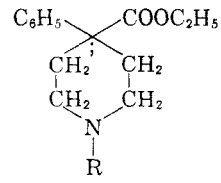
TABLE I

ETHYL 1-ALKYL-4-PHENYLPIPERIDINE-4-CARBOXYLATES



R—	Formula	Yield, %	M.P.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found	Activity[d]
$CH_3(CH_2)_5$—	$C_{20}H_{32}ClNO_2 \cdot HCl$	48.6	160.0–161.4	67.87	67.81	9.12	9.10	10.02	10.02	6.7
$CH_3(CH_2)_6$—	$C_{21}H_{34}ClNO_2 \cdot HCl$	78.0	146.4–149.0	68.54	68.40	9.31	9.26	9.64	9.49	3.3
$CH_3(CH_2)_7$—	$C_{22}H_{36}ClNO_2 \cdot HCl$	68.4	137.0–138.0	69.16	69.44	9.50	9.09	9.28	8.99	4.0
$CH_3(CH_2)_8$—	$C_{23}H_{38}ClNO_2 \cdot HCl$	43.0	132.4–134.2	69.76	69.58	9.67	9.47	8.95	8.77	2.5
$CH_3(CH_2)_9$—	$C_{24}H_{40}ClNO_2 \cdot HCl$	28.7	135.4–136.2	70.30	70.61	9.83	10.48	8.65	8.60	0
$CH_3(CH_2)_{11}$—	$C_{26}H_{44}ClNO_2 \cdot HCl$	16.4	131.6–132.6	71.27	71.35	10.13	10.01	8.09	8.16	0
CH_3 \ $CHCH_2CH_2$— / C_2H_5	$C_{20}H_{32}ClNO_2 \cdot HCl$	59.9	163.4–165.4	67.87	67.97	9.12	9.59	10.02	9.99	3.0
CH_3 \ CH— / C_4H_9	$C_{20}H_{31}NO_2$[c]	68.8	120–122	60.97	61.01	8.53	8.56	7.75[a]	7.78	5.8
C_2H_5 \ CH— / C_4H_9	$C_{21}H_{34}ClNO_2 \cdot HCl$	17.6	145.0–147.4	8.69[b]		8.70		9.63	9.54	1.7
C_2H_5 \ CH— / C_3H_7	$C_{20}H_{32}ClNO_2 \cdot HCl$	35.6	179.6–182.6	9.04[b]		8.95		10.02	9.99	0.23
Meperidine										1

[a] Analyzed for sulfur. [b] Analyzed for oxygen. [c] B. CH_3SO_3H salt. [d] Relative to meperidine.

precipitated after a few minutes of stirring. The product was collected, washed with ether and dried; yield 1089 g. (86%), m.p. 120–122°.

Anal. Calcd. for $C_{20}H_{31}NO_2 \cdot CH_3SO_3H$: C, 60.97; H, 8.53; S, 7.75. Found: C, 61.01; H, 8.56; S, 7.78.

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N-Substituted *N'*-Phenylureas

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A factor which stimulated growth in mature carrot phloem cells has been identified as 1,3-diphenylurea.[1] The possibility that other phenylurea derivatives might possess physiological activity is suggested by the fact that various structural modifications of another plant growth factor, Kinetin[2] [6-(2-furfurylamino)purine], have been found to be effective in stimulating biological responses in a number of assay systems. For example, the furfuryl group of Kinetin can be replaced, with retention of biological activity, by phenyl-,[3] ω-phenylalkyl-,[4] ω-cyclohexylalkyl-,[5] and heterocyclicaminopurines.[6] Accordingly, a number of substituted amines were condensed with phenylisocyanate to produce the corresponding *N*-substituted *N'*-phenylureas. These compounds were subsequently examined in several biological assay systems.

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TABLE I

N-SUBSTITUTED *N'*-PHENYLUREAS[a]

$$C_6H_5—NH—\overset{\overset{O}{\|}}{C}—NH—R$$

R	M.P.[b]	Empirical Formula	Calcd. C,%	Calcd. H,%	Calcd. N,%	Found C,%	Found H,%	Found N,%
3-Phenylpropyl-	87- 90	$C_{16}H_{18}N_2O$	75.56	7.13		75.30	7.03	
4-Phenylbutyl-	107–110	$C_{17}H_{20}N_2O$			10.44			10.44
5-Phenylpentyl-	98–100	$C_{18}H_{22}N_2O$	76.56	7.85	9.92	76.11	7.87	10.00
7-Phenylheptyl-	95- 96	$C_{20}H_{26}N_2O$			9.02			8.89
(2-Methyl-2-phenyl)ethyl-	136–137	$C_{16}H_{18}N_2O$	75.56	7.13		75.19	6.75	
2-α-Naphthylethyl-	154–156	$C_{19}H_{18}N_2O$	78.62	6.25		78.20	6.35	
3-Cyclohexylpropyl-	112–113	$C_{16}H_{24}N_2O$	73.80	9.29		73.66	8.90	
6-Cyclohexylhexyl-	117–120	$C_{19}H_{30}N_2O$	75.45	10.00	9.26	74.35	9.83	9.34
2-Pyridylmethyl-	128–130	$C_{13}H_{13}N_3O$	68.70	5.77	18.55	68.55	5.55	18.46
3-Pyridylmethyl-	103–105	$C_{13}H_{13}N_3O$	68.70	5.77		68.55	5.80	
4-Pyridylmethyl-	134–136	$C_{13}H_{13}N_3O$			18.50			18.88
2-Thenyl-	165–168	$C_{12}H_{12}N_2OS$	62.04	5.21	12.06	62.01	5.24	12.11
2-Furfuryl-	118–120	$C_{12}N_{12}N_2O_2$	66.65	5.59	12.96	66.77	5.79	13.04
3-Methoxypropyl-	248–249	$C_{11}H_{16}N_2O_2$			13.45			13.23

[a] The authors are indebted to Mr. B. S. Gorton for technical assistance with some of these syntheses. [b] M.p. are uncorrected.

The various *N*-substituted *N'*-phenylureas were prepared through the usual procedure by condensing the appropriate amine with phenylisocyanate under anhydrous conditions as indicated in the accompanying equation, and were obtained in essentially quantitative yields. Some physical

$$RNH_2 + C_6H_5—N=C=O \longrightarrow C_6H_5NHCONHR$$

properties and analytical data for the previously unreported derivatives which were prepared are summarized in Table I.

Because of the limited solubility of many of these *N*-substituted *N'*-phenylureas in water, most of the biological assays were carried out using a saturated aqueous solution of the compound as the highest concentration tested. The biological systems studied included an attempt to (a) augment the rate of lettuce seed germination,[7] (b) inhibit hydra tentacle regeneration,[8] (c) inhibit the growth of *Escherichia coli*, and (d) augment the growth inhibition of 2,4-diamino-6,7-diphenylpteridine in *Lactobacillus arabinosus*.[9] Under the testing conditions cited in the references, representative members of each of the homologous series of 6-substituted purine derivatives possessed a significant biological response; however, none of the *N*-substituted *N'*-phenylurea analogs were found to be appreciably active in any of these assay systems. Recently, these compounds were also tested for their ability to stimulate growth in carrot tissue, and no significant growth-promoting effects were observed; in contrast, several of the corresponding 6-substituted aminopurines were active in this test system.[10]

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The Mechanism of the *N,N*-Dichloro-*sec*-alkylamine Rearrangement

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In recent papers[1,2] on the rearrangement of *N,N*-dichloro-*sec*-alkylamines to α-amino ketones Baumgarten and coworkers visualize a mechanism similar to that proposed by Cram and Hatch[3,4] for the Neber rearrangement of oxime tosylates. A key intermediate in this reaction sequence is the dehydrohalogenation of the *N,N*-dichloroamine to

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