[Contribution from the Noyes Chemical Laboratory, University of Illinois]

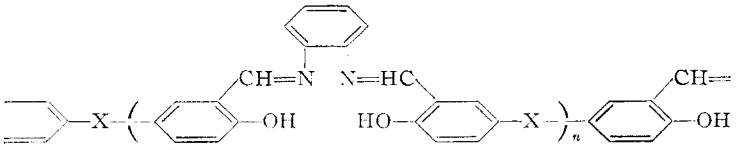
Heat Stability Studies on Chelates from Schiff Bases of Salicylaldehyde Derivatives. II

By C. S. Marvel and N. Tarköy[1]

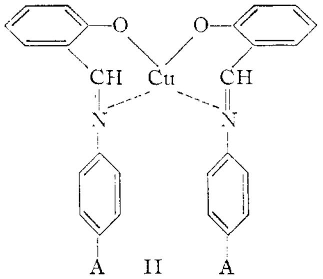
Received October 5, 1957

The influence of the sulfone group in the 5,5′-position of a bis-salicylaldehyde Schiff base upon the heat stabilities of the corresponding metal chelates was studied. Best stabilities were found in the nickel and cadmium chelates, showing, respectively, 0.09 and 0.27% weight loss per hour at 250° in air, the corresponding values for 300° being 1.1 and 1.3%. The greatly enhanced heat stability of these chelates as compared with the 5,5′-methylene-bis-salicylaldehyde series was interpreted in terms of increased acidity of the phenolic groups. The heat degradation of the cobalt, nickel, iron and cadmium chelates seems to be a thermal process.

In continuation of former work[2] on metal chelated aromatic polymeric Schiff bases of type I as an approach to the synthesis of heat-stable polymeric materials, the present study deals with the influence of electron-withdrawing groups, such as X in formula I, on the stability of these chelates.

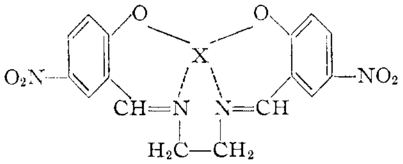

I, X = -SO_2-

Other factors being held constant, two electronic effects can be thought to enhance the stability of chelates of type I: (1) increasing the electron availability of the amine component of the Schiff base,[3] (2) increasing the acidity of the phenolic groups. The effectiveness of the first idea was clearly demonstrated by Calvin,[4] who reported that in compound II the stability of the metal chelate parallels the basicity of the amine and the order of increasing stability is A = $-NO_2$, $-SO_3Na$, $-C_6H_5$, -H, $-CH_3$, -OH, $-OCH_3$.

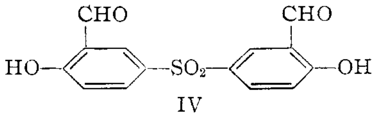

II

In order to test the effect of increasing phenol acidity on the stability of chelates of type I, the monomeric model compound III was prepared from 5-nitrosalicylaldehyde[5] and ethylenediamine. The chelates of III with the divalent metals cobalt, nickel, iron, copper and cadmium showed fair stability for short periods at 250° in air, but decomposed almost totally in 24 hours. Attributing this result mainly to the inherent instability of nitro-compounds, it was decided to synthesize a monomer of type I where X = $-SO_2-$. This group is sufficiently electron withdrawing, is known for high thermal stability[6] and seems also sterically suitable.[7]

Attempts to introduce aldehyde groups into the 3- and 3′-positions of 4,4-dihydroxy-diphenyl sulfone by either the Duff or Reimer–Tiemann reactions failed.[8]


III

The desired bis-salicylaldehyde 5,5′-sulfone (IV) then was obtained by the sequence of reactions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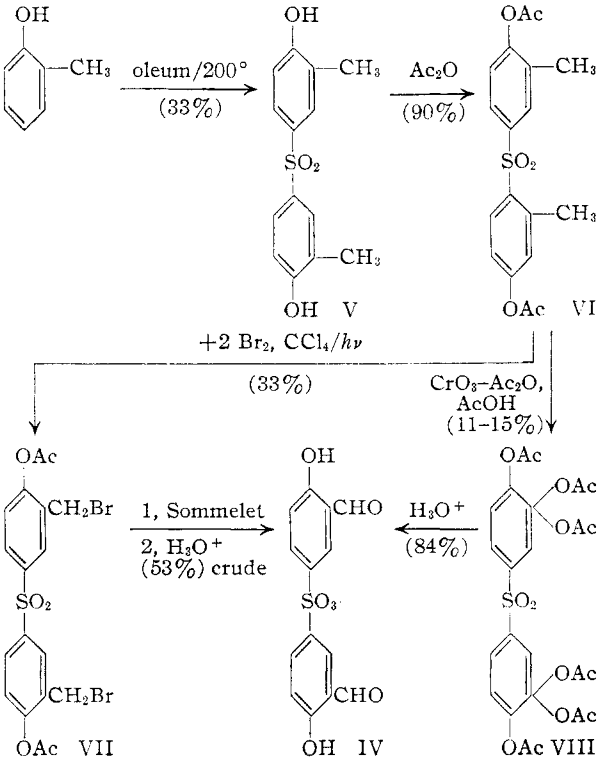

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[1] The work discussed herein was performed under contract number AF-33(616)-3772 with the Materials Laboratory of Wright Air Development Center, Wright–Patterson Air Force Base, Ohio; Lt. L. E. Coleman and Lt. Paul D. Shaw, project engineers.

[2] C. S. Marvel and N. Tarköy, This Journal, **79**, 6000 (1957).

[3] For the sake of resonance, however, only aromatic amines are desirable.

The condensation of *o*-cresol with fuming sulfuric acid furnished 3,3′-dimethyl-4,4′-dihydroxy-diphenyl sulfone (V),[9] which on treatment with acetic anhydride gave the corresponding diacetate VI. This diacetate VI could be converted by slow bromination to the bis-monobromide VII,[10] which by a Sommelet reaction furnished the desired bis-salicylaldehyde 5,5′-sulfone. An alternate route consisted in oxidizing the diacetate VI with chromic acid–acetic anhydride to the hexaacetate VIII, which upon warming with acid furnished the desired dialdehyde IV. This oxidative synthesis proved to be more useful for preparative purposes.

Acetic acid exhibited the same catalytic effect on the formation of the polymeric Schiff base (see formula I, X = $-SO_2-$), as discussed in the corresponding methylene-bis-salicylaldehyde series.[2] The polymer I shows an inherent viscosity of 0.05 (in dimethylformamide, concentration 1 g./100 ml.) which indicates a molecular weight of approximately 10,000; microanalysis and infrared data [bands in Nujol at 1150 and 1320 cm.$^{-1}$ (sulfone), 1620 cm.$^{-1}$ (conjugated —CH=N), a weak band at 1660 cm.$^{-1}$ (aldehyde end groups), broadness in the 2500–3200 cm.$^{-1}$ region (chelated OH) and a distinct band at 3550 cm.$^{-1}$ (methanol)] suggest that there is 1 mole of methanol held per monomer unit and the end groups are aldehyde.

The polymer I was chelated with the divalent metals cobalt, iron, nickel, copper and cadmium and the thermal stability of these chelates was tested by means of an exact thermobalance similar to that described by Winslow and Matreyek.[11] The results are given in Table I.

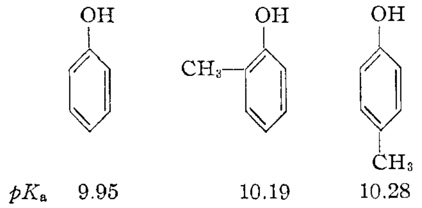
TABLE I

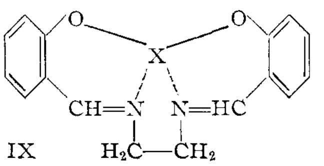
HEAT STABILITY DATA ON CHELATES OF POLYMER I

The tests were run on 200-mg. samples, placed in Pyrex vials of 8 mm. diameter and 53 mm. height. The average weight loss was calculated mostly over a 23-hr. heating period, with hourly readings during the first 7 hr. Accuracy of weighing was ±0.05 mg., maximum deviation from the indicated temperature being held within ±3°. Readings were started after 1 hr. heating, in order to eliminate drying loss errors and the hot/cold error of the balance system. At 300° in air the cadmium chelate showed an average weight loss of 1.3%/hr., the nickel chelate 1.1%/hr.

Chelating metal	Average % weight loss/hour at 250° In air	In nitrogen
Co	0.64	0.71
Ni	0.09	0.15
Fe	1.20	1.14
Cd	0.27	0.69
Cu	2.24	0.67

The striking enhancement of heat stability of these chelates (*e.g.*, 0.3% weight loss for Ni chelate in 3 hr. at 250°) compared with the methylene-bis-salicylaldehyde series (11–26% weight loss in 3 hr. at 250°) supports the idea of correlating phenol acidity to chelate stability. It might prove equally useful to think of the reported[2] non-steric destabilization of chelates of type IX, which occurs on introducing a CH_3- group in *o*- or *p*-position to the OH group, in terms of lowered acidity of the corresponding phenols.





IX

The interesting relative independence of the thermal stability values from the atmosphere (nitrogen or air) for the nickel, cobalt, iron and cadmium chelate suggests that the degradation of these compounds is thermal rather than oxidative.

Experimental[12]

Bis-5-nitrosalicylaldehyde-ethylenediimine (III).—Ethanolic solutions of 5-nitrosalicylaldehyde[5] and ethylenediamine, mixed in equimolar ratio, furnish immediately the Schiff base as a yellow powdery precipitate. Because of the extreme insolubility of this product, purification of the crude material was accomplished by sublimation at 240° (0.01 mm.) for six hours yielding a yellow powder, m.p. 275–277°.

Anal. Calcd. for $C_{16}H_{14}N_4O_6$: C, 53.63; H, 3.91. Found: C, 54.03; H, 4.13.

Chelation of 5-Nitrosalicylaldehyde-ethylenediimine (III) with Metals.—Upon mixing a solution of sublimed 5-nitrosalicylaldehyde-ethylenediimine in hot dimethylformamide (130 ml. will dissolve 1.0 g.) with equimolar amounts of bivalent acetates (iron, cobalt, copper, cadmium, nickel) dissolved in dimethylformamide, the colored metal chelates immediately precipitate. Only zinc failed to give a precipitate under these conditions. The colors of the precipitates are: iron = brown, cobalt = dark red, copper = greenish-gray, cadmium = light yellow, nickel = orange. None of these chelates was melted at 340°; the iron chelate violently decomposed around 330°. The precipitates were isolated by filtration, washed with dimethylformamide, water, ethanol and ether and (because of their insolubility) analyzed in the crude state after being dried at 80° (0.01 mm.) for 20 hours.

Anal. Calcd. for $C_{16}H_{12}N_4O_6Co$: C, 46.28; H, 2.89. Found: C, 46.28; H, 3.17. Calcd. for $C_{16}H_{12}N_4O_6Ni$: C, 46.30; H, 2.90. Found: C, 46.99; H, 2.90. Calcd. for $C_{16}H_{12}N_4O_6Fe$: C, 46.62; H, 2.19. Found: C, 45.21; H, 2.83. Calcd. for $C_{16}H_{12}N_4O_6Cd$: C, 40.99; H, 2.56. Found: C, 41.67; H, 2.60. Calcd. for $C_{16}H_{12}N_4O_6Cu$: C, 45.80; H, 2.86. Found: C, 43.64; H, 3.12.

3,3′-Dimethyl-4,4′-dihydroxy-diphenyl sulfone (V) was prepared according to a slightly modified procedure of Chattaway and Bell[9] as follows. One hundred grams of

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[4] M. Calvin and R. H. Bailes, THIS JOURNAL, **68**, 953 (1946).

[5] H. Ichibagase and S. Terada, *J. Pharm. Soc. Japan*, **72**, 876 (1952); *C. A.*, **47**, 6413a, b, c, d (1953); W. V. Miller, *Ber.*, **20**, 1927 (1887). The product can be sublimed without decomposition at 80° (0.01 mm.).

[6] W. E. Truce and D. D. Emrick, THIS JOURNAL, **78**, 6130 (1956).

[7] H. C. Brown, D. H. McDaniel and O. Häfliger, Chapter 14 in "Determination of Organic Structures by Physical Methods" by E. A. Braude and F. C. Nachod, Academic Press, Inc., New York, N. Y., 1955, p. 607.

[8] The Duff reaction is known to fail in the case of electron-seeking *p*-substituents; *cf.* L. M. Liggett and H. Diehl, *Proc. Iowa Acad. Sci.*, **52**, 191 (1945); J. C. Duff, *J. Chem. Soc.*, 547 (1941). The failure of the Reimer–Tiemann reaction probably is due also to the electronegativity of the *p*-sulfone group.

[9] F. D. Chattaway and A. E. Bell, *J. Chem. Soc.*, 43 (1934).

[10] Attempts to prepare the corresponding bis-dibromide proved unsuccessful.

[11] F. H. Winslow and W. Matreyek, *J. Polymer Sci.*, **22**, 315 (1956).

[12] The melting points are not corrected.

TABLE II

HEAT STABILITY DATA ON CHELATES OF III

Temperature 250°, in air; 200-mg. samples of chelate.

Chelate	Weight loss, %				
	1 hr.	2 hr.	3 hr.	4 hr.	20 hr.
Cd	0.5	0.5	0.5	0.5	54
Ni	6.5	6.5	6.5	6.5	Over 80
Fe	6.5	Over 80	..	..	.....
Cu	11.5	11.5	11.5	11.5	Over 80
Co	13.0	13.2	13.5	14.5	Over 80

freshly distilled *o*-cresol (b.p. 80° (11 mm.)) was heated under reflux (temperature of the oil-bath 180–185°) with a mixture of 12 ml. of 98% sulfuric acid and 14 ml. of 30% oleum for four hours. After that time the red liquid was poured into 2 liters of cold diluted sodium hydroxide solution. The alkaline solution was extracted with ether, the extracts discarded, the water layer acidified with concentrated hydrochloric acid and let stand overnight. The crude product was isolated by filtration, washed with buffer solution (*p*H = 7) and with water. After recrystallization from 50% ethanol (charcoal) the white crystals (42 g. = 33%) melted at 265–266° (uncorr.); literature = 268°.

Bis-salicylaldehyde 5,5'-Sulfone (IV).—Forty-three grams of 3,3'-dimethyl-4,4'-dihydroxy-diphenyl sulfone (0.155 mole), m.p. 265–266°, was heated under reflux with 430 ml. of acetic anhydride (reagent grade) for one hour. To the cold (5°) solution a cold (16°) mixture of 430 ml. of glacial acetic acid and 60 ml. of concentrated sulfuric acid was added slowly with stirring. The temperature of the mixture was kept at 5° (±3°) and over a period of one hour, with continuous stirring, 70 g. (0.700 mole) of chromic acid (Merck) was added slowly. After the addition was complete, stirring of the reaction mixture (temperature 5–10°) was continued for three hours. After this time the mixture was poured on about 8 liters of ice–water mixture and let stand overnight. The clear green solution was decanted, the thick residue dissolved in chloroform–ether (~ 1:2), washed with ferrous sulfate solution, with sodium carbonate solution (until the washing was alkaline), with water and dried with magnesium sulfate. The colorless solution was concentrated to about 50 ml., 500 ml. of ether added and the separated white crystals collected. The yield was 14.66 g., m.p. 166–170°. After recrystallization from acetone–petroleum ether, the hexaacetate weighed 10.590 g. (12% yield; it was found on repetition that the yield varies between 11 and 15%) and melted at 177–179°. The analytical sample was recrystallized three times from acetone–petroleum ether and melted at 178–179°.

Anal. Calcd. for $C_{28}H_{26}O_{14}S$: C, 52.52; H, 4.38. Found: C, 52.59; H, 4.53.

Twenty grams of this material was dissolved in a mixture of 700 ml. of ethanol, 233 ml. of water and 47 ml. of 97% sulfuric acid and heated under reflux for four hours. On cooling to 5° white crystals separated; they were washed with sodium acetate solution, with water and dried. The yield was 8.908 g. of white crystals (84% yield), m.p. 215–216°. The analytical sample of the bis-salicylaldehyde 5,5'-sulfone was recrystallized three times from acetone–petroleum ether and sublimed at 160° (0.01 mm.), m.p. 216–217°. The infrared spectrum (Nujol) shows bands at 1150 and 1320 cm.$^{-1}$ (sulfone), 1660 cm.$^{-1}$ (chelated-CHO) broadness in the 2500–3400 cm.$^{-1}$ region (chelated-OH).

Anal. Calcd. for $C_{14}H_{10}O_6S$: C, 54.90; H, 3.27; S, 10.45. Found: C, 55.04; H, 3.38; S, 10.41.

***o*-Dicresoldiacetate 4,4'-Sulfone.**—Twenty grams of the dicresol sulfone V (m.p. 268°) was heated under reflux with 150 ml. of acetic anhydride (reagent grade) for one hour. After the usual working up procedure, the crude product was recrystallized from ethanol. The yield was 19.5 g. m.p. 132–133° (90%).

Forty-two grams (0.116 mole, m.p. 132–133°) of *o*-dicresoldiacetate 4,4'-sulfone (VI) was dissolved in 800 ml. of pure carbon tetrachloride at reflux temperature. The reaction vessel was irradiated by the light of a 1000-watt bulb. Into this well-stirred solution a solution of 37.2 g. of bromine (4 × 0.116 mole) in 240 ml. of carbon tetrachloride was added slowly for 6 hours. The carbon tetrachloride was refluxed during the whole operation. After addition of bromine was completed, the reaction mixture was heated and stirred for 15 minutes, then cooled to 20°, the separated crystals isolated by filtration and recrystallized from acetone–petroleum ether. The yield was 20.0 g. of white crystals (33%), m.p. 177–178°. The analytical sample was recrystallized five times from acetone–petroleum ether and melted at 179.0–180.0°.

Anal. Calcd. for $C_{18}H_{16}O_6Br_2S$: C, 41.54; H, 3.08; Br, 30.77. Found: C, 41.84; H, 3.37; Br, 31.06.

One gram of this dibromide (VII), m.p. 177–178° (0.00192 mole), was dissolved in 12 ml. of pure chloroform and warmed on the water-bath for one-half hour with a solution of 0.540 g. (2 × 0.00192 mole) of hexamethylenetetramine in 7 ml. of chloroform; 1.47 g. (95%) of white crystals of the quaternary salt formed, which was heated under reflux in 30 ml. of 60% ethanol overnight (stirring). Then 3 ml. of concentrated hydrochloric acid was added and heating under reflux continued for one hour longer. After dilution with water and the usual working up procedure, 300 mg. of oily material containing some crystals was obtained. This on sublimation 160° (0.01 mm.) gave white crystals, m.p. 210–212° (mixed melting point with authentic sample of disalicylaldehyde 5,5'-sulfone, 213–214°). The infrared spectrum (Nujol) was identical with that of disalicylaldehyde 5,5'-sulfone obtained by the oxidative method.

Polymer Obtained from Salicylaldehyde 4,4'-Sulfone and *o*-Phenylenediamine (I).—One and two-hundredths grams of salicylaldehyde 5,5'-sulfone (IV) (0.0033 mole), m.p. 216–217°, was dissolved in 25 ml. of tetrahydrofuran and 100 ml. of glacial acetic acid. To this solution was added a well-stirred solution of pure *o*-phenylenediamine (m.p. 103°, 0.0033 mole) in 10 ml. of glacial acetic acid. On warming on the water-bath in about 10 seconds a bright yellow precipitate formed; after addition of 50 ml. of methanol, stirring was continued for 30 minutes. The product was isolated by filtration, washed with methanol and ether and dried. The yield was 975 mg. of yellow powder (78% yield), with an inherent viscosity of 0.05 (1% solution in dimethylformamide). The infrared spectrum (Nujol) shows bands at 1150 and 1920 cm.$^{-1}$ (sulfone), 1620 cm.$^{-1}$ (conjugated—CH=N—), a weak band at 1660 cm.$^{-1}$ (chelated aldehyde end groups), broadness in the 2500–3300 cm.$^{-1}$ region (chelated–OH) and a distinct band at 3350 cm.$^{-1}$ (methanol).

Anal. Calcd. for $(C_{20}H_{14}N_2O_4S \cdot CH_3OH)_n$: C, 61.50; H, 4.38; N, 6.83. Found: C, 61.82; H, 4.19; N, 6.62.

Chelation of the Polymer Obtained from *o*-Phenylenediamine and Salicylaldehyde 5,5'-Sulfone (I) with Metals.—The divalent metal acetates of cobalt, nickel, iron, copper, zinc and cadmium were dissolved in tetrahydrofuran (in some cases addition of water or acetic acid is necessary to complete dissolution) to give 0.1 molar solutions. To a stirred solution of 600 mg. of polymer in 10 ml. of dimethylformamide 36 ml. of the metal acetate solution was added slowly and stirring was continued in a closed vessel at room temperature for two days. The precipitates are colored: nickel = red-brown, cobalt = brown, iron = brown-violet, copper = light olive-green. The zinc chelate (yellow) always had a low carbon content and was not further examined. The cadmium chelate formed only under the following conditions: 419 mg. of polymer was dissolved in 10 ml. of dimethylformamide and mixed with a solution of 408 mg. (1.5 mmoles) of $Cd(OAc)_2 \cdot 2H_2O$ in 10 ml. of dimethylformamide; on heating this mixture under reflux for 20 minutes a light yellow precipitate of the cadmium complex formed. After filtering, the precipitates were washed with dimethylformamide, water, ethanol and ether, dried at room temperature (0.01 mm.) for two days and analyzed. The samples were hygroscopic; the erratic analytical values undoubtedly are due to partial solvation of the polymer chelates.

Anal. Calcd. for $(C_{20}H_{12}N_2O_4SFe)_n$: C, 55.53; H, 2.78; N, 6.48. Found: C, 56.18; H, 3.76; N, 5.85. Calcd. for $(C_{20}H_{12}N_2O_4SCo \cdot H_2O \cdot CH_3OH)_n$ (hexacovalent Co assumed): C, 51.97; H, 3.72; N, 5.77. C, 51.80; H, 3.81; N, 5.58.

Anal. Calcd. for $(C_{20}H_{12}N_2O_4SNi)_n$: C, 55.25; H, 2.70; N, 6.45. Found: C, 55.66; H, 3.50; N, 5.83. Calcd. for $(C_{20}H_{12}N_2O_4SCu)_n$: C, 54.65; H, 2.74; N, 6.37. Found: C, 55.10; H, 3.85; N, 5.51. Calcd. for $(C_{20}H_{12}N_2O_4SCd)_n$: C, 49.14; H, 2.46; N, 5.73. Found: C, 48.27; H, 4.30; N, 4.74.

We are indebted to Mr. Jozsef Nemeth of the Microanalytical Laboratory of the University of Illinois for the microanalyses, and to Mr. James Brader of the University of Illinois for the infrared data.

URBANA, ILLINOIS

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Synthesis of Aromatic Boronic Acids. Aldehydo Boronic Acids and a Boronic Acid Analog of Tyrosine[1]

BY H. R. SNYDER, ALBERT J. REEDY[2] AND WM. J. LENNARZ

RECEIVED SEPTEMBER 5, 1957

The synthesis of *o*- and *p*-bromomethylbenzeneboronic acids by the direct bromination of the tolueneboronic acids is described. *o*- and *p*-formylbenzeneboronic acids are prepared and some of their reactions with carbonyl reagents are studied. *p*-Bromomethylbenzeneboronic acid is converted to an analog of tyrosine having the boronic acid function in the place of the phenolic hydroxyl group.

Because of the numerous useful transformations to which benzyl halides and aromatic aldehydes can be submitted, it appeared probable that the substituted benzeneboronic acids carrying bromomethyl and aldehyde functions attached to the ring would be important intermediates for the synthesis of a variety of boron-containing aromatic compounds. Accordingly, a study of the synthesis and properties of *o*- and *p*-bromomethylbenzeneboronic acids and *o*- and *p*-formylbenzeneboronic acids was undertaken. Part of this work has been anticipated by Torssell,[3] who recently described the synthesis of all these compounds and the corresponding *m*-isomers. His method consisted in the introduction of one or two atoms of bromine into the methyl groups of the tolueneboronic acids, the aldehydes being obtained by hydrolysis of the dibromo derivatives. He chose the Ziegler reagent for the bromination because of the earlier report by Kuivila and Hendrickson[4] of the rapid brominolysis of aromatic boronic acids, whereby, for example, benzeneboronic acid is converted to bromobenzene. However, the experiments of Kuivila and Hendrickson[4] were conducted in 20% acetic acid, and it seemed to us by no means certain that direct bromination in anhydrous medium was excluded. It was found that in carbon tetrachloride solution and under the influence of light, *o*- and *p*-tolueneboronic acids were converted to the monobromomethyl derivatives in yields of about 90%. Torssell[3] obtained these compounds *via* the Ziegler bromination in approximately the same yield, and that method was also used in the present work.

The aldehyde synthesis contemplated consisted in the application of the Sommelet synthesis to the bromomethyl derivatives. This method proved satisfactory for the *p*-isomer, but with the *o*-bromomethyl derivative the yield was so low that it was impractical. The method developed for the *o*-aldehyde was essentially the same as that disclosed by Torssell,[3] except that we carried out the hydrolysis of the dibromomethyl derivative with alkali, whereas he employed sulfurous acid.

When *o*-bromomethylbenzeneboronic acid was extracted into aqueous 15% potassium hydroxide and the solution allowed to stand at room temperature for one hour before acidification, the product was the same as that obtained by Torssell[3] by hydrolysis with hot water and formulated as the cyclic ester I. This substance proved to be a remarkably stable boronic acid derivative. It resisted the action of dehydrating agents, being recovered unchanged even after treatment with refluxing thionyl chloride. It was also unexpectedly resistant to hydrolytic cleavage of the boronic function by acids or bases. For example, it was recovered almost quantitatively after refluxing for three hours with 10% hydrochloric acid, and even after fourteen hours the recovery was 50%. By contrast, only 10% of a sample of *p*-tolueneboronic acid was recovered after 1.5 hours, hydrolysis to toluene and boric acid having proceeded extensively. Similarly, compound I was recovered quantitatively after three hours of refluxing with 15% potassium hydroxide.

The low yield of the *o*-formylbenzeneboronic acid from the Sommelet reaction was due to the occurrence of another reaction of the primary amine which is an intermediate[5] in the Sommelet process. Under slightly different conditions from those under which the aldehydo boronic acid was obtained, there was produced a high melting substance whose analysis agreed with that calculated on the assumption of the addition of a molecule of formaldehyde and the loss of two molecules of water from the aminomethylbenzeneboronic acid. Of the structures considered (II, III, IV), only IV seems to accommodate the fact that the substance is soluble in dilute acids but insoluble in water and dilute alkali. If this is the actual structure the eight-membered ring is not highly stable, for conditions of diazotization convert the substance to the cyclic ester I.

p-Formylbenzeneboronic acid was found to undergo a number of the reactions characteristic of aromatic aldehydes, but in general only those

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[1] Part of this work was supported by a grant [AT(11-1)-314] from the U. S. Atomic Energy Commission.

[2] Phillips Petroleum Co. Fellow, 1955–1956.

[3] K. Torssell, *Arkiv Kemi*, **10**, 507 (1957).

[4] H. F. Kuivila and A. R. Hendrickson, THIS JOURNAL, **74**, 5068 (1952).

[5] S. J. Angyal, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954 p. 197.