# New Compounds

## Derivatives of 2-Hydroxy-*p*-phenetidine. I. Azomethines[1]

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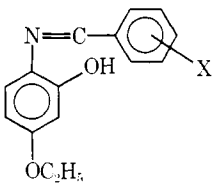
We have reported[2] an improved synthesis of 2-hydroxy-*p*-phenetidine. The *N*-acetyl derivative of this compound has recently been identified[3] as a toxic metabolite of *p*-acetophenetide (phenacetin) in the urine of cats, dogs, and humans. Since the azomethine linkage is not unknown, and even plays a role, in certain physiological reactions,[4] it occurred to us to prepare a series of compounds condensing this biologically interesting amine with various aryl aldehydes seeking compounds of possible therapeutic value. Twenty new compounds were made and are presented in Table I. Their ir spectra had a band at 1626–1618 $cm^{-1}$ (C=N stretching).[5]

TABLE I
AZOMETHINE DERIVATIVES OF 2-HYDROXY-*p*-PHENETIDINE




| Compound no. | X | Mp, °C | Yield,[a] % | Formula[b] |
|---|---|---|---|---|
| 1 | H[c] | 109–110 | 90 | $C_{15}H_{15}NO_2$ |
| 2 | 2-OH[c] | 151–152 | 90 | $C_{15}H_{15}NO_3$ |
| 3 | 3-OH[d] | 137–138 | 46 | $C_{15}H_{15}NO_3$ |
| 4 | 4-OH[c] | 108–109 | 60 | $C_{15}H_{15}NO_3$ |
| 5 | 3-$OCH_3$-4-OH[e] | 136–137 | 95 | $C_{16}H_{17}NO_4$ |
| 6 | 3,4-$CH_2O_2$[f] | 131–132 | 61 | $C_{16}H_{15}NO_4$ |
| 7 | 3,4-$(OCH_3)_2$[c] | 114–115 | 84 | $C_{17}H_{19}NO_4$ |
| 8 | 3,4,5-$(OCH_3)_3$[f] | 118–119 | 69 | $C_{18}H_{21}NO_5$ |
| 9 | 4-$NHCOCH_3$[c] | 190–191 | 81 | $C_{17}H_{18}N_2O_3$ |
| 10 | 4-$N(CH_3)_2$[e] | 167–168 | 77 | $C_{17}H_{20}N_2O_2$ |
| 11 | 2-$NO_2$[c] | 104–105 | 49 | $C_{15}H_{14}N_2O_4$ |
| 12 | 3-$NO_2$[c] | 119–120 | 61 | $C_{15}H_{14}N_2O_4$ |
| 13 | 4-$NO_2$[f] | 147–148 | 70 | $C_{15}H_{14}N_2O_4$ |
| 14 | 2-Cl[e] | 85–86 | 53 | $C_{15}H_{14}ClNO_2$ |
| 15 | 3-Cl[f] | 97–98 | 68 | $C_{15}H_{14}ClNO_2$ |
| 16 | 4-Cl[c] | 125–126 | 65 | $C_{15}H_{14}ClNO_2$ |
| 17 | 2,6-$Cl_2$[f] | 111–112 | 63 | $C_{15}H_{13}Cl_2NO_2$ |
| 18 | 3,4-$Cl_2$[c] | 117–118 | 63 | $C_{15}H_{13}Cl_2NO_2$ |
| 19 | 3,5-$Cl_2$[g] | 104–105 | 83 | $C_{15}H_{13}Cl_2NO_2$ |
| 20 | H[c] [cinnamylidene] | 115–116 | 57 | $C_{17}H_{17}NO_2$ |

[a] Yield after one recrystallization (EtOH). [b] All of the compounds had correct analyses for C, H, and N (within 0.4% of the theoretical) except compound 13: Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.79. Found: C, 62.70; H, 5.40; N, 9.85. All analyses were done by Dr. A. Bernhardt, Elbach über Engelskirchen, Germany. Aldehy deobtained from [c] The Matheson Co., Inc. [d] J. T. Baker Chemical Co. [e] Eastman Kodak Co. [f] Aldrich Chemical Co. [g] Synthesized in this laboratory by the method of H. S. Sharadamma, S. H. Kulkarni, P. B. Sattur, and K. S. Nargund, *J. Karnatak Univ.*, **1**, 61 (1956).

In addition to these azomethines, the parent amine and its *N*-acetyl derivative were tested in $BDF_1$ mice (with L1210 lymphoid leukemia) for antitumor activity by the Cancer Chemotherapy National Service Center, NCI. All of the compounds were inactive. It is of interest that whereas both 2-hydroxy-*p*-phenetidine and 2-hydroxy-*p*-acetophenetide were toxic at a dosage of 150 mg/kg (5/6 deaths with the amine, and 6/6 with the *N*-acetyl derivative), only one of the 20 azomethines caused a death at 400 mg/kg, the highest dose tested (**2**, Table I, 1 death of 6 mice tested).

### Experimental Section[6]

The condensations between the amine and the various aldehydes were performed as described in the following procedure for ***N*-benzylidene-2-hydroxy-*p*-phenetidine**. To a hot (60°) solution of 7.6 g (0.05 mol) of 2-hydroxy-*p*-phenetidine in 50 ml of EtOH, 5.3 g (0.05 mol) of PhCHO was added slowly and the mixture was boiled for 10 min. Upon cooling to room temperature, a creamy white precipitate came out giving 15.5 g (95%), mp 109–110°. One recrystallization from EtOH gave an analytical sample with the same melting point.

**Acknowledgment.**—We wish to thank Alice C. Lee for obtaining the ir spectra.

(5) K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day Inc., San Francisco, Calif., 1962, p 222; The usual range given for C=N is 1690–1640 $cm^{-1}$, but this is shifted by the effects of conjugation. The spectra were run on a Beckman IR-5 instrument (KBr disks).

(6) Melting points were determined on a Fisher-Johns block and are corrected to standards.

## 2,3-Dihydro-4(1H)-quinazolinone Derivatives

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As a part of a search for 2,3-dihydro-4(1H)-quinazolinone compounds with possible pharmacological activity,[1] some potential antipyretic, hypotensive, and CNS depressant 3-aminoalkyl-2,3-dihydro- and 3-amino-2,3-dihydro-4(1H)-quinazolinone derivatives were prepared; moreover, a series of 3-hydroxy-2,3-dihydro-4(1H)-quinazolinone derivatives was synthesized as possible antibacterial[2] and antifungal agents on the basis of the known activity of some benzohydroxamic and cyclic hydroxamic acids (Table I).

(1) Supported in part by Grant No. CA-01744 from the National Cancer Institute and by Career Development Award 5-K03-CA-14,991 (T.L.F.).

(2) M. J. Namkung and T. L. Fletcher, *J. Med. Chem.*, **12**, 348 (1969).

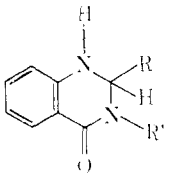
(3) A. Klutch, M. Harfenist, and A. H. Conney, *ibid.*, **9**, 63 (1966).

(4) D. E. Metzler, M. Ikawa, and E. E. Snell, *J. Amer. Chem. Soc.*, **76**, 648 (1954).

(1) G. Bonola, P. Da Re, M. J. Magistretti, E. Massarani, and I. Setnikar, *J. Med. Chem.*, **11**, 1136 (1968).

(2) Bacteriostatic 3-hydroxy-2,3-dihydro-4(1H)-quinazolinones have been quite recently reported by Farbwerke Hoechst A.-G., Netherland Appl. 6,609,924 (1967); *Chem. Abstr.*, **68**, 59609 (1968).

TABLE I



| No. | R | R' | Recrystn solvent[a] | Mp, °C | Yield, % | Formula | Analyses |
|---|---|---|---|---|---|---|---|
| 1 | H | $CH_2N$ | A | 144–145 | 60 | $C_{14}H_{19}N_3O_2$ | C, H, N |
| | | | B | 195–198[b] | | $C_{14}H_{19}N_3O_2 \cdot HCl$ | N, Cl |
| 2 | $C_6H_5$ | $CH_2N$ | A | 163–164 | 71 | $C_{20}H_{23}N_3O_2$ | C, H, N |
| | | | | 85[c] | | $C_{20}H_{23}N_3O_2 \cdot C_6H_3O_7N_3$[d] | N |
| 3 | 2-$HOC_6H_4$ | $CH_2N$ | B | 183–185 | 62 | $C_{20}H_{23}N_3O_2$ | C, H, N |
| | | | | 100–110[b] | | $C_{20}H_{23}N_3O_2 \cdot C_6H_3O_7N_3$[d] | C, H, N |
| 4 | 4-$HOC_6H_4$ | $CH_2N$ | C | 182–183 | 42 | $C_{20}H_{23}N_3O_3$ | C, H, N |
| 5 | 4-$ClC_6H_4$ | $CH_2N$ | C | 163–165 | 61 | $C_{20}H_{22}ClN_3O_2$ | C, H, Cl, N |
| 6 | H | $CH_2N$ | A | 137–138 | 65 | $C_{15}H_{21}N_3O$ | C, H, N |
| | | | B | 185–187[b] | | $C_{15}H_{21}N_3O \cdot HCl$ | N, Cl |
| 7 | $C_6H_5$ | $CH_2N$ | D | 100–112 | 84 | $C_{21}H_{25}N_3O$ | C, H, N |
| 8 | 2-$HOC_6H_4$ | $CH_2N$ | D | 153–155 | 54 | $C_{21}H_{25}N_3O_2$ | C, H, N |
| 9 | 4-$HOC_6H_4$ | $CH_2N$ | E | 180–182 | 37 | $C_{21}H_{25}N_3O_2$ | C, H, N |
| 10 | 4-$ClC_6H_4$ | $CH_2N$ | A | 157–158 | 34 | $C_{21}H_{24}ClN_3O$ | C, H, Cl, N |
| 11 | H | $(CH_2)_2N(C_2H_5)_2$ | F | 60–62 | 65 | $C_{14}H_{21}N_3O$ | C, H, N |
| | | | B | 159–162[b] | | $C_{14}H_{21}N_3O \cdot HCl$ | N, Cl |
| 12 | $C_6H_5$ | $(CH_2)_2N(C_2H_5)_2$ | B | 112–114 | 48 | $C_{20}H_{25}N_3O$ | C, H, N |
| 13 | 2-$HOC_6H_4$ | $(CH_2)_2N(C_2H_5)_2$ | D | 139[c] | 39 | $C_{20}H_{25}N_3O_2$ | C, H, N |
| 14 | 4-$HOC_6H_4$ | $(CH_2)_2N(C_2H_5)_2$ | B | 159–161 | 72 | $C_{20}H_{25}N_3O_2$ | C, H, N |
| 15 | 4-$ClC_6H_4$ | $(CH_2)_2N(C_2H_5)_2$ | F | 117–118 | 65 | $C_{20}H_{24}ClN_3O$ | C, H, Cl, N |
| 16 | H | $CH_2N$ | A | 131–132 | 53 | $C_{13}H_{19}N_3O$ | C, H, N |
| 17 | $C_6H_5$ | $CH_2N$ | C | 189–190 | 65 | $C_{20}H_{23}N_3O$ | C, H, N |
| 18 | 2-$HOC_6H_4$ | $CH_2N$ | D | 177–178 | 74 | $C_{20}H_{23}N_3O_2$ | C, H, N |
| 19 | 4-$HOC_6H_4$ | $CH_2N$ | E | 176–178 | 71 | $C_{20}H_{23}N_3O_2$ | C, H, N |
| 20 | 4-$ClC_6H_4$ | $CH_2N$ | C | 177–178 | 79 | $C_{20}H_{22}ClN_3O$ | C, H, Cl, N |
| 21 | H | $(CH_2)_2N(CH_3)_2$ | F | 104–105 | 82 | $C_{12}H_{17}N_3O$ | C, H, N |
| 22 | $C_6H_5$ | $(CH_2)_2N(CH_3)_2$ | B | 161–163 | 69 | $C_{18}H_{21}N_3O$ | C, H, N |
| 23 | 4-$HOC_6H_4$ | $(CH_2)_2N(CH_3)_2$ | C | 194–196 | 64 | $C_{18}H_{21}N_3O_2$ | C, H, N |
| 24 | $C_6H_5$ | $(CH_2)_2N(CH_3)_2$ | A | 142–143 | 67 | $C_{19}H_{23}N_3O$ | C, H, N |
| 25 | $C_6H_5$ | $N(CH_3)_2$ | A | 170–171 | 72 | $C_{16}H_{17}N_3O$ | C, H, N |
| 26 | 2-$HOC_6H_4$ | $N(CH_3)_2$ | C | 197–199 | 56 | $C_{16}H_{17}N_3O_2$ | C, H, N |
| 27 | 4-$HOC_6H_4$ | $N(CH_3)_2$ | C | 188–190 | 60 | $C_{16}H_{17}N_3O_2$ | C, H, N |
| 28 | 4-$ClC_6H_4$ | $N(CH_3)_2$ | A | 153–155 | 50 | $C_{16}H_{16}ClN_3O$ | C, H, Cl, N |
| 29 | 2-$HOC_6H_4$ | $NHC_6H_5$ | E | 193–195 | 79 | $C_{20}H_{17}N_3O_2$ | C, H, N |
| 30 | 4-$HOC_6H_4$ | $NHC_6H_5$ | H | 206–208 | 45 | $C_{20}H_{17}N_3O_2$ | C, H, N |
| 31 | 4-$ClC_6H_4$ | $NHC_6H_5$ | C | 208–210 | 71 | $C_{20}H_{16}ClN_3O$ | C, H, Cl, N |
| 32 | H | OH | B | 141–144 | 65 | $C_9H_9N_3O_2$ | C, H, N |
| 33 | $C_6H_5$ | $OCH_2CH_2N(CH_3)_2$ | H | 123–128 dec[e] | 35 | $C_{19}H_{21}N_3O_2$ | C, H, N |
| 34 | $C_6H_5$ | $OCH_2CH_2N$ | B | 144–147 | 30 | $C_{24}H_{24}N_3O_2$ | C, H, N |
| 35 | $C_6H_5$ | $OCH_2CH_2N$ | H | 139–143 dec[e] | 67 | $C_{21}H_{25}N_3O_2$ | C, H, N |
| 36 | $C_6H_5$ | $OCH_2C_6H_5$ | I | 170–173 | 81 | $C_{20}H_{18}N_2O_2$ | C, H, N |
| 37 | $C_6H_5$ | $OCH_2CH{=}CH_2$ | C | 142–144 | 77 | $C_{17}H_{16}N_2O_2$ | C, H, N |
| 38 | $C_6H_5$ | $OCH_2C{\equiv}CH$ | C | 178–180 | 71 | $C_{17}H_{14}N_2O_2$ | C, H, N |
| 39 | $C_6H_5$ | $OCOC_6H_5$ | C | 193–195 | 64 | $C_{21}H_{16}N_2O_3$ | C, H, N |
| 40 | $C_6H_5$ | $OCH_2COOCH_3$ | I | 140–143 | 68 | $C_{17}H_{16}N_2O_4$ | C, H, N |
| 41 | $C_6H_5$ | $OCH_2COOC_2H_5$ | C | 142–144 | 73 | $C_{18}H_{18}N_2O_4$ | C, H, N |
| 42 | $C_6H_5$ | $OCH_2COOH$ | A | 158–160 dec[e] | 20 | $C_{16}H_{14}N_2O_4$ | C, H, N |
| 43 | 2-$CH_3OC_6H_4$ | OH | C | 162–165 | 72 | $C_{15}H_{14}N_2O_3$ | C, H, N |
| 44 | 2-$CH_3OC_6H_4$ | $OCH_2COOC_2H_5$ | C | 150–153 | 73 | $C_{19}H_{20}N_2O_5$ | C, H, N |
| 45 | 4-$CH_3OC_6H_4$ | OH | B | 194–197 | 58 | $C_{15}H_{14}N_2O_3$ | C, H, N |
| 46 | 4-$CH_3OC_6H_4$ | $OCH_2CH_2N(CH_3)_2$ | A | 144–146 | 30 | $C_{20}H_{24}N_3O_2$ | C, H, N |
| 47 | 4-$CH_3OC_6H_4$ | $OCH_2CH_2N$ | C | 175–177 | 35 | $C_{21}H_{25}N_3O_4$ | C, H, N |

TABLE I (*Continued*)

| No. | R | R′ | Recrystn solvent[a] | Mp, °C | Yield, % | Formula | Analyses |
|---|---|---|---|---|---|---|---|
| 48 | 4-$CH_3OC_6H_4$ | $OCH_2CH_2N$⟨⟩ | C | 180–182 | 50 | $C_{22}H_{27}N_3O_3$ | C, H, N |
| 49 | 4-$CH_3OC_6H_4$ | $OCH_2COOC_2H_5$ | C | 128–130 | 67 | $C_{19}H_{20}N_2O_5$ | C, H, N |
| 50 | 2,3-$(CH_3O)_2C_6H_3$ | OH | C | 201–204 | 85 | $C_{16}H_{16}N_2O_4$ | C, H, N |
| 51 | 2,3-$(CH_3O)_2C_6H_3$ | $OCH_2CH_2N(CH_3)_2$ | J | 122–124 | 30 | $C_{20}H_{25}N_3O_4$ | C, H, N |
| 52 | 2,3-$(CH_3O)_2C_6H_3$ | $OCH_2CH_2N$⟨⟩O | H | 140–142 | 52 | $C_{22}H_{27}N_3O_5$ | C, H, N |
| 53 | 2,3-$(CH_3O)_2C_6H_3$ | $OCH_2CH_2N$⟨⟩ | H | 143–145 | 40 | $C_{23}H_{29}N_3O_4$ | C, H, N |
| 54 | 2,3-$(CH_3O)_2C_6H_3$ | $OCH_2COOC_2H_5$ | C | 126–128 | 66 | $C_{20}H_{22}N_2O_6$ | C, H, N |
| 55 | 3,4-$(CH_3O)_2C_6H_3$ | OH | C | 191–193 dec | 75 | $C_{16}H_{16}N_2O_4$ | C, H, N |
| 56 | 3,4-$(CH_3O)_2C_6H_3$ | $OCH_2CH_2N(CH_3)_2$ | C | 171–173 | 55 | $C_{20}H_{25}N_3O_4$ | C, H, N |
| 57 | 3,4-$(CH_3O)_2C_6H_3$ | $OCH_2CH_2N$⟨⟩O | C | 192–194 | 47 | $C_{22}H_{27}N_3O_5$ | C, H, N |
| 58 | 3,4-$(CH_3O)_2C_6H_3$ | $OCH_2CH_2N$⟨⟩ | C | 156–158 | 48 | $C_{23}H_{29}N_3O_4$ | C, H, N |
| 59 | 3,4-$(CH_3O)_2C_6H_3$ | $OCH_2COOC_2H_5$ | C | 155–157 | 75 | $C_{20}H_{22}N_2O_6$ | C, H, N |
| 60 | 2,5-$(CH_3O)_2C_6H_3$ | OH | C | 169–171 | 75 | $C_{16}H_{16}N_2O_4$ | C, H, N |
| 61 | 2,5-$(CH_3O)_2C_6H_3$ | $OCH_2CH_2N$⟨⟩ | H | 118–121 | 60 | $C_{23}H_{29}N_3O_4$ | C, H, N |
| 62 | 2,5-$(CH_3O)_2C_6H_3$ | $OCH_2COOC_2H_5$ | C | 155–157 | 65 | $C_{20}H_{22}N_2O_6$ | C, H, N |
| 63 | 2-$O_2NC_6H_4$ | OH | K | 208–211 dec | 84 | $C_{14}H_{11}N_3O_4$ | C, H, N |
| 64 | 3-$O_2NC_6H_4$ | OH | C | 192–194 | 85 | $C_{14}H_{11}N_3O_4$ | C, H, N |
| 65 | 4-$O_2NC_6H_4$ | OH | A | 122–123 dec | 73 | $C_{14}H_{11}N_3O_4$ | C, H, N |
| 66 | 4-$O_2NC_6H_4$ | $OCH_2CH_2N$⟨⟩O | B | 151–153 | 55 | $C_{20}H_{22}N_4O_5$ | C, H, N |
| 67 | 4-$O_2NC_6H_4$ | $OCH_2COOC_2H_5$ | C | 133–135 | 51 | $C_{18}H_{17}N_3O_6$ | C, H, N |
| 68 | 2-$ClC_6H_4$ | OH | C | 170–172 | 80 | $C_{14}H_{11}ClN_2O_2$ | C, H, N, Cl |
| 69 | 2-$ClC_6H_4$ | $OCH_2CH_2N$⟨⟩O | C | 190–192 | 60 | $C_{20}H_{22}ClN_3O_3$ | C, H, N, Cl |
| 70 | 2-$ClC_6H_4$ | $OCH_2COOC_2H_5$ | C | 157–159 | 90 | $C_{18}H_{17}ClN_2O_4$ | C, H, N, Cl |
| 71 | 2-Furyl | OH | D | 163–166 | 30 | $C_{12}H_{10}N_2O_3$ | C, H, N |
| 72 | 2-Furyl | $OCH_2CH_2N$⟨⟩·HCl | H | 197–201[b] | 50 | $C_{19}H_{23}N_3O_3\cdot HCl$ | C, H, N, Cl |
| 73 | 2-Furyl | $OCH_2COOC_2H_5$ | C | 128–129 | 72 | $C_{16}H_{16}N_2O_5$ | C, H, N |
| 74[f] | $C_6H_5$ | OH | B | 173–175 | 50 | $C_{15}H_{14}N_2O_2$ | C, H, N |
| 75[f] | $C_6H_5$ | $OCH_2CH_2N$⟨⟩O | J | 116–118 | 45 | $C_{21}H_{25}N_3O_3$ | C, H, N |
| 76[f] | $C_6H_5$ | $OCH_2CH_2N(CH_3)_2\cdot HCl$ | H | 181–184[b] | 60 | $C_{19}H_{23}N_3O_2\cdot HCl$ | C, H, N, Cl |
| 77[f] | $C_6H_5$ | $OCH_2COOC_2H_5$ | F | 108–110 | 50 | $C_{19}H_{20}N_2O_4$ | C, H, N |
| 78[g] | | OH | A | 193–195 | 10 | $C_{13}H_{16}N_2O_2$ | C, H, N |
| 79[h] | | $OCH_2CH_2N$⟨⟩O | A | 143–144 | 50 | $C_{16}H_{23}N_3O_3$ | C, H, N |
| 80[h] | | $OCH_2CH_2N$⟨⟩ | H | 130–135 dec[b] | 70 | $C_{17}H_{25}N_3O_2$ | C, H, N |
| 81[h] | | $OCH_2C_6H_5$ | F | 132–133 | 75 | $C_{17}H_{18}N_2O_2$ | C, H, N |

[a] A = $C_6H_6$, B = *i*-PrOH, C = 95% EtOH, D = AcOEt, E = $Me_2CO$, F = $C_6H_6$–ligroin, G = *i*-PrOH–$H_2O$, H = MeCN, I = MeOH, J = $C_6H_6$–cyclohexane, K = AcOH. [b] In sealed capillary tube. [c] Unsharp. [d] $C_6H_5O_7$ = citric acid. [e] On a Kofler bench. [f] 1-$CH_3$. [g] 2,2-Pentamethylene. [h] 2,2-$(CH_3)_2$.

## Experimental Section[3]

**N-(2-Piperidinoethyl)-2-aminobenzamide.**—To a solution of 12.8 g (0.1 mol) of *N*-(2-aminoethyl)piperidine in 400 ml of $H_2O$ was added 16.3 g (0.1 mol) of isatoic anhydride and the mixture was stirred for 0.5 hr at room temperature and for 0.5 hr at 45°. After standing overnight a saturated solution of $Na_2CO_3$ was added to ensure a complete separation of the product, which was collected, dissolved in dilute HCl, and precipitated from the filtered solution with excess $Na_2CO_3$: yield 20 g (81%), mp 130–132°. An analytical sample (from $C_6H_6$) melted at 130–132°. *Anal.* ($C_{14}H_{21}N_3O$) C, H, N. The dihydrochloride salt decomposes at about 200° (from 99% EtOH). *Anal.* ($C_{14}H_{21}N_3O\cdot 2HCl$) N, Cl.

**N-(2-Pyrrolidinoethyl)-2-aminobenzamide.**—To a solution of 11.4 g (0.1 mol) of 2-pyrrolidinoethylamine in 100 ml of 99% EtOH was added 16.3 g (0.1 mol) of isatoica nhydride and the mixture was refluxed for 1 hr. The residue obtained by evaporating the solvent was taken up in dilute HCl. The acid solution was made alkaline with excess $Na_2CO_3$ and the product which separated was collected and recrystallized from ligroin to yield 11.6 g (50%) of pure product, mp 100–101°. *Anal.* ($C_{13}H_{19}N_3O$) C, H, N.

**2-Methylaminobenzohydroxamic acid** was prepared as described[4] for 2-aminobenzohydroxamic acid, substituting methyl *N*-methylanthranilate for methyl anthranilate. After concentrating the reaction mixture, the sodium salt was collected and dissolved in $H_2O$. The filtered solution was made acid with AcOH and a cream-colored solid in 72% yield was obtained, mp 120–124°. An analytical sample ($C_6H_6$) melted at 122–124°. *Anal.* ($C_8H_{10}N_2O_2$) C, H, N.

**3-Aminoalkyl-2,3-dihydro-, 3-Amino-2,3-dihydro-, and 3-Hydroxy-2,3-dihydro-4(1H)-quinazolinone Derivatives.**

(3) Melting points are uncorrected and were determined on a Kofler micro hot stage unless otherwise specified. The uv absorptions of all the 2,3-dihydro-4(1H)-quinazolinone compounds were consistent with the given structures, *i.e.*, maxima around 220 and 345 nm (log ε *ca.* 4.5 and 3.4), respectively (*cf.* G. Bonola and E. Sianesi, *Ber.*, in press.). When analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values.

(4) A. W. Scott and B. L. Wood, *J. Org. Chem.*, **7**, 515 (1942).

**General Procedures.**—The products were prepared by condensing equimolar amounts of the appropriate 2-aminobenzamide or 2-aminobenzohydroxamic acid and of the aldehyde or ketone in absolute EtOH at room (**43**, **65**, **68**) or at boiling (**63**, **64**) temperature, in boiling aqueous EtOH in the presence of NaOH (**1**, **6**, **11**, **16**, **21**, **32**, **43**, **45**, **50**, **55**, **60**, **71**), or in boiling absolute EtOH in the presence of piperidine (**74**), dry HCl (**78**), or NaOEt (remaining products). Work-up followed as usual.

**3-*N*,*N*-Disubstituted Aminoethoxy-2,3-dihydro-4(1H)-quinazolinones. General Procedure.**—To 1 mol of the K salt of the 3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in *i*-PrOH, 1 mol of 2-dialkylaminoethyl chloride was added. The mixture was refluxed for 3–4 hr and filtered from KCl. The products either crystallized directly or were obtained by concentration. Recrystallization from an appropriate solvent gave pure bases except **72** and **76**, for which only the hydrochloride salts fulfilled the analytical requirements.

**3-Carbalkoxymethoxy-2,3-dihydro-4(1H)-quinazolinones. General Procedure.**—To a solution of 3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in 1 equiv of alcoholic KOH 1 equiv of alkyl bromoacetate was added and the mixture was allowed to stand till the product separated; **77** was obtained on dilution with $H_2O$.

**2-Phenyl-3-carboxymethoxy-2,3-dihydro-4(1H)-quinazolinone** (**42**) was obtained by hydrolysis at room temperature of the ester **41** with 1 equiv of methanolic KOH, work-up as usual.

**2-Phenyl-3-benzoyloxy-2,3-dihydro-4(1H)-quinazolinone** (**39**) was obtained by Schotten-Baumann acylation of 2-phenyl-3-hydroxy-2,3-dihydro-4(1H)-quinazolinone.

**2-Phenyl-3-benzyloxy-2,3-dihydro-4(1H)-quinazolinone** (**36**).—To a solution of 2.4 g (0.01 mol) of 2-phenyl-3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in 10 ml of methanolic 1 *N* KOH 1.3 g (0.01 mol) of $PhCH_2Cl$ was added. The mixture was refluxed for 1 hr and the product separated on cooling. In a similar way **2,2-dimethyl-3-benzyloxy-2,3-dihydro-4(1H)-quinazolinone** (**81**) was obtained after dilution with $H_2O$ of the reaction mixture.

**2-Phenyl-3-allyloxy-2,3-dihydro-4(1H)-quinazolinone** (**37**).—To a solution of 2.8 g (0.01 mol) of the potassium salt of 2-phenyl-3-hydroxy-2,3-dihydro-4(1H)-quinazolinone in 10 ml of DMF 0.8 g (0.01 mol) of allyl bromide was added. The reaction mixture was set for 4 hr at room temperature and then poured into $H_2O$. The separated oil was extracted in $CHCl_3$, and the extract was washed ($H_2O$), dried, and evaporated to give crude **37**. Similarly, **2-phenyl-3-propargyloxy-2,3-dihydro-4(1H)-quinazolinone** (**38**) was prepared.

## Hexachlorocyclopentadiene Adducts of Unsaturated Amides

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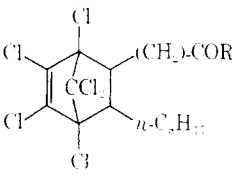
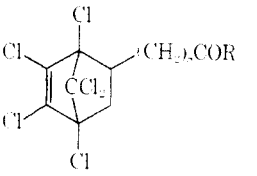
It was previously shown that monoolefinic compounds react with hexachlorocyclopentadiene to give Diels–Alder adducts, some of which have exceptional insecticidal activity.[2] Previous publications[3–5] from this laboratory have shown that many long chain amides possess antimycotic activity. In continuing these investigations a number of hexachlorocyclopentadiene adducts of unsaturated amides have been prepared and are presented in Table I.

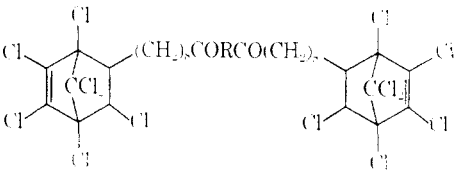
TABLE I



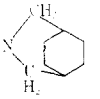
1–15



16, and 17



18

| No. | R | $n^{25}D$ | Density at 30° | Formula[a] |
|---|---|---|---|---|
| 1 | $N(CH_3)_2$ | | 1.1534 | $C_{12}H_{10}Cl_6NO$ |
| 2 |  | 1.5134 | 1.1593 | $C_{15}H_{10}Cl_6NO$ |
| 3 | $N(C_2H_5OCH_3)_2$ | 1.4943 | 1.1266 | $C_{15}H_{16}Cl_6NO_3$ |
| 4 |  | 1.5166 | 1.2132 | $C_{15}H_8Cl_6NO_2$ |
| 5 |  | 1.5118 | 1.1521 | $C_{15}H_{12}Cl_6NO$ |
| 6 |  | 1.5213 | 1.1675 | $C_{17}H_{12}Cl_6NO$ |
| 7 |  | 1.5157 | 1.1698 | $C_{15}H_{11}Cl_6N_2O$ |
| 8 | $N(C_2H_5)_2$ | 1.5031 | 1.1385 | $C_{17}H_{18}Cl_6NO$ |
| 9 | $N(C_2H_5)(CH_2)_3OC_2H_5$ | 1.4997 | 1.1337 | $C_{19}H_{22}Cl_6NO_2$ |
| 10 | $N(CH_3)$-*n*-$C_4H_9$ | 1.5043 | 1.1407 | $C_{17}H_{18}Cl_6NO$ |
| 11 | $N(CH_3)CH_2CH{=}CH_2$ | 1.5106 | 1.1618 | $C_{17}H_{16}Cl_6NO$ |
| 12 | $NHCH_2CH{=}CH_2$ | 1.5156 | 1.1922 | $C_{16}H_{12}Cl_6NO$ |
| 13 | $NHCH_2C_6H_5$ | 1.5346 | 1.2202 | $C_{20}H_{14}Cl_6NO$ |
| 14 |  | 1.5202 | 1.2213 | $C_{17}H_{12}Cl_6NO$ |
| 15 | *N*-$C_4H_8O$ | 1.5048 | 1.1443 | $C_{13}H_{13}Cl_6NO$ |
| 16 | $N(CH_2CH_2CH_2CH_3)$ | 1.5141 | 1.2455 | $C_{15}H_{23}Cl_6NO$ |
| 17 |  | 1.5322 | 1.3088 | $C_{21}H_{23}Cl_6NO$ |
| 18 |  | 1.5409 | 1.3115 | $C_{30}H_{16}Cl_{12}N_2O_2$ |

[a] All compounds were analyzed for N, and the analytical values were within ±0.4% of the calculated values.

### Experimental Section[6]

The densities were determined by pycnometer in a thermostated bath controlled to within 0.1°. Refractive indices were measured at 30.0 ± 0.1° with a precision Bausch and Lomb refractometer using the D Na line.

(1) A laboratory of the Southern Utilization Research and Development Division, ARS, USDA. Naming a company or product does not imply approval or recommendation by the Department over others which may also be suitable.

(2) E. K. Fields, *J. Amer. Chem. Soc.*, **76**, 2709 (1954).

(3) A. F. Novak, G. C. Clark and H. P. Dupuy, *J. Amer. Oil Chemists' Soc.*, **38**, 321 (1961).

(4) A. F. Novak, M. J. Fisher, S. P. Fore, and H. P. Dupuy, *ibid.*, **41**, 503 (1964).

(5) A. F. Novak, J. M. Solar, R. R. Mod, F. C. Magne, and E. L. Skau, *ibid.*, **46**, 249 (1969).

(6) Micro analyses are by Galbraith Laboratories, Knoxville, Tenn.