

[CONTRIBUTION FROM THE WELLCOME RESEARCH LABORATORIES]

Quaternary Piperazines with Anti-pinworm Activity¹

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The syntheses and properties of 100 piperazine monoquaternary salts prepared for a study of their anthelmintic activities, and of some related compounds, are reported. Most were prepared by standard methods, but attempts to decarboxylate three 1-carbethoxy-4-benzylquaternaries (table, lines 42, 49, 50) led to debenzilation. Anthelmintic activity (*Syphacia obvelata* in the mouse) is discussed briefly as a function of structure.

Consideration of the structures of a number of compounds active in a screening test (*Syphacia obvelata* in the mouse)² designed to find substances active against the pinworm of humans, *Enterobius vermicularis*, suggested that two structural features were common to piperazine, gentian violet and several other active series of compounds: all appeared likely to exist largely in the cationic form at physiological acidities,³ and all had a ring structure near the positive charge. It was thought of interest to prepare some other compounds combining these structural features. The piperazine ring, which occurs in many physiologically active compounds, was therefore given the positive charge induced by quaternization at one nitrogen. It was also anticipated that the well-known tendency of quaternary salts to be poorly absorbed on oral administration would result in negligible systemic toxicity to the host. The high therapeutic index of some of the first compounds prepared led to the synthesis of a large number of diverse piperazine monoquaternaries, whose properties are tabulated.

The thoroughly explored route to unsymmetrical piperazines by alkylation of 1-carbethoxypiperazine¹ was used to prepare most of the compounds. The quaternizations were done in acetone at about room temperature, since some of the higher quaternaries could not be crystallized readily from alcoholic solvents. Further, solvolysis of some halides competed with the slower quaternizations especially in methanol.

It was convenient to prepare large batches of the 1-carbethoxy-4-alkylpiperazines substituted with the smaller alkyl group and to then quaternize each of these with a number of larger alkyl bromides. In some cases, the alkyl iodides were used as quaternizing agents to speed up the reactions, but they were not as satisfactory since the hydriodides of the starting tertiary amines were sometimes the only isolable products.⁴

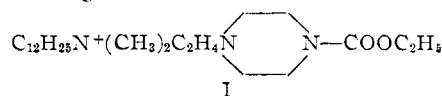
The quaternization of 1-carbethoxy-4-propargylpiperazine, e.g., with dodecyl bromide, was so slow as to be essentially unusable. This is, of course, an example of the well-known electron-attracting ability of the ethynyl group. Propargyl bromide was

therefore used to prepare quaternaries such as those on lines 38 and 71-79 of the table, and reacted rapidly as anticipated.⁵ Indeed, the dipropargyl quaternary was prepared readily (line 76).

To prepare the 1,1-dialkylpiperazinium halides without an amide function at N₄ (lines 1-10 of the table) decarboxylation of the corresponding 4-carbethoxy quaternaries by constant-boiling aqueous hydrochloric acid was generally used.⁶ The quaternary function at the other nitrogen did not appear to increase the rate of hydrolysis at the carbethoxy group appreciably more than the activation conferred by protonation of a tertiary nitrogen in this strongly acidic medium.

In the case of the attempted acid hydrolysis of 1-carbethoxy-4-methyl-4-benzylpiperazinium chloride and its 4-methyl-4-*p*-chlorobenzyl congener (table, lines 42 and 44), this treatment led to destruction of the quaternary with formation of 1-methylpiperazine (characterized both by benzylation and by formation of the phenylthiourea) and steam-distillable material resembling the corresponding benzyl halide. The related 1-carbethoxy-4-methyl-4-*p*-anisylpiperazinium chloride (table, line 50) gave what appeared to be a polymer in addition to the 1-methylpiperazine. Raney nickel-catalyzed hydrogenolysis⁷ of the 1-nitroso quaternary (table, line 100) was therefore used to prepare 1-methyl-1-benzylpiperazinium chloride.^{7,8}

The 1-alkyl-4-amides (other than the carbethoxy compounds) required for preparation of the corresponding quaternaries (table, groups B, C, D, F, G) were in general prepared by the methods previously reported.⁹ One exception is the preparation of the compound I, required to determine whether placing the quaternary grouping further from the ring would affect anthelmintic activity.



This was prepared from the commercially available aminoethylpiperazine which, on heating with benz-

(1) This paper is No. X on unsymmetrical piperazines from these laboratories. For the previous paper, see R. Baltzly, W. S. Ide and E. Lorz, *THIS JOURNAL*, **77**, 4809 (1955).

(2) K-F. Chan, *Am. J. Hyg.*, **56**, 22 (1952).

(3) The glycinamide quaternaries of A. J. Rachlin, *et al.*, A.C.S. Div. of Med. Chem. Abstracts, P.5M. (Apr. 8, 1956) also fit this category, as does cyanine dye No. 715 [cf. E. Perez-Santiago, J. Oliver-González and C. J. Thillet, *Am. J. Trop. Med. Hyg.*, **2**, 307 (1953)].

(4) E. D. Hughes and U. G. Shapiro, *J. Chem. Soc.*, 1177 (1937), have shown that the ratio of the E₁ elimination to the S_N2 hydrolysis of isopropyl iodide in alkaline ethanol-water solution is greater than for isopropyl bromide.

(5) The rapid reactions of propargyl chloride with ethoxide and with radioactive chloride have been reported by C. A. Vernon, *J. Chem. Soc.*, 4462 (1954), and that with ethoxide by L. F. Hatch and V. Chiola, *THIS JOURNAL*, **73**, 360 (1951). However, the occurrence of side reactions led to inconstancy of the rate, or incomplete reaction. Since the theoretical titer of acetylenic hydrogen is found in the quaternaries readily isolated in excellent yield from our quaternizations with propargyl bromide, it is hoped to measure the rate of this reaction more precisely as time permits.

(6) T. S. Moore, M. Boyle and V. M. Thorne, *J. Chem. Soc.*, 39 (1929).

(7) E. Lorz and R. Baltzly, *THIS JOURNAL*, **73**, 93 (1951).

(8) Details of this and of the other protecting methods studied will be reported separately.

(9) M. Harfenist, *THIS JOURNAL*, **76**, 4991 (1954).

TABLE I
 PROPERTIES OF PIPERAZINE QUATERNARIES

R	R'	X ⁻	M.p., °C.	Recrystn. solvents ^a	Calculated C	Analyses, % H	Found C	H
A: Compounds of type $\text{HN} \begin{array}{c} \boxed{} \\ + \end{array} \text{NRR}'\text{X}^-\text{HX}$								
1	CH ₃	CH ₃	Cl	219-220	W-M	38.51	8.62	38.57 8.79
2	CH ₃	<i>n</i> -C ₈ H ₁₇	Cl	178	A-B-E	Cl ⁻ 37.90		Cl ⁻ 38.19
3	CH ₃	<i>n</i> -C ₁₁ H ₂₃	I	175.5-177	A-B-E	Cl ⁻ 24.87		Cl ⁻ 24.87
4	CH ₃	<i>n</i> -C ₁₂ H ₂₅	Cl	158-159	A-Ac	I ⁻ 49.73		I ⁻ 50.00
5	CH ₃	<i>n</i> -C ₁₃ H ₂₇	Cl	109-120	A-Ac	Cl ⁻ 20.77		Cl ⁻ 20.60
6	CH ₃	<i>n</i> -C ₁₄ H ₂₉	Cl	144-145	A-EA-E	Cl ⁻ 19.95		Cl ⁻ 19.96
7	CH ₃	<i>n</i> -C ₁₆ H ₃₃	Br	105-108	A-EA	Cl ⁻ 19.19		Cl ⁻ 18.83
8	CH ₃	CH ₂ C ₆ H ₅	Cl	172-175 ^c	A-B-E	Br ⁻ 32.88		Br ⁻ 33.52
9	C ₂ H ₅	<i>n</i> -C ₈ H ₁₇	Cl	188-195	A-B-E	Cl ⁻ 27.02		Cl ⁻ 27.12
10	C ₄ H ₉	<i>n</i> -C ₁₀ H ₂₁	Cl	167.5-168	B-E	Cl ⁻ 23.68		Cl ⁻ 24.43
11	CH ₃	CH ₂ COOH ^b	Cl	230	W-Ip	Cl ⁻ 19.95		Cl ⁻ 20.23
						36.37	6.98	36.22 7.53
B: Compounds of type $\text{CH}_3\text{C}(=\text{O})\text{N} \begin{array}{c} \boxed{} \\ + \end{array} \text{NRR}'\text{X}^-$								
12	CH ₃	<i>n</i> -C ₁₄ H ₂₉	Br	166.5	Ac-E	Br ⁻ 19.06		Br ⁻ 19.11
13	CH ₃	CH ₂ C ₆ H ₅	Cl	225-226	Ac-E	Cl ⁻ 13.20		Cl ⁻ 13.34
C: Compounds of type $\text{C}_6\text{H}_5\text{C}(=\text{O})\text{N} \begin{array}{c} \boxed{} \\ + \end{array} \text{NRR}'\text{X}^-$								
14	CH ₃	CH ₃	I	216.5-217.5	AW-A	45.10	5.53	44.83 5.42
15	CH ₃	<i>n</i> -C ₄ H ₉	I	140-142	TBW-TB	49.49	6.49	49.08 6.25
16	CH ₃	<i>n</i> -C ₁₂ H ₂₅	Br	174.5-175.5	Ac-B-E	63.56	9.11	63.72 9.10
17	CH ₃	CH ₂ C ₆ H ₅	Cl	116-117	A-AE-E	Cl ⁻ 10.24		Cl ⁻ 10.48
D: Compounds of type $\text{CH}_3\text{OOCN} \begin{array}{c} \boxed{} \\ + \end{array} \text{NRR}'\text{X}^-$								
18	CH ₃	<i>n</i> -C ₁₂ H ₂₅	Br	192-193	MA	56.01	9.65	56.22 9.99
E: Compounds of type $\text{C}_6\text{H}_5\text{OOCN} \begin{array}{c} \boxed{} \\ + \end{array} \text{NRR}'\text{X}^-$								
19	CH ₃	CH ₃	I	197-199	A-E	34.40	6.10	34.55 6.46
20	CH ₃	C ₆ H ₅	Br	170.5-171.5	A-EA-E	42.82	7.72	42.71 7.53
21	CH ₃	<i>n</i> -C ₈ H ₁₇	I	123.5-124.5	A-EA	38.60	6.77	38.58 6.62
22	CH ₃	<i>i</i> -C ₈ H ₁₇	I	178	A-EA	38.60	6.77	38.17 7.04
23	CH ₃	<i>n</i> -C ₄ H ₉	I	104-107.5	A-EA-E	40.45	7.07	40.48 7.01
24	CH ₃	<i>n</i> -C ₈ H ₁₇	I	131.5-132.5	Ac-EA	42.17	7.35	42.48 7.74
25	CH ₃	<i>i</i> -C ₈ H ₁₇	I	133.5-134	A-EA-E	42.17	7.35	42.00 7.11
26	CH ₃	<i>n</i> -C ₆ H ₁₃	I	115-117.5	A-EA-E	43.75	7.61	43.87 7.49
27	CH ₃	<i>n</i> -C ₇ H ₁₅	Br	161-162	A-EA-E	51.27	8.89	50.75 8.81
28	CH ₃	<i>n</i> -C ₈ H ₁₇	Br	183-184	A-EA-E	52.59	9.10	52.67 9.10
29	CH ₃	<i>n</i> -C ₉ H ₁₉	I	107-108.5	A-EA	47.91	8.30	48.04 7.92
30	CH ₃	<i>n</i> -C ₁₀ H ₂₁	Br	203.5-204.5	Ac-EA	54.95	9.48	54.75 9.44
31	CH ₃	<i>n</i> -C ₁₁ H ₂₃	Br	198.5-199	Ac-EA	56.01	9.65	55.79 10.02
32	CH ₃	<i>n</i> -C ₁₂ H ₂₅	Br	216	D	56.99	9.81	56.56 10.08
33	CH ₃	<i>n</i> -C ₁₃ H ₂₇	Br	215.5-218.5	D	Br ⁻ 18.36		Br ⁻ 18.75
34	CH ₃	<i>n</i> -C ₁₄ H ₂₉	Br	203-203.5	A-EA-E	57.98	10.36	57.51 10.12
35	CH ₃	<i>n</i> -C ₁₅ H ₃₁	Br	201-202.5	Ac-EA; N-EA	59.63	10.23	59.30 10.32
36	CH ₃	<i>n</i> -C ₁₆ H ₃₃	Br	219-221	D	60.40	10.35	60.58 10.44
37	CH ₃	C ₆ H ₁₃ CH=CH ₂	I	111-113	EA	50.48	8.22	50.44 8.16
38	CH ₃	CH ₂ C≡CH	Br	151-152	A-EA	45.37	6.58	45.52 6.78
39	CH ₃	CH ₂ CH ₂ C≡CH	Tos ^d	146-148	Ac-E	57.63	7.12	57.74 7.08
40	CH ₃	CH ₂ C≡C-C ₄ H ₉	Br	123-125	Ac-B-E	Br ⁻ 22.92		Br ⁻ 22.48
41	CH ₃	C ₆ H ₅	I	137.5-138.5	A-Ac-E	I ⁻ 33.81		I ⁻ 34.23
42	CH ₃	CH ₂ C ₆ H ₅	Cl	185.5-186.5	A-EA-E	Cl ⁻ 11.66		Cl ⁻ 11.87
43	CH ₃	CH ₂ C ₆ H ₄ Cl(2)	Cl	165-167.5	Ac-E	Cl ⁻ 10.65		Cl ⁻ 10.60
44	CH ₃	CH ₂ C ₆ H ₄ Cl(4)	Cl	189	A-Ac-E	54.04	6.62	54.34 6.70
45	CH ₃	CH ₂ C ₆ H ₃ Cl ₂ (2,4)	Cl	178.3-179	A-B-E	Cl ⁻ 9.64		Cl ⁻ 9.21
46	CH ₃	CH ₂ C ₆ H ₃ Cl ₂ (3,4)	Cl	170-171	Ac-E	Cl ⁻ 9.64		Cl ⁻ 9.62
47	CH ₃	CH ₂ C ₆ H ₄ CH ₃ (2)	Br	200.5-202.5	A-Ac-E	Br ⁻ 22.38		Br ⁻ 22.63
48	CH ₃	CH ₂ C ₆ H ₄ CH ₃ (3)	Br	176-178	A-EA-E	Br ⁻ 22.38		Br ⁻ 22.32
49	CH ₃	CH ₂ C ₆ H ₄ CH ₃ (4)	Br	189-190	A-B-E	Br ⁻ 22.38		Br ⁻ 22.59
50	CH ₃	CH ₂ C ₆ H ₄ OCH ₃ (4)	Cl	189	N-EA	58.55	7.68	58.45 7.92
51	CH ₃	(CH ₂) ₂ C ₆ H ₅	I	194.5-195.5	A-EA-E; W	I ⁻ 31.40		I ⁻ 31.42
52	CH ₃	(CH ₂) ₃ C ₆ H ₅	Br	138.5-139.5	N-Ac-E	Br ⁻ 21.52		Br ⁻ 21.81
53	CH ₃	CH ₂ CH=CHC ₆ H ₅ ^e	Cl	157-158	Ac-EA-E	Cl ⁻ 10.92		Cl ⁻ 10.87
54	CH ₃	$\begin{array}{c} \text{C} \\ \parallel \\ \text{CH}_2\text{C}-\text{S}-\text{C} \\ \parallel \\ \text{C} \end{array}$	Cl	164-165	A-EA-E	Cl ⁻ 11.64		Cl ⁻ 11.62

TABLE I (continued)

R	R'	X ⁻	M.p., °C.	Recrystn. solvents ^a	Calculated C	Analyses, % H	Found C	Found H
E: Compounds of type $C_2H_5OOCN \begin{array}{c} \boxed{+} \\ \text{NRR}' \end{array} X^-$								
55	CH ₃	$\begin{array}{c} \text{CH}_2\text{C}=\text{C} \\ \parallel \quad \parallel \\ \text{C}-\text{S}-\text{C} \\ \parallel \\ \text{O} \end{array}$	Br	138-145	A-EA	Br ⁻ 22.88	Br ⁻ 22.68	
56	CH ₃	CH ₂ C-C ₆ H ₅	Br	172.5-175	N-EA	51.78	6.24	51.53 6.04
57	CH ₃	CH ₂ COOCH ₃	Cl	143-145	M-Ac-E	47.05	7.54	46.60 7.36
58	CH ₃	CH ₂ COOC ₂ H ₅	Cl	145.5-146.5	A-B-EA-E	48.89	7.86	48.68 7.90
59	CH ₃	CH ₂ COOC ₁₂ H ₂₅	Cl	113.5-116	M-B-E	Cl ⁻ 8.15	Cl ⁻ 8.26	
60	CH ₃	CH(CH ₃)COOC ₁₂ H ₂₅	Cl	75-77	Ac-E	Br ⁻ 16.20	Br ⁻ 16.25	
61	C ₂ H ₅	C ₂ H ₅	I	154-156	A-B-EA	38.60	6.77	38.35 7.04
62	C ₂ H ₅	<i>n</i> -C ₈ H ₁₇	I	106-109	Ac-E	47.88	8.27	48.29 8.55
63	C ₂ H ₅	CH ₂ C ₆ H ₅	Cl	133.5-134.5	N-Ac-E	Cl ⁻ 11.34	Cl ⁻ 11.14	
64	C ₄ H ₉	<i>n</i> -C ₁₀ H ₂₁	I	155.5-156.5	A-EA	52.18	8.98	52.55 8.92
65	CH ₂ CH=CH ₂	<i>n</i> -C ₈ H ₁₇	Br	154.5-155.5	Ac-E	Br ⁻ 20.42	Br ⁻ 20.58	
66	CH ₂ CH=CH ₂	<i>n</i> -C ₁₀ H ₂₁	Br	169	Ac-E	Br ⁻ 19.50	Br ⁻ 19.21	
67	CH ₂ CH=CH ₂	<i>n</i> -C ₁₂ H ₂₅	Br	177-177.5	Ac-E	Br ⁻ 17.86	Br ⁻ 18.05	
68	CH ₂ CH=CH ₂	CH ₂ CH=CH ₂	Br	172-173	A-Ac-E	Br ⁻ 25.04	Br ⁻ 25.00	
69	CH ₂ CH=CH ₂	CH ₂ CH=CH ₂	Cl	154-158	A-Ac-E	Cl ⁻ 12.91	Cl ⁻ 12.88	
70	CH ₂ CH=CH ₂	CH(CH ₃) COOC ₂ H ₅	Br	114.5-116	A-B-E	Br ⁻ 21.08	Br ⁻ 21.23	
71	CH ₂ C≡CH	<i>n</i> -C ₈ H ₁₇	Br	125-126	Ac-EA-E	Br ⁻ 20.52	Br ⁻ 20.85	
72	CH ₂ C≡CH	<i>n</i> -C ₁₀ H ₂₁	Br	125-127	Ac-EA	Br ⁻ 19.15	Br ⁻ 19.10	
73	CH ₂ C≡CH	<i>n</i> -C ₁₁ H ₂₃	Br	140.5-142.5	Ac-EA	Br ⁻ 18.53	Br ⁻ 18.36	
74	CH ₂ C≡CH	<i>n</i> -C ₁₂ H ₂₅	I	87-91	EA-B-E	I ⁻ 25.78	I ⁻ 25.23	
75	CH ₂ C≡CH	CH ₂ CH=CH ₂	Br	166-167	A-Ac-E	Br ⁻ 25.20	Br ⁻ 24.80	
76	CH ₂ C≡CH	CH ₂ C≡CH	Br	193.3-194.3	A-B	0.635% ^f	0.641% ^f	
77	CH ₂ C≡CH	CH ₂ C≡C-C ₄ H ₉	Br	119-121	Ac-EA-E	Br ⁻ 21.57	Br ⁻ 21.58	
78	CH ₂ C≡CH	C ₆ H ₅	Br	174.5-175.5	AW-Ac-E	Br ⁻ 22.62	Br ⁻ 22.77	
79	CH ₂ C≡CH	CH ₂ C ₆ H ₅	Cl	165-165.5	A-EA-E	63.39	7.12	63.31 7.05
80	CH ₂ CH ₂ C≡CH	<i>n</i> -C ₈ H ₁₇	Tos ^d	178-181	Ac-EA	N ^g 5.65	N ^g 5.38	
81	CH ₂ CH ₂ C≡CH	<i>n</i> -C ₁₀ H ₂₁	Tos ^d	193.5-195.5	Ac-EA	64.33	9.05	64.09 9.19
82	CH ₂ C ₆ H ₅	$\begin{array}{c} \text{CH}_2-\text{C}=\text{C} \\ \parallel \quad \parallel \\ \text{C}-\text{S}-\text{C} \\ \parallel \\ \text{O} \end{array}$	Br	163.5-166.5	A-B-E	Br ⁻ 18.79	Br ⁻ 18.71	
83	CH ₂ CH ₂ C ₆ H ₅	<i>n</i> -C ₁₂ H ₂₅	I	111-114	EA-E	I ⁻ 22.71	I ⁻ 22.22	
84	CH ₂ CH ₂ C ₆ H ₅	CH ₂ C ₆ H ₅	Cl	181.5-183	A-EA-E	Cl ⁻ 9.12	Cl ⁻ 9.13	
85	OCH ₃	<i>n</i> -C ₁₂ H ₂₅	I	142-143.5	Ac-E	I ⁻ 26.20	I ⁻ 26.30	
86	CH ₂ CH ₂ OH	<i>n</i> -C ₁₆ H ₃₃	Br	100-101	Ac	Br ⁻ 15.76	Br ⁻ 15.70	
F: Compounds of type $H_2NCON \begin{array}{c} \boxed{+} \\ \text{NRR}' \end{array} X^-$								
87	CH ₃	CH ₃	I	232.5-233.5	W-A-Ac	I ⁻ 44.50	I ⁻ 44.31	
88	CH ₃	CH ₃	Cl	247-247.5	M-Ac	Cl ⁻ 18.31	Cl ⁻ 18.55	
89	CH ₃	CH ₂ C ₆ H ₅	Cl	203 ^b	A-Ac	57.91	7.48	58.15 7.82
G: Compounds of type $(CH_3)_2NC \begin{array}{c} \parallel \\ \text{O} \\ \boxed{+} \\ \text{NRR}' \end{array} X^-$								
90	CH ₃	CH ₃	I	213-214	A-Ac-E	I ⁻ 40.51	I ⁻ 40.42	
91	CH ₃	<i>n</i> -C ₄ H ₉	I	136-137	A-Ac-E	40.57	7.38	40.51 7.26
92	CH ₃	<i>n</i> -C ₁₂ H ₂₅	Br	187-190	D	Br ⁻ 19.02	Br ⁻ 19.07	
93	CH ₃	CH ₂ C ₆ H ₅	Cl	175	A-Ac	Cl ⁻ 11.91	Cl ⁻ 11.59	
H: Compounds of type $(C_2H_5)_2NC \begin{array}{c} \parallel \\ \text{O} \\ \boxed{+} \\ \text{NRR}' \end{array} X^-$								
94	CH ₃	<i>n</i> -C ₁₀ H ₂₁	Br	158-163	Ac-E	Br ⁻ 19.00	Br ⁻ 18.97	
95	CH ₃	<i>n</i> -C ₁₂ H ₂₅	Br	167-169	Ac-EA	Br ⁻ 17.81	Br ⁻ 17.71	
96	CH ₃	<i>n</i> -C ₁₄ H ₂₉	Br	169-174	Ac-EA	Br ⁻ 16.78	Br ⁻ 17.39	
I: Compounds of type $ONN \begin{array}{c} \boxed{+} \\ \text{NRR}' \end{array} X^-$								
97	CH ₃	CH ₃	I	219-223	N-E	I ⁻ 46.78	I ⁻ 45.95	
98	CH ₃	CH ₃	Cl	257	M-Ac	Cl ⁻ 19.72	Cl ⁻ 19.96	
99	CH ₃	<i>n</i> -C ₁₂ H ₂₅	I	182.5-183	A-EA	48.07	8.52	47.97 8.40
100	CH ₃	CH ₂ C ₆ H ₅	Cl	197	A-EA-E	56.40	7.09	56.30 7.20
						Cl ⁻ 13.86	Cl ⁻ 14.11	

^a Recrystallization solvents were: A = absolute ethanol; AW = 95% ethanol; Ac = acetone; B = benzene; D = dioxane (purified); E = absolute ether; EA = ethyl acetate; Ip = isopropyl alcohol; M = methanol; MA = methyl acetate; N = nitromethane; TB = *t*-butyl alcohol; TBW = 2% water in TB; W = water. ^b Prepared by hydrolysis of the 1-carbomethoxy esters, lines 57 and 58. ^c Hydrate had m.p. 116°. ^d Tos = *p*-toluenesulfonate. ^e Assumed, but not proved to have been produced without allylic rearrangement. ^f Acetylenic H by method given in S. Siggia, "Quantitative Organic Analysis via Functional Groups," John Wiley and Sons, Inc., New York, N. Y., 1949, p. 55. The compound puffs on attempted microanalysis by standard methods for C and H. ^g Kjeldahl nitrogen, performed by Mrs. R. Purdey. ^h M.p. 215° on rapid heating.

(6) E. Lorz and R. Baltzly, *THIS JOURNAL*, **73**, 93 (1951).