c	$H_2C{=}CHCH_2$	78	140–143 (acetone/ether)	$C_{11}H_8F_3N_3O_3$ (287.2)	1755	Aceton-d_6: 4.97 (d, 2H, J = 8.0 Hz, $CH_2CH{=}CH_2$); 5.20–5.64 (m, 2H, $CH{=}CH_2$); 5.69–6.28 (m, 1H, $CH{=}CH_2$); 7.61–8.36 (m, 3H$_{arom}$)	287
1d	$(CH_3)_2CHCH_2$	77	187.5–189.5 ($CHCl_3$/ether)	$C_{12}H_{12}F_3N_3O_3$ (303.2)	1760	$CDCl_3$: 1.06 [d, 6H, J = 6.2 Hz, $(CH_3)_2CH$]; 1.81–2.45 [m, 1H, $(CH_3)_2CH$]; 4.28 (d, 2H, J = 6.2 Hz); CH_2); 7.6–8.41 (m, 3H$_{arom}$)	303
1e	$CH_3SCH_2CH_2$	78	115–116 Cacetone/ether)	$C_{11}H_{10}F_3N_3O_3S$ (321.3)	1770	Aceton-d_6: 2.22 (s, 3H, SCH_3); 3.00 (t, 2H, J = 6.2 Hz, SCH_2CH_2O); 5.74 (t, 2H, J = 6.2 Hz, SCH_2CH_2O); 6.99–8.63 (m, 3H$_{arom}$)	321
1f	9-Fluorenylmethyl	95	190–193 (acetone/ether)	$C_{22}H_{14}F_3N_3O_3$ (425.4)	1750	$CDCl_3$: 4.43 (m, 1H, H – 9); 4.90 (d, 2H, J = 6.4 Hz, CH_2); 7.20–8.33 (m, 11H$_{arom}$)	425

[a] Satisfactory microanalyses obtained: C ± 0.25, H ± 0.29, N ± 0.14.

Table 2. Compounds **2a–l** Prepared

Product	R^1	Y	Yield (%)	m.p. (°C) (solvent)	Molecular Formula[a] or Lit. m.p. (°C)	IR (KBr) $\nu_{C=O}$ (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ (ppm)	MS (*m/z*, M^+)
2a	$C_6H_5CH_2$	*i*-$C_3H_7CH(CO_2CH_3)NH-$	95	oil[b]	m.p. 54–55	1730	0.90 [q, 6H, J = 4.0 Hz, $(CH_3)_2CH$]; 2.13–2.33 [m, 1H, $(CH_3)_2CH$]; 4.22 (q, 1H, J = 4.0 Hz, NH(H); 5.48 (br, 1H, NH); 5.05 (s, 2H, $C_6H_5CH_2$); 7.27 (s, 5H, C_6H_5)	265
2b	$C_6H_5CH_2$		95	oil	$C_{13}H_{17}NO_3$ (235.3)	1700	1.44–2.35 (m, 4H, CH_2CH_2); 2.95–4.30 (m, 6H, CH_2NCHCH_2OH); 5.11 (s, 2H, $C_6H_5CH_2$); 7.30 (s, 5H, C_6H_5)	235
2c	Cl_3CCH_2	$C_6H_5CH_2NH-$	64	83–84 (ether)	$C_{10}H_{10}Cl_3NO_2$ (282.6)	1720	4.42 (d, 2H, J = 6.2 Hz, CH_2NH); 4.76 (s, 2H, CH_2); 5.24 (m, 1H, NH); 7.29 (s, 5H, C_6H_5)	282.5
2d	$H_2C=CHCH_2$	$C_6H_5CH_2CH(CO_2C_2H_5)NH-$	97	oil[c]	$C_{15}H_{19}NO_4$ (277.3)	1730	1.21 (t, 3H, J = 6.6 Hz, CH_2CH_3); 3.10 (d, 2H, J = 6.0 Hz, $C_6H_5CH_2$); 4.15 (q, 2H, J = 6.6 Hz, $CH_2(CH_3)$; 4.40–4.60 (m, 2H, CH_2OCO); 4.67 (brt, 1H, NHCH); 5.08–5.40 (m, 3H, $CHCH_2$, NH); 5.67–6.13 (m, 1H, CH_2CH); 7.27 (m, 5H, C_6H_5)	277
2e	$CH_3SCH_2CH_2$	$C_6H_5CH_2NH-$	80	oil	$C_{11}H_{15}NO_2S$ (225.3)	1700	2.13 (s, 3H, CH_3); 2.66 (t, 2H, J = 6.6 Hz, SCH_2); 4.21 (t, 2H, J = 6.6 Hz, CH_2, CH_2OCO), 4.29 (d, 2H, J = 5.2 Hz, CH_2NH); 5.02 (br s, 1H, NH); 7.21 (s, 5H, C_6H_5)	225
2f	9-Fluorenyl-methyl	$C_2H_5O_2CCH_2NH-$	98	105–107 (ether)	105–110[c]	1700	1.29 (t, 3H, J = 7.2 Hz, CH_2CH_3); 3.54; 3.54, 4.54 (m, 7H, 9-H, CH_2OCO, CH_2CO, CH_2CH_3); 5.35 (br, 1H, NH); 7.00–7.76 (m, 8H_{arom})	325
2g	$C_6H_5CH_2$	2-Furylmethyl	95	oil	$C_{13}H_{12}O_4$ (232.2)	1730	5.10, 5.13 (2 s, 2 × 2H, CH_2, $C_6H_5CH_2$); 6.25–6.48 (m, 2H, furfuryl H-3, H-4); 7.27–7.47 (m, 6H, C_6H_5, furfuryl H-5)	232
2h	$C_6H_5CH_2$	$H_3CCH=CHCH_2O$	68	oil	$C_{12}H_{14}O_3$ (206.2)	1750	1.67 (d, 3H, J = 5.2 Hz, CH_3); 4.49 (d, 2H, J = 5.2 Hz, OCH_2); 5.08 (s, 2H, $C_6H_5CH_2$); 5.50–6.00 (m, 2H, $CH=CH$); 7.25 (s, 5H, C_6H_5)	206
2i	Cl_3CCH_2	$H_3CCH=CHCH_2O$	53	oil	$C_7H_9Cl_3O_3$ (247.5)	1762	1.73 (d, 3H, J = 6.0 Hz, CH_3); 4.64 (d, 2H, J = 6.0 Hz, CH_2CH); 4.77 (s, 2H, CH_2O); 5.32–6.16 (m, 2H, $CH=CH$)	247.5
2j	$H_2C=CHCH_2$	2-Furylmethyl	58	oil	$C_9H_{10}O_4$ (182.2)	1748	5.64–6.21 (m, 5H, $CH_2=CHCH_2O$); 6.24–6.54 (m, 2H, furfuryl H-3, H-4); 7.34–7.47 (m, 1H, furfuryl H-5)	182
2k	$H_2C=CHCH_2$	—[d]	74	oil	$C_{14}H_{22}O_3$ (238.3)	1740	1.60 (s, 3H, $C-CH_3$); 1.67, 1.72 [2s, 2 × 3H, $C(CH_3)_2$]; 2.01–2.12 (m, 4H, CH_2CH_2); 4.60–4.64 (m, 2H, $CH_2=CHCH_2$); 4.66 (d, 2H, J = 8.0 Hz, $OCH_2CH=$); 5.24–5.28, 5.33–5.39 (2m, 1H each, $CH_2=CH-CH_2$); 5.05–5.10, 5.35, 5.41 (m, 2H, 2x $=CH$); 5.89–6.00 (m, 1H, $CH_2=CHCH_2O$)	238
2l	C_2H_5	—[d]	74	oil	$C_{13}H_{22}O_3$ (226.3)	1740	1.29 (t, 3H, J = 7.0 Hz, CH_2CH_3); 1.58 (s, 3H, CCH_3); 1.67, 1.70 [2s, 3H each, $C(CH_3)_2$]; 2.00–2.13 (m, 4H, CH_2CH_2); 4.18 (q, 2H, J = 7.0 Hz, CH_2CH_3); 4.63 (d, 2H, J = 7.2 Hz, $OCH_2CH=$); 5.04–5.09, 5.34–5.40 (m, 2H, 2x $=CH$)	

[a] Satisfactory microanalyses obtained: C ±0.30, H ±0.25, N ±0.21.
[b] $[\alpha]_D^{24} = -17.7°$ (c = 1.1 ethanol); Lit.[5] $[\alpha]_D^{20} = -18.9°$ (c = 1, methanol).
[c] $[\alpha]_D^{24} = -3.8°$ (c = 1.7, ethanol).
[d] $(CH_3)_2C=CH(CH_2)_2C(CH_3)=CHCH_2O-$

IR (KBr): ν = 1830, 1815 (C=O); 1605 cm^{-1} ($C=C_{arom}$).

^{1}H-NMR (Acetone-d_6): δ = 7.50–8.45 ppm (H_{arom}).

MS: m/z = 432 (M^+).

1-Alkoxy[6-(trifluoromethyl)benzotriazolyl] Carbonates 1a–f; General Procedure:

A solution of alcohol (3.5 mmol) in acetonitrile (2 ml) is added to BTBC (1.3 g, 3.0 mmol) in acetonitrile (150 ml) under stirring at room temperature. After 24 h the mixture is evaporated *in vacuo*, the residue is washed with aqueous sodium hydrogen carbonate (20 ml) and the precipitate is collected. The dried precipitate is recrystallized from appropriate solvent (Table 1).

Carbamates 2a–f and Carbonates 2g–l; General Procedure:

A mixture of active carbonate (**1**, 1 mmol and the appropriate amino compound (1 mmol) in acetonitrile (15 ml) or the appropriate alcohol (1 mmol) with DMAP (**1** mmol) in tetrahydrofuran is stirred at room temperature or at 0°C respectively. After 24 h, the mixture is evaporated and ethyl acetate (150 ml) is added to the residue. The organic layer is washed with 4% aqueous sodium hydrogen carbonate (80 ml), 0.5 normal hydrochloric acid (80 ml) and saturated brine (80 ml) and the solvent evaporated. The residue is purified by TLC on silica gel plates to afford the carbamates **2a–f** and carbonates **2g–l**.

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(1) This constitutes Part XIII of a series entitled *Studies on Activating Methods of Functional Groups*. Part XII: Takeda, K., Tsuboyama, K., Suzuki, A., Ogura, H. *Chem. Pharm. Bull.* **1985**, *33*, 2545.

(2) Ogura, H., Kobayashi, T., Shimizu, K., Kawabe, K., Takeda, K. *Tetrahedron Lett.* **1979**, 4745.
Ogura, H., Takeda, K. *Nippon Kagaku Kaishi* **1981**, 836.
Ogura, H., Sato, O., Takeda, K. *Tetrahedron Lett.* **1981**, *22*, 4817.
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Takeda, K., Akagi, Y., Saiki, A., Tsukahara, T., Ogura, H. *Tetrahedron Lett.* **1983**, *24*, 4569.
Takeda, K., Sawada, I., Suzuki, A. *Tetrahedron Lett.* **1983**, *24*, 445.

(3) Takeda, K., Tsuboyama, K., Yamaguchi, K., Ogura, H. *J. Org. Chem.* **1985**, *50*, 273.

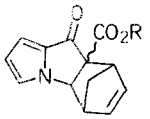
(4) Bodanszky, M., Klausner, Y.S., Ondetti, M.A. *Peptide Syntheses*, Wiley, New York 1976, p. 18.

(5) Miyoshi, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1489.

(6) Carpino, L.A., Ham, G.Y. *J. Org. Chem.* **1972**, *37*, 3404.

Errata and Addenda 1987

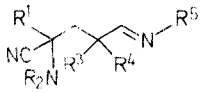
Hall, G., Sugden, J.K., Waghela, M.B.
Page 10. Line 3 of the Abstract should read: dropyrolizines ...
Page 14. The first word of Section 3.11. should be: Benzo[*b*]pyrrolizines.
Page 15. Formula **27** should be:



27

Page 15. The product referred to in Section 4.6., lines 4–5, should be: 10*H*-pyrrolizino[1,2-*b*]quinoline
Page 17. In Section 7., line 4 of the second paragraph should read: **34**.[182] ...

Ahlbrecht, H., von Daacke, A.
Page 24. Formula **8** should be:



8

Costisella, B., Keitel, I.
Page 45. In the heading of the experimental procedure, **6** should read **3** and **8** should read **7**.

Stoss, P., Merrath, P., Schlüter, G.
Page 174. Numbers 1 and 3 should be exhanged in formula **2a–f**.

Singh, G., Deb, B., Ila, H., Junjappa, H.
Page 286. Compounds **1** are 2-aroyl-2-arylthioketene dithioacetals.

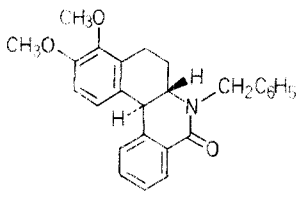
Asaad, F.M., Becher, J., Møller, J., Varma, K.S.
Page 301. Under the reaction scheme, the X group in compounds **3b,d** and **4b,d** should be $CO_2C_2H_5$.

Legrel, P., Baudy-Floc'h, M., Robert, A.
Page 306. The title should read: A One-Pot Synthesis of α-Halohydrazides from 2,2-Dicyanooxiranes.
Page 306. In the table under the reaction scheme, the second heading R^1 should be R^2.

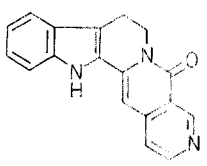
van der Goorbergh, J.A.M., van der Steeg, M., van der Gen, A.
Pages 314–317. The systematic names for the heterocycles involved are: 4,5-dioxo-3,4-dihydro-2*H*,5*H*-thiopyrano[3,2-*c*][1]benzopyrans **4** (RF 24756), 4,5-dioxo-2*H*,5*H*-thiopyrano[3,2-*c*][1]benzopyrans **7** (RF 24756), and 4,5-dioxo-1,3,4,4a,5,10b-hexahydro-2*H*-[1]benzopyrano[4,3-*b*]pyridines **8** (RF 24539).

Attanasi, O.A., Filippone, P., Santensanio, S., Serra-Zanetti, F.
Page 382. In the table under the reaction scheme, R^3 for **1b** should be $CO_2C_2H_5$ and R^3 for **1c** should be CO_2CH_3.

Campbell, A.L., Lenz, G.R.
Pages 428 and 446. Formulae **95** and **298** should be:



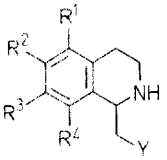
95



298

Page 437. The heading for Table 3 should be: Intermolecular ...

Pelletier, J.C., Cava, M.P.
Page 476. Formula **1a–m** should be:



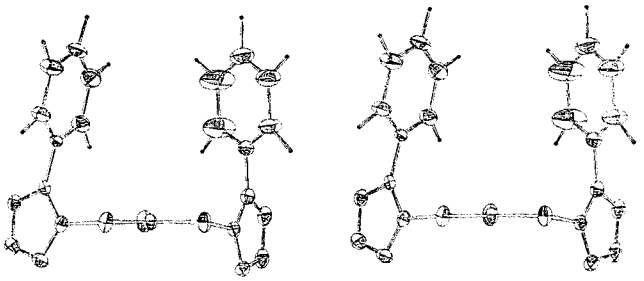
1a-m

L'abbé, G.
Page 528. Compound **45** should be named: 3-(2-pyridyl)-2,4-dithioxo-3,4-dihydro-2*H*-pyrido[1,2-*a*][1,3,5]triazine (RF 9177).

Evans, R.D., Schauble, J.H.
Page 551. Compounds **10** and **11** are tricyclo[2.2.1.0^{2,6}]heptane derivatives.

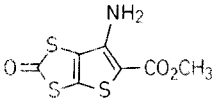
Takeda, K., Tsuboyama, K., Hoshino, M., Kishino, M., Ogura, H.
Page 559. The Y-group for **2g** and **2j** should be furfuryloxy.

Takeda, K., Tsuboyama, K., Takayanagi, H., Ogura, H.
Page 560. The following figure should appear after the 4th paragraph:



Eicher, T., Stapperfenne, U.
Page 625. Compounds **13a,b** are 6,7-dihydrofuro[2,3-*b*]pyridines (RF 7431), and compounds **15a,b** are 1,4-dihydrocyclopentimidazoles (RF 5892).

Dölling, W., Augustin, M., Ihrke, R.
Page 655. Formula **6** should be:



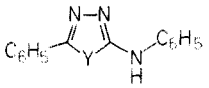
6

Mikołajczyk, M., Bałczewski, P.
Page 661. The second paragraph of ref. 21 should be ref. 22; refs. 22 and 23 should be 23 and 24, respectively.

Rösch, W., Regitz, M.
Page 692. Compounds **21a,b** are 2*H*-1,2,3-diazaphospholes.

Tietze, L.-F., Brumby, T., Pretor, M.
Page 702. Compounds **8** and **9** are 4a,10b-dihydro-4*H*,5*H*-pyrano[3,4-*c*][1]benzopyran-2-carboxylic esters.

Wamhoff, H., Zahran, M.
Page 877. Formula **18a,b** should be:



18a,b

Castaldi, G., Giordano, C.
Page 1039. The target compounds **3** are 1-bromoalkyl aryl ketones.