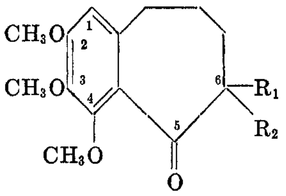
[Contribution from the Chemical Laboratory of the University of Utah]

SEVEN-MEMBERED RING COMPOUNDS.* VI.[1] BROMINATION OF 2,3,4-TRIMETHOXYBENZOSUBERONE

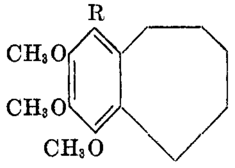
PETE D. GARDNER[2] AND W. J. HORTON

Received September 9, 1953

The work reported herein arose from an attempt to introduce a carbon chain in the 6-position of I. It was expected that the bromination of I using two moles of bromine would give 1,6-dibromo-2,3,4-trimethoxybenzosuberone which could then be treated with sodium acetoacetic ester.



I $R_1 = R_2 = H$
II $R_1 = R_2 = Br$
III $R_1 = H$; $R_2 = Br$
IV $R_1 = H$; $R_2 = I$



V R = H
VI R = Br

The bromination proceeded rapidly at 0° to yield a crystalline dibromide (91%). The reaction with sodium acetoacetic ester produced a monobromide (III) (93%). Similarly sodium malonic ester gave III (84%). The infrared absorption curve of III showed presence of the carbonyl group and the absence of non-benzenoid unsaturation thus eliminating dehydrohalogenation. Hence the attempted alkylations cleanly replaced one bromine by a hydrogen atom.

The identical monobromide (III) was produced (72%) if one mole of bromine was added to I. A mole of bromine on III gave the original dibromide which resisted further bromination. The dibromide was recovered (80%) when treated with bromine even though the solution was warmed briefly.

The properties of III suggested that the dibromide could not be the 1,6-compound since the remaining bromine atom in III could easily be replaced by hydrogen or by iodine. The monobromide liberated iodine from acidified potassium iodide suggesting an α-bromoketone. When it was refluxed with sodium iodide in acetone, a monoiodide was obtained (83%). Permanganate oxidation of III conclusively eliminated the 1-position since 3,4,5-trimethoxyphthalic anhydride was obtained.

With other reagents, the monobromide was decidedly unreactive. It was negative to boiling alcoholic silver nitrate and was recovered (83%) after 30 minutes in refluxing γ-collidine. It was also recovered after 7 hours in hot

---

* Presented at the W. E. Bachmann Memorial Session, Organic Chemistry Division, American Chemical Society, Chicago Meeting, September 8, 1953.

[1] The preceding paper is (1).

[2] From the doctoral dissertation of P. D. Gardner.

methanolic sodium acetoacetic ester. Methanolic sodium methoxide however gave a dark red solution and no crystalline product.

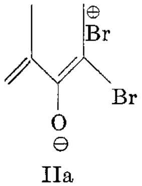
The dibromide was recovered from refluxing sodium acetate-acetic acid after 10 hours and it failed to react with boiling alcoholic silver nitrate or with 1.2% methanolic sulfuric acid. With methanolic potassium hydroxide, dark gums were formed which resisted purification. The dibromide gave III in excellent yield when refluxed with alcoholic sodium iodide but with a solution of sodium iodide in acetone, the monoiodide IV was obtained. Zinc dust in methanol or a palladium-catalyzed hydrogenation in ethanol-pyridine replaced both bromine atoms by hydrogen. However, if the catalytic reduction was conducted in acetic acid, the monobromide III, the ketone I, or the phenol VII (see below) could be obtained depending on the duration of the hydrogenation. The formula, II, best accounts for the behavior of the dibromide.

We had reached the above conclusions when we discovered a brief reference (2) to the bromination of I using pyridinium bromide perbromide. The product was reported to be stable to potassium acetate-acetic acid and was assigned the structure, 1-bromo-2,3,4-trimethoxybenzosuberone. Due to the proximity of the melting point to that of our monobromide III, a sample was obtained by the reported procedure (2) and found to be identical. It seems certain therefore that this compound is 6-bromo-2,3,4-trimethoxybenzosuberone.

An independent synthesis of 1-bromo-2,3,4-trimethoxybenzosuberone was attempted. The known δ-3,4,5-trimethoxyphenylvaleric acid (3) was brominated and the product gave 2-bromo-3,4,5-trimethoxybenzoic acid by permanganate oxidation. Cyclization of the brominated valeric acid resulted in loss of bromine with the production of I.

The bromosuberane VI was prepared from V and found to be similar to the monobromide III in inertness to silver nitrate or γ-collidine. When it was oxidized with permanganate, the expected 6-bromo-3,4,5-trimethoxyphthalic anhydride was obtained.

In order to draw together the various reactions of the dibromide II, it is proposed that the formation of a "positive bromine" is assisted not only by the presence of the second bromine atom but also by the electromeric shift to IIa, a form having stability due to coplanarity of the 5–6 double bond and the benzene ring (4). The more positive character of di- as compared to mono-halo compounds and of bromo as compared to chloro compounds is known (5, 6). The positive bromine might then be removed by (A) reduction with sodium iodide in alcohol or acetone, or by hydrogen iodide or (B) by reaction with the anion from acetoacetic ester or malonic ester. Due to the large excess of aceto-



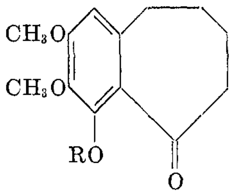
IIa

acetic ester anion, the brominated acetoacetic ester would react with the anion to give diethyl diacetylsuccinate. A high-boiling by-product was noted but not identified. It is well known that positive bromine compounds may brominate other molecules (6–8).

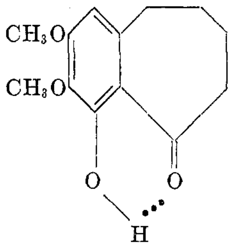
It must follow that the monoiodide IV must similarly be a "positive iodine" compound since the iodine is replaceable by hydrogen iodide or sodium acetoacetic ester in contrast to the monobromide. The replacement of iodine in IV using sodium acetate-acetic acid departs from the previous experience on these bromo compounds with sodium acetate. The appearance of free iodine suggests that concurrent iodide ion formation in glacial acetic acid provides hydrogen iodide which understandably reacts with IV.

In the case of the monobromide III, the "positive bromine" formation is facilitated by the attack of a proton from hydrogen iodide on the oxygen atom of III. The reaction of sodium iodide in acetone with III without release of free iodine probably involves a rearward approach (9). It then appears that the acetate ion and acetoacetic ester or malonic ester anions do not react with III because the halide is less positive than that in II or in the monoiodide IV.

In the catalytic hydrogenation of the dibromo compound II in acetic acid, a phenolic compound VII was obtained when the hydrogenation time was 3.5 hours. The hydrogen bromide produced in the reaction was the responsible reagent since the loss of the methyl group did not occur in alcohol-pyridine solution. Further, treating I with hydrogen bromide-acetic acid at room temperature for 4.5 hours gave VII (82%). It is of interest that the dibromide II is converted to III (70%) when the amount of catalyst is decreased and the time is shortened to 2.5 hours. The phenol VII was remethylated with dimethyl sulfate, since it is inert to diazomethane (11), producing I and thus indicating the absence of other changes in the original reaction. Ethylation of VII gave VIII since permanganate oxidation of VIII gave known 3-ethoxy-4,5-dimethoxyphthalic anhydride. The hydroxyl group in VII is thus established at position 4.



VII R = H
VIII R = C_2H_5



IX

The selective dealkylation of alkyl aryl ethers adjacent to a carbonyl group is known (10–13) but the removal of a methyl group under extremely mild conditions is possibly a feature of the proximity of the carbonyl oxygen in 4-alkoxybenzosuberones (13). The tentative formulation of a chelate form IX is suggested in analogy to known cases in 5- or 6-membered ring systems (11, 14). Further support for IX is obtained from the infrared absorption curve of VII

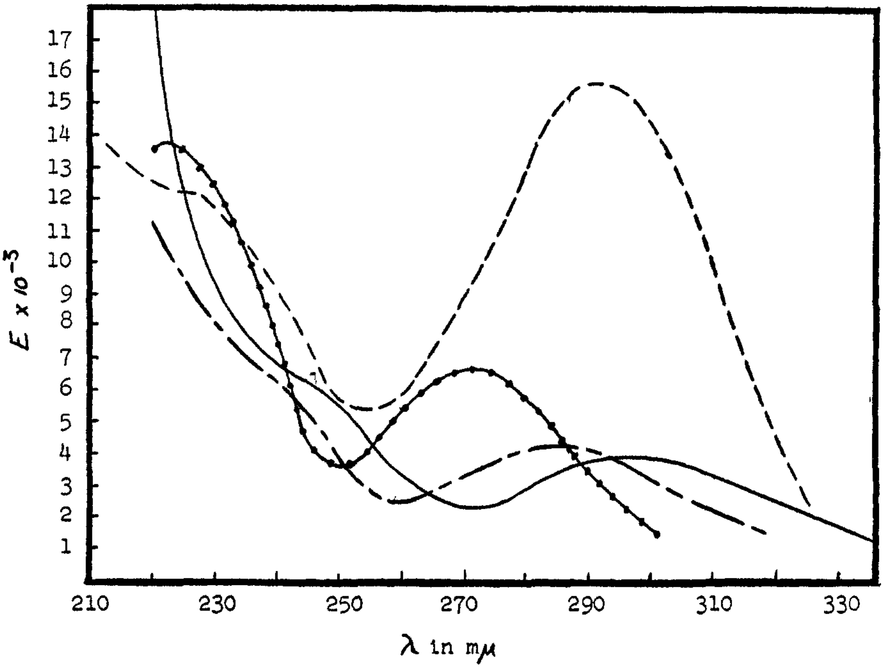


Fig. 1. Ultraviolet Absorption Spectra of:

2,3,4-Trimethoxybenzosuberone;	• • • • • • • • • • • • • • • • • •	I
2,3-Dimethoxy-4-hydroxybenzosuberone;	- - - - - - - - - - - - - - - - - -	VII
2,3,4-Trimethoxy-6-bromobenzosuberone;	— - — - — - — - — - — - —	III or IV
2,3,4-Trimethoxy-6,6-dibromobenzosuberone;	————————————	II.

which lacks bands for carbonyl or hydroxy groups and from the ultraviolet absorption curves of IX and I when compared with analogous 6- or 7-membered ring compounds (Fig. 1) (13, 14).

Acknowledgement. A Frederick Gardner Cottrell grant and financial assistance from the Utah Chapter of Sigma Xi are gratefully acknowledged. A portion of this work was completed in the laboratories of Merck and Company, Inc. We are indebted for their coöperation.

EXPERIMENTAL[3]

6,6-Dibromo-2,3,4-trimethoxybenzosuberone (II) (*a*) *From I.* A solution of 1.6 g. (0.0064 mole) of I suspended in 25 cc. of anhydrous ether was cooled to 0° and 2.24 g. (0.014 mole) of bromine in 5 cc. of anhydrous carbon tetrachloride was added dropwise during 20 minutes with swirling. The solution was allowed to warm to 20° and was then poured into 100 cc. of ice-water. The ether layer, washed twice with 5% sodium bicarbonate and with water, was dried and the ether was removed *in vacuo*. The solid residue deposited 2.24 g. (0.0055 mole) of nearly colorless flat rods or blades, m.p. 111–112.5° from ethyl acetate-petroleum ether (30–60°). Material from the mother liquor, crystallized from the same solvent, amounted to 0.13 g. (0.0003 mole) m.p. 105–109° (91%). Further purification from this solvent gave material m.p. 112–113°.

---

[3] Melting points are corrected.

Anal. Calc'd for $C_{14}H_{16}Br_2O_4$: C, 41.20; H, 3.95; Br, 39.17.
Found: C, 41.44; H, 3.83; Br, 39.23.

Recovered unreacted material below invariably melted at 125–126.5° but had an identical analysis and infrared absorption spectrum. Seeding with the higher modification produced this second form but the reverse experiment failed. If the lower-melting form was inserted in the bath at 116°, a double melting point was observed. The compound gave a bright orange color in concentrated sulfuric acid. It failed to react with boiling alcoholic silver nitrate. When refluxed with a solution of sodium acetate in acetic acid for 10 hours, 94% of II was recovered. The dibromide II was recovered (80%) after refluxing with 1 mole of bromine in 2:1 carbon tetrachloride-ether for 5 minutes. The dibromide failed to give a 2,4-dinitrophenylhydrazone. Hot methanolic potassium hydroxide gave a dark brown gum which yielded no crystalline product. When refluxed in 1.2% methanolic sulfuric acid, the dibromide was recovered unchanged.

(*b*) *From III.* When the monobromide below (1.082 g., 0.00305 mole) was treated with 0.540 g. (0.00339 mole) of bromine according to the procedure above, 0.852 g. (0.00209 mole, 64%) of II was obtained, m.p. 119–123°, undepressed when melted with material from (*a*).

6-Bromo-2,3,4-trimethoxybenzosuberone (III) (*a*) *From II.* A solution of 0.14 g. of sodium in 1.5 cc. of methanol, 15 cc. of benzene, and 1.04 g. of acetoacetic ester was combined with 1.68 g. (0.00413 mole) of the above dibromide and 8 cc. of dry benzene. The solution was refluxed for 4 hours. It was then treated in the usual manner and the oil III, after removal of acetoacetic ester by distillation at 1 mm., crystallized from methanol in colorless rods or rectangular prisms. The first crop, 1.17 g. (0.00356 mole) softened at 81°, m.p. 85–86° and the second, 0.094 g. (0.00029 mole) melted at 80–83° (93%). A sample repeatedly recrystallized from methanol melted at 85.2–86.2°.

Anal. Calc'd for $C_{14}H_{17}BrO_4$: C, 51.08; H, 5.21; Br, 24.28.
Found: C, 50.80; H, 5.20; Br, 24.48.

A similar experiment using sodium malonic ester gave III (84%) m.p. 81.5–85°. When sodium methoxide was used alone under conditions identical to those above, the solution became dark red after 1 hour. No crystalline product could be obtained.

(*b*) *From II using alcoholic sodium iodide.* A solution of 1.212 g. of II (0.00296 mole) in 30 cc. of absolute ethanol containing 3.0 g. of sodium iodide was refluxed for 2.5 hours. Free iodine was noted. The mixture was diluted with 50 cc. of water and extracted with ether. After washing with aqueous sodium sulfite and with water, 0.713 g., m.p. 83–85.5° (0.00216 mole, 73%) of slightly colored rods was obtained by distillation of the solvent. Further recrystallization from methanol gave III m.p. 86.2–87.4°, not changed when mixed with the material above.

The monobromide gave a negative test with 2,4-dinitrophenylhydrazine and did not react with hydroxylamine or hot alcoholic silver nitrate. By examination of the infrared absorption curve it contained a carbonyl group but no non-benzenoid unsaturation. With concentrated sulfuric acid a yellow-orange color was produced. The compound was recovered from hot γ-collidine (83%) after refluxing for 30 minutes. It liberated iodine from acidified aqueous alcoholic potassium iodide.

Oxidation of the monobromide III (1.0 g.) in aqueous pyridine with 6.0 g. of potassium permanganate (15) gave, after addition of 6 *N* sulfuric acid and solid sodium bisulfite followed by cooling in ice-water, 0.37 g. of crystalline material. Sublimation at 130–150°/0.2–0.3 mm. (bath temperature) gave 0.315 g., m.p. 130–143° raised to 143–145° by recrystallization from benzene; reported (16) for 3,4,5-trimethoxyphthalic anhydride, m.p. 143°. It formed the corresponding N-methylphthalimide, m.p. 126–128°; reported (17) for 3,4,5-trimethoxy-N-methylphthalimide, m.p. 127°. The phthalic anhydride obtained did not depress the melting point of material prepared by permanganate oxidation of authentic I.

When the monobromide III was treated for 7 hours with excess sodium acetoacetic ester as was done in its preparation above, it failed to react as shown by the recovery of III (77.5%) m.p. 84–86°, undepressed when mixed with authentic III.

(*c*) *From I.* Using equimolar portions of bromine and I and the procedure employed above, III was obtained (72%) m.p. 80.5–83°.

(*d*) *Using pyridinium bromide perbromide* (2). A solution of 1.00 g. (0.004 mole) of I in 15 cc. of acetic acid with 1.55 g. of 90% pyridinium bromide perbromide (0.0044 mole) was swirled for 2 minutes at 45°. After standing 10 minutes at 25°, it was poured into 75 cc. of water, cooled to 0°, and seeded with III. The colorless solid obtained at once, weighed 1.30 g. (0.00395 mole, 98.5%) m.p. 74–79°, sintering at 70°; reported (2) m.p. 79°. Recrystallization from methanol gave 1.07 g. (81%) m.p. 79–81°, not depressed when mixed with III above.

2,3,4-Trimethoxybenzosuberone from II (*a*) *By hydrogenation.* A mixture containing 1.090 g. (0.00267 mole) of II in 50 cc. of absolute ethanol and 2 cc. of pyridine with 0.497 g. of 5% palladium-carbon consumed 2 moles of hydrogen per mole of compound when shaken under hydrogen at room temperature and atmospheric pressure for 35 minutes. After removal of the catalyst and distillation of the solvent, a colorless solid (0.604 g., 0.00241 mole, 90%) was obtained m.p. 98–100°, not changed when mixed with known I.

(*b*) *By zinc dust.* The dibromide II (1.42 g.) with 5 g. of zinc dust in 25 cc. of methanol on the steam-bath for 20 minutes gave 0.75 g. (86%) of I.

2,3,4-Trimethoxybenzosuberane (V) (*a*) *From II.* A mixture of 0.90 g. (0.0022 mole) of the dibromide, 3.0 g. of zinc dust, and 15 cc. of acetic acid was refluxed for 1.75 hours. The cooled solution was poured into 100 cc. of water and extracted with ether. The water-washed ether solution on distillation gave a nearly colorless oil which crystallized from methanol. One-half gram (0.0021 mole, 95%) of colorless prisms (V), m.p. 62–65° gave after two crystallizations from methanol, m.p. 62.5–63.5°.

Anal. Calc'd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53.
Found: C, 71.11; H, 8.45.

(*b*) *From I.* A mixture containing 0.56 g. (0.0022 mole) of I and 0.56 g. of palladium-carbon in 25 cc. of acetic acid was shaken under hydrogen as above. After 85 minutes the product was obtained as above and crystallized from methanol in colorless prisms m.p. 56–61° (0.32 g., 0.0014 mole, 62%). A second crystallization from methanol gave V m.p. 62–62.6° not depressed on mixing with material from (*a*).

4-Bromo-1,2,3-trimethoxybenzosuberane (VI). To 4.00 g. (0.017 mole) of the suberane V in 25 cc. of ether at 0° was added 3.04 g. (0.19 mole) of bromine in 20 cc. of carbon tetrachloride with stirring. After warming to room temperature, the product was obtained as described above for the dibromination. The pale yellow oil gave 4.94 g. (0.0157 mole, 92%) of nearly colorless distillate, b.p. 121–123°/0.3 mm.

Anal. Calc'd for $C_{14}H_{19}BrO_3$: C, 53.34; H, 6.08; Br, 25.35.
Found: C, 53.75; H, 6.13; Br, 25.4.

The oil gave no precipitate with boiling alcoholic silver nitrate and was inert when refluxed with γ-collidine. It gave a dark orange-red color immediately with concentrated sulfuric acid. When oxidized with potassium permanganate as above (15), 6-bromo-3,4,5-trimethoxyphthalic anhydride, m.p. 133–134°, sintering at 128°, was obtained after sublimation *in vacuo* and crystallization from ether; reported (16) m.p. 132°.

6-Bromo-3,4,5-trimethoxy-N-methylphthalimide, prepared as above (17), sublimed at 170°/25 mm. (bath temperature). Recrystallization from methanol and resublimation at 125–128°/0.9 mm. gave material m.p. 127–128°.

Anal. Calc'd for $C_{12}H_{12}BrNO_5$: C, 43.65; H, 3.67.
Found: C, 43.97; H, 3.65.

When mixed with 3,4,5-trimethoxy-N-methylphthalimide above, it melted at 99–105°.

4-Hydroxy-2,3-dimethoxybenzosuberone (VII) (*a*) *From II.* The dibromo compound (0.561 g., 0.00138 mole) in 25 cc. of acetic acid was shaken for 3.5 hours under hydrogen at atmospheric pressure with 0.561 g. of 5% palladium-carbon. After treatment as above, 0.221 g. (0.000937 mole, 68%) crystallized from methanol, m.p. 116–118°. From four recrystallizations from methanol, nearly colorless octahedrons m.p. 117.5–118.5° were obtained.

Anal. Calc'd for $C_{13}H_{16}O_4$: C, 66.08; H, 6.83.
Found: C, 66.27; H, 7.05.

The compound dissolved in cold 5% sodium hydroxide and gave a brown-black color with alcoholic ferric chloride. It had an ultraviolet absorption maximum at 288 and at 223 mμ.

(Fig. 1). The infrared absorption curve failed to reveal either carbonyl or hydroxyl groups. It did not react when treated with excess ethereal diazomethane for 30 minutes at room temperature.

The *oxime* melted at 148–150° after crystallization from aqueous methanol and from ethyl acetate-cyclohexane.

Anal. Calc'd for $C_{13}H_{17}NO_4$: C, 62.13; H, 6.82.

Found: C, 62.39; H, 6.97.

The red *2,4-dinitrophenylhydrazone* after crystallization from acetone-methanol melted at 206–207° if inserted at 200° and heated 2° per minute.

Anal. Calc'd for $C_{19}H_{20}N_4O_7$: C, 54.80; H, 4.84.

Found: C, 54.51; H, 4.73.

The *acetate* crystallized from methanol as colorless diamonds m.p. 131–132°.

Anal. Calc'd for $C_{15}H_{18}O_5$: C, 64.73; H, 6.52.

Found: C, 64.52; H, 6.65.

By treatment of VII (39 mg.) in 20% potassium hydroxide with 0.7 cc. of dimethyl sulfate on the water-bath for 10 minutes followed by 0.7 cc. of the reagent and heating for 20 minutes, 15.3 mg. of I was obtained after recrystallization from methanol. It melted at 98.5–101°, not depressed when mixed with known I.

(*b*) *From I.* A solution of 1.00 g. (0.004 mole) of I in 15 cc. of acetic acid and 3.0 cc. of 30–32% hydrogen bromide in acetic acid was allowed to stand at room temperature for 4.5 hours. The solution was poured into water and the water was extracted with ether. The ether was washed twice with 10% sodium hydroxide. The alkaline washes on acidification at 0° gave 0.77 g. (0.0033 mole, 82%) of crystals m.p. 110–114°. From methanol 0.68 g. (m.p. 115–117°) was obtained which melted undepressed when mixed with material from (*a*) and which gave the same color with ferric chloride.

A reduction of 1.075 g. of II in 25 cc. of acetic acid with 0.780 g. of palladium-carbon for 2.5 hours gave 0.606 g. (70%) of III.

4-Ethoxy-2,3-dimethoxybenzosuberone (VIII). One gram (0.00424 mole) of VII in 5 cc. of 10% sodium hydroxide followed by 10 cc. of 45% potassium hydroxide was treated with 7 cc. of diethyl sulfate in two portions over a 10-minute period while heating on the steam-bath. After adding 10 cc. of potassium hydroxide and heating for 30 minutes, the addition of base was repeated, the oil was dissolved by the addition of methanol, and the solution was boiled for 30 minutes. The methanol was then removed by distillation and the product was obtained by ether extraction. Distillation of the ether gave 0.91 g. (0.00344 mole, 65%) of pale yellow oil. A central colorless drop was collected at 100–110°/1 mm. (bath temperature) in a cold-finger sublimer.

Anal. Calc'd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63.

Found: C, 67.92; H, 7.60.

The *2,4-dinitrophenylhydrazone* was an oil. The *oxime*, crystallized several times from benzene-petroleum ether (30–60°) and from cyclohexane, melted at 108–110°.

Anal. Calc'd for $C_{15}H_{21}NO_4$: C, 64.49; H, 7.58.

Found: C, 64.09; H, 7.42.

Oxidation of VIII with potassium permanganate (15) gave material which sublimed at 150–160°/0.08 mm. (bath temperature) and crystallized from ether m.p. 104–105°, sintering at 102°. A second sublimation gave a m.p. 103–105°; reported for 3-ethoxy-4,5-dimethoxyphthalic anhydride (17), m.p. 108°. The N-methylphthalimide melted at 90–92° after sublimation and recrystallization from ether; reported (17), m.p. 92°.

6-Iodo-2,3,4-trimethoxybenzosuberone (IV). One gram (0.00245 mole) of the dibromide was refluxed for 2 hours with a solution of 3.0 g. of sodium iodide in acetone. Free iodine and a solid appeared. The product was obtained by the method used on the dibromide and it was crystallized from methanol, m.p. 90–93° (0.460 g., 0.00122 mole, 50%). Further purification gave pale yellow plates, m.p. 102–102.5°.

Anal. Calc'd for $C_{14}H_{17}IO_4$: C, 44.69; H, 4.56; I, 33.74.

Found: C, 44.69; H, 4.76; I, 33.8.

The compound had an ultraviolet absorption maximum at 288 mμ (Fig. 1). It became orange in concentrated sulfuric acid and gave a strong positive test with acidified potassium iodide.

The identical amounts of reagents on 0.513 g. (0.00125 mole) of the monobromide III with refluxing for 3 hours gave 0.390 g. (0.00103 mole, 83%) of IV after crystallization from methanol. The m.p. 95–99° was not depressed on mixing with the above material. Free iodine was not liberated in the reaction to any appreciable extent.

One gram of IV (0.00266 mole) was refluxed for 1 hour in a solution containing sodium ethoxide (from 0.085 g. of sodium and 1 cc. of ethanol), 10 cc. of benzene, and 0.75 g. of acetoacetic ester. The red oil obtained from the reaction crystallized from methanol (0.33 g., 50%) and proved to be I, m.p. 96–99°. A second crystallization from methanol brought the melting point to 98–101° not depressed on admixture with I.

A solution of 0.75 g. of the iodide IV and 3.0 g. of anhydrous sodium acetate in 20 cc. of acetic acid was refluxed for 5.5 hours. Free iodine appeared in the condenser. From the washed ether extract, a solid was obtained which deposited 0.30 g. (60%) of I from methanol, m.p. 99–101°.

δ-2-Bromo-3,4,5-trimethoxyphenylvaleric acid. A solution containing 5.0 g. (0.0187 mole) of the valeric acid (3) (m.p. 65.5–67.5°) in 70 cc. of anhydrous carbon tetrachloride was treated at 0° with 3.0 g. (0.019 mole) of bromine in 25 cc. of the solvent with dropwise addition and stirring. After the 25-minute addition period, the temperature was allowed to rise to 25°. The nearly colorless solution was washed once with water and the solvent was distilled *in vacuo*. The residual material gave 5.9 g. (0.0175 mole, 93%) of a very pale yellow oil, b.p. 190–194°/0.3 mm. The oil solidified after standing at room temperature for 1 week. Two crystallizations from cyclohexane gave lustrous plates m.p. 57–58.4°.

Anal. Calc'd for $C_{14}H_{19}BrO_5$: C, 48.43; H, 5.52; Br, 23.02.

Found: C, 48.63; H, 5.60; Br, 22.73.

The *amide*, crystallized from aqueous methanol, melted at 83–84.5°.

Anal. Calc'd for $C_{14}H_{20}BrNO_4$: C, 48.56; H, 5.82.

Found: C, 48.66; H, 5.85.

Oxidation of 1.0 g. of the valeric acid with potassium permanganate gave 0.41 g., m.p. 145–147°. One recrystallization from ethyl acetate-petroleum ether (30–60°) gave colorless needles m.p. 150–151°, unchanged when mixed with 2-bromo-3,4,5-trimethoxybenzoic acid made by the bromination of 3,4,5-trimethoxybenzoic acid (18).

The above valeric acid (1.105 g.) in 28 g. of polyphosphoric acid was heated on the steam-bath with occasional swirling for 45 minutes. The product was isolated as reported (19) and the residual oil gave 0.254 g. (32%) of I, m.p. 99–101°, by chromatography on acid-washed alumina as the sole crystalline product.

SUMMARY

The bromination of 2,3,4-trimethoxybenzosuberone introduces bromine atoms into the 6 position. The reactions of the 6-halogensuberones are best understood in terms of the reactions of "positive halogens" and the order of decreasing "positiveness" is 6-iodo-, 6,6-dibromo-, and 6-bromo-2,3,4-trimethoxybenzosuberone.

2,3,4-Trimethoxybenzosuberone is hydrolyzed under unusually mild conditions. It is shown that the 4-methoxy group is lost probably due to the proximity of the carbonyl oxygen of the seven-membered ring.

SALT LAKE CITY 1, UTAH

REFERENCES

(1) GARDNER AND HORTON, *J. Am. Chem. Soc.*, **75**, 4976 (1953).

(2) CAUNT, CROW, HAWORTH, AND VODOZ, *J. Chem. Soc.*, 1631 (1950).

(3) Gardner, Horton, Thompson, and Twelves, *J. Am. Chem. Soc.*, **74**, 5527 (1952).
(4) Coplanarity in enol lactones of benzosuberone glyoxylates was previously proposed to account for their stability. Horton, Hummel, and Johnson, *J. Am. Chem. Soc.*, **75**, 944 (1953).
(5) Hirst and Macbeth, *J. Chem. Soc.*, **121**, 2169 (1922).
(6) Fisher, Snyder, and Fuson, *J. Am. Chem. Soc.*, **54**, 3665 (1932).
(7) Koelsch, *J. Am. Chem. Soc.*, **53**, 1147 (1931).
(8) Kröhnke and Timmler, *Ber.*, **69**, 614 (1936).
(9) It should be noted that the reaction of 6-bromobenzosuberone and cyanide ion has been reported. Tarbell, Wilson, and Ott, *J. Am. Chem. Soc.*, **74**, 6263 (1952).
(10) Koelsch and Prill, *J. Am. Chem. Soc.*, **67**, 1298 (1945).
(11) Schönberg and Aziz, *J. Am. Chem. Soc.*, **75**, 3265 (1953); Schönberg and Mustafa, *J. Chem. Soc.*, 746 (1946). These papers link insolubility in alkali and inertness to diazomethane to chelate structures.
(12) Reichstein, *Helv. Chim. Acta*, **10**, 396 (1927).
(13) Haworth, Moore, and Pauson, *J. Chem. Soc.*, 1045 (1948).
(14) Morton and Earlam, *J. Chem. Soc.*, 159 (1941).
(15) Bucher, *J. Am. Chem. Soc.*, **32**, 374 (1910).
(16) Lettré, Fernholz, and Hartwig, *Ann.*, **576**, 147 (1952).
(17) Manske and Holmes, *J. Am. Chem. Soc.*, **67**, 95 (1945).
(18) Feist and Dschu, *Festschrift A. Tschirch*, 23 (1926) [*Chem. Abstr.*, **22**, 3405 (1928)].
(19) Gilmore and Horton, *J. Am. Chem. Soc.*, **73**, 1413 (1951).