Neither compound nor the standards, administered intradermally or intraperitoneally, had an effect on the development of hemorrhage in the Arthus reaction. Both compounds produced comparable inhibition of local and systemic lesions in adjuvant-induced arthritis in the rat and of paralysis in experimental allergic encephalomylitis. These inhibitions were observed at or near toxic levels, but the toxicity was considered adjuvant-related. Morton and Chatfield11 had indicated that the adjuvant-induced arthritic rat probably does not detoxify compounds as efficiently as do normal rats because of impaired liver function. When II was tested in normal or adjuvant-treated rats at daily oral doses of 60 mg/kg a marked increase in lethality was observable by the eleventh day in the drug-adjuvant treated group (13/15) deaths), as compared with the drug, nonadjuvant treated group (2/15 deaths). II was more effective than I in decreasing cell induration in the delayed hypersensitivity skin reaction (tuberculin) in the guinea pig, in suppressing hemagglutinin production in the mouse, and in inhibiting TdR uptake by mouse thymus cells in culture. Neither compound was active as a membrane stabilizer. Both compounds demonstrated analgesic activity in the writhing and Randall-Sellito assays, and neither compound produced gastric erosions in the fasted rat. Because of the low acute oral toxicity of I and II in the rat and in the mouse and because they lack ulcerogenic potential, both compounds possess favorable therapeutic indices. These data indicate that both I and II possess antiinflammatory activity of considerable interest;

they compare favorably with indomethacin, phenylbutazone, and niflumic acid. Compound I has been selected for further toxicological studies.

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# Synthetic Antidiarrheal Agents.

## 2,2-Diphenyl-4-(4'-aryl-4'-hydroxypiperidino)butyramides

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The synthesis of a series of 2,2-diphenyl-4-(4'-aryl-4'-hydroxypiperidino)butyramides and the preliminary evaluation of their antidiarrheal activities are described. Intermediates are (tetrahydro-3,3-diphenyl-2furylidene)ammonium salts prepared from 4-bromo-2,2-diphenylbutyric acid (2). 4-(p-Chlorophenyl)-4hydroxy-N,N-dimethyl- $\alpha$ , $\alpha$ -diphenyl-1-piperidinebuty ramide HCl (30, loperamide) and 4-(4-chloro- $\alpha$ , $\alpha$ , $\alpha$ trifluro-m-tolyl)-4-hydroxy-N,N-dimethyl- $\alpha$ , $\alpha$ -diphenyl-1-piperidinebutyramide HCl (33, fluperamide) were approximately two times more potent than diphenoxylate and had a considerably better relative constipating specificity.

As part of a continuing effort to develop novel antidiarrheal agents, a series of 2,2-diphenyl-4-(4'-aryl-4'-hy droxypiperidino)butyramides of formula I were prepared. Diphenoxylate (IIa), a well-known antidiarrheal and potent inhibitor of the peristaltic relfex activity of guinea pig ileum in vitro, 2 belongs to a series of 1-(3-cyano-3,3diphenylpropyl)-4-phenylisonipecotic acid esters. With Ha the aim to synthesize analgesic type compounds devoid of analgesic action, but behaving as highly active inhibitors of gastrointestinal propulsion and defaecation, was achieved. The active metabolite of IIa, difenoxine (IIb),<sup>3</sup> was found to be five times more potent than IIa and to possess a better safety margin.4-8

The original objective of this study was to replace the cyano group of II by an amide function, but the approach led invariably to less active or inactive compounds. However, when the carboxyl substituent on the piperidine ring was replaced by a hydroxyl group as well, improvement in activity was found. This modification was surprising, since 4-aryl-4-piperidinols are typical moieties of neuroleptics,

$$\begin{array}{c|c} CON \\ \hline Ph_2C-CH-CHN \\ \hline R_1 & R_2 \\ \hline I & IIa, R = Et \\ b, R = H \\ \end{array}$$

such as haloperidol, trifluperidol, moperone, and clofluperol.9 Chemistry. The synthesis of the teritary butyramides I is outlined in Schemes I and II. Ring opening of 2,2-diphenyl-4-hydroxybutyric acid  $\gamma$ -lactone (1) with HBr in AcOH afforded 4-bromo-2,2-diphenylbutyric acid (2).10 Subsequent treatment of 2 with SOCl<sub>2</sub> and reaction of the intermediate acid chloride with an appropriate secondary amine yielded the corresponding (tetrahydro-3,3-diphenyl-2-furylidene)ammonium salts III (Table I). Compounds 3 rearranged spontaneously under the reaction conditions. The structure of ammonium salts III was evident from spectral data (Experimental Section) and from their reactivity. Compounds III

#### Scheme I

$$\begin{array}{c}
O & O \\
Ph & \longrightarrow Ph_2CCH_2CH_2Br \\
\hline
Ph & 2 \\
\hline
1 & \longrightarrow A \\
\hline
Ph & \longrightarrow Ph \\
\hline
III & IV$$

### Scheme II

$$\begin{array}{c|c}
 & CONMe_{2} \\
 & Ph \\
\hline
 & Ph \\
\hline
 & Ph \\
\hline
 & Ph_{2}CCH_{2}CH_{2}OH \\
\hline
 & Ph_{2}CCH_{2}CH_{2}OH \\
\hline
 & Ph \\
\hline
 & S \\
 & S \\
\hline
 & S \\
\hline$$

reacted extremely fast with 4-aryl-4-piperidinols IV to give the desired end products I. Treatment of dimethyl(tetrahydro-3,3-diphenyl-2-furylidene)ammonium bromide (4a) with aqueous base afforded 4-hydroxy-N,N-dimethyl-2,2-diphenylbutyramide (5), which was converted with SOCl<sub>2</sub> to the corresponding 4-chloro compound 6c. Compound 6c rearranged slowly to the corresponding ammonium salt of

type III upon warming in an inert solvent. Reaction of 6c with IV afforded end products I (Table II).

Primary and secondary butyramides I were prepared by substitution reaction of **6a** and **6b** with the appropriate 4-aryl-4-piperidinols IV. Compounds **6a** and **6b** were synthesized by ring opening of the corresponding 3,3-diphenyl-2-iminotetrahydrofurans **7a** and **7b** with HCl. <sup>11</sup> Quaternization of **7b** with MeI afforded ammonium iodide **4b**. Alkylation of **7a** with LiNH<sub>2</sub> and MeI yielded monomethylated compound **7b**.

The  $\beta$ - and  $\gamma$ -methyl-substituted butyramides I were prepared by condensation of the appropriately substituted (tetrahydro-3,3-diphenyl-2-furylidene)ammonium salts 11 and 14 with 4-aryl-4-piperidinols IV. The synthesis of 11 and 14 is outlined in Schemes III and IV. Treatment of 3-

#### Scheme III

cyano-3,3-diphenylisobutyric acid<sup>12</sup> with SOCl<sub>2</sub> followed by reduction of the intermediate acid chloride with NaBH<sub>4</sub> in DMF afforded the corresponding alcohol 9. Acid cyclization of 9 gave tetrahydro-4-methyl-3,3-diphenyl-2-furanimine (10). Alkylation of 10 followed by quaternization yielded ammonium iodide 11. Allylation of the appropriately N,N-disubstituted 2,2-diphenylacetamide 12 with NaNH<sub>2</sub> in xylene afforded the corresponding 2,2-diphenyl-4-pentenamide 13. Cyclization of 13 with HBr in AcOH

Table I. (Tetrahydro-3,3-diphenyl-2-furylidene)ammonium Salts

$(A') \stackrel{\uparrow}{N} O \qquad R_2 \qquad X^-$ $Ph \qquad R_1$								
Compd	$N \stackrel{A'}{_{\Delta}}$	$R_{_1}$	R <sub>2</sub>	X	Crystn solvent	Yield purified, %	Mp, °C	Formula <sup>a</sup>
4a	NMe,	Н .	Н	Br	i-BuCOMe	50	181-182	C H P-NO
4b	NMe <sub>2</sub>	H	H	Į.	i-BuCOMe	63	217-218	C <sub>18</sub> H <sub>20</sub> BrNO
11	NMe,	Me	H	Ī	i-BuCOMe	35	180-181	C <sub>18</sub> H <sub>20</sub> INO C <sub>19</sub> H <sub>22</sub> INO
14a	NMe,	H	Me	Br	i-BuCOMe	7 <b>4</b>	207-208	$C_{19}H_{22}BrNO$
14b	c-N(CH <sub>2</sub> ) <sub>4</sub>	H	Me	Br	i-BuCOMe	88	226-227	$C_{21}H_{24}BrNO$
15	NEt,	H	Н	Br	i-BuCOMe	58	172-174	$C_{20}H_{24}BrNO$
16	N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub>	H	H	Br	i-Pr <sub>2</sub> O	53	98-100	$C_{22}H_{24}BrNO$
17	NEtMe	Н	H	Br	Me <sub>2</sub> CO	50	172-173	$C_{19}H_{22}BrNO^{c}$
18	N-i-PrMe	Н	Н	Br	2		2,22,0	$C_{20}H_{24}BrNO^{b,c}$
19	NMe-n-Pr	Н	Н	Br	i-BuCOMe	49	170-172	$C_{20}H_{24}BrNO^c$
20	$NMeCH_2C_6H_5$	H	H	Br	i-BuCOMe	31	112-113	$C_{24}H_{24}BrNO^{c}$
21	c-N(CH <sub>2</sub> ) <sub>4</sub>	H	Н	Br	i-BuCOMe	45	186-188	$C_{20}H_{22}BrNO^c$
22	c-N(CH <sub>2</sub> ) <sub>5</sub>	H	H	Br	i-BuCOMe	52	166-167	$C_{21}^{20}H_{24}^{22}BrNO$
23	$c-N(CH_2)_5-m-CH_3$	H	H	Br	i-BuCOMe	70	198-199	$C_{22}^{21}H_{26}^{24}BrNO^{c}$
24	c-N(CH <sub>2</sub> ) <sub>5</sub> -p-CH <sub>3</sub>	H	H	Br	i-BuCOMe	40	193-194	$C_{22}^{22}H_{26}^{26}BrNO$
25	c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	H	Н	Br	i-BuCOMe	30	175-177	$C_{20}H_{22}BrNO_{2}$
26	NO CH3	Н	Н	Br	i-Pr₂O	30	143–144	C <sub>22</sub> H <sub>26</sub> BrNO <sub>2</sub>
	CH <sub>3</sub>							

<sup>&</sup>lt;sup>a</sup>Analyzed for C, H, and N. <sup>b</sup>Crude oil (not analyzed for C, H, and N). <sup>c</sup>The possibility of geometric isomerism due to restricted rotation of the C=N<sup>b</sup> bond was not further investigated.

Table II. 2,2-Diphenyl-4-(4'-aryl-4'-hydroxypiperidino)butyramides

$$CON$$
 $A'$ 
 $A'$ 
 $C-CH-CH-N$ 
 $R_1$ 
 $R_2$ 
 $R_4$ 

Comput   Na						$\odot$				
27		,,_A'\					Crystn	Yield		
NIMe	Compd	N_A-/	$R_1$	$R_2$	$R_3$	$R_4$	solvent	purified, %	Mp,°C	Formula <sup>a</sup>
NIMe	27	<del></del>	H	Н	4-C1	Н	<i>i</i> -RuCOMe	10	236_237	C H CIN O .HCl
29										C H N O HCI
30 NMe; H H H 4-Me H Me; CO 41 31 NMe; H H H 4-Me H Me; CO 41 32 NMe; H H H 3-Cl 3-Cl; Fibroth 80 33 NMe; H H H 4-Cl 3-Cl; Fibroth 80 33 NMe; H H H 4-Cl 3-Cl; Fibroth 64 34 NMe; H H H H H PhMe 60 35 NMe; H H H H H PhMe 60 36 NMe; H H H H H PhMe 60 37 NMe; H H H 3-Cl; H Fibroth 82 37 NMe; H H H 3-Cl; H Fibroth 82 37 NMe; H H H 2-Me Me; CO 41 38 NMe; H H 2-Me Me; CO 41 40 NE; H H 2-Me Me; CO 41 41 NE; H H 4-Cl 3-Cl; Fibroth 69 420-221 C, H, N, O; HCl 3-Cl; H, N, O;										C H CIN O .HC
31 NMe; H H 3-Cl 4-Cl 6-BucOMe 80 239-240 C_HL, NO, -HCl 33 NMe; H H H 4-Cl 3-CF, 6-PO-H 64 215-216 C_HL, CIN, O, -HCl 34 NMe; H H H H H PhMe 60 130-131 C_HL, NO, -HCl 35 NMe; H H H H H PhMe 60 130-131 C_HL, NO, -HCl 36 NMe; H H H 4-F H 6-BucOMe 64 123-124 C_HL, Bin, NO, -HCl 37 NMe; H H 4-F H 6-BucOMe 34 123-124 C_HL, Bin, NO, -HCl 37 NMe; H H 2-Me 4-Me 6-BucOMe 34 123-124 C_HL, Bin, NO, -HCl 0-PO-H 60 130-131 C_HL, NO, -HCl										C + CIN O + CI
32 NMe; H H H 4Cl 3-CF, FP0H 64  33 NMe; H H H 4Cl 3-CF, FP0H 64  34 NMe; H H H H H PPMe 60  35 NMe; H H H H H F PPME 60  36 NMe; H H H SCF, H FBUCOME 84  36 NMe; H H H SCF, H FBUCOME 84  37 NMe; H H H 2-ME FBUCOME 84  38 NMe; H H 2-ME SMCOME 84  39 NMe; H H 2-ME SMCOME 84  40 NE; H H 2-ME SMCOME 84  40 NE; H H 4Cl 3-CF, FBUCOME 85  41 NE; H H 4Cl 3-CF, FBUCOME 85  423-2246 C,H,H,N,O; HCl 0-5/-P70H 82  233-234 C,H,H,N,O; HCl 0-5/-P70H 82  248-249 C,H,H,N,O; HCl 0-5/-P70H 82  249-240 C,H,H,N,O; HCl 0-5/-P70H 82  249-241 C,H,		-								$C = H \cdot N \cdot O \cdot HC$
33 NMe; H H H 4-Cl 3-CF; PPOH 64 213-216 C <sub>2</sub> H <sub>2</sub> H <sub>2</sub> FN,O <sub>2</sub> ·HCl 35 NMe; H H H H H PPME 60 130-131 C <sub>2</sub> H <sub>2</sub> H <sub>2</sub> NO, H <sub>2</sub> O 135 NMe; H H H 4-B H PBuCOME 64 123-124 C <sub>2</sub> H <sub>2</sub> H <sub>2</sub> NN,O <sub>2</sub> ·H <sub>2</sub> O 136 NMe; H H 4-B H PPMC 82 233-234 C <sub>2</sub> H <sub>2</sub> H <sub>2</sub> FN,O <sub>2</sub> ·HCl 137 NMe; H H 2-Me 4-Me 4-Me 4-Me 4-Me 4-Me 4-Me 4-Me 4										$C_{30}H_{36}N_2O_2$ HC1
NMe;   H   H   H   H   FPME   60   130-131   C_yH_N,N_O, 1										$C_{29}^{11} C_{12}^{11} C_{1$
36 NMe, H H H 3-CF, H FBCOME 64 123-124 C.,H,BN,O,-H,O 36 NMe, H H H 4-F H FBCOME 34 183-186 (H,F,N,O,-HC) 37 NMe, H H H 2-Me 4-Me FBUCOME 34 123-124 C.,H,FN,O,-HCI-0.5FPOHD 38 NMe, H H B 2-Me 0-5-MeO THF 40 180-181 C.,H,N,O,-HCI-0.5FPOHD 39 NMe, H H B 2-Me 0-5-MeO THF 40 180-181 C.,H,N,O,-HCI-0.5FPOHD 40 NEt; H H H 2-Me 0-5-MeO THF 40 180-181 C.,H,N,O,-HCI-0.5FPOHD 41 NEt; H H H 4-CI 3-CF, FBUCOME 45 135-136 C.,H,FN,O,-HCI 42 NEt, H H H 3-CI 4-CI FPOH 60 124-8-249 C.,H,R,CI-N,O,-HCI 43 NEt, H H H 3-CF H FBUCOME 75 222-223 C.,H,FN,O,-HCI 44 NEt, H H H 3-CF H FBUCOME 75 222-223 C.,H,FN,O,-HCI 45 NEt, H H H 4-CI H FPOH 11 248-249 C.,H,R,CI-N,O,-HCI 46 NEt, H H H 4-CI H FBUCOME 75 222-223 C.,H,FN,O,-HCI 47 NICH,, H H H 4-CI H FBUCOME 56 187-188 C.,H,FN,O,-HCI-0.5FPOHC 48 NCH,, H H 4-CI 3-CF, FBUCOME 56 187-188 C.,H,FN,O,-HCI-0.5FPOHC 49 NCH,, H H 4-CI 3-CF, FBUCOME 56 187-188 C.,H,FN,O,-HCI-0.5FPOHC 40 NCH,, H H 3-CI 4-CI E-IOH 30 188-189 C.,H,FN,O,-HCI-0.5FPOHC 41 NCH,, H H 4-CI 3-CF, FBUCOME 56 187-188 C.,H,FN,O,-HCI-0.5FPOHC 42 NCH,, H H 3-CI 4-CI E-IOH 30 188-189 C.,H,FN,O,-HCI-0.5FPOHC 43 NCH,, H H 3-CI 4-CI E-IOH 30 188-189 C.,H,FN,O,-HCI-0.5FPOHC 44 NCH,, H H 3-CI 4-CI E-IOH 30 188-189 C.,H,FN,O,-HCI-0.5FPOHC 45 NCH,, H H 3-CI 4-CI E-IOH 30 188-189 C.,H,FN,O,-HCI-0.5FPOHC 46 NCH,, H H 3-CI 4-CI E-IOH 30 188-189 C.,H,FN,O,-HCI-0.5FPOHC 47 NCH,, H H 3-CI 4-CI E-IOH 30 188-189 C.,H,FN,O,-HCI 48 NCH,, H H 3-CI 4-CI H FBUCOME 61 187-184 C.,H,FN,O,-HCI-0.5FPOHC 48 NCH,, H H 3-CI 4-CI H FBUCOME 77 222-223 C.,H,FN,O,-HCI 49 NCH,, H H 3-CI 4-CI H BUCOME 78 242-243 C.,H,FN,O,-HCI 40 NCH,, H H 3-CI 4-CI H BUCOME 78 242-243 C.,H,FN,O,-HCI 41 NEt; H H H 4-CI H FBUCOME 78 242-243 C.,H,FN,O,-HCI 41 NEt; H H H 4-CI H FBUCOME 78 242-243 C.,H,FN,O,-HCI 41 NEt; H H H 4-CI H FBUCOME 78 242-243 C.,H,FN,O,-HCI 41 NEt; H H H 4-CI H FBUCOME 78 242-243 C.,H,FN,O,-HCI 41 NEt; H H H 4-CI H FBUCOME 78 242-243 C.,H,FN,O,-HCI 41 NEt; H H H 4-CI H FBUCOME 78 242-243 C.,H,FN,O,-HCI 41 NEt; H H H 4-CI H FBUCOME 78 242-243 C.,H,FN,O,-HCI 4										
36 NMe; H H H 3-CF, H FBUCOME 34 183-186 C <sub>1</sub> H <sub>2</sub> F,N <sub>0</sub> , HCl 0.54PrOHD 37 NMe; H H H 2-Me 4-Me 4-Me 4-Me 4-Me 4-Me 4-Me 4-Me 4		•								C H D-N O . H O
37 NMe. 38 NMe. 49 H H 2-Me 40 NEt. 40 NEt. 41 H H 2-Me 50 S-MeO 41 180-181 42 (L.H.F.N.O., -HC-H.O.) 41 NEt. 41 NEt. 42 H H H 4-CI 43 NEt. 44 H H 3-CI 44 S-PFO-H 45 NET. 45 NET. 46 NET. 47 ENCOME 48 S-PFO-H 48 S-PFO-H 49 S-PFO-H 40 NET. 40 NET. 41 NET. 42 NET. 43 NET. 44 NET. 45 NET. 46 H H 3-CI 46 NET. 47 ENCOME 48 S-PFO-H 48 S-PFO-H 49 S-PFO-H 40 NET. 48 S-PFO-H 40 NET. 49 S-PFO-H 40 NET. 40 NET. 41 NET. 41 NET. 42 NET. 43 NET. 44 NET. 44 NET. 45 NET. 46 H H 3-CI 46 NET. 47 ENCOME 48 S-PFO-H 49 S-PFO-H 40 NET. 48 ENCOME 49 S-PFO-H 40 NET. 49 ENCOME 49 ENCOME 49 ENCOME 49 ENCOME 49 ENCOME 40 NET. 40 NET. 41 NET. 42 NET. 43 NET. 44 NET. 44 NET. 45 NET. 46 NET. 47 ENCOME 48 ENCOME 49 ENCOME 49 ENCOME 49 ENCOME 40 EN										$C_{29}^{11}_{33}^{13}^{13}^{11}_{2}^{$
38   NMe										C H FN O .HCl. 0 5i-PrOHb
39										
40 NEt, H H 4-Cl 3-CF, FBuCOMe 69 220-221 C, H, ClF, N,O, HCl 41 NEt, H H 4-F H 7-BuCOMe 45 135-136 C, H, FN,O, 42 NEt, H H 3-Cl 4-Cl 7-POH 60 245-246 C, H, ClN,O, HCl 43 NEt, H H H H H H 7-POH 71 248-249 C, H, N,O, HCl 0.58-POH 44 NEt, H H H 3-CF, H 7-BuCOMe 75 222-223 C, H, F,N,O, HCl 0.58-POH 45 NEt, H H H 3-CF, H 7-BuCOME 75 222-223 C, H, F,N,O, HCl 0.58-POH 46 NEt, H H H 4-Cl H 7-POH 36 145-146 C, H, B, N,O, HCl 0.58-POH 47 NC(H,), H H H 4-Cl H 7-POH 36 145-146 C, H, B, N,O, HCl 0.58-POH 48 NC(H,), H H H 4-Cl H 7-BuCOME 56 187-188 (H, K,N,O, HCl 0.58-POH) 49 NC(H,), H H H 4-Cl H 7-BuCOME 56 187-188 (H, K,N,O, HCl 0.58-POH) 49 NC(H,), H H 3-Cl 3-CF, FBuCOME 30 188-189 (H, K,N,O, HCl 0.58-POH) 50 NC(H,), H H 3-Cl 3-CF, FBuCOME 40 117-118 (H, CN,O, HCl 0.58-POH) 51 NC(H,), H H 3-Cl 3-CF, FBuCOME 40 117-118 (H, CN,O, HCl 0.58-POH) 52 NC(H,), H H 4-Cl 3-CF, FBuCOME 40 117-118 (H, CN,O, HCl 0.58-POH) 53 NC(H,), H H 3-Cl 3-CF, FBuCOME 64 204-205 C, H, K,N,O, HCl 0.58-POH) 54 NC(H,), H H 3-CC, 3-CF, FBuCOME 64 204-205 C, H, K,N,O, HCl 0.58-POH) 55 NC(H,), H H 3-CC, 3-CF, FBuCOME 65 200-201 C, H, K,N,O, HCl 0.58-POH) 56 NC(H,), H H 3-CC, H H FBuCOME 65 211-253 (H, K,N,O, HCl 0.58-POH) 57 NC(H,), H H 3-CC, H H FBuCOME 65 243-244 (H, K,N,O, HCl 0.58-POH) 58 NC(H,), H H 3-CC, H H FBuCOME 65 243-244 (H, K,N,O, HCl 0.58-POH) 59 NC(H,CH,), O H H 4-Cl H FBuCOME 65 243-244 (H, K,N,O, HCl 0.58-POH) 61 NC(H,CH,), O H H 4-Cl H FBuCOME 78 242-243 (H, K,N,O, HCl 0.58-POH) 62 NNC(H,CH,), O H H 4-Cl H FBuCOME 78 242-243 (H, K,CN,O, HCl 0.58-POH) 63 NOCH, H H 4-Cl H FBuCOME 73 225-226 (H, H,K,N,O, HCl 0.58-POH) 64 NNC+PT H H 4-Cl H FBuCOME 73 225-226 (H, H,K,N,O, HCl 0.58-POH) 65 NNC(H,CH,), H H 4-Cl H FBuCOME 73 225-226 (H, H,K,N,O, HCl 0.58-POH) 66 NNC+PT H H 4-Cl H FBuCOME 73 225-226 (H, H,K,N,O, HCl 0.58-POH) 67 NNC+PT H H 4-Cl H FBuCOME 73 225-226 (H, H,K,N,O, HCl 0.58-POH) 78 NNCe, H Me 4-Cl H FBuCOME 71 215-216 (H, H,K,N,O, HCl 0.58-POH) 79 NNCe, H Me 4-Cl H FBuCOME 71 225-226 (H, H,K,N,O, HCl 0.58-POH) 71 NNCe, H Me 4-Cl H										C H N.O HNO
41 NEt; H H 4-F H 5-BuCOMe 45 135-136 C, 1,H,FN,O; 14C1 42 NEt; H H H 3-CI 4-CI 1-FPOH 60 245-246 C, 1,H,FN,O; 14C1 0.55-PrOH 43 NEt; H H H H H 1										C H CIF N O .HCl
42   NEt,										C H FN O
A3										$C_{\bullet}H_{\bullet}$ Cl N O $\bullet$ HCl
Mathematical Property   Mat										C H N O · HCl · O 5 <i>i</i> -PrOH
46 NE; H H H 4-BE H FBuCOMe 36 145-146 C, H, Bin O, 10, SH, O 47 eN(CH <sub>2</sub> ) <sub>4</sub> H H H 4-CL H FPOH 44 236-237 C, H <sub>2</sub> , CN, O <sub>2</sub> + CL 1-0, St-PrOHC 48 eN(CH <sub>2</sub> ) <sub>4</sub> H H H 4-CL H FBuCOME 62 192-193 C, H <sub>2</sub> , CN, O <sub>2</sub> + CL 1-0, St-PrOHC 48 eN(CH <sub>2</sub> ) <sub>4</sub> H H H 4-CL 3-CF <sub>2</sub> FBuCOME 62 192-193 C, H <sub>2</sub> , CN, O <sub>2</sub> + CL 1-0, St-PrOHC 50 eN(CH <sub>2</sub> ) <sub>4</sub> H H 3-CL 4-CL EIOH 49 200-201 C <sub>2</sub> , H <sub>2</sub> , CL N <sub>2</sub> , O <sub>2</sub> + CL 1-0, St-PrOHC 51 eN(CH <sub>2</sub> ) <sub>4</sub> H H 3-CL H FBuCOME 53 168-169 C, H <sub>2</sub> , CL N <sub>2</sub> , O <sub>2</sub> + CL 1-0, St-PrOHC 52 eN(CH <sub>2</sub> ) <sub>4</sub> H H 4-CL H FBuCOME 53 168-169 C, H <sub>2</sub> , CL N <sub>2</sub> , O <sub>2</sub> + CL 1-0, St-PrOHC 53 eN(CH <sub>2</sub> ) <sub>4</sub> H H 3-CL 4-CL FBuCOME 53 168-169 C, H <sub>2</sub> , CL N <sub>2</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 54 eN(CH <sub>2</sub> ) <sub>4</sub> H H 3-CL 4-CL M <sub>2</sub> , CO 37 202-203 C, H <sub>2</sub> , CL N <sub>2</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 55 eN(CH <sub>2</sub> ) <sub>3</sub> H H H 3-CL 4-CL M <sub>2</sub> , CO 37 202-203 C, H <sub>3</sub> , CL N <sub>2</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 56 eN(CH <sub>2</sub> ) <sub>3</sub> H H H 3-CL H FBuCOME 62 200-201 C, H <sub>3</sub> , CL N <sub>2</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 57 eN(CH <sub>2</sub> ) <sub>3</sub> H H H 3-CL H FBuCOME 62 200-201 C, H <sub>3</sub> , CL N <sub>2</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 58 eN(CH <sub>2</sub> ) <sub>3</sub> H H H 3-CL H FBuCOME 62 21-233 C, H <sub>3</sub> , CL N <sub>2</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 59 eN(CH <sub>2</sub> ) <sub>3</sub> O H H 3-CL H FBuCOME 65 243-244 C, H <sub>3</sub> , CL N <sub>2</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 60 eN(CH <sub>2</sub> ) <sub>3</sub> O H H 3-CL H FBuCOME 65 243-244 C, H <sub>3</sub> , CL N <sub>3</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 61 eN(CH <sub>2</sub> ) <sub>3</sub> O H H 3-CL H FBuCOME 65 243-244 C, H <sub>3</sub> , CL N <sub>3</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 62 eN(CH <sub>2</sub> ) <sub>3</sub> O H H 4-CL H FBuCOME 78 242-243 C, H <sub>3</sub> , CL N <sub>3</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 64 eN(CH <sub>2</sub> ) <sub>3</sub> O H H 4-CL H FBuCOME 78 242-243 C, H <sub>3</sub> , CL N <sub>3</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 65 eN(CH <sub>2</sub> ) <sub>3</sub> O H H 4-CL H FBuCOME 78 225-225 C, H <sub>3</sub> , CL N <sub>3</sub> , O <sub>3</sub> + CL 1-0, St-PrOHC 66 NMe-P-P H H 4-CL H FBuCOME 79 225-226 C, H <sub>3</sub> , CL N <sub>3</sub>										CHF.N O .HCl
NET										CHBrN.O. 0.5H.O
48										C. H. CIN O . HCl · 0.5 <i>i</i> -PrOH <sup>c</sup>
## ONICH_D_A H H 4-F H FBUCOME 62 192-193 C_H_CFN_O_C HC PO ONICH_D_A H H 3-CL 3-CF_S FBUCOME 30 188-189 C_H_CFN_O_C HC PO_NOCH_D_A H H 3-CL 3-CF_S FBUCOME 40 117-118 C_H_M_CLN_O_C HC PO_N CH_D_A H H 3-CL 4-CL E-OH 49 200-201 C_H_CLN_O_C HC PO_N CH_D_A H H 3-CL H FBUCOME 53 168-169 C_H_CFN_O_S HC PO_N CH_D_A H H 4-CL H FBUCOME 53 168-169 C_H_CFN_O_S HC PO_N CH_D_A H H 4-CL H FBUCOME 53 168-169 C_H_CFN_O_S HC PO_N CH_D_A H H 4-CL H FBUCOME 64 204-205 C_H_CFN_O_S HC PO_N CH_D_A H H 3-CF_S H FBUCOME 64 204-205 C_H_CFN_O_S HC PO_N CH_D_A H H 3-CF_S H FBUCOME 62 200-201 C_H_CFN_O_S HC PO_N CH_D_A H P 1 - PBUCOME 62 200-201 C_H_CFN_O_S HC PO_N CH_D_A P 1 - PBUCOME 62 200-201 C_H_CFN_O_S HC PO_N CH_D_A P 1 - PBUCOME 65 251-253 C_H_CFN_O_S HC PO_N CH_D_A P 1 - PBUCOME 65 251-253 C_H_CFN_O_S HC P 1 - PBUCOME 65 243-244 C_H_CFN_O_S HC P 1 - PBUCOME 65 243-245 C_H_CFN_O_S HC P 1 - PBUCOME 66 2241-242 C_H_CFN_O_S HC P 1 - PBUCOME 65 243-245 C_H_CFN_O_S HC P 1 - P		c-N(CH <sub>2</sub> ).								CHN.O.
## ONICH_D_A		c-N(CH <sub>a</sub> ).								CHFN.O.
50		c-N(CH <sub>a</sub> ).								CHClF.N.O.·HCl
51		c-N(CH <sub>a</sub> ).				4-C1				CHCl.N.O.·HCl
52 cN(CH <sub>2</sub> ) <sub>3</sub> H H 4 4-Cl H ibuCOMe 53 168-169 C <sub>3</sub> ,H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 53 cN(CH <sub>2</sub> ) <sub>3</sub> H H 3-Cl 3-CF <sub>5</sub> i-BuCOMe 64 204-205 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 55 cN(CH <sub>2</sub> ) <sub>5</sub> H H 3-CF <sub>5</sub> H ibuCOMe 62 200-201 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 55 cN(CH <sub>2</sub> ) <sub>5</sub> H H 3-CF <sub>5</sub> H ibuCOMe 51 240-241 C <sub>3</sub> +H <sub>3</sub> N <sub>2</sub> O <sub>5</sub> inCl 56 cN(CH <sub>2</sub> ) <sub>5</sub> H H H 3-CF <sub>5</sub> H ibuCOMe 51 240-241 C <sub>3</sub> +H <sub>3</sub> N <sub>2</sub> O <sub>5</sub> inCl 57 cN(CH <sub>2</sub> O <sub>1</sub> ) <sub>5</sub> H H 4-Cl H ibuCOMe 62 213-213 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 68 cN(CH <sub>2</sub> O <sub>1</sub> O <sub>2</sub> ) H H 3-CF <sub>5</sub> H ibuCOMe 62 213-214 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 69 cN(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> O H H 3-CF <sub>5</sub> H ibuCOMe 65 243-244 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 60 cN(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> O H H 3-CF <sub>5</sub> ibuCOMe 65 243-244 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 61 cN(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> O H H H 3-Cl H ibuCOMe 78 242-243 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 61 cN(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> O H H 4-Cl H ibuCOMe 78 242-243 C <sub>3</sub> +H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 62 cN(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> O H H 4-Cl H ibuCOMe 78 241-242 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 62 cN(CH <sub>3</sub> CH <sub>3</sub> ) <sub>2</sub> O H H 4-Cl H ibuCOMe 72 257-258 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 63 No CH <sub>3</sub> CN <sub>2</sub> O <sub>5</sub> inCl 64 cN(CH <sub>3</sub> ) <sub>2</sub> m-CH <sub>3</sub> H H 4-Cl H ibuCOMe 72 257-258 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 65 cN(CH <sub>3</sub> ) <sub>2</sub> m-CH <sub>3</sub> H H 4-Cl H ibuCOMe 78 241-242 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 66 NMeEt H H 4-Cl H ibuCOMe 78 235-236 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 66 NMee <sup>2</sup> in H H 4-Cl H ibuCOMe 78 235-236 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 66 NMee <sup>2</sup> in H H 4-Cl H ibuCOMe 78 235-236 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 67 NMen <sup>3</sup> in H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O <sub>5</sub> inCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H ibuCOMe 78 225-226 C <sub>3</sub> H <sub>3</sub> CIN <sub>2</sub> O		c-N(CH <sub>a</sub> ).								Carha FaNaOa HCl 2HaO
53 cN(CH <sub>2</sub> ) <sub>5</sub> H H 4 4-Cl 3-CF <sub>3</sub> i-BuCOMe 64 204-205 C <sub>3</sub> H <sub>3</sub> C(F)N <sub>2</sub> O <sub>3</sub> -HCl 55 cN(CH <sub>2</sub> ) <sub>5</sub> H H 3-Cl 4-Cl Me <sub>2</sub> CO 37 202-203 C <sub>2</sub> H <sub>3</sub> C(F)N <sub>2</sub> O <sub>3</sub> -HCl 55 cN(CH <sub>2</sub> ) <sub>5</sub> H H 3-CF <sub>3</sub> H i-BuCOMe 62 200-201 C <sub>3</sub> H <sub>3</sub> C <sub>3</sub> F <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 55 cN(CH <sub>2</sub> ) <sub>5</sub> H H H H H i-BuCOMe 51 240-241 C <sub>3</sub> H <sub>3</sub> P <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 57 cN(CH <sub>2</sub> ) <sub>2</sub> H H H 3-CF <sub>3</sub> H i-BuCOMe 62 213-214 C <sub>3</sub> H <sub>3</sub> P <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 58 cN(CH <sub>2</sub> OH <sub>2</sub> ) <sub>2</sub> H H 3-CF <sub>3</sub> H i-BuCOMe 62 213-214 C <sub>3</sub> H <sub>3</sub> P <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 59 cN(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> D H H 3-CF <sub>3</sub> H i-BuCOMe 65 243-244 C <sub>3</sub> H <sub>3</sub> P <sub>3</sub> C <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 60 cN(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> D H H 3-CF <sub>3</sub> i-BuCOMe 65 243-244 C <sub>3</sub> H <sub>3</sub> P <sub>3</sub> C <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 61 cN(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> D H H H H I i-PrOH 49 182-183 C <sub>3</sub> H <sub>3</sub> C <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 61 cN(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> D H H 4-Cl H Me <sub>2</sub> CO 72 257-258 C <sub>3</sub> H <sub>3</sub> C <sub>3</sub> CN <sub>2</sub> O <sub>3</sub> -HCl 62 cN(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> D H H 4-Cl H i-BuCOMe 36 241-242 C <sub>3</sub> H <sub>3</sub> C <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 63 NMe <sub>2</sub> CH <sub>3</sub> C		c-N(CH <sub>a</sub> ).								C., H., CIN, O.
54		c-N(CH <sub>2</sub> ),								C.H. CIF N.O. HCI
55 c-N(CH <sub>2</sub> ) <sub>2</sub> H H H 3-CF <sub>2</sub> H i-BuCOMe 62 200-201 C <sub>23</sub> H <sub>37</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> -HCl 56 c-N(CH <sub>2</sub> ) <sub>3</sub> H H H H i-BuCOMe 51 240-241 C <sub>23</sub> H <sub>37</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> -HCl 57 c-N(CH <sub>2</sub> ) <sub>3</sub> H H A 4-Cl H EtOH 66 251-253 C <sub>23</sub> H <sub>37</sub> N <sub>3</sub> O <sub>2</sub> -HCl 58 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>3</sub> O H H 3-CF <sub>2</sub> H i-BuCOMe 62 213-214 C <sub>23</sub> H <sub>36</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> -HCl 59 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>3</sub> O H H 3-Cl 3-CF <sub>3</sub> i-BuCOMe 65 243-244 C <sub>23</sub> H <sub>36</sub> C <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 60 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>3</sub> O H H 3-Cl 4-Cl i-BuCOMe 78 242-243 C <sub>33</sub> H <sub>36</sub> C <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 61 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>3</sub> O H H H 4-Cl H Me <sub>2</sub> CO 72 257-258 C <sub>33</sub> H <sub>36</sub> C <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 62 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H 4-Cl H i-BuCOMe 36 241-242 C <sub>33</sub> H <sub>36</sub> C <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 63 NO CH <sub>3</sub> 64 c-N(CH <sub>2</sub> ) <sub>2</sub> m-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 71 215-216 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 65 c-N(CH <sub>2</sub> ) <sub>2</sub> m-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 66 NMeEt H H 4-Cl H i-BuCOMe 78 190-191 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 67 NMen-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 68 NMei-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 73 225-226 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-BuCOMe 60 225-226 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 60 225-226 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 72 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 60 225-226 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 73 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>33</sub> H <sub>33</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 74 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 40 252-253 C <sub>33</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 75 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 43 193-194 C <sub>33</sub> H <sub>33</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 76 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 109-197 C <sub>33</sub> H <sub>33</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 77 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 47 109-197 C <sub>33</sub> H <sub>33</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 78 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 47 109-197 C <sub>33</sub> H <sub>33</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>24</sub> H <sub>35</sub> N <sub>2</sub> O <sub>2</sub> 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>24</sub> H <sub>35</sub> N <sub>2</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>24</sub> H <sub>35</sub> N <sub>2</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>24</sub> H <sub>35</sub> N <sub>2</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> )		c-N(CH <sub>2</sub> ),								CanHaeClaNaOa HCl
56 c-N(CH <sub>2</sub> ) <sub>2</sub> H H H H H H i-BuCOMe 51 240-241 C <sub>22</sub> H <sub>38</sub> N <sub>1</sub> O <sub>2</sub> -HCl 57 c-N(CH <sub>2</sub> ) <sub>3</sub> H H 4-Cl H EtOH 66 251-253 C <sub>22</sub> H <sub>37</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl <sup>2</sup> 58 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H 3-CF <sub>3</sub> H i-BuCOMe 62 213-214 C <sub>22</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 59 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H 3-CF <sub>3</sub> i-BuCOMe 65 243-244 C <sub>22</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 60 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H H 3-Cl i-BuCOMe 78 242-243 C <sub>31</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 61 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H H 4-Cl H Me <sub>2</sub> CO 72 257-258 C <sub>31</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 62 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H 4-Cl H Me <sub>2</sub> CO 72 257-258 C <sub>31</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 63 NO CH <sub>3</sub> H H 4-Cl H i-BuCOMe 36 241-242 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 64 c-N(CH <sub>2</sub> ) <sub>2</sub> -p-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 71 215-216 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 65 c-N(CH <sub>2</sub> ) <sub>2</sub> -p-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 66 NMeEt H H 4-Cl H i-BuCOMe 85 235-236 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 66 NMee-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 67 NMen-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 68 NMei-Pr H H 4-Cl H i-BuCOMe 73 225-226 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-BuCOMe 60 225-226 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 60 225-226 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 60 225-226 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 60 225-226 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 60 225-226 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 43 193-194 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 43 193-194 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 43 193-194 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 43 193-194 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 72 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 73 C <sub>32</sub> H <sub>32</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>2</sub> -HCl 74 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>32</sub>		c-N(CH <sub>2</sub> ),						62		Ca2H22F2N2O2 · HCl
57 c-N(CH <sub>2</sub> ) <sub>5</sub> H H 3-Cl H EtOH 66 251-253 C <sub>23</sub> H <sub>3</sub> ,ClN <sub>2</sub> O <sub>2</sub> -HCl <sup>d</sup> 58 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H 3-CF <sub>3</sub> H i-BuCOMe 62 213-214 C <sub>23</sub> H <sub>36</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 59 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H 4-Cl 3-CF <sub>3</sub> i-BuCOMe 65 243-244 C <sub>23</sub> H <sub>36</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 60 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H H 3-Cl i-BuCOMe 78 242-243 C <sub>3</sub> H <sub>36</sub> Cl <sub>1</sub> N <sub>2</sub> O <sub>3</sub> -HCl 61 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H H H H i-PrOH 49 182-183 C <sub>31</sub> H <sub>36</sub> N <sub>2</sub> O <sub>3</sub> -HCl 0-Si-PrOH 62 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H H 4-Cl H i-BuCOMe 72 257-258 C <sub>31</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 63 NO CH <sub>3</sub> H H 4-Cl H i-BuCOMe 74 241-242 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 64 c-N(CH <sub>2</sub> ) <sub>4</sub> m-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 74 215-216 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 65 c-N(CH <sub>3</sub> ) <sub>5</sub> p-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 66 NMeEn-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 67 NMe-n-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>3</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 68 NMe-i-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>3</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 69 NMe-h-Ph H 4-Cl H i-BuCOMe 78 190-191 C <sub>3</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 69 NMe-h-Ph H 4-Cl H i-BuCOMe 78 190-191 C <sub>3</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-BuCOMe 78 190-191 C <sub>3</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-BuCOMe 60 225-226 C <sub>31</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 72 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 60 258-259 C <sub>33</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 73 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 45 106-197 C <sub>30</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 74 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 40 200-201 C <sub>30</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 75 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>30</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 76 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 43 193-194 C <sub>30</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>3</sub> 77 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 43 193-194 C <sub>30</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>3</sub> 78 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 109-190 C <sub>31</sub> H <sub>36</sub> ClN <sub>3</sub> O <sub>3</sub> 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>36</sub> ClN <sub>3</sub> O <sub>3</sub> 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-167 C <sub>32</sub> H <sub>36</sub> ClN <sub>3</sub> O <sub>3</sub> 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-1687 C <sub>32</sub> H <sub>36</sub> ClN <sub>3</sub> O <sub>3</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>32</sub> H <sub>36</sub> ClN <sub>3</sub> O <sub>3</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 1206-207 C <sub>32</sub> H <sub>36</sub> ClN <sub>3</sub> O <sub>3</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 1206-207 C <sub>32</sub> H <sub>36</sub>		c-N(CH <sub>2</sub> ),								$C_{20}H_{20}N_{2}O_{2}\cdot HC1$
58		c-N(CH <sub>2</sub> ),						66		CaaHaaClNaOa · HCld
59										$C_{32}H_{35}F_{3}N_{2}O_{3}\cdot HC1$
60 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H H 3-Cl 4-Cl i-BuCOMe 78 242-243 C <sub>31</sub> H <sub>36</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 61 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H H H H i-PrOH 49 182-183 C <sub>31</sub> H <sub>36</sub> N <sub>2</sub> O <sub>3</sub> -HCl 0.5i-PrOH 62 c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O H H A 4-Cl H Me <sub>2</sub> CO 72 257-258 C <sub>31</sub> H <sub>36</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>3</sub> -HCl 0.5i-PrOH 63 NO CH <sub>3</sub> H H 4-Cl H i-BuCOMe 36 241-242 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 63 NO CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> -HCl 65 c-N(CH <sub>2</sub> ) <sub>2</sub> -p-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 65 NMeEt H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 67 NMe-n-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 68 NMe-i-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 69 NMeCH,Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-BuCOMe 60 225-226 C <sub>33</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> Me H 4-Cl H i-PrOH 45 200-201 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> Me H 4-Cl H i-PrOH 40 252-253 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H EtOOH 40 200-201 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H EtOOH 40 200-201 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 48 169-170 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 48 169-170 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NNC(H <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NNC(H <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NNC(H <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> -HCl NNC(H <sub>2</sub> ) <sub>4</sub>			Н	H		3-CF <sub>2</sub>	i-BuCOMe			C <sub>20</sub> H <sub>24</sub> ClF <sub>2</sub> N <sub>2</sub> O <sub>3</sub> ·HCl
61 c-N(CH <sub>2</sub> (H <sub>2</sub> ) <sub>2</sub> ) <sub>2</sub> O H H H H H H i-PrOH 49 182-183 C <sub>31</sub> H <sub>36</sub> N <sub>2</sub> O <sub>3</sub> ·HCl· 0.5i-PrOH 62 c-N(CH <sub>2</sub> (H <sub>2</sub> ) <sub>2</sub> ) <sub>2</sub> O H H H 4-Cl H Me <sub>2</sub> CO 72 257-258 C <sub>31</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>3</sub> ·HCl· 0.5i-PrOH 63 N O CH <sub>3</sub> H H 4-Cl H i-BuCOMe 36 241-242 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> ·HCl 64 c-N(CH <sub>2</sub> ) <sub>5</sub> ·m-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 65 c-N(CH <sub>2</sub> ) <sub>5</sub> ·p-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 66 NMeEt H H 4-Cl H PhMe 30 215-216 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 67 NMe-n-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 68 NMe-i-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 68 NMe-i-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>33</sub> H <sub>33</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-BuCOMe 60 225-226 C <sub>33</sub> H <sub>33</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 45 200-201 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> H M Me 4-Cl H i-BuCOMe 20 165-166 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> H M Me 4-Cl H i-BuCOMe 40 200-201 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 40 200-201 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 41 193-194 C <sub>36</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>2</sub> NO <sub>2</sub> ·HCl 71 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 41 193-194 C <sub>36</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>2</sub> NO <sub>2</sub> ·HCl 72 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 43 193-194 C <sub>36</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>2</sub> NO <sub>2</sub> ·HCl 73 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 73 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 73 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>36</sub> H <sub>36</sub> N <sub>3</sub> O <sub>2</sub> NO <sub>2</sub> ·HCl 73 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>36</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 74 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>36</sub> H <sub>36</sub> N <sub>3</sub> O <sub>2</sub> NO <sub>2</sub> ·HCl 74 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>36</sub> H <sub>36</sub> N <sub>3</sub> O <sub>2</sub> NO <sub>3</sub>		c-N(CH,CH,),O	Н	Н						$C_3$ , $H_3$ , $Cl_3$ N $_2$ O $_3$ · $HCl$
62	61		H	H	Н	Н	i-PrOH	49	182-183	$C_3H_{36}N_2O_3\cdot HCl\cdot 0.5i$ -PrOH
63 NOCH <sub>3</sub> H H 4-Cl H i-BuCOMe 36 241-242 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> ·HCl  64 c-N(CH <sub>2</sub> ) <sub>5</sub> ·m-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 71 215-216 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  65 c-N(CH <sub>2</sub> ) <sub>5</sub> ·p-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  66 NMeEt H H 4-Cl H PhMe 30 215-216 C <sub>33</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  67 NMe-n-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  68 NMe-i-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>3</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>3</sub> H <sub>3</sub> -ClN <sub>2</sub> O <sub>2</sub> ·HCl  70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-BuCOMe 60 225-226 C <sub>35</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  71 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  72 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  73 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 45 200-201 C <sub>3</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  74 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl  75 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 76 NMe <sub>2</sub> H Me 4-F H i-BuCOMe 43 193-194 C <sub>30</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 77 NMe <sub>2</sub> H Me H i-BuCOMe 48 169-170 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me H i-BuCOMe 48 169-170 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 48 169-170 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>32</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>32</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>32</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub>		c-N(CH <sub>2</sub> CH <sub>2</sub> ) <sub>2</sub> O	Н	Н	4-C1	Н	Me <sub>*</sub> CO	72	257-258	C.,H.,CIN,O.,HCI
63 NO H H H 4-Cl H i-BuCOMe 36 241-242 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>3</sub> ·HCl  64 c-N(CH <sub>2</sub> ) <sub>5</sub> ·m-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 71 215-216 C <sub>33</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  65 c-N(CH <sub>2</sub> ) <sub>5</sub> ·p-CH <sub>5</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>25</sub> H <sub>39</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  66 NMeEt H H 4-Cl H PhMe 30 215-216 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  67 NMe-n-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  68 NMe-i-Pr H H 4-Cl H i-BuCOMe 73 225-226 C <sub>35</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>35</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-PrOH 60 258-259 C <sub>35</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  71 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  72 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 45 200-201 C <sub>31</sub> H <sub>34</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl  74 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl  75 NMe <sub>2</sub> H Me 4-F H i-BuCOMe 43 193-194 C <sub>36</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 76 NMe <sub>2</sub> H Me 1 H i-BuCOMe 43 193-194 C <sub>36</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 77 NMe <sub>2</sub> H Me 1 H i-BuCOMe 43 193-194 C <sub>36</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>36</sub> Cl <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl  79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 57 166-196 C <sub>36</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 81 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 81 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 82 C-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 81 NMe <sub>2</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>36</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub>							2	· <del>-</del>		- 3135 2- 3
64 c-N(CH <sub>2</sub> ) <sub>5</sub> m-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 71 215-216 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 65 c-N(CH <sub>2</sub> ) <sub>5</sub> p-CH <sub>3</sub> H H 4-Cl H i-BuCOMe 85 235-236 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 66 NMeEt H H 4-Cl H PhMe 30 215-216 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 67 NMe-n-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 68 NMe-i-Pr H H 4-Cl H i-BuCOMe 73 225-226 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H i-BuCOMe 60 225-226 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> Me H 4-Cl H EtOH 60 258-259 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 72 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 45 200-201 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 74 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> ·HCl 75 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> 76 NMe <sub>2</sub> H Me 4-F H i-BuCOMe 43 193-194 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> 77 NMe <sub>2</sub> H Me H H i-BuCOMe 43 193-194 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me A-Cl 3-CF <sub>3</sub> i-BuCOMe 48 169-170 C <sub>3</sub> H <sub>3</sub> p(IN <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me A-Cl 3-CF <sub>3</sub> i-BuCOMe 48 169-170 C <sub>3</sub> H <sub>3</sub> p(IN <sub>3</sub> O <sub>2</sub> ) 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me A-Cl H i-BuCOMe 57 168-169 C <sub>3</sub> H <sub>3</sub> p(IN <sub>3</sub> O <sub>2</sub> 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me A-Cl H i-BuCOMe 71 206-207 C <sub>2</sub> H <sub>3</sub> p <sub>3</sub> p <sub>3</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me A-Cl H i-BuCOMe 71 206-207 C <sub>2</sub> H <sub>3</sub> p <sub>3</sub> p <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me A-Cl H i-BuCOMe 71 206-207 C <sub>2</sub> H <sub>3</sub> p <sub>3</sub> p <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me A-F H i-BuCOMe 27 186-187 C <sub>2</sub> P <sub>3</sub> p <sub>3</sub> p <sub>3</sub> N <sub>2</sub> O <sub>2</sub>	63	N O	Н	Н	4-C1	H	i-BuCOMe	36	241-242	C <sub>23</sub> H <sub>30</sub> ClN <sub>2</sub> O <sub>3</sub> ·HCl
65		CH <sub>3</sub>								
65	64	c-N(CH <sub>2</sub> ) <sub>5</sub> -m-CH <sub>3</sub>	H	Н	4-C1	Н	i-BuCOMe	71	215-216	C <sub>33</sub> H <sub>30</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl
66 NMeEt H H 4-Cl H PhMe 30 215-216 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 67 NMe-n-Pr H H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 68 NMe-i-Pr H H H 4-Cl H i-BuCOMe 73 225-226 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H EtOH 60 258-259 C <sub>32</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 72 NMe <sub>2</sub> Me H 4-Cl 3-CF <sub>3</sub> i-PrOH 45 200-201 C <sub>31</sub> H <sub>34</sub> ClF <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl 74 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl 75 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 76 NMe <sub>2</sub> H Me 4-F H i-BuCOMe 20 165-166 C <sub>30</sub> H <sub>35</sub> FN <sub>2</sub> O <sub>2</sub> 77 NMe <sub>2</sub> H Me H i-BuCOMe 43 193-194 C <sub>30</sub> H <sub>36</sub> N <sub>3</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> i-BuCOMe 48 169-170 C <sub>31</sub> H <sub>36</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 79 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> i-BuCOMe 48 169-170 C <sub>31</sub> H <sub>36</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>36</sub> N <sub>3</sub> O <sub>2</sub> 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>32</sub> H <sub>36</sub> N <sub>2</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>32</sub> H <sub>36</sub> P <sub>3</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H i-BuCOMe 27 186-187 C <sub>32</sub> H <sub>37</sub> FN <sub>2</sub> O <sub>2</sub>	65	c-N(CH <sub>2</sub> ) -p-CH <sub>2</sub>	Н	Н	4-C1	Н	i-BuCOMe		235-236	C, H, CIN, O, HCI
67 NMe-n-Pr H H 4-Cl H i-BuCOMe 78 190-191 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 68 NMe-i-Pr H H H 4-Cl H i-BuCOMe 73 225-226 C <sub>31</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 69 NMeCH <sub>2</sub> Ph H H 4-Cl H i-BuCOMe 60 225-226 C <sub>32</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H EtOH 60 258-259 C <sub>33</sub> H <sub>37</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 71 NMe <sub>2</sub> Me H 4-Cl H i-PrOH 54 196-197 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 72 NMe <sub>2</sub> Me H 4-Cl 3-CF <sub>3</sub> i-PrOH 45 200-201 C <sub>31</sub> H <sub>34</sub> ClF <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H i-PrOH 40 252-253 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl 74 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> ·HCl 75 NMe <sub>2</sub> H Me 4-F H i-BuCOMe 20 165-166 C <sub>30</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 76 NMe <sub>2</sub> H Me H i-BuCOMe 43 193-194 C <sub>30</sub> H <sub>36</sub> N <sub>2</sub> O <sub>2</sub> 77 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> H i-BuCOMe 48 169-170 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> i-BuCOMe 45 207-208 C <sub>31</sub> H <sub>35</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H i-BuCOMe 57 168-169 C <sub>32</sub> H <sub>35</sub> N <sub>2</sub> O <sub>2</sub> ·HCl 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 C <sub>32</sub> H <sub>35</sub> ClN <sub>2</sub> O <sub>2</sub> 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 27 186-187 C <sub>32</sub> H <sub>37</sub> F <sub>N</sub> O <sub>2</sub>				H	4-C1	Н	PhMe		215-216	$C_{30}H_{35}CIN_2O_2 \cdot HCl$
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			Н	H	4-C1	Н	i-BuCOMe		190-191	$C_{31}H_{37}CIN_2O_2 \cdot HCl$
$\begin{array}{cccccccccccccccccccccccccccccccccccc$			Н	H	4-C1	Н	i-BuCOMe		225-226	$C_{31}H_{37}ClN_2O_2 \cdot HCl$
70 N(CH <sub>2</sub> CH=CH <sub>2</sub> ) <sub>2</sub> H H 4-Cl H EtOH 60 258-259 $C_{33}H_{37}ClN_2O_2 \cdot HCl$ 71 NMe <sub>2</sub> Me H 4-Cl H <i>i</i> -PrOH 54 196-197 $C_{30}H_{35}ClN_2O_2 \cdot HCl \cdot 0.5i$ -PrOH 72 NMe <sub>2</sub> Me H 4-Cl 3-CF <sub>3</sub> <i>i</i> -PrOH 45 200-201 $C_{31}H_{34}ClF_3N_2O_2$ 73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H <i>i</i> -PrOH 40 252-253 $C_{31}H_{35}F_{3N}O_2 \cdot HCl$ 74 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 $C_{30}H_{35}ClN_2O_2$ 75 NMe <sub>2</sub> H Me 4-F H <i>i</i> -BuCOMe 20 165-166 $C_{30}H_{35}FN_2O_2$ 76 NMe <sub>2</sub> H Me H H <i>i</i> -BuCOMe 43 193-194 $C_{30}H_{35}FN_2O_2$ 77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{31}H_{35}F_3N_2O_2$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}ClF_3N_2O_2 \cdot HCl$ 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{35}N_2O_2 \cdot HCl$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{35}FN_2O_2$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}FN_2O_2$			Н	H	4-C1	Н	i-BuCOMe	60	225-226	$C_{35}H_{37}ClN_2O_2 \cdot HCl$
71 NMe <sub>2</sub> Me H 4-Cl H <i>i</i> -PrOH 54 196-197 $C_{30}H_{35}CIN_{2}O_{2} \cdot HCl \cdot 0.5i$ -PrOH 72 NMe <sub>2</sub> Me H 4-Cl 3-CF <sub>3</sub> <i>i</i> -PrOH 45 200-201 $C_{31}H_{34}CIF_{3}N_{2}O_{2}$ 73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H <i>i</i> -PrOH 40 252-253 $C_{31}H_{35}F_{3}N_{2}O_{2} \cdot HCl$ 74 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 $C_{30}H_{35}CIN_{2}O_{2}$ 75 NMe <sub>2</sub> H Me 4-F H <i>i</i> -BuCOMe 20 165-166 $C_{30}H_{35}FN_{2}O_{2}$ 76 NMe <sub>2</sub> H Me H H <i>i</i> -BuCOMe 43 193-194 $C_{30}H_{35}N_{2}O_{2}$ 77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{31}H_{35}F_{3}N_{2}O_{2}$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}CIF_{3}N_{2}O_{2} \cdot HCl$ 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{35}N_{2}O_{2} \cdot HCl$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{31}H_{35}F_{30}O_{2}$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}F_{30}O_{2}$		N(CH,CH=CH,),	Н	Н	4-C1	H	EtOH	60	258-259	CHCIN.OHCl
72 NMe <sub>2</sub> Me H 4-Cl 3-CF <sub>3</sub> <i>i</i> -PrOH 45 200-201 $C_{3i}H_{34}ClF_{3}N_{2}O_{2}$ 73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H <i>i</i> -PrOH 40 252-253 $C_{3i}H_{35}F_{3}N_{2}O_{2}$ ·HCl 74 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 $C_{3o}H_{35}ClN_{2}O_{2}$ 75 NMe <sub>2</sub> H Me 4-F H <i>i</i> -BuCOMe 20 165-166 $C_{3o}H_{35}FN_{2}O_{2}$ 76 NMe <sub>2</sub> H Me H H <i>i</i> -BuCOMe 43 193-194 $C_{3o}H_{35}N_{2}O_{2}$ 77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{3i}H_{35}F_{3}N_{2}O_{2}$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{3i}H_{34}ClF_{3}N_{2}O_{2}$ ·HCl 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{22}H_{36}N_{2}O_{2}$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{3i}H_{35}ClN_{2}O_{2}$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{3a}H_{37}F_{3}O_{2}$	71		Me	Н	4-C1		i-PrOH	54	196-197	$C_{30}H_{34}CIN_{2}O_{2}HCl \cdot 0.5i$ -PrOH
73 NMe <sub>2</sub> Me H 3-CF <sub>3</sub> H <i>i</i> -PrOH 40 252-253 $C_{31}H_{35}F_{3}N_{2}O_{2}$ HCl 74 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 $C_{30}H_{35}CIN_{2}O_{2}$ 75 NMe <sub>2</sub> H Me 4-F H <i>i</i> -BuCOMe 20 165-166 $C_{30}H_{35}FN_{2}O_{2}$ 76 NMe <sub>2</sub> H Me H H <i>i</i> -BuCOMe 43 193-194 $C_{30}H_{35}N_{2}O_{2}$ 77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{31}H_{35}F_{3}N_{2}O_{2}$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}F_{3}F_{3}N_{2}O_{2}$ 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{38}N_{2}O_{2}$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{38}N_{2}O_{2}$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}FN_{2}O_{2}$		NMe <sub>2</sub>		H	4-C1	3-CF <sub>3</sub>	i-PrOH		200-201	Ca.Ha.ClFaNaOa
74 NMe <sub>2</sub> H Me 4-Cl H EtOH 40 200-201 $C_{30}H_{35}CIN_2O_2$ 75 NMe <sub>2</sub> H Me 4-F H <i>i</i> -BuCOMe 20 165-166 $C_{30}H_{35}FN_2O_2$ 76 NMe <sub>2</sub> H Me H H <i>i</i> -BuCOMe 43 193-194 $C_{30}H_{36}N_2O_2$ 77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{31}H_{35}F_3N_2O_2$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}CIF_3N_2O_2$ ·HCl 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{36}N_2O_2$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{36}P_3O_2$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}FN_2O_2$			Me	H	3-CF <sub>3</sub>		i-PrOH	40	252-253	$C_{31}H_{35}F_{3}N_{2}O_{2}\cdot HCl$
75 NMe <sub>2</sub> H Me 4-F H <i>i</i> -BuCOMe 20 165-166 $C_{30}H_{35}FN_{2}O_{2}$ 76 NMe <sub>2</sub> H Me H H <i>i</i> -BuCOMe 43 193-194 $C_{30}H_{36}N_{2}O_{2}$ 77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{31}H_{35}F_{3}N_{2}O_{2}$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}Fi_{3}N_{2}O_{2}$ ·HCl 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{36}N_{2}O_{2}$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{32}Fi_{3}N_{2}O_{2}$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{32}FN_{2}O_{2}$			H	Me		Н	EtOH	40	200-201	$C_{30}H_{35}ClN_2O_2$
76 NMe <sub>2</sub> H Me H H <i>i</i> -BuCOMe 43 193-194 $C_{30}H_{36}N_2O_2$ 77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{31}H_{35}F_3N_2O_2$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}ClF_3N_2O_2 \cdot HCl$ 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{38}N_2O_2$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{37}ClN_2O_2$ 81 c-N(CH <sub>2</sub> ) <sub>6</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}FN_2O_2$				Me	4-F	H	i-BuCOMe	20		$C_{30}H_{35}FN_2O_2$
77 NMe <sub>2</sub> H Me 3-CF <sub>3</sub> H <i>i</i> -BuCOMe 48 169-170 $C_{31}H_{35}F_{3}N_{2}O_{2}$ 78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}ClF_{3}N_{2}O_{2}$ ·HCl 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{38}N_{2}O_{2}$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{37}ClN_{2}O_{2}$ 81 c-N(CH <sub>2</sub> ) <sub>6</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}FN_{2}O_{2}$		NMe,		Me	Н	H		43		$C_{30}H_{36}N_2O_2$
78 NMe <sub>2</sub> H Me 4-Cl 3-CF <sub>3</sub> <i>i</i> -BuCOMe 45 207-208 $C_{31}H_{34}ClF_{3}N_{2}O_{2} \cdot HCl$ 79 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me H H <i>i</i> -BuCOMe 57 168-169 $C_{32}H_{38}N_{2}O_{2}$ 80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{37}ClN_{2}O_{2}$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}FN_{2}O_{2}$				Me	3-CF <sub>3</sub>		i-BuCOMe	48		$C_{31}H_{35}F_{3}N_{2}O_{2}$
79 c-N( $\dot{C}H_2$ ) <sub>4</sub> H Me H H i-BuCOMe 57 168-169 $\dot{C}_{32}H_{38}N_2O_2$ 80 c-N( $\dot{C}H_2$ ) <sub>4</sub> H Me 4-Cl H i-BuCOMe 71 206-207 $\dot{C}_{32}H_{37}ClN_2O_2$ 81 c-N( $\dot{C}H_2$ ) <sub>6</sub> H Me 4-F H i-BuCOMe 27 186-187 $\dot{C}_{32}H_{37}FN_2O_2$	78	NMe <sub>2</sub>		Me		3-CF <sub>3</sub>	i-BuCOMe	45		C <sub>31</sub> H <sub>34</sub> ClF <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl
80 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-Cl H <i>i</i> -BuCOMe 71 206-207 $C_{32}H_{37}CIN_2O_2$ 81 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 4-F H <i>i</i> -BuCOMe 27 186-187 $C_{32}H_{37}FN_2O_2$	79	$c-N(\tilde{CH}_2)_4$	H	Me	Н			57		$C_{32}H_{38}N_2O_2$
81 c-N(CH <sub>o</sub> ) H Me 4-F H i-BuCOMe 27 $186-187$ C <sub>32</sub> H <sub>3</sub> FN <sub>2</sub> O <sub>2</sub>	80	c-N(CH <sub>2</sub> ) <sub>4</sub>		Me		H				
82 c-N(CH <sub>2</sub> ) <sub>4</sub> H Me 3-CF <sub>3</sub> H $i$ -BuCOMe 30 133-134 $C_{33}$ H <sub>37</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl·2H <sub>2</sub> O	81	c-N(CH <sub>2</sub> ) <sub>4</sub>	H	Me						C <sub>32</sub> H <sub>37</sub> FN <sub>2</sub> O <sub>2</sub>
	82	$c-N(CH_2)_4$	Н	Me	$3-CF_3$	Н	i-BuCOMe	30	133-134	C <sub>33</sub> H <sub>37</sub> F <sub>3</sub> N <sub>2</sub> O <sub>2</sub> ·HCl·2H <sub>2</sub> O

<sup>a</sup>Analyzed for C, H, and N. <sup>b</sup>C: calcd, 69.49; found, 69.01. <sup>c</sup>C: calcd, 68.28; found, 67.83. <sup>d</sup>C: calcd, 69.43; found, 68.91.

gave the desired 5-methyl-substituted ammonium bromides 14.

**Pharmacology**. For screening female Wistar rats were used.  $ED_{50}$  values with 95% confidence limits were computed by Finney's iterative method.<sup>13</sup> The oral antidiar-

rheal activity was assessed by measuring the protection from diarrhea caused by castor oil.<sup>4</sup> The analgesic activity was assessed by measuring the warm water induced tail withdrawal reflex.<sup>14</sup> The ratio of the  $ED_{50}$  value in the tail withdrawal test over the  $ED_{50}$  value which gives protection for

#### Scheme IV

$$\begin{array}{c} \text{Ph}_2\text{CHCON} & \text{A} \\ \text{A} \\ \text{Ph}_2\text{CH}_2\text{CH}_2\text{CH}=\text{CH} \\ 12 \\ \text{I} & \text{A} \\ \text{Ph} \\ \text{Ph} \\ 14 \end{array}$$

1 hr in the castor oil test was used as a criterion for the relative constipating specificity (RCS).

The results are summarized in Table III. All compounds

#### Results and Discussion

tested showed antidiarrheal activity. The combination of antidiarrheal potency and high relative constipating specificity was optimal when the amide group was tertiary, bearing two small alkyl groups, such as dimethylamino (30-39) or ethylmethylamino (66). Introduction of a secondary amide (28, 29) resulted in a tenfold decrease of antidiarrheal potency and primary amide 27 had a very low potency. When  $N < \frac{A}{A'}$  was diethylamino (40-46) the compounds were equipotent, but a twofold increase in analgesic potency worsened the RCS. The corresponding pyrrolidino compounds (47-52, 79-82) were two or three times less active but retained high RCS. The piperidino (53-57, 64, 65) and morpholino (58-63) derivatives showed a large decrease in antidiarrheal potency with the exception of compound 56 which had a high antidiarrheal potency and a high RCS.  $\beta$ -Methyl branching ( $R_1 = Me$ , 71–73) resulted in increased antidiarrheal potency but also in a sharp increase of analgesic potency, with consequent loss of RCS.  $\gamma$ -Methyl branching  $(R_2 = Me, 74-82)$  had similar influence although

Substitution on the 4-phenyl ring of the 4-piperidinol moiety was optimal for p-Cl (30), m-CF<sub>3</sub>, p-Cl (33), and p-Br (35). The unsubstituted compound 34 was a very potent antidiarrheal but also a strong analgesic. m-CF<sub>3</sub> (36) and p-F (37) substitution gave an increase in antidiarrheal potency but afforded too strongly analgesic compounds. p-Me substitution (31) resulted in a tenfold loss of potency, while m,p-diCl (32) and o,p-diMe (38) substitution retained antidiarrheal potency but gave a lower RCS.

Loperamide (30) and fluperamide (33) were selected for further investigation. They were approximately two times more potent than diphenoxylate (IIa) and 50 times more potent than codeine. Compared with IIa and codeine, 30 and 33 had a far superior relative constipating specificity (Table IV).

### **Experimental Section**

less pronounced.

Melting points were taken on a Tottoli melting point apparatus and are corrected. All compounds were routinely checked for their structure by uv and ir spectrometry (uv, Beckman DK-2A and ir, Perkin-Elmer 421). Nmr spectra were recorded by means of a Bruker HX-60 spectrometer. Where analyses are indicated by symbols of the elements, analytical results obtained for those elements were within  $\pm 0.4\%$  of the theoretical values.

4-Bromo-2,2-diphenylbutyric Acid (2). A mixture of 1 (600 g, 2.5 mol) and 48% HBr in AcOH (1200 ml) was stirred for 48 hr. The precipitate was collected by filtration, washed with  $\rm H_2O$  and PhMe,

Table III. Antidiarrheal Activity in Rats

Compd	ED <sub>50</sub> , a castor oil	ED <sub>50</sub> , b tail withdrawal	Rel constipating specificity <sup>c</sup>
27	5.00d	>40	>8
28	$0.16^{d}$	5	31
29	$1.00^{d}$	40	40
30	0.15 (0.11-0.20)	80	533
31	1.26 (0.53-2.99)	≥160	≥127
32	0.26 (0.18-0.40)	100	385
33	0.15 (0.11-0.21)	70	467
34	0.012 (0.006-0.021)	3.0	250
35	0.10 (0.06-0.17)	80	800
36	0.020 (0.010-0.042)	4.0	200
37	0.040 (0.019-0.085)	20	500
38	0.16 (0.10-0.27)	20	125
39	0.57 (0.37-0.86)	≥160	≥281
40	0.080 (0.042-0.153)	20	250
41	0.044 (0.024-0.079)	10	227
42	0.31 (0.20-0.48)	80	258
43	0.025 (0.014-0.045)	3.0	120
44	0.017 (0.007-0.037)	2.0	118 97
45 46	0.33 (0.21-0.52) 0.17 (0.11-0.25)	32 40	235
47	0.016 (0.009-0.030)	7.0	437
48	0.16 (0.10-0.58)	40	250
49	0.45 (0.31-0.66)	160	355
50	0.50 (0.25-0.98)	>320	>640
51	0.11 (0.07-0.17)	10	91
52	0.27 (0.18-0.40)	160	593
53	5.00d	>160	>32
54	2.50d	>160	>64
55	0.53 (0.29-0.94)	160	302
56	0.25 (0.17-0.38)	>320	>1280
57	1.76 (1.13-2.73)	>160	>91
58	0.63 (0.29-1.39)	>160	>251
<b>5</b> 9	1.26 (0.55-2.89)	>160	>127
60	$8.00^{d}$	>160	>20
61	0.50d	130	260
62	10 <b>d</b>	160	16
63	10 <i>d</i>	≥160	≥16
64	10 <sup>d</sup>	>160	>16
65	10 <b>d</b>	>160	>16
66	0.13 (0.07-0.29)	≥160	≥1231
67	0.54 <i>d</i>	>160	>296
68	0.54d	>160	>296
69	1.24 (0.56-2.72)	>160	>129
70	10d	>160	>16
71 72	0.025 (0.013-0.045) 0.028 (0.015-0.055)	1.0	40 45
73	0.028 (0.013-0.033)	1.25 1.25	208
74	0.070 (0.048-0.102)	20	286
7 <b>5</b>	0.070 (0.048-0.102)	20 20	622
76	0.057 (0.035-0.094)	20	351
77	0.022 (0.012-0.039)	2.5	114
78	0.060 (0.029-0.124)	2.5	42
79	1.26 (0.64-2.48)	>40	>32
80	0.42 (0.19-0.91)	40	95
81	1.26 (0.66-2.84)	>40	>32
82	2.07 (0.89-4.81)	>80	>39

 $^a$ mg/kg po at 1 hr after castor oil (confidence limits).  $^b$ mg/kg po (graphically estimated).  $^c$ ED<sub>50</sub> tail withdrawal/ED<sub>50</sub> castor oil (1 hr).  $^d$ Graphically estimated.

and crystallized from i-Pr<sub>2</sub>O to give pure 2 (670 g, 84%), mp 135–137°. Anal. ( $C_{16}H_{18}BrO_2$ ) C, H.

Dimethyl(tetrahydro-3,3-diphenyl-2-furylidene)ammonium Bromide (4a). To a suspension of 2 (227 g, 0.71 mol) in CHCl<sub>3</sub> (1500 ml) was added SOCl<sub>2</sub> (160 ml) dropwise. The mixture was refluxed for 4 hr and allowed to cool, and the solvent was removed in vacuo. The crude acid chloride (227 g, 93%) was used without purification. To a solution of dimethylamine (5.4 g, 0.12 mol) and Na<sub>2</sub>CO<sub>3</sub> (25.4 g, 0.24 mol) in H<sub>2</sub>O (100 ml) was added dropwise a solution of 4-bromo-2,2-diphenylbutyroyl chloride (33.8 g, 0.1 mol) in PhMe (100 ml), while the temperature was kept between 0 and 5°. The mixture was stirred for an additional 2 hr and extracted with CHCl<sub>3</sub>. The organic layer was dried (MgSO<sub>4</sub>) and the solvent removed in vacuo. The residue was crystallized from i-BuCOMe to give pure 4a (17.3 g, 50%): mp 181-182°; uv max (95% EtOH) 255 nm ( $\epsilon$ 

Table IV. Antidiarrheal Activity of Loperamide, Fluperamide, Diphenoxylate, and Codeine in Rats

			$\mathrm{ED}_{50}, b$				
Compd	1 hr	2 hr	4 hr	8 hr	tail withdrawal	$\mathrm{RCS}^c$	$\mathrm{LD}_{\mathfrak{so}}^{d}$
Loperamide	0.15 (0.11-0.20)	0.29 (0.23-0.38)	0.61 (0.45-0.83)	1.81 (1.25-2.63)	80	533	185 (135-254)
Fluperamide	0.15 (0.11-0.21)	0.20 (0.15-0.28)	0.31 (0.23-0.43)	0.77(0.51-1.16)	70	467	86 (48-156)
Diphenoxylate	0.16 (0.11-0.23)	0.54 (0.40-0.72)	1.41 (1.07-1.87)	4.77 (3.44-6.61)	6	37	221 (133-367)
Codeine	2.85 (1.87-4.35)	10.8 (8.7-13.5)	28.8 (21.5-38.6)	69.9 (50.1-97.7)	36	13	427 (302-603)

amg/kg po at stated hour after caster oil (confidence limits). bmg/kg po (graphically estimated). cED<sub>50</sub> tail withdrawal/ED<sub>50</sub> castor oil at 1 hr. dMortality after 7 days in mg/kg po (confidence limits).

540) and 261 (425); ir (KBr) 1675-1680 cm<sup>-1</sup> (C=N); nmr (CDCl<sub>2</sub>) δ 3.03 (s, 3), 3.50 (t, 2), 3.8 (s, 3), 4.89 (t, 2), and 7.51 ppm (s, 10). Anal. (C<sub>18</sub>H<sub>20</sub>BrNO) C, H, N. Other compounds prepared by this method were 15-26.

N,N-Dimethyl-2,2-diphenyl-4-hydroxybutyramide (5). A solution of 4a (7.5 g, 0.021 mol) in H<sub>2</sub>O (50 ml) was alkalized with aqueous NaOH and the mixture extracted with Et,O. The organic layer was dried (MgSO<sub>4</sub>) and the solvent removed in vacuo. The residue was crystallized from i-Pr<sub>2</sub>O to afford pure 5 (5.6 g, 94%), mp 131-132°. Anal. (C<sub>18</sub>H<sub>21</sub>NO<sub>2</sub>) C, H, N.

4-Chloro-N,N-dimethyl-2,2-diphenylbutyramide (6c). A mixture of 5 (12 g, 0.042 mol) = 4 SOCl<sub>2</sub> (6.4 g, 0.054 mol) in CHCl<sub>3</sub> (100 ml) was refluxed for 2 hr. The solvent was removed in vacuo and the residue crystallized from i-Pr<sub>2</sub>O to give pure 6c (7 g, 53%),

mp 136-137°. Anal. (C<sub>18</sub>H<sub>20</sub>ClNO) C, H, N. N-(Tetrahydro-3,3-diphenyl-2-furylidene)methylamine Hydrobromide (7b). To a mixture of 35% aqueous methylamine (100 g, 1.13 mol) and Na<sub>2</sub>CO<sub>3</sub> (106 g, 1 mol) in H<sub>2</sub>O (1000 ml) and PhMe (800 ml) was added dropwise 4-bromo-2,2-diphenylbutyroyl chloride (337.5 g, 1 mol) in PhMe (200 ml), while the temperature was kept between 0 and 5°. The mixture was allowed to come to room temperature and the precipitate collected by filtration. The solid was taken up into CHCl<sub>3</sub>, the solution dried (MgSO<sub>4</sub>), and the solvent removed in vacuo. The residue was crystallized from i-BuCOMe to afford pure 7b (223 g, 67%), mp 159-161°. Anal. (C<sub>17</sub>H<sub>17</sub>NO· HBr) C, H, N.

4-Chloro-N-methyl-2,2-diphenylbutyramide (6b). 7b (33.2 g, 0.1 mol) was converted to base in the usual way and dissolved in i-BuCOMe. The mixture was refluxed while dry HCl gas was bubbled through for 30 min. The solvent was removed in vacuo and the residue crystallized from i-Pr<sub>2</sub>O to give pure 6b (20.2 g, 70%), mp 150-152°. Anal. (C<sub>17</sub>H<sub>18</sub>CINO) C, H, N. Compound 6a was prepared similarly.

Dimethyl(tetrahydro-3,3-diphenyl-2-furylidene)ammonium Iodide (4b). A solution of 7b (12.6 g, 0.05 mol) and MeI (14.2 g, 0.1 mol) in i-BuCOMe was refluxed overnight. The solvent was removed in vacuo and work-up as for 4a afforded pure 4b (12.4 g, 63%): mp 217-218°; nmr (CDCl<sub>3</sub>) δ 2.99 (s, 3), 3.47 (t, 2), 3.82 (s, 3), 4.87 (t, 2), and 7.48 ppm (s, 10). Anal. ( $C_{18}H_{20}INO$ ) C, H, N.

Tetrahydro-4-methyl-3,3-diphenyl-2-furanimine Hydrochloride (10). 3-Cyano-3,3-diphenylisobutyric acid 8 (45 g, 0.17 mol) was refluxed with SOCl<sub>2</sub> (30 ml) in CHCl<sub>3</sub>. The solvent was removed in vacuo; the crude acid chloride was dissolved into DMF and added dropwise to a mixture of NaBH<sub>4</sub> (7.5 g) in DMF (150 ml). The mixture was stirred at room temperature overnight. AcOH (15 ml) was added and the mixture poured onto ice-H2O. The mixture was extracted with i-Pr<sub>2</sub>O, the organic layer was dried (MgSO<sub>4</sub>), and the solvent was removed in vacuo. The crude oil 9 (45 g) was dissolved into dry  $\rm Et_2O$  (250 ml) saturated with dry HCl gas. The mixture was left overnight at  $0^\circ$ . The solvent was removed in vacuo and the residue crystallized from i-BuCOMe to give pure 10 (20 g, 40%), mp  $186-189^{\circ}$ . Anal.  $(C_{17}H_{17}NO)$  C, H, N.

Dimethyl(tetrahydro-4-methyl-3,3-diphenyl-2-furylidene)ammonium Iodide (11). To a suspension of 10 (5.75 g, 0.02 mol) in THF (50 ml) was added in small portions LiNH<sub>2</sub> (0.92 g, 0.04 mol) and the mixture refluxed for 2 hr. MeI (14.2 g, 0.1 mol) was added dropwise and reflux continued for an additional 12 hr. The mixture was poured into H<sub>2</sub>O and extracted with i-BuCOMe. Further quaternization and work-up as described for 4b afforded pure

11 (2.8 g, 35%), mp 180-181°. *Anal.* (C<sub>19</sub>H<sub>22</sub>INO) C, H, N. *N,N*-Dimethyl-2,2-diphenyl-4-pentenamide (13a). To a mixture of 50% NaNH2 suspended in xylene (120 g, 1.5 mol) and PhMe (500 ml) was added dropwise N,N-dimethyl-2,2-diphenylacetamide (310 g, 1.3 mol) in PhMe (1000 ml). The mixture was refluxed for 1 hr, allyl bromide (212 g, 1.75 mol) was added drop-

wise, and reflux continued for 2 hr. H<sub>2</sub>O (500 ml) was added, and the organic layer was separated, dried (MgSO<sub>4</sub>), and evaporated. The residue was crystallized from i-Pr<sub>2</sub>O to give pure 13a (249 g, 69%), mp 110-112°. Anal. (C<sub>19</sub>H<sub>21</sub>NO) C, H, N.

Dimethyl(tetrahydro-5-methyl-3,3-diphenyl-2-furylidene)ammonium Bromide (14a). A solution of 13a (88 g, 0.31 mol) in AcOH (300 ml) was treated with HBr gas until saturation. The solvent was removed in vacuo and the residue crystallized from i-BuCOMe to afford pure 14a (83 g, 74%), mp 207-208°. Anal. (C<sub>19</sub>H<sub>22</sub>BrNO) C, H, N. Compound 14b was prepared similarly.

4-(p-Chlorophenyl)-4-hydroxy-N,N-dimethyl-α,α-diphenyl-1piperidinebutyramide Hydrochloride (30). From a suspension of 4p-chlorophenyl-4-piperidinol (4.2 g, 0.02 mol) and Na<sub>2</sub>CO<sub>3</sub> (8 g, 0.075 mol) in i-BuCOMe (250 ml), the H<sub>2</sub>O was removed with the aid of a Dean-Stark trap. Then 4a (7.6 g, 0.022 mol) was added, the mixture refluxed for 2 hr and filtered, and the solvent removed in vacuo. The residue was dissolved into i-PrOH and neutralized with HCl gas. Crystallization from i-PrOH afforded pure 30 (6 g, 58%), mp 222-223°. Anal. (C<sub>29</sub>H<sub>33</sub>ClN<sub>2</sub>O<sub>2</sub>·HCl) C, H, N. Other compounds prepared by this method were 31-82.

4-(p-Chlorophenyl)-4-hydroxy- $\alpha$ , $\alpha$ -diphenyl-1-piperidinebutyramide Hydrochloride (27). A suspension of 6a (6.85 g, 0.025 mol), 4-p-chlorophenyl-4-piperidinol (10.5 g, 0.05 mol), and a trace KI in i-BuCOMe (250 ml) was refluxed for 12 hr. Work-up as above afforded pure 27 (1.2 g, 10%), mp 236-237°. Anal. (C<sub>27</sub>H<sub>29</sub>ClN<sub>2</sub>O<sub>2</sub> HCl) C, H, N. Other compounds prepared by this method were 28

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