Mannich-Type Condensation of Hydroquinone, Formaldehyde, and Primary Amines

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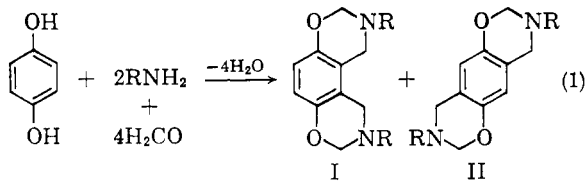
Disubstitution of hydroquinone by a Mannich-type condensation with formaldehyde and unhindered primary amines occurs preferentially in the 2,3-positions. A number of new 2,3- and 2,5-disubstituted hydroquinone derivatives are reported.

The preparation of *m*-benzoxazines by reaction of formaldehyde and primary amines with phenols,[1] polyhydroxybenzenes,[2,3] or naphthols[4] has been extensively investigated by Burke and co-workers. Their recent paper[3] concerned with the synthesis of bisoxazines[5] I and II (equation 1), by the condensation of hydroquinone, formaldehyde, and a primary amine in a molar ratio of 1:4:2, prompts this disclosure of our independent investigations of the reaction.



(1)

Burke, *et al.*, reported[3] the isolation of I and II in 12 and 72% yields, respectively, when utilizing benzylamine, and in 27 and 31% yields, respectively, from α-methylbenzylamine. Bisoxazine II was also obtained from several other primary amines, *i.e.*, methyl- (63%),[2] *t*-butyl- (76%),[3] allyl- (82%),[3] cyclohexyl- (43%),[2] and ethanolamines (53%),[3] although no corresponding I was isolated in these cases. Aniline and *p*-toluidine afforded 1,3,5-triarylhexahydro-*s*-triazines to the exclusion of bisoxazines.[6a]

In our studies, we found that both I and II were isolable in all cases examined (see Table I).[6b] Furthermore, I and not II was found to be the favored isomer unless its formation was sterically inhibited. The discrepancies between the present work and that of Burke and co-workers may be attributed to several factors. The high yields of II which they reported when employing methyl-, *t*-butyl-, allyl-, and benzylamines, were based on crude products prior to purification. Although evidently unrecognized, these crude products must have contained a considerable, if not predominant, amount of the more soluble isomer I. Their failure to isolate I in the cases of methyl-, *t*-butyl-, allyl-, and cyclohexylamines is probably due to its loss during subsequent recrystallizations of the crude product. On the other hand, the attempted fractionation of I from II when R = $C_6H_5CH_2$, based on their differences in solubility in boiling methanol, was ineffective, owing to the very low solubilities of both isomers in this medium.

TABLE I
YIELDS OF BISOXAZINES[a]

Case	R	Yield, % I	Yield, % II
a	CH_3	65	21
b	*i*-C_3H_7	51	40
c	*t*-C_4H_9	20	51
d	C_6H_{11}	50	34
e	$(CH_3)_2NCH_2CH_2$	45	15
f	$CH_2{=}CHCH_2$	62	22
g	$C_6H_5CH_2$	59	19
h	C_6H_5	[b]	21

[a] Prepared *via* bis(alkoxymethyl)amine procedure. See Experimental. [b] Yield not ascertained owing to losses incurred during separation of product from contaminating triazine.

The bisoxazines were prepared both by reaction of hydroquinone with formaldehyde and primary amines in the conventional manner,[1-4,6] and by reaction of hydroquinone with bis(alkoxymethyl)-amines (see Table II) prepared as shown below.

$$RNH_2 + 2H_2CO + 2R'OH \rightleftharpoons RN(CH_2OR')_2 + 2H_2O$$

Only one example of this latter type of compound, $RN(CH_2OR')_2$, has been previously reported,[7] although alkoxymethyldialkylamines, R_2NCH_2OR', have been used to prepare N,N-dialkylaminomethylphenols.[8] We have found the bis(alkoxymethyl)amine reagent to be particularly useful in the cases of N,N-dimethylaminoethylamine and aniline. However, for the other amines studied here, conversion to a bis(alkoxymethyl)amine

(1) W. J. Burke, *J. Am. Chem. Soc.*, **71**, 609 (1949); W. J. Burke, R. P. Smith, and C. Weatherbee, *ibid.*, **74**, 602 (1952).

(2) W. J. Burke and C. Weatherbee, *ibid.*, **72**, 4691 (1950).

(3) W. J. Burke, C. R. Hammer, and C. Weatherbee, *J. Org. Chem.*, **26**, 4403 (1961).

(4) W. J. Burke, M. J. Kolbezen, and C. W. Stephens, *J. Am. Chem. Soc.*, **74**, 3601 (1952); W. J. Burke, K. C. Murdock, and Grace Ec, *ibid.*, **76**, 1677 (1954).

(5) This is a convenient name used to refer to compounds I and II.

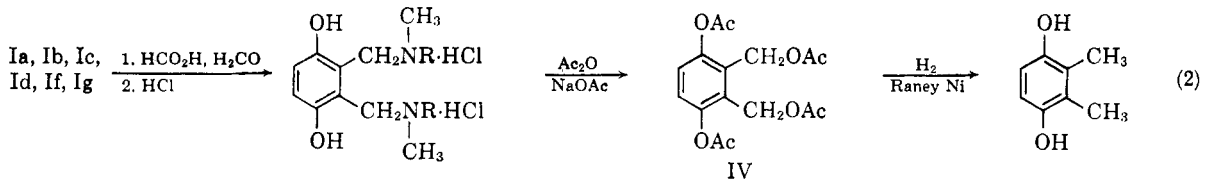
(6) (a) C. R. Hammer, dissertation for Ph.D. degree, University of Utah (1956); (b) After this manuscript was accepted for publication, a similar result was disclosed by M. E. Kuehne and E. A. Konopka *J. Med. Pharm. Chem.*, **5**, 257 (1962).

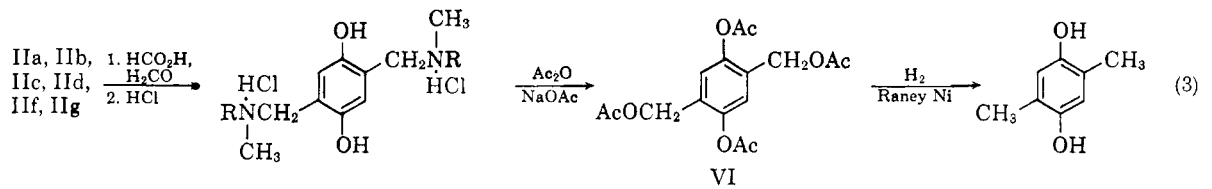
(7) Gertrude M. Robinson and R. Robinson, *J. Chem. Soc.*, **123**, 1532 (1932).

(8) H. F. Tseou and C. T. Yong, *J. Org. Chem.*, **4**, 123 (1939); J. H. Burckhalter, F. H. Tendick, E. M. Jones, W. F. Holcomb, and A. L. Rawlins, *J. Am. Chem. Soc.*, **68**, 1894 (1946).

TABLE II
BIS(ALKOXYMETHYL)AMINES
$RN(CH_2OR')_2$

R	R'	B.p., °C./mm.	$n^{25}D$	Yield, %	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
CH_3	i-C_4H_9	93/12	1.4167	65	65.0	12.3	6.9	64.9	12.3	6.7
i-C_3H_7	i-C_4H_9	119/11	1.4215	58	67.4	12.6	6.1	67.3	12.5	6.4
t-C_4H_9	i-C_4H_9	124/14	1.4265	51	68.5	12.3	5.7	68.8	12.5	5.9
C_6H_{11}	i-C_4H_9	103/0.5	1.4485	34	70.9	12.2	5.2	71.4	12.0	5.3
$(CH_3)_2NCH_2CH_2$	i-C_4H_9	106/0.5	1.4325	22	64.6	12.3	12.3	63.8	12.4	11.7
CH_2=$CHCH_2$	i-C_4H_9	113/13	1.4283	75	68.1	11.8	6.1	68.0	11.8	6.0
$C_6H_5CH_2$	C_2H_5	80/0.1	1.4849	51	70.1	9.4	6.2	70.1	9.3	6.6
$C_6H_5CH_2$	i-C_4H_9	114/0.07	1.4765	47	73.2	10.4	5.0	73.4	10.3	5.2
C_6H_5	C_2H_5	70/0.02	1.5085	51	68.9	9.1	6.7	69.2	9.4	6.8





Ia, IIa. R = CH_3 Id, IId. R = C_6H_{11}
Ib, IIb. R = i-C_3H_7 If, IIf. R = CH_2=$CHCH_2$
Ic, IIc. R = t-C_4H_9 Ig, IIg. R = $C_6H_5CH_2$

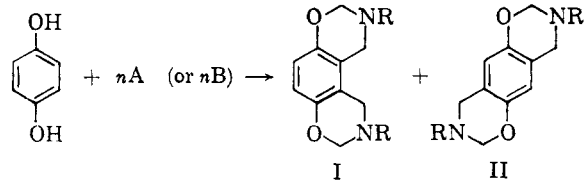
CHART I

afforded no pronounced advantage. It is important to note that substantially identical ratios of I to II were obtained using either bis(alkoxymethyl)-amine or the free amine and formaldehyde (see Table III). Use of excess amine and formaldehyde is recommended since it gives higher total yields of mixed isomers. The less soluble, higher melting isomer (II) was separated from the more soluble, lower melting isomer (I), on the basis of solubility differences. Crude I was then purified by column chromatography employing alumina.

The structures of the bisoxazines of Tables IV and V, with the exceptions of Ie, Ih (Table V) and IIe, IIh (Table IV) were proved, as shown in Chart I. The isomeric bisoxazines from methylamine (Ia and IIa) were converted to IV and VI whose structures were established by hydrogenolysis to the known 2,3- and 2,5-dimethylhydroquinones. After the structures of IV and VI were established, these compounds served as convenient reference compounds to which the structures of the remaining bisoxazines were related.

Structures of the isomeric pairs, Ie and IIe (R = $(CH_3)_2NCH_2CH_2$) and Ih and IIh (R = C_6H_5), were assigned by analogy based on the fact that in

TABLE III
YIELDS OF BISOXAZINES AS A FUNCTION OF REAGENT AND CONCENTRATION



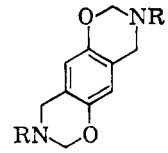
R	n	Reagent	Yield, % I	Yield, % II	Yield, % Total
$C_6H_5CH_2$	2	A	59	19	78
$C_6H_5CH_2$	2	B	47	13	60
$C_6H_5CH_2$	3	A	70	23	93
$C_6H_5CH_2$	3	B	66	15	81
CH_3	2	A	65	21	86
CH_3	2	B	56	13	69
CH_2=$CHCH_2$	2	A	62	22	84
CH_2=$CHCH_2$	2	B	41	15	56

A = $RN(CH_2OC_4H_9$-$i)_2$ B = $(RNH_2 + 2H_2CO)$

the other isomeric pairs examined, the higher melting, less soluble isomer possessed structure I. Corroborative evidence for these structural assignments was provided by nuclear magnetic resonance (n.m.r.) spectroscopy (see Table VI). In the cases

TABLE IV

3,7-DI-R-2,3,4,6,7,8-HEXAHYDRO-1,5-DIOXA-3,7-DIAZAANTHRACENE



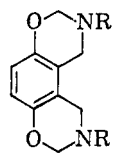
II

Case	R	M.p.,[a] °C.	Crystallization media[b]	Solubilities[c] Hot C_6H_6	Cold C_6H_6	Et_2O	Ligroin (B.p. 30–60°)	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
a	CH_3	182–184 182–183[d]	A	sls	vsls	i	i	65.4	7.3	12.7	65.2	7.3	12.6
b	i-C_3H_7	125–127	B	vs	s	vsls	i	69.6	8.7	10.1	69.4	8.4	10.0
c	t-C_4H_9	175–176 173–174[e]	B	vs	s	vsls	i	71.1	9.4	8.9	71.0	9.2	9.2
d	C_6H_{11}	161–163 161–162[d]	C	vs	s	vsls	i	74.2	8.9	7.9	74.1	8.8	7.9
e	$(CH_3)_2NCH_2CH_2$	111–113	B	vs	s	sls	i	64.7	8.9	16.8	64.7	8.7	16.5
f	$CH_2{=}CHCH_2$	137–139 139–140[e]	B	s	sls	vsls	i	70.6	7.4	10.3	70.6	7.4	10.1
g	$C_6H_5CH_2$	201–202 202–203[e]	A	sls	vsls	i	i	77.4	6.5	7.5	77.5	6.3	7.5
h	C_6H_5	186–188	B	s	sls	vsls	i	76.8	5.8	8.1	77.0	6.2	8.0

[a] Capillary, uncorrected. [b] A = benzene; B = benzene–ligroin (b.p. 30–60°); C = ethyl acetate. [c] vs = very soluble; s = soluble; sls = slightly soluble; vsls = very slightly soluble; i = insoluble. [d] Ref. 2. [e] Ref. 3.

TABLE V

3,6-DI-R-2,3,4,5,6,7-HEXAHYDRO-1,8-DIOXA-3,6-DIAZAPHENANTHRENE



I

Case	R	M.p.,[a] °C.	Crystallization media[b]	Solubilities[c] Hot C_6H_6	Cold C_6H_6	Et_2O	Ligroin (B.p. 30–60°)	Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
a	CH_3	95–97	A	vs	vs	s	i	65.4	7.3	12.7	65.4	7.3	12.7
b	i-C_3H_7	...[d]	...	vs	vs	s	sls	69.6	8.7	10.1	68.9	8.7	9.8
c	t-C_4H_9	95–98	B	vs	vs	vs	s	71.1	9.2	9.2	71.2	9.5	9.1
d	C_6H_{11}	82–83	B	vs	vs	s	sls	74.2	8.9	7.9	74.8	8.8	7.4
e	$(CH_3)_2NCH_2CH_2$	35–37	B	vs	vs	vs	s	64.7	9.0	16.8	64.3	9.0	16.4
f	$CH_2{=}CHCH_2$	48–50	B	vs	vs	vs	s	70.6	7.4	10.3	70.5	7.4	10.0
g	$C_6H_5CH_2$	142–143 143–144[e]	A	s	s	i	i	77.4	6.5	7.5	77.5	6.5	7.5
h	C_6H_5	125–127	A	s	sls	sls	i	76.8	5.8	8.1	76.7	5.7	8.2

[a] Capillary, uncorrected. [b] A = benzene–ligroin (b.p. 30–60°); B = ligroin (b.p. 30–60°) at −50°. [c] vs = very soluble; s = soluble; sls = slightly soluble; vsls = very slightly soluble; i = insoluble. [d] Sirup. [e] Ref. 3.

of Ia, Ic, and If, the chemical shifts of the *ortho* protons are 0.15–0.23 τ less than the chemical shifts of the *para* protons of the isomers, IIa, IIc, and IIf. Consistent with this observation, the chemical shifts of the *ortho* protons in the compounds assigned structures Ie and Ih are 0.17 and 0.20 τ lower than the shifts for the *para* protons of the compounds assigned structures IIe and IIh.

It is surprising that unhindered primary amines give I representing 2,3-disubstitution of hydroquinone in good yield, whereas secondary amines give 2,5-disubstituted hydroquinones in good yield.[9] For example, although we find that N-methylbenzylamine affords Vg (free base) in 72% yield, a 70% yield of Ig was obtained from benzylamine. The high yield of I formed in the case of unhindered primary amines and the repeated failure to isolate products of type III from secondary amines, suggests that primary amines react in the following manner.

The isoindoline intermediate (VII) arises from an *intramolecular* condensation not possible with secondary amines and is analogous to the initial *intermolecular* condensation. The formation of a

(9) W. T. Caldwell and T. R. Thompson, *J. Am. Chem. Soc.*, **61**, 1765 (1939).

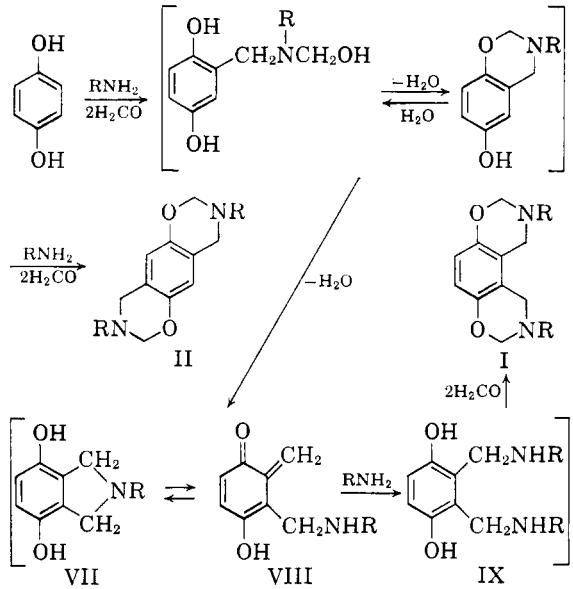


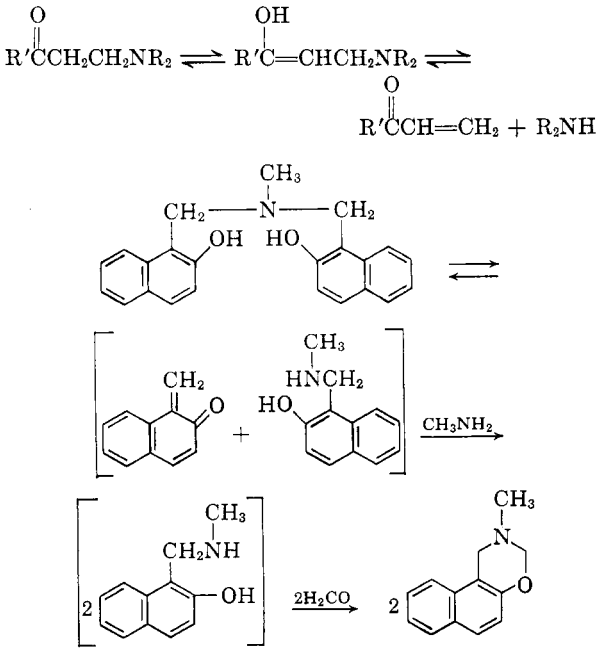
TABLE VI

CHEMICAL SHIFTS OF THE *ortho* AND *para* PROTONS

Case	Concentration in $CHCl_3$, %	τ^a *ortho*(I)	*para*(II)
a	5	3.36	3.58
c	10	3.45	3.60
f	10	3.38	3.61
e	10	3.39	3.59
h	5	3.35	3.52
h	10	3.34	...

[a] G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).

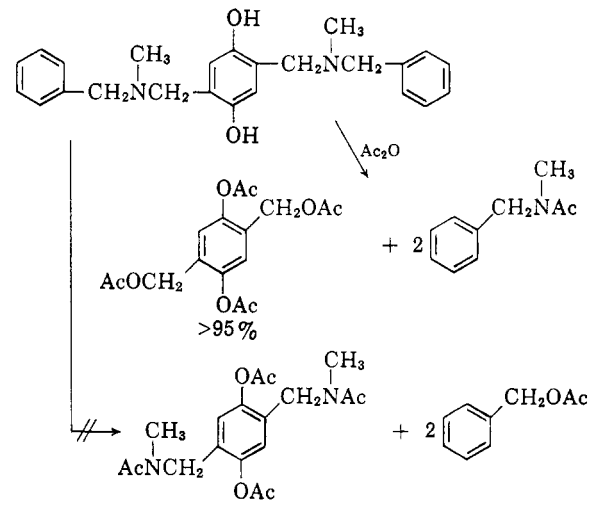
ketomethylene intermediate similar to VIII has been previously suggested[10] in amine exchange reactions and is analogous to the formation of olefins from Mannich bases.



(10) H. R. Snyder and J. A. Brewster, *J. Am. Chem. Soc.*, **70**, 4230 (1948).

The conversion of VII to IX is an amine interchange reaction analogous to the following reaction described by Burke.[4]

The different chemistry conferred on a benzylamine derivative by the presence of a potentially ketonic *ortho*-hydroxyl group is particularly well demonstrated by the following reaction in which we observe the specific cleavages shown.



Experimental

General Procedure for the Preparation and Isolation of Bisoxazines I and II (See Tables IV and V). A. Preparation. (a) From Bis(alkoxymethyl)amines.—To a refluxing solution of 2.0 moles of bis(alkoxymethyl)amine (see Table II) in 500 ml. of benzene was added a solution of 1.0 mole (110 g.) of hydroquinone in 250 ml. of ethanol. The addition required 10 min. The solution was refluxed for an additional 30 min. and then the solvents were removed under reduced pressure. Three times the residue was placed in 400 ml. of benzene and the solvent was removed. Except when R = C_6H_5, the residue at this point was a crystalline or semicrystalline mass. In the case of R = C_6H_5, it was found necessary to heat the residue for 15 min. at 110°/50 mm. before the reaction mixture could be induced to crystallize.

(b) **From Amine and Formaldehyde.**—To a suspension of 4.0 moles (120 g.) of paraformaldehyde in 500 ml. of ethanol was added 2.0 moles of the primary amine. The mixture was stirred until complete solution was effected and then heated to reflux. To it was added a solution of 1.0 mole (110 g.) of hydroquinone in 250 ml. of ethanol over a 10-min. period. The solution was refluxed for an additional 30 min. and then treated as described earlier.

Following previously described procedures,[2,3] formalin (37%) and dioxane could be substituted for paraformaldehyde and ethanol, respectively, without influencing the composition of the product.

B. Separation and Isolation.—Isolation of IIa–IIf from their respective reaction mixtures was effected by suspending the residue in 500 ml. of boiling ether, filtering it, and washing the crystalline residue with four 100-ml. portions of ether.

Crude IIg was obtained by suspending the residue in 500 ml. of boiling benzene, filtering it, and washing the collected crystals with four 100-ml. portions of cold benzene.

Crude IIh was isolated by dissolving the residue in 500 ml. of boiling benzene, followed by cooling to room temperature. The mixture was diluted with 200 ml. of ligroin (b.p. 60–90°), and the resulting crystals were filtered.

The crude products, IIa–IIh, thus obtained were recrystallized to constant melting points employing the media in Table IV. The yields and characterizations of IIa–IIh are listed in Tables I and IV, respectively.

Isomeric I was then isolated and purified in the following manner. After removal of crude II, the solvent was stripped. The residue was dissolved in a minimum amount of warm benzene and chromatographed on a column (5 × 45 cm.) of activated alumina, using 1 l. of benzene as a developer. The product obtained by concentration of the eluate was recrystallized to constant melting point from the media given in Table V, with the exception of Ib, which could not be induced to crystallize. The characterizations and yields of Ia–Ih are recorded in Tables V and I, respectively.

2,5-Bis(hydroxymethyl)hydroquinone Tetraacetate (VI) from II (See Equation 3).—Bisoxazines IIa, IIb, IIc, IId, IIf, and IIg were degraded to tetraacetate VI as in the following example. Following a previously described procedure,[2] a mixture of 7.44 g. (0.02 mole) of IIg, 8.0 ml. of 37% aqueous formaldehyde, and 25 ml. of 85% formic acid was heated for 12 hr. on a steam bath. After cooling, 10 ml. of concentrated hydrochloric acid was added and the solvents were removed under reduced pressure. The residue crystallized after trituration with ether. Recrystallization from water–ethanol yielded 8.0 g. (89%) of pure Vg, m.p. > 50°.

Anal. Calcd. for $C_{24}H_{30}Cl_2N_2O_2$: C, 64.1; H, 6.7; Cl, 15.8. Found: C, 64.2; H, 7.0; Cl, 15.7.

Acetolysis[11] of Vg was effected by refluxing a mixture of 4.5 g. (0.05 mole) of Vg, 8.2 g. (0.10 mole) of anhydrous sodium acetate, and 75 ml. of acetic anhydride for 16 hr. The light yellow reaction mixture was cooled and poured into 500 ml. of ice and water. After standing for 30 min., the product was collected by filtration. Recrystallization from ethanol afforded 1.5 g. (90%) of product VI, m.p. 117–119° (lit.,[11] m.p. 119°).

Anal. Calcd. for $C_{16}H_{18}O_8$: C, 56.8; H, 5.3. Found: C, 56.6; H, 5.1.

2,3-Bis(hydroxymethyl)hydroquinone Tetraacetate (IV) from I (See Equation 2).—In like manner, bisoxazines Ia, Ib, Ic, Id, If, and Ig were converted into their corresponding 2,3-bis(N-R-N-methylaminomethyl)hydroquinone dihydrochlorides (III) by reaction with formic acid and formaldehyde, followed by treatment with concentrated hydrochloric acid. These products were characterized in several instances as reported below.

IIIa (R = CH_3), m.p. 225–227° dec. *Anal.* Calcd. for $C_{12}H_{22}Cl_2N_2O_2$: C, 48.5; H, 7.4; Cl, 23.9. Found: C, 48.7; H, 7.5; Cl, 23.7.

IIIb (R = *i*-C_3H_7), m.p. 212–214° dec. *Anal.* Calcd. for $C_{16}H_{30}Cl_2N_2O_2$: C, 54.5; H, 8.5; Cl, 20.0. Found: C, 54.4; H, 8.6; Cl, 19.8.

IIId (R = C_6H_{11}), m.p. 229–234° dec. *Anal.* Calcd. for $C_{22}H_{38}Cl_2N_2O_2$: C, 61.0; H, 8.8; Cl, 16.4. Found: C, 60.7; H, 8.7; Cl, 16.1.

IIIg (R = $C_6H_5CH_2$), m.p. 173–176° dec. *Anal.* Calcd. for $C_{24}H_{30}Cl_2N_2O_2$: C, 64.1; H, 6.7; Cl, 15.8. Found: C, 63.9; H, 7.0; Cl, 15.5.

The acetolyses of IIIa, IIIb, IIIc, IIId, IIIf, and IIIg to IV were effected in the manner described for the acetolysis of V to VI. However, column chromatography was found beneficial in freeing the desired tetraacetate from a dark colored impurity formed during the acetolysis. For example, a mixture of 2,3-bis(dimethylaminomethyl)hydroquinone dihydrochloride (IIIa) (12.6 g., 0.042 mole), sodium acetate (7.0 g., 0.084 mole), and 150 ml. of acetic anhydride was refluxed for 18 hr. The dark colored reaction mixture was cooled and poured into 300 ml. of ice and water. The product crystallized over a 20-min. period and was collected by filtration. This material was dissolved in 50 ml. of benzene and chromatographed on a column (4 × 18 cm.) of Micro-Cel C.[12] Development was effected with 750 ml. of benzene. The crystalline solid (6.4 g., 45%) obtained from the effluent was recrystallized from ethanol, m.p. 106–108°.

Anal. Calcd. for $C_{16}H_{18}O_8$: C, 56.8; H, 5.3. Found: C, 56.5; H, 5.3.

2,5-Dimethylhydroquinone from VI.—Tetraacetate VI (135.2 g., 0.4 mole) in 350 ml. of ethanol was hydrogenated in the presence of commercial Raney nickel for 14 hr. at 150° and 4400 p.s.i. The mixture was filtered and the solvent was removed by distillation. The resulting crystals (22 g., 40%) were recrystallized twice from ethanol–ligroin (b.p. 30–60°); m.p. 213–215° (lit.,[13] m.p. 213–215°). A mixed melting point with authentic 2,5-dimethylhydroquinone was undepressed and the infrared spectra were identical.

2,3-Dimethylhydroquinone from IV.—Tetraacetate IV (23.5 g., 0.07 mole) was subjected to the hydrogenolysis conditions just described. Removal of the catalyst and evaporation of the solvent yielded a light-colored sirup. The sirup was dissolved in 200 ml. of boiling benzene, filtered and the filtrate was slowly cooled. Crystallization commenced and was completed by diluting the mixture with 200 ml. of ligroin (b.p. 30–60°), followed by refrigeration overnight. The product (1.2 g., 12.5%) had a melting point of 221–224° (lit.,[13] m.p. 221°). A mixed melting point with an authentic sample of 2,3-dimethylhydroquinone was undepressed and the infrared spectra were identical.

2,5-Bis(N-benzyl-N-methylaminomethyl)hydroquinone.—To a refluxing solution of N-methylbenzylamine (181.5 g., 1.5 mole) and paraformaldehyde (45 g., 1.5 mole) in 200 ml. of ethanol was added a solution of hydroquinone (55 g., 0.5 mole) in 250 ml. of ethanol. After refluxing for 2.5 hr., the mixture was concentrated under reduced pressure to three fourths of its initial volume. Dilution with 200 ml. of ligroin (b.p. 30–60°) yielded 99 g. of product. An additional 41 g. of product was obtained as a second crop. Recrystallization of the combined products from chloroform–ligroin (b.p. 30–60°) produced 135.8 g. (72%) of white needles, m.p. 178–180°, which were identical with the product obtained by neutralization of Vg with aqueous sodium bicarbonate.

Anal. Calcd. for $C_{24}H_{28}N_2O_2$: C, 76.6; H, 7.4; N, 7.4. Found: C, 76.8; H, 7.3; N, 7.4.

Acetolysis of 2,5-Bis(N-benzyl-N-methylaminomethyl)-hydroquinone.—A mixture of 2,5-bis(N-benzyl-N-methylaminomethyl)hydroquinone (24.4 g., 0.065 mole) and 250 ml. of acetic anhydride was refluxed for 18 hr. The reaction mixture was concentrated to a sirup and then poured into ice and water. The product (VI) immediately crystallized and was collected by filtration. Recrystallization from ethanol produced 20.8 g. (95%) of pure VI, m.p. 117–119°.

Bis(isobutoxymethyl)amines (See Table II).—To a rapidly stirred suspension of 300 g. (10 moles) of paraformaldehyde in 2 l. of isobutyl alcohol was slowly added 5 moles of the primary amine. The reaction mixture was stirred until solution was complete. The solution was then refluxed and the water removed as a water–alcohol azeotrope. The desired product was then isolated by distillation through a 14-in. column packed with glass helices.

Bis(ethoxymethyl)amines (See Table II).—The procedure just given was followed, using 1 l. of benzene and 1 l. of ethanol instead of 2 l. of isobutyl alcohol.

N.m.r. Spectra (See Table VI).—The spectra were obtained at room temperature using a Varian Associates V-4300B high resolution spectrometer at 60 Mc. The chemical shifts relative to internal tetramethylsilane were measured by the audio-frequency side-band technique.

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