in dry ether (100 ml) were added ethyl acetoacetate (10 g, 0.077 mol) and concentrated sulfuric acid (0.02 ml) at −78°. The reaction mixture was maintained at 0–5° for 10 days. The crystals (1.5 g, 70%) were isolated, and recrystallization from ethyl acetate gave compound **7**: mp 142–143°; ν_{max}^{KBr} 1763 (C=O), 1700 (C=O), 1689 cm^{-1} (C=O); λ_{max}^{EtOH} 268 mμ (log ε 4.05), 329 (3.74); nmr ($CDCl_3$) τ 8.57 (t, 3, $-CH_2CH_3$), 7.42 (s, 3, $-CH_3$), 5.54 (q, 2, $-CH_2CH_3$), 4.35 (s, 1, C=CH–); enolic –OH group (by $FeCl_3$ test). The molecular weight was found to be 280 ($CHCl_3$, osmotic method) (calcd for $C_{12}H_{10}O_7$, 266).

Anal. Calcd for $C_{12}H_{10}O_7$: C, 54.14; H, 3.79. Found: C, 53.89; H, 3.94.

4-Hydroxy-7-methyl-2H,5H-pyrono[3,2-*c*]pyrone (11).—In a 200-ml autoclave were placed acetone (40.7 g, 0.72 mol), carbon suboxide (8.7 g, 0.12 mol), dry ether (110 ml), and concentrated sulfuric acid (0.3 ml). The autoclave was maintained at 20° for 14 days, and heated to 60° for 1 day. The resinoid was separated on a filter, and 1.0 g (8%) of solid was extracted with ether from the resinoid. The recrystallization from ethyl acetate gave compound **8**: mp 225°; ν_{max}^{KBr} 1762 (C=O), 1695 (C=O), 1638 cm^{-1} (C=O); λ_{max}^{EtOH} 271 mμ (log ε 4.17), 330 (3.93); nmr ($CDCl_3$) τ 7.60 (s, 3, CH_3), 4.50 (s, 1, C=CH), 3.78 (s, 1, C=CH). The molecular weight found to be 180 (Rast method) (calcd for $C_9H_6O_5$, 194.1).

Anal. Calcd for $C_9H_6O_5$: C, 55.68; H, 3.14. Found: C, 55.81; H, 3.04.

Registry No.—Carbon suboxide, 12076-43-6; acetylacetone, 123-54-6; benzoylacetone, 93-91-4; ethyl acetoacetate, 141-97-9; acetone, 67-6-41; **1a**, 19926-37-5; **2**, 1198-08-9; **3**, 17313-47-2; **4**, 19926-40-0; **9**, 19926-41-1; **11**, 4860-88-2.

Novel Formation of the Benzil from 2-(Dimethylaminomethyl)benzaldehyde under Benzoin Condensation Conditions[1]

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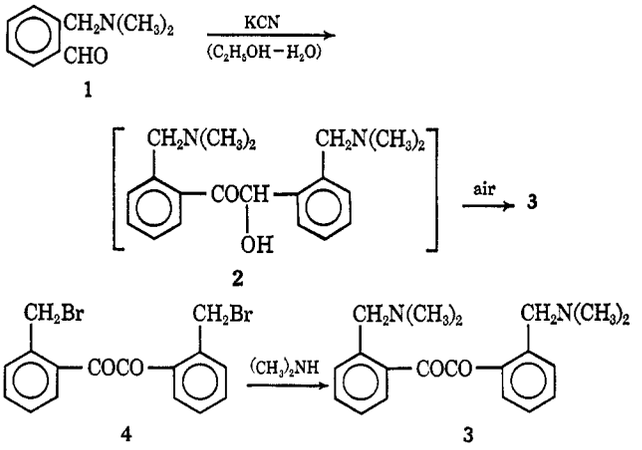
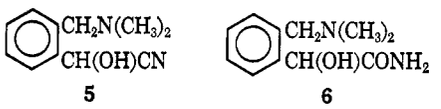
Although many examples of the benzoin condensation of an aromatic aldehyde by an alkali cyanide in ethanol–water have been reported,[2] none appears to have been accompanied by oxidation to form the benzil instead of the benzoin. In fact, subsequent conversion of the benzoin into the benzil has generally been effected by moderate or strong oxidizing agents.[3]

We have found that 2-(dimethylaminomethyl)benzaldehyde (**1**) undergoes the benzoin condensation under the usual conditions to form directly 2,2′-bis(dimethylaminomethyl)benzil (**3**) in about 50% yield. Presumably diaminobenzoin **2** was an intermediate which was oxidized by air. The starting compound **1** was prepared from the reaction of the lithium derivative of benzyldimethylamine with N,N-dimethylformamide and from the Grignard reagent of 2-bromobenzyldimethylamine and triethyl orthoformate. The first method is the one of choice. The diaminobenzil **3** was independently synthesized from 2,2′-dimethylbenzil through the dibromo derivative **4** (see Experimental Section).



The structure of the diaminobenzil **3** was supported by analysis and absorption spectra. The infrared spectrum showed a carbonyl peak at 5.98 μ but no hydroxyl peak. The nmr spectrum showed the methyl protons and methylene protons as singlets and an aromatic proton multiplet in the ratio 12:4:8. The mass spectrum showed the highest peak at *m/e* 324, with the base peak at *m/e* 162, and a reasonably intense peak at *m/e* 58 [$(CH_3)_2N^+{=}CH_2$] as might be expected for a benzil[4a] and for a benzyldimethylamine.[4b]

That diaminobenzoin **2** was an intermediate was supported by effecting the reaction under nitrogen in the absence of air. The resulting crude product evidently consisted of mainly **2** as indicated by its nmr spectrum, which also showed the presence of very little **3**. Some of the cyanohydrin **5** may have been present. Recrystallization of this crude product from hot ethanol afforded diaminobenzil **3** in almost quantitative yield.



In addition to the yellow diaminobenzil **3**, there was isolated from the reaction mixture a white solid which was shown by high resolution mass spectrometry and elemental analysis to have the elemental composition $C_{11}N_{16}N_2O_2$. Its infrared and nmr spectra are consistent with hydroxyaminoamide **6**, which would be the partial hydrolysis product of the cyanohydrin **5**. Cyanohydrins are known to be intermediates in the benzoin condensation[5] but formation of a hydroxyamide such as **6** as a by-product appears not to have been reported previously. As might be expected, the methylene group of **6** showed geminal coupling, having an AB pattern in its nmr spectrum which is characteristic of methylene groups *ortho* to an asymmetric center.[6]

(1) Supported by Public Health Service Grant No. CA-04455 from the National Cancer Institute.

(2) (a) W. S. Ide and J. S. Buck, *Org. Reactions*, **4**, 60 (1948); (b) C. D. Shacklett and H. A. Smith, *J. Amer. Chem. Soc.*, **75**, 2655 (1953).

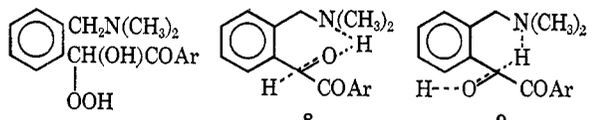
(3) (a) R. Adams and C. S. Marvel, *Org. Syn.*, **1**, 25 (1921); (b) J. van Alphen, *Rec. Trav. Chim. Pays-Bas*, **48**, 1112 (1929); (c) B. Klein, *J. Amer. Chem. Soc.*, **63**, 1474 (1941); (d) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed, Longmans, Green and Co., London, England, 1957, p 715; (e) H. T. Clarke and E. E. Dreger, *Org. Syn.*, **6**, 6 (1926); (f) E. Fischer, *Ann. Chem.*, **211**, 214 (footnote) (1882).

(4) (a) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1967, p 138; (b) pp 297–309.

(5) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, pp 394–397.

(6) J. C. Randall, R. L. Vaulx, M. E. Hobbs, and C. R. Hauser, *J. Org. Chem.*, **30**, 2035 (1965); J. C. Randall, J. J. McKleskey, III, P. Smith, and M. E. Hobbs, *J. Amer. Chem. Soc.*, **86**, 3229 (1964).

The mechanism of the air oxidation of intermediate diaminobenzoin **2** to form diaminobenzil **3** has not been established. We suggest that the function of the tertiary amino group in **2** is to weaken the C–H bond of the methine hydrogen *via* hydrogen bonding in an intermediate such as **8** or **9** and thus facilitate either the formation of the peroxide **7** or transfer of the hydrogen atom to oxygen to form an intermediate radical. A peroxide similar to **7** has been demonstrated to be an intermediate in the air oxidation of benzaldehyde.[7] In addition, hydride transfer from **2** to **1** to form the corresponding amino alcohol and **3** is possible since our material balance accounted for only 53–63%. However, in contrast to our observations, such a mechanism would not require the presence of air.



7 **8** **9**

Although this air oxidation of a benzoin to form a benzil under benzoin condensation conditions appears to be novel, air oxidation of benzoin in the presence of the relatively strong base, alcoholic alkali, has been reported.[8] We have observed that benzoin fails to undergo noticeable air oxidation in the presence of benzyldimethylamine under the usual benzoin condensation conditions; apparently an intramolecular mechanism, as indicated in **8** or **9**, is required for facile autoxidation.

It should be mentioned that the present method of synthesis of aminoaldehyde **1** appears to be more convenient than that reported previously, which involved several steps; the last step of the earlier synthesis involved ozonolysis of 2-(dimethylaminomethyl)styrene.[9]

Experimental Section

Melting and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 137 Infracord. Nmr spectra were taken on a Varian A-60 instrument operating at 60 MHz and are reported relative to tetramethylsilane as internal standard.[10] Mass spectra were obtained on an Associated Electrical Industries MS-902 spectrometer operated at 70 eV.[11] Ether was dried at reflux over lithium aluminum hydride and was used freshly distilled. Anhydrous magnesium sulfate was employed as the drying agent. Analyses were performed by M-H-W Laboratories, Garden City, Mich.

Preparation of 2-(Dimethylaminomethyl)benzaldehyde (1). A. *n*-Butyllithium Method.—Lithiobenzyldimethylamine (**10**) was prepared under nitrogen from 40.5 g (0.30 mol) of benzyldimethylamine in 300 ml of dry ether and 255 ml of 2.35 *M* (0.60 mol) of *n*-butyllithium in hexane[12] (stirred 22 hr) as described previously.[13] To the stirred solution of **10** was added dropwise 44.4 g (0.63 mol) of freshly distilled N,N-dimethylformamide (vigorous reaction). The resulting solution was stirred for 2 hr, then poured onto a mixture of 125 ml of concentrated HCl and 1 kg of crushed ice. The layers were separated. The cold, aqueous acidic solution was washed twice with ether, and made basic with solid NaOH. The resulting mixture was extracted three times with ether, and the combined ethereal extract was dried. The solvent was removed, and the residue was distilled to give 25.6 g (52%) of 2-(dimethylaminomethyl)benzaldehyde (**1**): bp 112–114° (9.5 mm); bp 122–123° (14 mm) [lit.[9] bp 122–123° (14 mm)]; ir (CCl_4) 5.90 μ (C=O); nmr (CCl_4) δ 2.17 (s, 6 H, $2CH_3N$), 3.67 (s, 2 H, $ArCH_2N$), 7.3–7.4 (m, 3 H), 7.7–7.9 (m, 1 H), 10.30 (2, 1 H, CHO).

B. Grignard Method.—2-Bromobenzyldimethylamine, bp 101–103° (10 mm) [lit.[14] bp 104–106° (9 mm)], was prepared in 71% yield from 140 g (0.64 mol) of *o*,α-dibromotoluene[15] and 100 g (2.23 mol) of anhydrous dimethylamine in 100 ml of ether (Dry Ice–acetone bath) by a modification of an earlier procedure.[14]

2-Bromobenzyldimethylamine (64.2 g, 0.30 mol) was converted into its Grignard reagent[14] with 9 g (0.4 g-atom) of magnesium in 250 ml of dry ether, and the solution was stirred for 1 hr. Freshly distilled triethyl orthoformate (59.3 g, 0.40 mol) was added slowly, and the resulting mixture was stirred at reflux for 21 hr. Water (500 ml) was slowly added, and the mixture was extracted continuously with ether for 24 hr. The ethereal solution was extracted with 500 ml of 3 *M* HCl. The acidic solution was heated near reflux for 3 hr, then cooled and made basic with solid NaOH. The resulting mixture was extracted with ether. After drying, the ethereal extract was evaporated, and the residue was distilled to give 17.5 g (40%) of benzyldimethylamine (identified by vpc retention time) and 19.5 g (39%) of **1**, bp 104–106° (8 mm); the nmr spectrum was indistinguishable from that of **1** obtained by method A.

Benzoin Condensation of 2-(Dimethylaminomethyl)benzaldehyde (1). A. Under Usual Conditions (in Air).[2b]—A mixture of 19.5 g of aminoaldehyde **1**, 2.5 g of KCN, and 15 ml each of 95% EtOH and water was refluxed (solution) for 2 hr. The solution was cooled overnight, and the resulting precipitate was removed by filtration to give 5.72 g of yellow needles of 2,2′-bis(dimethylaminomethyl)benzil (**3**), mp 136–145°. The filtrate was refluxed with an additional 3.5 g of KCN for another 2 hr, chilled, and seeded. The resulting precipitate was again removed by filtration to give 2.19 g of yellow needles of **3**, mp 146–151°. The filtrate was extracted with ether and the solvent was removed from the ethereal extract. The residue was steam distilled to give, after recrystallization from 95% EtOH, 1.30 g of **3** as yellow needles, mp 148–151°. The total yield of **3** was 9.21 g (50%). Four crystallizations from EtOH gave an analytical sample: mp 149.5–150.5°; ir (CCl_4) 5.98 μ (C=O); nmr (CCl_4) δ 2.10 (s, 12 H, $4NCH_3$), 3.63 (s. 4 H, $2ArCH_2N$), 7.3–7.6 (m, 8 H); mass spectrum, *m/e* (relative intensity) 324 (25), 250 (26), 207 (10), 179 (18), 178 (11), 163 (13), 162 (100), 132 (11), 119 (43), 91 (48), 58 (16).

Anal. Calcd for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64. Found: C, 74.24; H, 7.64; N, 8.67.

Concentration of the mother liquor obtained from crystallization of the final crop of **3** afforded apparently hydroxy-2-(dimethylaminomethyl)phenylacetamide (**6**, white needles): mp 180–181°; ir ($CHCl_3$) 2.85, 2.88, 2.95, and 5.95 μ; nmr ($CDCl_3$) δ 2.23 (s, 6 H, $2NCH_3$), 3.20 (d, 1 H, J = 13 Hz) and 3.80 (d, 1 H, J = 13 Hz) ($ArCH_2N$), 5.13 [s, 1 H, ArCH(OH)CO], 6.2–6.6 (b, 1 H, OH), 7.1–7.4 (m, 4 H), 7.7–8.0 (b, 2 H, NH_2); mass spectrum, *m/e* (relative intensity) 208 (1), 165 (30), 164 (92), 163 (98), 162 (13), 135 (15), 134 (15), 120 (32), 119 (100), 118 (58), 92 (15), 91 (68), 90 (11), 65 (15), 58 (74), 46 (45), 44 (51).

Anal. Calcd for $C_{11}H_{16}N_2O_2$: C, 63.44; H, 7.74; N, 13.45; mol wt, 208.1212. Found: C, 63.24; H, 7.91; N, 13.56; mol wt (mass spectroscopy), 208.1216.

B. Under Nitrogen.—A solution of 12 g of KCN in 25 ml of water was added to a solution of 16.3 g of aminoaldehyde **1** in 75 ml of 95% EtOH which had been flushed with oxygen-free nitrogen[16] for 2 hr. Nitrogen was passed through the mixture for 0.5 hr and the mixture was refluxed for 2 hr (solution) under a blanket of nitrogen. After cooling, the solution was diluted with 200 ml of water, and nitrogen was bubbled through the resulting mixture for 0.5 hr. The mixture was kept at −20° for 3 days, and then filtered to give 6.87 g of a light yellow solid: nmr ($CDCl_3$) δ 2.03 (s), 2.12 (s), 2.17 (s), 2.25 (s), many small peaks

(7) Reference 5, p 708.
(8) L. Michaelis and E. S. Fetcher, *J. Amer. Chem. Soc.*, **50**, 1246 (1937).
(9) H. W. Bersch and R. Meyer, *Arch. Pharm.*, **287**, 613 (1954).
(10) In nmr descriptions: s = singlet, d = doublet, m = multiplet, b = broad.
(11) We thank Dr. David Rosenthal for the mass spectral determinations, which were done at the Research Triangle Mass Spectrometry Center supported by Special Facility Grant No. FR-00330-01, National Institutes of Health.
(12) Obtained from Alfa Inorganics, Inc., Beverly, Mass.
(13) F. N. Jones and C. R. Hauser, *J. Org. Chem.*, **27**, 701 (1962).
(14) F. N. Jones and C. R. Hauser, *ibid.*, **27**, 4389 (1962).
(15) F. DeTar and L. A. Carpino, *J. Amer. Chem. Soc.*, **78**, 475 (1956).
(16) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley & Sons, Inc., New York, N. Y., 1967, p 393.

2.5–3.1, 3.53 (d, J = 4 Hz), and AB system with doublets centered at 3.75 and 4.17 (J = 12 Hz), 5.97 (d, J = 4 Hz), 7.0–7.3 (m). This crude product was dissolved in 150 ml of absolute EtOH at room temperature, and 700 ml of water was added to give yellow solid, mp 102–130°, the nmr spectrum of which was almost indistinguishable from that of pure **3**. Recrystallization from hot 95% EtOH gave pure **3**, mp and mmp 149–151°.

Independent Synthesis of Diaminobenzil 3.—A solution of 32.76 g (0.205 mol) of bromine in 100 ml of CCl_4 was added dropwise during 4 hr to a hot, stirred solution of 23.8 g (0.1 mol) of 2,2′-dimethylbenzil[2b] in 500 ml of CCl_4 containing a few crystals of benzoyl peroxide; during this time, the reaction mixture was irradiated with a2 50-W sun lamp. The product crystallized on cooling (ice bath) and was filtered. It was then washed with cold CCl_4 to give 17.32 g (44%) of the crude 2,2′-di(bromomethyl)benzil (**4**): mp 145–155° (decomposes to a black tar); ir ($CHCl_3$) 5.97 μ (C=O); nmr ($CDCl_3$) δ 5.04 (s, 4 H, 2Ar-CH_2Br), 7.2–7.7 (m, 8 H). The nmr spectrum of the filtrate obtained on removing crude **4** showed peaks indicating the presence of non-, mono-, and dibrominated methyl groups in the mixture of benzils remaining. Three crystallizations of **4** from CCl_4 gave a sample: mp 155–156° (decomposes to a black tar); mass spectrum, m/e (relative intensity) 398 (0.08), 396 (0.14), 394 (0.08), 318 (0.2), 317 (1.2), 316 (1.7), 315 (1.2), 314 (1.4), 200 (10), 199 (100), 198 (10), 197 (100), 119 (15), 118 (93), 90 (37), 89 (19). The sample was not analytically pure.

The crude dibromobenzil **4** (1.25 g, 3.2 mmol) was added to anhydrous dimethylamine (*ca.* 40 ml) and the mixture stirred at reflux (Dry Ice–acetone condenser) for 2 hr. The mixture was poured into water, dilute $NaHCO_3$ solution was added, and the aqueous mixture was extracted with ether. The ethereal extracts were dried and evaporated. The residue was recrystallized from 95% EtOH to give 0.72 g (70%) of **3** as yellow needles, mp and mmp 149–151°. The infrared spectra of the two samples were indistinguishable.

Failure of Autoxidation of Benzoin in the Presence of a Tertiary Amine.—A solution of benzoin (2.12 g, 0.01 mol), KCN (0.5 g), and benzyldimethylamine (1.35 g, 0.01 mol) in 95% EtOH (40 ml) was refluxed for 24 hr, cooled, and the precipitate (white needles) was filtered to give 1.30 g (62%) of benzoin, mp and mmp 132–133°. Vpc of the mother liquor showed no peak for benzil, but did show a peak for benzoin. Probably more benzoin could have been recovered from the mother liquor.

Registry No.—**1**, 19886-78-3; **3**, 19922-49-7; **4**, 19886-79-4; **6**, 19886-80-7; benzoin, 119-53-9.

Bromination of Silver and Sodium Stilbenecarboxylates

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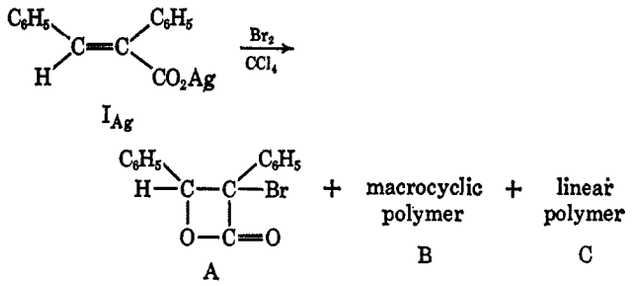
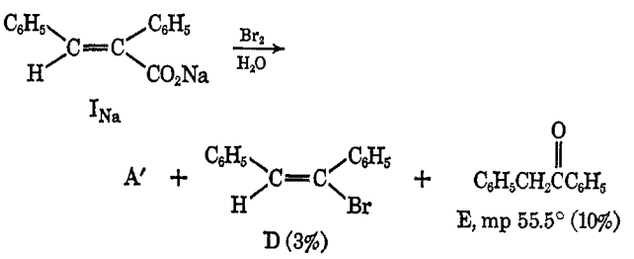
In 1957, Berman and Price[2] reported that sodium *cis*- and *trans*-stilbene-α-carboxylates were brominated to give good yields of the corresponding bromostilbenes. We have been unable to confirm this report, nor have others.[3,4] Our further studies have, however, led to the isolation of bromo-β-lactone A and its macrocyclic (B) and linear polymer C which we wish to report here.



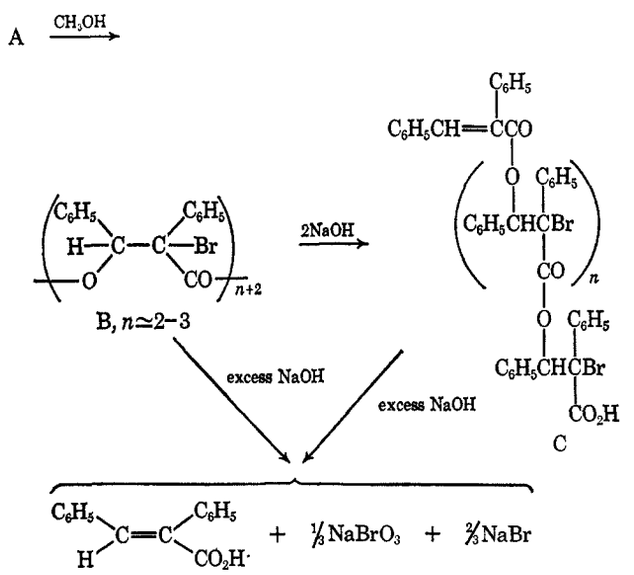
The product obtained from the sodium salt in water almost certainly included a β-lactone (ir absorbance at 1850 cm^{-1}) but it could not be separated by chromatography. Unlike β-lactone A, it failed to produce macrocyclic polymer B on warming in methanol, suggesting A′ may be a geometric isomer of A.



The *trans* salts (II_{Ag} and II_{Na}) gave essentially the same results, except that *no* bromostilbene was isolated from II_{Na} and the recovered acid was I, *not* II.

The formation of a bromolactone is analogous to the similar reaction reported for dimethylmaleic acid.[5] The lactone, readily identified by its ir absorbance at 1850 cm^{-1}, was obtained as an oil.

The macrocyclic polymer was readily converted into a linear polymer by 2 equiv of base. On more vigorous conditions, both polymers were degraded to I and sodium bromate,[6] with consumption of 2 equiv of base per unit. The cleavage of any one of the ester links in B could occur more readily than further reaction of these links in C due to ring strain in B, more favorable



(1) From the Ph.D. Dissertation of H. W. Blunt, 1965.

(2) J. D. Berman and C. C. Price, *J. Amer. Chem. Soc.*, **79**, 5474 (1957).

(3) B. B. Jarvis and W. Protz, Department of Chemistry, University of Maryland, College Park, Md.; *J. Org. Chem.*, **33**, 874 (1968).

(4) W. Brown and S. Jankowski, Argonne National Laboratories, Argonne, Ill., private communication.

(5) D. S. Tarbell and P. D. Bartlett, *J. Amer. Chem. Soc.*, **59**, 408 (1937).

(6) A. G. Cotton and G. Wilkinson ["Advanced Inorganic Chemistry," John Wiley & Sons, Inc., New York, N. Y., 1962] report the equilibrium constant (K = 10^{15}) heavily favors disproportionation of hypobromite to bromate and bromide.