[CONTRIBUTION FROM THE CARBOHYDRATE LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE]

FLUORO-ACETYL DERIVATIVES OF SUGARS. III. OPTICAL ROTATION AND ATOMIC DIMENSION (CONTINUED)

BY D. H. BRAUNS

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In addition to other reported fluoro-acetyl derivatives of sugars,[1] the present article reports the preparation of fluoro-triacetyl-*l*-arabinose as a stable, pure, crystalline substance. The specific rotation of the compound was found to be +138.2° in chloroform solution. Ryan and Mills[2] have prepared chloro-triacetyl-arabinose but do not mention its specific rotation. Chavanne[3] reported the preparation of chloro- and bromo-triacetyl-arabinose (prepared from *l*-arabinose $[\alpha]_D = +105.2$) in the crystalline form, and gave for their specific rotations in chloroform solution —224.8° and —283.5°, respectively. Even if Chavanne had been mistaken in the reading of the *sign* of the rotation, the reported *magnitudes* of the rotations would have constituted an exception to the relationship between specific rotations and atomic diameters observed by the author, inasmuch as the ratio of the differences of the specific rotations would have been (Cl-F) : (Br-Cl) = 87 : 59, whereas the ratio of the respective differences of Bragg's atomic diameters is (Cl-F) : (Br-Cl) = 87 : 34.

Starting from the same lot of *l*-arabinose ($[\alpha]_D = +104°$) from which the fluoro compound had been obtained, the author has prepared chloro- and bromo-triacetyl-*l*-arabinose and also iodo-triacetyl-*l*-arabinose. All these derivatives were obtained in large transparent crystals. The last compound is the least stable, so that the values for its rotations are less certain than the others.

On determining the specific rotations of all these compounds, the data given by Chavanne were found to be entirely erroneous, the signs being + in all cases and the ratios between the differences in specific rotation from one halogen to another being comparable with the differences in atomic diameter given by Bragg. These results also suggest that a revision of the specific rotations of the chloro and bromo derivatives of xylose (see preceding article[1b]), if made with the same care as for the other reported values, may reveal an improved agreement. (This revision, also that for other quoted values, will be published in a forthcoming article.)

The specific and molecular rotations of the derivatives in question, in comparison with the atomic diameters, are shown in Table I. Regarding

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[1] THIS JOURNAL, **45**, (a) 833, (b) 2381 (1923).

[2] Ryan and Mills, *J. Chem. Soc.*, **79**, 706 (1901).

[3] Chavanne, *Compt. rend.*, **134**, 661 (1902).

the interpretation of the data compiled, reference is made to the discussion in the preceding article.[4]

TABLE I

COMPARISON OF ROTATIONS WITH ATOMIC DIAMETERS IN HALOGEN-TRIACETYL DERIVATIVES OF *l*-ARABINOSE

	Rotations				Atomic diameter differences (reduced)
Halogen	Molecular	Differences	Specific	Differences	
F	+ 384		+138.2		
		336		106	106
Cl	+ 720		+244.4		
		253		43	41
Br	+ 973		+287.1		
		335		52	62
I	+1308		+339.1		

The experimental error involved in the method of determining the specific rotation (as followed throughout this work) was ascertained for fluoro-acetyl-arabinose and is recorded in the experimental part.

Experimental Part

Fluoro-triacetyl-*l*-arabinose.—Starting[5] with β-tetra-acetyl-*l*-arabinose prepared from *l*-arabinose ($[\alpha]_D = +104°$), the manner of preparation of this compound is the same as described by the author for[6] fluoro-tetra-acetyl-glucose.

The resulting colorless sirup crystallized readily when stirred with petroleum ether. Ten g. of β-tetra-acetyl-*l*-arabinose yielded about 7 g. of impure product. It was recrystallized by dissolving it in about 450 cc. of boiling water, filtering the solution with the aid of a hot-water funnel and gradually cooling the filtrate in ice water. In this way brilliant needles were obtained. A few crystallizations yielded a product of constant rotation. The yield of pure substance was about 6 g.; m. p., 117–118°. After the third crystallization, 0.6017 g. in chloroform in a volume of 24.9767 cc. produced a rotation in a 4-dm. tube of 13.301 circular degrees to the right; hence, $[\alpha]_D^{20} = +138.02°$. The result of the determination after the fourth crystallization is reported below and leads to $[\alpha]_D^{20} = +138.18 \pm 0.04$ (m.e.) of the pure compound. It is stable, colorless, odorless and tasteless[7] and is very soluble in the usual organic solvents, from which it cannot be efficiently recrystallized. The action of hydrofluoric acid on α-tetra-acetyl-*l*-arabinose yields the identical compound.

Analyses.[8] Subs., 0.2152: CO_2, 0.3763; H_2O, 0.1068. Subs., 0.6228: CaF_2, 0.0825. Subs., 0.5000: 320.82 cc. of 0.1 *N* NaOH; 248.86 cc. of 0.1 *N* H_2SO_4. Subs., 2.5783, 4.2713, 6.0871: C_6H_6, 100; ΔF, 0.456°, 0.785°, 1.043°. Calc. for $C_{11}H_{15}O_7F$: C, 47.46; H, 5.44; F, 6.83; 71.91 cc. of 0.1 *N* NaOH for AcOH + HF; mol. wt., 278. Found: C, 47.68; H, 5.55; F, 6.45; 71.96 cc. of 0.1 *N* NaOH; mol. wt., 283, 272, 291.

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[4] Ref. 1 b, p. 2384. See also *Physica,* **3,** 69 (1923).

[5] Hudson and Dale, THIS JOURNAL, **40,** 994 (1918).

[6] Brauns, *ibid.,* **37,** 1283 (1915).

[7] Whereas the α- and β-tetra-acetyl-arabinose are bitter, the derived halides have no taste, a remarkable exception to the bitter taste of corresponding hexose derivatives.

[8] For description of methods of analysis, see Ref. 1 a, p. 835.

The experimental error involved in the determination of the specific rotation was ascertained by performing the determination five times (on different days) for the same lot of pure fluoro-triacetyl-*l*-arabinose (Table II). The preceding crystallization of this preparation gave for approximately the same concentration the value $[\alpha]_D^{20} = +138.02°$. The solvent used was U. S. P. chloroform. For work with the bromo and iodo compounds, it was specially purified by shaking with water, drying over sodium sulfate and distilling, the first and last fraction of the distillate being discarded. This purification was performed on each day that the solvent was used. Investigations with chloro-triacetyl-arabinose showed that identical rotations are obtained with U. S. P. chloroform (1% alcohol) and purified chloroform.

TABLE II

DETERMINATION OF ERROR OF SPECIFIC ROTATION OF FLUORO-TRIACETYL-*l*-ARABINOSE

Volume of flask, 24.9767 cc. at 20°. Length of tube, 4 dm.

Weighed amt......	0.6046	0.6094	0.6052	0.6012	0.6069
Reading, α_D^{20}.....	+ 13.37	+ 13.481	+ 13.409	+13.308	+ 13.429
$[\alpha_D^{20}]$.............	+138.08	+138.13	+138.33	+138.21	+138.16

Excluding the presence of impurities in this stable compound we derive $[\alpha]_D^{20} = +138.18 \pm 0.04$ (m.e.).

Chloro-triacetyl-*l*-Arabinose.—Chavanne[3] and Ryan and Mills[2] prepared the compound by the action of the required amount of acetyl chloride on arabinose at room temperature. The method was not found satisfactory in the hands of the author, as the reaction is slow and incomplete. Good results were obtained by boiling 6.5 g. of *l*-arabinose with 24 cc. (an excess) of acetyl chloride and a small amount of zinc chloride[9] on a water-bath. After about 15 minutes the arabinose was dissolved, forming a slightly colored solution. The reaction product was dissolved in a small amount of chloroform and washed thrice with ice water. The chloroform solution was further dried with calcium chloride, filtered, and the chloroform evaporated with a dry current of air, leaving a thick sirup, which crystallized readily upon adding a small amount of ether and stirring. The crystals were filtered by suction and recrystallized from ether. The yield was about 5 g. of pure substance; m. p., 146–147° (Chavanne, 148–149°). After three crystallizations the specific rotation was constant; 0.6024 g. of the third crystallization in chloroform in a volume of 24.9767 cc. produced a rotation in a 4-dm. tube at 20° of +23.591 circular degrees; hence, $[\alpha]_D^{20} = +244.52°$; 0.6083 g. of the same lot of pure substance gave a rotation of +23.802 circular degrees under identical conditions; hence, $[\alpha]_D^{20} = +244.32°$. The average, +244.4°, is taken as the specific rotation of the pure substance. The compound is fairly stable, colorless, odorless and tasteless, and is soluble in organic solvents except petroleum ether.

Analyses. Subs., 0.2128: CO_2, 0.3516; H_2O, 0.0988. Subs., 0.2015: AgCl, 0.0977. Calc. for $C_{11}H_{15}O_7Cl$: C, 44.81; H, 5.13; Cl, 12.04. Found: C, 45.06; H, 5.19; Cl, 11.99.

Bromo-triacetyl-*l*-Arabinose.—Chavanne[3] prepared the compound by the action of the required amount of acetyl bromide on arabinose at the temperature of an ice-and-salt mixture. The reaction was found to be very slow in the hands of the author and was for this reason modified by first cooling the mixture with an ice-and-salt mixture,

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[9] See Hudson and Johnson, THIS JOURNAL, **37,** 2751 (1915).

then with ice water and finally allowing the water to warm during the course of a few hours to room temperature. The reaction product was dissolved in a small amount of chloroform and washed four times with ice water. The chloroform solution was dried with calcium chloride, filtered and the chloroform evaporated with a dry current of air to a thick sirup, which crystallized readily on stirring with a small amount of ether. The crystals were filtered by suction and recrystallized from ether. The yield was about 4 g. of pure substance from 10 g. of arabinose; m. p., 138–139° (Chavanne, 137°). After three crystallizations the specific rotation was constant; 0.4651 g. of the third crystallization in purified chloroform in a volume of 24.9767 cc. at 20° produced a rotation in a 4-dm. tube at 20° of +21.386 circular degrees, hence $[\alpha]_D^{20} = +287.11°$, which is taken as the specific rotation of the pure substance. The pure compound is fairly stable, colorless, odorless and tasteless and may be kept for a few weeks without decomposition in a vacuum desiccator in an ice box. It is soluble in organic solvents except petroleum ether.

Analyses. Subs., 0.2150: CO_2, 0.3085; H_2O, 0.0856. Subs., 0.1609: AgBr, 0.0886. Calc. for $C_{11}H_{15}O_7Br$: C, 38.93; H, 4.46; Br, 23.57. Found: C, 39.13; H, 4.45; Br, 23.43.

Iodo-triacetyl-*l*-Arabinose.—The method of E. Fischer and H. Fischer[10] for the preparation of iodo-tetra-acetyl-glucose was followed. Four g. of α-tetra-acetyl-*l*-arabinose was dissolved in 3 cc. of glacial acetic acid in a graduated tube with accurately ground stopper by gently heating it on a steam-bath. To the cooled solution was added 22 cc. of a saturated solution of hydriodic acid in glacial acetic acid and the mixture was kept for one hour at room temperature. It was then poured into a mixture of ice water and chloroform and shaken. The shaking of the chloroform solution with ice water was repeated thrice. The chloroform solution was dried with calcium chloride and filtered and the chloroform was evaporated by a dry current of air, leaving a thick sirup, which crystallized readily upon stirring with some ether. The impure, yellow crystals were pressed lightly between hardened filter paper and recrystallized from absolute ether, especial care being taken to avoid elevated temperature and contact with moisture and metals. By slowly evaporating the ether in a dry current of air beautiful, large, brilliant crystals which are devoid of any yellow color can be obtained. When a colorless ether solution is slightly warmed or allowed to take up moisture it gradually turns yellow, finally becoming dark brown. Different preparations gave after recrystallization specific rotations of +337.5°, +338.8° and +339.06°. The last value was obtained with 0.6146 g. in purified chloroform in a volume of 24.9767 cc. at 20°. This solution produced a rotation in a 4-dm. tube at 20° of +33.375 circular degrees; hence, $[\alpha]_D^{20} = +339.06°$, which is taken as the specific rotation of the pure substance, since analysis of this preparation gave data agreeing with the required calculated values. The compound is not stable but can be kept for several weeks in a desiccator over sodium hydroxide in an ice box. It is colorless, odorless and tasteless and is soluble in organic solvents except petroleum ether.

Analyses. Subs., 0.2037: CO_2, 0.2566; H_2O, 0.0687. Subs., 0.1529: AgI, 0.0930. Calc. for $C_{11}H_{15}O_7I$: C, 34.19; H, 3.92; I, 32.87. Found: C, 34.35; H, 3.77, I, 32.87.

Summary

Upon comparing the optical rotations of mono-halogen triacetyl-*l*-arabinoses the differences Cl-F, Br-Cl and I-Br in specific rotations are found to be approximately proportional to the differences in atomic diameters recorded by Bragg, being thus in harmony with the simple relation

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[10] E. Fischer and H. Fischer, *Ber.*, **43,** 2535 (1910).

between specific rotations and atomic diameters previously found for the analogous derivatives of glucose, cellose, xylose and fructose. The methods of preparation, properties and analyses of fluoro-, chloro-, bromo- and iodotriacetyl-*l*-arabinose are given.

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[CONTRIBUTION FROM THE DRUG CONTROL LABORATORY IN COÖPERATION WITH THE COLOR LABORATORY, BUREAU OF CHEMISTRY, UNITED STATES DEPARTMENT OF AGRICULTURE]

THE IDENTIFICATION OF PHENOLS BY MEANS OF THE SPECTROSCOPE[1]

BY SAMUEL PALKIN AND H. WALES

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In a previous paper[2] attention was called to the use of diazo-*p*-nitrobenzene as a test reagent for guaiacol sulfonate ("thiocol"). The advantages of this reagent over other diazonium salts for color reactions were shown. The similarity in the behavior of the different phenols toward color-producing reagents and the limitation of the eye in distinguishing between the different shades produced, render color tests in themselves of little value in identifying the individual phenols. It is only when the colors produced are subjected to critical analysis by the spectroscope that positive identification becomes possible.

The frequency with which phenolic compounds occur in medicinal preparations, the small quantities in which they are found, and the admixture of various other compounds, make the problem of identifying any individual phenol in such products a very difficult one.

Gsell,[3] in a comprehensive review of the subject of phenol identification, has shown that wide differences in absorption spectra of the phthaleins of the various phenols exist, and that these afford a very positive means for their identification. Once prepared, the phthaleins are no doubt of diagnostic value, but the exacting conditions (such as absence of water, limitation in temperature range and comparative freedom from contaminating substances) necessary for the phthalein condensation detract much from the usefulness of this reaction, particularly as applied to complex medicinal preparations.

Investigation by the authors has shown that the ease with which the azo dyes can be prepared, under the conditions most common in practical analysis, makes this means particularly well adapted for the identification of phenols in medicinal preparations. The most useful general reagent

[1] Presented at the Washington meeting of the American Chemical Society, April, 1924.

[2] S. Palkin, *J. Ind. Eng. Chem.*, **10**, 618 (1918).

[3] Gsell, *Z. anal. Chem.*, **55**, 417 (1916).