"Ortho Effects" of the Halogen Atoms in the Reactions of 3-Bromo-2,6-dimethoxybenzaldehyde and 2-Chloro-3-bromo-6-methoxybenzaldehyde with Aluminium Chloride

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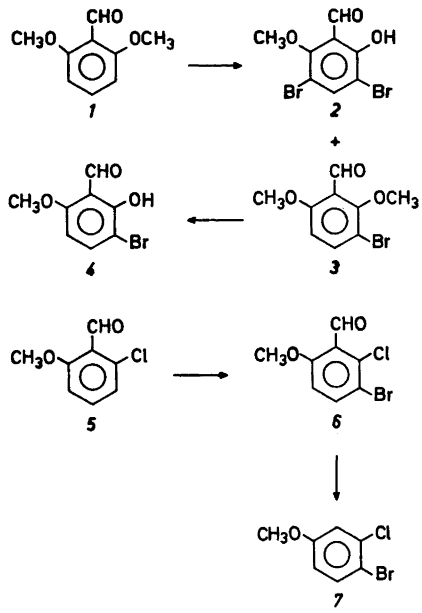
The sign of the stereospecific long range coupling between the aldehyde proton and the aromatic proton in the 3-position in salicylaldehydes has recently been determined using an elegant double resonance technique.[1] Before this technique was developed, a number of attempts were made to synthesize a 2,3-disubstituted 6-hydroxybenzaldehyde, in which the sign of the coupling could be determined by "simple" double resonance methods. These attempts failed but led to some interesting chemical results.



A simple route to the desired type of compounds seemed to be the introduction of a substituent in the 3-position of a 2-substituted 6-methoxybenzaldehyde, followed by demethylation. 2,6-Dimethoxybenzaldehyde (*1*) was therefore brominated and demethylated but only the "wrong" aldehyde (*4*) was obtained.

In another attempt, 2-chloro-6-methoxybenzaldehyde (*5*) was brominated and then treated with aluminium chloride or boron tribromide. Rapid decarbonylation to (*7*) occurred instead of the expected demethylation.

The bromination of 2,6-dimethoxybenzaldehyde (*1*) yielded also the mono-demethylated dibromide (*2*). The absence of 3,5-dibromo-2,6-dimethoxybenzaldehyde indicates that this compound is demethylated with exceptional ease. Presumably, the effect of the bromine atoms is to polarize the carbon-oxygen bond of the methoxy group. The fact that 3-bromo-2,6-dimethoxybenzaldehyde (*3*) is demethylated exclusively in the 2-position indicates that the polarization is an "ortho effect".[2] The facile decarbonylation of 3-bromo-2-chloro-6-methoxybenzaldehyde, presumably a reverse Friedel-Crafts acylation, indicates that here the chlorine atom excerts an "ortho effect" on the bond between the aldehyde group and the aromatic nucleus. It is tempting to describe the effect of the halogen atoms as a field effect, operating through space rather than through the π-system.

Experimental. 3-Bromo-2,6-dimethoxybenzaldehyde (*3*)[4] was prepared by bromination of (*1*) with bromine in glacial acetic acid at room temperature. M.p. 49–53°, yield 75 %. The alkali soluble part of the bromination product was 3,5-dibromo-2-hydroxy-6-methoxybenzaldehyde (*2*), m.p. 117–119°, yield 6 %.

3-Bromo-2-hydroxy-6-methoxybenzaldehyde (*4*)[4] was obtained from (*3*) by refluxing with aluminium chloride for 5 min in benzene. M.p. 109–110°. NMR (δ) 3.80 (s, OCH_3), 6.78 (d) and 7.70 (d) (aromatic protons), 10.28 (CHO), 12.00 (OH).

2-Chloro-6-methoxybenzaldehyde (*5*)[4] was prepared by photodibromination of 2-chloro-6-methoxytoluene [3] followed by hydrolysis. M.p. 61–62°.

2-Chloro-3-bromo-6-methoxybenzaldehyde (*6*)[4] was prepared by bromination of (*5*). M.p. 80–88°, NMR: (δ) 3.9 (s, OCH_3), 6.80 (d) and 7.70 (d) (aromatic protons), 10.32 (CHO).

Attempted demethylation of *2-chloro-3-bromo-6-methoxybenzaldehyde* (*6*) was done by refluxing

for 5 min with aluminium chloride in benzene or by reaction with boron tribromide in methylene chloride for 12 h at −78°. A semi-crystalline product, 2-chloro-4-methoxybromobenzene (*7*) was obtained. NMR: 3.90 (s, OCH_3), 7−7.5 (m, aromatic H). There is no absorption corresponding to the hydrogen of the aldehyde group.

1. Forsén, S., Alm, T., Gestblom, B., Rodmar, S. and Hoffman, R. A. *J. Mol. Spectry.* **17** (1965) 13.
2. See, *e.g.*, Charton, M. *J. Am. Chem. Soc.* **91** (1969) 6649 and 624; Noyce, D. S., Bastian, N., Lau, P.T.S., Monson, R. S. and Weinstein, B. *J. Org. Chem.* **34** (1969) 1247.
3. Noelting, E. *Ber.* **37** (1904) 1015.
4. The compound gave a satisfactory C, H analysis.

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Bacterial Carotenoids XXXIV* C_{50}-Carotenoids

7.** A C_{50}-Carotenyl-D-glucoside from *Sarcina lutea*

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Several glycosides of C_{40}-carotenoids have been reported in recent years.[1,2] The occurrence of C_{50}-carotenyl glycosides has not been demonstrated before. We now report on the isolation and structure of a C_{50}-carotenyl-D-glucoside present in *Sarcina lutea*.

Details of the isolation will be reported elsewhere.[3] The glucoside (*1*) represented 20 % of the total carotenoid. *1* required as eluent from the cellulose column 30−40 % acetone in petroleum ether, $R_F = 0.45$ on Schleicher and Schüll No. 287 paper (50 % acetone in benzene), abs.max. 418, 440, and 468 nm in acetone, quantity available *ca.* 3 mg crude *1*. The peracetate (*2*), obtained on acetylation with acetic anhydride in pyridine, had $R_F = 0.63$ on the above kieselguhr paper (10 % acetone in petroleum ether) and abs. max. 417, 439, and 469 nm in acetone. The per(trideutero)acetate (*3*) was prepared in analogous manner, using hexadeuteroacetic anhydride and deuteropyridine. *2* and *3* were purified by TLC on kieselgel G (30 % acetone in petroleum ether).

The absorption spectra of *1*, *2*, and *3* were in agreement with an aliphatic nonaene chromophore. The M−92/M−106 ratio in the mass spectra of *2* and *3* was further in agreement with the values found for carotenoids with nine conjugated double bonds in the acyclic chain.[3,4] The mass spectra of the acetates (*2* and *3*) showed fragments in the lower part indicative of a hexoside. In the case of *2* these fragments corresponded to those found by Biemann *et al.*[5] for peracetylated hexoses and later encountered in acetylated carotenoid hexosides.[3,6] Analogous fragments with the appropriate mass shifts were observed for *3*, see Scheme 1. The hexose was liberated by hydrolysis of *1* (2 mg) in 0.15 N hydrogen chloride in methanol overnight, and the methyl glycoside thus obtained hydrolysed with 0.04 N polystyrene sulphonic acid.[7] The resulting reducing sugar was purified by descending paper chromatography using pyridine-ethyl acetate-water (2:5:7) [8] and spraying parallel test spots of glucose with aniline-phthalic acid reagent [9] in order to localize the sugar zone. In co-chromatography tests (System 5 [10]) with glucose and galactose ($R_{glucos} = 0.88$) the unknown hexose had $R_{glucos} = 0.99$. The paper-chromatographically purified sugar was identified as D-glucose by oxidation with D-glucose oxidase providing gluconic acid and hydrogen peroxide. The hydrogen peroxide was determined by peroxidase-catalyzed dehydrogenation of *o*-dianisidine.[11] Spectrophotometric determination and correlation with a calibration curve for D-glucose, permits quantitative determination of D-glucose on the 10 μg scale.

The molecular ion in the mass spectrum of *2* at *m/e* 1076 was in agreement with $C_{66}H_{92}O_{12}$. The molecular ion of *3* at *m/e* 1091 ($C_{66}H_{77}D_{15}O_{12}$) provided confirmation for this assignment and showed that *2* and

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