except that NaCl was not added in the incubation medium. Uptake was determined by dilution with 5 mL of incubation medium without NaCl. Samples were centrifuged at 20000g at 4 °C for 15 min, and radioactivity was evaluated in pellets after dilution in 1 mL of Proposol (New England Nuclear).

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Registry No. 1, 56-12-2; 2, 5130-17-6; 3, 102629-73-2; 4, 102629-74-3; 5, 498-95-3; 6, 68464-00-6; 7, 498-96-4; 8, 85375-85-5; 9, 85375-88-8; 10, 134525-28-3; 11, 89203-64-5; 12, 89203-55-4; 13, 53602-00-9; 14, 132033-96-6; 15, 98943-12-5; 16, 98976-55-7; 17, 134420-65-8; 18, 71622-29-2; 19, 71622-34-9; 20, 134455-45-1; 21, 1217-82-9; 22a, 5303-65-1; 22c, 59663-70-6; 22d, 10039-64-2; 22e, 134420-70-5; 22f, 134420-71-6; 23b, 134420-67-0; 23e, 134420-72-7; 23f, 134420-73-8; 24a, 95629-08-6; 24b, 134420-74-9; 24c, 134420-75-0; 24d, 134420-76-1; 24e, 134420-77-2; 24f, 134420-78-3; 25a, 116140-33-1; 25b, 134420-79-4; 25c, 134420-80-7; 25e, 134420-81-8; 25f, 134420-82-9; 28a, 116140-36-4; 28b, 134420-83-0; 28c, 134420-84-1; 28e, 134420-85-2; 28f, 134420-86-3; 29b, 134420-68-1; 29c, 134420-87-4; 29f, 134420-88-5; 30b, 134420-69-2; 30c, 134420-89-6; 30e, 134420-90-9; 30f, 134420-91-0; 32b, 24410-84-2; 32c, 1552-67-6; 32e, 6048-08-4; 32f, 134420-92-1; 33a, 6335-80-4; 33b, 134420-93-2; 33c, 134455-46-2; 33e, 134420-94-3; 33f, 134420-95-4; cyclopropyldiphenylmethanol, 5785-66-0; 4,4-diphenylbutanol, 56740-71-7; ethyl acrylate, 140-88-5; triphenyl(carbethoxymethyl)phosphonium bromide, 1530-45-6; benzylamine, 100-46-9.

3-Thienyl- and 3-Furylaminobutyric Acids. Synthesis and Binding $GABA_B$ Receptor Studies[1]

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Baclofen (β-(*p*-chlorophenyl)-GABA) is a selective agonist for the bicuculline-insensitive $GABA_B$ receptor. The search for new compounds that bind to the $GABA_B$ receptor is very important to clarify structural requirements. We report herein the synthesis and the binding studies of variously substituted 3-thienyl- and 3-furylaminobutyric acids. 4-Amino-3-(5-methyl-2-thienyl)butyric acid (**5d**) and 4-amino-3-(5-chloro-2-thienyl)butyric acid (**5h**) are potent and specific ligands for $GABA_B$ receptor. The IC_{50} values for the displacement of (*R*)-(−)-[^{3}H]baclofen are 1.34 and 0.61 μM for **5d** and **5h**, respectively, as compared to 0.33 μM for baclofen.

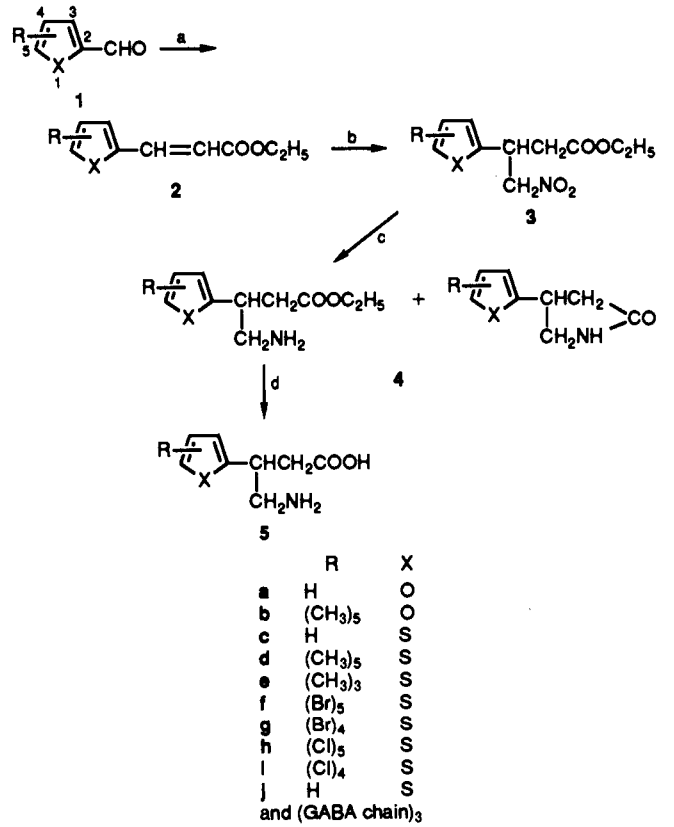
The neutral amino acid γ-aminobutyric acid (GABA) is an inhibitory neurotransmitter concerned with the control of neuronal activity in the mammalian central nervous system and with the regulation of many physiological mechanisms.[2] Within the central and peripheral nervous system, GABA has been shown to act through at least two distinctly different receptor sites,[3] termed $GABA_A$ and $GABA_B$ receptors, with different binding properties.[4,5] Accumulating evidence suggests that $GABA_B$ receptors are predominantly located presynaptically.[6] However, in a recent report, postsynaptically located $GABA_B$ receptor have been described.[7] $GABA_B$ receptors have also been detected and characterized in a variety of tissue preparations of peripheral origin.[8]

Until now, β-(*p*-chlorophenyl)-GABA (baclofen) was the selective agonist for the $GABA_B$ receptor. Analogues of baclofen, saturated or unsaturated, have been synthesized and tested for $GABA_B$ receptor affinity. These compounds showed no selective action at $GABA_B$ receptor sites in vitro.[9] The only new agonist available is (3-aminopropyl)phosphinic acid, which is a potent displacer of baclofen in binding studies.[10] However, this compound can act as a partial agonist under certain conditions.[11]

In recent papers, the phosphonic analogue of baclofen (phaclofen) and two sulfonic analogues (saclofen and 2-hydroxysaclofen) have been shown to be antagonists at $GABA_B$ receptors.[12,13] We recently described the synthesis of 3-(benzo[*b*]furan-2-yl)-GABA, new selective ligands of $GABA_B$ sites,[14] which are specific $GABA_B$ receptor antagonists.[15,16]

In the course of our work and in attempts to elucidate the structural requirements for access to the $GABA_B$ receptor,[14] we report the synthesis and the binding studies of new 3-heteroaryl-GABA analogues. These racemic compounds, especially **5d** and **5h**, are potent and specific

Scheme I[a]



	R	X
a	H	O
b	$(CH_3)_5$	O
c	H	S
d	$(CH_3)_5$	S
e	$(CH_3)_3$	S
f	$(Br)_5$	S
g	$(Br)_4$	S
h	$(Cl)_5$	S
i	$(Cl)_4$	S
j	H	S

and (GABA chain)$_3$

[a] Reagents: (a) $(C_6H_5)PCHCOOC_2H_5/C_6H_6$/reflux; (b) CH_3NO_2/Triton B/85 °C; (c) Raney Ni/H_2; (d) NaOH/EtOH/reflux.

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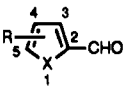
Table I

compd	R	yield, %	mp, °C; bp, °C	formula	anal.	method
2a	2-furyl					ref 17
2b	5-methyl-2-furyl	70	128–130 (13 mmHg)	$C_{10}H_{12}O_3$	C, H, O	A
2c	2-thienyl					ref 17
2d	5-methyl-2-thienyl	70–80	100 (0.2 mmHg)	$C_{10}H_{12}O_2S$	C, H, O, S[a]	A
2e	3-methyl-2-thienyl	83	94 (0.1 mmHg)	$C_{10}H_{12}O_2S$	C, H, O, S	A
2f	5-bromo-2-thienyl	80	172–178 (13 mmHg)	$C_9H_9O_2SBr$	C, H, O, S, Br	A
2g	4-bromo-2-thienyl	75	68–70	$C_9H_9O_2SBr$	C, H, O, S, Br[b]	A
2h	5-chloro-2-thienyl	78	100–102 (0.1 mmHg)	$C_9H_9O_2SCl$	C, H, O, S, Cl	A
2i	4-chloro-2-thienyl	77	135–136 (0.4 mmHg)	$C_9H_9O_2SCl$	C, H, O, S, Cl	A
2j	3-thienyl	76	148–150 (13 mmHg)	$C_{10}H_{10}O_2S$	C, H, O, S	A
3a	2-furyl	74	172–175 (13 mmHg)	$C_{10}H_{13}NO_5$	C, H, N, O	B
3b	5-methyl-2-furyl	66	128–130 (0.4 mmHg)	$C_{11}H_{15}NO_5$	C, H, N, O	B
3c	2-thienyl	46	138–145 (0.3 mmHg)	$C_{10}H_{13}NO_4S$	C, H, N, O, S	B
3d	5-methyl-2-thienyl	45	148–150 (0.4 mmHg)	$C_{11}H_{15}NO_4S$	C, H, N, O, S	B
3e	3-methyl-2-thienyl	57	138–142 (0.1 mmHg)	$C_{11}H_{15}NO_4S$	C, H, N, O, S	B
3f	5-bromo-2-thienyl	61	168 (0.2 mmHg)	$C_{10}H_{12}NO_4SBr$	C, H, N, O, S, Br[c]	B
3g	4-bromo-2-thienyl	72	preparative HPLC	$C_{10}H_{12}NO_4SBr$	C, H, N, O, S, Br	B
3h	5-chloro-2-thienyl	64	150–155 (0.4 mmHg)	$C_{10}H_{12}NO_4SCl$	C, H, N, O, S, Cl	B
3i	4-chloro-2-thienyl	62	140–145 (0.4 mmHg)	$C_{10}H_{12}NO_4SCl$	C, H, N, O, S, Cl	B
3j	3-thienyl	66	150–152 (0.2 mmHg)	$C_{10}H_{13}NO_4S$	C, H, N, O, S	B
5a	2-furyl	53	172–175 (173)	$C_8H_{11}NO_3$	C, H, N, O	D
5b	5-methyl-2-furyl	53	154–156	$C_9H_{13}NO_3$	C, H, N, O	D
5c	2-thienyl	42	198–200 (206)	$C_8H_{11}NO_2S$	C, H, N, O, S	D
5d	5-methyl-2-thienyl	53	184–186	$C_9H_{13}NO_2S$	C, H, N, O, S	D
5e	3-methyl-2-thienyl	14	187–188	$C_9H_{13}NO_2S{\cdot}H_2O$	C, H, N, O, S[d]	D
5f	5-bromo-2-thienyl	55	176–178	$C_8H_{10}NO_2SBr$	C, H, N, O, S, Br[e]	D
5g	4-bromo-2-thienyl	25	190–191	$C_8H_{10}NO_2SBr$	C, H, N, O, S, Br[f]	D
5h	5-chloro-2-thienyl	25	181–182	$C_8H_{10}NO_2SCl$	C, H, N, O, S, Cl	D
5i	4-chloro-2-thienyl	24	173–174	$C_8H_{10}NO_2SCl$	C, H, N, O, S, Cl	D
5j	3-thienyl	30	204–205	$C_8H_{11}NO_2S{\cdot}H_2O$	C, H, N, O, S	D

[a] Anal.: O calcd 16.30, found 16.80. [b] O calcd 12.26, found 11.52. [c] S calcd 9.95, found 10.42. [d] O calcd 22.11, found 21.70. [e] O calcd 12.11, found 12.61. [f] O calcd 12.11, found 12.57.

Table II. Binding Results (IC_{50},[a] μM)



compd	R	X	[^{3}H]muscimol binding $GABA_A$	(*R*)-(−)-[^{3}H]baclofen[b] binding $GABA_B$
5a	H	O	>100	>100
5b	$(CH_3)_5$	O	>100	>100
5c	H	S	>100	9.72
5d	$(CH_3)_5$	S	>100	1.34
5e	$(CH_3)_3$	S	>100	124
5f	$(Br)_5$	S	>100	1.86
5g	$(Br)_4$	S	>100	39.1
5h	$(Cl)_5$	S	>100	0.61
5i	$(Cl)_4$	S	>100	45.3
5j	H	S	>100	20.9
		(GABA chain)$_3$		
GABA			0.10	0.04
baclofen			–	0.33 (0.18[c])
β-(*o*-chlorophenyl)-GABA				0.80[c]
β-(*p*-fluorophenyl)-GABA				1.33[c]
β-(*m*-chlorophenyl)-GABA				20[c]
β-(*p*-hydroxyphenyl)-GABA				>100[d]
β-phenyl-GABA				>100[c]

[a] Results were means of two experiments done in triplicate. [b] See ref 18 for details. [c] See ref 3. [d] See ref 14.

ligands for the $GABA_B$ receptor with IC_{50} values similar to IC_{50} values of baclofen.

Chemistry. The synthetic strategy is illustrated in Scheme I. Treatment of thiophenecarboxaldehydes or

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furancarboxaldehydes **1a–j** with (carbethoxymethylene)-triphenylphosphorane in benzene at reflux temperature gave adducts **2a–j**, which were treated by nitromethane at 85 °C to afford the nitro esters **3a–j**. Catalytic hydrogenation of compounds **3a–j** at atmospheric pressure leads to mixtures (**4a–j**) of amino esters and lactams. These mixture (**4a–j**) were used in the next step without further purification and hydrolyzed by heating with excess sodium hydroxide in aqueous ethanol to obtain amino acids **5a–j** after purification by ion-exchange chromatography. Synthesis of compounds **5a** and **5c** has previously been reported in low yield by a multistep synthesis.[17] Table I list the physical data of the synthesized compounds. Title compounds **5** were characterized by ^1H and ^{13}C NMR spectroscopy and analytical HPLC.

Biochemistry. The pharmacological data are summarized in Table II, showing the activities of the ligands assessed on the basis of displacement of [^3H]muscimol or of (*R*)-(−)-[^3H]baclofen from rat brain membranes according to the previously described procedures.[18] All compounds **5a–j** were tested for their ability to displace [^3H]muscimol from rat brain membranes ($GABA_A$ sites) and also to displace [^3H]baclofen ($GABA_B$ sites) from rat brain membranes.

$GABA_A$ Sites. The compounds tested (up to 100 μM) failed to displace more than 20% of the tritium-labeled ligand specifically bound to $GABA_A$ receptors. The addition of increasing concentrations of unlabeled GABA and muscimol produced a dose-dependent reduction in binding. The IC_{50} for GABA and muscimol were 0.03 and 0.01 μM, respectively.

$GABA_B$ Sites. Two compounds (**5d–5h**) potently displaced binding of (*R*)-(−)-[^3H]baclofen to $GABA_B$ sites on rat whole brain synaptic membranes. The degress of displacement were concentration dependent, and **5d** and **5h** had IC_{50} values of 1.34 and 0.61 μM, respectively. The IC_{50} value for baclofen was 0.33 μM.

Discussion

. The therapeutic effects of baclofen (Lioresal, a drug marketed by Ciba-Geigy Ltd.) on certain types of spasticity[3] have prompted synthesis of a variety of structurally related compounds. However, these compounds showed little or no effect on the $GABA_B$ receptor in vitro. In the literature, baclofen is the reference selective agonist at the $GABA_B$ receptor and the only new agonist is the (3-aminopropyl)phosphinic acid.[10] Recently Kerr and coworkers have described phaclofen, saclofen, and 2-hydroxysaclofen as antagonists.[12,13] From the published results of structure–activity studies, it appeared that the alterations of the amino acid as well as of the aromatic moieties of baclofen have resulted in substantial or complete loss of activity. Considerable effort has been directed toward structure–activty relationships in order to develop agonists or antagonists.

The present data show the specificity of our baclofen analogues for $GABA_B$ receptor since compounds **5c–j** discriminate perfectly against $GABA_A$ and $GABA_B$ receptors. In the binding test, compounds **5d** and **5h** displace (*R*)-(−)-[^3H] baclofen respectively with IC_{50} values of 1.34 and 0.61 μM. In a previous report,[14] we have proposed some structural requirements for binding to the $GABA_B$ receptor. The 5-position of the thiophene ring could be compared to the "para" position in the aromatic ring: **5f** (IC_{50} = 1.86 μM) > **5g** (IC_{50} = 39.1 μM) and **5h** (IC_{50} = 0.61 μM) > **5i** (IC_{50} = 45.3 μM). These results are comparable with the previous works on modification of the 4-chlorophenyl ring in baclofen (*p*-Cl > *o*-Cl > *p*-F > *m*-Cl ≫ not substituted).[3] The binding results of these compounds are included for comparison in Table II. The presence of a substituent at the C5 on the five-membered heterocyclic ring is important for binding: **5d** (IC_{50} = 1.34 μM) > **5c** (IC_{50} = 9.72 μM) ≫ **5e** (IC_{50} = 124 μM); **5f** (IC_{50} = 1.86 μM) > **5g** (IC_{50} = 39.1 μM); and **5h** (IC_{50} = 0.61 μM) ≫ **51** (IC_{50} = 45.3 μM). The lack of this substituent increases of the IC_{50} (**5c**) and the presence of substituent at other positions (C4 or C3) leads to a great loss of activity. Previous results obtained with the 4-hydroxybaclofen analogue showed it was completely inactive in binding $GABA_B$ tests.[14] In the present paper, our results suggest also that the substituent in the para position on the aromatic or pseudoaromatic ring should be of lipophilic nature to observe high affinity. The higher activity of thienyl analogues (**5c** ≫ **5a** and **5d** ≫ **5b**) could be explained by the higher electronegativity of the oxygen atom in comparison with that of the sulfur atom. So, for both compounds **5a** and **5b**, the ammonium group might be folded toward the oxygen atom. Therefore, the distance between the carboxylate and ammonium moieties could be not favorable for $GABA_B$ receptor structure. This hypothesis is grounded by analogy with the structural results obtained with benzofuran analogues. For these compounds, in the solid state, the X-ray crystallographic data confirm the presence of a van der Waals contact between the ammonium group and benzofuran oxygen atom.[19] From the

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present and previous results,[14] the following hypothesis can be proposed to obtain compounds presenting an affinity for $GABA_B$ receptor. Three common features should be present: (a) an ammonium and a carboxylate group, (b) an aromatic or pseudoaromatic ring without substituent in the meta or ortho position, (c) a lipophilic group in the para position.

Experimental Section

Chemistry. Melting points were determined on a Büchi SMP 20 apparatus and are not corrected. IR (in KBr pellets) spectra were recorded on a Beckman Acculab IV spectrometer. ^1H NMR were recorded with a Bruker WP 80 pulsed Fourier transform spectrometer, using $(CH_3)_4Si$ as an internal standard, except for the compound dissolved in D_2O, where sodium 3-(trimethylsilyl)propanesulfonate was used. ^{13}C NMR (broad band decoupling) were recorded in D_2O. Elemental analyses were performed by C.N.R.S.-Vernaison and were in agreement with the calculated values within 0.4%. UV spectral characteristics have been exploited by HPLC-DAD (diode array detector) to confirm peak homogeneity and purity for final amino acids. Analytical HPLC was carried out on a LKB metering pump. The detection was performed with a DAD HP 1040 connected to an HP 9000 computer on a Lichrosorb Merkx RP 18 column. The preparative separations were performed on a Jobin-Yvon Modulprep HPLC system with R.I. (Refractive Index) lota detector and the Spectro Monitor D variable wavelength detector with a 40-mm i.d. column of silica gel (10–40 μm). Starting aldehydes 1 are commercially available or prepared according to literature procedures.[20,21]

General Procedure for Synthesis of Ethyl 3-Substituted Prop-2-enoate Derivatives 2a–j. Method A. (Carbethoxymethylene)triphenylphosphorane (34.84 g, 0.1 mol) was added to a stirred solution of the appropriate aldehyde **1a–j** (0.1 mol) in 200 mL of anhydrous benzene. The mixture was refluxed for 7 h under a nitrogen atmosphere. After evaporation of benzene, the crude residue was stirred for 1 h with diethyl ether, and the triphenylphosphine oxide was crystallized out and was separated by filtration. The solvent was evaporated and the oily residue was distilled under reduced pressure. Compound **2i** was chromatographed (95:5 toluene/CH_2Cl_2) and isolated as a oil. An analytical sample was distilled.

Compound **2d** displayed the following: IR 1710 (C=O); ^1H NMR ($CDCl_3$) δ 1.33 (t, 3 H, J = 7 Hz), 2.50 (s, 3 H), 4.26 (q, 2 H, J = 7 Hz), 6.09 (d, 1 H, J = 15.4 Hz), 6.70 (dd, 1 H, J = 3 Hz), 7.04 (d, 1 H, J = 3 Hz), 7.70 (d, 1 H, J = 15.4 Hz).

General Procedure for the Synthesis of Ethyl 3-Substituted 4-Nitrobutanoate Derivatives 3a–j. Method B. A stirred solution of esters **2a–j** (0.05 mol) in 100 mL of CH_3NO_2 with 4 mL of Triton B was heated at 85 °C for 18 h. After cooling, the reaction medium was acidified to pH 2 M HCl and 50 mL of H_2O was added. The mixture was extracted with diethyl ether portions. The combined extracts were washed with water, dried, and evaporated in vacuo, giving a crude oil, which was further purified by distillation under reduced pressure. Compound **3g** was purified by chromatography (99:1 toluene/petroleum ether) and isolated as a yellow oil. Compound **3i** was chromatographed (95:5 petroleum ether/EtOAc) and a pure analytical sample was distilled.

Compound **3d** displayed the following: IR 1730 (C=O); ^1H NMR ($CDCl_3$) δ 1.28 (t, 3 H, J = 7 Hz), 2.45 (s, 3 H), 2.84 (d, 2 H, J = 7 Hz), 4.20 (q, 2 H, J = 7 Hz), 4.20–4.50 (m, 1 H), 4.70 (d, 2 H, J = 7 Hz), 6.50–6.75 (m, 2 H).

General Procedure for Hydrogenation of 3a–j to a Mixture of 4a–j. Method C. The nitro esters **3a–j** (0.02 mol) were shaken in 200 mL of ethanol with Raney nickel catalyst at room temperature under an atmospheric pressure of hydrogen. After completion of the reaction, the catalyst was separated by filtration and the solvent evaporated under vacuum to furnish a mixture of amino esters and lactams **4a–j** used in the next step without further purification. For all compounds, the yield of reaction (mixture of amino ester and lactam) was between 50% and 80%. The proportion of two compounds was estimated to be roughly 50–50 by ^1H NMR spectral data.

General Procedure for Synthesis of 3-Substituted 4-Aminobutanoic Acids 5a–j. Method D. The mixture of **4a–j** (0.01 mol) was refluxed for 1 h in 40 mL of alcohol (95 °C) and 10 mL of 10 N NaOH. After cooling, the solution was evapored to dryness and the crude product was dissolved in water (50 mL) and acidified to pH 1 with 10% HCl. The aqueous layer was washed with small portions of diethyl ether and evaporated under vacuum. The residue was suspended in CF_3COOH (3 mL) and adsorbed on Dowex 50 W, H^+ form ion-exchange resin (10 mL), washed with water, and eluted with 5% NH_4OH. The ammonium solution was evaporated to dryness under vacuum and the residue recrystallized from the appropriate solvent.

Compound **5d** displayed the following: IR 3200–2500 (OH), 1580 (C=O); ^1H NMR (DMSO-d_6) ϑ 2.47 (s, 3 H), 2.59 (d, 2 H, J = 7 Hz), 2.80 (d, 2 H, J = 6.3 Hz), 3.20 (q, 1 H, J = 6.4 Hz), 6.60 (m, 2 H); ^1H NMR (D_2O) ϑ 2.20 (d, 3 H, J = 0.9 Hz), 2.20–2.50 (m, 2 H), 2.70–3.50 (m, 2 H), 3.30–3.55 (m, 1 H), 6.46 (dq, 1 H), 6.60 (d, 1 H); ^{13}C NMR (D_2O) ϑ 15.60 (CH_3), 38.02 (CH_2CO), 44.05 (CH), 45.98 (CH_2N), 126.49, 127.24, 141.27, 141.45 (4 C, thienyl), 180.28 (CO); MS, m/e 200 (M + 1, 44), 199 (20), 181 (4), 170 (100). The purity of this compound was controlled by analytical HPLC analysis: Lichrosorb RP 18, 5-μm column, 4 mm × 25 cm (Merck), eluent 80:20 CH_3OH/H_2O, flow rate 0.7 mL/min, t_R 3.45 min, λ_{max} 220 nm.

Biochemical Assays. Crude synaptic membranes (CSM) were prepared from whole rat brain according to the method of Enna and Snyder.[18] The binding assay procedures were described in a previous paper.[14]

Registry No. **1a**, 98-01-1; **1b**, 620-02-0; **1c**, 98-03-3; **1d**, 13679-70-4; **1e**, 5834-16-2; **1f**, 4701-17-1; **1g**, 18791-75-8; **1h**, 7283-96-7; **1i**, 57500-51-3; **1j**, 498-62-4; **2a**, 623-20-1; **2b**, 34265-56-0; **2c**, 13979-15-2; **2d**, 14779-23-8; **2e**, 133933-41-2; **2f**, 108373-19-9; **2g**, 58963-64-7; **2h**, 133933-42-3; **2i**, 133933-43-4; **2j**, 50266-60-9; **3a**, 133933-44-5; **3b**, 133933-45-6; **3c**, 133933-46-7; **3d**, 133933-47-8; **3e**, 133933-48-9; **3f**, 133933-49-0; **3g**, 133933-50-3; **3h**, 133933-51-4; **3i**, 133933-52-5; **3j**, 133933-53-6; **4a** (amino ester), 133933-54-7; **4a** (lactam), 133933-64-9; **4b** (amino ester), 133933-55-8; **4b** (lactam), 133933-65-0; **4c** (amino ester), 133933-56-9; **4c** (lactam), 133933-66-1; **4d** (amino ester), 133933-57-0; **4d** (lactam), 133933-67-2; **4e** (amino ester), 133933-58-1; **4e** (lactam), 133933-68-3; **4f** (amino ester), 133933-59-2; **4f** (lactam), 133933-69-4; **4g** (amino ester), 133933-60-5; **4g** (lactam), 133933-70-7; **4h** (amino ester), 133933-61-6; **4h** (lactam), 133933-71-8; **4i** (amino ester), 133933-62-7; **4i** (lactam), 133933-72-9; **4j** (amino ester), 133933-63-8; **4j** (lactam), 133933-73-0; **5a**, 133933-74-1; **5b**, 133933-75-2; **5c**, 133933-76-3; **5d**, 133933-77-4; **5e**, 133933-78-5; **5f**, 133933-79-6; **5g**, 133933-80-9; **5h**, 133933-81-0; **5i**, 133933-82-1; **5j**, 133933-83-2; Ph_3P=CHCOOEt, 1099-45-2.

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