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SUBSTITUTED METHYL α -D-GLUCOPYRANOSIDES: A RELATIONSHIP BETWEEN STRUCTURE AND THIN-LAYER CHROMATOGRAPHIC BEHAVIOR

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SUMMARY

Twenty substituted methyl α -D-glucopyranosides were separated by thin-layer chromatography with solvent mixtures of toluene and ethyl acetate. From R_F values and the MARTIN equation relating R_M with R_F , a relationship between chemical structure and chromatographic behavior was determined. Group constants, position parameters, and a solvent parameter were evaluated. Using these values, an R_M can be calculated from the number of functional groups, their position on a methyl α -D-glucopyranosyl group, and a solvent parameter.

INTRODUCTION

Numerous studies have been carried out on the relationship between structure and chromatographic behavior. A linear relationship between a derived function of the R_F value and the group(s) in a molecule was postulated by MARTIN¹ for liquid-liquid partition chromatography and later applied by SPORER AND TRUEBLOOD² to adsorption chromatography. This relationship takes the form

$$R_M = \log (1/R_F - 1) = G_0 + aG_x + bG_y + \dots G \quad (1)$$

where G_0 = constant of elementary group; G_x, G_y, \dots = constant of the group α ($\alpha = x, y, \dots$); G = constant dependent on adsorbent and solvent.

Many papers³⁻⁵ have confirmed experimentally the validity of the MARTIN relationship.

This paper aims to establish empirical group constants from the R_F values of substituted methyl α -D-glucopyranosides and the effect of position on the R_M . These data can assist in determining molecular structure.

EXPERIMENTAL

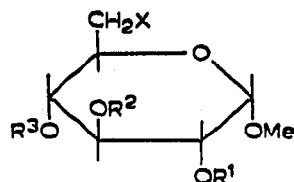
All substituted methyl 6-deoxy-6-halo- α -D-glucopyranosides were prepared according to a published technique⁶. Throughout the chromatographic work Silica

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Gel G* with the same lot number was used. Glass plates were cleaned⁷, dried and spread with Silica Gel G to a thickness of 0.25 mm and air-dried 18 h before use. After the compounds were spotted (25–35 μ g), the plate was developed in a sandwich chamber to a scribed line 13 cm above the spotting point, which was 1 cm above the edge. After the solvent front had reached the scribe line, the plate was removed from the solvent within 30 sec and the solvent evaporated in an air stream. The compounds were detected by spraying with a solution of ethanol–water–sulfuric acid (10:5:1) and heating until charred. Since R_F values are reproducible only under strictly controlled conditions, the adsorbent layer thickness and preparation, plate configuration, chamber, solvent development distance and amount of compound spotted were standardized. As a check on reproducibility, one set of compounds with each solvent system (Example Nos. 17–20, 1–4, 13–16 and 5–8 with toluene–ethyl acetate 1:1, 5:1, 10:1, 20:1, and toluene, respectively) was used as a standard. From six developed

TABLE I

R_F VALUES OF SUBSTITUTED METHYL α -D-GLUCOPYRANOSIDES^a



Example No.	Substitution				R_F values $\times 100$ Toluene–ethyl acetate				
	R^1	R^2	R^3	X	1:1	5:1	10:1	20:1	Toluene
1	Ac	Ac	Ac	OTs	55	20	8	4	0
2				Cl	62	31	16	9	1
3				Br	65	34	17	10	1
4				I	68	37	20	11	1
5	BzO	BzO	BzO	OTs	81	55	47	25	4
6				Cl	89	68	62	43	16
7				Br	90	70	64	47	22
8				I	94	74	68	51	24
9	BzO	BzO	Ms	OMs	57	23	10	6	0
10				Cl	78	56	37	21	3
11				Br	78	58	37	23	3
12				I	79	61	40	27	4
13	Ts	BzO	BzO	OTs	82	52	38	19	5
14				Cl	89	63	54	33	9
15				Br	89	65	57	36	10
16				I	91	68	58	39	14
17	Ms	Ac	Ac	OMs	32	5	1	0	0
18				Cl	57	20	13	5	0
19				Br	58	21	13	5	0
20				I	60	24	14	7	0

^a Ac = acetyl; BzO = benzoyl; Ms = methanesulfonyl; Ts = *p*-toluenesulfonyl.

* The mention of firm names or trade products does not imply that they are endorsed or recommended by the Department of Agriculture over other firms or similar products not mentioned.

plates, the highest and lowest R_F values of the standard set were discarded. If the standard deviation of the remaining set of four R_F values exceeded 2% of the mean of the standard, the observations were discarded; if not, the mean was listed in Table I.

RESULTS AND DISCUSSION

From eqn. 1 the group constants G_x, G_y, \dots were considered as the functional groups attached in methyl α -D-glucopyranosides to position C_2, C_3, C_4 and C_6 . As a consequence, the coefficients a, b, \dots were position parameters indicating the effect of a position on the R_M independent of the attached group. G_0 would be the constant for the methyl α -D-glucopyranosyl group. Since solvent mixtures were used, a parameter*, \log (weight % ethyl acetate), based on a Freundlich isotherm, was included for the G -term in eqn. 1. Eqn. 1 would take a form shown in eqn. 2.

$$R_M = \log (1/R_F - 1) = G_0 + aG_2 + bG_3 + cG_4 + dG_6 + e \log W \quad (2)$$

where G_0 = constant of methyl α -D-glucopyranosyl group; G_n = constant of group attached at position n of glucoside; W = weight % ethyl acetate; a, b, c, d = position parameter; e = constant dependent on adsorbent.

With toluene the R_F values of the glucosides were too low to be significant and were not used here. Example No. 17 R_F values were also too low and were excluded. A group constant for an iodo group on C_6 was defined as 1.00. As a first approximation of other group constants the ratio of the Hammett aliphatic σ -values^b was used or the constants were estimated.

Multiple linear regression analysis of eqn. 2 with the estimated group constants yielded a correlation coefficient exceeding 0.9. By varying the group constants and observing the standard error of estimate in the coefficients a, b, \dots in eqn. 2, it was apparent that two sets of group constants were needed. One set was needed for groups on C_6 (primary carbon) and another set for groups on C_2, C_3, C_4 (secondary carbon).

Group constants which best fit the data are recorded in Table II and the calculated coefficients are recorded in Table III.

TABLE II
GROUP CONSTANTS

Primary carbon		Secondary carbon	
Group, R	Value	Group, R	Value
MsO	2.49	Ms	1.74
TsO	1.67	Ts	1.20
Cl	1.20	Ac	0.92
Br	1.13	BzO	0.90
I	1.00 ^a		

^a Value assigned by definition.

* A parameter based on weight per cent of ethyl acetate, mole per cent of ethyl acetate, or SNYDER'S^b solvent parameter gave results nearly identical as to the effect on R_M .

With the values in Tables II and III, an R_M -calculated was compared to the R_F -observed for 76 compounds. A multiple correlation coefficient of 0.99 was found with a standard error of estimate (in the R_M) of 0.07. A plot of this R_M -calculated vs. R_F -observed is shown in Fig. 1.

TABLE III

G_0 , COEFFICIENTS AND STANDARD ERROR FOR EQN. 2

Coefficient	Value	Standard error
G_0	-36.897	0.950
a	0.256	0.033
b	38.164	1.049
c	0.1417	0.029
d	0.505	0.025
e	-1.225	0.024

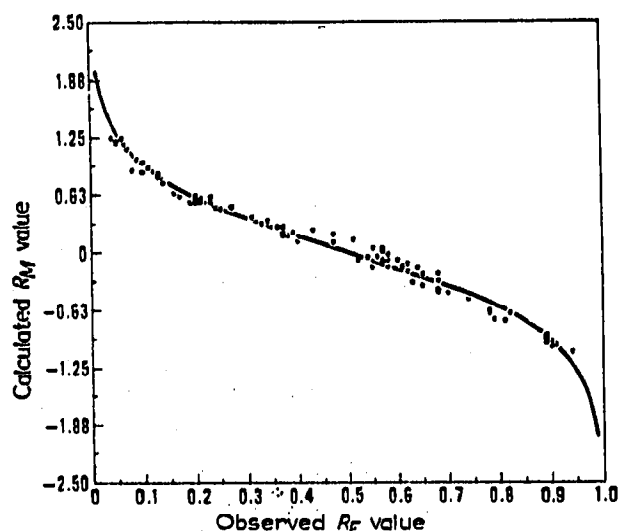


Fig. 1. Plot of R_M -calculated vs. R_F -observed. —, Theory, $R_M = \log(1/R_F - 1)$; ···, calculated R_M from eqn. 2.

In Table II the group constants reveal how a mesyl group strongly influences the migration of glucosides. This influence is readily observed in examples 9-12 and 17-20 in Table I. To a lesser degree this influence is observed at the secondary carbons in examples 2-4 vs. 18-20 and 6-8 vs. 10-12. Where comparable, the group constants on a secondary carbon were less than the value on a primary carbon.

From Table III the values of the position parameters a , b and c show that a functional group at C_3 strongly influences migration when compared to the same functional group at C_2 and C_4 . The reason for the large coefficient at C_3 is unknown.

The results point out the validity of the MARTIN equation between R_M and R_F , a linear relationship between the R_M value and the number of functional groups and their configuration. Although determined for only one series of related glucosides, the group constants would probably remain unchanged for any other similar series. This knowledge will assist the laboratory worker in estimating how a group influences R_M .

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