

Selectivity for Phosphate and Citrate with Benzyltin-Based Polymer Membrane Electrodes*

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ABSTRACT

Response properties are reported for membrane electrodes prepared by incorporating bis(p-fluorobenzyl)tin dichloride, bis(p-chlorobenzyl)tin dichloride, and tris(p-chlorobenzyl)tin chloride into plasticized poly(vinyl chloride) membranes. These electrodes respond selectively to dibasic phosphate and tribasic citrate. The magnitude of response and the degree of selectivity are affected by the method of pretreating the membrane. The highest level of selectivity is obtained for tribasic citrate from electrodes based on bis(p-fluorobenzyl)tin dichloride after conditioning with citrate. This electrode possesses a limit of detection for citrate of $0.4 \mu\text{M}$ at pH 7.0 with response times ranging from 2 to 5 minutes. Selectivity for citrate is demonstrated over phosphate, thiocyanate, iodide, bromide, nitrate, acetate, lactate, pyruvate, ascorbate, and chloride.

KEY WORDS: Potentiometry, Phosphate, Citrate, Anion selective electrodes.

INTRODUCTION

Several unique strategies are currently being pursued for the development of anion-selective membrane electrodes [1]. Membrane electrodes with high selectivity for dibasic phosphate have been prepared by incorporating selected organotin complexes into plasticized poly(vinyl chloride) membranes [2-4]. A structure/activity relationship has been proposed for derivatives of dibenzyltin dichloride [4]. Experimentally, we have noted that selectivity for phosphate improves in the order of bis(p-methylbenzyl)tin dichloride, dibenzyltin dichloride, and bis(p-chlorobenzyl)tin dichloride [4]. These findings indicate a strong correlation between the Hammett constant for substituents on the benzyl ring and the relative response to phosphate. We have postulated that Hammett constants can be used to predict the relative selectivity for a series of membrane electrodes based on derivatives of dibenzyltin dichloride. As a first test of this hypothesis, bis(p-fluorobenzyl)tin dichloride has been synthesized and the corresponding membrane electrode has been prepared and characterized. The selectivity properties of this electrode corroborate the proposed structure/activity relationship.

As part of our characterization of dibenzyltin electrodes, we have uncovered an unusually high selectivity for the tribasic form of citrate relative to all other anions tested. Citrate response has been found for electrodes based on bis(p-chlorobenzyl)tin dichloride, bis(p-fluorobenzyl)tin dichloride, and tris(p-chlorobenzyl)tin chloride. Unlike the response to phosphate, the magni-

tude of the response to citrate appears independent of the electronegativity of substituents on the benzyl ring.

The construction and characterization of membrane electrodes based on these organotin compounds are described. Special attention is given to the selectivity of these electrodes and the effect membrane pretreatment has on the resulting electrode selectivity.

EXPERIMENTAL

Apparatus

Electrode potentials were measured with a previously described potentiometer [5]. This device is capable of monitoring eight electrodes simultaneously and each potential is measured relative to a single reference electrode. Electrode potentials were collected with an IBM 9000 laboratory computer. A Corning model 476067 double junction silver-silver chloride reference electrode was used throughout with 3 M potassium chloride as the inner solution and 1 M lithium acetate as the outer solution. All measurements were made with stirred solutions in a thermostatted glass jacketed cell coupled with a Fisher model 90 water bath. The entire system was housed in a copper-wire Faraday cage.

Reagents

High molecular weight poly(vinyl chloride) (PVC), p-chlorobenzyl chloride, p-fluorobenzyl chloride, and tetrahydrofuran (THF) were purchased from Aldrich

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Chemical Co. (Milwaukee, WI). Tin mesh (-150, +325 mesh) was purchased from Cerac, Inc. (Pittsburgh, PA). Dibutylsebacate was from Eastman Kodak Co. (Rochester, NY), and Dimethylformamide was from EM Scientific (Gibbstown, NJ). HPLC grade toluene was purchased from Fisher Scientific (Pittsburgh, PA). All other compounds were reagent grade materials purchased from common suppliers. Solutions were prepared with Type I grade distilled-deionized water which was obtained by passing the house distilled water through a Milli-Q three house water purification unit.

Procedures

Bis(p-fluorobenzyl)tin dichloride, bis(p-chlorobenzyl)tin dichloride, and tris(p-chlorobenzyl)tin chloride were prepared by essentially the same procedure described earlier for the other dibenzyltin derivatives [2-4], which follows the original synthesis of Kinugawa *et al.* [6]. Briefly, bis(p-fluorobenzyl)tin dichloride was obtained by reacting p-fluorobenzyl chloride directly with tin metal in toluene, and the reaction product was recrystallized in 2-propanol. Tris(p-chlorobenzyl)tin dichloride was made by reacting p-chlorobenzyl chloride with tin metal in water, and the product was recrystallized in cyclohexane. Bis(p-chlorobenzyl)tin dichloride was prepared by a redistribution reaction of tris(p-chlorobenzyl)tin chloride with tin tetrachloride in toluene. Recrystallization was performed in toluene for this last product.

Percent yields were 9.3, 56, and 32% for bis(p-fluorobenzyl)tin dichloride, tris(p-chlorobenzyl)tin chloride, and bis(p-chlorobenzyl)tin dichloride, respectively. The melting point for bis(p-fluorobenzyl)tin dichloride ranged from 175 to 180°C which compared nicely with the literature value of 179 to 180°C [6]. Tris(p-chlorobenzyl)tin chloride melted between 116 and 118°C which was slightly higher than the reported value of 114 to 116°C [6]. The bis(p-chlorobenzyl)tin dichloride decomposed between 205 and 208°C which matches the reported decomposition temperature of 205°C [6]. All organotin compounds were stored in a vacuum desiccator to protect against degradation by hydrolysis.

Electrodes were fabricated by casting polymeric membranes directly over the open end of a short segment of Nalgene tubing that had been wedged onto the end of a 1 mL size disposable pipet tip. Membrane casting solutions were prepared by dissolving 35.1 mg of the organotin compound, 65.6 mg of high molecular weight poly(vinyl chloride), 24.8 mg of dimethylformamide, and 70.6 mg of dibutylsebacate in 1.5 mL of tetrahydrofuran. Freshly cast membranes were allowed to air dry overnight before use. Electrode construction was completed by adding a 0.1 M potassium chloride internal reference solution and a silver-silver chloride internal reference electrode.

Eight electrodes of the same type were characterized simultaneously by immersing the electrode tips into a single solution. All eight electrodes, along with a single reference electrode, were connected to the potentiometer,

and the potentials were recorded as a function of time. Electrode responses to particular anions were obtained by equilibrating the electrode in a 50 mL aliquot of a working buffer and then monitoring the potential for a series of microliter additions of a standard solution of the anion. The working buffer was composed of 10 mM Trizma base adjusted to pH 7.00 \pm 0.01 with sulfuric acid. The pH of the solution was monitored continuously and adjustments were made with either potassium hydroxide or sulfuric acid as needed to maintain a pH of 7.00 \pm 0.01. All species added to the solution were carefully noted to permit accurate calculation of ion activities after each addition. Activities were obtained by using activity coefficients calculated by the Davies equation [7], and ionic strength corrections were made for all acid dissociation constants.

Electrode potentials were recorded when the rate of potential change was less than 0.5 mV/min. Potential changes were calculated as the difference between the steady-state potential in the solution of interest and the steady-state potential of a corresponding blank solution. Response times were calculated as the time between when the standard addition was made and when the potential was recorded. Selectivity coefficients were calculated as the ratio of ion activities corresponding to a specified potential change [4].

RESULTS AND DISCUSSION

Response to Phosphate

Electrodes prepared with bis(p-fluorobenzyl)tin dichloride respond preferentially to phosphate compared to many common inorganic anions. Mean responses for a series of tested anions are presented in a Nernstian plot in Figure 1. In this experiment, all electrode membranes were pretreated by exposing each membrane to 10 mM phosphate for several minutes before calibration. This preconditioning step was found to be required in earlier investigations with these organotin compounds [2-4]. The steady-state response to phosphate is characterized by a slope of -31.5 mV/decade, a linear range from 0.43 to 11.2 mM, and a limit of detection of 86 μ M. As was found for previously characterized electrodes based on derivatives of dibenzyltin, the slope for the phosphate response suggests a preferential response to the dibasic form of phosphate. Inspection of the data in Figure 1 reveals an overall selectivity pattern of dibasic phosphate > thiocyanate > iodide \gg bromide \approx nitrate \approx acetate > chloride.

The relative response to phosphate displayed by bis(p-fluorobenzyl)tin electrodes follows that predicted by the electronegativity of the substituent on the benzyl ring. The reported Hammett constant for the p-fluoro group is 0.06 compared to values of -0.17, 0.00, and 0.23 for p-methyl, hydrogen, and p-chloro groups, respectively [8,9]. The relative responses of the various dibenzyltin electrodes are compared in the Figure 1 inset by plotting the experimentally measured limit of detection for dibasic phosphate as a function of the corresponding

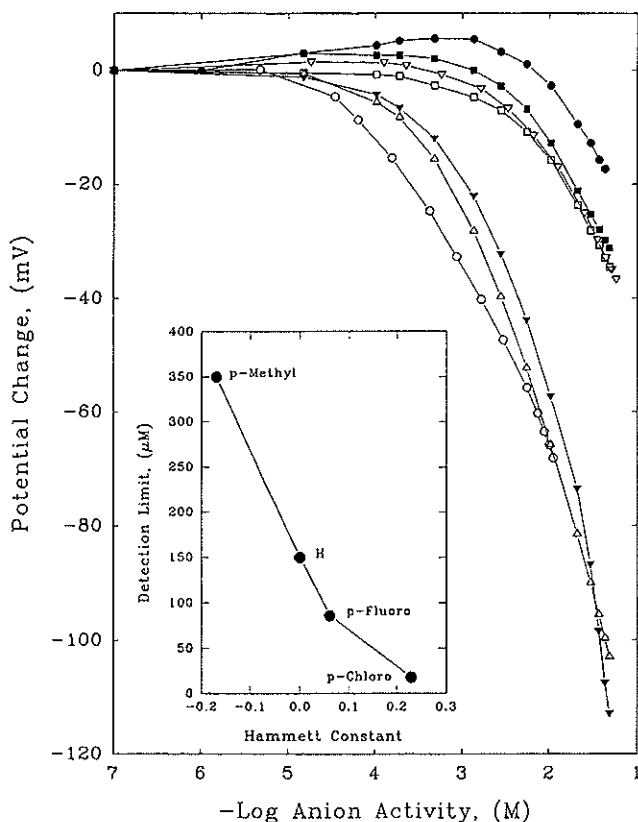


FIGURE 1. Mean responses to a variety of common inorganic anions for electrodes prepared with bis(*p*-fluorobenzyl)tin dichloride: dibasic phosphate (open circles), thiocyanate (open up-triangles), iodide (closed down-triangles), bromide (open squares), acetate (open down-triangles), nitrate (closed squares), and chloride (closed circles). Inset shows the correlation between limit of detection for dibasic phosphate and Hammett constant for substituents on the benzyl ring.

Hammett constant. Results for the bis(*p*-fluorobenzyl)tin electrodes fit very well with earlier results for the other electrodes [4], which serves to corroborate our proposed structure/activity relationship.

Response to Citrate

During our selectivity evaluation of the bis(*p*-fluorobenzyl)tin electrode, we discovered a surprisingly large response to citrate. Such a response was surprising, because citrate is near the bottom of the Hofmeister series and, hence, it is not typically considered a potential interference for anion selective membrane electrodes. The response by bis(*p*-fluorobenzyl)tin electrodes to citrate motivated an examination of the citrate response by bis and tris (*p*-chlorobenzyl)tin electrodes. Each of the organotin electrodes tested responded to citrate, and the magnitude of response depended strongly on the membrane conditioning procedure.

Mean electrode responses are presented in Figure 2A for bis(*p*-fluorobenzyl)tin and bis(*p*-chlorobenzyl)tin

electrodes that had been preconditioned by exposure to phosphate followed by calibration in a pH 7.00 Tris-H₂SO₄ buffer. This preconditioning treatment was the same as the one used earlier when testing for responses to phosphate. The results in Figure 2A reveal that responses at low activities are essentially identical for these two types of electrodes. For bis(*p*-fluorobenzyl)tin, the response slope is -19.6 mV/decade over a linear range from 5.4 to 38.7 μ M with a limit of detection of 0.4 μ M. For bis(*p*-chlorobenzyl)tin, the slope is -20.1 mV/decade over a linear range from 5.4 to 65.3 μ M with a limit of detection of 0.4 μ M. These response properties are summarized in Table 1. The two responses diverge rather dramatically, however, as the citrate activity approaches millimolar levels. The response by bis(*p*-chlorobenzyl)tin electrodes demonstrates a typical "hook" appearance which is characteristic of the formation of an anionic species in the membrane. A hook is observed when the concentration of the anionic species reaches a critical level in the membrane and cations are attracted into the membrane electrostatically, thereby reversing the direction of the potential change. On the other hand, the slope of the response curve for the bis(*p*-fluorobenzyl)tin electrodes increases to 50 mV/decade at higher citrate activities. Although this latter response is unusual, it was observed in all four trials of eight electrodes.

Response slopes at low activities for both the bis(*p*-fluorobenzyl)tin and bis(*p*-chlorobenzyl)tin electrodes suggest a preferential response to the tribasic form of citrate. To investigate this observation further, the response to citrate was examined in an acetate buffer at pH 5.5, where both dibasic and tribasic forms of citrate would be present in nearly equal proportions. The response slope at pH 5.5 was essentially the same as that measured at pH 7.0. In addition, the calculated limit of detection for tribasic citrate was nearly identical at both pH values.

Electrodes prepared with bis(*p*-fluorobenzyl)tin and bis(*p*-chlorobenzyl)tin and pretreated with citrate, as opposed to phosphate, give much different response curves. Mean responses for these electrodes in a pH 7.00 Tris-H₂SO₄ buffer are presented in Figure 2B. Compared to the responses in Figure 2A, the citrate pretreatment lowers the overall magnitude of response to citrate which results in poorer limits of detection. The slope, dynamic range, and limit of detection are listed in Table 1 for each of these electrodes. Slopes for both the bis(*p*-chlorobenzyl)tin and bis(*p*-fluorobenzyl)tin electrodes indicate response to the tribasic form of citrate.

Figure 2B reveals that the response by citrate treated tris(*p*-chlorobenzyl)tin electrodes (open circles) is poor with a slope of only -5.4 mV/decade over a limited range of activities. The citrate response can be improved significantly, however, by not pre-exposing the membrane to citrate. The mean response curve for a series of tris(*p*-chlorobenzyl)tin electrodes is presented in Figure 2B (closed circles). Here, the electrodes were calibrated after only a period in the pH 7.0 Tris-H₂SO₄ buffer. The resulting response slope is -35.1 mV/decade which suggests response to the dibasic form of citrate. Re-

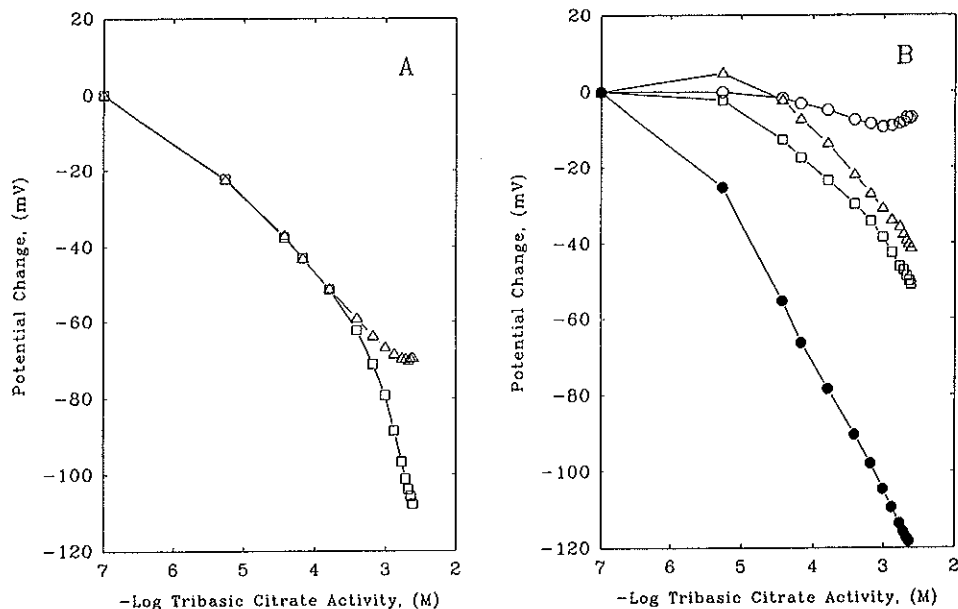


FIGURE 2. Mean responses to citrate for organotin electrodes. Plot A shows responses by bis(p-fluorobenzyl)tin electrodes (squares) and bis(p-chlorobenzyl)tin electrodes (triangles) after pretreatment with phosphate. Plot B shows responses by bis(p-fluorobenzyl)tin electrodes (open squares), bis(p-chlorobenzyl)tin electrodes (open triangles), and tris(p-chlorobenzyl)tin electrodes (open circles) after pretreatment with citrate. Plot B also shows the response from tris(p-chlorobenzyl)tin electrodes after no pretreatment (closed circles).

sponse curves measured at pH 6.0 likewise possessed mean slopes of -31.3 mV/decade. Assuming preferential response to dibasic citrate, the response at pH 7.0 ranges from 0.4 to 156 μM with a limit of detection of 0.06 μM . Essentially the same dynamic range was measured at pH 6.0, but the limit of detection increased to 0.5 μM . Unfortunately, the response of the nontreated electrodes decayed continuously over the period of several days. On the second day, for example, the slope decreased to -29.11 , the dynamic range shifted by one order of magnitude to higher activities, and the limit of detection increased to 8.3 μM .

Response times for responses to citrate are essentially the same for all electrodes tested after each of the pretreatments. Five minute response times are typically observed at low activities, and the response times decrease to approximately 2 minutes at the higher activities. In some cases, response times are as long as 8 minutes at the lowest activities. Electrodes pretreated with phosphate require less time to reestablish the baseline

potential compared to electrodes treated with citrate. The mean recovery time for the phosphate-treated electrodes is 2.0 and 2.4 minutes for bis(p-chlorobenzyl)tin and bis(p-fluorobenzyl)tin electrodes, respectively. Mean recovery times for the same electrodes treated with citrate are 15.0 and 13.3 minutes, respectively. Recovery times for the tris(p-chlorobenzyl)tin electrodes treated with citrate range from 16 to 31 minutes.

Selectivity coefficients for tribasic citrate over a series of inorganic and organic anions indicate that bis(p-fluorobenzyl)tin provides superior selectivity for citrate compared to bis(p-chlorobenzyl)tin, regardless of the preconditioning treatment. Table 2 summarizes all selectivity coefficients measured in this investigation. Bis(p-chlorobenzyl)tin electrodes display a selective response to citrate over phosphate of one order of magnitude, and the method of conditioning is not important. The bis(p-fluorobenzyl)tin electrodes, on the other hand, demonstrate nearly two orders of magnitude higher selectivity for citrate when membranes are treated with

TABLE 1 Citrate Response Properties for Dibenzyltin Electrodes

Dibenzyltin Compound	Slope (mV/decade)		Dynamic Range (μM)		Detection Limit (μM)	
	Phosphate ^a	Citrate ^b	Phosphate ^a	Citrate ^b	Phosphate ^a	Citrate ^b
Bis(p-chlorobenzyl)tin	-20.1	-22.0	5.4-65.3	37-2400	0.4	36.2
Bis(p-fluorobenzyl)tin	-19.6	-18.9	5.4-38.7	37-2400	0.4	7.0

^aElectrodes conditioned with phosphate.

^bElectrodes conditioned with citrate.

TABLE 2 Potentiometric Selectivity Coefficients for the Bis(p-Chlorobenzyl)tin and Bis(p-Fluorobenzyl)tin Electrodes

Anion	Bis(p-Chlorobenzyl)tin		Bis(p-Fluorobenzyl)tin	
	Log K^{pot} (phos) ^a	Log K^{pot} (cit) ^b	Log K^{pot} (phos) ^a	Log K^{pot} (cit) ^b
Dibasic phosphate	-0.92	-0.96	-1.53	-3.02
Thiocyanate	-0.93	—	-1.78	—
Iodide	-2.23	—	-2.23	—
Nitrate	-2.95	—	-3.54	—
Bromide	-3.03	—	-3.13	—
Chloride	-3.80	-2.67	-4.19	-3.00
Acetate	-3.04	—	-3.19	—
Lactate	—	-2.18	—	-2.55
Pyruvate	—	-2.00	—	-2.82
Ascorbate	—	-1.54	—	-2.40

^aElectrodes conditioned with phosphate.

^bElectrodes conditioned with citrate.

phosphate and over three orders of magnitude higher selectivity after citrate pretreatment. After treatment with citrate, electrodes display a cationic type response at low activities of the test anions, which indicates the formation of an anionic species in the membrane upon complexation with citrate. The incorporation of small amounts of a lipophilic cation might effectively counterbalance this anionic species, thereby eliminating this cationic response. Overall, the best selectivity for citrate is obtained with the bis(p-fluorobenzyl)tin electrodes treated with citrate.

All organotin electrodes tested have a significant response to pH over the region from 5.5 to 10. This pH response is likely caused by complexation between the tin compound and hydroxide from solution. Additionally, the formation of tin oxide is readily apparent as the solution pH is increased. Clearly, strong buffering is required and the ideal pH range is from 3.5 to 5.5. The effect of pH below 3.3 has not been assessed.

The functional lifetime of these electrodes represents their most significant limitation. Slow and continual degradation in the response is observed over the course of several days. For example, Figure 3 shows a series of mean response curves for the bis(p-fluorobenzyl)tin electrodes over the course of 25 days. Although the response degrades slowly over time, a significant response is still present on the 25th day. Stabilization of the response is essential before these electrodes will be practical for commercialization.

CONCLUSIONS

The selectivity patterns for both bis(p-fluorobenzyl)tin and bis(p-chlorobenzyl)tin electrodes indicate a preferential response to citrate compared to all tested inorganic and organic anions. The fact that the preconditioning procedure has such a dramatic affect indicates that the membrane chemistry plays a critical role in electrode selectivity. Improvements are needed in terms of stability of the membrane chemistry responsible for these selective responses. In terms of relative response to

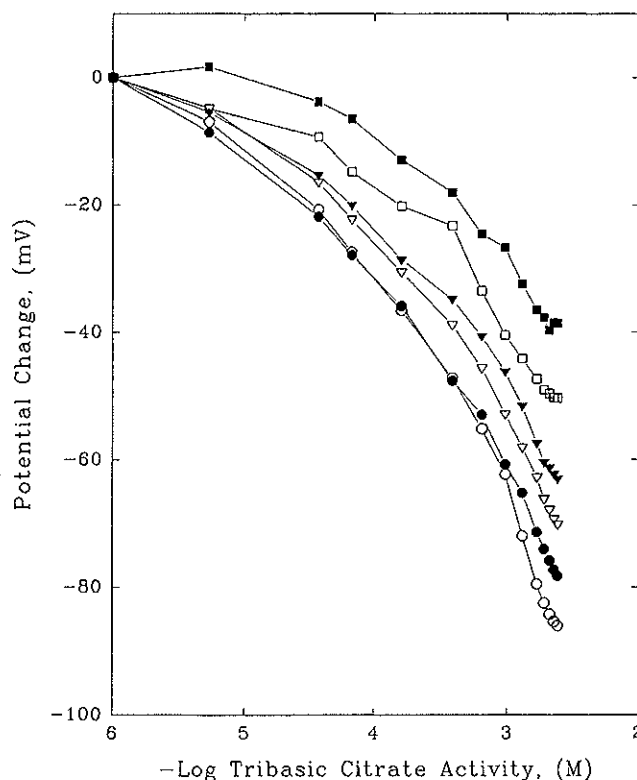


FIGURE 3. Mean responses to citrate for bis(p-fluorobenzyl)tin electrodes over time: day 1 (open circles), day 3 (closed circles), day 5 (open triangles), day 10 (closed triangles), day 18 (open squares), and day 25 (closed squares).

phosphate, the bis(p-fluorobenzyl)tin electrodes corroborate the proposed structure/activity relationship. There appears to be a difference in the fundamental mechanisms of response to phosphate and citrate, which is exemplified by the fact that bis(p-chlorobenzyl)tin is best for phosphate while bis(p-fluorobenzyl)tin is better for

citrate. It might be possible to separate these two mechanisms and develop selective electrodes for each anion once the actual chemical basis for these responses is identified and understood.

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