Table I. Rate Coefficients[a] and Isotope Effects for Reactions of Alkyl Halides with Nucleophiles

reagent:	$CF_3CH_2O^-$	H_2NS^-	$CF_3CF_2CH_2O^-$	HS^-	$(CF_3)_2CHO^-$	Cl^-	Br^-
PA[b] (kcal mol^{-1})	362	362	357	351	345	333	323
chlorides							
MeCl	2.20 ± 0.02 (−10)	1.46 ± 0.07 (−10)	1.01 ± 0.02 (−10)	1.21 ± 0.03 (−11)			
EtCl	2.48 ± 0.05 (−10)	3.81 ± 0.14 (−11)	5.88 ± 0.15 (−11)	nr[c]			
i-PrCl	4.31 ± 0.19 (−10)	nr	8.46 ± 0.36 (−11)	nr			
i-PrCl-d_6	1.88 ± 0.05 (−10)	nr	1.79 ± 0.09 (−11)	nr			
k_H/k_D	**2.3 ± 0.1**		**4.7 ± 0.3**				
t-BuCl	6.07 ± 0.35 (−10)	nr	1.69 ± 0.05 (−10)	nr			
t-BuCl-d_9	2.85 ± 0.09 (−10)	nr	5.14 ± 0.33 (−11)	nr			
k_H/k_D	**2.1 ± 0.1**		**3.3 ± 0.2**				
bromides							
MeBr	8.93 ± 0.20 (−10)	7.04 ± 0.03 (−10)	8.48 ± 0.21 (−10)	3.17 ± 0.10 (−10)	2.74 ± 0.13 (−11)	2.72 ± 0.14 (−11)	
MeBr-d_3		6.75 ± 0.18 (−10)	8.58 ± 0.18 (−10)	3.27 ± 0.03 (−10)	3.14 ± 0.01 (−11)	3.40 ± 0.19 (−11)	
k_H/k_D		**1.04 ± 0.03**	**0.99 ± 0.04**	**0.97 ± 0.03**	**0.87 ± 0.04**	**0.80 ± 0.06**	
EtBr	1.24 ± 0.04 (−9)	9.05 ± 0.16 (−10)	9.86 ± 0.42 (−10)	1.95 ± 0.13 (−10)	7.83 ± 0.33 (−12)		
EtBr-d_5	1.13 ± 0.04 (−9)	9.07 ± 0.29 (−10)	8.52 ± 0.29 (−10)	1.91 ± 0.05 (−10)	6.71 ± 0.35 (−12)		
k_H/k_D	**1.10 ± 0.06**	**1.00 ± 0.04**	**1.16 ± 0.06**	**1.02 ± 0.07**	**1.17 ± 0.08**		
i-PrBr	1.39 ± 0.04 (−9)	3.49 ± 0.09 (−10)	1.07 ± 0.02 (−9)	2.05 ± 0.05 (−12)	4.24 ± 0.17 (−12)		
i-PrBr-d_6	1.16 ± 0.03 (−9)	3.34 ± 0.03 (−10)	8.14 ± 0.41 (−10)	2.25 ± 0.11 (−12)	<2.20 (−12)		
k_H/k_D	**1.20 ± 0.05**	**1.04 ± 0.03**	**1.32 ± 0.07**	**0.91 ± 0.05**	**>1.9**		
t-BuBr	1.33 ± 0.01 (−9)	1.30 ± 0.05 (−10)	1.16 ± 0.08 (−9)	nr			
iodides							
MeI				7.44 ± 0.14 (−10)		1.66 ± 0.03 (−10)	2.89 ± 0.09 (−11)
MeI-d_3				7.35 ± 0.20 (−10)		1.98 ± 0.02 (−10)	3.78 ± 0.08 (−11)
k_H/k_D				**1.01 ± 0.03**		**0.84 ± 0.02**	**0.76 ± 0.03**

[a] Units are cm^3 molecule^{-1} s^{-1}. Errors are 1 standard deviation and reflect relative accuracy. Absolute errors, approximately ±20%. [b] Proton affinity of the nucleophile. [c] No reaction.

isotope effects undetectable. We have recently completed a comprehensive survey of the rates of reaction of primary, secondary, and tertiary chlorides and bromides with a variety of nucleophiles in the gas phase.[11] From this study we were able to identify nucleophiles that react relatively inefficiently, thereby giving isotope effects an opportunity to manifest themselves. We also came to the unexpected conclusion that, while sulfur and oxygen anions of the same basicity react at essentially the same rate by the S_N2 mechanism, oxygen anions are much more efficient than sulfur anions in inducing E2 reactions. For example, as shown in Table I, methyl chloride, which must undergo substitution, reacts somewhat more rapidly with H_2NS^- than with $CF_3CF_2CH_2O^-$. In contrast, isopropyl and *tert*-butyl chloride fail to react with H_2NS^- but react readily with the alkoxide. We therefore concluded that the latter reactions are eliminations.

These conclusions are confirmed by the isotope effects reported in this paper. As Table I shows, methyl bromide and iodide show either no isotope effect or an inverse secondary isotope effect with nucleophiles of all types. For example, CD_3Br reacts with Cl^- 1.25 times more rapidly than does CH_3Br. Thus the zero point energy difference between hydrogen and deuterium is greater in the transition state than it is in the ground state. These results are consistent with those reported for S_N2 reactions in solution.[12] In contrast, ethyl, isopropyl, and *tert*-butyl chlorides and bromides show appreciable to large isotope effects with appropriate nucleophiles whose attacking atom is oxygen, but no isotope effect with those nucleophiles with sulfur as the attacking atom. For example, isopropyl chloride reacts 4.7 times more rapidly with pentafluoropropoxide ion than does its hexadeuterio analogue, and *tert*-butyl chloride reacts 3.3 times more rapidly than does *tert*-butyl chloride-d_9. We have not found a sulfur nucleophile that reacts with either of these chlorides at a measurable rate. However, a comparison among sulfur and oxygen anions can be made using alkyl bromides as substrates. As predicted, sulfur anions react with ethyl and isopropyl bromide with no isotope effect or with a slight inverse isotope effect while oxygen anions react with these same substrates with appreciable normal isotope effects. The most reasonable explanation is that the former react by S_N2 and the latter mainly by E2 reactions.

The observation of such relatively large isotope effects in such rapid processes serves to emphasize yet again how the unique energetics of gas-phase ion–molecule interactions can give rise simultaneously to fast yet selective reactions. The ability to measure such subtle effects in the solvent-free environment of the gas phase should allow more precise computational modeling and perhaps give rise to a better understanding of the nature of isotope effects, particularly those secondary ones associated with the S_N2 reaction.[13]

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation under Grants CHE-8815459 and CHE-8815446 and discussions with Prof. Saul Wolfe.

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Photoinduced Porphyrin-to-Quinone Electron Transfer across Oligospirocyclic Spacers

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Structural determinations of bacterial photosynthetic reaction centers[2,3] have prompted many studies of photoinduced intramolecular electron transfer (ET) in models having linked porphyrins,[4,5] porphyrin–quinones (PQ)[5,6] and other donor–acceptor

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Table I. Lifetimes and Yields for Porphyrin–Quinone Compounds in 1-Butanol

compd	Φ_F[a]	Φ_T[b]	Φ_{ET}[c]	τ,[d] ps	τ_{CR},[e] ps	τ_{ET},[f] ps
5a (control)	0.027	0.90		1600 ± 100		
4a	0.002	0.06	0.94	105 ± 10	30 ± 5	112
4b	0.011	0.35	0.61	625 ± 50	250 ± 50	1025
4c	0.021	0.68	0.25	1200 ± 100		4800
4d	0.026	0.88	0.03	(1560)		5880

[a] Fluorescence yield: for **5a**, calculated from measured $^1P^*$ lifetime and natural radiative lifetime of 60 ns for metalloporphyrins ($\Phi_F = 0.03$ for ZnTTP in benzene); **4a–d** referenced to **5a**. [b] Triplet yield: **5a** assumed same as ZnTTP; **4a–d** referenced to **5a**. [c] P^+Q^- yield from $^1P^*$ calculated from fluorescence/lifetime data. [d] Measured lifetime of $^1P^*$ for control (τ_C) and PQ's (τ_{PQ}). [e] Measured P^+Q^- (charge recombination) lifetime. [f] Inherent τ for electron transfer calculated from fluorescence/lifetime data.

types.[5,7] The distance dependence of PQ ET has been studied for only two model systems. In these systems, the linkers were extended by one and two bicyclo[2.2.2]octane units[8] or by one and two nonhomologous alkyl bonds.[9] Theory suggests that the rate of ET through space should fall off with increasing R_e, the PQ edge-to-edge separation, according to the relationship $k_{ET} \propto \exp(-\beta R_e)$ where β is a constant.[5a,c] When R_e happens to equal the number of linker σ-bonds (see below), numerically identical β values obtain for both through-space and per-bond ET pathways.[5c] Apparent values of β for the above spacer extensions respectively are ≥ 1.5–1.9 (per angstrom and per bond) and 2.3 Å^{-1} (2.6/bond). It is important to understand how ET in PQ and other systems is mediated by the linker electronic structure and why the above β values are substantially larger than those (0.7–1.0) reported for photoinduced (and thermal) ET of *non*-PQ systems across *rigid* aliphatic linkers.[5,7] We report here a comprehensive study that addresses these questions.

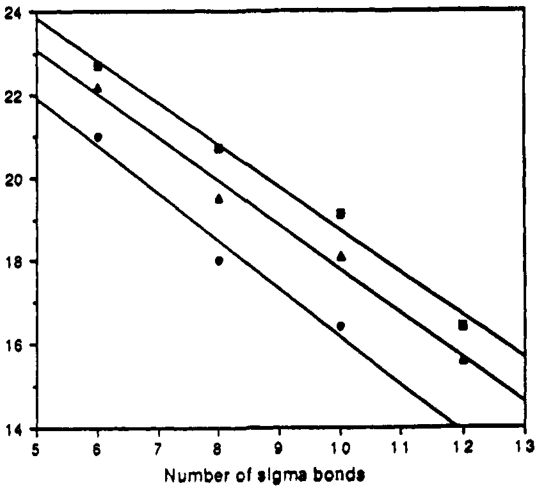

Figure 1. Least-squares exponential fits to the equation $k_{ET} = 10^{12}A \exp(-\beta N_\sigma)$ for **4a–d**. The values of β for *n*-BuOH (■), pyridine (▲), and MeCN (●) respectively are 1.03, 1.06, and 1.15 per bond; respective A values are 3.7, 2.1, and 1.0.

The rigid homologous spirocyclic spacers of our models **4a–d** (Scheme I) control R_e and minimize complications due to rotational degrees of freedom.[10,11] Attachment of the spacers directly to a pyrrole carbon rather than to a *meso*-phenyl group, which carries considerable porphyrin HOMO (A_{2u}) character,[12] allows the β values to reflect the operative ET distances.[13] Observed β values for both ET and charge recombination (CR) of our models are compared with the reported[8,9] and predicted relative β values for spirocyclic, bicyclo[2.2.2]octane, and alkane spacers.[14-16]

The PQ models **4a–d** were prepared as shown in Scheme I. Diester **1**[17] was O-methylated and reduced to a diol, which was converted to a dichloride and cyclized[18] to give diester **2**. Malonate-based spiroannulation reactions[19] were used to transform **2** to the homologous oligospirocycles **3a–d**. The 1,4-dimethoxynaphthalene rings of **3a–d** were oxidized[20] to the corresponding naphthoquinone diols, which were converted to **4a–d** by acetal exchange using 1-(dimethoxymethyl)tetratolylporphyrin,[21] followed by metalation with $Zn(acac)_2$. Controls **5a** and **5b** were prepared by using diols **3a** and **3b**. The PQ models and controls were characterized by 400-MHz ^1H NMR spectroscopy ($CDCl_3$, C_6D_6, C_6D_5N, CD_3CN, and *n*-BuOH-d_{10} at 25 °C). Despite the possibilities for rotation about the porphyrin–acetal bond through an angle Ψ, flexing of the spirofused rings,[22] and coordination of a fifth ligand to zinc,[23] the spectra indicate an average solution conformation for **4a–d** with an apparent plane of symmetry

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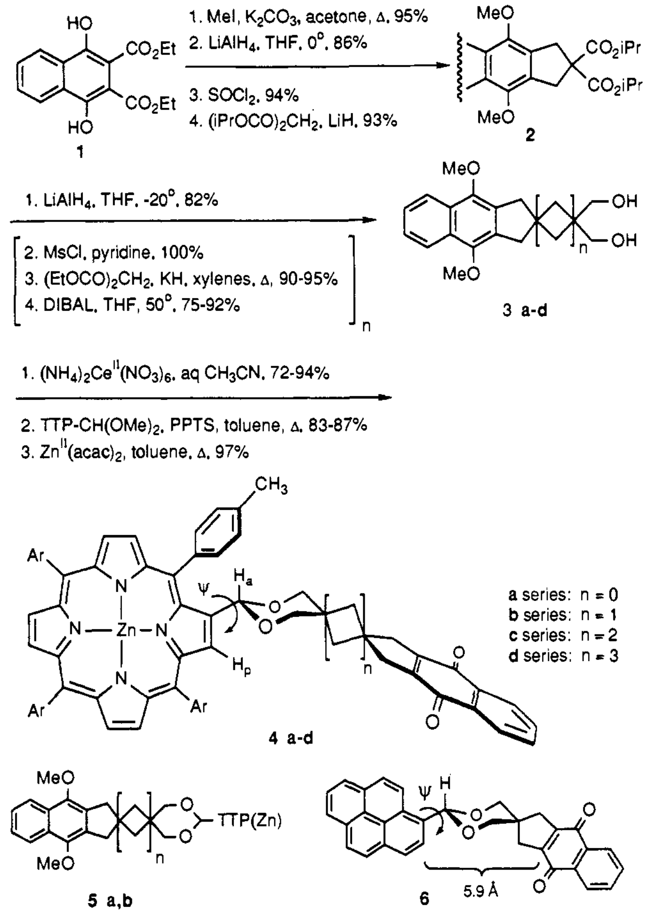
Scheme I



containing the acetal proton H_a and the porphyrin plane (see Scheme I). H_a is shifted upfield by >1 ppm to δ 5.35 ± 0.07 in $CDCl_3$ by ring-current shielding from the tolyl substituent,[24] and the porphyrin ring proton H_p is deshielded (to about 0.4 ppm downfield from the distal porphyrin ring protons) by through-space interaction with the acetal oxygens.[25] The spectra are also consistent with two rapidly equilibrating mirror image conformations having torsion angles Ψ of, say, +45° and −45°, values that approximate those observed in the solid state for **6**[26] (36°, 47°, two independent molecules) and a related 2-(2-chlorophenyl)-1,3-dioxane derivative (48°).[27]

Electronic solution spectra of **4a–d** and **5a,b** are superimposable with those of ZnTTP, suggesting the retention of local D_{4h} symmetry[28] and precluding strong PQ electronic coupling. Controls **5a,b** and models **4a–d** exhibit characteristic ZnTTP fluorescence (≈600 nm (Q_{00}) and ≈650 nm) whose excitation profile follows the Q band absorptions. Typical solvent shifts in the Q_{00} emission[29] cause the $^1P^*$ states of our models to lie respectively at 2.04, 2.03, and 2.01 eV in MeCN, *n*-BuOH, and pyridine. The redox potential[30a,b] of the annulated naphthoquinones (−0.75 V, MeCN, SCE) is ≈0.1 V lower than that of strain-free 2,3-dialkylnaphthoquinones such as the menaquinone acceptor in *R. viridis*.[31] ZnTTP should be ≈0.05 V more easily oxidized[32] than ZnTPP, whose oxidation potential is at ≈0.8 V vs SCE in the solvents of interest.[33] In MeCN, neglecting the coulombic work term, $-\Delta G_{ET}$ for photoinduced formation of P^+Q^- is ≈0.5 V and $-\Delta G_{CR}$ for charge recombination of P^+Q^- to afford ground-state PQ is ≈1.5 V.[34] ΔG_{ET} is less than optimal since the total Marcus reorganization energy reported for the formation of P^+Q^- species in polar solvents is 0.7–0.9 V,[10,35,36] about 0.6 V of which results from solvation of P^+.[37]

Transient absorption spectra were measured at room temperature by using a femtosecond apparatus already described.[38] The observed (see below) $^1P^*$ lifetimes (τ_C) of controls **5a** and **5b** were both 1.6 (1) ns in *n*-BuOH and MeCN; lifetimes of the PQ models **4a–d** (τ_{PQ}) varied with solvent and with the number of spirocyclobutane rings. ET rates were calculated as $k_{ET} = (1/\tau_{PQ}) - (1/\tau_C)$. Similar values of k_{ET} were obtained from the relationship $\Phi_C/\Phi_{PQ} = 1 + k_{ET}\,(1.6 \times 10^{-9}\ s)$ where Φ_{PQ} and Φ_C are the steady state fluorescence quantum yields of the PQ models and controls, respectively. Transient absorbance changes at times of 1 ps to 3 ns reveal the spectra and lifetimes of the $^1P^*Q$ and $^3P^*Q$ states[39] and of the P^+Q^- species. The spectral transparency of the quinone radical anions[40] and ground-state PQ and controls in the $\lambda > 600$ nm region along with the persistence of $^3P^*Q$ on the nanosecond time scale simplifies the kinetic analysis.[41] The P^+Q^- spectra thus obtained are similar to those reported for $ZnTPP^+$[42] and those we obtained for the control radical cations prepared by oxidation with $AgClO_4$.[43] Results of the photophysical analysis of the PQ models in *n*-BuOH are presented in Table I, and the k_{ET} data for *n*-BuOH (ϵ = 17.8), pyridine (ϵ = 12.3), and MeCN (ϵ = 38.0) are summarized in Figure 1. Corrections for variations in the reorganization energy with solvent and PQ separation were not applied and would appear to be small.

The ET rates are attenuated per bond (and per angstrom) according to β values (Figure 1) of 1.03–1.15. Structural studies of spiro[3.3]heptane and dispiro[3.1.3.1]decane derivatives[22] and of **6**[26] suggest that the R_e distances in **4a–d** are ≈5.9 Å + (2.18 Å/spirocyclobutane), or 5.9, 8.1, 10.2, and 12.1 Å, respectively, for σ-pathways of 6, 8, 10, and 12 bonds. Comparable β values were reported for both thermal and photoinduced intramolecular ET in non-PQ systems across rigid aliphatic linkers.[5,7] The higher β values reported for the PQ models[8,9] noted above may arise from intrinsic differences in linker orbital pathways and energetics or from some other factors such as insufficient data points or linker rotational freedom. Recent theoretical studies[14-16] of the orbital pathway factors predict that the β values (per σ-bond) of spiroalkane and bicyclo[2.2.2]octane linkers respectively should be 0.693 (ln 2) and 0.549 (0.5 ln 3) smaller than the β for alkane spacers.

The CR rates for **4a** and **4b** yield a β of 0.97 $Å^{-1}$ (1.06/bond). This value is lower than that reported (2.1 $Å^{-1}$) for the alkane-

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linked PQ system[9] and comparable to the value observed for CR in rigid non-PQ models.

In summary. ET rates for the homologous PQ models **4a–d** have been established both by steady state fluorescence and transient spectral studies. Spectroscopic identification of the P^+Q^- transients definitively relates diminished $^1P^*$ lifetimes and fluorescence yields to ET and also affords the CR rate of P^+Q^- to PQ. Observed β values show that the distance and σ-bond dependence of ET in rigidly linked PQ and non-PQ systems can be comparable. The observed and theoretically predicted abilities of these three PQ linkers to promote ET diminish the order spirocycles > bicyclo[2.2.2]octanes > alkanes. This result supports the view that long-range ET occurs through bonds.[5,7,44–46]

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Photoregulation of α-Chymotrypsin by Its Immobilization in a Photochromic Azobenzene Copolymer

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Photoregulation of enzymes is of broad interest as a means for developing macromolecular light signal amplification devices and targeted therapeutic agents. In previous studies[1–8] photoregulation of the biocatalyst was made possible by chemical modification of either the enzyme's active site or the protein backbone with photochromic compounds. Another approach involved the application of photochromic inhibitors, acting as effectively in only one of the photochromic isomers. Nevertheless, none of the known examples exhibits complete "on-off" photoswitchable activity. Here we report on a novel approach for photostimulation of enzymes by their immobilization in photochromic polymer matrices. We find that immobilization of α-chymotrypsin in a cross-linked photochromic copolymer of acrylamide and 4-(methacryloylamino)azobenzene (**1**) leads to complete "on-off" photoregulation of the enzyme, at a certain composition of the copolymer matrix. Previous studies have emphasized photoregulated physical properties of photochromic polymer assemblies such as viscosity,[9–11] wettability,[12] sol-gel transition,[13] electric potential,[14] and size changes.[15] The present study highlights the application of photochromic polymers as reaction media for photoregulation of biocatalysts.

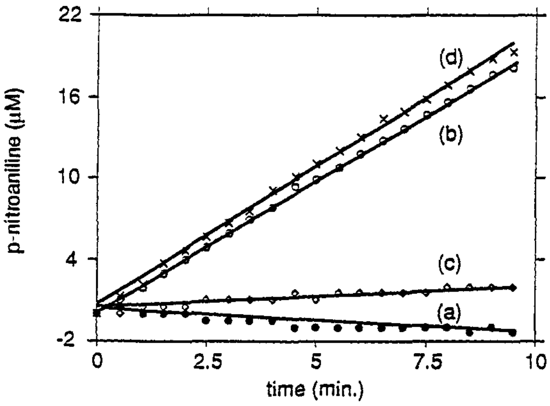
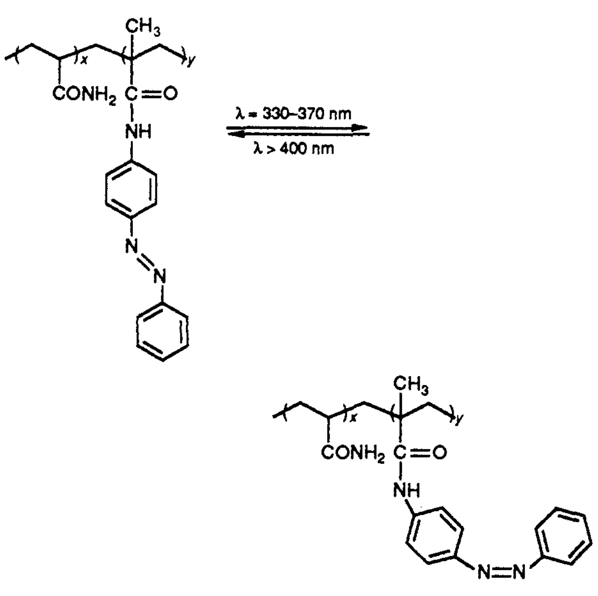


Figure 1. Rate of hydrolysis of **2**, 5.7×10^{-3} M, by α-chymotrypsin, 47.6 units, immobilized in an acrylamide–**1** copolymer (0.5 mol %): (a) hydrolysis by the enzyme in *trans*-**1**-acrylamide copolymer form; (b) after illumination, λ = 330–370 nm and in the presence of *cis*-**1**-acrylamide copolymer, (c) after further illumination of the polymer, λ > 400 nm, and re-formation of *trans*-**1**-acrylamide; (d) after additional illumination, λ = 330–370 nm, and regeneration of *cis*-**1**-acrylamide. Before each run the polymer gel is washed with TEA buffer (pH = 7.8) and new substrate solution is introduced to maintain similar initial concentrations of the substrate.

Immobilization of α-chymotrypsin (E.C. 3.4.21.1, 585 units) in the photochromic polymer is accomplished by radical copolymerization of acrylamide (375 mg) and **1**, 0–1 mol %, using *N*,*N*′-methylenebis(acrylamide) (20 mg) as a cross-linker in the presence of the enzyme. The resulting polymer gel that includes the enzyme is thoroughly washed. The polymer contains *trans*-azobenzene components and exhibits reversible photochromic properties (eq 1). Upon illumination of the polymer assembly, λ = 330–370 nm, isomerization to the *cis*-azobenzene unit occurs.



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