

**403.** *Optical Rotatory Dispersion in the Carbohydrate Group.*  
*Part IV. Tetramethyl  $\gamma$ -Mannonolactone.*

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It was found by Haworth, Hirst, and Smith (J., 1930, 2659) that the rotatory power of certain methylated lactones displayed remarkable variations with solvent, the differences being most evident with those lactones which possess *cis*-methoxy-groups on the second and third carbon atoms; *e.g.*, tetramethyl  $\gamma$ -mannonolactone (I) has  $[\alpha]_D + 65^\circ$  in water and  $-49^\circ$  in benzene, whilst the epimeric tetramethyl  $\gamma$ -gluconolactone (II) has high positive rotations which vary only moderately from solvent to solvent. The vicinal effect of the *cis*-methoxy-groups is as marked in this instance as it is in the case of  $\alpha$ -derivatives of mannose, which fail to obey even approximately Hudson's isorotation rules.

We have studied a typical example of an  $\alpha$ -mannose derivative in Part III (this vol., p. 1151) and have found that a quantitative correlation between the glucose and mannose series of derivatives is rendered doubly difficult on account of the different types of optical rotatory dispersion exhibited by these epimeric substances. The lactones exhibit yet additional complications by virtue of the induced dissymmetry of the carbonyl group, which, in certain cases already studied (Lowry and Gore, *Proc. Roy. Soc.*, 1932, *A*, 135, 13;

Levene and Marker, *J. Chem. Physics*, 1933, 1, 662), has been found to contribute a large and sometimes a dominating influence to the rotation in the visible region.



The rotatory dispersion of tetramethyl  $\gamma$ -mannonolactone has now been investigated, and in all the solvents employed, with the single exception of water, it is anomalous. An interesting explanation of the rotational behaviour of the lactone follows from an analysis of the observations. The rotatory power in alcohol, chloroform, benzene, acetone, and dioxan can be expressed by two-term Drude equations with terms of opposite sign. The corresponding frequency constants (see Table I) differ only slightly throughout the range of non-aqueous solvents and indicate that the rotation in these solvents depends essentially on two centres of absorption, one situated in the Schumann region in the neighbourhood of  $\lambda$  1500, and the other near to  $\lambda$  2500. The former may be identified with the normal frequencies found in aliphatic ethers, and the latter is to be associated with the lactonic CO group.

TABLE I.

*Tetramethyl  $\gamma$ -mannonolactone in various solvents.*

Solvent.	$[\alpha]_D^{25}$ .	$c$ .	$\lambda_1^2$ .	$\lambda_2^2$ .	$k_1^*$ .	$k_2^*$ .	$k_1/k_2$ .
Water .....	+ 59.8°	4.2	—	0.049	—	+ 17.8	—
Acetone .....	+ 4.95	3.2	0.022	0.065	— 6.816	+ 7.361	— 0.926
Alcohol .....	— 0.78	5.1	0.027	0.0575	— 12.25	+ 10.89	— 1.125
Chloroform .....	— 3.48	16.5	0.020	0.064	— 9.835	+ 6.521	— 1.508
Dioxan .....	— 14.7	15.36	0.022	0.063	— 13.15	+ 7.26	— 1.812
Benzene .....	— 31.7	16.31	0.026	0.061	— 19.04	+ 7.85	— 2.427
Ether .....	— 36.8	1.73	0.02	0.064	— 18.91	+ 5.66	— 3.339

\* The values for  $k_1$  and  $k_2$  refer to specific rotations.

In water, the low-frequency term alone remains and the rotation is expressible by a single-term equation; the contributions of all the centres of dissymmetry other than the induced centre cancel one another so completely that their net resultant is negligible. In the organic solvents the cancellation of these terms is less complete and their resultant, except in the case of acetone, is a negative term whose numerical value is sufficiently great in the visual region to render the observed rotation negative. The observations now recorded are of special interest in their bearing on Hudson's rule correlating the rotation of  $\gamma$ -lactones of sugar acids with the configuration of the fourth carbon atom. The rule holds with very few exceptions throughout the series of unmethylated  $\gamma$ -lactones (see Freudenberg and Kuhn, *Ber.*, 1931, 64, 703), and applies also to the rotations of many methylated lactones in aqueous solution. Tetramethyl  $\gamma$ -mannonolactone is one such case, and it now appears that the lactone follows the rule in aqueous solution because under these conditions the induced dissymmetry of the carbonyl group united by an ester linkage to the fourth carbon atom overpowers the rotational effect of the rest of the molecule. When this union is broken, the residual induced effect (due mainly to  $C_2$ ) is greatly diminished and in 2 : 3 : 5 : 6-tetramethyl mannonic acid, which shows simple rotatory dispersion in the negative region, the rotation is controlled by the Schumann bands of the remainder of the molecule. The position is similar to that found in the phenylhydrazides of sugar acids, where the direction of rotation of the compound is determined *via* an induced effect by the configuration of the groups on the second carbon atoms. The present experiments reveal that when tetramethyl  $\gamma$ -mannonolactone is dissolved in certain organic solvents, this induced effect (due mainly to  $C_4$ ) may be less in magnitude than the contribution of the remainder of the molecule. Since the two effects are here of opposite sign, it follows that the rotation may in the visual region be positive in some solvents and negative in

others. The sensitivity to solvent influence is exhibited in a striking manner by the variation of the specific rotation of the lactone in the same solvent (benzene) but at different concentrations :

$c$ .....	1.2	1.9	3	16
$[\alpha]_D^{20}$ .....	-49°	-48°	-46°	-32°

On account of this variation it is not possible at this stage to attempt a correlation between the rotational data ( $k_1$  and  $k_2$ ) and the nature of the solvent, but it is obvious that the position of water as a solvent is unique with respect to this lactone. It is hoped to enquire further into this and other problems raised in the present paper by extension of the work to lactones and other derivatives in which the result of variation in the vicinal effect can be studied.

The absorption spectrum of tetramethyl  $\gamma$ -mannonolactone has been investigated for solutions in water, alcohol, and chloroform. In no case was an absorption band detectable, but the results, which are shown graphically in the fig., give indications of a step-out in the region of  $\lambda$  2200 for the aqueous and alcoholic solutions. Since it is frequently found that the observed peak of an optically active absorption band lies some little distance on the high-frequency side of the frequency calculated for rotational data, it is possible that the step-out and the low-frequency term of anomalous dispersion equation may be correlated with one another.

#### EXPERIMENTAL.

The tetramethyl  $\gamma$ -mannonolactone was prepared partly by Levene and Simms's method (*J. Biol. Chem.*, 1925, 65, 46) and partly by that of Haworth, Hirst, and Stacey (*J.*, 1932, 2481). The specimens used had been purified by fractional distillation under diminished pressure, followed by five crystallisations from light petroleum; m. p. 108°,  $[\alpha]_D^{25} + 59.8^\circ$ ,  $[\alpha]_{5461}^{25} + 71.4^\circ$  in water ( $c$ , 4.2). The rotations recorded in the following tables were measured by the methods previously described (Part I). Readings from  $\lambda$  6708 to 4887 inclusive were obtained visually; all others were photographic measurements.

#### Tetramethyl $\gamma$ -Mannonolactone in Water.

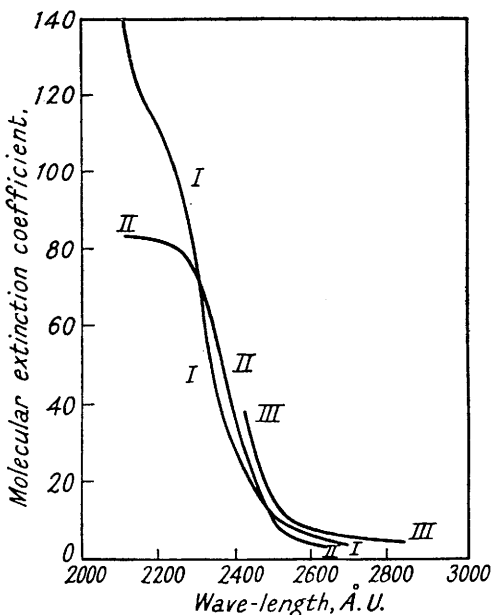
$c$ , 4.216;  $t$ , 25°;  $l$ , 2 dm.;  $[\alpha]_\lambda^{25} = 11.86\alpha_\lambda$ ;  $\alpha_\lambda = 1.50/(\lambda^2 - 0.049)$ .

$\lambda$ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.	$\lambda$ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.	$\lambda$ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.
6708	+3.79°	+3.74°	+0.05°	4307	+10.94°	+10.99°	-0.05°	3317	+24.42°	+24.58°	-0.16°
6292	4.36	4.32	+0.04	4115	12.44	12.47	-0.03	3216	27.42	27.56	-0.14
5893	5.04	5.03	+0.01	3946	13.94	14.06	-0.12	3135	30.42	30.44	-0.02
5805	5.22	5.20	+0.02	3816	15.44	15.52	-0.08	3064	33.41	33.42	-0.01
5515	5.91	5.88	+0.03	3701	16.92	17.05	-0.13	2985	37.41	37.41	$\pm 0$
5225	6.75	6.70	+0.05	3546	19.43	19.55	-0.12	2907	42.40	42.25	+0.15
4920	7.82	7.77	+0.05	3422	21.93	22.03	-0.10	2805	50.39	50.54	-0.15
4556	9.44	9.46	-0.02								

In this solvent the rotatory dispersion is almost simple.

2 : 3 : 5 : 6-Tetramethyl Mannonic Acid in Water.—The rotation of the acid was determined in the following way. A quantity of the lactone was weighed into a graduated flask, a slight excess of sodium hydroxide added, and at the end of 2 hours the exact amount of hydrochloric acid was added to neutralise the alkali. The flask was then filled to the mark with water.

Absorption spectrum of tetramethyl  $\gamma$ -mannonolactone.



I. In water. II. In alcohol. III. In chloroform.

The rotation may be affected to some slight extent by the presence of dissolved sodium chloride;  $[\alpha]_D^{25} - 24.1^\circ$ ,  $[\alpha]_{5461}^{25} - 28.2^\circ$  ( $c$ , 3.1936, calculated as lactone);  $t$ ,  $25^\circ$ ;  $l$ , 2 dm.

$$[\alpha]_\lambda^{25} = 15.66^\circ \alpha_\lambda; \alpha_\lambda = -0.509/(\lambda^2 - 0.016).$$

$\lambda$	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.	$\lambda$	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.	$\lambda$	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.
6708	-1.20	-1.17	-0.03	5515	-1.78	-1.77	-0.01	4310	-2.99	-3.00	+0.01
6292	1.35	1.34	-0.01	5225	1.98	1.98	$\pm 0$	4295	3.03	3.02	-0.01
6104	1.43	1.43	$\pm 0$	4887	2.29	2.28	-0.01	3780	3.99	4.01	+0.02
5893	1.54	1.54	$\pm 0$	4887*	2.28	2.28	$\pm 0$	3430	4.99	5.01	+0.02
5805	1.58	1.58	$\pm 0$								

\* Photographic reading.

The rotatory dispersion within this range of wave-lengths is simple.

*Tetramethyl  $\gamma$ -Mannonolactone in Ethyl Alcohol.*

$c$ , 5.106;  $t$ ,  $25^\circ$ ;  $l$ , 2;  $[\alpha]_D^{25} - 0.9^\circ$ ;  $[\alpha]_{5461}^{25} - 0.1^\circ$ ;  $[\alpha]_\lambda^{25} = 9.79\alpha_\lambda$ ;  $\alpha_\lambda = -1.251297/(\lambda^2 - 0.027) + 1.112292/(\lambda^2 - 0.0575)$ .

6708	-0.13	-0.13	$\pm 0$	4958	+0.24	+0.19	+0.05	2984	+14.86*	+15.09	-0.23
6292	0.10	0.11	+0.01	4620	0.54	0.42	+0.12	2900	19.86*	19.91	-0.05
6104	0.07	0.07	$\pm 0$	4202	0.88*	0.97	-0.09	2832	25.84*	25.47	+0.37
5893	0.08	0.07	-0.01	4132	1.24*	1.11	+0.13	2765	32.82*	33.39	-0.47
5805	0.06	0.06	$\pm 0$	3850	1.88*	1.94	-0.06	2710	42.80*	42.84	-0.04
5515	0.01	0.00	-0.01	3650	2.88*	2.92	-0.04	2667	52.72†	53.25	-0.43
5461	0.00	+0.01	-0.01	3425	4.88*	4.74	+0.14	2620	68.68†	68.76	-0.08
5225	+0.11	+0.07	+0.04	3265	6.88*	6.93	-0.05	2606	76.64†	76.24	+0.04
4887	+0.20	+0.22	-0.02	3092	10.88*	10.95	-0.07	2567	100.32†	100.33	-0.01

\* Observed with  $l = 1$ , and doubled.

† „ „ „  $l = 0.25$ , and multiplied by 8.

The lactone exhibits visual anomaly in ethyl-alcoholic solution.

*Tetramethyl  $\gamma$ -Mannonolactone in Acetone.*

$c$ , 3.236;  $t$ , 20;  $l$ , 2 dm.;  $[\alpha]_D^{20} + 4.95^\circ$ ;  $[\alpha]_{5461}^{20} + 6.85^\circ$ ;  $[\alpha]_\lambda^{20} = 15.47\alpha_\lambda$ ;  $\alpha_\lambda = -0.44406/(\lambda^2 - 0.022) + 0.4758/(\lambda^2 - 0.065)$ .

6300	+0.25	+0.26	-0.01	5300	+0.50	+0.50	$\pm 0$	4400	+1.15	+1.13	+0.02
6050	0.30	0.30	$\pm 0$	5180	0.55	0.55	$\pm 0$	4075	1.65	1.65	$\pm 0$
5750	0.35	0.36	-0.01	4994	0.65	0.64	+0.01	3956	1.90	1.92	-0.02
5640	0.40	0.39	+0.01	4835	0.75	0.74	+0.01	3868	2.15	2.17	-0.02
5450	0.45	0.45	$\pm 0$	4585	0.95	0.94	+0.01				

All the above are photographic measurements. The rotatory dispersion is of the type termed "quasi-anomalous" (Lowry and Cutter, J., 1925, 127, 608).

*Tetramethyl  $\gamma$ -Mannonolactone in Chloroform.*

$c$ , 16.51;  $t$ ,  $25^\circ$ ;  $l$ , 2 dm.;  $[\alpha]_D^{25} - 3.48^\circ$ ;  $[\alpha]_{5461}^{25} - 3.12^\circ$ ;  $[\alpha]_\lambda^{25} - 3.0284\alpha_\lambda$ ;  $\alpha_\lambda = -3.248/(\lambda^2 - 0.020) + 2.4854/(\lambda^2 - 0.064)$  (A);  $\alpha_\lambda = -2.9381/(\lambda^2 - 0.01362) + 2.1534/(\lambda^2 - 0.06548)$  (B).

$\lambda$	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$ (B).	Diff.	$\alpha_{\text{calc.}}$ (A).	Diff.	$\lambda$	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$ (B).	Diff.	$\alpha_{\text{calc.}}$ (A).	Diff.
7200*	-1.06°	-1.07°	+0.01°	-1.05°	-0.01°	4227	+1.21°	+1.18°	+0.03°	+1.20°	+0.01°
6300*	1.18	1.17	-0.01	1.15	-0.03	4220	1.26	1.26	$\pm 0$	1.24	+0.02
6292	1.16	1.17	+0.01	1.15	-0.01	4069	2.20	2.18	+0.02	2.16	+0.04
5805	1.13	1.15	+0.02	1.14	+0.01	3847	4.25	4.23	+0.02	4.21	+0.04
5515	1.06	1.09	+0.03	1.08	+0.02	3650	7.20	7.22	-0.02	7.22	-0.02
5225	0.93	0.95	+0.02	0.95	+0.02	3520	10.25	10.22	+0.03	10.23	+0.02
5054	0.80	0.81	+0.01	0.81	+0.01	3375	15.19	15.17	+0.02	15.21	-0.02
4887	0.65	0.63	-0.02	0.63	-0.02	3272	20.24	20.23	+0.01	20.29	-0.05
4680	0.33	0.28	-0.05	0.29	-0.04	3141†	30.38	30.35	+0.03	30.42	-0.04
4560	0.00	0.00	$\pm 0$	0.01	+0.01	3055†	40.48	40.46	+0.02	40.45	-0.03
4484	+0.21	+0.21	$\pm 0$	+0.20	+0.01						

\* Photographic measurements.

† Measurements with a 1 dm. tube ( $\times 2$ ).

The observed maximum rotation in the negative region was  $\alpha_{6300} = -1.18^\circ$  [Calc. for equation (A),  $-1.15^\circ$ ; for (B),  $-1.17^\circ$ ]. The observed wave-length for zero rotation was  $\lambda$  4560 [Calc. for (A),  $\lambda$  4558; for (B),  $\lambda$  4556]. Both the above equations gave calculated values in good agreement with the observed values, and it appears that equally satisfactory alternative solutions can be derived in which  $\lambda_1^2$  varies between 0.0136 and 0.020 whilst  $\lambda_2^2$  varies between 0.0655 and 0.064 respectively. In general, if  $\lambda_1^2$  in the high-frequency term is reduced it is found

that the corresponding value of  $\lambda_2^2$  in the low-frequency term must be increased, and *vice versa*. Still other equations were examined in which the values of  $\lambda_1^2$  ranged from 0.0015 to 0.0136 and those of  $\lambda_2^2$  from 0.069 to 0.0648 respectively; with these, good agreement could be obtained in the visual and near ultra-violet but deviations occurred in the further ultra-violet. No satisfactory three-constant equation ( $\lambda_1^2 = 0$ ) could be derived. It became clear that no equation would even approximately fit the observations unless it contained a low-frequency term in which  $\lambda_2^2$  had a value close to 0.065 and a high-frequency term in which  $\lambda_1^2$  was not greater than 0.022.

*Tetramethyl  $\gamma$ -Mannonolactone in Ether.*

$c$ , 1.728;  $t$ , 20°;  $l$ , 2 dm.;  $[\alpha]_D^{20^\circ} = 36.8^\circ$ ;  $[\alpha]_{3461}^{20^\circ} = 43.5^\circ$ ;  $[\alpha]_\lambda^{20^\circ} = 28.97\alpha_\lambda$ ;  $\alpha_\lambda = -0.6528/(\lambda^2 - 0.02) + 0.1955/(\lambda^2 - 0.064)$ .

$\lambda$ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.	$\lambda$ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.	$\lambda$ .	$\alpha_{\text{obs.}}$	$\alpha_{\text{calc.}}$	Diff.
6300	-1.15°	-1.14°	-0.01°	4770	-1.95°	-1.95°	±0°	4135	-2.50°	-2.49°	-0.01°
6025	1.25	1.25	±0	4640	2.05	2.05	±0	4085	2.55	2.55	±0
5780	1.35	1.36	+0.01	4515	2.15	2.15	±0	4035	2.60	2.59	-0.01
5555	1.45	1.46	+0.01	4400	2.25	2.26	+0.01	3975	2.65	2.65	±0
5365	1.55	1.57	+0.02	4290	2.35	2.35	±0	3925	2.70	2.70	±0
5115	1.70	1.71	+0.01	4185	2.45	2.45	±0	3850	2.77	2.77	±0
4975	1.80	1.80	±0								

All the above measurements were photographic. The rotatory dispersion is anomalous. The observed and calculated value of  $\lambda$  for the point of inflexion was  $\lambda$  3900.

*Tetramethyl  $\gamma$ -Mannonolactone in Benzene.*

$c$ , 16,306;  $t$ , 25°;  $l$ , 1 dm.;  $[\alpha]_D^{25^\circ} = 31.7^\circ$ ;  $[\alpha]_{3461}^{25^\circ} = 36.9^\circ$ ;  $[\alpha]_\lambda^{25^\circ} = 6.1327\alpha_\lambda$ ;  $\alpha_\lambda = -3.10481/(\lambda^2 - 0.02576) + 1.2793/(\lambda^2 - 0.06106)$ .

6708	-4.01	-4.03	+0.02	4202	-9.50	-9.51	+0.01	3393	-11.08	-11.08	±0
6292	4.54	4.56	+0.02	4060	10.00	10.00	±0	3384	11.05	11.05	±0
6104	4.82	4.84	+0.02	3910	10.50	10.49	-0.01	3348	10.91	10.89	-0.02
5893	5.17	5.19	+0.02	3828	10.74	10.74	±0	3338	10.81	10.84	+0.03
5805	5.33	5.34	+0.01	3790	10.85	10.85	±0	3283	10.49	10.48	-0.01
5515	5.89	5.89	±0	3730	11.00	11.00	±0	3232	9.99	9.97	-0.02
5225	6.51	6.52	+0.01	3713	11.04	11.04	±0	3163	8.98	8.98	±0
4887	7.36	7.37	+0.01	3691	11.08	11.08	±0	3113	7.97	7.95	-0.02
4681	7.99	7.96	-0.03	3405	11.12	11.12	±0	3060	6.44	6.47	+0.03
4424	8.75	8.77	+0.02								

The rotatory dispersion is anomalous. The calculated maximum value of  $\alpha_\lambda$  in the negative region was  $-11.28^\circ$  at  $\lambda$  3526. The observed value, obtained by interpolation, was  $-11.30^\circ$  at  $\lambda$  3530. The point of inflexion occurred at  $\lambda$  4046 ( $\alpha = -10.05^\circ$ ; calc. values). The observed values (by interpolation) were  $\lambda$  4050 and  $\alpha = -10.05^\circ$ . For  $\alpha = 0^\circ$  the wave-length is 2929 (calc.).

*Tetramethyl  $\gamma$ -Mannonolactone in Dioxan.*

$c$ , 15.36;  $t$ , 25°;  $l$ , 2 dm.;  $[\alpha]_D^{25^\circ} = 14.7^\circ$ ;  $[\alpha]_{3461}^{25^\circ} = 16.76^\circ$ ;  $[\alpha]_\lambda^{25^\circ} = 3.255\alpha_\lambda$ ;  $\alpha_\lambda = -4.04123/(\lambda^2 - 0.02188) + 2.23009/(\lambda^2 - 0.062806)$ .

6708	-3.68	-3.68	±0	4300	-6.54	-6.54	±0	3580	-3.91	-3.92	+0.01
6292	4.12	4.11	-0.01	4150	6.51	6.51	±0	3508	2.96	2.95	-0.01
5805	4.72	4.69	-0.03	4110	6.48	6.48	±0	3445	1.86	1.86	±0
5515	5.07	5.08	+0.01	4070	6.44	6.44	±0	3404	0.97	0.97	±0
5225	5.48	5.49	+0.01	4010	6.36	6.35	-0.01	3375	0.30	0.30	±0
5054	5.74	5.73	-0.01	3907	6.11	6.08	-0.03	3363	+0.03	+0.04	-0.01
4887	5.97	5.97	±0	3873	5.99	5.96	-0.03	3308	1.68	1.67	+0.01
4680	6.24	6.23	-0.01	3760	5.46	5.45	-0.01	3254	3.66	3.66	±0
4805	6.11	6.08	-0.03	3688	4.96	4.97	+0.01	3169	7.80	7.83	-0.04
4695	6.26	6.21	-0.05	3632	4.46	4.46	±0	3140	9.60	9.64	-0.04
4530	6.41	6.40	-0.01								

The rotatory dispersion is anomalous. The calculated maximum value of  $\alpha$  in the negative region was  $-6.54^\circ$  at  $\lambda$  4253. The observed value, obtained by interpolation, was  $-6.56^\circ$  at  $\lambda$  4250. The point of inflexion was at  $\lambda$  5000,  $\alpha = -5.80^\circ$  (Calc. :  $\lambda$  4993,  $\alpha = 5.82$ ). For  $\alpha = 0^\circ$ , the observed wave-length is  $\lambda$  3364 (Calc. :  $\lambda$  3364).

The authors thank the Government Grant Committee of the Royal Society for a grant.

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[Received, July 7th, 1934.]