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Thermal polymerization of some glucofuranose derivatives*

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ABSTRACT

Methyl α,β-D-glucofuranoside (**1**) and 1,2-*O*-isopropylidene-α-D-glucofuranose (**2**) have been polymerized thermally, using 0.1% phosphoric acid as catalyst. The resulting alcohol-insoluble polymers were analyzed by gel-permeation chromatography and methylation analysis. The two starting materials gave polymers that were very similar in molecular-weight distribution and in glycosyl-linkage composition. The proportion of furanosyl residues in the polymer, estimated by the relative proportions of furanosyl and pyranosyl residues that could be determined unequivocally by methylation analysis, was ~35–40%; higher than is found when glucopyranosides are polymerized, but indicating that significant furanose–pyranose isomerization had occurred during the polymerization process.

INTRODUCTION

As a part of a program to study chemical mechanisms of pyrolysis of polysaccharides, we have previously synthesized highly branched glucans by acid-catalyzed thermal polymerization of 1,6-anhydro-β-D-glucopyranose, and of methyl and phenyl glucopyranosides[1]. These methods will subsequently be used to synthesize isotopically labeled glucans for pyrolysis studies. To extend these studies, we have now polymerized two different glucofuranose derivatives using similar acid catalysis. The thermal polymerization of glycosides was first observed with 2-deoxyfuranosides by Stacey *et al.*[2,3] They found that the reaction was a condensation polymerization which, in the case of methyl 2-deoxy-α,β-D-galactofuranoside[4], resulted in an oligosaccharide having an approximate d.p. of 4–8 (cryoscopic). Accordingly, it was anticipated that the glucofuranosides would be found to polymerize at least as readily as the pyranosides.

In the study reported herein, we have investigated the acid-catalyzed, thermal polymerization of methyl α,β-D-glucofuranoside (**1**) and of 1,2-*O*-isopropylidene-α-D-glucofuranose (**2**).

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RESULTS AND DISCUSSION

Polymerization and isolation of the polymers. — (a) Methyl α,β-D-glucofuranoside (**1**). Compound **1** was synthesized from D-glucurono-1,4-lactone by treatment with acidic methanol followed by sodium borohydride[5]. The colorless, oily product, purified by preparative l.c., was a mixture of the β- and α-anomers in 93:7 molar ratio, as determined by g.l.c. of the trimethylsilyl ethers and by ^{13}C-n.m.r. spectroscopy. No pyranosides were observed.

To determine the best acid conditions for polymerization, thermogravimetry (t.g.) was performed on **1** with and without various acid catalysts and Fig. 1 shows some resultant t.g. and differential thermogravimetric (d.t.g.) curves. Without acid catalyst, t.g. of **1** showed only a single thermal event (as indicated by weight loss), which probably included polymerization and subsequent degradation, as well as anhydride formation and distillation. The final low yield (5%) of char suggested that the latter two forms of weight loss were more significant than the former. Of the acids and concentrations studied, the addition of 0.1% phosphoric acid resulted in a maximum separation of the thermal profile into two major events (Fig. 1). We interpreted the low-temperature d.t.g. peak as due to loss of methanol to form a polymer (see Scheme 1), and the second peak as due to thermal decomposition of the polymer. Such decomposition is usually associated with dehydration of the polymer and also loss of low-molecular-weight carbon-containing compounds. The spike in the low-temperature d.t.g. peak of the acid-treated material was variable from one experiment to another and was associated with bubbling in the oily sample, probably due to rapid loss of methanol. It was concluded that maximum production of polymer would thus entail heating of the sample through the low-temperature thermal event and cooling it before subsequent decomposition occurred.

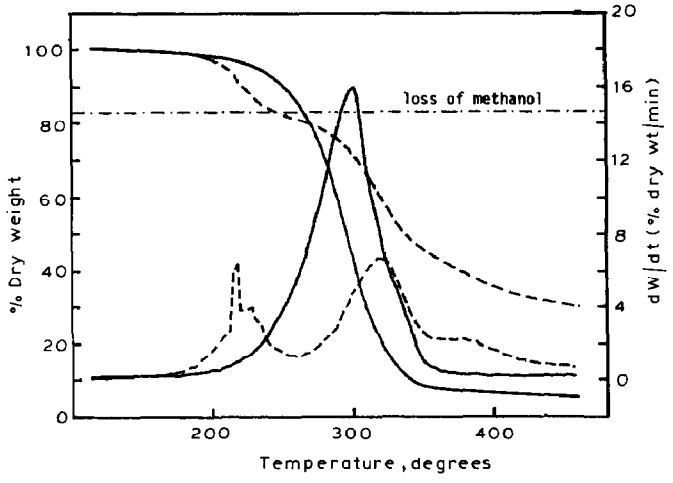


Fig. 1. Thermal analysis of **1** with (---) and without (—) 0.1% phosphoric acid.

TABLE I

Glucans from the thermal polymerization of **1** and **2**

Substrate, catalyst	*Polymerization conditions*	*Yield of polymer (%)*[a]	*Anhydro-glucose content (%)*[b]
1, 0.1% H_3PO_4	185°, 30 min[c]	73	90
2, none	196°, 150 min[c]	13	n.d.[d]
2, 0.1% H_3PO_4	170°, 130 min[e]	80	92
2, 0.5% H_3PO_4	164°, 60 min[f]	47	n.d.

[a] Expressed as a percentage of the theoretical yield of polymer. [b] Determined by phenol–sulfuric acid colorimetric analysis. [c] In an oil-bath. [d] Not determined. [e] In oil-bath for 70 min, followed by 60 min in an oven. [f] In an oven.

To produce the polymer on a large scale, compound **1**, containing 0.1% phosphoric acid was heated under the temperature regimes shown in Table I. The sample was periodically weighed, to determine when the theoretical weight loss had been obtained. At this time, heating was terminated. The resulting glassy material was dissolved in water and precipitated by dropwise addition of the solution to ethanol, to a final ethanol concentration of 95%. The washed and dried precipitate is hereafter referred to as "poly-**1**". The yield of this polymer (Table I) was somewhat higher than those previously reported[1] from glucopyranosides and the glucose content determined colorimetrically was high, demonstrating that the synthetic polymer was largely a glucan. This result also probably precludes any significant presence of interglucose *ether* linkages.

The alcohol-soluble fraction was trimethylsilylated and analyzed by g.l.c. Only 22% of the weight could be accounted for by this analysis. No residual starting material was found. Instead the analyzable portion of the alcohol-soluble material was comprised largely of 1,6-anhydro-β-D-glucopyranose (**5**, 3%), 1,6-anhydro-β-D-glucofuranose (**3**, 9%), methyl α- and β-D-glucopyranoside (6%), and D-glucose (4%). The remainder was probably comprised of oligosaccharides.

(b) 1,2-O-isopropylidene-D-glucofuranose (**2**). T.g. of **2** gave irreproducible results, but indicated the occurrence of two regions of weight loss. The irreproducibility was caused by distillation of **2** and subsequent crystallization in cooler parts of the thermal balance, including the "hang-down" wire. There was apparently also some loss of acetone and consequent polymer formation and the second thermal event was probably associated with thermal degradation of the polymer. T.g. of **2** containing 0.1% phosphoric acid gave the results shown in Fig. 2, which were reproducible. The initial thermal event occurred at a lower temperature than in the absence of acid and was no longer associated with visible distillation of **2**. Furthermore, the initial thermal event terminated shortly after the theoretical weight loss of acetone had occurred, suggesting that polymerization had proceeded successfully.

Compound **2** was polymerized on a large scale using three different concentrations of phosphoric acid, namely 0, 0.1, and 0.5% (Table I). The thermal conditions varied, depending on the acid concentration. If excessive foaming and thus poor

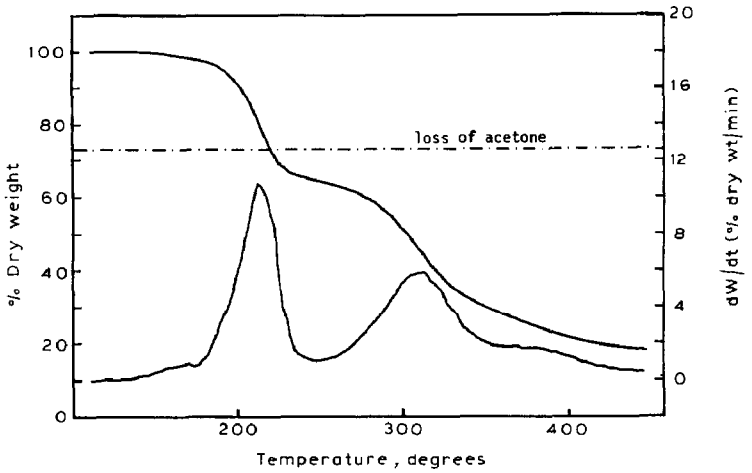


Fig. 2. Thermal analysis of **2** with 0.1% phosphoric acid.

heat-transfer occurred, the sample was moved from the oil-bath to a thermostatically controlled oven. As expected from the thermogravimetric results, the sample without acid gave some polymer, but the yield was low (Table I). The addition of 0.1% phosphoric acid greatly enhanced the yield of polymer. Increasing the phosphoric acid concentration to 0.5% and using the heat treatment shown in Table I gave only a moderate yield of polymer. The polymer made from **2** with 0.1% phosphoric acid was further characterized and will hereafter be referred to as "poly-**2**".

The alcohol-soluble fraction produced during the formation of poly-**2** was trimethylsilylated and analyzed by g.l.c. As was the case with poly-**1**, no residual starting material was found and the major portion of the alcohol-soluble material was not detected by this method. However, it did contain 2.4% 1,6-anhydro-β-D-glucopyranose (**5**) and 4.5% 1,6-anhydro-β-D-glucofuranose (**3**).

*Partial characterization of the polymers. — (a) Poly-***1**. Gel-permeation chromatography was used to determine the approximate molecular-weight distribution of the polymer (Fig. 3). The manufacturer's published calibration of this gel, using linear dextrans[6] shows a fractionation range from $\sim 4 \times 10^5$ to ~700 daltons. Subject to there being no major effect on gel permeation due to extensive branching, poly-**1** appears to embrace components covering the whole of this molecular-weight range, with the weight distribution shifted toward the low-molecular-weight end. Similar polydispersity, though with less high-molecular-weight component, was also observed with synthetic polymers made from glucopyranosides[1].

An estimate of the number-average molecular weight (MW_n) was made by analyzing poly-**1** for methanol end groups, using hydrolysis followed by g.s.c. analysis for methanol. A value of ~1 methoxy group per 50 glucosyl residues was obtained, corresponding to $MW_n \sim 8 \times 10^3$. This method assumes that the aglycons of all reducing-terminal residues are methanol. Since there is a possibility that some of the polymer molecules may terminate with reducing glucosyl or 1,6-anhydroglucosyl resi-

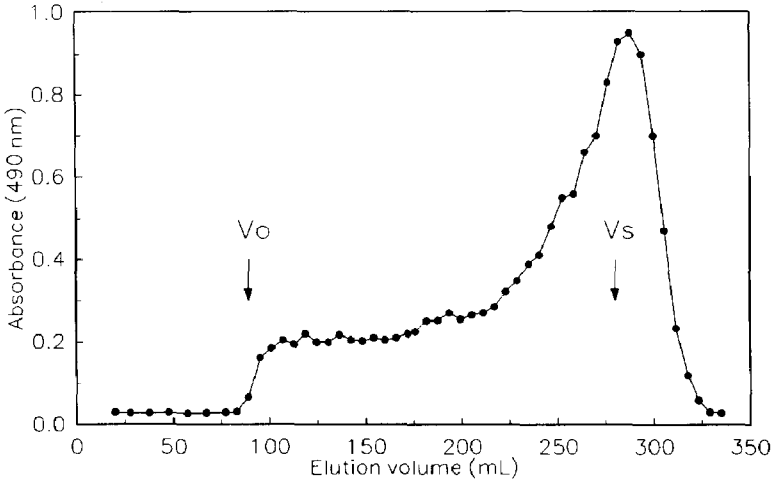
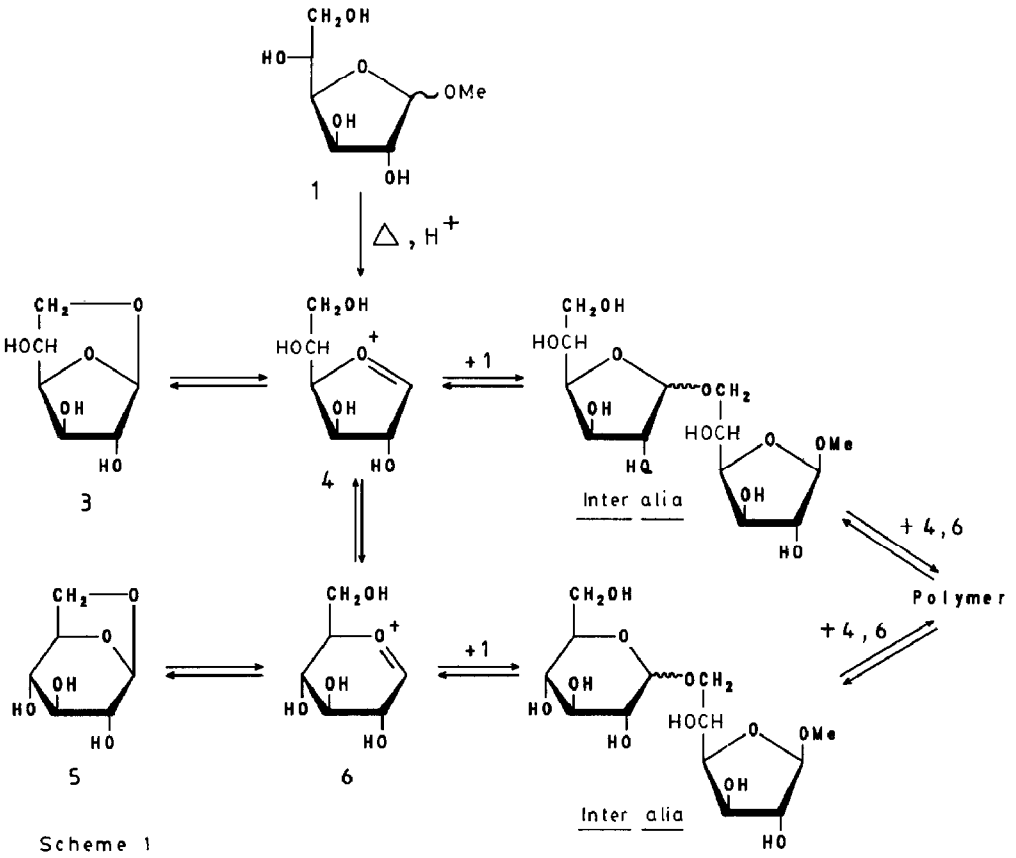


Fig. 3. Gel-permeation chromatography of poly-1 on Sephadex G-200. The arrows show the elution volumes (leading edge) of Blue Dextran (V_o) and sodium chloride (V_s).

dues, the estimated MW_n is a maximum value. The relatively low amount of residual methoxyl groups was substantiated by the lack of a distinct singlet at $\delta \sim 3.4$ in the ^{1}H-n.m.r. spectrum of poly-**1**. This singlet was clearly visible at 3.36 p.p.m. in the spectra of glucans made from methyl glucopyranosides[1]. The latter glucans therefore probably had significantly lower average molecular weight[1] ($MW_n \sim 2 \times 10^3$) than the present poly-**1**, perhaps because of the relatively facile formation of the glucofuranosyl cation.

Complete methylation of poly-**1** proved to be difficult, with a modified Hakomori methylation procedure[7] resulting in a severely undermethylated product. The best results were obtained using powdered NaOH as a catalyst for methylation[8], or the multiple-methylation procedure of Harris *et al.*[7] The application of these procedures, while still resulting in some incomplete methylation, gave a product that was sufficiently methylated to permit some general conclusions about the polymer structure. The following results were obtained using NaOH as the methylation catalyst.

Methylation analysis of poly-**1** (Table II) revealed that many of the glucosyl residues were in the furanose ring form, but that a large portion of the residues were in the pyranose form. Interconversion of the ring form from the furanose ring of the starting material to the pyranose form is most likely due to isomerization of the glucosyl cation[9] during the polymerization process (**4** → **6**, Scheme 1). The proportion of furanosyl to pyranosyl residues in poly-**1** could not be rigorously determined because several of the products of methylation analysis could have arisen from either furanosyl or pyranosyl units. The reductive cleavage method of Jun and Gray[10] was also applied in trial experiments. In theory, this method is capable of distinguishing between pyranosyl and furanosyl residues; however, the lack of furanosyl reference compounds and the difficulty of interpreting mass spectra of new products, led us to abandon this approach. Therefore, an approximation of the proportion of furanosyl residues was made by measuring the proportion of derivatives that could be unambiguously assigned as



Scheme 1

furanose. This content of unequivocal furanose units (26%) was much higher than that obtained from the synthetic polymers of glucopyranosides (3–5%)[1]. This observation suggests that polymerization occurs more rapidly than the **4** → **6** equilibration shown in Scheme 1.

Both pyranosyl and furanosyl residues showed a preference for linking through the sterically accessible primary hydroxyl group at C-6, although almost every possible linkage was found. This was also observed with synthetic glucans from glucopyranosides[1].

*(b) Poly-***2**. The G-200 gel-permeation chromatography elution profile of poly-**2** (data not shown) was very similar to that of poly-**1**, indicating a similar molecular-weight distribution. The presence of isopropylidene groups was indicated in ^{1}H-n.m.r. spectroscopy by a broad singlet at 1.41 p.p.m. Integration of this singlet relative to all of the other C-H signals showed one isopropyl moiety for every 12 sugar residues. This amount of residual isopropylidene groups was substantiated by analysis of poly-**2** for acetone, using hydrolysis followed by g.s.c. analysis. The difference between the "end-group" analyses of poly-**1** and poly-**2** was possibly due to the presence of anhydroglucose end-groups in the former. In addition, poly-**2** may have retained some isopropyli-

TABLE II

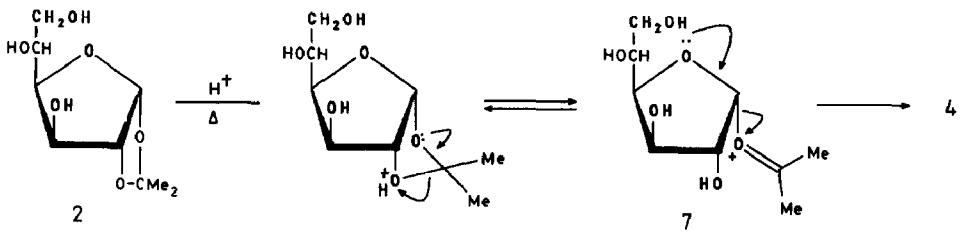
Methylation analyses of the synthetic glucans (in normalized mole %)

Location of methyl groups	*Deduced linkage*	*Ring form*	*Molar ratio*	
			*Poly-***1**	*Poly-***2**
2,3,4,6	T[c]	*p*	18	18
2,3,5,6	T	*f*	12	8
2,3,4	6	*p*	13	13
2,3,5	6	*f*	5	4
2,3,6	4 or 5	*p* or *f*	5	5
2,4,6	3	*p*	3	4
2,5,6[a]	3	*f*	6	7
3,4,6	2	*p*	2	2
2,3[b]	4,6 or 5,6	*p* or *f*	11	12
2,4	3,6	*p*	1	2
2,5	3,6	*f*	1	2
2,6	3,4 or 3,5	*p* or *f*	6	5
3,5	2,6	*f*	1	1
3,6	2,4 or 2,5	*p* or *f*	1	1
4,6	2,3,6	*p*	1	1
5,6	2,3,6	*f*		1
2	3,4,6 or 3,5,6	*p* or *f*	5	6
3	2,4,6 or 2,5,6	*p* or *f*	3	2
4	2,3,6	*p*	2	3
6	2,3,4 or 2,3,5	*p* or *f*	2	1
None	2,3,4,6 or 2,3,5,6	*p* or *f*	2	1

[a] Includes some (~40%?) 3,5,6-tri-*O*-methyl-D-glucitol. [b] Includes small amounts (~10%?) of 3,4-di-*O*-methyl-D-glucitol. [c] Nonreducing terminal residue.

dene groups at positions other than end groups through migration or cross-linking.

The methylation analysis of poly-**2** was very similar to that of poly-**1**. The only discernable difference was a slightly lower proportion of terminal glucofuranosyl residues. The similarity of the two methylation analyses strongly suggested that the polymers were formed mostly from the same monomeric species, namely, the glucofuranosyl **4** and pyranosyl **6** cations. The formation of such cations from **2** is obviously more complex than from methyl glucofuranoside. One possible mechanism is shown in Scheme 2. While there is no evidence for intermediate **7**, its presence and incorporation



Scheme 2

into the polymer by attack of a hydroxyl nucleophile from a polymer molecule at the central isopropyl carbon could explain the large amount of residual isopropylidene groups in poly-**2**. The effect on the polymer structure would thus be similar to "normal" pyrolytic transglycosylation.

Thus the thermal polymerization of **1** and **2** resulted in very similar polymers with respect to size, polydispersity, and linkage pattern. These glucans contain a significant proportion of glucofuranosyl residues and are being used as substrates for pyrolysis studies aimed at elucidating the mechanisms of thermal degradation of polysaccharides.

EXPERIMENTAL

Methyl α,β-D-glucofuranoside (**1**). — The title compound was synthesized from D-glucuronolactone (15 g suspended in 150 mL of MeOH) as described[5], except that Amberlite IR-120 cation-exchange resin (H^+ form, 4.75 g) was used as a catalyst. Following reduction[5] with $NaBH_4$, the title compound was isolated by column chromatography on silica gel in 76% yield and a portion of this product was further purified by l.c. on a Waters Radial-pak RP-18 column (10 cm × 8 mm) eluted with water. The colorless oil had ^{13}C-n.m.r. data in excellent agreement with the literature[11] for a ~10:1 mixture of β:α anomers. G.l.c. of the trimethylsilylated oil demonstrated the presence of only two components in 93:7 ratio.

Polymerization and isolation of polymer. — Phosphoric acid was incorporated into the glucofuranose derivatives **1** and **2** by dissolution in MeOH, addition of a methanolic solution of H_3PO_4, and removal of the solvent by rotary evaporation at ambient temperature followed by drying *in vacuo* over P_2O_5. The substrate (0.2–5 g) was placed in an open Erlenmeyer flask and immersed in an oil-bath at the desired temperature. The sample was periodically stirred, removed, and weighed. If excessive foaming could not be controlled by stirring and inadequate heat transfer was deemed to be a problem, the sample was removed to a thermostatically controlled oven. After heating, the glassy material was dissolved in water (5 mL) and added dropwise to EtOH (95 mL) with rapid stirring. Occasionally, vigorous shaking was necessary to accelerate precipitation of the polymer. The sample was centrifuged and the supernatant evaporated to dryness, yielding the alcohol-soluble fraction. The pellet was washed with EtOH (× 3) then acetone (× 3), and dried *in vacuo*, yielding the polymer as a white powder.

Analytical methods. — Thermogravimetry was performed on a Perkin–Elmer TGS-2 microbalance in a manner similar to that described earlier[1]. Trimethylsilylation was performed using Pierce TriSil[12]. The resulting mixtures were analyzed by g.l.c. on an HP-1 fused-silica capillary column (12 m × 0.2 mm i.d.). Gel-permeation chromatography was performed as described previously[1], and the collected fractions were analyzed colorimetrically using the phenol–H_2SO_4 assay[13]. ^1H-N.m.r. spectroscopy was performed at 90 MHz in D_2O using *tert*-BuOH as internal standard (1.20 p.p.m.). Determination of methanol end groups in poly-**1** was carried out by acid hydrolysis (M H_2SO_4, 120°, 2 h) and g.s.c. analysis (isothermal at 90°) of MeOH as described previously[1]. Analysis of methyl α-D-glucopyranoside by this method resulted in a 93% recovery of MeOH.

The same procedures were applied for the determination of acetone from poly-**2**, except that 0.1M H_2SO_4, 100°, 1 h was used and the g.s.c. analysis was carried out isothermally at 150°. Analysis of **2** by this procedure resulted in a 97% recovery of acetone. Polysaccharides were methylated in Me_2SO with MeI and powdered NaOH as catalyst[8]. The methylated polysaccharide was recovered from the methylation mixture by dialysis followed by lyophilization. Partially-methylated alditol acetates were prepared and analyzed as described previously[12]. The g.l.c. response factors of Sweet *et al.*[14] were applied.

ACKNOWLEDGMENTS

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