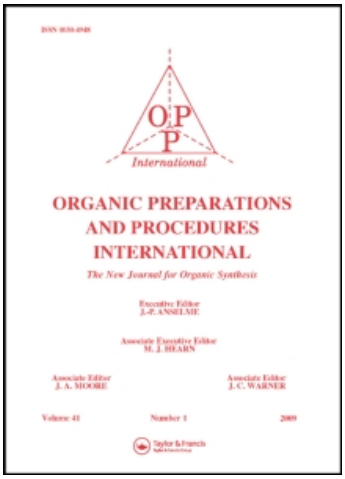

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Desroses, Matthieu , Laconde, Guillaume , Depreux, Patrick and Hénichart, Jean-Pierre(2004) 'SYNTHESIS OF UNSYMMETRICAL DIALKOXY QUINAZOLINES', Organic Preparations and Procedures International, 36: 5, 445 — 452
To link to this Article: DOI: 10.1080/00304940409356628
URL: http://dx.doi.org/10.1080/00304940409356628

ORGANIC PREPARATIONS AND PROCEDURES INT., 36 (5), 445-452 (2004)

SYNTHESIS OF UNSYMMETRICAL DIALKOXY QUINAZOLINES

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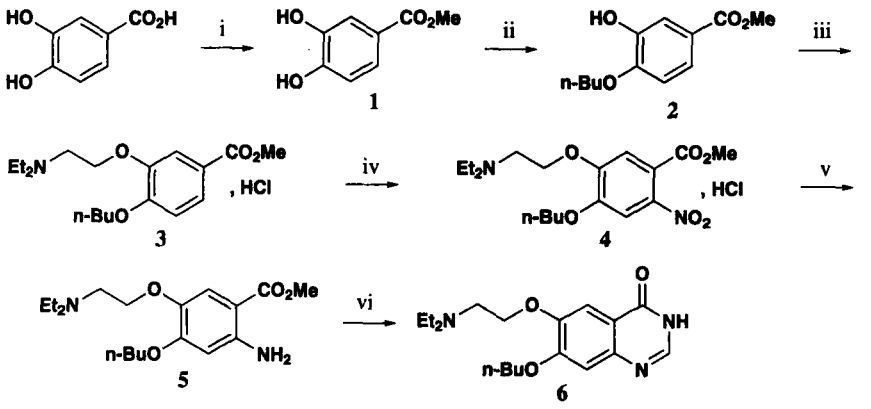
Quinazoline-derived compounds are gaining greater importance and wider use, mainly as the result of their applications in medicinal chemistry. For example, several quinazolines derivatives have been examined as inhibitors of a variety of transmembrane growth factor receptors,[1,2] or as inhibitors of farnesyl protein transferase,[3] in order to find some new method for the treatment of human cancer. They have also been developed as inhibitors of NF-κB activation[4] as a potential method for treating inflammatory diseases. Although this class of compounds is widely exploited, only few derivatives bear different ether side-chains at the 6- and 7-positions of the quinazoline ring. Furthermore, to our knowledge, different ethers of the phenolic groups of catechols[5] and more specifically of dihydroxyquinazolines derivatives are not well documented. Herein, we present an efficient route to quinazolines bearing different substituents, such as *n*-butoxy- and diethylaminoethoxy- groups at the 6- and 7-positions of the quinazoline ring *(Scheme 1)*.



i) $SOCl_2$, MeOH, reflux; ii) K_2CO_3, *n*-C_4H_9I, acetone; iii) K_2CO_3, $Et_2N(H_2C)_2Cl$•HCl, acetone, reflux; iv) HNO_3 (100%), $SnCl_4$, CH_2Cl_2, –25°C; v) $SnCl_2$, conc. HCl, 100°C; vi) $HCOONH_4$, $HCONH_2$, 140°C

Scheme 1

Commercially available 3,4-dihydroxybenzoïc acid was converted to its methyl ester **1** in quantitative yield.[6] Various procedures for the Williamson's reaction were then investigated to monoalkylate the hydroxy group of **1** *para* to the ester. Attempt using a solid-liquid phase-transfer system with polyethylene glycol (PEG) as phase-transfer agent, in dioxane under reflux and $NaHCO_3$ (one eq.) as the base[7] was unsuccessful. Alternatives procedures were then investigated.

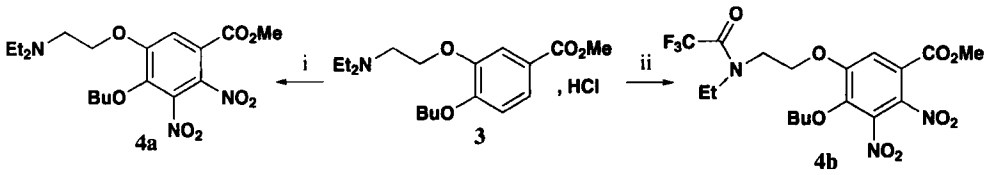
It was first decided to have available reference samples of the mono- and dibutylated products. This reaction was performed in refluxing acetone with an excess of K_2CO_3 and 1-iodobutane. Compound **2** and the *bis*-ether were thus obtained in 33% and 51% yield respectively. Attempts to monobutylate at the *para* hydroxy group of the ester group were then investigated. In none of these cases was the *bis*-ether isolated (*Table 1*). The best yield of **2** was

Table 1. Preparation of Compound **2**.

Method	Yield (%)	Base (equiv.)	Time (hrs)	Temp. (°C)	Solvent	*n*-BuI (equiv)
1[8]	20	K_2CO_3 (1.0)	18	Δ	acetone	1.0
2[8]	16	$NaHCO_3$ (1.0)	18	Δ	acetone	1.0
3[9]	42	NaH (0.9)	48	RT	DMF	0.9
4[9]	54	NaH (1.0)	48	RT	DMF	1.0
5[8]	40	K_2CO_3 (1.0)	18	RT	acetone	1.0
6[9]	40	NaH (0.9)	18	Δ	DMF	0.9

achieved by treatment of compound **1** with one eq. each of NaH and 1-iodobutane in DMF at room temperature for two days (*Table 1, Entry 4*). However, due to the easier procedure and work-up, selective introduction of *n*-butyl substituent was performed in 40% yield using one equivalent of 1-iodobutane and K_2CO_3 in acetone at room temperature over 18 h (*Table 1, Entry 5*). Alkylation of the free hydroxy group of **2** with 2-(diethylamino)ethyl chloride hydrochloride in K_2CO_3 in refluxing acetone, gave **3** in quantitative yield.

The nitration of **3** carried out in a fuming nitric and sulfuric acids mixture at –20°C, did not lead to desired compound **4** but rather to compound **4a** in only 5% yield. The bis-nitrated structure was confirmed by COSY and ROESY experiments. The main result of this reaction was a complex mixture of degradation products. It was therefore necessary to develop new approaches. Attempted selective nitrations with fuming nitric acid at room temperature in acetic acid or acetic anhydride[10] were unsuccessful. Treatment of **3** with fuming nitric acid in trifluoroacetic anhydride[11] led to compound **4b** in 15% yield. The structure **4b** was established by NMR experiments; a ^{19}F NMR (which suggested the presence of the fluorine atom), a ^{13}C NMR (which showed the presence of N-CO-CF_3 group), and a HSQC and HMBC NMR (which confirmed the positions of the nitro groups). The formation of **4** was not expected, although this N-dealkylation trifluoroacetylation has been observed in previous studies.[12]

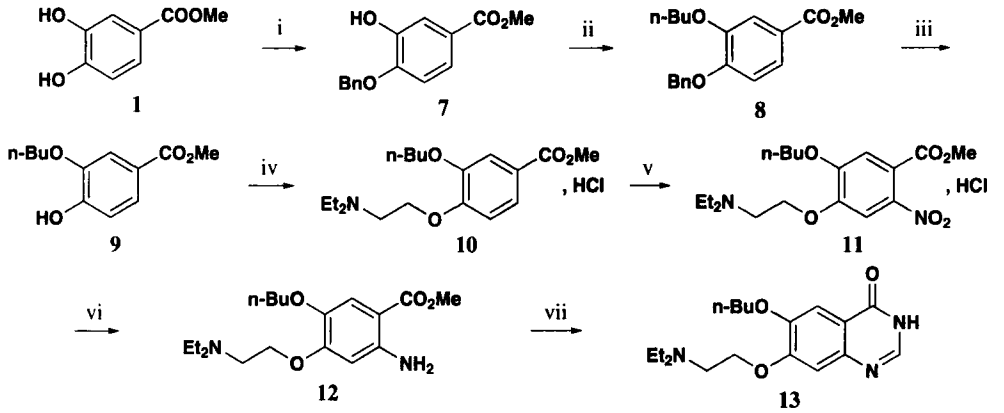


i) HNO_3 (100%), H_2SO_4 (97%), -20°C; ii) HNO_3 (100%), $(CF_3CO)_2O$

Scheme 2

A third approach, using a Claycop reagent (mixture of montmorillonite and cupric nitrate) in the presence of acetic anhydride in methylene chloride at room temperature,[13] led to a complex mixture from which the desired product was not isolated. Nitration of compound **3** in nitric acid (68%) at 0°C[14] provided the desired intermediate **4** in 30% yield. This yield could be increased to 65%, using fuming nitric acid with tin(IV) chloride in methylene chloride at –25°C.[15] The position of the nitro group was confirmed by COSY and ROESY experiments.

Amine **5** was obtained in 61% yield by reduction with iron powder in acetic acid during 1 h (*Method A*). The yield was improved to 66% yield in 30 minutes by using tin(II) chloride in conc. hydrochloric acid (*Method B*). The quinazoline **6** was then obtained in 66% yield, as described by Robba *et al.*,[16] by treatment of compound **5** with ammonium formate in formamide at 140°C. In order to validate this strategy, we decided to employ the same synthetic route to acquire isomer **13** (*Scheme 3*). This synthesis was accomplished by first benzylation of **1** in



i) K_2CO_3, BnBr, acetone; ii) K_2CO_3, *n*-C_4H_9I, acetone, reflux; iii) H_2, Pd/C, MeOH; iv) K_2CO_3, $Et_2N(CH_2)_2Cl$•HCl, acetone, reflux; v) HNO_3 (100%), $SnCl_4$, CH_2Cl_2, –25°C; vi) $SnCl_2$, HCl, 100°C; vii) $HCOONH_4$, $HCONH_2$, 140°C

Scheme 3

acetone at room temperature, using one equivalent of K_2CO_3 and benzyl bromide. The position of the benzyl group was confirmed by COSY and ROESY experiments. In the next step, the free phenol group of the intermediate **7** was alkylated with 1-iodobutane, using K_2CO_3 in refluxing acetone, to give **8** in 96% yield. After hydrogenolysis of the benzyl protective group in 94% yield, the free hydroxy group of compound **9** was alkylated with 2-(diethylamino)ethyl chloride

hydrochloride using K_2CO_3 in refluxing acetone. Intermediate **10** was obtained in 91% yield. The quinazoline **13** was then prepared with a similar strategy used to afford **6**. Nitration of compound **10** with fuming nitric acid with tin(IV) chloride in methylene chloride at –25°C, followed by the reduction of the nitro group using tin(II) chloride in conc. hydrochloric acid at 100°C, furnished **12** in 79% yield. This compound was cyclized to the quinazoline **13** using ammonium formate in formamide at 140°C with 60% yield.

EXPERIMENTAL SECTION

Mps were determined in open capillary tubes using a BÜCHI B-530 melting point apparatus and are uncorrected. Infrared spectra were obtained using a BRUKER VECTOR 22. ^{1}H NMR spectra were recorded using a BRUKER AC 300P spectrometer in DMSO-d_6 or in $CDCl_3$ at ambient temperature. Compound **1** was synthetised according to described procedure.[6]

Methyl 4-Butoxy-3-hydroxybenzoate (2).- To a solution of **1** (10g, 0.06 mol) in acetone (400 mL) was added K_2CO_3 (8.30 g, 0.06 mol). The mixture was stirred 15 min. and then a solution of 1-iodobutane (7 mL, 0.06 mol) in acetone (100 mL) was added slowly dropwise. The mixture was stirred 2 days at room temperature and filtered. The filtrate was concentrated *in vacuo* and the oily residue was washed with H_2O. The resulting precipitate was collected, washed successively with H_2O and petroleum ether, and dried *in vacuo*. Recrystallization from cyclohexane gave 8.62 g (64%) of white crystals, mp 113-115°C. IR: 3700-3000 (OH), 1699 (CO) cm^{-1}. ^{1}H NMR: ($CDCl_3$): δ 0.99 (t, 3H, J = 7.40 Hz), 1.52 (m, 2H), 1.84 (m, 2H), 3.88 (s, 3H), 4.11 (t, 2H, J = 6.45 Hz), 5.70 (s, 1H), 6.88 (d, 1H, J = 9.10 Hz), 7.58-7.64 (m, 2H).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 63.99; H, 7.05

Methyl 4-Butoxy-3-(2-diethylaminoethoxy)benzoate Hydrochloride (3).- A mixture of **2** (5.47 g, 0.024 mol), K_2CO_3 (16.6 g, 0.122 mol) and 2-(diethylamino)ethyl chloride hydrochloride (8.6 g, 0.048 mol) in acetone (80 mL) was refluxed for 16 hrs. The inorganic solid was filtered off and the filtrate concentrated *in vacuo*. The oily residue was dissolved in diethyl ether (50 mL) and a solution of diethyl ether saturated with gaseous HCl was added (30 mL). The resulting precipitate was collected, washed with diethyl ether and dried *in vacuo* to afford **3** (8.78 g, 100%) as HCl salt (a white solid), mp 148.5-150°C. IR: 2588 and 2488 (NH), 1716 (CO) cm^{-1}. ^{1}H NMR: ($CDCl_3$): δ 0.99 (t, 3H, J = 7.20 Hz), 1.42-1.54 (m, 8H), 1.83 (m, 2H), 3.33 (m, 4H), 3.53 (t, 2H, J = 4.60 Hz), 3.89 (s, 3H), 4.05 (t, 2H, J = 6.70 Hz), 4.53 (t, 2H, J = 4.60 Hz), 6.89 (d, 1H, J = 8.70 Hz), 7.55 (d, 1H, J = 2.00 Hz), 7.64 (dd, 1H, J = 8.70 and 2.00 Hz), 12.46 (s, 1H).

Anal. Calcd for $C_{18}H_{30}ClNO_4$: C, 60.07; H, 8.40; N, 3.89. Found: C, 60.27; H, 8.43; N, 4.18

Methyl 4-Butoxy-5-(2-diethylaminoethoxy)-2-nitrobenzoate Hydrochloride (4).- To a solution of **3** (3 g, 0.0083 mol) in CH_2Cl_2 (111 mL) cooled at –25°C, was added dropwise a solution of $SnCl_4$ (2.7 mL, 0.025 mol) and fuming HNO_3 (1mL, 0.025 mol) in CH_2Cl_2 (30 mL). After stirring at –25°C for 5 hrs, water was added (75 mL). The layers were separated by decantation.

The aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated *in vacuo*. The oily residue was dissolved in diethyl ether and a solution of diethyl ether saturated with gaseous HCl was added (30 mL). The resulting precipitate was collected, washed with diethyl ether and dried *in vacuo* to provide **4** (2.20g, 65%) as HCl salt (a white solid), mp 124.2-124.8°C. IR: 1728 (CO), 1520 (NO_2) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.99 (t, 3H, J = 7.57 Hz), 1.45 (m, 8H), 1.80 (m, 2H), 3.25 (m, 4H), 3.55 (m, 2H), 3.85 (s, 3H), 4.05 (t, 3H, J = 6.62 Hz), 4.62 (m, 2H), 7.10 (s, 1H), 7.38 (s, 1H).

Anal. Calcd for $C_{18}H_{29}ClN_2O_6$: C, 53.40; H, 7.22; N, 6.92. Found: C, 53.51; H, 7.30; N, 6.62

Methyl 4-Butoxy-5-(2-diethylaminoethoxy)-2,3-dinitrobenzoate (4a).- To a mixture of fuming nitric (5.2 mL) and sulfuric (3.3 mL) acids at –20°C was added **3** (1 g, 0.0027 mol). After stirring at –20°C for 6 hrs, the reaction mixture was hydrolyzed by adding glacial H_2O. A solution of K_2CO_3 (5%) was added to obtain a pH ~8 and the mixture was extracted with ethyl acetate. The organic layer was washed with H_2O, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 9.9/0.1) to provide **4a** (0.06g, 5%) as a yellow oil. IR: 1740 (CO) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.99 (t, 3H, J = 7.40 Hz), 1.07 (t, 6H, J = 7.10 Hz), 1.43 (m, 2H), 1.71 (m, 2H), 2.64 (q, 4H, J = 7.10 Hz), 2.94 (m, 2H), 3.90 (s, 3H), 4.15-4.29 (m, 4H), 7.44 (s, 1H).

Anal. Calcd for $C_{18}H_{27}N_3O_8$: C, 52.29; H, 6.58; N, 10.16. Found: C, 52.50; H, 6.62; N, 9.86.

Methyl 4-Butoxy-5-{2-[ethyl-(2,2,2-trifluoroacetyl)-amino]-ethoxy}-2,3-dinitrobenzoate (4b).- A mixture of **3** (1 g, 0.0027 mol), fuming HNO_3 (0.6 mL, 0.0135 mol) in trifluoroacetic anhydride (20 mL) was stirred at room temperature for 18 hrs. The reaction mixture was hydrolyzed with glacial H_2O. A solution of K_2CO_3 (5%) was added to obtain a pH ~8 and the mixture was extracted with ethyl acetate. The organic layer was washed with H_2O, dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH 9.8/0.2) to afford **4b** (0.20 g, 15%) as a white solid, mp 121.4-123.7°C. IR: 1721 (CO), 1682 (CO) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.90 (t, 3H, J = 7.40 Hz), 1.22 (t, 3H, J = 7.10 Hz), 1.35 (m, 2H), 1.60 (m, 2H), 3.08 (m, 2H), 3.47 (m, 2H), 3.90 (s, 3H), 4.21 (t, 2H, J = 6.60 Hz), 4.52 (m, 2H), 7.50 (s, 1H).

Anal. Calcd for $C_{18}H_{22}F_3N_3O_9$: C, 44.91; H, 4.61; N, 8.73. Found: C, 44.66; H, 4.62; N, 8.69

Methyl 2-Amino-4-butoxy-5-(2-diethylaminoethoxy)benzoate (5).

Method A.- To a suspension of **4** (1 g, 0.0025 mol) in acetic acid (30 mL) was added iron powder (1.51 g, 0.0025 mol) and conc. HCl (0.5 mL). The reaction mixture was refluxed for 1 h and filtered. The filtrate was concentrated *in vacuo* and the resulting residue was dissolved in acetone (30 mL). The suspension was filtered and the filtrate concentrated *in vacuo* to afford **5** (0.515 g, 61%) as an brown oil. IR: 3571 (NH_2), 1684 (CO) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.95 (t, 3H, J = 7.22 Hz), 1.12 (t, 6H, J = 7.22 Hz), 1.48 (m, 2H), 1.80 (m, 2H), 2.52 (q, 4H, J = 7.22 Hz), 2.85 (t, 2H, J = 6.24 Hz), 3.80 (s, 3H), 3.95 (m, 4H), 5.55 (s, 2H), 6.10 (s, 1H), 7.32 (s, 1H).

Anal. Calcd for $C_{18}H_{30}N_2O_4$: C, 63.88; H, 8.93; N, 8.28. Found: C, 63.75; H, 9.05; N, 8.35

Method B.- A suspension of **4** (1 g, 0.0025 mol) in conc. HCl (25 mL) was heated at 50-60°C for 5 minutes. A solution of $SnCl_2$ (2.33 g, 0.015 mol) in conc. HCl (20 mL) was added dropwise. The reaction mixture was heated at 100°C for 45 minutes. The solid formed was collected and dissolved in H_2O (300 mL). A solution of sodium hydroxide (2 N) was added to obtain a pH ~8-9. The aqueous solution was then extracted with ethyl acetate (3 x 100 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to give **5** (0.78 g, 91%) as a brown oil. Its NMR spectrum is identical to that obtained with method A.

7-Butoxy-6-(2-diethylaminoethoxy)-3H-quinazolin-4-one (6).- A mixture of **5** (1 g, 0.003 mol), $HCOONH_4$ (0.9 g, 0.009 mol) and $HCONH_2$ (1 mL, 0.015 mol) was heated at 140°C for 16 hrs. The mixture reaction was hydrolyzed (50 mL) and extracted with CH_2Cl_2. The separated aqueous layer was neutralized with a saturated K_2CO_3 solution. The resulting precipitate was collected to afford **6** (0.66 g, 66%) as a white solid, mp 201.8-202.2°C. IR: 1659 (CO), 1611 (NH) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.99 (t, 3H, J = 7.22 Hz), 1.10 (t, 6H, J = 7.22 Hz), 1.52 (m, 2H), 1.92 (m, 2H), 2.68 (q, 4H, J = 7.22 Hz), 2.98 (t, 2H, J = 5.58 Hz), 4.10 (m, 2H), 4.20 (m, 2H), 7.10 (s, 1H), 7.55 (s, 1H), 7.98 (s, 1H).

Anal. Calcd for $C_{18}H_{27}N_3O_3$: C, 64.84; H, 8.16; N, 12.60. Found: C, 65.10; H, 7.98; N, 12.48

Methyl 4-Benzyloxy-3-hydroxybenzoate (7).- As described for **2**, recrystallization from diisopropyl ether gave intermediate **7** as a pale yellow solid (10.42 g, 67%), from **1** (10 g, 0.06 mol) in acetone (400 mL), K_2CO_3 (8.30 g, 0.06 mol) and a solution of benzyl bromide (7 mL, 0.06 mol) in acetone (100 mL); mp 127.6-129°C. IR: 3392 (OH), 1693 (CO) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 3.89 (s, 3H), 5.18 (s, 2H), 5.70 (s, 1H), 6.96 (d, 1H, J = 8.20 Hz), 7.38-7.47 (m, 5H), 7.58-7.64 (m, 2H).

Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 69.90; H, 5.52

Methyl 4-Benzyloxy-3-butoxybenzoate (8).- To a solution of **7** (1 g, 0.0039 mol) in acetone (50 mL) was added K_2CO_3 (1.10 g, 0.0078 mol). The mixture was stirred 10 min. and 1-iodobutane (0.91 mL, 0.0078 mol) was added. The reaction mixture was refluxed for 5 hrs. The inorganic solid was filtered off and the filtrate was concentrated *in vacuo*. The resulting solid residue was washed successively with H_2O and petroleum ether. Recrystallization from ethanol-water (95/5) gave 1.18 g (96%) of white crystals, mp 54.7-55.8°C. IR: 1716 (CO) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 1.01 (t, 3H, J = 7.75 Hz), 1.55 (m, 2H), 1.86 (m, 2H), 3.89 (s, 3H), 4.09 (t, 2H, J = 6.70 Hz), 5.20 (s, 2H), 6.92 (d, 1H, J = 8.30 Hz), 7.27-7.48 (m, 5H), 7.56-7.65 (m, 2H).

Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.89; H, 7.10

Methyl 3-Butoxy-4-hydroxybenzoate (9).- To a solution of **8** (1 g, 0.0032 mol) in methanol (50 mL) was added Pd/C (0.2 g). The reaction mixture was stirred under hydrogen atmosphere at room temperature for 2 days, filtered, and evaporated *in vacuo*. The oily residue was treated with petroleum ether and the resulting precipitate was collected. Recrystallization from petroleum ether gave 0.67 g (94%) of white crystals, mp 61-62.2°C. IR: 3405 (OH), 1701 (CO) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.99 (t, 3H, J = 7.30 Hz), 1.50 (m, 2H), 1.82 (m, 2H), 3.88 (s, 3H), 4.10 (t, 2H,

J = 6.85 Hz), 5.70 (s, 1H), 6.93 (d, 1H, J = 8.30 Hz), 7.54 (s, 1H), 7.62 (d, 1H, J = 8.30 Hz).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.46; H, 7.23

Methyl 3-Butoxy-4-(2-diethylaminoethoxy)benzoate Hydrochloride (10).- Starting from **9** (2 g, 0.009 mol), compound **10** was synthesized using the same procedure as that for **3**. Recrystallization from toluene gave 2.55 g (91%) of white crystals, mp 116-118°C. IR: 2608 and 1483 (NH^+), 1717 (CO) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.98 (t, 3H, J = 7.35 Hz), 1.38-1.60 (m, 8H), 1.77 (m, 2H), 3.30 (m, 4H), 3.53 (m, 2H), 3.89 (s, 3H), 4.02 (m, 2H), 4.57 (t, 2H, J = 4.20Hz), 6.89 (d, 1H, J = 8.35 Hz), 7.53 (d, 1H, J = 2.00 Hz), 7.63 (dd, 1H, J = 8.35 and 2.00 Hz), 12.44 (s, 1H).

Anal. Calcd for $C_{18}H_{30}ClNO_4$: C, 60.07; H, 8.40; N, 3.89. Found: C, 60.30; H, 8.49; N, 4.05

Methyl 5-Butoxy-4-(2-diethylaminoethoxy)-2-nitrobenzoate Hydrochloride (11).- Starting from **10** (5 g, 0.014 mol), compound **11** was obtained using the same procedure as that for **4**. 3.8 g (67%) of a white solid were prepared, mp 119-120°C. IR: 1734 (CO), 1530 (NO_2) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 1.00 (t, 3H, J = 7.30 Hz), 1.50 (m, 8H), 1.80 (m, 2H), 3.30 (q, 4H, J = 7.23 Hz), 3.60 (t, 2H, 6.24 Hz), 3.80 (s, 3H), 4.10 (t, 2H, J = 6.30 Hz), 4.60 (t, 2H, J = 6.24 Hz), 6.80 (s, 1H), 7.40 (s, 1H), 12.50 (m, 1H).

Anal. Calcd for $C_{18}H_{29}ClN_2O_6$: C, 53.40; H, 7.22; N, 6.92. Found: C, 53.57; H, 7.34; N, 7.09

Methyl 2-Amino-5-butoxy-4-(2-diethylaminoethoxy)benzoate (12).- As described for **5**, intermediate **12** was obtained as an oil (0.33 g, 79%), from **11** (0.50 g, 0.0012 mol) and tin(II) chloride (0.93 g, 0.006 mol) in conc. HCl (23 mL). IR: 3480 and 3385 (NH_2), 1685 (CO), 1624 (NH_2) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.91 (t, 3H, J = 7.20 Hz), 1.01 (t, 6H, J = 7.20 Hz), 1.40 (m, 2H), 1.68 (m, 2H), 2.58 (m, 4H), 2.88 (t, 2H, J = 6.26 Hz), 3.85 (s, 3H), 3.88 (t, 2H, J = 6.57 Hz), 4.00 (t, 2H, J = 6.26 Hz), 5.50 (s, 2H), 6.10 (s, 1H), 7.30 (s, 1H).

Anal. Calcd for $C_{18}H_{30}N_2O_4$: C, 63.88; H, 8.93; N, 8.28. Found: C, 64.05; H, 9.05; N, 8.32

6-Butoxy-7-(2-diethylaminoethoxy)-3H-quinazolin-4-one (13).- Similarly to the procedure described for **6**, the title compound was prepared starting from **12** (0.89 g, 0.0026 mol), as a white solid (0.53 g, 60%), mp: 154-157°C. IR: 1689 (CO), 1609 (NH) cm^{-1}. ^1H NMR: ($CDCl_3$): δ 0.95 (t, 3H, J = 7.20 Hz), 1.06 (t, 6H, J = 7.00 Hz), 1.45 (m, 2H), 1.80 (m, 2H), 2.64 (q, 4H, J = 7.18 Hz), 2.96 (t, 2H, J = 6.11 Hz), 4.08 (t, 2H, J = 6.46 Hz), 4.17 (t, 2H, J = 6.11 Hz), 7.11 (s, 1H), 7.54 (s, 1H), 8.01 (s, 1H).

Anal. Calcd for $C_{18}H_{27}N_3O_3$: C, 64.84; H, 8.16; N, 12.60. Found: C, 64.68; H, 8.22; N, 12.35

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(Received May 18, 2004; in final form September 11, 2004)