azepine.[17] The mixture was refluxed with stirring for 1 hr. and then cooled in ice while a solution of 27.1 g. (0.10 mole) of I in 50 ml. of dimethylformamide was added dropwise below 10°. The solution was stirred at 60–70° for 2 hr. and allowed to stand overnight at room temperature. The major portion of the solvent was removed under reduced pressure and the residue was poured into 500 ml. of cold water. The insoluble material was extracted with three 200-ml. portions of methylene chloride; the combined organic layers were dried, filtered, and evaporated. The resulting dark oil was chromatographed on Woelm neutral alumina (elution with hexane) to give 17.85 g. (60.7%) of XII as a colorless, noncrystallizable oil.

(17) W. Schindler and F. Hafliger, U. S. Patent 2,764,580 (Sept. 25, 1956).

5-(2-Aminooxyethyl)dibenzazepine Hydrochloride (XIII).—A mixture of 17.7 g. (0.060 mole) of XII, 75 ml. of 8 *N* hydrochloric acid, and 75 ml. of ethanol was refluxed for 1 hr. and steam distilled for 1 hr. The solution was concentrated under reduced pressure and the dark residue was dissolved in ethanol. The ethanolic solution was filtered through a pad of charcoal, and the almost colorless filtrate was treated with ether and cooled. The crystalline product was filtered and dried to give 11.4 g. (65.5%) of off-white solid, m.p. 184.5–187° dec. Three recrystallizations of this material from ethanol–ether afforded pure XIII as shiny, white platelets, m.p. 188–189° dec.

Anal. Calcd. for $C_{16}H_{19}ClN_2O$: C, 66.08; H, 6.59; N, 9.64. Found: C, 65.93; H, 6.60; N, 9.48.

The Reaction between β-Keto Esters and Arylamines in the Presence of Polyphosphoric Acid. II.[1] Ethyl Acetoacetate and Its α-Alkyl Derivatives and Arylamines

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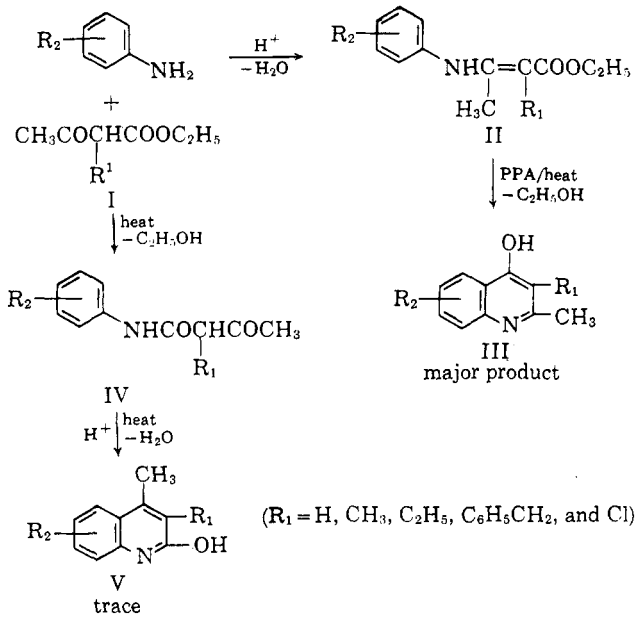
Received April 6, 1964

4-Hydroxyquinaldines have been synthesized directly from ethyl acetoacetate, or its α-alkyl derivatives and arylamines using polyphosphoric acid. The intermediate acetoacetanilides and ethyl β-arylaminocrotonates have been prepared and cyclized to hydroxyquinolines with polyphosphoric acid. The isomeric 5- and 7-substituted 4-hydroxyquinaldines derived from *meta*-substituted arylamines have been separated.

Recently the first direct synthesis of 4-hydroxy- and 2-hydroxyquinolines by the Conrad–Limpach[2] and Knorr[3] reactions, respectively, from arylamines and ethyl benzoylacetate has been effected using polyphosphoric acid (PPA).[1a]

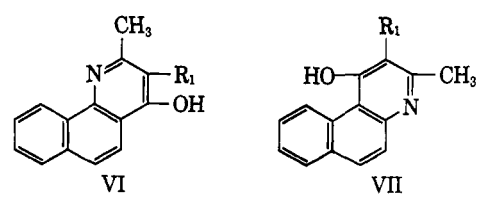
The condensation of a variety of arylamines with a number of other β-keto esters I in the presence of polyphosphoric acid has now led to the preparation of 4-hydroxyquinaldines III, the yields of which were generally higher than those obtained by the two-stage Conrad–Limpach reaction. Small amounts of the isomeric 2-hydroxylepidines V were isolated in some instances. The intermediate ethyl β-arylaminocrotonates II were not isolated. Cyclization of the crotonates with polyphosphoric acid gave higher yields of III than when heated in Dowtherm.



(R1 = H, CH_3, C_2H_5, $C_6H_5CH_2$, and Cl)

4-Nitroarylamines condensed readily with β-keto esters in the presence of polyphosphoric acid to give high yields of the 6-nitro-4-hydroxyquinaldines, the structures of which were proved by their reduction and deamination to the corresponding 4-hydroxyquinaldines. Arylamines containing a nitro group *ortho* or *meta* to the amino group, even in the presence of activating methoxy, or methyl groups in the molecule, failed to condense with β-keto esters in the presence of polyphosphoric acid.

The 1- and 2-naphthylamines reacted with β-keto esters to give the corresponding 4-hydroxy-7:8-benzoquinaldines VI and 4-hydroxy-5:6-benzoquinaldines VII, respectively.



(R1 = H, CH_3, and C_2H_5)

Mixtures of the isomeric 5- and 7-substituted 4-hydroxyquinaldines were formed when *meta*-substituted arylamines were used. The proportions of the 5- and 7-isomers were found to depend on the nature of the *meta* substituent. When the latter was a methoxy group the 7-isomer predominated, while with a methyl,

(1) (a) Part I: B. Staskun and S. S. Israelstam, *J. Org. Chem.*, **26**, 3191 (1961); (b) A. K. Mallams and S. S. Israelstam, *Chem. Ind.* (London), 952 (1963).

(2) M. Conrad and L. Limpach, *Ber.*, **20**, 944 (1887); **21**, 523, 1649 (1888); **24**, 2990 (1891).

(3) L. Knorr, *Ann.*, **236**, 69 (1886); *Ber.*, **17**, 540 (1884).

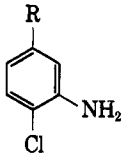
TABLE I

RATIOS OF 5- AND 7-SUBSTITUTED 4-HYDROXYQUINALDINES

meta substituent	β-Keto ester (I), R_1	Ratio of 5-isomer:7-isomer
CH_3O	H	1:1.7
CH_3O	CH_3	1:3.6
CH_3O	C_2H_5	1:2.2
CH_3	H	8.4:1
CH_3	CH_3	3.3:1
CH_3	C_2H_5	Mainly 5-isomer
Cl	H	1.4:1
Cl	CH_3	2.6:1
Cl	C_2H_5	1.4:1

or a chloro group the 5-isomer predominated (Table I).[4]

The identity of the 5-isomer was proved in each case by an unambiguous synthesis. This was achieved by blocking one of the *ortho* positions in the arylamine with a chloro group to give the arylamines VIII, which were then condensed with β-keto esters in the presence of polyphosphoric acid to give the corresponding 8-chloro-4-hydroxy-5-substituted quinaldines. Dehalogenation of the latter gave the desired 5-isomers.



VIII

(R = CH_3, CH_3O, and C_2H_5O)

The 5- and 7-chloro-4-hydroxyquinaldines and their 3-methyl homologs were identified by their melting points and by their infrared absorption spectra (Table II).

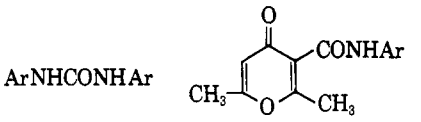
TABLE II

INFRARED ABSORPTION DATA FOR 5- AND 7-CHLORO-3-ALKYL-4-HYDROXYQUINALDINES

Isomer	Band frequency, cm.$^{-1}$ [a] 3-CH_3	3-C_2H_5	Origin of the band[b]
5-	805 (vs)	810 (vs)	Three free hydrogen atoms in the aromatic ring
7-	828 (m)	833 (m)	Two free hydrogen atoms in the aromatic ring
	865 (s)	870 (s)	One free hydrogen in the aromatic ring
	768 (vs)	778 (vs)	C—Cl absorption band for C=C—Cl

[a] vs = very strong; s = strong; m = medium. [b] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., Methuen and Co., Ltd., London, 1958; M. H. Palmer, *J. Chem. Soc.*, 3645 (1962).

The anilides[3] IV (R_1 = H; R_2 = H, 2-CH_3, 4-CH_3O, and 2,4-diCH_3) and acetoacet-1- and -2-napthalides on heating either with small amounts or with an excess of polyphosphoric acid gave traces of the corresponding arylamine, thus showing that negligible hydrolysis occurred at the amide group. The only products formed were the 2-hydroxylepidines V (R_1 = H) and it was noted that the corresponding 4-hydroxyquinaldines III (R_1 = H) were not isolated even when small amounts of polyphosphoric acid were used to effect the cyclization.[10,11] The anilides, in the presence of equimolar amounts of the corresponding arylamines, on heating with excess polyphosphoric acid gave mixtures of the 2-hydroxylepidines V (R_1 = H) and the 4-hydroxyquinaldines III (R_1 = H), while, with small amounts of polyphosphoric acid, the only products formed were the corresponding diarylureas IX.



IX X

The anilides IV (R_1 = H; R_2 = 2-CH_3O, 2-C_2H_5O, 4-C_2H_5, 4-Cl, 4-Br, 4-Cl-2-CH_3O, and 4-NO_2) on heating with small amounts of polyphosphoric acid gave the 4-hydroxyquinaldines III (R_1 = H). In each case hydrolysis occurred at the amide group of the anilide since the corresponding arylamines were isolated among the products of the reaction. When excess polyphosphoric acid was used, the 2-hydroxylepidines V (R_1 = H) were formed, and the competing amide hydrolysis became negligible except in the case of the halo- and nitro-substituted anilides IV (R_1 = H; R_2 = 4-Cl, 4-Br, 4-Cl-2-CH_3O, and 4-NO_2).[12] The anilides IV (R_1 = H; R_2 = 2-Cl, 2-Br, 2,4-di-Cl, and 2,5-di-Cl) on heating with small amounts, or with excess polyphosphoric acid, gave the 4-hydroxyquinaldines III (R_1 = H) and the 3-arylcarbamyl-2,6-dimethyl-4-pyrones X (Ar = 2-ClC_6H_4, 2-BrC_6H_4, 2,4-$Cl_2C_6H_3$, and 2,5-$Cl_2C_6H_3$).[15] Acetoacet-2-nitroanilide (IV, R_1 = H; R_2 = 2-NO_2) decomposed on heating with polyphosphoric acid to give 2-nitroaniline[12] and an intractable tar.[16]

The results show that 4-hydroxyquinaldines III (R_1 = H) are only formed from acetoacetanilides IV (R_1 = H) in the presence of polyphosphoric acid, under conditions where hydrolysis occurs at the amide group. The ease with which hydrolysis occurs was found to depend on the nature, the positions of the substituents in the acetoacetanilide, and on the amount of polyphos-

(4) It should be noted that the rates of isomers quoted refer to polyphosphoric acid cyclizations at 170°. Previous research on the Conrad–Limpach reaction has shown that the ratio of isomers is a function not only of the nature of the *meta* substituent in the arylamine, but also of the nature of the thermal solvent used to cyclize the crotonate[5-8] and the temperature at which the cyclization is effected.[9] The present work further demonstrates the dependence of the ratio of isomers on the nature of the α-substituent in the β-keto ester.

(5) C. C. Price, N. J. Leonard, and R. H. Reitsema, *J. Am. Chem. Soc.*, **68**, 1256 (1946).

(6) B. P. Bangdiwala and C. M. Desai, *J. Indian Chem. Soc.*, **30**, 655 (1953).

(7) B. P. Bangdiwala and C. M. Desai, *Current Sci.* (India), **21**, 256 (1952).

(8) E. A. Steck, L. L. Hallock, A. J. Holland, and L. Y. Fletcher, *J. Am. Chem. Soc.*, **70**, 1012 (1948).

(9) A. M. Spivey and F. H. S. Curd, *J. Chem. Soc.*, 2656 (1949).

(10) B. Staskun, *J. Org. Chem.*, **29**, 1153 (1964).

(11) Staskun[1a,10] and Israelstam[1a] reported that on heating benzoylacetanilide and polyphosphoric acid (1:1) at 140° a mixture of 2-hydroxy-4-phenylquinoline and 4-hydroxy-2-phenylquinoline was obtained. When excess polyphosphoric acid was used only the 2-hydroxy-4-phenylquinoline was formed.

(12) Nitro- and chloroacetoacetanilides have been reported[13,14] to undergo extensive hydrolysis at the amide group even in the presence of an excess of concentrated sulfuric acid.

(13) J. L. C. Marais and O. G. Backeberg, *J. Chem. Soc.*, 2207 (1950).

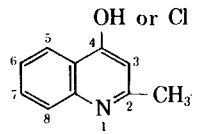
(14) J. Joubert, M.S. Dissertation, University of the Witwatersrand, 1961.

(15) Proof of the structures of the 3-arylcarbamyl-2,6-dimethyl-4-pyrones is dealt with in a subsequent paper by one of us [A. K. Mallams, *J. Org. Chem.*, **29**, 3555 (1964)].

(16) No crystalline material was obtained from the tar.

TABLE III

DIRECT SYNTHESIS OF 4-HYDROXY- AND 4-CHLOROQUINALDINES



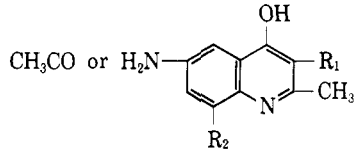
Substituents					4-Hydroxyquinaldines					4-Chloroquinaldines				
						Yield,		Nitrogen, %			Yield,		Nitrogen, %	
3	5	6	7	8	Formula	%	M.p., °C.	Calcd.	Found	Formula	%	M.p., °C.	Calcd.	Found
H	H	H	H	Br	$C_{10}H_8BrNO$[a]	82	208–210[b]			$C_{10}H_7BrClN$	94	74–75	5.46	5.40
H	H	Cl	H	Cl	$C_{10}H_7Cl_2NO$[c]	54	292–294[d]			$C_{10}H_6Cl_3N$	96	153–154	5.68	5.76
H	Cl	H	H	Cl	$C_{10}H_7Cl_2NO$	62	265–267	6.14	6.22	$C_{10}H_6Cl_3N$	95	121–122	5.68	5.70
H	H	Cl	H	CH_3O	$C_{11}H_{10}ClNO_2$[e]	60	247–250	6.26	6.31	$C_{11}H_9Cl_2NO$	99	141–142	5.79	5.84
H	H	NO_2	H	H	$C_{10}H_8N_2O_3$	76	400[f]			$C_{10}H_7ClN_2O_2$	98	146–148[g]		
H	H	NO_2	H	CH_3	$C_{11}H_{10}N_2O_3$	62	380 dec.	12.84	13.01	$C_{11}H_9ClN_2O_2$	95	177–179	11.84	11.68
H	H	NO_2	H	CH_3O	$C_{11}H_{10}N_2O_4$	61	309–312 dec.	11.97	12.07	$C_{11}H_9ClN_2O_3$	93	194–195 dec.	11.09	11.18
H	CH_3	H	H	Cl	$C_{11}H_{10}ClNO$	48	231–233.5	6.75	6.84	$C_{11}H_9Cl_2N$	100	85–86	6.19	6.36
H	CH_3O	H	H	Cl	$C_{11}H_{10}ClNO_2$	63	191–194	6.26	6.32	$C_{11}H_9Cl_2NO$	100	125–126.5	5.79	5.84
CH_3	H	H	H	CH_3	$C_{12}H_{13}NO$	94	313–317 dec.	7.49	7.56	$C_{12}H_{12}ClN$	98	51–52	6.81	6.90
CH_3	CH_3	H	H	H	$C_{12}H_{13}NO$	46[h,i] (98[j], 35[k])	337–340 dec.	7.49	7.60	$C_{12}H_{12}ClN$	100	94–96	6.81	6.93
CH_3	H	H	CH_3	H	$C_{12}H_{13}NO$	14[h,i] (98[j])	322–325	7.49	7.62	$C_{12}H_{12}ClN$	100	83–85	6.81	6.93
CH_3	H	CH_3	H	H	$C_{12}H_{13}NO$	94	340–344 dec.	7.49	7.58	$C_{12}H_{12}ClN$	95	90–91	6.81	6.84
CH_3	CH_3O	H	H	H	$C_{12}H_{13}NO_2$	16[h,l] (74[j], 20[m])	320–323 dec.	6.90	7.01	$C_{12}H_{12}ClNO$	100	149–50.5	6.32	6.48
CH_3	H	H	CH_3O	H	$C_{12}H_{13}NO_2$	57[h,l] (74[j], 33[m])	295–298[n]			$C_{12}H_{12}ClNO$	100	116.5–118	6.32	6.45
CH_3	H	H	H	C_2H_5O	$C_{13}H_{15}NO_2$	92	223–225	6.45	6.48	$C_{13}H_{14}ClNO$	97	109–110	5.94	5.97
CH_3	H	H	C_2H_5O	H	$C_{13}H_{15}NO_2$	(77[j], 33[k])	277–278	6.45	6.56	$C_{13}H_{14}ClNO$	100	95–96.5	5.94	6.09
CH_3	H	C_2H_5O	H	H	$C_{13}H_{15}NO_2$	92	279–281	6.45	6.47	$C_{13}H_{14}ClNO$	97	115–116	5.94	6.03
CH_3	H	H	H	Cl	$C_{11}H_{10}ClNO$	79	255–257	6.75	6.83	$C_{11}H_9Cl_2N$	94	87.5–88.5	6.19	6.31
CH_3	H	Cl	H	H	$C_{11}H_{10}ClNO$	82	340–344 dec.	6.75	6.84	$C_{11}H_9Cl_2N$	97	125–126	6.19	6.22
CH_3	H	H	H	Br	$C_{11}H_{10}BrNO$	98	233–235	5.56	5.64	$C_{11}H_9BrClN$	98	95–96	5.18	5.23
CH_3	H	Br	H	H	$C_{11}H_{10}BrNO$	98	339–342 dec.	5.56	5.65	$C_{11}H_9BrClN$	93	101.5–103	5.18	5.24
CH_3	H	Cl	H	Cl	$C_{11}H_9Cl_2NO$	85	302–305 dec.	5.79	5.86	$C_{11}H_8Cl_3N$	96	112–113	5.37	5.46
CH_3	Cl	H	H	Cl	$C_{11}H_9Cl_2NO$	98	238–240	5.79	5.83	$C_{11}H_8Cl_3N$	95	158–159	5.37	5.38
CH_3	H	Cl	H	CH_3O	$C_{12}H_{12}ClNO_2$	83	213–215	5.90	5.96	$C_{12}H_{11}Cl_2NO$	96	125–126	5.47	5.36
CH_3	H	NO_2	H	H	$C_{11}H_{10}N_2O_3$	76	375–380 dec.[o]			$C_{11}H_9ClN_2O_2$	96	167–169[p]		
CH_3	H	NO_2	H	CH_3	$C_{12}H_{12}N_2O_3$	67	327–330 dec.	12.07	12.20	$C_{12}H_{11}ClN_2O_2$	98	159–161	11.18	11.36
CH_3	H	NO_2	H	CH_3O	$C_{12}H_{12}N_2O_4$	58	290–293	11.29	11.18	$C_{12}H_{11}ClN_2O_3$	96	197–199	10.51	10.04
CH_3	CH_3	H	H	Cl	$C_{12}H_{12}ClNO$	82	186–188.5	6.32	6.40	$C_{12}H_{11}Cl_2N$	100	129–131	5.83	5.76
CH_3	CH_3O	H	H	Cl	$C_{12}H_{12}ClNO_2$	67	166–169	5.90	5.97	$C_{12}H_{11}Cl_2NO$	100	129.5–131	5.47	5.54

CH_3	C_2H_5O	H	H	Cl	$C_{13}H_{14}ClNO_2$	79	167–169	5.57	5.62	$C_{13}H_{13}Cl_2NO$	100	105–106	5.18	5.33
CH_3	H	H	Benzo		$C_{15}H_{13}NO$	77	354–359 dec.	6.28	6.37	$C_{15}H_{12}ClN$	85	109–110	5.80	5.91
CH_3	Benzo		H	H	$C_{15}H_{13}NO$	98	370–375 dec.[q]			$C_{15}H_{12}ClN$	85	135.5–137	5.80	5.75
C_2H_5	H	H	H	H	$C_{12}H_{13}NO$	99	286–289[r]			$C_{12}H_{12}ClN$	92	34–36	6.81	6.86
C_2H_5	H	H	H	CH_3	$C_{13}H_{15}NO$	83	284–287 dec.	6.97	6.99	$C_{13}H_{14}ClN$	94	41–42	6.38	6.46
C_2H_5	CH_3	H	H	H	$C_{13}H_{15}NO$	55[h,s–u] (95[i])	311–314	6.97	7.10	$C_{13}H_{14}ClN$	100	66.5–68	6.38	6.32
C_2H_5	H	CH_3	H	H	$C_{13}H_{15}NO$	91	329–332 dec.	6.97	7.02	$C_{13}H_{14}ClN$	96	60–61	6.38	6.49
C_2H_5	CH_3O	H	H	H	$C_{13}H_{15}NO_2$	22[h,v] (73[i])	287–290 dec.	6.45	6.57	$C_{13}H_{14}ClNO$	100	71–72.5	5.94	6.08
C_2H_5	H	H	CH_3O	H	$C_{13}H_{15}NO_2$	48[h,v] (73[i])	262–264	6.45	6.49	$C_{13}H_{14}ClNO$	100	71–73	5.94	6.07
C_2H_5	H	CH_3O	H	H	$C_{13}H_{15}NO_2$	80	287–290 dec.[w]			$C_{13}H_{14}ClNO$	97	71–72	5.94	6.01
C_2H_5	H	H	H	C_2H_5O	$C_{14}H_{17}NO_2$	79	235–238	6.06	6.19	$C_{14}H_{16}ClNO$	98	78–79	5.61	5.80
C_2H_5	H	C_2H_5O	H	H	$C_{14}H_{17}NO_2$	83	258–261	6.06	6.14	$C_{14}H_{16}ClNO$	97	85–87	5.61	5.62
C_2H_5	H	H	H	Cl	$C_{12}H_{12}ClNO$	77	245–248	6.32	6.31	$C_{12}H_{11}Cl_2N$	96	42–43	5.83	5.89
C_2H_5	Cl	H	H	H	$C_{12}H_{12}ClNO$	39[h,x] (80,[j] 32[m])	346–350 dec.	5.32	6.39	$C_{12}H_{11}Cl_2N$	100	84–85.5	5.83	5.91
C_2H_5	H	H	Cl	H	$C_{12}H_{12}ClNO$	27[h,x] (80,[j] 25[m])	334–338	6.32	6.42	$C_{12}H_{11}Cl_2N$	100	79–80.5	5.83	5.96
C_2H_5	H	Cl	H	H	$C_{12}H_{12}ClNO$	77	345–348 dec.	6.32	6.36	$C_{12}H_{11}Cl_2N$	96	77–78	5.83	5.92
C_2H_5	H	H	H	Br	$C_{12}H_{12}BrNO$	90	232–234	5.27	5.36	$C_{12}H_{11}BrClN$	95	47.5–48.5	4.92	5.00
C_2H_5	H	Br	H	H	$C_{12}H_{12}BrNO$	90	348–352 dec.	5.27	5.44	$C_{12}H_{11}BrClN$	97	71.5–73	4.92	4.98
C_2H_5	H	CH_3	H	CH_3	$C_{14}H_{17}NO$	72	276–279	6.51	6.53	$C_{14}H_{16}ClN$	96	83–84	6.00	6.03
C_2H_5	H	Cl	H	Cl	$C_{12}H_{11}Cl_2NO$	69	267–269	5.47	5.58	$C_{12}H_{10}Cl_3N$	95	73–74	5.08	5.12
C_2H_5	Cl	H	H	Cl	$C_{12}H_{11}Cl_2NO$	92	205–207	5.47	5.39	$C_{12}H_{10}Cl_3N$	94	63–64	5.08	5.16
C_2H_5	H	Cl	H	CH_3O	$C_{13}H_{14}ClNO_2$	63	218–220	5.57	5.65	$C_{13}H_{13}Cl_2NO$	93	138.5–139.5	5.19	5.30
C_2H_5	H	NO_2	H	H	$C_{12}H_{12}N_2O_3$	75	355–360 dec.	12.07	12.21	$C_{12}H_{11}ClN_2O_2$	96	133–135	11.18	11.29
C_2H_5	H	NO_2	H	CH_3	$C_{13}H_{14}N_2O_3$	65	308–311	11.39	11.30	$C_{13}H_{13}ClN_2O_2$	95	165–167	10.59	10.39
C_2H_5	H	NO_2	H	CH_3O	$C_{13}H_{14}N_2O_4$	57	265–268	10.69	10.80	$C_{13}H_{13}ClN_2O_3$	92	197–199	9.98	9.86
C_2H_5	CH_3	H	H	Cl	$C_{13}H_{14}ClNO$	62	165.5–168	5.94	6.08	$C_{13}H_{13}Cl_2N$	100	39–40	5.51	5.67
C_2H_5	CH_3O	H	H	Cl	$C_{13}H_{14}ClNO_2$	62	185–187	5.57	5.60	$C_{13}H_{13}Cl_2NO$	100	87.5–88.5	5.18	5.27
C_2H_5	H	H	Benzo		$C_{16}H_{15}NO$	74	327–329	5.91	6.02	$C_{16}H_{14}ClN$	93	75–76	5.48	5.56
C_2H_5	Benzo		H	H	$C_{16}H_{15}NO$	84	303–306[q]			$C_{16}H_{14}ClN$	89	89–91	5.48	5.61
Cl	H	H	H	Cl	$C_{10}H_7Cl_2NO$	44	293–295	6.14	6.25					
$C_6H_5CH_2$	H	H	H	H	$C_{17}H_{15}NO$	84	273–277	5.62	5.75	$C_{17}H_{14}ClN$	90	77–79	5.23	5.38

[a] Picrate, m.p. 196–198°. *Anal.* Calcd. for $C_{16}H_{11}BrN_4O_8$: N, 11.99. Found: N, 12.18. [b] S. N. Munavalli, S. N. Kulkarni, and K. S. Nargund [*J. Karnatak Univ.*, **1**, 23 (1956)] report m.p. 204–206°. [c] Picrate, m.p. 214–215°. *Anal.* Calcd. for $C_{16}H_{10}Cl_2N_4O_8$: N, 12.26. Found: N, 12.43. [d] G. K. Hughes and F. Lions [*J. Proc. Roy. Soc. N. S. Wales*, **71**, 458 (1938)] report m.p. 290°. [e] Picrate, m.p. 226–228°. *Anal.* Calcd. for $C_{17}H_{13}ClN_4O_9$: N, 12.38. Found: N, 12.56. [f] W. O. Kermack and A. P. Weatherhead [*J. Chem. Soc.*, 563 (1939) report m.p. >400°. [g] Lit.[f] m.p. 142°. [h] As calculated from the weight of the corresponding 4-chloro isomer obtained from the chromatographic separation. [i] Recovered mixture of 5- and 7-isomers = 14%. [j] Total yield of both 5- and 7-substituted 4-hydroxyquinaldines obtained in the direct synthesis. [k] Yield of isomer obtained by fractional crystallization from dilute hydrochloric acid. [l] Recovered mixture of 5- and 7-isomers = 18%. [m] Yield of isomer obtained by fractional crystallization from ethanol. [n] C. C. Price and W. G. Jackson [*J. Am. Chem. Soc.*, **68**, 1282 (1946)] report m.p. 293–295° dec. [o] Lit.[f] m.p. 380°. [p] A. Adams and D. H. Hey [*J. Chem. Soc.*, 2092 (1950)] report m.p. 171.5°. [q] R. Gillis, F. Lions, and E. Ritchie [*J. Proc. Roy. Soc. N. S. Wales*, **73**, 258 (1940)] report m.p. >300°. [r] M. Conrad and L. Limpach[2] report m.p. 290°. [s] Recovered mixture of 5- and 7-isomers = 27%. [t] A 3% yield of 2-chloro-3-ethyl-5(or 7-)-methyllepidine, m.p. 82–83° (*Anal.* Calcd. for $C_{13}H_{14}ClN$: N, 6.38. Found: N, 6.49), was obtained in the chromatographic separation. [u] No pure 7-isomer could be isolated by chromatography. [v] Recovered mixture of 5- and 7-isomers = 20%. [w] J. M. L. Stephen, J. M. Tonkin, and J. Walker [*J. Chem. Soc.*, 1034 (1947)] report m.p. 290°. [x] Recovered mixture of 5- and 7-isomers = 17%.

TABLE IV

AMINOQUINALDINES AND CORRESPONDING ACETYL DERIVATIVES

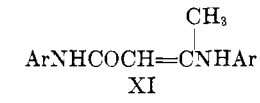


Substituent		Aminoquinaldines					Acetyl Derivatives					
R_1	R_2	Formula	Yield, %	M.p., °C.	Nitrogen % Calcd.	Nitrogen % Found	Fluorescence in ethanol	Formula	Yield, %	M.p., °C.	Nitrogen % Calcd.	Nitrogen % Found
H	H	$C_{10}H_{10}N_2O$	90	330–333 dec.[a]			Blue-red	$C_{12}H_{12}N_2O_2$	81	365 dec.[b]		
CH_3	H	$C_{11}H_{12}N_2O$	94	334–338 dec.[c]			Blue-red	$C_{13}H_{14}N_2O_2$	87	370–373 dec.[d]		
C_2H_5	H	$C_{12}H_{14}N_2O$	93	287–290	13.87	14.06	Yellow-green	$C_{14}H_{16}N_2O_2$	85	347–350 dec.	11.48	11.63
H	CH_3	$C_{11}H_{12}N_2O$	89	288–291	14.89	15.00	Blue	$C_{13}H_{14}N_2O_2$	93	310–313	12.17	12.39
CH_3	CH_3	$C_{12}H_{14}N_2O$	91	312–315 dec.	13.85	14.00	Blue-red	$C_{14}H_{16}N_2O_2$	88	352–356 dec.	11.48	11.60
C_2H_5	CH_3	$C_{13}H_{16}N_2O$	92	245–248	12.96	12.80	Blue	$C_{15}H_{18}N_2O_2$	84	332–336	10.85	10.76
H	CH_3O	$C_{11}H_{12}N_2O_2$	92	246–248	13.73	13.50	Blue	$C_{13}H_{14}N_2O_3$	92	340–344 dec.	11.39	11.48
CH_3	CH_3O	$C_{12}H_{14}N_2O_2$	90	264–267	12.84	13.00	Pale blue	$C_{14}H_{16}N_2O_3$	92	331–334	10.76	10.92
C_2H_5	CH_3O	$C_{13}H_{16}N_2O_2$	90	228–231	12.07	11.90	Blue-red	$C_{15}H_{18}N_2O_3$	88	336–339	10.22	10.07

[a] Lit. m.p. 345° (footnote *f*, Table III). [b] Lit. m.p. 365° (footnote *f*, Table III). [c] Lit. m.p. 326° (footnote *f*, Table III). [d] Lit. m.p. 385° (footnote *f*, Table III).

phoric acid used to effect cyclization.[17] Of these three factors the first two appear, on the basis of the results obtained with the acetoacetanilides, to be the most important. Thus while the anilides IV (R_1 = H; R_2 = H, 2-CH_3, 4-CH_3, 4-CH_3O, and 2,4-di-CH_3) would be expected on the basis of Staskun's postulate[10,17] to be monoprotonated in the presence of small amounts of polyphosphoric acid and therefore undergo hydrolysis to the arylamines with subsequent formation of the 4-hydroxyquinolines, no such hydrolysis occurred irrespective of whether the anilides were monoprotonated or diprotonated. Similarly the anilides IV (R_1 = H; R_2 = 2-Cl, 2-Br, 2,4-Cl_2, and 2,5-Cl_2) on heating with a considerable excess of polyphosphoric acid (1:40), where according to Staskun[10,17] diprotonation of the anilides would be expected to occur, underwent extensive hydrolysis at the amide group and consequently did not form the 2-hydroxylepidines. The nature of the substituents in the acetoacetyl portion of the anilide also has a marked effect on the ease of hydrolysis of the amide group. Thus while ω-bromoacetoacet-2-chloroanilide cyclized readily in the presence of excess polyphosphoric acid to give 4-bromomethyl-2-hydroxyquinoline, acetoacet-2-chloroanilide (IV, R_1 = H; R_2 = Cl) underwent considerable hydrolysis in the presence of the same amount of polyphosphoric acid.

In order to account for the above reactions it is suggested that the arylamines liberated by the hydrolysis of the anilides IV (R_1 = H) condense with unchanged anilides to give the anil–anilides XI[18] by an intermolecular reaction,[10] followed by their subsequent cyclization to the 4-hydroxyquinaldines under the prevailing reaction conditions.



XI

The fact that a 4-hydroxyquinaldine is formed when the anilide IV (R_1 = H; R_2 = H, 2-CH_3, 4-CH_3, 4-CH_3O, and 2,4-di-CH_3) is heated in the presence of the arylamine and polyphosphoric acid, but not in the absence of the arylamine, lends further support to the above mechanism. The formation of diarylureas IX from these anilides in the presence of the arylamine and very small amounts of polyphosphoric acid can readily be explained in terms of the mechanism proposed by Roberts and Edwards[19] for the formation of diarylureas from acetoacetanilides IV (R_1 = H), or anil–anilides XI and arylamines. The small amount of polyphosphoric acid present in the reaction mixture is insufficient to cyclize either the anilide IV (R_1 = H) or the anil–anilide XI, thus accounting for the formation of the diarylurea IX as the only product.

Experimental[20]

The Direct Synthesis of 4-Hydroxyquinaldines.—The arylamine (0.0125 mole), ethyl acetoacetate or its α-alkyl derivatives I (R_1 = H, CH_3, C_2H_5, Cl, and $C_6H_5CH_2$) (0.025 mole), and 5 g. of polyphosphoric acid were heated with stirring at 170° for 1 hr. The reaction mixture was neutralized with dilute sodium hydroxide and the precipitated 4-hydroxyquinaldine was washed with water, triturated with ether, and crystallized from ethanol, acetic acid, or dimethylformamide. Mixture melting points with the corresponding 4-hydroxyquinaldines obtained by cyclization of the ethyl β-arylaminocrotonates II[21] with polyphosphoric acid showed no depression.

(17) Staskun[10] has postulated that benzoylacetanilides in polyphosphoric acid (1:1) are monoprotonated at the amide group and hence hydrolyze to arylamines, whereas in excess polyphosphoric acid diprotonation occurs rendering the anilides less susceptible to hydrolysis with the result that cyclization occurs to give 2-hydroxy-4-phenylquinolines.

(18) Although the anil–anilides XI were not isolated from the actual reaction mixtures (*cf.*, Staskun[10] also failed to isolate the anil–anilides in the case of the benzoylacetanilides), the anil–anilides XI (Ar = 1-naphthyl and 2-naphthyl) were prepared[3] and cyclized to the quinaldines VI (R_1 = H) and VII (R_1 = H), respectively, by heating with polyphosphoric acid.

(19) R. M. Roberts and M. B. Edwards, *J. Am. Chem. Soc.*, **72**, 5537 (1950).

(20) Melting points were determined on a Kofler block and are uncorrected. Infrared spectra were measured on a Perkin-Elmer Infracord Model 137 spectrophotometer in the solid state using a potassium bromide disk.

(21) S. Coffey, J. K. Thomson, and F. J. Wilson, *J. Chem. Soc.*, 856 (1936).

TABLE V

CYCLIZATION OF ACETOACETANILIDES ($ArNHCOCH_2COCH_3$) WITH POLYPHOSPHORIC ACID

Ar	Anilide:PPA, w./w. ratio	Method	Yield of 2-hydroxy-quinoline, %	Yield of 4-hydroxy-quinaldine, %[a]	Other products yield, %
C_6H_5[b]	3:1	A	Nil	Nil	Intractable gum
		B	Nil	Nil	Diarylurea IX (20)
	1:1	A	11	Nil	Nil
	1:5	A	89	Nil	Nil
		B	15	4	Nil
2-$CH_3C_6H_4$	3:1	A	Nil	Nil	Intractable gum
		B	Nil	Nil	Diarylurea IX (12)
	1:1	A	31[c]	Nil	Nil
	1:5	A	99	Nil	Nil
		B	24	15	Nil
4-$CH_3C_6H_4$	3:1	B	Nil	Nil	Diarylurea IX (6)
	1:1	A	99[d]	Nil	Nil
	1:5	A	99	Nil	Nil
		B	45	26	Nil
2-$CH_3OC_6H_4$	1:1	A	Nil	22	Nil
	1:5	A	93	Nil	Nil
4-$CH_3OC_6H_4$	1:1	A	20	Nil	Nil
	1:5	A	66	Nil	Nil
		B	13	50	Nil
	1:10	A	50	Nil	Nil
2-$C_2H_5OC_6H_4$	1:1	A	Nil	16	Nil
	1:5	A	76	Nil	Nil
4-$C_2H_5OC_6H_4$	1:1	A	16	25	Nil
2-ClC_6H_4	1:2	A	Nil	1	Pyrone X[e] (81)
	1:5	A	Nil	1	Pyrone X (66)
	1:10	A	Nil	2	Pyrone X (52)
	1:40	A	Nil	Nil	Pyrone X (30)
4-ClC_6H_4	1:1	A	Nil	25	Nil
	1:5	A	Nil	29	Nil
	1:10	A	31	Nil	Nil
2-BrC_6H_4	1:1	A	Nil	6	Pyrone X[f] (5)
	1:5	A	Nil	1	Pyrone X (43)
	1:10	A	Nil	Nil	Pyrone X (37)
	1:40	A	Nil	Nil	Pyrone X (16)
4-BrC_6H_4	1:1	A	Nil	18	Nil
	1:5	A	14[g]	22	Nil
	1:15	A	29	Nil	Nil
2,4-$(CH_3)_2C_6H_3$	3:1	B	Nil	Nil	Diarylurea IX (5)
	1:1	A	86	Nil	Nil
	1:5	A	99	Nil	Nil
		B	31	33	Nil
	1:20	A	99	Nil	Nil
2,4-$Cl_2C_6H_3$[h]	1:1[i]	A	Nil	5	Pyrone X[j] (5)
	1:5	A	Nil	16	Pyrone X (16)
	1:10	A	Nil	5	Pyrone X (40)
	1:40	A	Nil	Nil	Pyrone X (24)
2,5-$Cl_2C_6H_3$	1:1	A	Nil	2	Pyrone X[k] (11)
	1:5	A	Nil	20	Pyrone X (7)
	1:15	A	Nil	11	Pyrone X (5)
	1:40	A	Nil	5	Pyrone X (1)
4-Cl-2-CH_3O-C_6H_3	1:1	A	Nil	22	Nil
	1:5	A	Nil	32	Nil
	1:40	A	9[l]	Nil	Nil
4-$NO_2C_6H_4$[m]	1:1	A	Nil	16	Nil
	1:10	A	Nil	20	Nil
1-Naphthyl	1:1	A	73[n]	Nil	Nil
	1:10	A	87[n]	Nil	Nil
2-Naphthyl	1:1	A	73[o]	Nil	Nil
	1:10	A	92[o]	Nil	Nil
C_6H_5 (ω-Br)	1:5	A	94[p,q]	Nil	Nil
2-ClC_6H_4 (ω-Br)	1:10	A	32[r,q]	Nil	Nil

[a] The odor of acetone was detected in the vapors from the reaction. [b] Cyclization with concentrated sulfuric acid (1:1 or 2:1) at 100° gave only 2-hydroxylepidine in 51 and 25% yields, respectively. [c] 2-Chloro-8-methyllepidine (93%), m.p. 66–67°. *Anal.* Calcd. for $C_{11}H_{10}ClN$: N, 7.31. Found: N, 7.42. [d] 2-Chloro-6-methyllepidine (90%), m.p. 102–104°. *Anal.* Calcd. for $C_{11}H_{10}ClN$: N, 7.31. Found: N, 7.49. [e] M.p. 201–204°. [f] M.p. 195–196.5°. [g] 6-Bromo-2-chlorolepidine (94%), m.p. 141–143°. *Anal.* Calcd. for $C_{10}H_7BrClN$: N, 5.46. Found: N, 5.51. [h] Acetoacet-2,4-dichloranilide on heating with equal weights or large excesses of either 74% or concentrated sulfuric acid gave 85–93% yields of 2,4-dichloroaniline as the only product. [i] On one occasion only, these

TABLE V (*Continued*)

conditions gave 6,8-dichloro-2-hydroxylepidine (16%), m.p. 241–243°. *Anal.* Calcd. for $C_{10}H_7Cl_2NO$: N, 6.14. Found: N, 6.17. The infrared spectrum showed a carbonyl peak at 1670 cm.$^{-1}$(s), which is typical of 2-quinolones [N. J. McCorkindale, *Tetrahedron*, **14**, 223 (1961)]. The other product of the reaction was 6,8-dichlor-4-hydroxyquinaldine (5%), the infrared spectrum of which showed a carbonyl peak at 1620 cm.$^{-1}$(s). Numerous repetitions of the experiment gave only the products listed in Table V. [j] M.p. 232–235°. [k] M.p. 179–181°. [l] M.p. 214–216°. *Anal.* Calcd. for $C_{11}H_{10}ClNO_2$: N, 6.26. Found: N, 6.35. The infrared spectrum showed a carbonyl peak at 1670 cm.$^{-1}$(s). [m] Acetoacet-2-nitroanilide decomposed on heating with polyphosphoric acid. [n] 2-Hydroxy-7:8-benzolepidine. [o] 2-Hydroxy-5:6-benzolepidine. The linear 2-hydroxy-6:7-benzolepidine was not formed. [p] M.p. 262–265° dec. A mixture melting point with 3-bromo-2-hydroxylepidine prepared by bromination of 2-hydroxylepidine using bromine water was 215–260°.[3] The infrared spectra were also dissimilar. [q] Cyclization of the anilide with concentrated sulfuric acid gave an identical product. [r] 4-Bromomethyl-2,8-dichlorolepidine (60%), m.p. 94–96°. *Anal.* Calcd. for $C_{10}H_6BrCl_2N$: N, 4.81. Found: N, 4.92.

The 4-hydroxy-6-nitroquinaldines were extracted from the reaction mixtures with excess, boiling, 16% sodium hydroxide, which was then neutralized with glacial acetic acid. The 4-hydroxyquinaldines gave orange colorations with aqueous alcoholic ferric chloride. The 4-chloroquinaldines were prepared by refluxing the 4-hydroxyquinaldines with excess freshly distilled phosphorus oxychloride for 10 min. and were crystallized from dilute ethanol.

The mixtures of isomeric 5- and 7-substituted 4-hydroxyquinaldines were fractionally crystallized from ethanol or dilute hydrochloric acid to give only one isomer in a pure state in most instances. Owing to the insolubility in the usual chromatographic solvents, the mixtures of 5- and 7-substituted 4-hydroxyquinaldines were converted in quantitative yield to the corresponding 4-chloroquinaldines as described above and the isomers separated by column chromatography on alumina using benzene as the eluent, some of the mixed isomers being recovered in each case. The 4-chloroquinaldines were reconverted in high yield to the corresponding 4-hydroxyquinaldines by heating with glacial acetic acid in a sealed tube at 190–200° for 7 hr. The results are given in Table III.[22]

6-Amino-4-hydroxyquinaldines.—4-Hydroxy-6-nitroquinaldines were reduced to the corresponding 6-amino-4-hydroxyquinaldines by the method of Halcrow and Kermack.[23] The 6-acetylaminoquinaldines were formed on heating with a mixture of acetic acid and acetic anhydride. The results are given in Table IV.

Deamination of the 6-Amino-4-hydroxyquinaldines.—The cooled mixture of the 6-amino-4-hydroxyquinaldine (1 g.), 20 ml. of concentrated hydrochloric acid, and 15 ml. water was diazotized, and the resulting solution was treated dropwise with 6 ml. 50% (w./w.) hypophosphorous acid at 0° during 1 hr., the resulting solution being allowed to stand for 24 hr. at 0°. Neutralization, followed by reduction in volume of the solution gave the corresponding 4-hydroxyquinaldines in 59–86% yield. The melting points were identical with those reported in Table III and showed no depression on admixture with the corresponding 4-hydroxyquinaldines from the direct synthesis.

Reductive Dehalogenation of the 5-Substituted 8-Chloro-4-hydroxyquinaldines.—A mixture of 3 g. of the 3,5-disubstituted 8-chloro-4-hydroxyquinaldine V (R_1 = H, CH_3, and C_2H_5 and R_2 = CH_3 and CH_3O; R_1 = CH_3 and R_2 = C_2H_5O), 3 g. of active Raney nickel, 15 ml. of 8% sodium hydroxide, 150 ml. of ethanol, and hydrogen were stirred for 8 hr. at room temperature in an hydrogenator at atmospheric pressure. On standing overnight no further absorption of hydrogen occurred, 0.96 to 0.99 mole of hydrogen having been taken up by the solution. The solution was filtered and the Raney nickel was extracted with excess boiling ethanol. The volume of the combined filtrates was reduced to 100 ml. After neutralizing with glacial acetic acid, the solution was evaporated to dryness and the crude quinaldine was crystallized to constant melting point from aqueous dimethylformamide. The dehalogenated quinaldines were obtained in 83–97% yield were identical with the corresponding 5-substituted 4-hydroxyquinaldines described in Table III (melting point and mixture melting point). The corresponding 4-chloroquinaldines were prepared as before and found to be identical with those described in Table III (melting point and mixture melting point). 4-Chloro-5-methoxyquinaldine, m.p. 95–96°, prepared in this manner has not been described in Table III.

Anal. Calcd. for $C_{11}H_{10}ClNO$: N, 6.74. Found: N, 6.84.

ω-Bromoacetoacetanilides.—A solution of 40 g. of acetoacetanilide in 120 ml. of glacial acetic acid was treated dropwise with a solution of 36.1 g. of bromine in 181 g. of glacial acetic acid containing a small crystal of iodine, over a period of 1 hr. at room temperature. The mixture was stirred further for 3 hr. and poured into water to give ω-bromoacetoacetanilide (84%) which was crystallized from benzene, m.p. 136–138° dec.[24] The product was identical (infrared spectra and mixture melting point) with ω-bromoacetoacetanilide prepared by the method of Hasegawa,[25] or Cook, *et al.*[26]

Similarly, ω-bromoacetoacet-2-chloroanilide was prepared in 86% yield. m.p. 72–74°.

Anal. Calcd. for $C_{10}H_8BrClNO_2$: N, 4.82. Found: N, 4.94.

Cyclization of Acetoacetanilides with Polyphosphoric Acid. Method A.—The acetoacetanilide and polyphosphoric acid (see Table V for ratios) were heated at 140° for 1 hr. with stirring and the reaction mixture was neutralized with sodium hydroxide. The crude precipitate was triturated with 8% sodium hydroxide (100 ml./g. of mixture) at room temperature. The insoluble products were removed by filtration and found to be either 2-hydroxyquinolines, diarylureas, or 3-arylcarbamyl-2,6-dimethyl-4-pyrones.[15] Neutralization of the alkaline filtrate with glacial acetic acid gave the 4-hydroxyquinoline (Table V).

Method B.—The acetoacetanilide, an equimolar quantity of the corresponding arylamine, and polyphosphoric acid were treated as in method A. The alkali-insoluble material consisted of either the 2-hydroxyquinoline or the diarylurea, the 4-hydroxyquinoline being soluble in alkali (Table V).

The melting points of the 2-hydroxyquinolines, the 2-chloroquinolines, and the diarylureas were identical with those recorded in the literature.[27] The 4-hydroxyquinaldines were identical with the corresponding products from the direct synthesis (Table III).

Cyclization of Anil–Anilides with Polyphosphoric Acid.—A mixture of 0.5 g. of β-1-naphthylaminocrotono-1-naphthylamide[3] (XI, Ar = 1-naphthyl) and 2.5 g. of polyphosphoric acid were heated at 140° for 30 min. and the reaction mixture was neutralized to give a quantitative yield of 4-hydroxy-7:8-benzoquinaldine, which was crystallized from dimethylformamide, m.p. and m.m.p. 328–332° dec.

4-Hydroxy-5:6-benzoquinaldine, m.p. 346–350° dec., was obtained in quantitative yield when XI (Ar = 2-naphthyl)[3] was similarly treated.

Acknowledgment.—One of us (A. K. M.) wishes to express his gratitude to the Sir Ernest Oppenheimer Memorial Trust for the award of a fellowship.

(22) Only data for those compounds which have not previously been reported in the literature are given in Table III, with the exception of the nitroquinaldines. In addition, 4,5-dichloroquinaldine was found to have m.p. 104.5–106, whereas A. M. Spivey and F. H. S. Curd[9] reported m.p. 89°.

(23) B. E. Halcrow and W. O. Kermack, *J. Chem. Soc.*, 415 (1945).

(24) C. M. Mehta and G. H. Patel [*Current Sci.* (India), **30**, 15 (1961)] and C. M. Mehta, J. M. Trivedi, and G. H. Patel [*J. Sci. Ind. Res.* (India), **20B**, 460 (1961)] have claimed that bromination under similar conditions gave α-bromoacetoacetanilide.

(25) M. Hasegawa, *Pharm. Bull.* (Tokyo), **1**, 50 (1953).

(26) D. J. Cook, R. E. Bowen, P. Sorter, and E. Daniels, *J. Org. Chem.*, **26**, 4949 (1961).

(27) Where the compounds have not previously been described in the literature, data is given in Table V.

3-Arylcarbamyl-2,6-dimethyl-4-pyrones Formed by the Action of Polyphosphoric Acid on o-Haloacetoacetanilides

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Received May 25, 1964

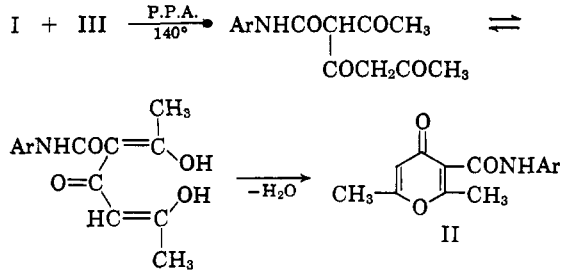
The treatment of *o*-haloacetoacetanilides with polyphosphoric acid gave a new series of substituted pyrones (3-arylcarbamyl-2,6-dimethyl-4-pyrones). The structures of these compounds were established by degradation studies and their characteristic infrared absorptions. Acid hydrolysis using 70% sulfuric acid caused the 4-pyrone ring to rupture at the ether bond.

On heating the *o*-haloacetoacetanilides I with polyphosphoric acid at 140° the corresponding 4-hydroxyquinaldines and 3-arylcarbamyl-2,6-dimethyl-4-pyrones II were formed.[2] The formation of 4-hydroxyquinaldines from acetoacetanilides in the presence of polyphosphoric acid has been shown to occur through anil–anilide intermediates, the formation of which depends upon heterolytic fission of the anilides at the amide group to give the arylamines.[2,3] The formation of 3-arylcarbamyl-2,6-dimethyl-4-pyrones II is also dependent upon heterolytic fission of the anilides. Thus while acetoacet-2-toluidide, which undergoes negligible fission to the arylamine in polyphosphoric acid,[2] did not form a pyrone of the type II, the anilides I, which undergo heterolytic fission in polyphosphoric acid, gave rise to the pyrones II. The initial formation of a carbonium ion III from the anilides I in polyphosphoric acid is consistent with the proposal of Duffy and Leisten.[4]

$$\underset{\text{I}}{\text{ArNHCOCH}_2\text{COCH}_3} \xrightarrow[140°]{\text{P.P.A.}} \text{ArNH}_2 + \underset{\text{III}}{\text{CH}_3\text{COCH}_2\text{CO}^+}$$

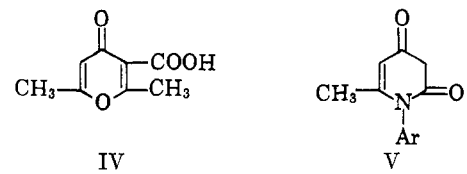
Ar = 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 2,5-$Cl_2C_6H_3$, and 2-BrC_6H_4

The carbonium ion III can react with the acetoacetanilides I to give the 3-arylcarbamyl-2,6-dimethyl-4-pyrones II. The intermediates were not isolated.

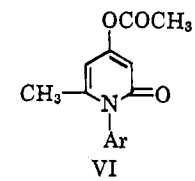


Acid hydrolysis of the 3-arylcarbamyl-2,6-dimethyl-4-pyrones II using 70% sulfuric acid gave the previously known[5] 2,6-dimethyl-4-pyrone-3-carboxylic acid (IV), the corresponding arylamine ($ArNH_2$ where Ar = 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 2,5-$Cl_2C_6H_3$, and 2-BrC_6H_4), and in addition the corresponding 1-aryl-2,4-diketo-6-methyl-1,2,3,4-tetrahydropyridines Va.

The pyridones Va were very soluble in cold dilute alkali, cold concentrated acids, and hot dilute acids, and, as no effervescence occurred with hot aqueous sodium carbonate, the acidic character was attributed to an enolic group. This was substantiated on treatment with an aqueous–alcoholic ferric chloride solution, when an orange color developed on standing for about 1 hr.[6] The basic properties of these compounds were attributed to a tertiary nitrogen atom as no primary amino group was present as shown by the failure of these compounds to diazotize and no NH-stretching bands were visible in the infrared spectra. On warming with acetic anhydride O-acylation occurred to give the 4-acetoxy-1-aryl-2-keto-6-methyl-1,2-dihydropyridines VI.

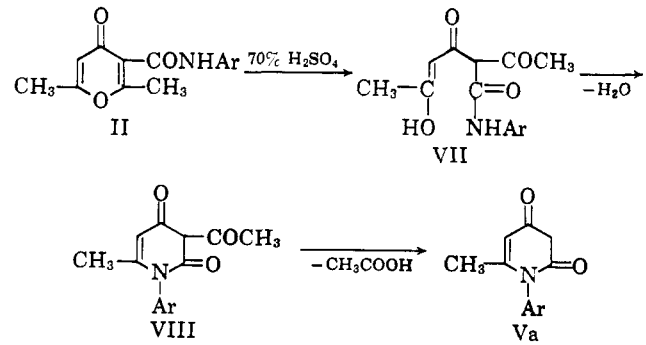


a, Ar = 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 2,5-$Cl_2C_6H_3$, and 2-BrC_6H_4
b, Ar = C_6H_5



Ar = 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 2,5-$Cl_2C_6H_3$, and 2-BrC_6H_4

The structures of the pyridones Va were established by a known synthesis.[7] The formation of the pyridones Va during the acid hydrolysis of the 3-arylcarbamyl-2,6-dimethyl-4-pyrones II must involve a rupture of the 4-pyrone ring at the ether bond with subsequent cyclization of the intermediates VII to give the 3-acetylpyridones VIII. The latter, in the presence of 70% sulfuric acid, were hydrolyzed to the corresponding pyridones Va. The intermediates VII and VIII were not isolated.



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