aqueuse restant après l'extraction au C_6H_6 est traitée selon la technique indiquée ci-dessus pour l'obtention de IIIa. Le précipité obtenu à l'issu du traitement cristallise de l'EtOH en donnant 4.5 g d'amino-2 morpholino-4 *s*-triazine IIIf. IR ν_{max}^{KBr} cm^{-1}: 3400 et 1650. Spectre de masse *m/e* 181 (M^+).

Action de IVa—f sur V——Les condensations ont été effectuées de façon analogue à celle utilisée lors de l'action de IVa sur I, à partir de 0.5 g (0.02 atomes) de Na, 0.024 moles de chlorhydrate de IVa—f et 3.7 g (0.02 moles) de V dans 30 ml d'EtOH anhydre. On obtient ainsi les *s*-triazines IIIa—f.

Synthése des IIIa—f à Partir des IVa—f et du Formiate d'Ethyle——On abandonne à température ambiante pendant 15 hr, un mélange de 0.5 g (0.02 atomes) de Na, 0.02 moles de chlorhydrate de IVa—f et de 1.6 g (0.02 moles) de formiate d'éthyle dans 30 ml d'EtOH anhydre, puis chauffe à ébullition pendant une demie heure. Le mélange réactionnel est ensuite concentré sous pression réduite et dilué par addition d'eau. Il apparaît alors un précipité que l'on essore et qui cristallise d'un mélange d'EtOH et de dioxane (IIIe et IIIf cristallise de l'EtOH).

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Studies on the Glucaric Acid Pathway in the Metabolism of D-Glucuronic Acid in Mammals. II.[1] Excretion of D-Glucaric Acid in Urine after Administration of Several Monosaccharides and Their Derivatives to Mammals[2]

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D-Glucaric acid (V) was identified as normal constituent of human urine[4] and a new oxidative metabolic pathway of D-glucuronolactone (I) to V in mammalian systems was demonstrated by Marsh.[5,6,7] The tentative reaction mechanism involved in the conversion of I into V is indicated briefly in Chart 1. The physiological significance of this new metabolic pathway of I may lie in the production of an endogenous β-glucuronidase inhibitor, because if D-glucaro-(1→4)-lactone (III) were present, which is known to be the most powerful inhibitor of the enzyme,[8] it could play an important role in controlling glucuronide hydrolysis *in vivo*, although no conclusive evidence for this is yet available.

For accurate determination of V in urine a chemical method has been developed recently in this laboratory[1] in place of the enzymic assay worked out by Marsh.[4] This paper describes the determination of urinary excretion of V in man, rat and guinea pig by using the chemical method after administration of several monosaccharides and their derivatives. The primary purpose of the present work is to find out the compound(s), whose oral administration to man could bring about the more increased urinary excretion of V compared with I.

1) Part I: M. Ishidate, M. Matsui, and M. Okada, *Anal. Biochem.*, **11**, 176 (1965).
2) Part of this work was presented at the 84th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1964.
3) Location: *Takada 3-chome, Toshima-ku, Tokyo*; *a*) Present address: *National Institute of Hygienic Sciences, Kamiyoga 1-chome, Setagaya-ku, Tokyo.*
4) C.A. Marsh, *Biochem. J.*, **86**, 77 (1963).
5) C.A. Marsh, *Biochem. J.*, **87**, 82 (1963).
6) C.A. Marsh, *Biochem. J.*, **89**, 108 (1963).
7) C.A. Marsh, *Biochem. J.*, **99**, 22 (1966).
8) G.A. Levvy, *Biochem. J.*, **52**, 464 (1952).

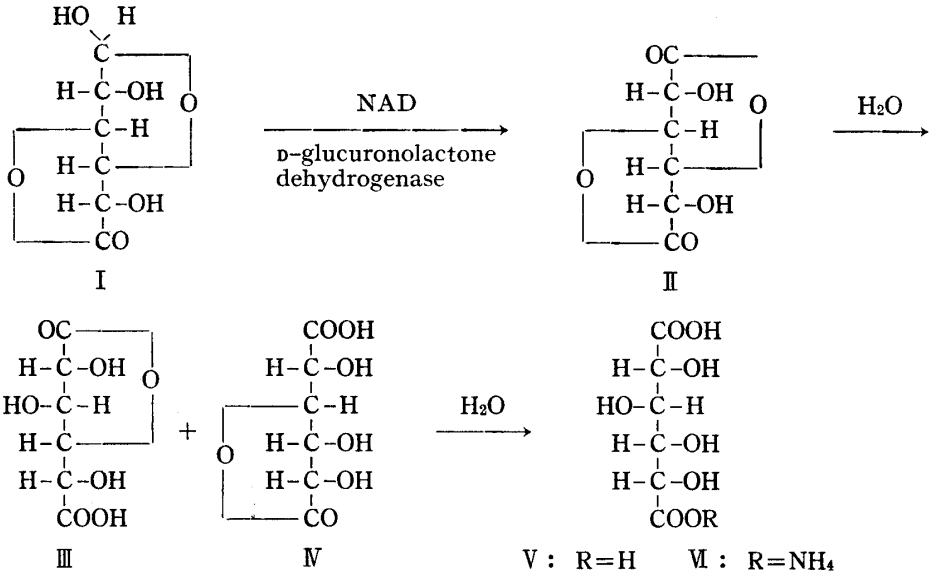


Chart 1

The amounts of V in 24-hour urines of normal human subjects determined by the chemical method are shown in Table I (fourth column). Conversions (%) of I administered orally to human subjects into V are also indicated in the same table. The conversion (average 16%) of I into V was in good agreement with that observed by Marsh.[4] The increase of urinary

Table I. Urinary Excretion of D-Glucaric Acid (V) after Oral Administration of D-Glucuronolactone (I), Sodium D-Glucuronate (VII) and D-Glucuronamide (VIII) to Human Subjects

Subjects (sex, age)	Compound	Dose (g)	D-Glucaric acid in urine (mg/24 hr)			
			Before dosage	After dosage 0—24 hr	After dosage 24—48 hr	Conversion[a] (%)
M (M. 29)	I	5	15	656	58	11
M (M. 29)	I	1	15	183	26	15
S (M. 20)	I	5	14	815	49	14
S (M. 20)	I	1	14	161	18	13
O (M. 40)	I	1	19	199	29	16
W (M. 31)	I	1	24	208	34	16
H (M. 33)	I	1	12	247	26	21
St (M. 27)	I	1	23	247	30	19
Tm (M. 52)	I	1	17	236	25	19
T (M. 67)	I	1	17	216	29	18
Sd (F. 26)	I	1	12	180	21	15
Sh (F. 32)	I	1	16	189	26	15
O (F. 36)	I	1	12	182	15	15
T (F. 60)	I	1	17	187	22	15
M (M. 29)	VII	1	15	14	20	—
O (M. 40)	VII	1	19	29	20	1
Ta (F. 25)	VIII	1	11	20	19	1.6
M (M. 29)	VIII	1	15	16	11	—
Sd (F. 26)	VIII	1	12	11	9	—

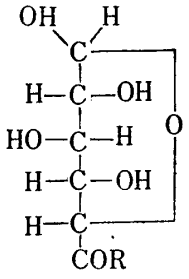
a) Calculated as follows, taking the first case as example:

$$\text{conversion (\%)} = \frac{(656+58)-15\times 2}{5000\times 1.2^{b)}} \times 100 = 11.4$$

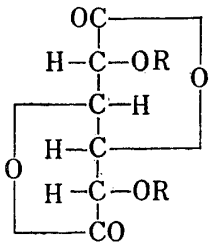
When this value is less than 0.5 it is indicated as a bar.

b) $\frac{\text{molecular weight of V}}{\text{molecular weight of I}} = \frac{210}{176} \fallingdotseq 1.2$

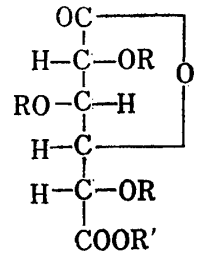
excretion of V in human subjects after oral dosage of I was marked in the first 24 hours, returning to normal value after 48 hours. On the other hand, oral administration of sodium D-glucuronate (VII) and D-glucuronamide (VIII) had a slight effect on the excretion of V as shown in the same table.



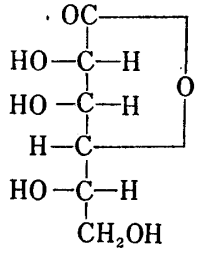
VII : R=ONa
VIII : R=NH_2



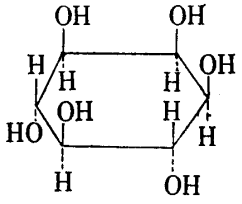
IX : R=$COCH_3$
X : R=COC_6H_5



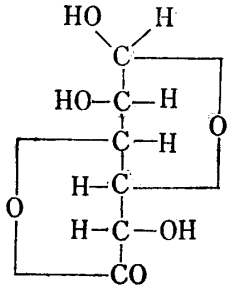
XI : R=$COCH_3$, R'=H
XII : R=H, R'=CH_3
XIII : R=H, R'=C_2H_5



XIV



XV



XVI

Chart 2

Oral administration of D-glucaro-(1→4) (6→3)-dilactone (II) to human subjects, which has been suggested[5,7] to be the initial product in the enzymic oxidation of I to V and obtained recently in pure crystalline state by chemical synthesis,[9] resulted in a marked increase of the urinary excretion of V, amounting to more than 50% of the dose. A considerable increase of the excretion of V in urine was observed after oral dosage of III or D-glucaro-(6→3)-lactone (IV) which are also involved in the conversion of I into V. The conversions were equivalent to several per cent or slightly more of the dose, thus being much less than that (16%) observed with I. On the other hand, oral administration of V itself or ammonium hydrogen D-glucarate (VI) had no appreciable effect on the urinary excretion of V. These results are shown in Table II.

Since it has been found that II is unstable and rapidly converted into III, IV and V in aqueous solution,[9,10] its diacetate, 2,5-di-O-acetyl-D-glucaro-(1→4) (6→3)-dilactone (IX)[9] was administered orally to human subjects in anticipation of the similar effect on the urinary excretion of V as that observed with II. The diacetate is much more stable than II and has been demonstrated to possess more powerful and durable inhibiting action on mice liver-β-glucuronidase *in vivo* than II or III.[11] As anticipated a striking increase of the urinary excretion of V was attained after oral dosage of IX to human subjects, which was equivalent to about 50% of the dose. 2,5-Di-O-benzoyl-D-glucaro-(1→4)(6→3)-dilactone (X) and 2,3,5-tri-O-acetyl-D-glucaro-(1→4)-lactone (XI) did not have any appreciable effect on the urinary excretion of V, while methyl or ethyl D-glucaro-(1→4)-lactonate (XII, XIII) had a strinking effect. These results are shown in Table III.

9) Y. Hirasaka and K. Umemoto, *Chem. Pharm. Bull.* (Tokyo), **13**, 325 (1965).
10) Y. Hirasaka, K. Umemoto, M. Sukegawa, and I. Matsunaga, *Chem. Pharm. Bull.* (Tokyo), **13**, 677 (1965).
11) R. Iida, S. Nagata, M. Kakimoto, H. Akaike, H. Watanabe, and A. Shioya, *Jap. J. Pharmacol.*, **15**, 88 (1965).

Table II. Urinary Excretion of D-Glucaric Acid (V) after Oral Administration of 1 g of D-Glucaro-(1→4) (6→3)-dilactone (II), D-Glucaro-(1→4)-lactone (III), D-Glucaro-(6→3)-lactone (IV), V and Ammonium Hydrogen D-Glucarate (VI) to Human Subjects

Subjects (sex, age)	Compound	D-Glucaric acid in urine (mg/24 hr)			
		Before dosage	After dosage		Conversion[a] (%)
			0—24 hr	24—48 hr	
M (M. 29)	II	15	731	38	61
M (M. 29)	II	15	669	—	>55
O (M. 40)	II	19	850	43	71
O (M. 40)	II	19	844	52	71
K (M. 26)	II	16	487	—	>41
M (M. 29)	III	15	98	14	8
S (M. 20)	III	14	100	13	9
St (M. 27)	III	15	112	13	10
Sh (F. 32)	III	18	85	15	7
O (F. 36)	III	12	71	18	6
M (M. 29)	IV	15	79	18	6
S (M. 20)	IV	14	46	15	3
M (M. 29)	V	15	22	9	—
O (M. 40)	V	16	15	9	—
M (M. 29)	VI	15	21	11	—
S (M. 20)	VI	14	22	12	—

a) See Table I a).

Table III. Urinary Excretion of D-Glucaric Acid (V) after Oral Administration of 2,5-Di-O-acetyl-D-glucaro-(1→4) (6→3)-dilactone (IX), 2,5-Di-O-benzoyl-D-glucaro-(1→4)(6→3)-dilactone (X), 2,3,5-Tri-O-acetyl-D-glucaro-(1→4)-lactone (XI), Methyl D-Glucaro-(1→4)-lactonate (XII) and Ethyl D-Glucaro-(1→4)-lactonate (XIII) to Human Subjects

Subjects (sex, age)	Compound	Dose (g)	D-Glucaric acid in urine (mg/24 hr)			
			Before dosage	After dosage		Conversion[a] (%)
				0—24 hr	24—48 hr	
O (M. 42)	IX	1.5	16	643	38	54
M (M. 31)	IX	1.5	15	660	27	52
K (M. 27)	IX	1.5	11	546	16	45
O (F. 38)	IX	1.5	14	508	26	42
M (M. 31)	X	0.91	14	14	15	—
O (M. 43)	XI	0.76	16	25	15	—
A (M. 25)	XI	0.76	13	19	16	—
T (M. 32)	XI	0.76	15	15	14	—
O (M. 43)	XII	1	15	903	—	>87
K (M. 28)	XII	1	12	709	—	>68
O (F. 40)	XII	1	12	673	—	>65
M (F. 28)	XII	1	11	604	—	>59
A (M. 25)	XIII	1	12	608	—	>61
M (F. 28)	XIII	0.96	12	519	—	>55

a) See Table I a).

Table IV. Urinary Excretion of Hexaric Acid[a] after Oral Administration of L-Gulonolactone (XIV), *meso*-Inositol (XV), D-Mannuronolactone (XVI) and D-Glucose (XVII) to Human Subjects

Subjects (sex, age)	Compound	Dose (g)	Hexaric acid in urine (mg/24 hr)			
			Before dosage	After dosage 0—24 hr	After dosage 24—48 hr	Conversion[b] (%)
M (M. 29)	XIV	1	15	20	14	—
O (M. 40)	XIV	1	19	18	—	—
M (M. 29)	XV	1	15	16	—	—
O (M. 40)	XV	1	16	14	16	—
O (M. 40)	XVI	1	16	256	—	>20
M (M. 29)	XVI	1	15	208	29	17
M (M. 29)	XVI	2	15	340	—	>14
M (M. 29)	XVII	10	15	21	16	—
O (M. 40)	XVII	10	16	18	15	—

a) As indicated in the previous paper,[1] the chemical assay used for the determination of D-glucaric acid (V) is not specific for V but is applicable to the hexaric acid in general. In the case of XVI, the observed increase in urinary hexaric acid excretion is not due to V but to D-mannaric acid.[8]
b) See Table I *a*).

Besides the above compounds which are mostly derivatives of V, L-gulonolactone (XIV), *meso*-inositol (XV), D-mannuronolactone (XVI) and D-glucose were administered orally to human subjects. XIV is involved in the D-glucuronic acid——L-ascorbic acid shunt as well as in the D-glucuronic acid——L-xylulose cycle, while XV is convertible into D-glucuronic acid in mammalian systems.[12] Among these monosaccharides only XVI had a marked effect on the urinary excretion of hexaric acid as shown in Table IV. This increase in urinary hexaric acid excretion has been disclosed to be due to D-mannaric acid.[13]

Table V. Excretion Rate of D-Glucaric Acid (V) estimated with 24-Hour Human Urine after Oral Administration of D-Glucuronolactone (I), D-Glucaro-(1→4) (6→3)-dilactone (II), D-Glucaro-(1→4)-lactone (III) and 2,5-Di-O-acetyl-D-glucaro-(1→4)(6→3)-dilactone (IX)

Subjects (sex, age)	Compound	Dose (g)	V (mg/24 hr)	Urinary excretion rate of V (%) Time (hr) after administration 2	4	6	8	24
O (M. 40)	I	1	211	42	64	73	80	100
M (M. 29)	I	1	174	39	62	76	82	100
M (M. 29)	I	5	526	26	49	63	80	100
K (M. 26)	I	5	646	21	55	79	85	100
M (M. 29)	II	1	669	48	74	86	90	100
O (M. 40)	II	1	507	44	74	85	91	100
M (M. 29)	III	1	85	38	63	73	81	100
O (M. 40)	III	1	131	34	65	79	86	100
M (M. 29)	III	5	462	45	74	84	89	100
O (M. 40)	III	5	677	53	72	84	90	100
O (M. 40)	IX	1.5	808	38	72	84	90	100
O (F. 37)	IX	1.5	683	32	69	74	83	100

12) S. Hollmann, "Non-Glycolytic Pathways of Glucose Metabolism," translated and revised by O. Touster, Academic Press, New York, 1964, pp. 83—114.
13) M. Matsui, M. Okada, and M. Ishidate. *J. Biochem.* (Tokyo), **57**, 715 (1965); *Chem. Pharm. Bull.* (Tokyo), **17**, 1005 (1969)

Time course of the excretion of V into urine after oral administration of I, II, III and IX to human subjects was estimated with the 24-hour urine. The result indicated that in all cases more than 80% of the total amount of V in the 24-hour urine was excreted in the initial 8 hours (Table V).

Urinary excretion of V after ingestion of I, II, III and IX in rat and guinea pig are shown in Table VI and VII respectively. Some interesting facts indicated in these tables are as follows: 1) Administration of I to rat had no or a very slight effect on the excretion of V, while in guinea pig a considerable effect was observed especially in the oral administration. In this connection, it should be noticed that rat is able to synthesize L-ascorbic acid from I, while guinea pig, monkey and man are the only mammals known to be unable to synthesize it fromI; 2) Conversions (%) of I and II given orally in guinea pig or rat into V were much less than those observed in man; 3) Intraperitoneal or intravenous injection of II in rat and guinea pig resulted in a striking increase of urinary excretion of V; 4) Intraperitoneal or intravenous injection of III in rat and guinea pig had a marked effect on the excretion of V, while oral ad-

Table VI. Urinary Excretion of D-Glucaric Acid (V) after Dosage of D-Glucuronolactone (I), D-Glucaro-(1→4) (6→3)-dilactone (II), D-Glucaro-(1→4)-lactone (III) and 2,5-Di-O-acetyl-D-glucaro-(1→4) (6→3)-dilactone (IX) in Rat

No.	Compound	Dose (mg)	Method of dosage	D-Glucaric acid in urine (mg/24 hr)			
				Before dosage	After dosage 0—24 hr	After dosage 24—48 hr	Conversion[a] (%)
1	I	20	*p.o.*[b]	0.75	0.84	0.57	—
2	I	200	*p.o.*	0.53	1.37	0.62	—
3	I	20	*i.p.*[c]	0.67	0.72	0.62	—
4	I	200	*i.p.*	0.68	2.98	0.69	1
4	I	20	*i.v.*[d]	0.81	1.14	0.63	1
1	II	21	*p.o.*	0.75	5.90	1.00	20
4	II	21	*p.o.*	0.83	4.72	0.73	16
6	II	21	*p.o.*	0.93	6.10	1.10	20
2	II	20	*i.p.*	0.74	17.1	1.03	67
5	II	21	*i.p.*	0.91	18.7	0.97	70
3	II	20	*i.v.*	1.03	13.4	1.17	51
4	II	18	*i.v.*	0.94	14.5	1.07	64
5	II	18	*i.v.*	0.99	15.8	1.03	71
2	III	20	*p.o.*	0.66	9.55	0.66	45
3	III	20	*p.o.*	0.81	8.88	0.58	40
1	III	19	*i.p.*	0.92	8.24	0.73	39
2	III	23	*i.p.*	0.77	11.9	0.61	48
1	III	23	*i.v.*	0.62	18.7	0.66	77
3	III	22	*i.v.*	0.80	16.3	0.62	75
7	IX	30	*p.o.*	0.95	8.45	0.70	31
8	IX	30	*p.o.*	1.14	7.40	0.75	26
7	IX	30	*i.p.*	0.78	10.25	1.30	39
8	IX	30	*i.p.*	0.79	8.40	1.05	31

a) See Table I a). b) *per os* c) intraperitoneal injection d) intravenous injection

14) E. Boyland, "The Biochemistry of Bladder Cancer," Charles C. Thomas Publisher, Springfield, Illinois, 1963.
15) E. Boyland, D.M. Wallace, and D.C. Williams, *Brit. J. Cancer*, **11**, 578 (1957); E. Boyland, D.M. Wallace, P.R.D. Avis, and C.H. Kinder, *Brit. J. Urol.*, **36**, 563 (1964); E. Boyland, C.H. Kinder, D. Manson, and D.M. Wallace, *Invest. Urol.*, **2**, 439 (1965).
16) Y. Yonese, H. Takayasu, M. Okada, and M. Ishidate, Abstracts of Papers, 9th International Cancer Congress, Tokyo, October 1966, p. 700; Y. Yonese, *Jap. J. Urol.*, **59**, 243 (1968).

Table VII. Urinary Excretion of D-Glucaric Acid (V) after Dosage of D-Glucuronolactone (I), D-Glucaro-(1→4) (6→3)-dilactone(II) and D-Glucaro-(1→4)-lactone (III)in Guinea Pig

No.	Compound	Dose (mg)	Method of dosage	D-Glucaric acid in urine (mg/24 hr)			
				Before dosage	After dosage 0—24 hr	After dosage 24—48 hr	Conversion[a] (%)
1	I	20	*p.o.*[b]	0.77	1.94	0.69	5
2	I	20	*p.o.*	0.73	2.63	1.06	8
3	I	200	*p.o.*	0.82	15.4	0.97	6
4	I	200	*p.o.*	0.97	12.6	1.50	5
3	I	20	*i.p.*[c]	1.01	1.68	0.83	3
4	I	20	*i.p.*	0.90	1.38	1.16	2
1	I	200	*i.p.*	1.20	2.69	0.89	0.6
2	I	200	*i.p.*	0.81	4.27	1.11	1.4
3	II	20	*p.o.*	1.19	4.76	1.04	15
4	II	20	*p.o.*	1.71	4.66	1.66	12
5	II	18	*p.o.*	1.38	4.85	1.22	16
6	II	18	*p.o.*	1.28	4.44	1.08	14
1	II	20	*i.p.*	1.16	16.7	1.20	64
7	II	20	*i.p.*	1.23	15.5	1.39	59
8	II	20	*i.p.*	1.48	18.1	1.22	69
1	III	21	*p.o.*	1.15	1.63	0.97	2.2
2	III	20	*p.o.*	0.88	1.57	0.78	3.4
4	III	21	*p.o.*	1.19	1.73	0.96	2.5
7	III	21	*p.o.*	1.17	1.74	1.01	2.7
2	III	21	*i.p.*	0.85	15.1	0.70	67
3	III	21	*i.p.*	1.32	16.3	1.10	71
4	III	20	*i.p.*	1.12	17.8	1.24	85
7	III	20	*i.p.*	1.08	19.8	0.91	95

a)See Table I *a*). b) *per os* c) intraperitoneal injection

ministration resulted in a striking increase of urinary excretion of V only in rat; 5) Oral and intraperitoneal ingestion of IX had a somewhat similar effect on the excretion of V in rat.

On the basis of their experimental results as well as theoretical considerations,[14] clinical application of the ammonium salt of III was made by Boyland and others in an attempt to prevent the development of bladder tumor.[15] While they found no beneficial effects of the compound on the bladder tumor in man, they noticed that administration of the compound did not reduce sufficiently the urinary β-glucuronidase activity. They found further that the administered compound was metabolized very rapidly and only less than 5% of the dose was excreted in urine.

Principally based on the findings obtained in the present work about the urinary excretion of V after oral administration of II and IX in man, they are being used in clinical trials, in terms of prevention of bladder tumor recurrences.[16]

Materials and Methods

Meterials——*meso*-Inositol (XV) and D-glucose were commercial samples. D-Glucaro-(1→4)-lactone (monohydrate) (III) and D-glucaro-(6→3)-lactone (IV) were prepared as described by Bose, *et al.*[17] D-Glucuronolactone (I), D-glucaro-(1→4) (6→3)-dilactone (II), D-glucaric acid (V), ammonium hydrogen D-glucarate (VI), sodium D-glucuronate (VII), D-glucuronamide (VIII), 2,5-di-O-acetyl-D-glucaro-(1→4) (6→3)-dilactone (IX), 2,5-di-O-benzoyl-D-glucaro-(1→4) (6→3)-dilactone (X), 2,3,5-tri-O-acetyl-D-glucaro-(1→4)-

17) R.J. Bose, T.L. Hullar, B.A. Lewis, and F. Smith, *J. Org. Chem.*, **26**, 1300 (1961).

lactone (XI), methyl D-glucaro-(1→4)-lactonate (XII), ethyl D-glucaro-(1→4)-lactonate (XIII), L-gulonolactone (XIV) and D-mannuronolactone (XVI) were obtained from Chugai Pharmaceutical Co., Ltd.

Urine Samples——Samples of human urines were obtained from this laboratory. From rats (male Donryu rats, body weight: 300—350 g) and guinea pigs (male, body weight: 450—550 g) maintained on normal diets in metabolism cages 24-hour urine samples were collected without any preservative in the collecting vessels. Urines were stored at 0° if examined within 24 hr of collection, or otherwise stored at −20°.

Method of Administration——To man test compounds were administered orally with water. Freshly prepared aqueous solutions of I, II and III were given orally in 1 ml to rat and guinea pig using stomach tube or catheter. For intraperitoneal or intravenous injection I, II and III were dissolved in 0.9% saline just before use and given in 1 ml. IX was suspended in 5% *gummi arabicum* solution and the suspension was given orally or intraperitoneally in 1 ml.

Determination of D-Glucaric Acid (V)——Determination of V in urine was performed according to "Procedure I" of the method reported earlier.[1]

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Synthesis of Coumurrayin

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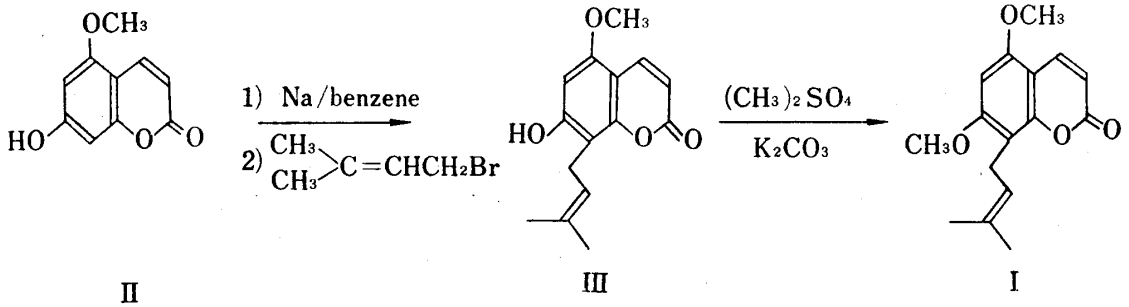
Recently, the structure of coumurrayin which was isolated from the ripe fruits of *Murraya paniculata* (L.) JACK (Rutaceae) has been elucidated as I by E. Ramstad, *et al.*[2] This paper deals with the synthesis of coumurrayin (I) from 7-hydroxy-5-methoxycoumarin (II).[3]



II III I

When sodium salt of II was treated with freshly distilled 1-bromo-3-methyl-2-butene in dry benzene under reflux, the 3-methyl-2-butenyl substituent was introduced to the expected C_8-position in II leading to 7-hydroxy-8-(3-methyl-2-butenyl)-5-methoxycoumarin (III). The structure of III was supported by the infrared (IR) absorption bands (in KBr) at 3360, 1690, 1600 and 1575 cm^{-1} and the nuclear magnetic resonance (NMR) spectrum of III taken in deuteropyridine, 1.67 (3H, broad singlet), 1.96 (3H, broad singlet), 3.80 (2H, broad doublet, J=7 cps) and 5.65 ppm (1H, broad triplet, J=7 cps), indicating the presence of a 3-methyl-

1) Location: *Yagotourayama, Tenpaku-cho, Showa-ku, Nagoya.*
2) E. Ramstad, W.C. Lin, T. Lin and W. Koo, *Tetrahedron Letters*, **1968**, 811.
3) T.R. Seshadri and M.S. Sood, *Indian J. Chem.*, 3, 354 (1965) [*C.A.*, **63**, 18009 (1965)].