Competition between Cyclization and Dehalogenation in the Photochemistry of Cinnamylphenols with Halogen Substituents at the Phenolic and Styrenic Chromophores

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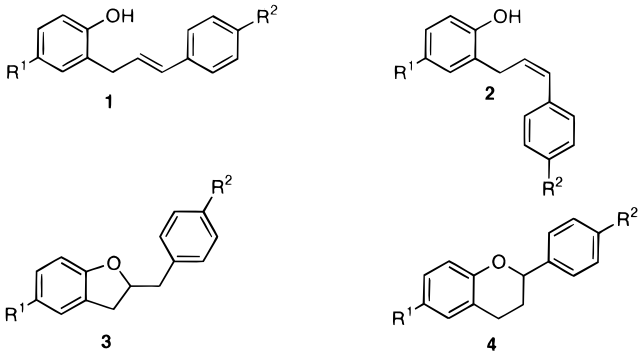
Introduction

Bichromophoric compounds have attracted considerable interest as suitable models for the study of key photochemical processes, such as energy or electron transfer.[1] Besides, they have found application in a number of fields, including the reproduction of biological phenomena (i.e. photosynthesis) or the design of new materials (i.e. photoconducting polymers).[2] Compounds derived from *trans*-2-cinnamylphenol (**1a**) are bichromophoric systems containing phenolic and styrenic units, connected through a methylene spacer. These systems are simple and versatile models in which small structural variations (such as substitution in both aromatics rings) allow to control the photophysical and photochemical behavior, reproducing at will intramolecular proton, electron, or energy transfer.[3,4]

The photochemistry of the parent *trans*-2-cinnamylphenol (**1a**) has been investigated in some detail.[3] The products obtained upon irradiation of **1a** are *cis*-2-cinnamylphenol (**2a**), 2-benzyl-2,3-dihydrobenzofuran (**3a**), and 2-phenyl-3,4-dihydro-2*H*-benzopyran (**4a**). Photocyclization to **3a** and **4a** has been rationalized through an excited-state proton transfer (ESPT) mechanism involving the excited singlet states of the phenol and styrene chromophores. It has been speculated that formation of dihydrobenzofuran **3a** takes place from the phenolic singlet, while dihydrobenzopyran **4a** arises from the styrenic singlet.[3] In the present work, halogen substituents have been incorporated to both aromatic rings with two main purposes: (i) to modify the relative energies of both chomophores and (ii) to provide an alternative pathway for deactivation of the excited states, by means of the carbon−halogen bond cleavage. It was expected that the substitution-dependent variations in the product selectivity could help to confirm the above excited-state assignment. In fact, the results show a complete inhibition in the formation of five-membered ring products when halogen is attached to the phenolic ring. Besides, solvent-derived products involving cleavage of the carbon−halogen bond are obtained in a number of cases. These facts constitute a convincing experimental support in favor of the initially proposed reaction mechanism.



a: $R^1 = R^2 = H$
b: R1 = Cl, $R^2 = H$
c: R^1 = Br, $R^2 = H$
d: $R^1 = H$, R^2 = Cl
e: $R^1 = H$, R^2 = Br
f: R^1 = Ph, $R^2 = H$
g : $R^1 = H$, R^2 = Ph

Results and Discussion

The required cinnamylphenols were prepared by treatment of 4-chloro- and 4-bromophenol with cinnamyl chloride in strong basic medium (compounds **1b**,**c**) or by reduction of the corresponding 2-hydroxychalcones with $LiAlH_4/AlCl_3$ in THF (compounds **1d**,**e**). Irradiation experiments were carried out in benzene (using quartz-filtered light) or in acetone (through Pyrex). All the samples were thoroughly deoxygenated before irradiation. The obtained results are presented in Table 1.

The substrates substituted at the phenolic ring were studied first. When the chloro derivative **1b**[5] was irradiated in benzene, a mixture of the cis isomer **2b**, the dihydrobenzopyran **4b**,[6] and the solvent-derived cyclic ethers **3f**[4] and **4f** [4] (Table 1, entry 2) was obtained. In the case of compound **1c**, irradiation under the same conditions led to **3f** and **4c**[6],**f** (Table 1, entry 4). When these results are compared with those previously obtained for the parent compound *trans*-2-cinnamylphenol (**1a**),[3] two differences appear particularly remarkable: the absence of the five-membered ring products **3b**,**c** and the formation of cyclic derivatives related to *trans*-2-cinnamyl-4-phenylphenol (**1f**).[4] If photocyclization to **3b**,**c** were to occur from the excited phenolic singlet, as previously hypothesized, the existence of a new competing reaction pathway (cleavage of the carbon−halogen bond) should result in a less efficient formation of such products. Actually, this was found to be the case.

Thermodynamic considerations show that complete C−X homolysis is possible upon excitation. Thus, the singlet energies of compounds **1b**,**c**, obtained from their fluorescence spectra (see Table 2), were found to be 98 and 97 kcal/mol, respectively,[7] while the corresponding

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(2) Balzani, V.; Scandola, F. *Supramolecular Photochemistry*; Ellis Horwood Limited: Chichester, 1991.
(3) Jiménez, M. C.; Márquez, F.; Miranda, M. A.; Tormos, R. *J. Org. Chem.* **1994**, *59*, 197.
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(6) Bauer, D. J.; Selway, J. W. T.; Batchelo, J. F.; Tisdale, M.; Caldwell, I. C.; Young, D. A. B. *Nature (London)* **1981**, *292*, 369.
(7) Similar values were found for 4-chlorophenol and 4-bromophenol in Wehry, E. L.; Rogersm L. B. *J. Am. Chem. Soc.* **1965**, *87*, 4234.

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Table 1. Irradiations of *trans*-2-Cinnamylphenols 1a−e

				product yield (%)				
entry	compd	condns[a]	conv	**2**	**3**	**4**	**3f** or **3g**	**4f** or **4g**
1	**1a**	A	80	25	45		30	
2	**1b**	A	55	35		30	25	10
3	**1b**	B	70	100				
4	**1c**	A	40			30	60	10
5	**1c**	B	60	100				
6	**1d**	A	49	54	14		32	
7	**1d**	B	53	100				
8	**1e**	A	42	18	tr	15	47	19
9	**1e**	B	60	100				

[a] A; benzene, quartz; B; acetone, Pyrex. [b] tr = trace.

Table 2. Photophysical Data of Compounds 1b−e at Room Temperature in Hexane (λ_{exc} = 270 nm)

compd	$\lambda_{max\ emission}$ (nm)	E_S (kcal/mol)	ϕ_F
1b	310	98	0.001
1c	311	97	<0.001
1d	322	92	0.009
1e	325	91	0.002

C−X bond energies in the model compounds chlorobenzene and bromobenzene are only 95 and 75 kcal/mol.[8] To rule out the possibility that the benzene-derived products could be formed by secondary photolysis of the halogen-containing cyclic ethers, compounds **4b**,**c** were submitted to irradiation under the same conditions. No significant reaction was observed in this control experiment, which indicates that *trans*-2-cinnamyl-4-phenylphenol (**1f**) is formed first, via addition of the aryl radical **I** to the solvent. The subsequent photochemical transformation of **1f** into **3f** and **4f** is a known process.[4]

In principle, dehalogenation could also occur from an excited triplet state. This appeared less likely, as the values of triplet energies (ca. 60−70 kcal/mol)[9] are too low to fulfill the thermodynamic requirements, unless some degree of C−C bond making occurs concomitantly with C−X bond breaking.[10] To check this point, photolysis of **1b**,**c** was carried out using acetone as photosensitizer. Under these conditions, compounds **3f** and **4f** were not formed, and the only process observed was trans/cis isomerization (Table 1, entries 3 and 5). Hence, dehalogenation does not appear to take place from an excited triplet.[11−14]

In a second stage of the work, the cinnamylphenols subtituted at the styrenic ring were investigated. When compound **1d**, bearing a chlorine, was photolyzed in benzene through quartz (Table 1, entry 6), the reaction mixture was found to contain the cis isomer **2d**, together with the cyclic ethers **3d** and **4d**.[6] In this case, no products derived from reaction of **1d** with the solvent were observed, which is in agreement with the fact that the singlet energy (92 kcal/mol, see Table 2)[15] is lower than the energy required to break the chlorine−carbon bond. On the other hand, the lack of an efficient pathway for photochemical deactivation of the phenolic singlet explains formation of the dihydrobenzofuran **3d**, as in the parent compound **1a**.

Finally, direct photolysis of the brominated cinnamylphenol **1e** under the same conditions (Table 1, entry 8) produced compounds **2e**, **3g**,[16] and **4e**,**g**.[16] Only traces of **3e** were detected.[17] Now, the energy content of the excited singlet (91 kcal/mol, Table 2) is clearly high enough to cleave the carbon−bromine bond. Thus, the aryl radical **II** is formed, and then radical addition to the solvent takes place. Again, the dihydrobenzopyran **4e** was irradiated under the same conditions; its photostability confirmed that photodehalogenation is the primary photochemical step in the sequence of events leading to **4g**.

As stated above for the analogues **1b**,**c** with halogen substituents at the phenolic ring, the only reaction occurring from the excited triplet states of **1d**,**e** was found to be *trans* to *cis* photoisomerization. This was assessed by using acetone as photosensitizer (Table 1, entries 7 and 9).

In summary, the introduction of chlorine and bromine in both the phenolic and the styrenic rings of a bichromophoric cinnamylphenol produces a decrease of the corresponding singlet excited-state energies. When such energies lie above those required to cleave the carbon−halogen bond, photodehalogenation (followed by solvent addition) efficiently competes with photocyclization (Scheme 1). This is specially remarkable in the case of the compounds substituted at the phenolic chromophore, where formation of dihydrobenzofurans is completely prevented. These observations support the previous assumption that the phenolic singlet gives rise to five-membered ring compounds, while the styrenic singlet leads to the isomeric six-membered ring analogues.

Experimental Section

UV spectra were recorded in cyclohexane; λ_{max} (nm) and log ϵ values (in parentheses) are given for each absorption band. IR spectra were obtained with a GC−FTIR instrument; ν_{max} (cm^{-1}) is given for all the absorption bands. ^1H NMR spectra were measured in $CDCl_3$ with a 300-MHz instrument; chemical shifts are reported in δ (ppm) values, using TMS as internal standard. Mass spectra were obtained under electron impact; the ratios *m*/*z* and the relative intensities (%) are indicated for the significant peaks. Fluorescence spectra were recorded in hexane. Isolation and purification were done by conventional column chromatography on silica gel using dichloromethane as eluent or by means of isocratic HPLC equipment provided with a semipreparative column, using hexane/ethyl acetate as eluent.

General Irradiation Procedure. Solutions of 0.02 g of the substrates in 20 mL of benzene or acetone were placed into quartz or Pyrex tubes surrounding a centrally positioned quartz cooling jacket containing a 125 W medium-pressure Hg lamp and irradiated under argon for 1 h. The reaction mixtures were analyzed by GC-MS and ^1H NMR.

Synthesis of the Substrates and the New Compounds. Preparation of the Substrates 1b,c.[3,18] The sodium salt

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(11) An additional possibility would be triplet-state dehalogenation via formation of excimers.[12−14] Although the contribution of this route cannot be ruled out at the present stage of the work, it appears less likely in view of the close relationship between lack of dehalogenation and singlet energy deficit.

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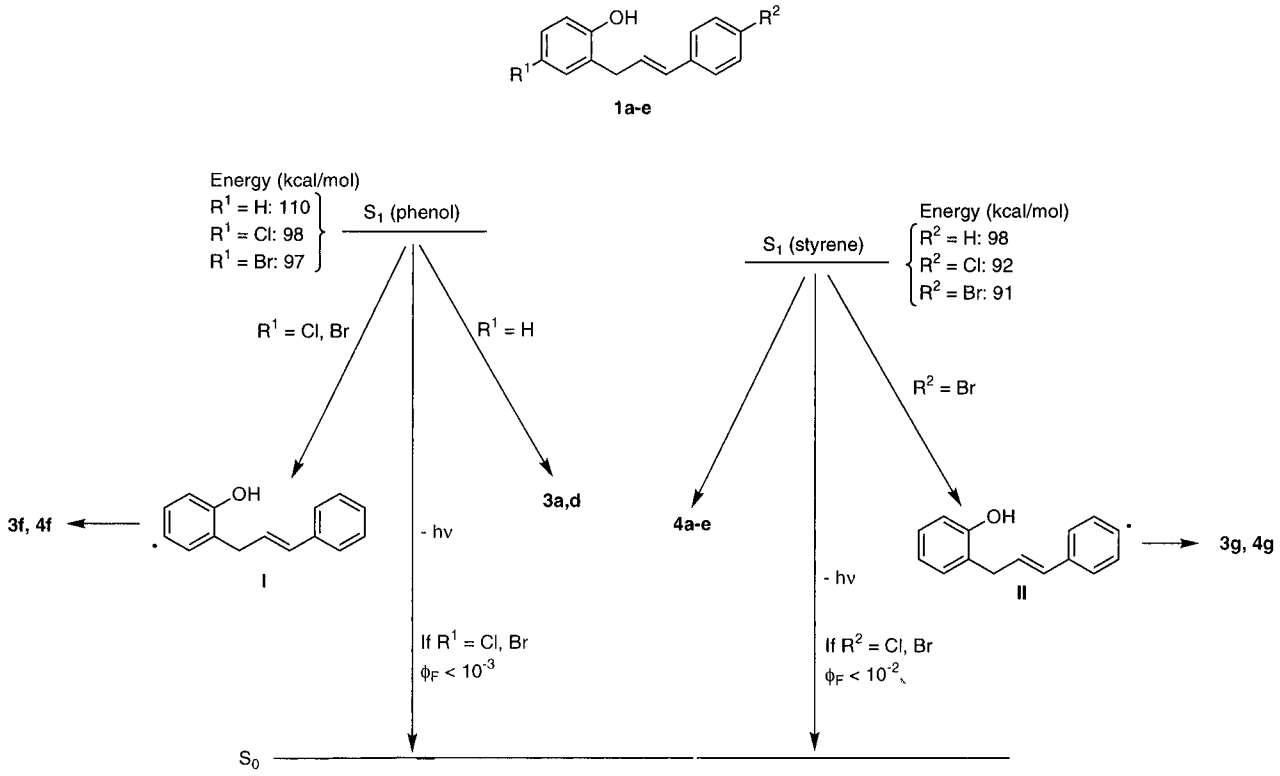
(15) A similar value was found for 4-chlorostyrene in Brede, O.; David, f.; Steenken, S. *J. Photochem. Photobiol. A: Chem.* **1996**, *97*, 127.

(16) Jiménez, M. C.; Miranda, M. A.; Tormos, R. *Tetrahedron* **1997**, *53*, 14729.

(17) MS spectra data for **3e**: 290 (M^+ (^{81}Br), 7), 288 (M^+ (^{79}Br), 8), 237 (6), 119 (100), 118 (28), 117 (8), 92 (9), 91 (52), 89 (12), 78 (4), 77 (7).

Scheme 1



obtained from 40.0 mmol of 4-chloro- or 4-bromophenol was added to *trans*-cinnamyl chloride (6.10 g, 40.0 mmol) in 100 mL of benzene. After the mixture was refluxed for 5 h, the solvent was distilled and the residue was treated with 100 mL of Claisen's alkali (35.00 g of potassium hydroxide in 25 mL of water and methanol up to 100 mL). The alkaline solution was washed with hexane, acidified with HCl, and extracted with methylene chloride. Evaporation of the solvent gave a residue which was submitted to column chromatography.

Preparation of the Substrates 1d,e. The cinnamylphenols **1d**,**e** were prepared by reduction of the corresponding *trans*-2-hydroxychalcones (previously synthesized by condensation of 2-hydroxyacetophenone with 4-chloro or 4-bromobenzaldehyde)[19] with $LiAlH_4/AlCl_3$, using tetrahydrofuran as solvent.[20] Final purification was done by column chromatography.

Alternative Synthesis of Compound 3d. (*Z*)-2-[(4-Chlorophenyl)methylene]-3(2*H*)-benzofuranone[21] (1.0 mmol) in ethyl acetate (25 mL) was hydrogenated in the presence of palladium/charcoal (11%) until consumption of 75 mL of hydrogen. The solution was filtered and on evaporation afforded the pure dihydrobenzofuran **3d** in quantitative yield.

***trans*-4-Bromo-2-cinnamylphenol (1c)** (43%): oil.;UV 284 (3.4), 227 (sh, 4.0), 216 (4.1); FTIR 3651 (OH), 3559 (OH), 3070, 3032, 1485, 1409, 1308, 1258, 1205, 1160, 1105, 966, 812, 733, 628; ^{1}H NMR 7.19−7.36 (m, 7H), 6.67 (d, 1H), 6.49 (d, J = 16 Hz, 1H), 6.31 (dt, J_1 = 16 Hz, J_2 = 6 Hz, 1H), 5.14 (s, 1H), 3.50 (d, J = 6 Hz, 2H); MS 290 (M^+(^{81}Br), 43), 288, (M^+(^{79}Br), 43), 209 (100), 199 (22), 197 (23), 131 (19), 118 (29), 115 (23), 104 (48), 91 (19), 77 (18). Anal. Calcd for $C_{15}H_{13}BrO$: C, 62.30; H, 4.53; Br, 27.63. Found: C, 62.25; H, 4.46; Br, 26.95.

***trans*-2-[3-(4-Chlorophenyl)-2-propenyl]phenol (1d)** (45%): UV 259 (3.9), 219 (3.8); FTIR 3650 (OH), 3585 (OH), 3075, 3033, 2914, 1590, 1491, 1321, 1254, 1207, 1095, 1014, 966, 834, 748; ^{1}H NMR 7.20 (AA′BB′, 4H), 7.14−7.18 (m, 2H), 6.88 (t, J = 8 Hz, 1H), 6.74 (t, J = 8 Hz, 1H), 6.26−6.34 (m, 2H), 5.31 (s, 1H), 3.49 (d, J = 6 Hz, 2H); MS 246 (M^+(^{37}Cl), 24), 246, (M^+(^{35}Cl), 72), 209 (70), 138 (100), 131 (34), 119 (79), 115 (55), 107 (20), 91 (58), 89 (30), 77 (43); exact mass calcd for $C_{15}H_{13}$35ClO 244.0655, found 244.0661.

***trans*-2-[3-(4-Bromophenyl)-2-propenyl]phenol (1e)** (55%): UV 260 (4.2), 215 (4.1); FTIR 3650 (OH), 3589 (OH), 3076, 3032, 2914, 1588, 1488, 1321, 1254, 1207, 1075, 1011, 966, 832, 748; ^{1}H NMR: 7.19−7.40 (m, 2H), 7.21 and 7.38 (AA′BB′, 4H), 6.93 (t, J = 8 Hz, 1H), 6.81 (t, J = 8 Hz, 1H), 6.39 (m, 2H), 4.85 (s, 1H), 3.54 (d, J = 6 Hz, 2H); MS 290 (M^+(^{81}Br), 25), 288, (M^+(^{79}Br), 27), 209 (70), 184 (71), 182 (66), 131 (48), 119 (97), 115 (94), 91 (100), 77 (82); exact mass calcd for $C_{15}H_{13}{}^{79}$BrO 288.0150, found 288.0141.

***cis*-4-Chloro-2-cinnamylphenol (2b)**: UV 283 (3.3), 247 (sh, 3.7), 215 (4.1); FTIR 3651 (OH), 3590 (OH), 3069, 3027, 1598, 1488, 1412, 1310, 1258, 1204, 1161, 1109, 914, 810, 757; 701; ^{1}H NMR 7.05−7.39 (m, 8H), 6.70 (d, J = 12 Hz, 1H), 5.81 (dt, J_1 = 12 Hz, J_2 = 7 Hz, 1H), 5.02 (s, 1H), 3.61 (d, J = 7 Hz, 2H); MS 246 (M^+ (^{37}Cl), 18), 244 (M^+ (^{35}Cl), 49), 209 (63), 165 (27), 153 (46), 152 (31), 131 (28), 115 (65), 91 (72), 77 (60). Anal. Calcd for $C_{15}H_{13}ClO$: C, 73.59; H, 5.35; Cl, 14.51. Found: C, 73.21; H, 5.46; Cl, 13.82.

***cis*-4-Bromo-2-cinnamylphenol (2c)**: UV 283 (3.4), 230 (4.1), 216 (4.1); FTIR 3650 (OH), 3585 (OH), 3068, 3025, 1598, 1485, 1407, 1307, 1258, 1202, 1161, 1103, 873, 809, 700, 628; ^{1}H NMR 7.25−7.40 (m, 7H), 6.65−6.70 (m, 2H), 5.81 (dt, J_1 = 12 Hz, J_2 = 7 Hz, 1H), 4.92 (s, 1H), 3.61 (d, J = 7 Hz, 2H); MS: 290 (M^+ (^{81}Br), 11), 288 (M^+ (^{79}Br), 12), 209 (35), 118 (36), 115 (38), 104 (100), 91 (80), 78 (26), 77 (36), 51 (29). Anal. Calcd for $C_{15}H_{13}BrO$: C, 62.30; H, 4.53; Br, 27.63. Found: C, 62.22; H, 4.49; Br, 27.35.

***cis*-2-[3-(4-Chlorophenyl)-2-propenyl]phenol (2d)**: UV 248 (3.9), 219 (3.9); FTIR 3649 (OH), 3601 (OH), 3075, 3026, 1589, 1490, 1401, 1321, 1255, 1203, 1093, 1015, 841, 748; ^{1}H NMR 7.25 and 7.30 (AA′BB′, 4H), 7.08−7.15 (m, 2H), 6.88 (dt, J_1 = 7 Hz, J_2 = 1 Hz, 1H), 6.76 (d, J = 8 Hz, 1H), 6.56 (d, J = 12 Hz, 1H), 5.81 (dt, J_1 = 12 Hz, J_2 = 7 Hz, 1H), 4.82 (s, 1H), 3.61 (dd, J_1 = 7 Hz, J_2 = 2 Hz, 2H); MS 246 (M^+(^{37}Cl), 29), 246, (M^+(^{35}Cl), 75), 209 (100), 165 (24), 140 (28), 138 (83), 131 (40), 119 (45), 115 (67), 91 (56), 77 (49); exact mass calcd for $C_{15}H_{13}$-^{35}ClO 244.0655, found 244.0649.

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***cis*-2-[3-(4-Bromophenyl)-2-propenyl]phenol (2e)**: UV 251 (4.2), 216 (4.0); FTIR 3650 (OH), 3601 (OH), 3075, 3026, 2914, 1587, 1488, 1402, 1321, 1255, 1203, 1075, 1040, 1012, 839, 786, 748; ^{1}H NMR 7.19 and 7.47 (AA′BB′, J = 8 Hz, 4H), 7.09−7.15 (m, 2H), 6.89 (dt, J_1 = 7 Hz, J_2 = 1 Hz 1H), 6.77 (t, J = 8 Hz, 1H), 6.54 (d, J = 11 Hz, 2H), 5.88 (dt, J_1 = 11 Hz, J_2 = 7 Hz, 2H), 4.81 (s, 1H), 3.61 (dd, J_1 = 7 Hz, J_2 = 2 Hz, 2H); MS 290 (M^+(^{81}Br), 27), 288, (M^+(^{79}Br), 28), 209 (72), 184 (67), 182 (73), 171 (41), 169 (43), 131 (47), 119 (100), 91 (87), 77 (71); exact mass calcd for $C_{15}H_{13}{}^{79}BrO$ 288.0150, found 288.0140.

2-(4-Chlorobenzyl)-2,3-dihydrobenzofuran (3d): FTIR 3079, 2950, 1598, 1483, 1229, 1169, 1096, 1015, 986, 869, 796, 745; ^{1}H NMR 7.55−6.69 (m, 8H), 4.91 (m, 1H), 3.14 (m, 2H), 2.89 (m, 2H); MS 246 (M^+(^{37}Cl), 4), 244 (M^+(^{35}Cl), 12), 125 (9), 120 (9), 119 (100), 118 (16), 91 (49), 77 (4); exact mass calcd for $C_{15}H_{13}{}^{35}ClO$ 244.0655, found 244.0646.

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