

Anal. Calcd. for $C_{11}H_{16}N_2Cl$: C, 62.70; H, 7.18; N, 13.30; Cl, 16.83. Found: C, 62.36; H, 6.97; N, 13.36; Cl, 16.98.

Nitriles used were either commercially available or were prepared according to the method of Marxer.¹⁰

1-Aminoethylimidazolines (XVIII) (*cf.* Table II). **General Procedure.**—The appropriate nitrile (0.2 mole) was mixed with 0.22 mole of diethylenetriamine or *N,N*-dimethyldiethylenetriamine, and 200–500 mg. of dry hydrogen sulfide was passed into this mixture. The resulting solution was heated in an oil-bath at 90–120° until evolution of ammonia was complete, this taking sometimes only a few minutes and sometimes 7–8 hr. Usually a temperature of 100–105° was sufficient. The resulting imidazolines were usually distilled twice and the dihydrochlorides prepared.

1,1'-Bisimidazolinyethanes (XIX) (*cf.* Table III) **General Procedure:** Bis-[2,*p*-chloroanilinomethylimidazoliny-(1)]-ethane (XIX/8).—Dry hydrogen sulfide (400 mg.) was

passed into a mixture of 49.98 g. (0.3 mole) of *p*-chloroanilinoacetonitrile and 21.93 g. (0.15 mole) of triethylenetetramine. This was heated in an oil-bath at 110°, when a rapid evolution of ammonia occurred, lasting for 1 hr. and becoming very slow during the next 6 hr. The reaction product crystallized on addition of 200 ml. of ethyl acetate. Crystals of XIX/8 were isolated and washed with ethyl acetate, when they had m.p. 162° (slight sintering at 149°). Since this base conformed to the expected analytical results, the hydrochloride was prepared without further purification, by dissolving in alcohol and adding 2 equivalents of alcoholic hydrochloric acid; hydrochloride m.p. 228–231°.

Generally, the bases of Table III decomposed on distillation, with the exception of XIX/1 and XIX/2. When they did not crystallize upon addition of ethyl acetate, the solution was evaporated, dissolved in dilute hydrochloric acid, the oil reprecipitated by dilute ammonia in the cold and taken up in ethyl acetate or alcohol to prepare the hydrochloride.

BASEL, SWITZERLAND

(10) A. Marxer, *Helv. Chim. Acta.*, **37**, 166 (1954).

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, RESEARCH LABORATORIES, THE WILLIAM S. MERRELL CO.]

Central Stimulants. α,α -Disubstituted 2-Piperidinemethanols and 1,1-Disubstituted Heptahydroöxazolo[3,4-*a*]pyridines

BY FREDERICK J. McCARTY, CHARLES H. TILFORD AND M. G. VAN CAMPEN, JR.

RECEIVED JULY 19, 1956

A series of α,α -disubstituted-2-piperidinemethanols was prepared and converted to the corresponding 2-piperidinemethanols by hydrogenation. Heptahydroöxazolo[3,4-*a*]pyridine derivatives of some of the piperidinemethanols were also prepared. A number of the piperidinemethanols and heptahydroöxazolidines possess central stimulant activity.

This investigation was a continuation of the search for new therapeutic agents in the α,α -disubstituted-2-piperidinealkanol series. A previous paper¹ described the synthesis of a series of α,α -disubstituted-2-piperidine-ethanols and the related octahydropyrid[1,2-*c*]oxazines. A number of these compounds had diuretic and anti-fungal properties.

The piperidinemethanols of the present investigation are analogs of α,α -diphenyl-2-piperidinemethanol hydrochloride^{2,3} which possesses central stimulant activity.⁴ Generally, these piperidinemethanols were prepared by hydrogenation of the corresponding pyridinemethanols. Some of them were treated with formaldehyde to yield the oxazolidine derivatives. The synthetic methods used for preparing the intermediate pyridinemethanols are shown.

Previous examples of Grignard reactions in which other pyridyl ketones were substituted in the literature.^{5–7} The preparation of α -phenyl- α -(2-thienyl)-2-pyridinemethanol (Table I, 35A) was recently reported.⁸

The synthesis of di- and tripyridinemethanols⁹

(1) C. H. Tilford and M. G. Van Campen, Jr., *THIS JOURNAL*, **76**, 2431 (1954).

(2) C. H. Tilford, R. S. Shelton and M. G. Van Campen, Jr., *ibid.*, **70**, 4001 (1948).

(3) H. W. Werner and C. H. Tilford, U. S. Patent 2,624,739 (1953).

(4) B. B. Brown and H. W. Werner, *J. Pharmacol. Exptl. Therap.*, **110**, 180 (1954).

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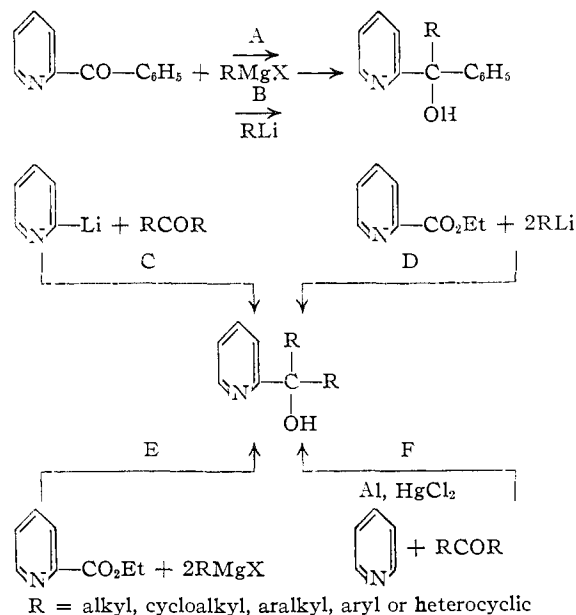
(6) K. Winterfeld and F. W. Holschneider, *Arch. Pharm.*, **273**, 315 (1935).

(7) N. Sperber, D. Papa, E. Schwenk and M. Sherlock, *THIS JOURNAL*, **71**, 887 (1949).

(8) J. Heer, E. Sury and K. Hoffmann, *Helv. Chim. Acta*, **38**, 134 (1955).

(9) J. P. Wibaut, A. P. de Jonge, H. G. P. Van der Voort and P. Ph. H. L. Otto, *Rec. trav. chim.*, **70**, 1054 (1951).

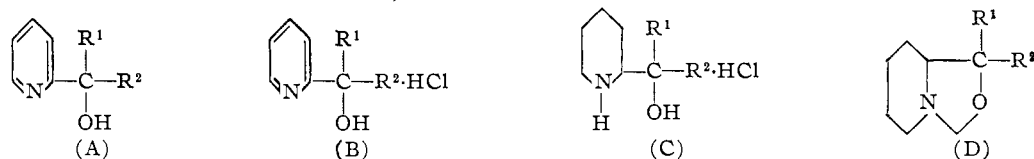
and other pyridinemethanols by reaction of lithio agents with ketones have been carried out.¹⁰ A ketone synthesis from ethyl picolinate and 2-pyridyllithium has been reported to yield tri-2-pyridinemethanol as a by-product.⁹ Preparation



of α,α -dimethyl-2-pyridinemethanol from ethyl picolinate and methylmagnesium iodide has been reported.¹¹ A series of pyridinemethanols, mainly of the type in which one R group is alkyl, has been prepared² by condensation of pyridine with the ap-

(10) A. J. Nunn and K. Schofield, *J. Chem. Soc.*, 589 (1952).

(11) W. Sobocki, *Ber.*, **41**, 4103 (1908).

TABLE I
 SUBSTITUTED PYRIDINEMETHANOLS, PIPERIDINEMETHANOLS AND HEPTAHYDROÖXAZOLOPYRIDINES


No.	R ¹	R ²	Method	M.p., °C. cor. ^a	Yield, %	Formula	Carbon, %		Hydrogen, %	
							Calcd.	Found	Calcd.	Found
1A	Phenyl	Phenyl	A	104-106	79	C ₁₈ H ₁₈ ON ^b				
1B	Phenyl	Phenyl	G	181-182		C ₁₈ H ₁₈ ONCl ^b	72.85	72.27	5.44	5.35
1C	Phenyl	Phenyl	I	312-324	92	C ₁₈ H ₂₂ ONCl ^b	71.15	71.10	7.30	7.29
1D	Phenyl	Phenyl	K	117-121	92	C ₁₉ H ₂₁ ON	81.69	82.41	7.58	8.19
1D	Phenyl	Phenyl		158-159		C ₂₃ H ₂₅ O ₅ N ^c	69.86	69.88	6.38	6.73
1D	Phenyl	Phenyl		182-183		C ₁₉ H ₂₂ ONCl ^d	72.26	72.33	7.02	7.21
2A	Phenyl	<i>o</i> -Tolyl	B	95-96	82	C ₁₉ H ₁₇ ON	82.89	83.16	6.23	6.35
2B	Phenyl	<i>o</i> -Tolyl	G	190-192		C ₁₉ H ₁₈ ONCl	73.21	73.19	5.82	5.89
2C	Phenyl	<i>o</i> -Tolyl	I	296-297	56	C ₁₉ H ₂₄ ONCl	71.79	71.73	7.61	7.82
3A	Phenyl	<i>m</i> -Tolyl	B	90-91	86	C ₁₉ H ₁₇ ON	82.89	82.90	6.23	6.42
3B	Phenyl	<i>m</i> -Tolyl	G	193-195		C ₁₉ H ₁₈ ONCl	73.21	73.22	5.82	5.87
3C	Phenyl	<i>m</i> -Tolyl	I	290-291	69	C ₁₉ H ₂₄ ONCl	71.79	71.91	7.61	7.84
3D	Phenyl	<i>m</i> -Tolyl	K	134-136	33	C ₂₄ H ₂₇ O ₅ N ^c	70.40	70.55	6.65	6.61
4A	Phenyl	<i>p</i> -Tolyl	A	83-85	89	C ₁₉ H ₁₇ ON	82.89	82.98	6.23	6.34
4B	Phenyl	<i>p</i> -Tolyl	G	193-195		C ₁₉ H ₁₈ ONCl	73.21	72.87	5.82	6.09
4C	Phenyl	<i>p</i> -Tolyl	I	316-318	69	C ₁₉ H ₂₄ ONCl	71.79	71.79	7.61	7.76
5A	Phenyl	<i>p</i> -Ethylphenyl	B	59-61	62	C ₂₀ H ₁₉ ON	83.00	82.87	6.62	6.58
5B	Phenyl	<i>p</i> -Ethylphenyl	G	156-157		C ₂₀ H ₂₀ ONCl	73.72	73.89	6.19	5.90
5C ₁	Phenyl	<i>p</i> -Ethylphenyl	I	323-324	47	C ₂₀ H ₂₆ ONCl	72.40	71.74	7.90	7.91
5C ₂	Phenyl	<i>p</i> -Ethylphenyl ^e	I	271-273	20	C ₂₀ H ₂₆ ONCl	72.40	71.70	7.90	7.69
6A	Phenyl	2,5-Dimethylphenyl	B	93-95	72	C ₂₀ H ₁₉ ON	83.00	83.09	6.62	6.56
6B	Phenyl	2,5-Dimethylphenyl	G	175-177		C ₂₀ H ₂₀ ONCl	73.72	73.43	6.19	6.31
6C	Phenyl	2,5-Dimethylphenyl	I	280-282	45	C ₂₀ H ₂₆ ONCl	72.40	72.25	7.90	8.12
6D	Phenyl	2,5-Dimethylphenyl	K	116-117	70	C ₂₁ H ₂₅ ON	82.05	82.01	8.20	8.03
6D	Phenyl	2,5-Dimethylphenyl		200-203		C ₂₅ H ₂₉ O ₅ N ^c	70.91	71.03	6.90	7.02
7A	Phenyl	Mesityl	B	147-148	77	C ₂₁ H ₂₁ ON	83.14	83.23	6.98	6.95
7B	Phenyl	Mesityl	G	192-193		C ₂₁ H ₂₂ ONCl	74.20	74.21	6.53	6.46
7C	Phenyl	Mesityl	I	271-272	39	C ₂₁ H ₂₆ ONCl	72.91	72.80	8.16	8.23
8A	<i>p</i> -Tolyl	<i>p</i> -Tolyl	E	119-121	68	C ₂₀ H ₁₉ ON	83.01	82.83	6.62	6.62
8B	<i>p</i> -Tolyl	<i>p</i> -Tolyl	G	181-183		C ₂₀ H ₂₀ ONCl	73.72	73.77	6.19	6.25
8C	<i>p</i> -Tolyl	<i>p</i> -Tolyl	I	316-317	74	C ₂₀ H ₂₆ ONCl	72.40	72.57	7.90	7.96
9A	<i>o</i> -Tolyl	<i>o</i> -Tolyl	D	119-120	74	C ₂₀ H ₁₉ ON	83.01	83.08	6.62	6.87
9B	<i>o</i> -Tolyl	<i>o</i> -Tolyl	G	193-194		C ₂₀ H ₂₀ ONCl	73.72	73.58	6.19	6.18
9C	<i>o</i> -Tolyl	<i>o</i> -Tolyl	I	255-256	92	C ₂₀ H ₂₆ ONCl	72.40	72.28	7.90	7.86
9D	<i>o</i> -Tolyl	<i>o</i> -Tolyl	K	224-226	60	C ₂₁ H ₂₆ ONCl ^d	73.36	73.39	7.62	7.65
10A	Phenyl	Benzyl	A	104-105	58	C ₁₉ H ₁₇ ON	82.89	82.78	6.23	6.50
10B	Phenyl	Benzyl	G	188-190		C ₁₉ H ₁₈ ONCl	73.21	72.85	5.82	5.93
10C ₁	Phenyl	Benzyl	I	235-236	79	C ₁₉ H ₂₄ ONCl	71.79	71.44	7.61	7.77
10C ₂	Phenyl	Benzyl ^e	I	284-286	10	C ₁₉ H ₂₄ ONCl	71.79	72.08	7.61	7.75
10D	Phenyl	Benzyl ^f	K	114-116	46	C ₂₄ H ₂₇ O ₅ N ^c	70.40	70.21	6.65	6.74
11A	Phenyl	1-Naphthyl	B	148-149	44	C ₂₂ H ₁₇ ON	84.84	84.76	5.50	5.32
11B	Phenyl	1-Naphthyl	G	186-188		C ₂₂ H ₁₈ ONCl	75.96	75.74	5.22	5.33
11C	Phenyl	1-Naphthyl	I	283-284	83	C ₂₂ H ₂₄ ONCl	74.66	74.44	6.83	6.54
12A	Phenyl	<i>p</i> -Chlorophenyl	C	110-111	68	C ₁₈ H ₁₄ ONCl	73.09	72.84	4.77	4.80
12B	Phenyl	<i>p</i> -Chlorophenyl	G	215-216		C ₁₈ H ₁₅ ONCl ₂	65.08	64.99	4.55	4.71
12C ₁	Phenyl	<i>p</i> -Chlorophenyl ^f	J	124-125		C ₁₈ H ₂₀ ONCl ^g	71.64	71.57	6.68	6.88
12C ₁	Phenyl	<i>p</i> -Chlorophenyl	I	320	22	C ₁₈ H ₂₁ ONCl ₂	63.90	64.26	6.26	6.39
12C ₂	Phenyl	<i>p</i> -Chlorophenyl ^e	I	276	68	C ₁₈ H ₂₁ ONCl ₂	63.90	64.38	6.26	6.37
12D	Phenyl	<i>p</i> -Chlorophenyl ^f	K	99-100	74	C ₁₈ H ₂₀ ONCl	72.73	72.76	6.43	6.35
13A	Phenyl	<i>o</i> -Chlorophenyl	C	125-127	42	C ₁₈ H ₁₄ ONCl	73.09	72.96	4.77	4.80
13B	Phenyl	<i>o</i> -Chlorophenyl	G	208-209		C ₁₈ H ₁₅ ONCl ₂	65.08	64.67	4.55	4.34
13C	Phenyl	<i>o</i> -Chlorophenyl	J	172		C ₁₈ H ₂₀ ONCl ^g	71.64	71.88	6.68	6.63
13C	Phenyl	<i>o</i> -Chlorophenyl	I	276-277	94	C ₁₈ H ₂₁ ONCl ₂	63.90	64.28	6.26	6.48
14B	Phenyl	<i>m</i> -Chlorophenyl ^h	B	194-196	24	C ₁₈ H ₁₅ ONCl ₂	65.07	64.86	4.55	4.76
14C	Phenyl	<i>m</i> -Chlorophenyl	I	304-305	83	C ₁₈ H ₂₁ ONCl ₂	63.90	63.95	6.26	6.40
14D	Phenyl	<i>m</i> -Chlorophenyl	K	83-85	64	C ₁₈ H ₂₀ ONCl	72.73	72.92	6.43	6.47

TABLE I (Continued)

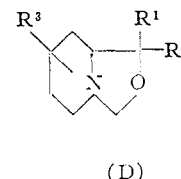
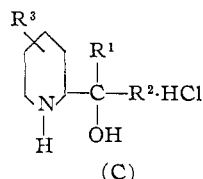
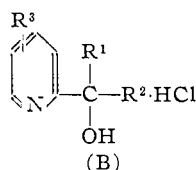
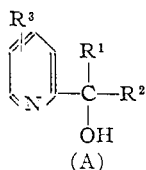
No.	R	R ¹	Method	M.p., °C. cor. ^a	Yield, %	Formula	Carbon, %		Hydrogen, %	
							Calcd.	Found	Calcd.	Found
14D	Phenyl	<i>m</i> -Chlorophenyl		126-128		C ₂₃ H ₂₄ O ₆ NCl ^f	64.26	64.21	5.63	5.75
15A	Phenyl	<i>p</i> -Bromophenyl	C	96	68	C ₁₈ H ₁₄ ONBr	63.53	63.52	4.15	4.23
15B	Phenyl	<i>p</i> -Bromophenyl	G	203-204		C ₁₈ H ₁₅ ONBrCl	57.39	57.36	4.01	4.09
15C ₁	Phenyl	<i>p</i> -Bromophenyl	I	314-315	20	C ₁₈ H ₂₁ ONBrCl	56.48	56.38	5.53	5.59
15C ₂	Phenyl	<i>p</i> -Bromophenyl ^g	I	275-276	22	C ₁₈ H ₂₁ ONBrCl	56.48	56.37	5.53	5.75
16A	Phenyl	<i>p</i> -Fluorophenyl	C	83-85	40	C ₁₈ H ₁₁ ONF	77.40	77.41	5.05	5.10
16B	Phenyl	<i>p</i> -Fluorophenyl	G	187-189		C ₁₈ H ₁₅ ONFCl	68.45	68.52	4.79	4.94
16C	Phenyl	<i>p</i> -Fluorophenyl	I	288-289	67	C ₁₈ H ₂₁ ONFCl	67.17	67.21	6.58	6.45
17A	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl	C	88-89	24	C ₁₈ H ₁₅ ONCl ₂	65.46	65.47	3.97	4.16
17B	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl	G	187-193		C ₁₈ H ₁₅ ONCl ₃	58.95	58.93	3.85	3.82
17C	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl	J	83-84	97	C ₁₈ H ₁₉ ONCl ₂ ^o	64.29	64.27	5.70	5.81
17C	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl	I	309-310	80	C ₁₈ H ₂₀ ONCl ₂	58.01	58.24	5.41	5.48
17D	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl	K	169-171	81	C ₁₉ H ₁₉ ONCl ₂	65.52	65.32	5.50	5.82
17D	<i>p</i> -Chlorophenyl	<i>p</i> -Chlorophenyl		132-134		C ₂₃ H ₂₃ O ₅ NCl ₂ ^g	59.50	59.38	4.99	5.18
18A	<i>p</i> -Chlorophenyl	<i>o</i> -Chlorophenyl	C	110-112	33	C ₁₈ H ₁₅ ONCl ₂	65.46	65.44	3.97	4.09
18B	<i>p</i> -Chlorophenyl	<i>o</i> -Chlorophenyl	G	182-192		C ₁₈ H ₁₄ ONCl ₃	58.95	59.15	3.85	4.05
18C ₁	<i>p</i> -Chlorophenyl	<i>o</i> -Chlorophenyl	I	273-275	68	C ₁₈ H ₂₀ ONCl ₃	58.01	58.22	5.41	5.60
18C ₂	<i>p</i> -Chlorophenyl	<i>o</i> -Chlorophenyl ^h	I	306-307	13	C ₁₈ H ₂₀ ONCl ₃	58.01	57.88	5.41	5.40
19A	<i>p</i> -Bromophenyl	<i>p</i> -Bromophenyl ⁱ	C	102-103	27	C ₁₈ H ₁₃ ONBr ₂	51.58	51.71	3.13	3.14
19C	<i>p</i> -Bromophenyl	<i>p</i> -Bromophenyl	I	306-307	61	C ₁₈ H ₂₀ ONBr ₂ Cl	46.82	47.30	4.37	4.67
20B	Phenyl	<i>p</i> -Hydroxyphenyl ^k	C	165-167	16	C ₁₈ H ₁₆ O ₂ NCl	69.01	69.17	5.15	5.24
20C	Phenyl	<i>p</i> -Hydroxyphenyl	I	213-214	40	C ₁₈ H ₂₂ O ₂ NCl	67.60	67.58	6.94	7.07
21A	Phenyl	<i>p</i> -Anisyl	A	120-122	80	C ₁₉ H ₁₇ O ₂ N	78.33	77.92	5.88	5.91
21B	Phenyl	<i>p</i> -Anisyl	G	158-160		C ₁₉ H ₁₉ O ₂ NCl	69.61	69.48	5.53	5.61
21C	Phenyl	<i>p</i> -Anisyl	I	285-286	33	C ₁₉ H ₂₄ O ₂ NCl	68.35	68.58	7.25	7.22
22A	Phenyl	<i>p</i> -Phenetyl ^l	A	110-112	45	C ₂₀ H ₁₉ O ₂ N	78.65	78.58	6.27	6.44
22C ₁	Phenyl	<i>p</i> -Phenetyl	I	276-277	25	C ₂₀ H ₂₆ O ₂ NCl	69.06	68.97	7.54	7.70
22C ₂	Phenyl	<i>p</i> -Phenetyl ^m	I	235	36	C ₂₀ H ₂₆ O ₂ NCl	69.06	68.92	7.54	7.66
23A	Phenyl	3,4-Methylenedioxyphenyl	C	112-114	52	C ₁₉ H ₁₄ O ₃ N	74.75	74.16	4.95	5.01
23B	Phenyl	3,4-Methylenedioxyphenyl	G	190-192		C ₁₉ H ₁₆ O ₃ NCl	66.76	66.69	4.72	4.69
23C	Phenyl	3,4-Methylenedioxyphenyl	I	259-260	74	C ₁₉ H ₂₂ O ₃ NCl	65.62	65.73	6.38	6.43
24A	Phenyl	2-Methoxy-1-naphthyl	C	103-105	72	C ₂₃ H ₁₉ O ₂ N	80.92	80.66	5.61	5.62
24B	Phenyl	2-Methoxy-1-naphthyl	G	142-144		C ₂₃ H ₂₀ O ₂ NCl	73.11	73.24	5.34	5.29
24C	Phenyl	2-Methoxy-1-naphthyl	I	256	20	C ₂₃ H ₂₆ O ₂ NCl	71.97	71.88	6.84	6.89
25A	<i>p</i> -Benzyloxyphenyl	<i>p</i> -Benzyloxyphenyl	C	123-126	62	C ₃₂ H ₂₇ O ₃ N	81.15	80.96	5.75	5.72
25B	<i>p</i> -Benzyloxyphenyl	<i>p</i> -Benzyloxyphenyl	G	146-147		C ₃₂ H ₂₉ O ₃ NCl	75.35	74.84	5.53	6.02
25C	<i>p</i> -Hydroxyphenyl	<i>p</i> -Hydroxyphenyl	I	229-230	20	C ₁₈ H ₂₂ O ₃ NCl	64.39	64.26	6.61	6.75
26A	<i>p</i> -Anisyl	<i>p</i> -Anisyl	C	90-91	85	C ₂₀ H ₁₉ O ₃ N	74.76	74.87	5.96	6.13
26B	<i>p</i> -Anisyl	<i>p</i> -Anisyl	G	154-156		C ₂₀ H ₂₀ O ₃ NCl	67.13	67.39	5.63	5.71
26C	<i>p</i> -Anisyl	<i>p</i> -Anisyl	I	261-262	72	C ₄₀ H ₂₆ O ₃ NCl	66.01	66.34	7.21	7.33
27A	<i>p</i> -Phenetyl	<i>p</i> -Phenetyl ⁿ	D	93-94	19	C ₂₂ H ₂₃ O ₃ N	75.63	75.79	6.63	6.61
27C	<i>p</i> -Phenetyl	<i>p</i> -Phenetyl	I	219	77	C ₂₂ H ₃₀ O ₃ NCl	67.42	67.52	7.72	7.72
28A	Phenyl	<i>p</i> -Aminophenyl	C ^j	73-75	1.5	C ₁₈ H ₁₅ ON ₂	78.24	78.20	5.84	5.79
28C	Phenyl	<i>p</i> -Aminophenyl ^k	I	188-190	19	C ₁₈ H ₂₄ ON ₂ Cl ₂	60.84	60.82	6.81	6.81
29A	Phenyl	<i>p</i> -Dimethylaminophenyl ^l	B	152-153	62	C ₂₀ H ₂₀ ON ₂	78.90	78.76	6.62	6.80
29C	Phenyl	<i>p</i> -Dimethylaminophenyl	I	233-234	11	C ₂₄ H ₃₅ O ₅ N ₂ ^m	66.96	66.82	7.96	7.94
30A	<i>p</i> -Dimethylamino-phenyl	<i>p</i> -Dimethylamino-phenyl	D	148-151	61	C ₂₂ H ₂₅ ON ₃	76.07	75.92	7.26	7.38
30B	<i>p</i> -Dimethylamino-phenyl	<i>p</i> -Dimethylamino-phenyl	G	248-250		C ₂₂ H ₂₃ ON ₃ Cl ₃ ⁿ	57.82	57.64	6.18	6.75
30C	Phenyl	Phenyl	I	256-258	63	C ₂₂ H ₃₄ ON ₃ Cl ₃ ⁿ	57.10	57.13	7.41	7.56
31A	Phenyl	<i>p</i> -Trimethylsilyl-phenyl	B	74-76	65	C ₂₁ H ₂₃ ONSi	75.63	75.54	6.95	7.21
31B	Phenyl	<i>p</i> -Trimethylsilyl-phenyl	G	171-173		C ₂₁ H ₂₄ ONSiCl	68.19	68.48	6.54	6.31
31C	Phenyl	<i>p</i> -Trimethylsilyl-phenyl	J	100-102		C ₂₁ H ₂₉ ONSi ^o	74.30	74.22	8.61	8.93
31C	Phenyl	<i>p</i> -Trimethylsilyl-phenyl	I	347-348	35	C ₂₁ H ₃₀ ONSiCl	67.08	66.70	8.04	7.99
32B	Phenyl	2-Pyridyl ^p	G	171-172		C ₁₇ H ₁₅ ON ₂ Cl	68.33	68.07	5.06	4.93
32B	Phenyl	2-Pyridyl	G	180-193		C ₁₇ H ₁₆ ON ₂ Cl ₂ ^o	60.91	60.68	4.81	4.92
32C	Phenyl	2-Pyridyl	I	201-202	75	C ₁₇ H ₂₁ ON ₂ Cl	66.98	66.87	6.94	7.00
32C ₁	Phenyl	2 Piperidyl	I	340	29	C ₁₇ H ₂₈ ON ₂ Cl ₂ ^o	58.80	58.70	8.14	8.26
32C ₂	Phenyl	2 Piperidyl ^q	I	282	45	C ₁₇ H ₂₈ ON ₂ Cl ₂ ^o	58.80	58.71	8.14	8.31
33A	Phenyl	β -Indolyl ^r	A	178-179	6	C ₂₀ H ₁₅ ON ₂	80.00	79.97	5.37	5.40
33C	Phenyl	β -Indolyl	I	156-159	29	C ₂₂ H ₂₅ O ₃ N ₂ ^m	72.12	72.20	7.15	7.19
34A	Phenyl	2-Furyl	C ^o	60-62	40	C ₁₆ H ₁₃ O ₂ N	76.49	76.47	5.21	5.15
34B	Phenyl	2-Furyl	G	164-166		C ₁₆ H ₁₄ O ₂ NCl	66.79	66.76	4.90	5.05

TABLE I (Continued)

No.	R	R ¹	Method	M.P., °C. cor. ^a	Yield, %	Formula	Carbon, %		Hydrogen, %	
							Calcd.	Found	Calcd.	Found
34C	Phenyl	2-Furyl	I	224-226	30	C ₁₆ O ₂ O ₂ NCl	65.40	65.50	6.86	6.94
34C ₁	Phenyl	2-Tetrahydrofuryl	I	228-230	38	C ₁₆ H ₂₁ O ₂ NCl	64.52	64.69	8.12	8.07
35A	Phenyl	2-Thienyl ^l	C	84-86	65	C ₁₆ H ₁₃ ONS	71.90	71.92	4.90	4.87
35B	Phenyl	2-Thienyl	G	156-158		C ₁₆ H ₁₄ ONSCl	63.27	63.49	4.64	4.83
36C	2-Thienyl	2-Thienyl ^l	H	124-125	56	C ₁₄ H ₁₇ ONS ₂ ^g	60.17	60.39	6.14	6.30
36C	2-Thienyl	2-Thienyl	G	240-241	94	C ₁₄ H ₁₃ ONS ₂ Cl	53.24	53.16	5.74	5.86
36D	2-Thienyl	2-Thienyl	K	211-212	80	C ₁₅ H ₁₃ ONS ₂ Cl ^d	54.94	54.81	5.53	5.61
37A	Phenyl	Cyclopropyl	B ^e	82-84	92	C ₁₅ H ₁₅ ON	79.97	80.10	6.71	6.76
37B	Phenyl	Cyclopropyl	G	122-124		C ₁₅ H ₁₅ ONCl	68.85	68.72	6.16	6.16
37C	Phenyl	Cyclopropyl	I	224-226	95	C ₁₅ H ₂₂ ONCl	67.28	67.36	8.28	8.35
38A	Phenyl	Cyclopentyl	A	65-67	35	C ₁₇ H ₁₉ ON	80.62	80.86	7.56	7.43
38B	Phenyl	Cyclopentyl	G	110-110 ^f		C ₁₇ H ₂₀ ONCl	70.45	70.48	6.96	7.21
38C	Phenyl	Cyclopentyl	I	273-274	96	C ₁₇ H ₂₆ ONCl	69.01	69.35	8.85	8.71
39A	Phenyl	Cyclohexyl ⁱ	C	71-73	62	C ₁₈ H ₂₁ ON	80.86	81.12	7.92	7.99
39C	Phenyl	Cyclohexyl	I	325-326	77	C ₁₈ H ₂₃ ONCl	69.75	69.72	9.11	9.11
40B	Phenyl	1-Cycloheptyl ^h	B	166-167		C ₁₉ H ₂₂ ONCl	72.27	72.24	7.02	7.13
40C	Phenyl	Cycloheptyl	I	289-290	93	C ₁₉ H ₃₀ ONCl	70.45	70.50	9.34	9.29
40D	Phenyl	Cycloheptyl	K	140-142	25	C ₄₄ H ₆₂ O ₆ N ₂ ^u	73.91	73.82	8.74	8.66
41A	Phenyl	1-Methyl 3-(2-propyl)- cyclopentyl ⁱ	C	71-76	60	C ₂₁ H ₂₇ ON	81.50	81.93	8.80	8.82
41C ₁	Phenyl	1-Methyl-3-(2-propyl)- cyclopentyl	I	215-216	7	C ₂₁ H ₃₄ ONCl	71.66	71.60	9.74	9.91
41C ₂	Phenyl	1-Methyl-3-(2-propyl)- cyclopentyl	I	295-298	13	C ₂₁ H ₃₄ ONCl ^e	71.66	71.56	9.74	9.65
41C ₃	Phenyl	1-Methyl-3-(2-propyl)- cyclopentyl	I	260-263	17	C ₂₁ H ₃₄ ONCl ^e	71.66	71.65	9.74	9.59
42A	Phenyl	4-Methylcyclohexyl ⁱ	A	109-111	60	C ₁₉ H ₂₃ ON	81.10	81.19	8.24	8.13
42C	Phenyl	4-Methylcyclohexyl	I	320-321	60	C ₁₉ H ₃₀ ONCl	70.45	70.51	9.34	9.49
43C	Phenyl	4-Ethylcyclohexyl ^o	I	330-351	80	C ₂₀ H ₂₂ ONCl	71.09	70.87	9.55	9.53
44A	Phenyl	Bicyclo[2,2,1]-5-hepten-2-yl	C	91-92	63	C ₁₉ H ₁₉ ON	82.25	82.56	6.90	6.89
44C	Phenyl	Bicyclo[2,2,1]-2-heptyl	I	310-311	27	C ₁₉ H ₂₆ ONCl	70.90	70.84	8.77	8.72
44D	Phenyl	Bicyclo[2,2,1]-2-heptyl	K	129-132	23	C ₂₄ H ₃₁ O ₆ N ^e	69.72	69.86	7.56	7.47
45A	<i>p</i> -Anisyl	Cyclopropyl	A ^e	95-96	93	C ₁₆ H ₁₇ O ₂ N	75.27	75.23	6.72	6.82
45B	<i>p</i> -Anisyl	Cyclopropyl	G	172-173		C ₁₆ H ₁₉ O ₂ NCl	65.86	65.85	6.22	6.39
45C ₁	<i>p</i> -Anisyl	Cyclopropyl	I	286-287	40	C ₁₆ H ₂₄ O ₂ NCl	64.52	64.52	8.12	8.23
45C ₂	<i>p</i> -Anisyl	Cyclopropyl ^e	I	229-230	33	C ₁₆ H ₂₄ O ₂ NCl	64.42	64.51	8.12	8.27
46A	Cyclohexyl	Cyclohexyl	C	79-81	84	C ₁₈ H ₂₇ ON	79.07	79.18	9.96	10.06
46B	Cyclohexyl	Cyclohexyl	G	237-240		C ₁₈ H ₂₈ ONCl	69.77	69.89	9.11	9.24
46C	Cyclohexyl	Cyclohexyl	I	280-281	71	C ₁₈ H ₃₄ ONCl	68.43	68.56	10.85	10.99
47C	Phenyl	2-Propyl ^o	I	306-307	75	C ₁₈ H ₂₄ ONCl	66.76	66.97	8.96	9.02
48C	2-Propyl	2-Propyl ^o	I	309-311	13	C ₁₂ H ₂₆ ONCl	61.12	60.99	11.12	10.97
49A	<i>i</i> -Butyl	<i>i</i> -Butyl	C	78-80 ^e	36	C ₁₄ H ₂₃ ON	75.99	76.13	10.48	10.61
49B	<i>i</i> -Butyl	<i>i</i> -Butyl	G	144-145		C ₁₄ H ₂₄ ONCl	65.23	65.26	9.38	9.29
49C	<i>i</i> -Butyl	<i>i</i> -Butyl	I	167-168	90	C ₁₄ H ₃₀ ONCl	63.72	63.85	11.46	11.58
50C	Hydrogen	1-Phenylcyclohexyl ^h	I	269-270	84	C ₁₈ H ₂₈ ONCl	69.75	69.51	9.11	8.98
51C	Hydrogen	3,4-Methylenedioxyphenyl ^o	I	192-195	15	C ₁₃ H ₁₈ O ₃ NCl	57.45	57.67	6.67	6.68
-CR ¹ R ² -										
52A		1-Indanylidene	C	79-81	80	C ₁₄ H ₁₃ ON	79.59	79.35	6.20	6.36
52B		1-Indanylidene	G	164-166		C ₁₄ H ₁₄ ONCl	67.88	68.01	5.70	5.96
52C ₁		1-Indanylidene	I	200-202	65	C ₁₄ H ₂₀ ONCl	66.25	66.10	7.94	7.86
52C ₂		1-Indanylidene ^e	I	203-205	25	C ₁₄ H ₂₀ ONCl	66.25	66.29	7.94	8.05
52D		1-Indanylidene ^f	K	150-151	22	C ₁₉ H ₂₃ O ₅ N ^e	66.08	66.29	6.71	6.88
53A		1-Tetrahydrylidene	C	77-78	76	C ₁₆ H ₁₆ ON	79.97	80.00	6.72	6.83
53B		1-Tetrahydrylidene	G	186-187		C ₁₆ H ₁₆ ONCl	68.85	68.97	6.16	6.26
53C		1-Tetrahydrylidene	I	205-207	75	C ₁₆ H ₂₂ ONCl	67.26	67.14	8.28	8.14
54A		9-Fluorenylidene	C	130-131	62	C ₁₈ H ₁₃ ON	83.38	83.14	5.05	5.21
54B		9-Fluorenylidene	G	222-223		C ₁₈ H ₁₄ ONCl	73.06	73.16	4.77	4.87
54C		9-Fluorenylidene	I	269-270	66	C ₁₈ H ₂₀ ONCl	71.64	71.80	6.68	6.90
54D		9-Fluorenylidene	K	96-98	90	C ₁₈ H ₁₉ ON	82.28	82.23	6.91	6.85
55A		9-Xanthylidene	C	120-121	69	C ₁₈ H ₁₅ O ₂ N	78.51	78.08	4.76	4.69
55B		9-Xanthylidene	G	189-192		C ₁₈ H ₁₄ O ₂ NCl	69.34	69.34	4.53	4.63
55C		9-Xanthylidene	I	224-227	67	C ₁₈ H ₂₀ O ₂ NCl	68.01	68.58	6.34	6.44
56A		10-Thioxanthylidene	C	186-187	62	C ₁₈ H ₁₃ ONS	74.21	74.37	4.50	4.60
56B		10-Thioxanthylidene	G	190-192		C ₁₈ H ₁₄ ONSCl	65.94	66.19	4.30	4.35
56C		10-Thioxanthylidene	I	283-285	48	C ₁₈ H ₂₀ ONSCl	64.74	65.40	6.04	6.22

TABLE I (Continued)

No.	R ¹	R ²	Method	M. p., °C cor. ^a	Yield, %	Formula	Carbon, %		Hydrogen, %	
							Calcd.	Found	Calcd.	Found
57A	9-Anthrylidene		C	126-128	49	C ₁₉ H ₁₅ ON	83.48	83.39	5.53	5.53
57B	9-Anthrylidene		G	240		C ₁₉ H ₁₆ ONCl	73.65	73.91	5.21	5.25
57C	9-Anthrylidene		I	272-274	80	C ₁₉ H ₂₂ ONCl	72.25	72.31	7.02	7.17
57D	9-Anthrylidene		K	162-164	82	C ₂₀ H ₂₁ ON	82.44	82.29	7.27	7.37
57D	9-Anthrylidene			168-169	80	C ₂₁ H ₂₅ O ₅ N ^c	70.75	70.62	6.18	6.23
58C	1-Bornylidene ^w		I	288-289	88	C ₁₅ H ₂₃ ONCl	65.79	65.55	10.30	10.26
59C ₁	1-Fenchylidene ^w		I	249-250	87	C ₁₅ H ₂₃ ONCl	65.79	65.71	10.30	10.25
59C ₂	1-Fenchylidene ^e		I	217-221		C ₁₅ H ₂₃ ONCl	65.79	65.68	10.30	10.37



No.	R ¹	R ²	R ³	Method	M. p., °C cor. ^a	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
60A	Phenyl	Phenyl	4-Methyl	F ^g	112-114	38	C ₁₉ H ₁₇ ON	82.89	83.30	6.23	6.40
60B	Phenyl	Phenyl	4-Methyl	G	205-207		C ₁₉ H ₁₈ ONCl	73.21	73.20	5.82	5.94
60C	Phenyl	Phenyl	4-Methyl	I	316-317	79	C ₁₉ H ₂₄ ONCl	71.79	71.80	7.61	7.74
61A	<i>p</i> -Tolyl	<i>p</i> -Tolyl	4-Methyl	F ^g	107-109	52	C ₂₁ H ₂₁ ON	83.14	83.13	6.98	7.07
61B	<i>p</i> -Tolyl	<i>p</i> -Tolyl	4-Methyl	G	180-183		C ₂₁ H ₂₂ ONCl	74.20	74.28	6.53	6.27
61C	<i>p</i> -Tolyl	<i>p</i> -Tolyl	4-Methyl	I	303-304	58	C ₂₁ H ₂₈ ONCl	72.91	72.92	8.16	8.04
61D	<i>p</i> -Tolyl	<i>p</i> -Tolyl	7-Methyl	K	295	85	C ₂₂ H ₂₈ ONCl ^d	73.81	73.97	7.88	8.40
62B	Phenyl	Hydrogen	4-Ethyl	F ^g	131-133	19	C ₁₄ H ₁₆ ONCl	67.33	67.92	6.46	6.64
62C	Phenyl	Hydrogen	4-Ethyl	I	205-207	50	C ₁₄ H ₂₂ ONCl	65.73	65.75	8.67	8.62
63A	Phenyl	Phenyl	6-Methyl	D	88-91	39	C ₁₉ H ₁₇ ON	82.90	82.71	6.23	6.32
63B	Phenyl	Phenyl	6-Methyl	G	171-176		C ₁₉ H ₁₈ ONCl	73.19	73.18	5.82	5.98
63C	Phenyl	Phenyl	6-Methyl	J	103-104	87	C ₁₉ H ₂₃ ON ^e	81.10	80.98	8.24	8.34
63C	Phenyl	Phenyl	6-Methyl	I	278-279	89	C ₁₉ H ₂₄ ONCl	71.78	71.83	7.61	7.59
63D	Phenyl	Phenyl	5-Methyl	K	121-123	69	C ₂₀ H ₂₃ ON	81.86	81.70	7.90	7.92
63D	Phenyl	Phenyl	5-Methyl		220-222		C ₂₀ H ₂₄ ONCl ^d	72.82	72.89	7.33	7.34

^a The hydrochlorides melted with some decomposition. ^b Previously reported in ref. 2; 1C also reported in ref. 3. ^c Acid maleate salt. ^d Hydrochloride salt. ^e A more soluble racemic modification obtained by fractional crystallization. ^f Prepared from the C₁ racemate. ^g Free base. ^h The corresponding free base was prepared by the method given in this row and isolated as an oil; 14A, b.p. 166-176° (10 mm.), 40A, b.p. 135-150° (0.2 mm.), yield 29%. ⁱ Converted to an oily hydrochloride salt. ^j The crude oil (70 g.) from the decomposed reaction mixture was distilled and gave 1 g. of the desired base with the remainder as polymerized residue. ^k Prepared by hydrogenation of a 25-g. fraction of crude pyridinemethanol, b.p. 124-142° (0.1 mm.), obtained by method B. ^l Converted to an impure crystalline hydrochloride salt, m.p. 243-248°. ^m 29C is a diacetate salt; 33C is an acetate salt. ⁿ Trihydrochloride. ^o Dihydrochloride. ^p The free base was prepared by method B; yield 73%, m.p. 96-97° (ref. 9, m.p. 96.5-97.5°). ^q Also prepared by method A (21% yield) by addition of 2-benzoylpyridine to 2-furylmagnesium iodide. ^r Ref. 8; 35A, m.p. 82-83°; 36C, m.p. 123-125°. ^s Cyclopropyl 2-pyridyl ketone substituted for 2-benzoylpyridine in this method. ^t Hygroscopic. ^u Neutral maleate salt. ^v Prepared by hydrogenation of 5 C₁. ^w Intermediates are reported in ref. 2. ^x Boiling point (0.1 mm.). ^y Prepared by hydrogenation of the pyridine ring and keto-group of 1-phenylcyclohexyl 2-pyridyl ketone hydrochloride. See Experimental for ketone preparation. ^z For procedure see method C of ref. 2. Method and yield given for 62B refers to the free base, isolated as an oil, b.p. 141-143° (0.3 mm.). Yields are based on carbonyl reactant.

appropriate ketone in the presence of mercuric chloride and aluminum.

Synthesis of pyridinemethanols by the Hammick reaction^{7,12-15} offered an attractive alternative method because of its simplicity. However, condensation of picolinic acid with aromatic ketones under various conditions gave poor yields or none of the desired products.

A few anomalous reactions were encountered in the course of preparing pyridinemethanols by methods A, B and C. The reaction of cyclopentylmagnesium bromide with 2-benzoylpyridine (method A) yielded 35% of the desired product,

(12) P. Dyson and D. L. Hammick, *J. Chem. Soc.*, 1724 (1937).

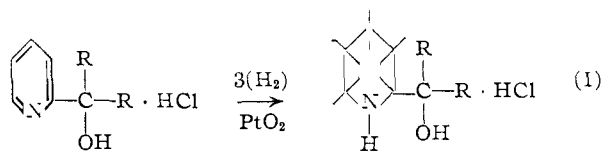
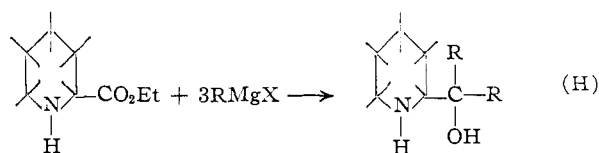
(13) B. R. Brown, *ibid.*, 2577 (1949).

(14) N. H. Cantwell and E. V. Brown, *THIS JOURNAL*, **75**, 1489 (1953).

(15) M. R. Buchdahl and T. O. Soine, *J. Am. Pharm. Assoc.*, **41**, 225 (1952).

α -cyclopentyl- α -phenyl-2-pyridinemethanol (Table I, 38A) and 36% of the reduction product, α -phenyl-2-pyridinemethanol. A method B type reaction between *o*-chlorophenyllithium (from *o*-chlorobromobenzene and *n*-butyllithium) and 2-benzoylpyridine was unsuccessful. However, the desired product, α -(*o*-chlorophenyl)- α -phenyl-2-pyridinemethanol (Table I, 13A) was obtained from a method C reaction. Reactions between 2-pyridyllithium and the following ketones (method C) were unsuccessful: *p*-iodobenzophenone, *p,p'*-dihydroxybenzophenone and acridone. The reaction involving *p*-iodobenzophenone apparently did not take place, since 84% of the ketone was recovered from the reaction mixture. The desired product (Table I, 30A) from the reaction involving *p,p'*-dimethylaminobenzophenone was obtained by method D.

The piperidinemethanols were prepared by methods H and I.



α,α -Di-(2-thienyl)-2-piperidinemethanol (Table I, 36C) was prepared by method H. After this work had been completed, a similar preparation of this compound was reported.⁸ The synthesis of the N-methyl derivative of 36C has also been described.¹⁶ These papers also reported the reaction of 2-benzoylpiperidine⁸ and its N-methyl derivative¹⁶ with 2-thienylmagnesium bromide to produce the corresponding piperidinemethanols.

Most of the piperidinemethanols of Table I were prepared from the intermediate pyridinemethanols by method I. The hydrogenation of pyridinemethanols containing an R group vulnerable to hydrogenation was carried out by interrupting the reaction after 3 molar equivalents of hydrogen had been absorbed. In this manner the 2-furyl (34C), 4-ethylphenyl (5C₁, 5C₂) and 2-pyridyl (32C, monohydrochloride) piperidinemethanols were obtained. When the reaction was allowed to proceed until 5 or 6 molar equivalents of hydrogen had been absorbed, the 2-tetrahydrofuryl (34C₁), 4-ethylcyclohexyl (43C) and 2-piperidyl (32C₁, 32C₂) piperidinemethanols were obtained. The dipiperidyl dihydrochlorides (32C₁, 32C₂) were prepared from 32B dihydrochloride rather than from 32B monohydrochloride. A comparison of the ultraviolet spectra of the more highly saturated compounds 34C₁, 43C, 32C₁ and 32C₂ with the corresponding compounds containing 2-furyl (34C), 4-ethylphenyl (5C₁, 5C₂) and 2-pyridyl (32C, monohydrochloride) groups showed higher molecular extinction coefficients for the latter compounds (see Table II). A similar comparison of infrared spectra of these compounds also showed differences in absorption.

α,α -Di-(*p*-hydroxyphenyl)-2-piperidinemethanol·HCl (Table I, 25C) was prepared by a hydrogenation-hydrogenolysis reaction of α,α -di-(*p*-benzyloxyphenyl)-2-pyridinemethanol·HCl (25B). The hydrogenation of 10-(2-pyridyl)-10-thioxanthol·HCl (Table I, 56B) with platinum oxide as the catalyst proceeded satisfactorily, but a similar hydrogenation of the pyridyl group of α -phenyl- α -(2-thienyl)-2-pyridinemethanol·HCl (35B) was unsuccessful.

Many of the compounds prepared by method I contained two asymmetric carbon atoms and two racemic modifications of the piperidine compounds often were isolated by fractional crystallization. The two fractions were recrystallized until constant melting points were obtained, but it was not deter-

mined whether the products were pure racemates or constant melting mixtures of racemates. Three constant melting crops were obtained for compound 41C of Table I, which has three asymmetric carbon atoms. In several cases the racemic modifications showed differences in degree of pharmacological activity.

One example of the conversion of a piperidinemethanol to a substituted heptahydrooxazolo[3,4-a]pyridine by heating α -methyl-2-piperidinemethanol and formalin with excess hydrochloric acid in water has been reported.¹⁷ The oxazolidine derivatives of this investigation were usually prepared by heating the piperidinemethanol base (or its hydrochloride salt and an equivalent of sodium bicarbonate) with formalin in methanol. When the hydrochlorides were used in the reaction without sodium bicarbonate, they were recovered unchanged in most cases. A comparison of the infrared spectra of the piperidinemethanols with that of the oxazolidine derivatives clearly showed the absence of the characteristic absorption band for tertiary hydroxyl groups at 3300 cm.⁻¹ in the latter compounds.

Initial attempts to convert 1,1-diphenylheptahydrooxazolo[3,4-a]pyridine to the hydrochloride salt with equivalents of aqueous or alcoholic hydrogen chloride yielded α,α -diphenyl-2-piperidinemethanol hydrochloride. However, subsequent reactions did give a stable hydrochloride salt of the oxazolidine (Table I, 1D), when excess amounts of aqueous or alcoholic hydrogen chloride were used.

Pharmacological Activity.—Many of the substituted α,α -diaryl-2-piperidinemethanols were characterized by central stimulant activity. The compounds were administered orally to mice and degree of stimulation determined by the photoelectric cell method.¹⁸ One of the most potent compounds was the parent α,α -diphenyl-2-piperidinemethanol hydrochloride.⁴ The potency was usually sustained when one of the phenyl rings had alkyl, alkoxy, hydroxy, fluorine, chlorine or dimethylamino substituents in the *para* position. Substitution of these groups in the *ortho* or *meta* position of one ring or in the *para* positions of both rings generally decreased the potency by a considerable amount. Replacement of one of the phenyl rings with 2-piperidyl, 2-furyl or 2-tetrahydrofuryl groups or both of the phenyl rings by 2-thienyl groups decreased the potency slightly. The other piperidinemethanols had either little or no central stimulant activity. The heptahydrooxazolo[3,4-a]pyridine derivatives were in general less potent than the corresponding piperidinemethanols.

Acknowledgment.—Evaluation of central stimulant activity was carried out in these laboratories under the direction of Drs. H. W. Werner and B. B. Brown. We are grateful for the special assistance of Drs. Geraldine L. Krueger, Edwn R. Andrews, Mr. Paul L. Tiernan, Mr. Loyd Kasbo and Mr. Martin Gordon in various phases of this work. We also wish to express our thanks to Mr.

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William F. Boyd for infrared spectra and Dr. E. D. Carkhuff and Mr. Eno Thuss for the ultraviolet spectra.

TABLE II
ULTRAVIOLET^a SPECTRA

No.	λ_{\max} , m μ	ϵ	No.	λ_{\max} , m μ	ϵ
5C ₁	257	557	32C ₂	266	146
5C ₂	263	551		260	210
	257	556		256	232
	252	501		250	175
43C	270	172	34C	262	198
	261	277		256	262
	255	233	34C ₁	262	176
32C	260	4485		256	229
32C ₁	266	146		249	223
	260	210			
	256	229			
	250	173			

^a Spectra were determined in 1-cm. silica cells at 25° with a Cary ultraviolet spectrophotometer. Water was used as the solvent.

Experimental

Intermediate Ketones.—Most of the ketones were obtained from commercial sources. The following ketones were synthesized by previously described methods: cyclohexyl phenyl ketone,¹ 1-methyl-3-isopropylcyclopentyl phenyl ketone,¹ bicyclo[2.2.1]heptene-2-yl phenyl ketone,¹ thioxanthone,¹ di-(*p*-benzyloxyphenyl) ketone,¹⁹ 2-methoxy-1-naphthyl phenyl ketone,²⁰ 3,4-methylenedioxybenzophenone²¹ and *o*-chlorobenzophenone.²² Other ketones were prepared as follows:

(a) *p*-Iodobenzophenone.—A solution of 63 g. (0.32 mole) of *p*-aminobenzophenone in 500 ml. of acetic acid was cooled to -15°. Thirty grams (0.43 mole) of sodium nitrite dissolved in 170 ml. of concentrated sulfuric acid was added slowly at -15 to 5°. The mixture thickened, was stirred for 3 hr. and the temperature was allowed to rise to 25°. The reaction mixture was poured into 2 l. of ice-water and treated with a solution of 75 g. (0.45 mole) of potassium iodide in 300 ml. of water containing 1 g. of copper powder. The mixture was warmed at 60–70° until evolution of nitrogen ceased, and sodium bisulfite solution was added to remove iodine color. The red solid was removed by filtration to give 78 g. of crude material. Three recrystallizations from methanol yielded 24 g. (24.3%), m.p. 93–97°; reported²³ m.p. 101°.

(b) *p*-Fluorobenzophenone.—An ether solution of *p*-fluorophenylmagnesium bromide²⁴ was prepared from 81 g. (0.33 g. atom) of magnesium turnings, 50 g. (0.28 mole) of *p*-fluorobromobenzene and 600 ml. of anhydrous ether. The solution was cooled to -45° and 28.8 g. (0.28 mole) of benzonitrile added rapidly with stirring. The reaction mixture was allowed to stand over the weekend; ether was removed by distillation, and the imino intermediate was decomposed by refluxing with 300 ml. of 10% hydrochloric acid for 1 hr. The mixture was extracted with ether and the desired product crystallized from petroleum ether to give 30 g. (54%) of yellow crystals, m.p. 47–49°; reported²³ m.p. 52°.

(c) 1-Phenylcyclohexyl 2-Pyridyl Ketone.—To 2.1 g. (0.30 g. atom) of lithium wire in 100 ml. of anhydrous ether was added 21.4 g. (0.15 mole) of *n*-butyl bromide in 80 ml. of anhydrous ether at -20° over a period of 30 minutes. The butyllithium solution was cooled to -50°, and 21 g. (0.13 mole) of 2-bromopyridine was added during a 10-minute period, the temperature being maintained below -40°. The mixture was stirred for 20 minutes, cooled to -60° and

19 g. (0.10 mole) of 1-phenylcyclohexyl cyanide²⁵ added. The reaction mixture was allowed to warm to room temperature, 100 ml. of 20% hydrochloric acid was added and the mixture was refluxed for about 30 minutes. The mixture was made alkaline with 10% sodium hydroxide; the ether layer was separated and concentrated on the steam-bath. The residue was crystallized from 40–60° petroleum ether; yield 10 g. (38%), m.p. 75–78°.

Anal. Calcd. for C₁₅H₁₉ON: C, 81.47; H, 7.22. Found: C, 81.25; H, 7.17.

The hydrochloride melting at 137–139° was hygroscopic and did not give a satisfactory analysis.

Anal. Calcd. for C₁₅H₁₉ON·HCl: C, 71.64; H, 6.68. Found: C, 70.02; H, 6.71.

(d) Cyclopropyl 2-Pyridyl Ketone.—This ketone was prepared by the above procedure c using 15.4 g. (2.2 g. atoms) of lithium wire, 150 g. (1.1 moles) of *n*-butyl bromide, 174 g. (1.1 moles) of 2-bromopyridine and 67 g. (1.0 mole) of cyclopropyl cyanide. The ether solution from the decomposed reaction mixture was fractionally distilled, and the desired ketone was collected at 112–115° (11 mm.), m.p. 36–37°, yield 47 g. (32%).

Anal. Calcd. for C₉H₉ON: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.60; H, 6.15; N, 9.32.

The hydrochloride salt melted at 159–160° dec.

Anal. Calcd. for C₉H₉ON·HCl: C, 58.85; H, 5.49. Found: C, 58.66; H, 5.57.

Intermediate Halo-compounds.—All of the halo compounds used in the preparation of Grignard and lithium agents were commercially available except the following: *p*-bromoethylbenzene,²⁶ (*p*-chlorophenyl)-trimethylsilane²⁷ and 1-chlorocycloheptene.²⁸

Ethyl 6-Methylpicolinate.—A mixture of 100 g. (0.66 mole) of 6-methylpicolinic acid, 170 g. of ethanol and 167 g. of concd. sulfuric acid was refluxed for 4 hr. The reaction mixture was distilled under reduced pressure on the steam-bath to remove most of the unchanged ethanol, and the residue was treated with 200 ml. of concd. ammonium hydroxide. The oil that formed was extracted with benzene and fractionally distilled, b.p. 122–126° (10 mm.), yield 68 g. (63%), *n*_D²⁰ 1.5060.

Anal. Calcd. for C₉H₁₁O₂N: C, 65.45; H, 6.71. Found: C, 65.28; H, 6.61.

2-Pyridinemethanols by the Hammick Reaction.—Previous investigations^{7,12–15} of the Hammick reaction have been concerned primarily with the reaction of aromatic aldehydes and aromatic alkyl ketones with picolinic acid. A yield of 14.5% of α,α -diphenyl-2-pyridinemethanol has been reported⁷ by refluxing a 6:1 ratio of benzophenone to picolinic acid in *p*-cymene for 6 hr. It was found that this yield could be increased to 25% by adding the acid over a 1–3 hr. period to a refluxing *p*-cymene solution of benzophenone (total reflux period of 7.5 hr.). This yield was duplicated when *p*-chlorobenzophenone was substituted for benzophenone. However, none of the desired product could be isolated when *p,p'*-dichlorobenzophenone, *o,p'*-dichlorobenzophenone, *p*-hydroxybenzophenone or xanthone was substituted for benzophenone under these conditions. For a similar reaction of benzophenone with catalytic amounts of triethylamine present, the yield of α,α -diphenyl-2-pyridinemethanol was decreased to 8%. None of the desired product could be isolated when a solution of picolinic acid in pyridine was substituted for solid picolinic acid or when ethylamine or dimethylformamide was substituted for *p*-cymene as solvent.

Substituted 2-Pyridinemethanols (Table I).—The various synthetic methods are illustrated by representative examples. Significant variations from the examples are described separately and in footnotes to the table.

(a) α -Benzyl- α -phenyl-2-pyridinemethanol (Method A).—To the Grignard reagent prepared from 126 g. (1.0 mole) of benzyl chloride, 29 g. (1.2 g. atoms) of magnesium turn-

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(21) W. Borsche, *Ann.*, **526**, 1 (1936).

(22) P. J. Montagne and S. A. Koopal, *Rec. trav. chim.*, **29**, 139 (1910).

(23) S. A. Koopal, *ibid.*, **34**, 115 (1915).

(24) Lithium did not react with *p*-fluorobromobenzene in an attempted preparation of *p*-fluorophenyllithium.

(25) C. H. Tilford, M. G. Van Campen, Jr., and R. S. Shelton, *THIS JOURNAL*, **69**, 2902 (1947).

(26) J. W. Copenhaver, M. F. Roy and C. S. Marvel, *ibid.*, **57**, 1311 (1935).

(27) C. A. Burkhard, *ibid.*, **68**, 2103 (1946).

(28) E. A. Braude, W. F. Forbes and E. A. Evans, *J. Chem. Soc.*, 2202 (1933).

ings and 500 ml. of dry ether cooled to -20° was added 166 g. (0.9 mole) of 2-benzoylpyridine in 150 ml. of dry ether. After complete addition of the ketone, the mixture was allowed to warm up to $25-30^{\circ}$ and decomposed with ammonium chloride solution. The mixture was filtered and the precipitate washed with water; yield 160 g. (58%), m.p. $100-101^{\circ}$. The ether layer from the filtrate was evaporated to one-half volume and diluted with 2 volumes of $70-90^{\circ}$ petroleum ether, cooled and filtered; yield 53 g. (19%) of additional product melting at $101-102^{\circ}$. An analytical sample recrystallized from methanol melted at $104-105^{\circ}$.

The reaction of cyclopentylmagnesium bromide with 2-benzoylpyridine yielded 35% of the desired product (Table I, 38A) and 36% of α -phenyl-2-pyridinemethanol, m.p. $78-79^{\circ}$; reported² m.p. $76-78^{\circ}$. A mixed melting point with an authentic sample was not lowered. The Grignard reagent for 33A (Table I) was prepared from indole and isopropylmagnesium chloride in benzene in place of ethylmagnesium iodide in anisole.²⁹

(b) α -(α -Naphthyl)- α -phenyl-2-pyridinemethanol (Method B).—A solution of 100 g. (0.48 mole) of α -bromonaphthalene in 100 ml. of dry ether was added to 6.7 g. (0.96 g. atom) of lithium in 350 ml. of dry ether over a period of 1-2 hr. under reflux. To the naphthyllithium thus formed was added 80 g. (0.43 mole) of 2-benzoylpyridine in 100 ml. of dry ether at -20° . The mixture was allowed to warm to 25° and aqueous ammonium chloride solution was added. The ether layer was separated, evaporated to a volume of 200 ml. and diluted with 300 ml. of hot $70-90^{\circ}$ petroleum ether. The solution was cooled to -12° and filtered; yield 65 g. (44%), m.p. $142-144^{\circ}$. An analytical sample recrystallized from methanol melted at $148-149^{\circ}$.

The lithium agents for compounds 14B and 32B (Table I) were prepared by exchange reactions of *n*-butyllithium with *m*-bromochlorobenzene³⁰ and with 2-bromopyridine,⁹ respectively.

(c) α -(4-Bromophenyl)- α -phenyl-2-pyridinemethanol (Method C).—An ether solution of *n*-butyllithium was prepared from 6.9 g. (1.0 g. atom) of lithium and 68.5 g. (0.5 mole) of *n*-butyl bromide in 600 ml. of dry ether at -10° , under nitrogen. The mixture was stirred for a period of 1.5 hr. until the lithium had dissolved. The solution was cooled to -60° , and 71 g. (0.45 mole) of 2-bromopyridine dissolved in 100 ml. of dry ether was added over a 15-minute period at -60 to -40° . The stirred solution was again cooled to -60° , and 105 g. (0.40 mole) of 4-bromobenzophenone suspended in 200 ml. of dry ether was added. The mixture was stirred at about -40° for a 2 hr. period; the temperature was allowed to rise to 20° , and the reaction mixture was decomposed with aqueous ammonium chloride solution. Unchanged ketone was removed by filtration and the ether layer was evaporated to give the crystalline product. Two recrystallizations from methanol yielded 84 g. (62%), m.p. $95-97^{\circ}$. An analytical sample melted at $95-96^{\circ}$.

A variation in the ratio of pyridyllithium and ketone was necessary for compounds 20B and 28A (Table I). A molar ratio of 2:1 and 3:1, respectively, was used to allow for reaction of the hydroxyl and amino groups.

(d) α, α -Di-(*p*-dimethylaminophenyl)-2-pyridinemethanol (Method D).—To 6.94 g. (1.0 g. atom) of lithium in 500 ml. of dry ether was added 100 g. (0.5 mole) of *p*-bromo-*N,N*-dimethylaniline in 100 ml. of dry ether over a period of 1 hr. with refluxing and stirring.³¹ The mixture was cooled to -40° and 30 g. (0.2 mole) of ethyl picolinate in 100 ml. of ether was added during 30-40 minutes. The mixture was allowed to warm to room temperature and then refluxed 45 minutes. The reaction mixture was decomposed with aqueous ammonium chloride solution and filtered. The crude product was recrystallized from methanol; yield 42 g. (61%), m.p. $120-125^{\circ}$. An analytical sample melted at $148-151^{\circ}$.

The preparation of compound 63A (Table I) by this method required the substitution of ethyl 6-methylpicolinate for ethyl picolinate.

(e) α, α -Di-(*p*-tolyl)-2-pyridinemethanol (Method E).—The Grignard reagent was prepared by the addition of 171

g. (1.0 mole) of *p*-bromotoluene in 200 ml. of dry ether to 23 g. (0.95 g. atom) of magnesium turnings in 300 ml. of dry ether over a period of 1.5 hr. Ethyl picolinate (75 g., 0.5 mole) was dissolved in 100 ml. of ether and added to the Grignard reagent with stirring over a period of 45 minutes. The reaction mixture was decomposed with ammonium chloride solution and about 250 ml. of dry toluene was added. The ether toluene layer was diluted with 3 volumes of petroleum ether ($40-60^{\circ}$) and evaporated to a volume of 1 l., cooled and filtered; yield 93 g. (67%), m.p. $112-118^{\circ}$. An analytical sample recrystallized from methanol melted at $119-121^{\circ}$.

Substituted-2-Pyridinemethanol Hydrochlorides (Method G).—The free bases in crystalline or oily form were dissolved in methanol and treated with the theoretical amount of alcoholic hydrogen chloride solution. The alcoholic solution was then diluted with ether or ethyl acetate until a faint cloudiness persisted or crystallization was induced. The mixture was then cooled to -12° and the hydrochloride salt removed by filtration. Crystalline hydrochlorides were not isolated for the following compounds of Table I: 19B, 22B, 28B, 33B, 39B, 41B, 42B and 44B.

Substituted-2-Piperidinmethanols (Table I). α, α -Di-(2-thienyl)-2-piperidinmethanol (Method H).—A solution of 98 g. (0.6 mole) of 2-bromothiophene in 100 ml. of dry ether was added to 14.5 g. (0.6 g. atom) of magnesium turnings in 250 ml. of dry ether over a period of an hour with stirring and refluxing. The thienylmagnesium bromide solution thus prepared was cooled to -20° during 20-30 minutes addition of 18 g. (0.115 mole) of ethyl pipercolinate in 50 ml. of dry ether. The temperature of the mixture was allowed to rise to $25-30^{\circ}$, and the reaction mixture was decomposed with aqueous ammonium chloride solution. The ether solution was separated and concentrated on the steam-bath to approximately 250 ml. The concentrate was diluted with 3 volumes of hot petroleum ether, cooled at -12° overnight and filtered; yield 18 g. (56%), m.p. $124-126^{\circ}$. An analytical sample recrystallized from methanol melted at $124-125^{\circ}$. The reported melting point is $123-125^{\circ}$.⁸

Hydrogenation of 2-Pyridinemethanols (Method I). (a) **General Procedure.**—A mixture of 0.2 mole of the substituted pyridinemethanol hydrochloride, 200 ml. of methanol and 0.6-0.8 g. of platinum oxide catalyst was shaken with hydrogen at 3 to 4 atmospheres pressure in a Parr hydrogenation apparatus until the theoretical amount (0.6 mole) of hydrogen had been absorbed. The catalyst was removed by filtration and the filtrate concentrated to about one-fourth volume. Approximately 200 ml. of ethyl acetate or ether was added, the solution was cooled to -12° and then filtered to obtain the crystalline piperidinmethanol hydrochloride.

The pyridinemethanol base with an equivalent of alcoholic or aqueous hydrogen chloride can be substituted for the pyridinemethanol hydrochlorides in this procedure. Compounds 29C and 33C (Table I) were prepared by hydrogenation of the free base in methanol with an equivalent of glacial acetic acid. During several of the hydrogenations, the piperidinmethanol hydrochlorides precipitated, and it was necessary to dissolve the product by heating with larger quantities of solvent before removing the catalyst by filtration.

(b) **Partial Hydrogenation:** α -(*p*-Ethylphenyl)- α -phenyl-2-pyridinemethanol.—A mixture of 49 g. (0.15 mole) of α -(*p*-ethylphenyl)- α -phenyl-2-pyridinemethanol-HCl, 300 ml. of methanol and 0.8 g. of platinum oxide was hydrogenated (initial pressure 60 lb.) until 3.3 molar equivalents of hydrogen were absorbed. The reaction mixture was filtered to remove catalyst and concentrated. Crystallization yielded 23 g. (47%) of product, m.p. $310-311^{\circ}$. An analytical sample melted at $323-324^{\circ}$. A second crop was obtained; yield 5 g. (10%), m.p. $290-291^{\circ}$. A third crop of 10 g. (20%), m.p. $271-273^{\circ}$, probably representing a second racemic modification, was also obtained. The melting point of a mixture of the first and third crops was $268-270^{\circ}$.

A 5-g. (0.015 mole) sample of the highest melting racemate was further hydrogenated as above and yielded 4 g. (80%) of the ethylcyclohexyl derivative (Table I, 43C), m.p. $330-331^{\circ}$. When mixed in equal amounts with starting material, the melting point was $311-313^{\circ}$. The ultraviolet spectrum of the product exhibited lower molecular extinction coefficients than the starting material (see compounds 5C₁, 5C₂ and 43C of Table II). The starting material and product were both converted to free bases which

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(30) H. Gilman, R. V. Christian and S. M. Spatz, *This Journal*, **68**, 979-981 (1946).

(31) R. K. Robins and B. E. Christensen, *J. Org. Chem.*, **16**, 324 (1951).

melted at 84–86° and 96–98°, respectively. An equal mixture of the free bases melted at 73–75°.

α -Phenyl- α -(2-pyridyl)-2-pyridinemethanol-HCl.—Partial hydrogenation was carried out as in the preceding example. The reaction was interrupted when the theoretical amount of hydrogen for the saturation of one pyridyl ring had been absorbed. α -Phenyl- α -(2-pyridyl)-2-piperidinemethanol-HCl (Table I, no. 32C) was obtained in 75% yield, m.p. 201–202°. The hydrogenation of α -phenyl- α -(2-pyridyl)-2-pyridinemethanol-2HCl (Table I, 32B-dihydrochloride) with 6 molar equivalents of hydrogen yielded α -phenyl- α -(2-piperidyl)-2-piperidinemethanol-2HCl (Table I, 32C₁ and 32C₂). The ultraviolet spectra of 32C₁ and 32C₂ exhibited much lower molecular extinction coefficients than those of 32C (see Table II).

α -(2-Furyl)- α -phenyl-2-pyridinemethanol.—Saturation of the pyridyl group with hydrogen was carried out by an interrupted reaction as described above and gave a 30% yield of α -(2-furyl)- α -phenyl-2-piperidinemethanol (Table I, 34C), m.p. 224–226°. A subsequent hydrogenation of 34B with 5 molar equivalents of hydrogen gave a 38% yield of α -phenyl- α -(2-tetrahydrofuryl)-2-piperidinemethanol (Table I, no. 34C₁); m.p. 226–228°. The melting point of an equal mixture of 34C and 34C₁ was lowered 3°. The latter compound also exhibited lower molecular extinction coefficients as shown in Table II.

An attempted hydrogenation of the pyridine ring of α -phenyl- α -(2-thienyl)-2-pyridinemethanol (Table I, 35B) by this procedure was unsuccessful. Hydrogen was not absorbed (with heating at 65°), and the reaction mixture turned black.

(c) **Hydrogenation-Hydrogenolysis of α,α -Di-(*p*-benzyloxyphenyl)-2-pyridinemethanol.**—A mixture of 3.2 g. (0.006 mole) of α,α -di-(*p*-benzyloxyphenyl)-2-pyridinemethanol HCl (Table I, 25B), 30 ml. of methanol and 0.2 g. of platinum oxide was hydrogenated until 5 molar equivalents of hydrogen was absorbed. The product (Table I, 25C) was isolated as described in the preceding examples to give 0.4 g. (20%), m.p. 227–229° dec. An analytical sample recrystallized from methanol-ether melted at 229–230°.

α,α -Disubstituted-2-Piperidinemethanol Free Bases (Method J).—The appropriate piperidinemethanol hydrochloride was dissolved in methanol, and a slight excess of 5% aqueous sodium hydroxide was added. The mixture was cooled, filtered, the precipitate washed with water and recrystallized from 2-propanol or 75–90° petroleum ether. In some cases, the piperidinemethanol hydrochlorides were suspended in hot benzene or benzene-ether mixtures and stirred with aqueous sodium hydroxide solution. The free bases were then isolated from the organic layers. Free bases which could not be crystallized were used without identification to prepare oxazolidine derivatives. Crystalline free bases obtained by these procedures are reported in Table I.

Substituted Heptahydrooxazolo[3,4-a]pyridines (Method K).—A mixture of 0.02 mole of piperidinemethanol base and 3.0 ml. (0.037 mole) of formalin in 50 ml. of methanol was refluxed 16 hr. About 25 ml. of methanol was removed and the solution cooled and filtered. The products were recrystallized from methanol, ethyl acetate or 75–90° petroleum ether.

Several hydrochlorides (Table I, compounds IC, 2C, 3C, 5C₁, 6C, 12C₁, 12C₂, 14C, 15C₁, 15C₂, 16C, 17C, 18C₁, 19C, 20C, 22C₁, 37C, 41C₃, 49C, 50C and 60C) were originally used in this procedure but were recovered unchanged.

However, three oxazolidine derivatives (Table I, compounds 9D, 36D and 61D) were prepared by using the piperidinemethanol hydrochloride in the above procedure. Four compounds (1D, 52D, 54D and 57D) of Table I were prepared by using the piperidinemethanol hydrochloride with an equivalent of sodium bicarbonate in the above procedure.

The heptahydrooxazolo[3,4-a]pyridines were converted to acid maleate salts by adding an equivalent of maleic acid to the base in methanol. Subsequent addition of ethyl acetate or ether usually precipitated the salt. The products were recrystallized from methanol-ether mixtures. Several attempts to prepare neutral maleate salts by adding one-half equivalent of maleic acid were unsuccessful, except for compound 40D (Table I). The attempted preparation of a maleate or fumarate salt of compound 63D (Table I) was unsuccessful and resulted in recovery of 90% of the starting base. However, the hydrochloride salt of this compound was prepared readily. The conversion of compound 1D to a hydrochloride salt in methanol was accomplished by using an excess of either alcoholic or aqueous hydrogen chloride. When equivalents of these reagents were used, some splitting of the oxazolidine ring unexpectedly occurred, and varying amounts of α,α -diphenyl-2-piperidinemethanol hydrochloride also were obtained.

Additional support for the structure of 1,1-diphenylheptahydrooxazolo[3,4-a]pyridine was obtained by a procedure previously described¹ for analogous compounds. A solution of 0.5 g. of the base 1D (Table I) in 10% hydrochloric acid was slowly distilled, and the evolved formaldehyde was isolated as its 2,4-dinitrophenylhydrazone, m.p. 156–159°. A mixture with an authentic sample of formaldehyde 2,4-dinitrophenylhydrazone (m.p. 164–166°) melted at 157–160°. The residue in the distillation flask was made alkaline with sodium hydroxide solution, filtered and recrystallized twice from methanol to give 0.2 g. of recovered 1,1-diphenylheptahydrooxazolo[3,4-a]pyridine, m.p. 116–120°. When mixed with an authentic sample of this compound the melting point was not depressed.

1-Methyl- α,α -diphenyl-2-piperidinemethanol.—A mixture of 16 g. (0.06 mole) of α,α -diphenyl-2-piperidinemethanol, 16 g. (0.2 mole) of formalin and 24 g. (0.4 mole) of 98–100% formic acid was refluxed for a period of 36 hr. The reaction mixture was cooled, made alkaline with 5% sodium hydroxide and the oil extracted with 150 ml. of hot petroleum ether. The ether layer was cooled and filtered to give 13 g. (77%) of product melting at 90–92°. A second crop was obtained; yield 2.2 g. (13%), m.p. 88–90°. A mixture of this compound with 1,1-diphenylheptahydrooxazolo[3,4-a]pyridine (Table I, 1D) melted at 78–81°.

Anal. Calcd. for C₁₉H₂₃ON: C, 81.10; H, 8.24. Found: C, 81.20; H, 8.31.

1-Methyl- α,α -diphenyl-2-piperidinemethanol Methobromide.—A mixture of 12 g. (0.043 mole) of 1-methyl- α,α -diphenyl-2-piperidinemethanol, 50 ml. of methanol and 25.5 ml. (0.2 mole) of 77% methanolic methyl bromide was heated at 75° in a capped bottle for 24 hr. The reaction mixture was diluted with three volumes of ether and filtered to give 16 g. (98%) of product melting at 265–266°. Recrystallization from 70% methanol gave 11 g. (68%), m.p. 266–267°.

Anal. Calcd. for C₂₀H₂₅ONBr: C, 63.83; H, 6.97. Found: C, 63.30; H, 7.02.

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