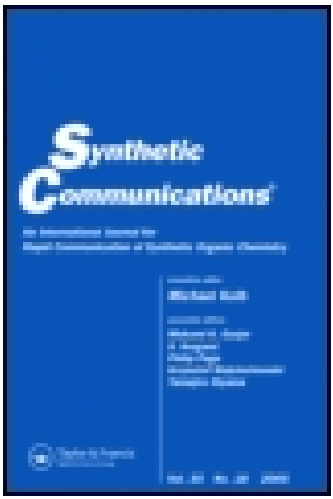

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A Simple Method for the Synthesis of Carbamates

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A SIMPLE METHOD FOR THE SYNTHESIS OF CARBAMATES

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Abstract:A new method for carbamate synthesis using aryl and alkylamines with sodium hydride and diethylcarbonate in dry benzene is described .

Carbamate derivatives are known to have pesticide[1] , insecticide[2], antibiotic[3], and other pharmacological properties. They also are useful intermediates in the synthesis of polyurethanes[4]. In connection with our studies on structure-biological-activities-relationships and synthetic methods, we now report here an alternative method for the synthesis of N-aryl and N-alkylcarbamates starting from readily available chemicals.

The preparation of carbamates has been acomplished in many ways. Among some important synthetic methods, are the reaction of: carbamyl chloride with an alcohol or metal alkoxide[5] and the reaction of cyanogen chloride or gaseous cyanic acid with an alcohol[6].

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Other well know methods reported are the reaction of a chloroformate with ammonia[7]; from isocyanate[8]; reaction of amide with lead tetra-acetate[9]; from isonitriles[10]; from cyanates with organic halides[11]; reductive carbonylation of aromatic nitro compounds with $Ru_3(CO)_{12}$ or $Ru(CO)_3(PPh_3)_2$ and methanol[12]; enzymatic oxidative convertion of thio to oxo by Baker's Yeast[13]; from azides[13] ; an alcohol with trichloroacetyl isocyanate[14]; amines and alkylhalides employing a solid liquid phase-transfer technique[15]; etc. One of them, reported by Porta[16], used aliphatic amines with diethylcarbonate and catalyzed the transformation with different Lewis acids. However, this method could not be extended to the synthesis of N-arylcarbamates.

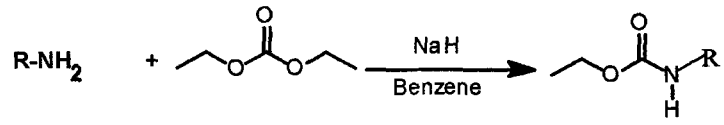
EXPERIMENTAL

General Method:

Sodium hydride (50 % in mineral oil) was added to a mixture of the amine (0.1mol) and freshly distillate diethylcarbonate (0.12 mol) in dry benzene (50 ml); the mixture to was vigorously stirred at room temperature for 1 h and then refluxed until the amine has reacted (t.l.c.) . The reaction mixture was treated with a water/ethanol mixture (1:1) (50 ml) and filtered through Celite, follow by washing of the Celite cake with ethanol, the combinated filtrate and washes were evaporated under reduced pressure (rotatory evaporator) . The residue was extracted with ethyl acetate(3 X 50 ml) and the organic extracts were dried with anhydrous sodium sulfate and concentrated to give a residue. The final purification of the product was accomplished by column chromatography (silica gel; *n*-hexane/ ethylacetate 60/40) which furnished the products.

The results are summarized in the table . Melting points were obtained on a Fisher Apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 283 and Nicolet FT 55K. The proton nuclear magnetic resonance

TABLE



R	Time (h)	Yield (%)	mp(°C)lit or Molecular Formula
4-(1-Pyrroyl)phenyl	*2.5*	*80*	135-136, $C_{13}H_{14}N_2O_2$[a]
4-Acetylphenyl	*1.5*	*80*	151-153 [17]
3-Chlorophenyl	*1.5*	*93*	oil [18]
4-Bromophenyl	*6.0*	*68*	oil [19]
3-Iodophenyl	*8.0*	*95*	oil, $C_9H_{10}NO_2I$ [b]
4-Methoxyphenyl	*5.0*	*57*	65-68 [20]
4-Cyclohexylphenyl	*15.0*	*83*	125-128, $C_{15}H_{21}NO_2$[c]
4-Nitrophenyl	*2.0*	*46*	108-110, [21]
4-n-Butylphenyl	*6.0*	*85*	oil, $C_{13}H_{19}NO_2$[d]
3,5-Dimethoxyphenyl	*13.0*	*47*	79-81, $C_{11}H_{15}NO_4$[e]
4-Hydroxyphenyl	*2.5*	*85*	110-112 [22]
n-Octyl	*1.0*	*78*	oil, [23]
n-Hexyl	*1.5*	*80*	oil, $C_9H_{18}NO_2$[f]
Cyclohexyl	*1.0*	*55*	oil [24]
n-Butyl	*1.0*	*70*	oil [25]

Elemental Analyses: calc. a) C 68.81, H 6.13, found C 68.76, H 6.10; b) C 37.12, H 3.46, found C 37.05, H 3.41; c) C 72.83, H 8.56, found C 72.53, H 8.50; d) C 70.54, H 8.66, found C 70.48, H 8.60; e) C 58.66, H 6.71, found C 58.62, H 6.67; f) C 62.74, H 10.54, found C 62.69, H 10.52.

spectra were recorded on a Varian FT-80, 80 MHz spectrometer. Mass spectra were recorded on a Shimadzu GCMS-2000A and HP 5995 at 70 eV. The UV spectra were recorded on a Perkin Elmer 552 spectrophotometer, using ethanol as solvent.

[4-(1-Pyrroyl)phenyl]carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz), δ (ppm), 7.35(m, 4H), 7.0(dd, 2H-Hα pyrrole), 6.6 (brs, 1H, NH), 6.25(dd, 2H, Hβ pyrrole), 4.25(q, 2H, CH_2), 1.30(t , 3H). IR (KBr): 3318, 1703 cm^{-1}. MS m/z(%), M^+: 230(100), 202 [M^+-C_2H_4](18), 184 [202- H_2O](40), 157 [M^+-$C_3H_5O_2$](73).

(4-Acetylphenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz), δ (ppm) 7.70(dd, 4H), 6.80(brs, 1H,),6.50 (brs, 1H, N-H), 4.25(q, 2H), 2.3(s , 3H). 1.25(t, 3H). IR (KBr): 3305, 2890, 1725 cm^{-1}. MS m/z(%), M^+: 207(67), 192 [M^+-CH_3](100). UV λ_{max} 202 nm (Log ε= 4.33), λ_{max} 210 nm (Log =3.95), λ_{max} 285 nm (Log ε=4.08).

(3-Chlorophenyl) carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$-DMSO, 200 MHz) δ (ppm), 7.8 (m, 1H), 7.35 (m, 3H), 6.8 (brs, 1H, NH), 4.30 (q, 2H), 1.3 (t, 3H). IR (film): 3350, 2985, 1700 cm^{-1}. MS m/z (%) M^+: 199 (62), (100), 126 [M^+-$C_3H_5O_2$](100).

(4-Bromophenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz), δ (ppm) 7.7(m, 1H), 7.2(m, 3H), 6.75(brs, 1H, NH), 4.25(q, 2H), 1.3(t, 3H). IR (film $CHCl_3$): 3300, 2900, 1715 cm^{-1}. MS m/z(%), M^+: 243(70), 171 [M^+-$C_3H_5O_2$](100). UV λ_{max} 237 nm (Log ε= 4.086), λ_{max} 257 nm (Log ε=2.938), λ_{max} 285 nm (Log ε= 4.44).

(3-Iodophenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz), δ (ppm) 7.8(m, 1H), 7.35(m, 2H), 6.95 (m, 1H), 6.60(brs, 1H, NH), 4.2(q, 2H), 1.3(t, 3H). IR (film $CHCl_3$): 3320, 3100, 2900, 1710 cm^{-1}. MS m/z(%), M^+: 291(87), 92 (100). UV λ_{max} 228 nm (Log ε =2.98), λ_{max} 278 nm (Log ε = 4.345),.

(4-Methoxyphenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz),δ (ppm) 7.10(dd, 4H), 6.4(brs, 1H, NH), 4.15(q, 2H), 3.8 (s , 3H). 1.30 (t, 3H). IR (KBr): 3105, 2800, 1700 cm^{-1}. MS m/z(%), M^+: 195 (51.1), 167 [M^+-C_2H_4](20). 122 [M^+-$C_3H_5O_2$](100) . UV λ_{max} 287 nm (Log ε= 3.28), λ_{max} 238 nm (Log ε =4.58), λ_{max} 202 nm (Log ε=4.26).

(4-Cyclohexylphenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz),δ (ppm) 7.2(dd, 4H), 6.4(brs, 1H, NH), 4.20 (q, 2H), 2.3 (m , 1H). 1.30(m, 13H). IR (KBr): 3330, 2910, 1700 cm^{-1}. MS m/z(%), M^+: 247 (100), 218 [M^+-C_2H_5](10). 91(23) . UV λ_{max} 235 nm (Log ε= 4.35), λ_{max} 202 nm (Log ε =3.89).

(4-Nitrophenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz), δ (ppm)7.85(dd, 4H), 6.9(brs, 1H, NH), 4.25(q, 2H), 1.30(t, 3H). IR (KBr): 3390, 2995, 1740 cm^{-1}. MS m/z(%), M^+: 210 (100), 165 [M^+-C_2H_5O](10) . UV λ_{max} 315 (Log ε = 4.0), λ_{max} 217 nm (Log ε = 3.85), λ_{max} 202 nm (Log ε =3.82).

(4-Butylphenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz), δ (ppm)7.20(dd, 4H), 6.45(brs, 1H, NH), 4.20(q, 2H), 2.52 (t , 2H). 1.25 (m,7H), 0.9 (t, 3H). IR (film) : 3320, 2920, 1710 cm^{-1}. MS m/z(%), M^+: 221 (36.6), 178 [M^+-C_3H_8](100). UV λ_{max} 210 nm (Log ε= 4.19), λ_{max} 235 nm (Log ε =4.42).

(3,5-Dimethoxyphenyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 80 MHz), δ (ppm), 6.65(brs, 1H, NH), 6.55(d, 2H), , 6.15(t, 1H), 4.2 (q, 2H), 3.75 (s,6H), 1.25(t, 3H). IR (film) : 3498, 2920, 1720 cm^{-1}. MS m/z(%), M^+: 225 (100), 180 [M^+-$C_2H_5O_2$](10) . UV λ_{max} 240 nm (Log ε = 9.44), λ_{max} 212 nm (Log ε =4.62).

(4-Hydroxyphenyl) carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$-DMSO, 200 MHz) δ (ppm), 8.35 (brs, 1H, OH), 7.34 (brs, 1H, NH), 6.90 (dd, 4H), 4.18 (q, 2H), 1.3 (t, 3H) . IR, (KBr) 3342, 3303, 3031, 2924, 1703 cm^{-1}. MS m/z(%), M^+: 181 (50), 163 [M^+-C_2H_4](20), 135 , 108 (100) .

n-Octylcarbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 200 MHz), δ (ppm) 4.65 (

brs, 1H, NH), 4.10 (q, 2H), 3.15 (q, 2H), 1.48 (m, 2H), 1.25 (m, 13H), 0.85 (t, 3H). IR (film) : 3328, 2925, 1700 cm^{-1}. MS m/z(%), M^+:201 (6), 102 (100).

n-Hexylcarbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 200 MHz),δ (ppm) 4.60 (brs, 1H, NH), 4.05 (q, 2H), 3.10 (q, 2H), 1.40 (m, 2H),1.20 (m, 9H), 0.85 (t, 3H). IR (film) : 3331, 2955, 1699 cm^{-1}. MS m/z(%), M^+: 173 (5), 102 (100).

(4-Cyclohexyl)carbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 200 MHz), δ (ppm)4. 5 (brs, 1H, NH), 4.3 (q, 2H), 1.7 (m, 11 H), 1.1 (t, 3H). IR (film) : 3300, 2985, 1700 cm^{-1}. MS m/z(%), M^+: 171 (15), 126 (100) .

n-Butylcarbamic acid ethyl ester: ^{1}H-NMR ($CDCl_3$, 200 MHz), δ (ppm) 4.62 (brs, 1H, NH), 4.05 (q, 2H), 3.10 (q, 2H), 1.40 (m, 2H),1.20 (m, 5H), 0.85 (t, 3H). IR (film) : 3331, 2955, 1699 cm^{-1}. MS m/z(%), M^+:145 (8), 102 (100) .

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