Table I. Physical Properties of Fe_4S_4 Clusters at 25 °C under Ar (λ_{max} (ϵ), half-life,[a] and $E^{1/2}$ (versus Ag/AgCl))

	$Fe_4S_4((SPh\text{-}m\text{-}S)_2CD)_2$ (**2**)	$Fe_4S_4(SPh\text{-}m\text{-}SCD)_4$ (**3**)	$Fe_4S_4(SPh\text{-}m\text{-}SMe)_4$ (**4**)
in H_2O (10 mM phosphate buffer, pH 7.0)	428 nm (17 000) 120 h −0.58 V	468 nm (17 000) 70 h −0.55 V	468 nm[b] 5.6 h[b] −0.54 V[b]
in DMF	441 nm (17 500) c −0.94 V[d]	458 nm (17 000) c −0.93 V[d]	463 nm (17 300) c −0.92 V[d]

[a] By monitoring the decreases of the characteristic absorptions of clusters at 420–470 nm. [b] 5% DMF–95% 10 mM phosphate buffer, pH 7.0. [c] No appreciable spectral changes were observed for several days. [d] 100 mM $n\text{-}Bu_4NBr$.

by applying −0.50 V versus Ag/AgCl of the anodic potential in over 95% yield based on the spectral absorbance (see Figure 1).

The present synthetic clusters **2** and **3** are soluble in water[12] without any solubilizing reagents, and a small amount of **4** (ca. 0.1 mM) is also able to be solubilized in 5% DMF–H_2O. The reduction potentials of **2**, **3**, and **4** in aqueous solution at pH 7.0 were observed to be −0.58, −0.55, and −0.54 V versus Ag/AgCl, respectively. Observed positive shifts of reduction potentials by the solvent change ($E^{1/2}_{H_2O} - E^{1/2}_{DMF} = 0.36\text{–}0.38$ V) lie within the range of those reported for other synthetic clusters.[6]

The most remarkable characteristics of **2** and **3** are their stabilities in aqueous solution. The half-lives at pH 7.0 (25 °C) of **2** and **3** in the aqueous phosphate buffer, without any additional thiols, are greater than 120 and 70 h, respectively, based on absorbance changes of the electronic spectra of **2** and **3**, while that of the reference cluster **4** is only 5.6 h in 5% DMF–H_2O. Thus, **2** and **3** are 21- and 13-fold more stable than **4** in aqueous solution, respectively, though the stability of **4** is higher than that expected from the data reported for other clusters having alkylthiolate ligands.[13] Since consideration of CPK space filling molecular models of **2** and **3** shows that the primary OH groups of cyclodextrin can attack iron atoms of the cluster core *intramolecularly*, present enhanced stabilities of **2** and **3** may be attributed to the favorable shift of ligand exchange equilibrium toward the cluster formation by the competition of water with these primary OH groups of cyclodextrin.[2]

Finally, it should be noted that the λ_{max}'s of the electronic spectra of **3** and **4** show a small red shift when the solvent is changed from DMF to H_2O rather than the blue shift usually reported for alkylthiolate clusters, while **2** shows the normal blue shift.[6] Although at the present stage it is not clear whether the observed red shift is the general trend for arenethiolate clusters or not, there is a possibility that a mechanism other than the solvation on sulfur atoms,[6] such as steric effects,[14] is operating for the absorption shift by solvent change in the present case.

The present new iron–sulfur clusters have great advantage in that the hydrophobic pockets of cyclodextrins may be available as recognition sites for substrates such as an electron donors and/or acceptors. Applications of these water soluble clusters, especially focusing on **2**, are now in progress in our laboratory.

Acknowledgment. We thank Toshio Tanaka and Koji Tanaka, Osaka University, for their kind advice on the electrochemical experiments for the present compounds.

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Absolute Rates of Dimerization and Cycloaddition of 3,4-Dimethylenefuran and 3,4-Dimethylenethiophene by Nanosecond Time-Resolved Spectroscopy[1a]

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3,4-Dimethylenefuran (**1**) and 3,4-dimethylenethiophene (**2**) can be generated in fluid solutions from the corresponding diazenes, **3** and **4**,[3-5] and from the corresponding bis-allenes, **5** and **6**.[6-8] The capture of the singlet[3-5,9] biradicals **1** and **2** by alkenes to give cycloadducts (**7**) is believed to involve the same intensely colored species (**1**, λ_{max} = 560 nm; **2**, λ_{max} = 572 nm) observed spectroscopically from **3** and **4** immobilized in low-temperature glasses or flash photolyzed in solution, although heretofore no direct evidence on this point has been available.

We now report direct time-resolved spectroscopic observations of the kinetic behavior of these transients generated from diazenes **3** and **4** by nanosecond flash photolysis.[10] Deoxygenated samples of **3** or **4** in either CH_3CN or toluene solution in a 3 × 7 mm static cell (initial optical densities about 0.4 at 337 nm) were kept at 260–263 K to minimize thermal decomposition and subjected to 337-nm laser pulses. Transient spectra with maxima at about 560 (**1**) and 572 (**2**) nm were observed with an optical multichannel analyzer. Typically, the pulses produced initial transient concentrations of (1–2) × 10^{-5} M. The decay of the transient absorption with time was monitored by a photomultiplier-transient digitizer system.

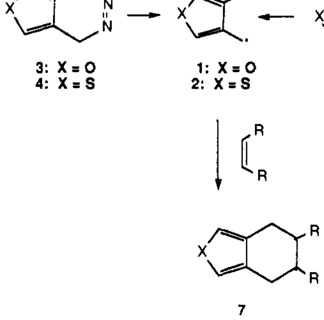

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Table I. Rates of Cycloaddition of 3,4-Dimethylenefuran (**1**) and 3,4-Dimethylenethiophene (**2**) with Alkenes at 260–263 K[a]

	1		**2**		
alkene	10^6k[b]	k_{rel} (direct)[g]	10^6k[b]	k_{rel} (direct)[g]	k_{rel} (compet)[h]
maleic anhydride[c]	1200	20	570	57	90
fumaronitrile[d]	320	5.1	11	1.1	1.5
dimethyl fumarate[e]	63	1.0	10	1.0	1.0
acrylonitrile[f]	0.42	0.0067	0.024	0.0024	0.0083

[a] In CH_3CN solvent. [b] In M^{-1} s^{-1}. [c] Concentration range 0–0.011 M. [d] 0–0.014 M. [e] 0–0.048 M. [f] 0–2 M. [g] Determined from absolute rate measurements (present work). [h] Determined from competition experiments (ref 6a).

The disappearance of both species could be fitted to second-order kinetics with rate constants ($2k_t$ in M^{-1} s^{-1}) for dimerization[3] as follows: for **1** (CH_3CN), 3.3×10^{10}; for **1** (toluene), 1.6×10^{10}; for **2** (CH_3CN), 9.3×10^9; for **2** (toluene), 5.5×10^9, each value being the average of four separate determinations. The probable uncertainty in the dimerization rate constants is about 50%, primarily because the extinction coefficients (in M^{-1} cm^{-1}) of the biradicals (**1**, 5300; **2**, 5400) are known to an accuracy of only about 20%.[11] The rates, especially those for the furan **1**, approach the diffusive encounter-controlled limit of about 10^{10} M^{-1} s^{-1} under these conditions.

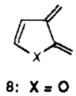
In the presence of large excesses of alkenes, the transients are quenched with pseudo-first-order kinetics. The rate constants in all cases are linear ($r \geq 0.99$ in most cases) in the alkene concentration, and the limiting rate constant at zero quencher concentration, extrapolated by a least-squares fit and converted to second-order form, is in good agreement with the dimerization rate constant determined as described above. The bimolecular rate constants are shown in Table I.

The values for the dimerization rate constants may be pertinent to the question[12] of the statistical spin effect in monoradical–monoradical reactions. Absolute rates for most of such processes seem to cluster around 2×10^9 M^{-1} s^{-1} rather than the calculated encounter-controlled limit of 10^{10} M^{-1} s^{-1}. This has prompted the conjecture that reaction may occur in only a quarter of the encounters, since only this fraction of the radical pairs will be singlet. However, the present reaction partners are *singlet biradicals*, whose pairs necessarily are singlet. Hence product formation is spin-allowed from all encounters. Perhaps the consequent increase in efficiency of combination contributes to the exceptionally high rates observed here.

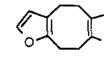
Table I shows that the effect of structure on the relative reactivities of alkenes toward the biradical **2** is essentially the same whether measured by competition experiments[6a] or by the present absolute rates (compare the last two columns). This leaves little doubt that the species responsible for the formation of cycloadducts in preparative experiments[3,6a] are indeed the purple substances[3–5,6b] whose kinetic behavior now has been observed directly.

The absolute rates of the cycloaddition reactions also are extremely fast (Table I). With stereochemically labeled alkenes, these reactions are ≥99% stereospecifically syn additions[3,11] which most probably pass over four-center, Diels–Alder-like transition states. However, the cycloaddition rates of **1** and **2** with alkenes exceed those[13] of even the most reactive Diels–Alder pairs by many orders of magnitude. For example, the **1**–maleic anhydride reaction is faster than that of cyclopentadiene–tetracyanoethylene, one of the fastest Diels–Alder cases, by a factor of about 3×10^5; the factor becomes 10^{10} in a structurally more closely related case, cyclopentadiene–maleic anhydride. These large enhancements of reactivity probably are caused by the small frontier orbital gap[13] in the reaction of alkenes with these electron-rich biradicals and by the much greater exothermicity (about 80 kcal/mol as compared to the 40 kcal/mol of the Diels–Alder reaction).

The dimerization rates of the species **1** and **2** greatly exceed those of their isomers, 2,3-dimethylenefuran (**8**),[14a] and 2,3-dimethylenethiophene (**9**),[14b] respectively. Compound **8**, for example, is persistent in solution at −78 °C in a concentration of about 0.2 M, from which a rough value for its dimerization rate constant of about 10^{-3} M^{-1} s^{-1} can be calculated. Thus, the dimerization of **1** is some 10^{13} times as fast as that of **8**! Although



8: X = O
9: X = S



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the dimerization of **8**, helped by the creation of two aromatic furan units in the dimer **10**, has a substantial thermodynamic driving force (about 60 kcal/mol[15]), the exothermicity of the dimerization of the biradical **1** (about 100 kcal/mol[15]) remains much greater. One can hardly refrain from the conclusions that this difference is a major cause of the large rate effects and that the latter constitute dramatic experimental demonstrations of the consequences of non-Kekulé character.

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Total Synthesis of Amphimedine

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The unusual structure of amphimedine (**1**), a cytotoxic alkaloid recently isolated from a Pacific sponge,[1] was elucidated by using long-range C–H and C–C NMR correlations. Amphimedine belongs to a small group of highly unsaturated fused pentacyclic alkaloids isolated from marine organisms[2] and is loosely related to the mimosamycin-type family of antibiotics.[3] In this communication we report the first total synthesis of amphimedine.

In the retrosynthetic analysis (Scheme I), amphimedine can be derived from diazaanthraquinone **2**, available by a hetero-Diels–Alder reaction[4] of 2-azadiene **3**[5,6] with the quinoline-5,8-

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