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SOLVENT EXTRACTION STUDIES USING TETRACYCLINE AS A COMPLEXING AGENT

X. DETERMINATION OF THE STABILITY CONSTANTS FOR THE COMPLEXES OF THORIUM AND TETRACYCLINE*

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Stability constants for thorium complexes with tetracycline were determined by the methods of average number of ligands, the limiting value, the two parameters and by weighted least squares. The solvent extraction technique was used to obtain the required data for the determination of the constants.

Introduction

Separation of uranium from thorium using solvent extraction and tetracycline hydrochloride (TC) as complexing agent has been previously reported.[1] It was shown that diethylenetriaminepentaacetic acid (DTPA) is a good masking agent for thorium allowing the complexation of uranium by TC, which is extracted by the organic solvent benzyl alcohol, while thorium is complexed by DTPA. The complex Th-DTPA is not extracted into benzyl alcohol.

If ethylenediaminetetraacetic acid (EDTA) is used as masking agent for the complexing reaction of thorium by TC, the masking action is only partly efficient to prevent extraction of thorium by TC as Th–TC complex. This together with the fact that DTPA is an efficient masking agent for thorium when uranium is separated from thorium by extraction of U(uranyl) – TC into benzyl alcohol would indicate that the stability constants of Th – TC complexes should be larger than the stability constant of Th – EDTA, but smaller than Th – DTPA.

SAKAGUCHI et al.[2] have determined the values for the stability constants of thorium with the derivatives of TC for which the complexes metal: ligand would

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be in a 1 : 1 proportion. In this way the stability constants of Th-chlorotetracycline and Th-oxytetracycline were found to be lg K = 5.96 and lg K = 4.43, respectively.

In this work the formation or stability constants of $Th(TC)_n$, for n = 1, 2, 3 and 4 are determined by the methods of average number, two parameters, limiting value and least squares.[3]

Theory

To calculate stability constants the following correlation was used

$$D = I_o/I_a = K_D \beta_4 [A]^4 / \sum_{n=0}^{4} \beta_n [A]^n \qquad (1)$$

where
- D – distribution ratio of Th;
- I_o, I_a – activities of the ^{234}Th tracer in the organic and aqueous phases, respectively;
- K_D – distribution constant of the complex $Th(TC)_4$;
- $[A]$ – concentration of the ligand ion in the aqueous phase;
- β_n (n = 1, 2, 3, 4) – formation constants for the complexes $Th(TC)_n$ (charges are omitted for simplicity).

By using a ^{234}Th tracer, the concentration of the metal (tracer plus carrier) can be made much smaller than the initial concentration of the ligand. The amount of ligand in the complex molecule can thus be ignored and the following mass balance correlation will prevail

$$V_o C_o = [HA]_o V_o + ([HA] + [A])\, V \qquad (2)$$

where
- V_o, V – volumes of organic and aqueous phases, respectively;
- C_o – initial concentration of tetracycline in the organic phase;
- $[HA]_o$ – concentration of tetracycline in the organic phase, after equilibration;
- $[HA]$, $[A]$ – concentration of the ligand in the aqueous phase, after equilibration; (organic phase is indicated by subscript o; no subscript in the concentration formula indicates aqueous phase).

Concentration of the free ligand TC, [A], was calculated considering TC as being a monoacid in the pH interval of 1.0 to 3.0, with a pK_1 value equal to 3.39.[4] Hydrogen dissociation of the phenolic diketone and dimethylamino groups are too small[5] for pH values smaller than 5.5.

Concentration of free ligand was calculated by the equation[4]

$$pA = pK_1 - pH - \lg C_o V_o / (1 + D' V_o V^{-1})(1 + K_1 [H]^{-1}) V \qquad (3)$$

where K_1 – first dissociation constant of TC;
D' – distribution ratio for the ligand TC; D' values are taken from reference 4.

General correlations used for calculating the stability constants were already presented in Ref.[4], for the complexes of lanthanides elements and TC, $Ln(TC)_n$, with n = 1, 2 and 3. The same correlations will be used in this paper for $Th(TC)_n$ complexes, with n = 1, 2, 3 and 4.

Since in the case of calculation of stability constants for lanthanide-TC,[4] the method of limiting value was not applied, a brief presentation of the correlations used will be made here.[3]

The parameters f_{4-n} are defined in the following way

$$f_{4-n} = \beta_n / \beta_4 \qquad (4)$$

Eq. (1) is transformed to give

$$F_o = 1/D = (1 + f_1 [A]^{-1} + f_2 [A]^{-2} + f_3 [A]^{-3} + f_4 [A]^{-4}) / K_D \qquad (5)$$

$$F_1 = (K_D/D - 1)[A] = f_1 + f_2 [A]^{-1} + f_3 [A]^{-2} + f_4 [A]^{-3} \qquad (6)$$

$$F_2 = (F_1 - f_1)[A] = f_2 + f_3 [A]^{-1} + f_4 [A]^{-2} \qquad (7)$$

$$F_3 = (F_2 - f_2)[A] = f_3 + f_4 [A]^{-1} \qquad (8)$$

$$F_4 = (F_3 - f_3)[A] = f_4 \qquad (9)$$

β_n values are calculated after determination of f_{4-n} values. f_{4-n} and K_D are determined by drawing the curves of F_o, F_1, F_2, F_3 and F_4 versus $[A]^{-1}$. Next the slopes of the curves at $[A]^{-1} \rightarrow 0$ are determined as well the ordinate values at this point.

Experimental

Solutions

All reagents used were of analytical grade. Benzyl alcohol was equilibrated with water prior to the extraction experiments and vice versa, the water was saturated with benzyl alcohol. Deionized water and distilled in a quartz apparatus was used throughout.

TC was synthesized and purified by "Laborterápica Bristol". Fresh TC solution was prepared every day, since the ligand molecules decompose in aqueous solution at room temperature. Solutions were used within six hours after preparation.

Thorium nitrate solutions were standardized by gravimetry [6] These solutions were used for titration experiments to determine the metal: ligand ratio and as carrier for ^{234}Th in the extraction experiments.

Sodium perchlorate solution used as supporting electrolyte was prepared from $NaClO_4 \cdot H_2O$ in order to given an aqueous phase with an ionic strength of 0.10M.

Carrier-free solutions of ^{234}Th were prepared in accordance with Abráo[7] using uranyl nitrate solutions.

Complex formation between thorium and tetracycline

Potentiometric titrations. TC has three ionizable hydrogens corresponding to the tricarbonylmethane, phenolic diketone and dimethylamino groups. The dissociation constants are $pK_1 = 3.39$, $pK_2 = 7.44$ and $pK_3 = 8.85$, respectively.[4] The complexation position of thorium in the TC molecule was determined by potentiometric titrations of TC solutions in the presence and absence of thorium. Sodium hydroxide was used for titration. Fig. 1 shows the formation of the Th - TC complexes at pH values smaller than 5.5. At these pH values the dissociation of the tricarbonylmethane group occurs indicating that thorium is linked to the TC molecule through the tricarbonylmethane group.

Conductometric titrations. Fig. 2 shows the results of conductometric titrations of thorium with TC, indicating formation of the species in which the metal : ligand ratios are equal to 1 : 1, 1 : 2, 1 : 3 and 1 : 4. Curve B does not show the 1 : 4 complex since the dilution of the solution being titrated is too high to give precise results.

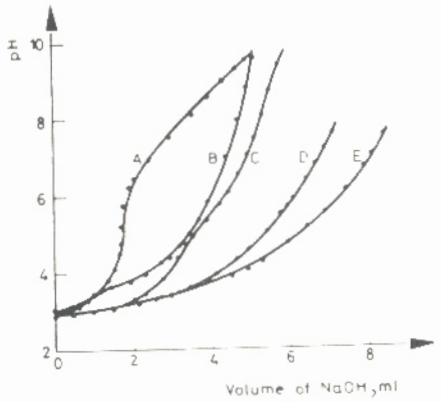

Fig. 1. Potentiometric titration of TC ($9.2 \cdot 10^{-3}$M) with NaOH (0.10M). Relation Th – TC : A – no Th; B – 1 : 1; C – 1 : 2; D – 1 : 3; E – 1 : 4

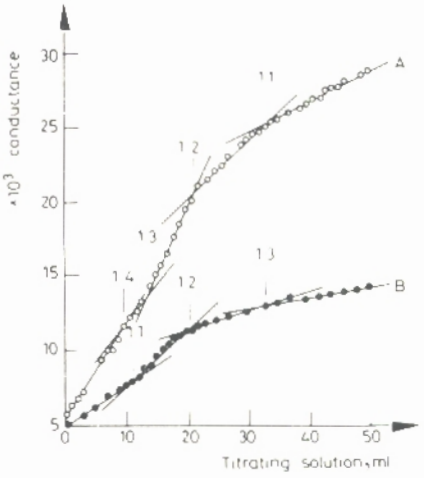

Fig. 2. Conductometric titrations of TC: A – 40 ml TC $9.2 \cdot 10^{-3}$M + 110 ml of water titrated with $Th(NO_3)_4$ 0.01M; B – 10 ml of $Th(NO_3)_4$ 0.01M + 140 ml of water titrated with Th $9.2 \cdot 10^{-3}$M. (In curve B formation of the 1 : 4 complex is not indicated since solutions corresponding to this proportion are too dilute for detection by the conductometer)

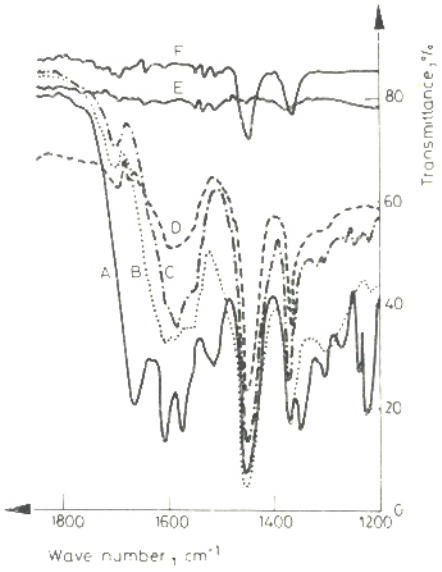

Fig. 3. Infrared absorption spectrum of Th – TC compounds: A – TC; B – Th(TC); C – Th(TC)
D – $Th(TC)_4$; E – KBr cells; F – Nujol oil

Infrared absorption spectra. Complexation position of thorium with the TC molecule was also checked by means of infrared absorption spectrophotometry.

Th – TC complexes were prepared in accordance with BAKER and BROWN,[8] at a pH value of 2.5 and a reaction time of 150 min. The mixture was kept under agitation during this time. The compound formed was dried at room temperature in a vacuum-desiccator.

TC and $Th(TC)_n$ were emulsified in mineral oil (Nujol) and spectra were registered by means of a Perkin–Elmer spectrophotometer, model 180, using KBr cells with 4 mm thick walls and a 38.5 X 19.5 mm window.

TC shows three absorption bands, at 1580, 1610 and 1670 cm^{-1}, which are not present in the spectrum of Th – TC; instead, a large band, at approximately 1600 cm^{-1}, is presented by Th – TC (Fig. 3). Since the absorption corresponding to the value at 1600 cm^{-1} is due to vibration of the –C=O group it is seen that thorium is linked to the TC molecule via the tricarbonylmethane group.

Solvent extraction experiments. Thorium is not linked through the dimethylamino group to the TC molecule since thorium is extracted by benzyl alcohol

Table 1
Percent extraction (%E) of the thorium complex with DTC, ATC and TC

DTC		ATC		TC	
pH	%E	pH	%E	pH	%E
0.95	2.2	1.00	12.3	0.82	14.9
1.29	11.5	1.30	66.6	0.95	25.4
1.64	32.5	1.73	94.7	1.29	68.2
1.97	59.4	2.12	98.8	1.64	91.8
2.20	73.3	2.81	99.4	1.69	91.2
2.62	84.7	2.92	99.8	2.15	98.7
2.84	89.9	3.12	99.8	2.37	99.4
3.30	95.3	3.65	98.5	2.94	99.7

$[DTC] = [ATC] = [TC] = 2 \cdot 10^{-3}$M.
$[Th] = 1.05 \cdot 10^{-5}$M.
$[NaClO_4] = 0.10$M.
Organic solvent: benzyl alcohol.
Shaking time: 30 min at 25.0±0.5 °C.
DTC – dedimethylaminotetracycline.
ATC – anhydrotetracycline.

solutions of dedimethylaminotetracycline (DTC) and DTC has no dimethylamino group. On the other side, thorium is extracted by anhydrotetracycline (ATC) that has, also, the tricarbonylmethane group in the same way as TC and DTC. Results are shown in Table 1.

Thorium ions, Th^{4+}, are not extracted into benzyl alcohol without TC, as shown in Table 2. The extraction of thorium into benzyl alcohol does take place only when TC is dissolved in the organic phase, indicating the formation of the Th – TC complex. NASTASI and LIMA[9] have also shown the formation of this complex by means of the variation of the wavelength of maximum absorbance for TC and the wavelength of maximum absorbance for the compound Th – TC.

Determination of the equilibration time for extraction. The percent extraction (%E) of the Th – TC complex into benzyl alcohol was determined as function of shaking time. In one series of experiments Th – TC was initially dissolved in the organic phase; another series was carried out in which the aqueous phase was the one where thorium was initially dissolved. Results presented in Table 3 show that equilibrium is attained rather rapidly at low or high pH's of the aqueous phase. A 30 min shaking time was chosen for the extraction experiments.

Table 2
Results of thorium extraction
into benzyl alcohol without tetracycline

pH	%E
1.55	0.01
1.80	0.24
2.10	0.37
2.45	0.12

$[Th] = 2.9 \cdot 10^{-4}$M.
$[NaClO_4] = 0.10$M.
Shaking time: 30 min at
25.0±0.5 °C

Table 3
Results of determination
of the equilibration time for extraction

Time, min	pH = 1.50		pH = 2.55	
	I*	II*	I	II
	%E	%E	%E	%E
5	47.5	52.4	97.7	98.7
30	51.7	51.2	98.3	98.9
60	52.2	50.8	98.4	98.6
120	50.4	49.7	98.6	98.6

$[TC] = 7.5 \cdot 10^{-4}$M, $[Th] = 2 \cdot 10^{-5}$M, $[NaClO_4] = 0.10$M.
Temperature: 25.0±0.5 °C
*I and II indicate whether Th was initially present in the aqueous phase or the organic phase, respectively.

Experimental procedure for determination of the distribution ratios. The extraction system consisted of 5 ml TC solution in benzyl alcohol and 5 ml aqueous solution of ^{234}Th plus thorium carrier and sodium perchlorate at a concentration of 0.10M. The pH of the aqueous phase was adjusted by adding a dilute solution of perchloric acid or sodium hydroxide. Concentration of thorium varied from 10^{-5}M to 10^{-4}M, achieved by adding thorium carrier. The TC concentration in the organic solvent varied from $7.5 \cdot 10^{-4}$M to $5 \cdot 10^{-3}$M.

The phases were equilibrated at 25.0 ± 0.5 °C by shaking in a mechanical stirrer for 30 min. After equilibration, the phases were separated by centrifugation and aliquots of each phase were taken and counted using a well-type NaI(Tl) scintillation counter 5.4 × 4.5 cm, coupled to a single channel analyzer.

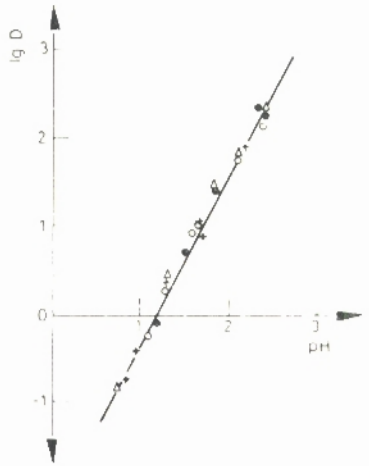

Fig. 4. Distribution ratio of Th vs. pH. TC = 0.01M; [Th]: ○ – $4.0 \cdot 10^{-6}$M; + – $1.0 \cdot 10^{-5}$M; △ – $8.3 \cdot 10^{-5}$M; ● – $1.0 \cdot 10^{-4}$M

Identification of the type of complexes formed. The formation of poly- or mononuclear complexes was checked by measuring the distribution ratio (lg D) of thorium at a constant concentration of TC ($2 \cdot 10^{-3}$M) and varying the pH, at various parametric concentrations of thorium. Results are presented in Table 4 and Fig. 4.

Table 4
Distribution ratio lg D as a function of pH for different concentrations of thorium

[Th], M							
$4.0 \cdot 10^{-6}$		$1.0 \cdot 10^{-5}$		$8.3 \cdot 10^{-5}$		$1.0 \cdot 10^{-4}$	
pH	lg D	pH	lg D	pH	lg D	pH	lg D
1.04	−0.2550	0.82	−0.7556	0.75	−0.8651	1.18	0.0855
1.28	0.2585	0.95	−0.4679	1.30	0.3966	1.18	0.0833
1.58	0.9105	1.29	0.3308	1.82	1.4456	1.50	0.6963
1.65	1.0015	1.64	1.0515	2.10	1.7917	1.82	1.3950
2.08	1.7517	1.69	0.8446	2.37	2.3312	2.35	2.2954
2.33	2.1740	2.15	1.9006			2.42	2.2108
		2.37	2.2554				

[TC] = $2 \cdot 10^{-3}$M.

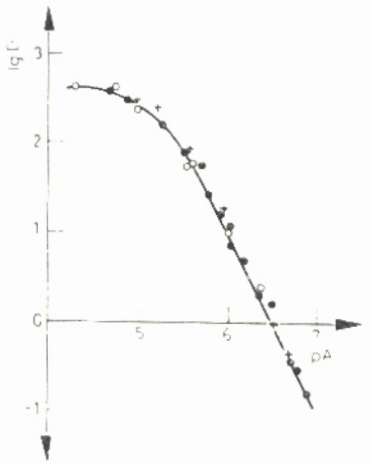

Fig. 5. Distribution ratio of Th vs. pA as a function of TC concentration. [Th] = $10^{-4} - 10^{-5}$M; [TC] = $5.0 \cdot 10^{-3}$M (○); $2.0 \cdot 10^{-3}$M (●); $7.5 \cdot 10^{-4}$M (+)

From this Figure it can be seen that lg D is linearly correlated with the pH in the interval 1.0 to 2.5.

Student's t test and F test[10] applied to the values of Table 4 show that the straight lines corresponding to the four metal concentrations are coincident at a confidence level of 95%. This indicates that the distribution ratio is not dependent of the metal concentration in the interval of 10^{-5}M to 10^{-4}M, which shows the formation of mononuclear complexes of the type $Th(TC)_n$.[3]

To check if the complexes are of the general formula $MA_n(OH)_p(HA)_r$, $MA_n(OH)$ or MA_n the distribution ratios, lg D, were determined as a function of the cologarithm of the concentration of free ligand (pA) for various initial concentrations of TC. Fig. 5 shows that the distribution ratios (lg D) are function's only of pA for various initial concentrations of TC, indicating the formation of complexes of the type MA_n.[3]

The formation of negatively charged complexes of the type $[Th(TC)_n]^{4-n}$, with $n > 4$, was ruled out. If such complexes existed in the pH interval of 1.0 to 3.0, the curve of Fig. 5, lg D versus pA, would show a maximum value for lg D or a plateau followed by a decrease of lg D for decreasing pA values.[11]

The fact that lg D is a function only of pA in the pH interval examined, for various TC concentrations, indicates that no hydroxo complexes are formed. Hydrolysis of thorium in this pH interval was not taken into account since this would occur only at pH values higher than 3.5.[12]

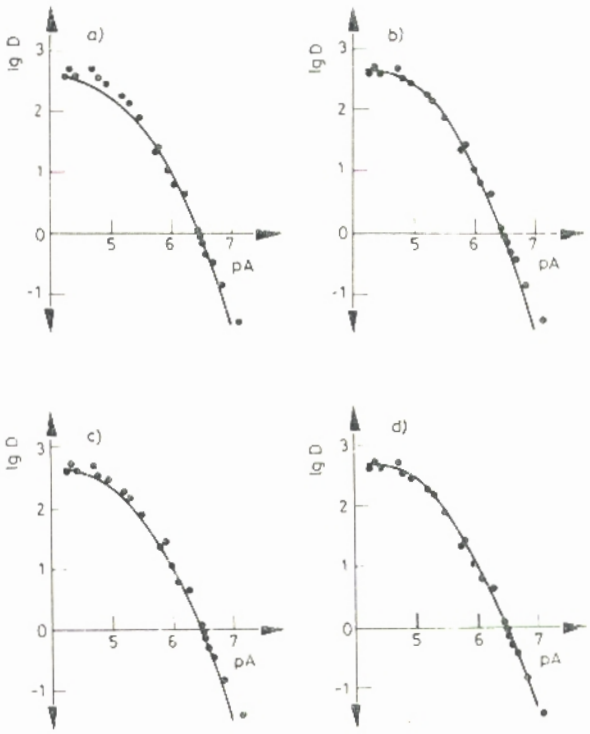

Fig. 6. Distribution ratio of Th vs. pA. Dots represent experimental values and the curves are calculated values using constants obtained by the four methods: two-parameter (a); limiting value (b); average number (c); least squares (d)

It was also assumed that only uncharged complexes $Th(TC)_4$ are dissolved and extracted by the organic solvents, especially for those of low dielectric constant.[3,11]

Stability constants

Results for the constants are presented in Table 5. It can be seen that a good agreement is found for all four methods.

ROSSOTTI[13] suggests that the calculated values of the stability constants should be substituted into the basic equation [Eq. (1)] to check if such substitution reproduces the experimental data. In Fig. 6 are presented the experimental values of lg D versus pA (dots) as well as the calculated curves for lg D using the formation constants listed in Table 5.

Table 5
Stability constants for the complexes of thorium with tetracycline

Method	lg β_1	lg β_2	lg β_3	lg β_4	K_D
Two parameters	7.3	13.8	19.5	24.4	–
Limiting value	7.1	13.5	18.5	24.0	500
Average number	7.6	14.1	19.6	24.6	–
Least squares	7.0±0.4	14.2±0.3	18.9±0.5	24.6±0.3	507±46

$NaClO_4$ = 0.10M, temperature = 25.0±0.5 °C.
The constants β_n are expressed in units corresponding to $(litre)^n/(mol)^n$.

Discussion

In Fig. 6 it is seen that the constants calculated by the two-parameter method give a curve that is mostly displaced from the experimental points, relative to the three other methods. This displacement can be explained considering that this method gives only approximate values for the constants, since the correlations used for the calculations are exact only if there are one or two chemical species and if the ratio of two consecutive constants k_n is the same,[14] that is

$$k_1/k_2 = k_2/k_3 = k_3/k_4 = 10^{2b} \tag{10}$$

To evaluate the errors in the determination of the constants by the least-squares method, the error σ_D in the measurement of D, was considered as being a constant percentage of D, i.e., $\sigma_D = PD$ with P taken equal to 10%. The weight w_i for an individual observation i is defined as (cf. Ref.[15])

$$w_i = 1/\sigma_i^2$$

The values of the computed parameters or their standard deviations (a_n and σ_{an}) in the equation used to calculate the formation constants by the least-squares method* do not change if the weight of all observations is changed by multiplying

*Note:

$$Z = \sum_{n=0}^{4} a_n [A]^n \tag{11}$$

where

$$Z = [A]^3 \, D^{-1} \qquad \text{and} \qquad a_n = \beta_n/K_D \, \beta_4 \tag{12}$$

the variances by a constant factor. However, the value of S_{min} where

$$S_{min} = \sum_{i=1}^{L} w_i V_i^2 \qquad (13)$$

does change. V_i is the difference between the measured value of the function and the value calculated with the best set of parameters at that point. As shown by DEMING[15] and FISHER,[16] S_{min} has the same distribution as the χ^2 function with k degrees of freedom, which are equal to the number of observations or experimental points (L), minus the number corresponding to the number of parameters in Eq. (11), i.e., $k = L - N$. When the mathematical model represented by Eq. (11) and the weights w_i are consistent with the experimental data, the mean value of χ^2/k will be equal to 1 with a range of ±0.5 at a 70% confidence level.[17] A 70% level is a rather stringent condition. The test was applied giving a χ^2/k value equal to 1.30.

For the limiting value method the graphs of F_3 and F_4 versus $[A]^{-1}$ were not used since the errors of such values were rather large. Values for f_3 and f_4 were instead obtained from the graph of F_5 versus [A], with

$$F_5 = (K_D/D - 1)[A]^4 = f_4 + f_3[A] + f_2[A]^2 + f_1[A]^3 \qquad (14)$$

*

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