Tetrahedron Vol. 26, pp 4293 to 4299 Pergamon Press 1970. Printed in Great Britain

PHOTOCHEMISTRY OF HETEROCYCLIC COMPOUNDS—III

THE PHOTOCHEMICAL DECOMPOSITION OF 5,5-DIALKOXYBARBITURIC ACIDS[1]

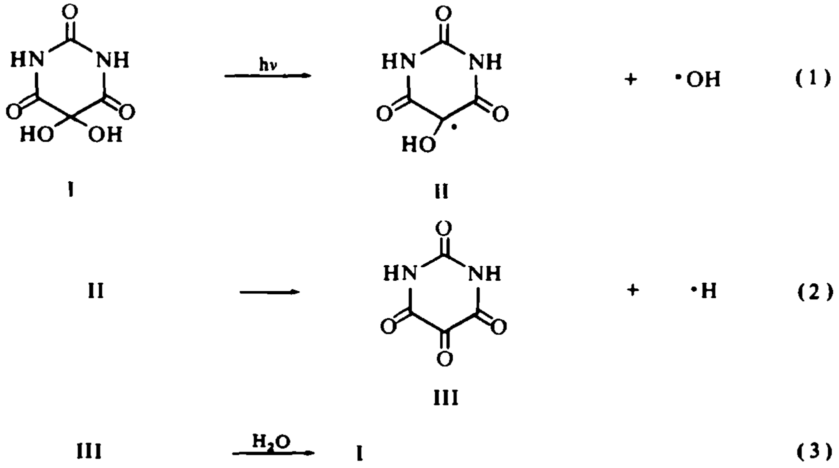
Y. Otsuji, S. Wake and E. Imoto
Department of Applied Chemistry, Faculty of Engineering, University of Osaka Prefecture, Sakai, Osaka, Japan

(*Received in Japan* 18 *March* 1970; *Received in the UK for publication* 29 *April* 1970)

Abstract—Irradiation of an aqueous solution of 5,5-dimethoxybarbituric acid (IVa) with ultraviolet light gave 5,5'-dimethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl (VIII), formaldehyde, methane and other decomposition products. Similarly, irradiation of an aqueous solution of 5,5-diethoxybarbituric acid (IVb) afforded 5,5'-diethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl (VII), acetaldehyde, methane, ethane and other decomposition products. These results led to the conclusion that the photochemical reactions of IVa and IVb in water are initiated by homolytic cleavage of C—OR bond resulting in the formation of 5-alkoxyperhydro-2,4,6-trioxo-5-pyrimidyl radical and followed by a homolytic cleavage of the O—R bond in the radical.

Some properties of 5,5-dialkoxybarbituric acids and their derivatives in the dark are also presented.

In the previous paper,[1] we have shown that alloxan monohydrate (I) undergoes homolytic cleavage upon irradiation of an aqueous solution with ultraviolet light to give an hydroxyl radical and 5-hydroxyperhydro-2,4,6-trioxo-5-pyrimidyl radical (II) which then decomposes to form alloxan and a hydrogen atom.

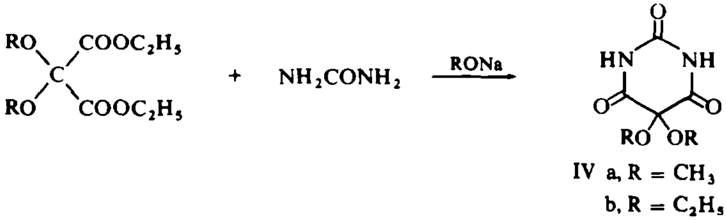


In this paper, we present evidence that 5,5-dialkoxybarbituric acids also undergo a type of photodecomposition reaction similar to those represented in equations (1)–(3).

RESULTS AND DISCUSSION

Preparation and properties of 5,5-dialkoxybarbituric acids and related compounds

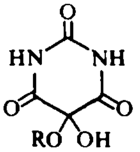
5,5-Dimethoxy- and 5,5-diethoxybarbituric acid (IVa and IVb), used for irradiation, were prepared by the base-catalyzed condensation of the corresponding dialkoxymalonate with urea.[2]


IV a, R = CH_3
b, R = C_2H_5

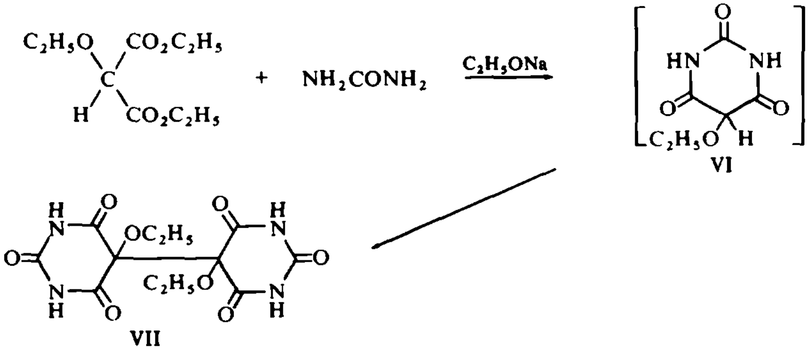
(4)

These compounds were stable in water in the dark. Even when they were allowed to stand in boiling water, the compounds remained unchanged and were recovered almost in quantitative yields. Careful paper chromatographic examinations of the aqueous solutions of the compounds by the method of Said and Fleita[3] indicated that no alloxan monohydrate (I), a hydrolysis product, was present in the solution.

All attempts to obtain IVa and IVb from anhydrous alloxan (III) and alcohols were unsuccessful. In these experiments, however, crystalline compounds were obtained which gradually decomposed on standing under atmospheric conditions to give I. Although these compounds could not be isolated in a pure form, it is conceivable that their structure is represented by the hemiketal form (V).[4, 5]


V a, R = CH_3
b, R = C_2H_5

We also attempted to prepare 5-ethoxybarbituric acid (VI) by the base-catalyzed condensation of diethyl ethoxymalonate with urea. However, the condensation gave 5,5′-diethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl (VII) instead of VI. This result suggests that, once formed, VI is immediately oxidized by air to VII. This is consistent with the fact that dialuric acid is readily oxidized to alloxantin upon exposure to air.[6]


VI
VII

(5)

Photodecomposition of 5,5-dimethoxybarbituric acid (IVa)

Irradiation of an deaerated aqueous solution of IVa with a low-pressure mercury lamp gave formaldehyde, 5,5′-dimethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl (VIII) and other unidentified solid decomposition products and evolved a gaseous mixture of methane, CO_2, CO and hydrogen. Formaldehyde was identified as its 2,4-dinitrophenylhydrazone. The structure of VIII was confirmed by its elemental analysis and spectral properties.

Table 1 shows the results of VPC analysis of the evolved gas. The proportion of component gases in the evolved gas varied with the irradiation time. The ratio of CO_2 or CO to methane increased with increase of the irradiation time. The analysis of the solid products identified is summarized in Table 2.

TABLE 1. PROPORTION OF THE GAS EVOLVED UPON IRRADIATION OF 5,5-DIMETHOXYBARBITURIC ACID (IVa) IN WATER[a]

Irradiation time (h)	Total volume of gas evolved (ml)	Molar ratio of the component gases CO_2	: CO	: CH_4	: H_2
7	0·8	5·5	0·5	1	1·9
14	1·6	7·6	1·5	1	2·2
21	2·0	9·9	2·2	1	1·3

[a] Initial concentration of IVa was 2·5 × 10^{-2}M.

TABLE 2. SOLID PRODUCTS IDENTIFIED ON IRRADIATION OF 5,5-DIALKOXYBARBITURIC ACIDS IN WATER

A. 5,5-Dimethoxybarbituric acid (IVa)[a]

Irradiation time (h)	Yields of the solid products (mmole) IVa[b]	VIII · $2H_2O$	2,4-D of HCHO[c]
7	0·59	0·19	1·2
3	2·7	0·06	0·32

B. 5,5-Diethoxybarbituric acid (IVb)[d]

Irradiation time (h)	Yields of the solid products (mmole) IVb[b]	VII	2,4-D of CH_3CHO[c]
7	2·3	0·23	1·5
3	4·4	0·09	0·89

[a] A soln of 1·5 g (8 mmoles) of IVa in 300 ml of water was irradiated.

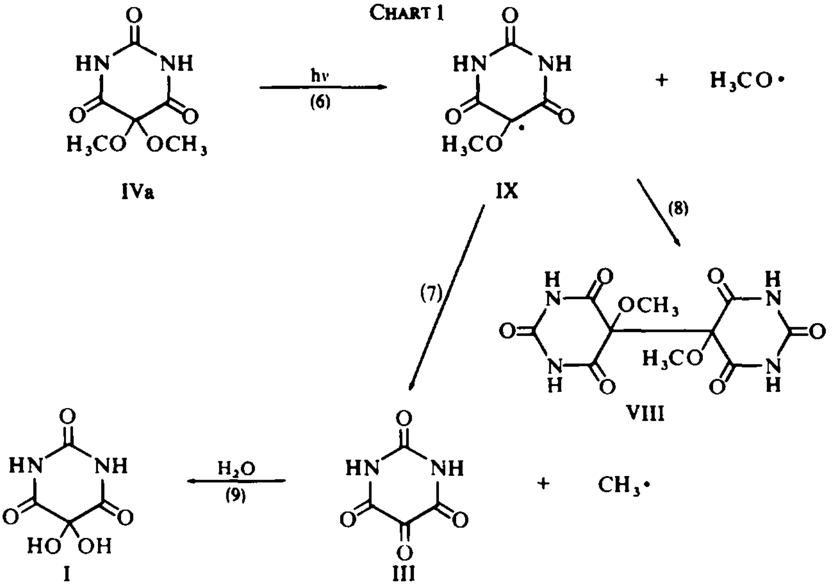
[b] The starting material recovered after irradiation.

[c] 2,4-D represents 2,4-dinitrophenylhydrazone.

[d] A soln of 1·5 g (6·9 mmoles) of IVb in 300 ml of water was irradiated.

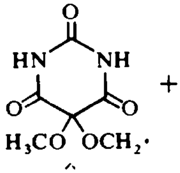
A mechanism proposed to explain the above results is given in Chart 1. The first step of the photochemical reaction is homolytic cleavage of the C—OCH_3 bond (path 6) in the excited state of IVa, which results in the formation of methoxyl radical and 5-methoxy perhydro-2,4,6-trioxo-5-pyrimidyl radical (IX). A similar cleavage reaction has also been proposed for the photochemical decompositions of alloxan monohydrate and ninhydrin.[1,7] The radical IX can then react in two different

Chart 1



ways. Either it decomposes to give methyl radical and alloxan (III) (path 7), or it dimerizes to give VIII (path 8). The methyl and methoxyl radicals thus produced would lead to the formation of methane and formaldehyde. A speculative mechanism for the formation of these compounds is represented as (10)–(13). CO and CO_2 can be

$$2CH_3O\cdot \rightarrow CH_2O + CH_3OH \qquad (10)$$

$CH_3O\cdot + IVa \rightarrow$  $+ CH_3OH$ (11)

$$\cdot CH_3 + IVa \rightarrow X + CH_4 \qquad (12)$$

$$X \rightarrow CH_2O + IX \qquad (13)$$

produced by the fragmentation reactions of I, IVa, VIII, IX or other intermediates. That the ratio of CO or CO_2 to methane increases with increase of irradiation time may suggest that in the initial stage of the photochemical reaction the pathways (6)–(13) predominate over the fragmentation reactions which lead to CO and CO_2. Hydrogen can be formed by the photodecomposition reaction of I, produced by reactions (7) and (9), by the mechanism proposed previously.[1] Alloxan was in fact detected in the reaction mixture by the method of Said and Fleita.[3]

Photodecomposition of 5,5-diethoxybarbituric acid (IVb)

Irradiation of a deaerated aqueous solution of IVb with a low-pressure mercury lamp gave acetaldehyde, 5,5′-diethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl (VII) and unidentified decomposition products accompanied by evolution of gas. Acetaldehyde was identified as its 2,4-dinitropheylhydrazone. The structure of VII was established from its elemental analysis and spectral properties. VPC analysis of the evolved gas showed that it consisted of a mixture of ethane, methane, CO, CO_2 and hydrogen. In this case the content of ethane in the evolved gas was very small. For example, when a $2\cdot5 \times 10^{-2}$M solution of IVb was irradiated for 20 h, the total volume of evolved gas was 2·3 ml and the molar ratio of component gases in the gas was as follows; $CO_2:H_2:CO:CH_4:C_2H_6 = 4:3:2:1: < 0\cdot1$. The solid products obtained are summarized in Table 2. Alloxan was also detected in the reaction mixture. These results for IVb can be explained in terms of a similar mechanism to that shown for the photodecomposition of IVa. In the case of IVb, methane can be produced through the decomposition of ethoxyl radical[8] (14).

$$C_2H_5O\cdot \rightarrow CH_3\cdot + HCHO \qquad (14)$$

The conclusion to be drawn from this investigation is that the photochemical decompositions of IVa and IVb are initiated by homolytic cleavage of C—OR bond and the resulting 5-alkoxyperhydro-2,4,6-trioxo-5-pyrimidyl radical then decomposes to yield alkyl radical and alloxan or couples to form a dimer of the radical, VIII or VII. Complex fragmentation reactions take place though independently to some extent. This investigation would provide strong support of the mechanism proposed for the photochemical decomposition of water catalyzed by alloxan monohydrate in the previous paper.[1]

EXPERIMENTAL

M.ps are uncorrected. UV spectra were recorded with a Hitachi EPU-2U recording spectrophotometer. IR spectra were obtained with a Hitachi EPI-S_2 infrared spectrophotometer. Microanalyses were performed with a Yanagimoto MT-1 CHN Corder. NMR spectra were obtained on a Hitachi H-60 high resolution NMR spectrometer, using TMS as internal standard. VPC analysis of gases was performed with a Hitachi KGL-2 gas chromatograph; H_2, CO and CO_2 were analyzed as described in the previous paper,[1] and methane and ethane were analyzed using columns packed with molecular sieve 5A and activated charcoal, respectively. All gas volumes reported in this paper are shown as values at NTP. Water used in this investigation was purified by distillation of deionized water.

Dimethyl dimethoxymalonate. A soln of 200 g diethyl dibromomalonate[9] in 70 ml dry MeOH was added gradually to a soln of 41 g sodium in 650 ml dry MeOH with stirring at such a rate as to keep the temp of the soln below 50°. Stirring was continued at room temp for 5 h. Dry HCl was then passed into the soln until the mixture became weakly acidic. Ppt was removed by filtration and the filtrate was evaporated. The residue was extracted with 200 ml ether, and this extract evaporated. Distillation of the residue gave 22 g (18%) of the product, b.p. 97–105° (1 mm); NMR (CCl_4) τ 6·65 (s, 6H) and 6·20 (s, 6H); IR (CCl_4) 1770 cm^{-1}. (Found: C, 43·69; H, 6·17. Calc for $C_7H_{12}O_6$: C, 43·75; H, 6·29%).

Diethyl diethoxymalonate. This compd was prepared in the manner described above from diethyl dibromomalonate and NaOEt in EtOH. The product was purified by distillation, b.p. 105–114° (2 mm) (lit.[10] 225°); IR (CCl_4) 1760 and 1740 cm^{-1}. The NMR spectrum (CCl_4) showed two triplets at τ 8·79 and 8·72 (J = 7 cps, 12H, methyl of $-OCH_2CH_3$ and $-COOCH_2CH_3$), a quartet at τ 6·45 (J = 7 cps, 4H, methylene of $-OCH_2CH_3$) and a quartet at τ 5·80 (J = 7 cps, 4H, methylene of $-COOCH_2CH_3$). The yield of this compd was 19%.

5,5-Dimethoxybarbituric acid (IVa). A soln of 17 g dimethyl dimethoxymalonate in 30 ml dry MeOH was added with stirring to a soln of 2·5 g sodium and 6 g urea in 70 ml dry MeOH. The mixture was refluxed with stirring for 8 h, cooled and then acidified with dry HCl. The solvent was evaporated and the residue extracted with 100 ml ether. The extract was evaporated and the residue, which solidified on scratching with a spatula, was recrystallized from $CHCl_3$–MeOH to give 8 g (48%) of IVa, m.p. 147–149°; NMR (DMSO-d_6) τ 6·62 (s, $-OCH_3$); IR (KBr) 3300, 3200, 1790 and 1730 cm^{-1}; UV (H_2O) λ_{max} 275 mμ (ε = $1\cdot2 \times 10^2$). (Found: C, 38·02; H, 4·35; N, 14·78. Calc for $C_6H_8N_2O_5$: C, 38·30; H, 4·29; N, 14·89%).

5,5-Diethoxybarbituric acid (IVb). This was prepared from diethyl diethoxymalonate and urea in a manner similar to that described above and purified by recrystallization from water, m.p. 164–165° (lit.[2]

165°); IR (KBr) 3250, 3150, 1780 and 1720 cm^{-1}; UV (H_2O) λ_{max} 275 mμ (ε = 1·2 × 10^2). The yield of this compd was 44%.

Diethyl ethoxymalonate. This was prepared by the method of Wislicenus and Huenzesheimer,[11] the thermal decomposition of diethyl ethoxyoxaloacetate[12] at 180–200°, and purified by distillation under reduced press, b.p. 80–85° (2 mm) (lit.[11] 228°); NMR (CCl_4) two triplets at τ 8·77 and 8·72 (J = 7 cps, 9H, methyl of —$CO_2CH_2CH_3$ and —OCH_2CH_3), 6·41 (q, J = 7 cps, 2H, —OCH_2—), 5·82 (q, J = 7 cps, 4H, —CO_2CH_2—) and 5·73 (s, 1H, $\mathrm{HC}\!\overset{/}{\underset{\backslash}{-}}$); IR ($CHCl_3$) 1760 and 1730 cm^{-1}. The yield was 82%.

Reaction of diethyl ethoxymalonate with urea. A soln of 12 g diethyl ethoxymalonate in 20 ml dry EtOH was added with stirring to 50 ml ethanolic soln containing 1·4 g sodium and 3·6 g urea. The mixture was refluxed with stirring for 6 h, cooled, acidified slightly with dry HCl and then evaporated to dryness. The residue was washed with ether, then with water. Recrystallization from dioxan gave 7 g (70%) 5,5′-diethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl (VII), m.p. 306–307° dec; NMR (DMSO-d_6) τ 8·95 (t, J = 7 cps, 6H, methyl of —OCH_2CH_3) and τ 6·59 (q, J = 7 cps, 4H, methylene of —OCH_2CH_3); IR (KBr) 3250, 3150, 1760, 1730 and 1705 cm^{-1}. (Found: C, 42·35; H, 3·97; N, 16·17. Calc for $C_{12}H_{14}N_4O_8$: C, 42·11; H, 4·12; N, 16·37%).

Reactions of alloxan anhydride (III). III was obtained by sublimation of its monohydrate (I) at 200° under a press of 0·05 mm. The product was intensely yellow and decomposed at about 250°.[4]

A. *Reaction with MeOH.* 1 g of III was dissolved in 15 ml of absolute MeOH to give a red soln. Dry HCl was added at which the colour changed from red through yellow to colourless. MeOH was driven off under reduced press to give 0·8 g of crystalline compd, m.p. 142–147°. The IR spectrum (KBr) was almost identical with that of I. On standing under atmospheric conditions, this compd gradually reverted to I, m.p. 235–238° dec.

B. *Reaction with EtOH.* To a red suspension of 1 g of III in 15 ml dry EtOH was added dry HCl. A similar work-up to that described above gave 0·7 g of a colourless crystalline compd, m.p. 132–135°. The IR spectrum was almost identical with that of I. This compd also reverted to I on standing under atmospheric conditions.

C. *Reaction with triethyl formate.* To a soln of 1 g of III and 2 g triethyl formate in 15 ml dry EtOH was added dry HCl. During addition the colour of the soln changed from red to yellow. A small amount of $CaCl_2$ was added to the soln, which was then warmed at 80° for 5·5 h. The solvent was driven off under reduced press and the residue extracted with 40 ml ether. Anhydrous Na_2CO_3 was added to the extract and separated by filtration. The ether was then evaporated to give a colourless crystalline compd, m.p. 140–150°. This compd again reverted to I on standing under atmospheric conditions.

Photochemical reaction of 5,5-dimethoxybarbituric acid (IVa). A soln of 1·5 g (8 mmoles) of IVa in 300 ml water was placed in a cylindrical vessel and N_2 was bubbled through the soln for 30 min. The soln was then irradiated with a 15 W Taika low-pressure mercury immersion lamp under N_2 at room temp for 7 h. After irradiation, 30 ml of the irradiated soln was pipetted into an aq soln of 2,4-dinitrophenylhydrazine. Filtration gave 0·026 g (0·12 mmole) of the 2,4-dinitrophenylhydrazone of formaldehyde: the total yield of the hydrazone produced from 8 mmoles of IVa was therefore 0·26 g (1·2 mmoles). The hydrazone thus obtained melted at 160–162° after recrystallization from EtOH and was identical with the authentic sample in every respect.

The irradiated soln remaining (270 ml) was evaporated to dryness under reduced press. The residue was extracted thoroughly with 50 ml ether and an unextracted red-brown solid (A) was separated by filtration. The ether extract was evaporated and the residue recrystallized from $CHCl_3$–MeOH to give 0·1 g of the starting material (IVa), m.p. 145–147°; the total recovery of IVa was therefore 0·11 g (7%).

The red-brown solid A was extracted with 10 ml water and filtered to separate an unextracted solid from an aqueous soln (B). The solid was then recrystallized from water to give 0·06 g of 5,5′-dimethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl dihydrate (VIII); the total yield of VIII from 1·5 g of IVa was thus 0·066 g (5%). This compd decomposed at 306–307°. The IR spectrum (KBr) showed absorptions at 3500, 1750, 1715 cm^{-1} and complex absorptions between 3100–2850 cm^{-1}. (Found: C, 34·37; H, 3·95; N, 15·80. Calc for $C_{10}H_{14}N_4O_{10}$: C, 34·29; H, 4·03; N, 16·00%).

Finally, evaporation of the aqueous soln B gave 1 g of a complex mixture of unidentified decomposition products; the total yield of these products from 1·5 g of IVa was therefore 1·1 g.

Irradiation was also carried out similarly for 3 h. The recovered starting material, formaldehyde, VII and unidentified decomposition products were obtained, the results being summarized in Table 2.

Photochemical reaction of 5,5-diethoxybarbituric acid (IVb). A soln of 1·5 g (6·9 mmoles) of IVb in 300 ml distilled water in a cylindrical reaction vessel was irradiated as described above. However, in this case an outlet from the reaction vessel was connected through vinyl tubing to a flask which contained an aq soln of 2,4-dinitrophenylhydrazine. Irradiation was carried out under N_2 for 7 h at room temp. The solvent was evaporated to dryness under reduced press. The residue was extracted thoroughly with 50 ml ether and filtered to separate an unextracted solid (A). The ether extract was evaporated to dryness and the residue recrystallized from water to give 0·5 g (33·3 %) of the starting material IVb. The ether insoluble solid A was extracted with 20 ml water and then filtered to separate an unextracted solid from an aqueous soln (B). This solid was recrystallized from dioxan to give 0·08 g (7 %) of 5,5′-diethoxybiperhydro-2,4,6-trioxo-5-pyrimidyl (VII), m.p. 301–303° dec. The compd VII was identical in every respect with the compd produced by the reaction of diethyl ethoxymalonate with urea. Evaporation of the aqueous filtrate B gave 0·75 g of a complex mixture of unidentified decomposition products. On the other hand, filtration of the aq 2,4-dinitrophenylhydrazine soln gave 0·33 g (1·5 mmoles) of the 2,4-dinitrophenylhydrazone of acetaldehyde. This hydrazone melted at 162–164° after recrystallization from EtOH and was identical with the authentic sample in every respect.

Irradiation was also carried out for 3 h. The results are summarized in Table 2.

Identification of alloxan. Alloxan was detected in the photochemical reaction mixture of IVa and IVb by means of paper chromatography.[3] Two eluents, $BuOH$-$AcOH$-H_2O and $BuOH$-$HCOOH$-H_2O, were used. In every case alloxan gave a blue fluorescent spot, with the same R_f value as that of the authentic sample, under UV light after exposure to NH_3 vapour.

Detailed analysis of the evolved gas. The same apparatus and procedure as those previously described[1] were employed for the detailed analysis of the evolved gases.

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