### REACTIONS OF SYRINGALDEHYDE INVOLVING HALOGENATION

By K. R. KAVANAGH AND J. M. PEPPER

In a manner similar to that whereby vanillin may be prepared by the oxidation of softwood lignins, a mixture of vanillin and syringaldehyde would be so obtained by the oxidation of hardwood lignins. The value of this preparation of these aromatic aldehydes as pure chemicals would be increased if their separation could be achieved readily. Pearl and Dickey (8) have summarized the various laboratory methods that have been used. A paper chromatographic separation has subsequently been described by Stone and Blundell (12). The aim of the present work, in part, was to determine whether syringaldehyde (VIII) could be separated from vanillin (VII) by bromination or iodination of the VII under conditions wherein no reactions occurred with the VIII. The halogenation of vanillin in the reactive 5-position is well established, but there have been no reports on any similar introduction of halogen into the syringaldehyde molecule. Any such reaction would be expected to be minimized owing to the absence of any such activated position ortho to the phenolic hydroxyl group. The decreased ortho-directing tendency of methoxyl groups, due likely to steric effects, has been pointed out by Rosenwald (11). Syringaldehyde was treated with iodine under similar conditions to those used for the preparation of 5-iodovanillin (9), that is, iodine dissolved in a potassium iodide solution was added slowly to an alkaline solution of the aldehyde. A dense, black, iodine-containing product resulted which gave no definite melting point. A similar iodination of a 1:1 molar mixture of vanillin and syringaldehyde was then attempted using an amount of iodine equimolar to the vanillin with which it was thought reaction would be more rapid. The same black product resulted and was not studied further. In the attempts to brominate syringaldehyde according to the procedure for the preparation of 5-bromovanillin (6), the previously unreported 2-bromosyringaldehyde (I), m.p. 186-187°C., was obtained. On repeating this reaction with equimolar amounts of vanillin, syringaldehyde, and bromine, a precipitate resulted which consisted of a mixture of 5-bromovanillin (m.p. 164°C.) and I. Neither of the halogenation methods appeared to be a practical means of separation of mixtures of VII and VIII. The 2-bromosyringaldehyde (I) was identified by analyses and conversion to the known derivatives.

Repeated attempts to convert syringic acid (III) to the reference compound 2-bromosyringic acid (II) according to the direct bromination procedure of Levine (5) were unsuccessful. It is interesting to note that Bogert and Plaut (1) reported a similar failure. 2-Bromo-3,4,5-trimethoxybenzoic acid (V) was made from 3,4,5-trimethoxybenzoic acid (IV) according to the method of Feist and Dschu (3) only if the powdered iron catalyst that they recommend was omitted; otherwise, unchanged IV was recovered. The oxidation of I with silver oxide according to the method used by Pearl (7) for the oxidation of vanillin gave a product having the required properties

216

KAVANAGH & PEPPER: REACTIONS OF SYRINGALDEHYDE INVOLVING HALOGENATION 217



of II. Other structure proof of I was obtained by its methylation with diazomethane to VI, which was subsequently oxidized with potassium permanganate to a product V, identical with that obtained from IV. Since the reaction of aromatic aldehydes with diazomethane may give rise to the mixture of products shown as VI (2), no purification was attempted at this stage in the belief that all such products would be oxidized to V.

Two derivatives, the oxime and the acetate of 2-bromosyringaldehyde, were prepared as pure compounds and their analyses reported.

#### EXPERIMENTAL

## A. Iodination Studies

Syringaldehyde (5 gm.) (9) was reacted with iodine under the same relative conditions as those used for the preparation of 5-iodovanillin (9). A black residue (5.5 gm.) resulted, which gave a positive Beilstein test, had no definite melting point but charred slowly to leave a residue. A similar treatment of equimolar amounts of syringaldehyde (5 gm.), vanillin (4.2 gm.), and iodine (7 gm.) again resulted in a similar black precipitate (9.3 gm.).

#### B. Bromination Studies

Syringaldehyde (6 gm.) was reacted with bromine under the same relative conditions as those used for the preparation of 5-bromovanillin (6). The resulting light yellow product (4.7 gm.) was recrystallized three times from glacial acetic acid; colorless needles, m.p. 186–187°C. A similar treatment of

## CANADIAN JOURNAL OF CHEMISTRY. VOL. 32

equimolar (0.017 mole) amounts of syringaldehyde (3 gm.) and vanillin (2.5 gm.) with bromine (1.4 gm.) (0.0087 mole) gave rise to a white product (1.5 gm.) which, after two recrystallizations from ethanol, yielded a product (m.p. 152–155°C.) (0.9 gm.) whose mixed melting point (159–161°C.) with an authentic sample (m.p. 164°C.) indicated that it was mainly 5-bromovanillin. A further experiment using an equimolar (0.017 mole) amount of bromine yielded a product which, after recrystallization from ethanol, weighed 2.0 gm., m.p. 135–143°C.

## C. Preparation and Identification of 2-Bromosyringaldehyde

### Preparation

Several runs were made to study the optimum conditions of preparation of this new compound. Neither decreasing the rate of addition of bromine nor refluxing the reaction mixture for from 15 min. to six hours after complete addition materially affected the yield. The following procedure illustrated the sythesis. Syringaldehyde (6 gm.) was dissolved, with warming, in glacial acetic acid (15 ml.). To this hot solution was added, dropwise, over a period of 20 min., a solution of bromine (5.3 gm.) in acetic acid (10 ml.). The crude reaction product which separated was removed by filtration; weight, 6.2 gm. After recrystallization from glacial acetic acid, then ethanol, colorless needles resulted. Yield, 3.8 gm., m.p. 186–187°C. Calc. for C<sub>9</sub>H<sub>9</sub>O<sub>4</sub>Br: mol. wt. 261; C, 41.4; H, 3.48; Br, 30.6; OCH<sub>3</sub>, 23.8%. Found: mol. wt. (Rast) 262, 265; C, 41.55, 41.60; H, 3.65, 3.60; Br, 30.7, 30.86; OCH<sub>3</sub>, 23.2, 23.6%.

2-Bromosyringaldehyde oxime.—The oxime was prepared in the usual way; m.p. 132–133° C.\* Calc.for  $C_9H_{10}O_4BrN$ : C, 39.2; H, 3.65; OCH<sub>3</sub>, 22.5%. Found: C, 39.9, 39.2; H, 4.1, 4.0; OCH<sub>3</sub>, 22.2%.

2-Bromosyringaldehyde acetate.—This monoacetate was prepared according to the method used for the preparation of the analogous derivative of vanillin (10). Recrystallization from ethanol gave white needles, m.p. 113.5–114.5°C. Calc. for  $C_{11}H_{11}O_5Br$ : C, 43.62; H, 3.66; OCH<sub>3</sub>, 20.4%. Found: C, 43.70; H, 3.82; OCH<sub>3</sub>, 20.4, 19.9%.

#### Identification

Synthesis of 2-bromo-3,4,5-trimethoxybenzoic acid (IV).—Starting with 3,4,5-trimethoxybenzoic acid the method of Feist and Dschu (3) was followed but the required product, m.p. 148.5–150°C. (reported (3), 148°C.) was obtained only if the powdered iron catalyst, mentioned in their procedure, was omitted.

Oxidation of 2-bromosyringaldehyde to 2-bromosyringic acid.—To the washed silver oxide prepared from silver nitrate (2.4 gm.) (7) was added water (24 ml.), sodium hydroxide (2.8 gm.), and 2-bromosyringaldehyde (2 gm.). After gentle heating with stirring for 20 min., the solution was filtered and the

<sup>\*</sup>It was observed that this oxime, after recrystallization from either ethanol-water or water alone, melted at  $100-102^{\circ}$ C. after air-drying. Further drying in an Abderhalden drier or in a vacuum desiccator raised the melting point to  $132-133^{\circ}$ C. This suggested that the oxime forms a stable hydrate of unknown exact composition. Calc. for  $C_9H_{19}O_4BrN.8/2$   $H_2O:OCH_3$ , 20.4%. Found for the product, m.p.  $100-102^{\circ}$ C:  $OCH_3$ , 20.4, 20.2, 20.8%.

residue washed with hot water. The combined filtrate was acidified with sulphur dioxide gas but no precipitate formed. To recover any unreacted aldehyde, dilute sulphuric acid (7 ml.) was added and the solution boiled until the sulphur dioxide had been removed. After standing, a precipitate was removed and was shown to be starting material (35% recovery). The remaining filtrate was extracted with ether. This extract was dried and the excess solvent removed to leave a residue (1.0 gm.). Two recrystallizations from dilute acetic acid gave pale yellow crystals (0.6 gm.) m.p. 153–155°C. in good agreement with that of 155°C. reported by Levine (5). Calc. for C<sub>9</sub>H<sub>9</sub>O<sub>5</sub>Br: C, 39.0; H, 3.28; OCH<sub>3</sub>, 22.4%. Found: C, 39.2; H, 3.38; OCH<sub>3</sub>, 22.2%.

Conversion of 2-bromosyringaldehyde to 2-bromo-3,4,5-trimethoxybenzoic acid.—To a suspension of 2-bromosyringaldehyde (4 gm.) in ether (300 ml.) was added an ethereal solution of diazomethane prepared from nitrosomethylurea (20.6 gm.). After 2.5 hr. stirring at around 0°C. a clear solution resulted after which the ether and excess diazomethane were allowed to evaporate at room temperature. The residual yellow oil was dissolved in ether (100 ml.) and this solution extracted with 5% sodium hydroxide (2 × 100 ml.). The ether layer, after drying, was concentrated to leave an orange-colored oil (4.3 gm.) which was used directly in the next step.

The method of Head and Robertson (4) for the oxidation of a substituted benzaldehyde to the corresponding acid was first tested by the successful conversion of veratraldehyde to veratric acid in 60% yield, after recrystallization from dilute acetone. To the methylated product (4.3 gm.) obtained above, dissolved in acetone (100 ml.), was added with swirling a solution of potassium permanganate (1.62 gm.) in water (50 ml.) over a period of one hour at 50-55°C. During the next hour, further permanganate (0.38 gm. in 10 ml. water) was added. The mixture was cooled to 0°C., cleared with sulphur dioxide, and the acetone evaporated. Some white crystals and a yellow oil separated, which, after decantation of the water, were treated with saturated sodium bicarbonate (50 ml.) which dissolved only the crystals. From this solution, after acidification, a white precipitate (0.8 gm.) was obtained. Reoxidation of the oil resulted in a further amount (0.2 gm.) of product. These were combined and after recrystallization from dilute ethanol gave the required product, m.p. 146-148°C. A mixed melting point with synthetic V was undepressed. Calc. for C<sub>10</sub>H<sub>11</sub>O<sub>5</sub>Br: C, 41.3; H, 3.81; OCH<sub>3</sub>, 31.9%. Found: C, 42.1, 41.6; H, 3.94, 4.16; OCH<sub>3</sub>, 31.6, 31.8%.

# ACKNOWLEDGMENT

The authors wish to thank the Saskatchewan Research Council for the award of a Graduate Research Fellowship to one of them (K. R. K.). The Howard Smith Chemicals Limited, kindly donated the vanillin used in this investigation.

<sup>1.</sup> BOGERT, M. T. and PLAUT, E. J. Am. Chem. Soc. 37: 2729. 1915.

Die Chemie. Newer methods of preparative organic chemistry. Interscience Publishers Inc., New York. 1948. p. 522.

FEIST, K. and DSCHU, G. L. Festschr. A. Tschirch, 23-29. 1926. (Chem. Abstr. 22: 3405. 1928.)
HEAD, F. S. H. and ROBERTSON, A. J. Chem. Soc. 2432. 1931.
LEVINE, A. A. J. Am. Chem. Soc. 48: 797. 1926.
MCIVOR, R. A. and PEPEER, J. M. Can. J. Chem. 31: 298. 1953.
PEARL, I. A. J. Am. Chem. Soc. 68: 429. 1946.
PEARL, I. A. and DICKEY, E. E. J. Am. Chem. Soc. 73: 863. 1951.
PEPPER, J. M. and MACDONALD, J. A. Can. J. Chem. 31: 476. 1953.
PISOVSCHI, T. J. Ber. 43: 2137. 1910.
ROSENWALD, R. H. J. Am. Chem. Soc. 74: 4602. 1952.
STONE, J. E. and BLUNDELL, M. J. Anal. Chem. 23: 771. 1951.

RECEIVED SEPTEMBER 29, 1953. DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SASKATCHEWAN, SASKATOON, SASK.

220