similar systems are under further investigation.

Experimental Section

Lucigenin, as the nitrate salt, was a commercial sample and was recrystallized from ethanol before use. The counterion is electroinactive in the potential range studied and did not influence the voltammetric results. Cells, electrodes, reference electrodes, and voltammetric instrumentation were as previously described.[44,45] Beckman platinum-bottoned electrodes (No. 39273) were used as working electrodes for cyclic voltammetry.

Acknowledgment. Professor M. G. Ettlinger, University of Copenhagen, is gratefully acknowledged for his stimulating interest in this work. We express our gratitude to Dr. L. Nadjo, Université de Paris-VII, for helpful discussions concerning previously reported[12] voltammetric data. We thank the Norwegian Research Council for Science and the Humanities for support for E.A.

(44) E. Ahlberg, B. Svensmark, and V. D. Parker, *Acta Chem. Scand., Ser. B*, **B34**, 53 (1980).

(45) O. Hammerich and V. D. Parker, *J. Am. Chem. Soc.*, **96**, 4289 (1974).

Electron-Transfer Chemistry of the Merostabilized 3,5,5-Trimethyl-2-morpholinon-3-yl Radical

John M. Burns, Donald L. Wharry, and Tad H. Koch*

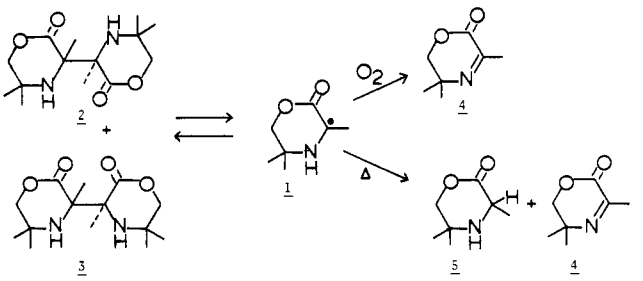
Contribution from the Department of Chemistry, University of Colorado, Boulder, Colorado 80309. *Received July 10, 1980*

Abstract: Reductions of 5,6-dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (**6**) to 5,5-dimethyl-3-phenyl-2-morpholinone (**8**), 2-benzoyl-4,4-dimethyl-2-oxazoline (**9**) to 2-(hydroxyphenylmethyl)-4,4-dimethyl-2-oxazoline (**10**), 4-(diphenylmethylene)-2,5-cyclohexadienone (**12a**) to diphenyl(*p*-hydroxyphenyl)methane (**14a**), 4-[bis(4-hydroxyphenyl)methylene]-2,5-cyclohexadienone (**12b**) to tris(*p*-hydroxyphenyl)methane (**14b**), benzil (**17**) to benzoin, and substituted benzils (**17a-c**) to substituted benzoins by 3,5,5-trimethyl-2-morpholinon-3-yl radical are described. Intermediate radicals 5,5-dimethyl-3-phenyl-2-morpholinon-3-yl (**7**), diphenyl(*p*-hydroxyphenyl)methyl (**13a**), and tris(*p*-hydroxyphenyl)methyl (**13b**) are characterized by EPR spectroscopy. Kinetic analyses of the reductions of **6**, **9**, **17**, and **17a-c** are described, and mechanisms and rate laws are shown in Schemes II, III, and VII. Reduction reactions most likely occur by electron transfer. Evidence for electron transfer includes an isotope effect for disproportionation of **1** equal to 1.10 ± 0.09, correlation of the logarithm of the relative rates of reduction of benzils with σ^+ with a ρ of 1.7 ± 0.1, and observation of electron transfer from **1** to tetracyanoethylene, dianisyloxoammonium perchlorate (**21**), and paraquat (**20**).

Radicals bearing electron-donating and electron-withdrawing substituents have unusual stability and persistence. The synergistic effect of this substitution has been described by Katritzky and co-workers as merostabilization,[1] by Balaban and co-workers in terms of push-pull stabilization,[2] and by Viehe as a captodative substituent effect.[3] The preparation, stability, and reactivity of these radicals have been recently reviewed by Viehe and co-workers.[4] The only mode of reactivity described is basically radical combination. We report in detail our results, previously communicated,[5] on the one electron-transfer reactivity of an aminocarboxy-substituted free radical, 3,5,5-trimethyl-2-morpholinon-3-yl (**1**, Scheme I).

We have reported that 3,5,5-trimethyl-2-morpholinon-3-yl is formed when a mixture of the meso and *dl* dimers (**2** and **3**, respectively) of the radical are dissolved in benzene, chloroform, or ethanol solvent at ambient temperature.[6] In chloroform solvent the $\Delta H°$ and $\Delta H^{\ddagger}$ for formation of **1** are 22 and 27 kcal/mol, respectively.[6,7] The facility of bond homolysis and the persistence

Scheme I



of **1** have been discussed in terms of dipolar resonance stailization of **1**.[6] The methylmorpholinonyl radical **1** oxidizes in air to 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) and disproportionates upon being heated at 80 °C to a 50:50 mixture of **4** and 3,5,5-trimethyl-2-morpholinone (**5**).

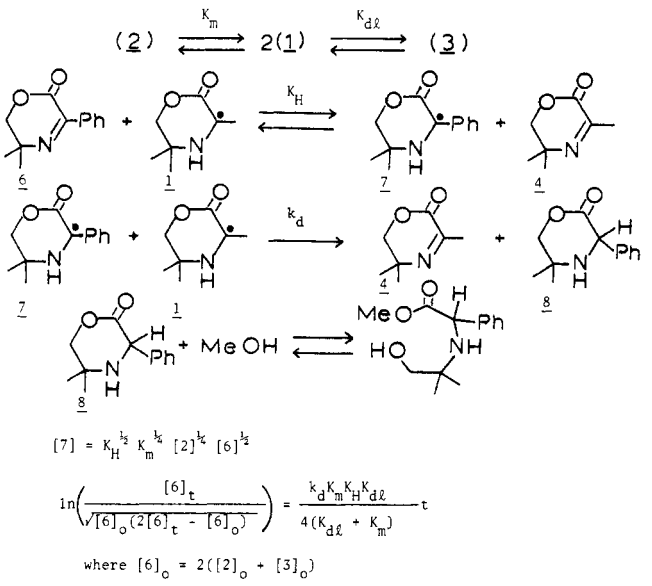
Results and Discussion

Reduction of 5,6-Dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (6) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). A mixture of the meso and *dl* radical dimers **2** and **3** reacts with 5,6-dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (**6**) in degassed methanol solvent to give a new radical species characterized by EPR spectroscopy as 5,5-dimethyl-3-phenyl-2-morpholinon-3-yl (**7**). The EPR spectrum shows a *g* value of 2.003 99 and the

(1) Baldock, R. W.; Hudson, P.; Katritzky, A. R.; Soti, F. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1422.
(2) Balaban, A. T.; Caproin, M. T.; Negoita, N.; Baican, R. *Tetrahedron* **1977**, *33*, 2249.
(3) Stella, L.; Janousek, R.; Merényi, R.; Viehe, H. G. *Angew. Chem., Int. Ed Engl.* **1978**, *17*, 691.
(4) Viehe, H. G.; Merényi, R.; Stella, L.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 917.
(5) Burns, J. M.; Wharry, D. L.; Koch, T. H. *J. Am. Chem. Soc.* **1979**, *101*, 2750.
(6) Koch, T. H.; Olesen, J. A.; DeNiro, J. *J. Am. Chem. Soc.* **1975**, *97*, 7285.
(7) Bennett, R. W.; Wharry, D. L.; Koch, T. H. *J. Am. Chem. Soc.* **1980**, *102*, 2345.

0002-7863/81/1503-849$01.00/0

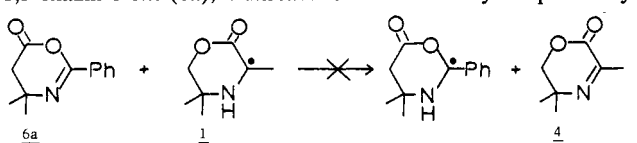
Scheme II



following splitting pattern: N, 1:1:1, 6.52 G; N–H, 1:1, 3.95 G; ortho and para H, 1:3:3:1, 2.01 G; meta H, 1:2:1, 0.81 G. In methanol-d_4 solvent the hydrogen on nitrogen exchanges for deuterium, and the EPR spectrum shows an N–D, 1:1:1 splitting of 0.66 G in place of the N–H splitting. The EPR spectra were verified by spectrum simulation.

The phenylmorpholinonyl radical **7** is persistent for a period of days and does not dimerize or combine with **1** as indicated by ^{1}H NMR spectroscopy. Upon being heated for a prolonged time **7** is reduced quantitatively to 5,5-dimethyl-3-phenyl-2-morpholinone (**8**), and the radical dimers **2** and **3** are oxidized to 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**). The phenylmorpholinone **8** was identified spectroscopically by comparison with a sample prepared by catalytic hydrogenation of **6**. The phenylmorpholinone is somewhat unstable and exists in equilibrium with a ring-opened product, methyl 2-phenyl-2-(1,1-dimethyl-2-hydroxyethyl)aminoacetate, identified by ^{1}H NMR spectroscopy.

A molecule which contains a permutation of the imino lactone functionality of **6**, namely, 4,5-dihydro-4,4-dimethyl-2-phenyl-1,3-oxazin-6-one (**6a**), is unreactive with the methylmorpholinonyl



radical **1**. No EPR signal other than that from **1** is observed from a mixture of **2**, **3**, and **6a**, and heating a mixture of **2**, **3**, and **6a** yields only the products of disproportionation of **1**. This result was not unexpected since the permutation transformed an electron-withdrawing substituent at the radical site into a moderate electron-donating substituent and, consequently, reduced the merostabilization.

A mechanism for the production of the phenylmorpholinone **8** is shown in Scheme II and is suggested by the following evidence. The relative intensity of the EPR spectrum of the phenylmorpholinonyl radical **7** at ambient temperature is directly proportional to the square root of the concentration of **6** (obsd 1.49, theoretical 1.41) and the fourth root of the concentration of the radical dimers **2** and **3** (obsd 1.23, theoretical 1.19). Furthermore, the intensity of the EPR spectrum of **7** is significantly diminished upon the addition of trimethyloxazinone **4**. Under the conditions of the intensity measurements, the reduction of **7** to **8** was slow, and the concentration of the methylmorpholinonyl radical **1** was low relative to the concentration of the phenylmorpholinonyl radical. As indicated by the expression for the concentration of **7** in Scheme II, the observed effect of concentration on relative EPR signal intensities is consistent with rapid equilibrium steps

Table I. Rate of Reduction of **6** by **1**[a]

t, min	[6], mol/L	t, min	[6], mol/L	t, min	[6], mol/L
0	0.250	1316	0.187	3289	0.155
60	0.229	1524	0.174	3542	0.155
120	0.223	1700	0.170	4157	0.151
195	0.217	1813	0.168	4650	0.147
325	0.211	2067	0.170	4980	0.141
463	0.204	2706	0.161	5537	0.142
662	0.201	2893	0.159	6937	0.136

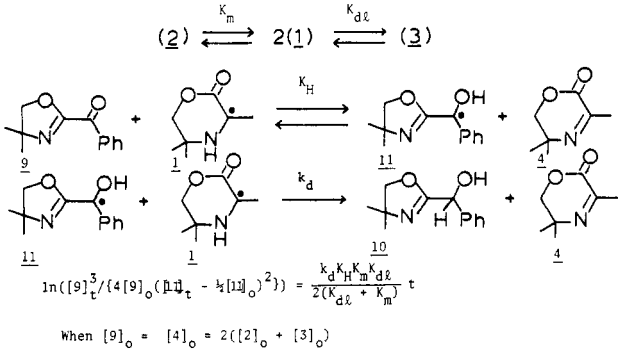
[a] The concentration of a mixture of radical dimers **2** and **3** was 0.125 M in methanol-d_4 solvent, and the temperature was 35 ± 0.1 °C.

Table II. Rate of Reduction of **9** by **1** in the Presence of **4**[a]

t, min	[9], mol/L	t, min	[9], mol/L	t, min	[9], mol/L
0	0.500	1135	0.400	2715	0.334
105	0.484	1410	0.378	3420	0.332
420	0.453	1725	0.366	4115	0.300
730	0.421	2190	0.344	4980	0.293
925	0.414				

[a] The concentrations of a mixture of radical dimers **2** and **3** and methyloxazinone **4** were 0.250 and 0.500 M, respectively, and the temperature was 35 ± 0.1 °C.

Scheme III

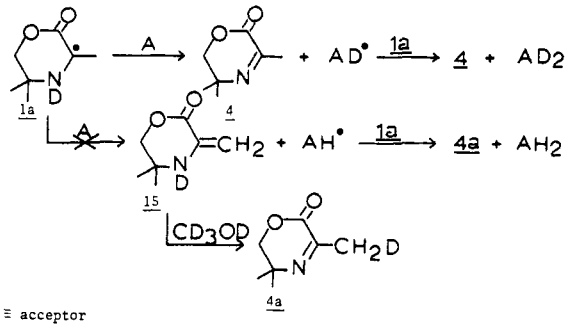


designated by constants K_m, K_{dl}, and K_H prior to a slower reaction of radical intermediates. The rate of reduction of the phenyloxazinone **6** to the phenylmorpholinone **8** is consistent with the integrated rate law shown in Scheme II for over 90% of the reaction at 35 °C for a methanol solution that is 0.250 M in **6** and 0.125 M in radical dimers **2** and **3**. The concentration of **6** as a function of time as determined by ^{1}H NMR spectroscopy is shown in Table I. In the absence of an excess of **6**, disproportionation of **1** to **4** and **5** is competitive with reduction of **7** toward the end of the reaction. A plot of ln $([6]_t/([6]_0(2[6]_t - [6]_0)^{1/2}))$, the integrated rate law for the mechanism in Scheme II, vs. time (t) is linear with a slope of $(7.9 \pm 0.3) \times 10^{-3}$ s^{-1}. The data in Table I are inconsistent with disproportionation of **7** to **6** and **8** as the rate-controlling step in that a corresponding plot of the appropriate integrated rate law vs. t is nonlinear.

Reduction of 2-Benzoyl-4,4-dimethyl-2-oxazoline (9) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). Methylmorpholinonyl **1** in chloroform solvent selectively reduces the carbonyl functional group of 2-benzoyl-4,4-dimethyl-2-oxazoline (**9**) to give 2-(hydroxyphenylmethyl)-4,4-dimethyl-2-oxazoline (**10**), identified by comparison of its spectral properties with those of an authentic sample.[8] An intermediate radical other than **1** was not observed by EPR spectroscopy. The reduction is quantitative in radical dimers **2** and **3** when approximately a 100% excess of **9** is employed. In the absence of a large excess of the carbonyl compound, disproportionation of the methylmorpholinonyl radical **1** to **4** and **5** is competitive with reduction of **9**. The rate of reduction of oxazoline **9** in a chloroform solution that is 0.500 M in oxazoline, 0.250 M in radical dimers **2** and **3**, and 0.500 M in methyl-

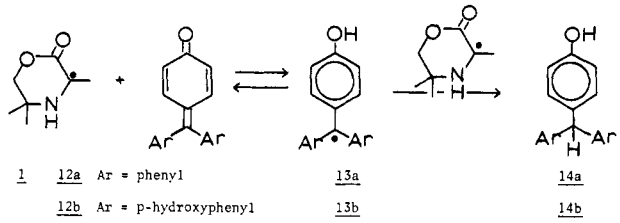
(8) Hansen, J. F.; Wang, S. *J. Org. Chem.* **1976**, *41*, 3635.

Scheme IV



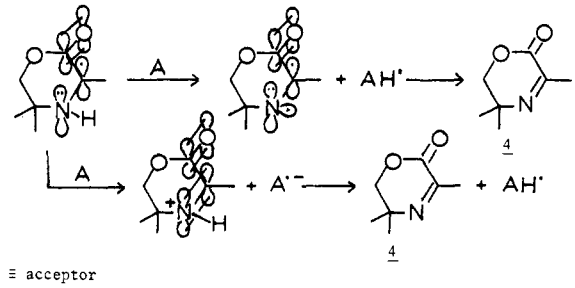
oxazinone **4** is consistent with a mechanism analogous to that proposed in Scheme II for the reduction of the phenyloxazinone **6** and shown in Scheme III. The concentration of **9** as a function of time as determined by ^{1}H NMR spectroscopy is shown in Table II. In the absence of the initial concentration of methyloxazinone **4**, the rate-controlling step shifts from the first hydrogen atom transfer to the second hydrogen atom transfer as the reaction proceeds. A plot of the integrated rate law for the stated reaction conditions and proposed mechanism, $\ln([9]_t^3/(4[9]_0([11]_t - {}^1/_2[11]_0)^2))$, vs. t is linear for over 90% of the reaction with a slope equal to $(4.0 \pm 0.1) \times 10^{-4}$ s^{-1}. The kinetic measurements were again inconsistent with disproportionation of **11** to **9** and **10** as the rate-controlling step.

Reduction of 4-(Diphenylmethylene)-2,5-cyclohexadienone (12a) and 4-[Bis(4-hydroxyphenyl)methylene]-2,5-cyclohexadienone (12b). The methylmorpholinonyl radical **1** transfers a hydrogen atom to the carbonyl of 4-(diphenylmethylene)-2,5-cyclohexadienone (**12a**) and to the carbonyl of 4-[bis(4-hydroxyphenyl)methylene]-2,5-cyclohexadienone (**12b**). A chloroform solution of **2**, **3**, and **12a** at ambient temperature gives an EPR signal with a g value of 2.003 53 and the following splitting pattern: ortho H, 1:6:15:20:15:6:1, 2.57 G; meta H, 1:6:15:20:15:6:1, 1.13 G; para H, 1:2:1, 2.80 G; O–H, 1:1, 0.12 G. Similarly, a dimethyl sulfoxide solution of **2**, **3**, and **12b** gives an EPR signal with a g value of 2.003 81 and the following splitting pattern: ortho H, 1:6:15:20:15:6:1, 2.48 G; meta H, 1:6:15:20:15:6:1, 1.00 G; O–H, 1:3:3:1, 0.11G. The EPR spectra were assigned to the diphenyl(*p*-hydroxyphenyl)methyl radical (**13a**) and the tris(*p*-hydroxyphenyl)methyl radical (**13b**), respectively. These radicals have not been previously characterized. Upon prolonged heating of **12a** and **12b** with radical dimers **2** and **3**, reduction quantitatively to diphenyl(*p*-hydroxyphenyl)methane (**14a**) and tris(*p*-hydroxyphenyl)methane (**14b**) occurs.

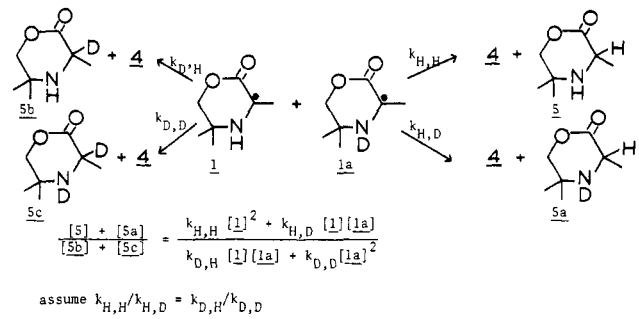


Determination of the Hydrogen Atom Transferred from 3,5,5-Trimethyl-2-morpholinon-3-yl (1). The hydrogen atom transferred from 3,5,5-trimethyl-2-morpholinon-3-yl (**1**) could have been either the hydrogen bonded to nitrogen or the hydrogen bonded to the 3-methyl carbon. Loss of a hydrogen bonded to the 3-methyl carbon would yield initially the enamine **15** which would tautomerize to the imine **4** (Scheme IV). The hydrogen bonded to the nitrogen of **1** was established as the hydrogen transferred in three reactions, disproportionation of **1** to **4** and **5**, reduction of **6** to **8**, and reduction of **9** to **10**, by deuterium-labeling experiments. The indicated reactions were performed in methanol-d_4 solvent in which the N–H protons of **2** and **3** exchange for deuterons, and the reaction mixtures at termination were observed by ^{1}H NMR spectroscopy. In all three experiments the methyloxazinone **4** contained no deuterium, and the methine proton absorptions of the reduced products **5**, **8**, and **10** were absent. As proposed in Scheme IV, formation of the enamine intermediate **15** would have led to deuterium incorporation in **4** at the 3-methyl substituent and no deuterium incorporation at the methine position of the reduced products.

Scheme V



Scheme VI



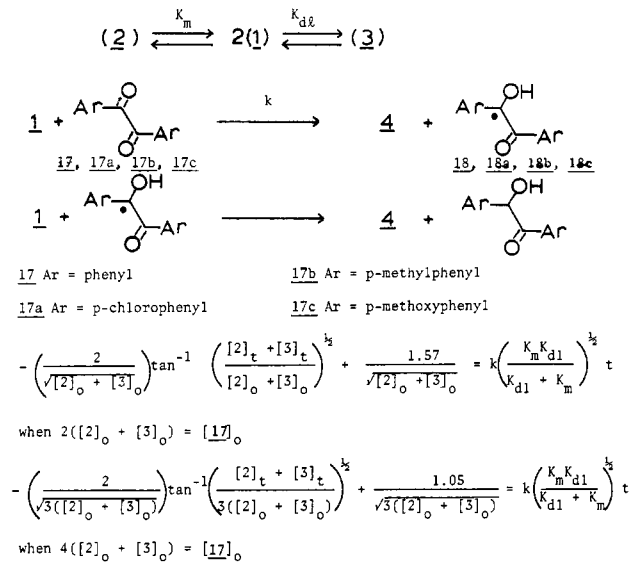
Electron-Transfer Mechanism for Hydrogen Atom Transfer. The redox reactions described for the methylmorpholinonyl radical **1** could occur by two distinct mechanisms, direct hydrogen atom transfer or electron transfer followed by proton transfer (Scheme V). It is interesting to note that direct transfer of a hydrogen atom from the nitrogen of **1** without simultaneous electronic internal conversion would produce an n,π^* state of **4** which probably lies 60–70 kcal/mol above the ground state, whereas electron transfer from the π system of **1** followed by proton transfer from the nitrogen would produce the ground state of **4**.

We have probed three redox reactions of **1** for evidence which might distinguish between these mechanistic alternatives. First, the deuterium kinetic isotope effect for the disproportionation of methylmorpholinonyl radical **1** to **4** and **5** was measured. The deuterium kinetic effect was determined by examining deuterium incorporation at the 3-position of 3,5,5-trimethyl-2-morpholinone (**5**) from 17% disproportionation of a solution in which the ratio of the concentration of methylmorpholinonyl radical to *N*-(dueteriomethyl)morpholinonyl radical varied from 50:50 to 47:53 during the course of the reaction. The mixture of deuterated and undeuterated radicals was prepared from partially deuterated radical dimers **2** and **3**, and the ratio was measured by double integration of a region of the EPR spectrum in which the absorptions of the two radicals were distinct and equally intense. A deuterium kinetic isotope effect of 1.10 ± 0.09 was calculated from the integration of the ^{1}H NMR spectrum of the reaction mixture by assuming that the average ratio of methylmorpholinonyl radical to *N*-(deuteriomethyl)morpholinonyl radical was 48.5:51.5 and that, for a rate-controlling hydrogen atom transfer, the possible secondary deuterium isotope effects with respect to the hydrogen atom acceptor are equal ($k_{H,H}/k_{H,D} = k_{D,H}/k_{D,D}$; see Scheme VI).

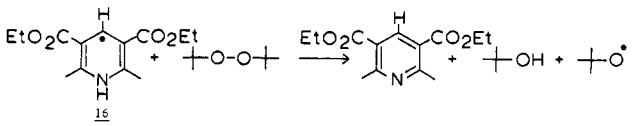
The magnitude of the kinetic isotope effect suggests that the rate-controlling step of the disproportionation is electron transfer. Approximations of the maximum possible primary kinetic isotope effects for cleavage of N–H and C–H bonds at 25 °C are 9.2 and 6.9, respectively.[9] Although the maximum isotope effect for a

(9) Hine, J. "Physical Organic Chemistry"; McGraw-Hill: New York, 1962; p 86.

Scheme VII



hydrogen atom transfer mechanism is not anticipated since the transition state for disproportionation of **1** would probably not be symmetrical, a value in the range of 2–3 would be consistent with literature precedent and an approximate exothermicity of less than 10 kcal/mol.[10] Gibian and Corley have determined indirectly that k_H/k_D for disproportionation of methylphenylmethyl radical is 1.87 at 118 °C[12] which extrapolates to 2.03 at 72 °C.[13] Saltiel and Curtis have obtained a k_H/k_D of 3.1 at 30 °C for the hydrogen atom transfer from 6-(benzoyloxy)-1,3-cyclohexadien-5-yl radical to oxygen.[14] This isotope effect extrapolates to 2.7 at 72 °C. For hydrogen atom abstraction from toluene by bromine, k_H/k_D is 4.6, and the reaction is exothermic by 10 kcal/mol.[15] Huyser and co-workers have noted an isotope effect of 2.39 at 125 °C for the hydrogen atom transfer reaction of the pyridinyl radical **16** to di-*tert*-butyl peroxide.[16,17] No isotope effect



was observed in the reduction of acetyl peroxide by **16**. For this latter reaction an electron-transfer mechanism was proposed on the basis of this and other evidence.

The second redox reaction probed for evidence of the mechanism for hydrogen atom transfer was the reduction of benzil to benzoin. 3,5,5-Trimethyl-2-morpholinon-3-yl (**1**) selectively reduces one carbonyl of benzil (**17**) to give benzoin in chloroform solvent. Intermediate radicals other than **1** were not observed in the EPR spectrum, and the reduction was again quantitative in radical dimers **2** and **3** as determined by ^{1}H NMR spectroscopy when approximately a 100% excess of benzil was employed. As a probe of the reaction mechanism, the effect of substituents in the 4- and 4'-positions of benzil on the rate in chloroform solvent was measured. For at least the first 30% of reaction (18% for 4,4'-dimethoxybenzil (**16c**)), the rates of reduction of benzil and the 4,4'-disubstituted benzils were consistent with the first hydrogen atom transfer being the rate-controlling step (Scheme VII). Under the reaction conditions less than 1% disproportionation of methylmorpholinonyl radical **1** was observed through the first half-life of **2** and **3** with a 100% excess of 4,4'-dichlorobenzil (**17a**) and 4,4'-dimethylbenzil (**17b**) and with a 300% excess of 4,4'-dimethoxybenzil (**17c**). The concentrations of **17** and **17a–c** as a function of time as determined by ^{1}H NMR spectroscopy are shown in Table III, and the slopes of the plots of the respective integrated rate laws vs. time (Scheme VII) for the first portion of the reaction are shown in Table IV. As can be seen from the equations in Scheme VII the ratios of the slopes give the ratios of the rate constants for the second step of the mechanism, and these are also reported in Table IV. The electron-withdrawing substituent chlorine enhances the rate of reduction, and the electron-donating substituents, methyl and methoxyl, retard the rate of reduction. The kinetic data are linear in σ^+, and a plot of log (k/k_0) vs. σ^+ gives a ρ of 1.7 ± 0.1. Correlation with σ^+ indicates that resonance effects are significant[18] presumably in the transition state as well as the ground state.

The Hammett correlation is consistent with a rate-controlling electron transfer for step 2 of Scheme VII. For this mechanism, electron-withdrawing substituents should facilitate the reaction through resonance interactions in the ground state and the transition state which likely resembles the radical anion. Correspondingly, electron-donating substituents should retard the electron transfer through resonance interactions in both the ground and transition states.

It is more difficult to conclude that a direct hydrogen atom transfer is inconsistent with the data in Table IV. The effects of substituents on the stability of radial **18**, which is also merostabilized, and on the transition state which it likely resembles are unknown. Since the hydrogen atom would most likely be

Table III. Rate of Reduction of Benzils by **1**[a]

benzil	[2 + 3], mol/L	time, min	benzil	[2 + 3], mol/L	time, min
17	0.0800	0	17b	0.0800	0
	0.0738	20		0.0768	20
	0.0676	40		0.0690	60
	0.0635	60		0.0632	100
	0.0567	90		0.0569	150
	0.0517	120		0.0520	200
	0.0426	220		0.0490	250
	0.0392	260		0.0447	350
17a	0.0800	0		0.0370	470
	0.0739	20	17c	0.0800	0
	0.0691	40		0.0759	20
	0.0636	60		0.0694	60
	0.0548	90		0.0658	100
	0.0479	140		0.0581	190
	0.0424	170		0.0536	250
	0.0402	200		0.0506	320
				0.0423	460

[a] The concentrations of **17**, **17a**, and **17b** were 0.160 M, and the concentration of **17c** was 0.320 M. The temperature was 50 ± 1 °C.

Table IV. Slopes of Plots of Data in Table III According to the Integrated Rate Laws in Scheme VII for the Initial Reaction

benzil	10^3(slope)	correln coeff	k/k_0
17	6.76	0.999	1
17a	7.23	0.997	1.07
17b	4.05	0.999	0.60
17c	1.70	0.984	0.25

(10) An approximation of the exothermicity of the disproportionation of **1** can be made, neglecting $\Delta H°_{soln}$. The $\Delta H°$ of homolysis of radical dimers **2** and **3** is approximately 20 kcal/mol in a nonpolar solvent.[6] The bond dissociation energy of a carbon–carbon single bond is 84 kcal/mol.[11] Hence the resonance energy of each methylmorpholinonyl radical **1** must be approximately 32 kcal/mol. Using bond-dissociation energies for the bonds formed (C-H, 91 kcal/mol; C=N – CN, 143–73 kcal/mol; the bond broken, N—H, 93 kcal/mol) and the resonance energy of the radical, the exothermicity is approximately 4 kcal/mol.

(11) March, J. "Advanced Organic Chemistry: Reactions, Mechanisms, and Structures"; McGraw-Hill: New York, 1977; p 28.

(12) Gibian, M. J.; Corley, R. C. *J. Am. Chem. Soc.* **1972**, *94*, 4178.

(13) Gibian, M. J.; Corley, R. C. *Chem. Rev.* **1973**, *73*, 441.

(14) Saltiel, J.; Curtis, H. C. *J. Am. Chem. Soc.* **1971**, *93*, 2056.

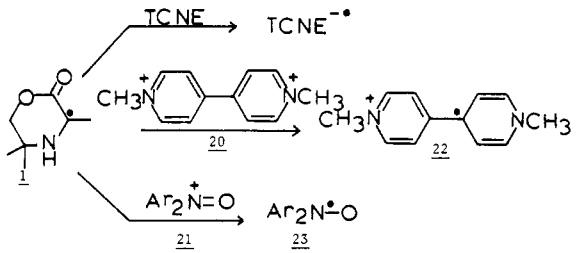
(15) Wiberg, K. B.; Slaugh, L. H. *J. Am. Chem. Soc.* **1958**, *80*, 3033.

(16) Huyser, E. S.; Kahl, A. A. *J. Org. Chem.* **1970**, *35*, 3742.

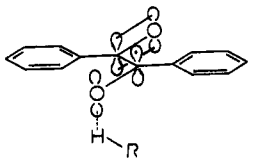
(17) Huyser, E. S.; Harmony, J. A. K.; McMillian, F. L. *J. Am. Chem. Soc.* **1972**, *94*, 3176.

(18) Brown, H. C.; Okamoto, Y. *J. Am. Chem. Soc.* **1958**, *80*, 4979.

Scheme VIII



delivered to the π bond of one carbonyl of benzil in a direct hydrogen atom transfer, the OH functional group of the incipient radical (**19**) could not serve as an effective electron donor in



19

merostabilization. Hence, the phenyl and benzoyl groups would most likely serve as the electron-donating and electron-withdrawing groups, respectively, of the incipient radical. The same substituent would then have an opposite effect on the two groups. The predominant effect would most likely reside with the phenyl group since the benzoyl group is electron withdrawing regardless of substitution. A reasonable prediction is that electron-donating substituents would stabilize and electron-withdrawing substituents would destabilize the transition and ground states. Hence, for the direct hydrogen transfer mechanism the substituent effects would probably be small and opposite those observed.

A possible model for the direct hydrogen atom transfer mechanism to benzil is hydrogen atom abstraction from desoxybenzoin. Relative rates of hydrogen atom abstraction from phenyl-substituted desoxybenzoins ($XC_6H_4CH_2COPh$) by bromine correlate with σ constants, and a Hammett plot gives a ρ of -0.92.[19] In general, for hydrogen atom abstraction from benzylic carbons, correlations with both σ and σ^+ have been observed, and ρ is generally negative.[20] Correlation with σ^+ is more likely with appreciable bond breaking in the transition state.[21] The sign of ρ for hydrogen atom abstraction is then the same as that predicted in the above analysis.

Hydrogen atom transfer from α-hydroxylalkyl radicals to ketones is a reaction analogous to that described here. Huyser and Neckers have measured substituent effects on transfer to substituted acetophenones.[22] A ρ value of 1.6 was obtained from a logarithmic plot of relative rates vs. σ. A direct hydrogen atom transfer mechanism was favored; however, an electron transfer mechanism was not considered.

The third redox reaction studied to determine the mode of reactivity of methylmorpholinonyl was reaction with electron acceptors. An acetonitrile solution 0.06 M in radical dimers **2** and **3** and 0.12 M in tetracyanoethylene (TCNE) gave a nine-line EPR spectrum with a g value of 2.002 89 ± 0.000 12 and a hyperfine coupling constant of 1.58 ± 0.01 G. The spectrum is identical within experimental error with the spectrum previously reported for the tetracyanoethylene radical anion.[23] The ultimate products of the reaction solution were not isolated and identified due to the complexity of the product mixture. Similarly, paraquat (**20**) and dianisyloxoammonium perchlorate (**21**) reacted with **1** to give the radical cation **22**[24] and dianisylnitroxide (**23**),[25] respectively (Scheme VIII).

On the basis of the foregoing discussion the mechanisms described in Schemes II, III, and VII are somewhat over simplified. Steps which are shown as hydrogen atom transfers are most likely electron transfers followed by rapid proton transfers. The kinetic analyses, however, basically remain the same.

It is interesting to note that the selectivity of reactions of phenylmorpholinonyl radical **7** with methylmorpholinonyl radical **1** (step 3, Scheme II) and hydroxyphenyloxazolinylmethyl radical **11** with methylmorpholinonyl radical **1** (step 3, Scheme III) can be rationalized in terms of electron transfer. The selectivity for reaction of **7** with **1** occurs even though the concentration of **7** is much higher than the concentration of **1**. Because of extended conjugation with the phenyl substituents in **7** and **11** the π^* orbital receiving the electron is probably of lower energy than the π^* orbital of **1** donating the electron. For the possible competing processes, disproportionation of **7** and **11**, the orbitals involved are of equal energy.

Analogies in the Literature. The hydrogen atom transfer reactions of the methylmorpholinonyl radical **1** find precedent in photoreduction reactions. Reversible hydrogen atom transfer has been proposed as part of the reaction mechanism for the photoreduction of benzophenone by ethers[26] and alcohols[27] and for the chemical-sensitized photoreduction of imines.[28]

Analogous electron-transfer mechanisms have been proposed for the reaction of pyridinyl radicals with acyl peroxides[16,17] as mentioned above and for the reaction of 1-ethyl-4-(carbomethoxy)pyridinyl radical with *p*-nitrobenzyl chloride.[29] Electron transfer from α-hydroxyalkyl radicals to nitroaromatic compounds,[30] biacetyl,[30] *N*-ethylmaleimide,[31] and *N*-methylnicotinamide salts[32] has been described. Recently, a number of papers have reported the probable one-electron-transfer reactivity of nicotinamide adenine dinucleotide (NADH),[32] the radical from nicotinamide adenine dinucleotide (NAD·),[33] and of model systems for NADH.[34,35] In many respects the reactivity of **1** parallels the reactivity of NADH and NAD·.

Summary. We have shown that the merostabilized radical 3,5,5-trimethyl-2-morpholinon-3-yl (**1**) can be used to generate other stable radicals, some not easily prepared by other techniques, and to reduce some functionalities by formally transferring the hydrogen atom bonded to nitrogen. The mechanism for hydrogen atom transfer is most likely a rate-controlling electron transfer from the electron rich π system followed by a rapid proton transfer from nitrogen. Because merostabilized radicals are, in general, electron rich, electron transfer will probably prove to be a common mode of reactivity for this type of radical.

Experimental Section

Melting and boiling points are uncorrected. All melting points were measured with a Fisher-Johns melting point apparatus. Infrared spectra were recorded with a Perkin-Elmer Model 337 infrared spectrophotometer and mass spectra with a Varian MAT CH-5 mass spectrometer. ^1H NMR spectra were obtained by using Varian A-60A and EM-390 spectrometers. All kinetic experiments were performed with the EM-390 spectrometer. Proton chemical shifts are reported in parts per million on the δ scale from internal tetramethylsilane. EPR spectra were recorded with a Varian V-4500 spectrometer, and splitting constants are

(19) Low, T. P.; Lee, K. H. *J. Chem. Soc. B* **1970**, *5*, 535.
(20) Russell, G. A. In "Free Radicals"; Kochi, J. K., Ed.; McGraw-Hill: New York, 1973; Vol. 1, p 275.
(21) Russell, G. A. *J. Org. Chem.* **1958**, *23*, 1407.
(22) Huyser, E. S.; Neckers, D. C. *J. Am. Chem. Soc.* **1963**, *85*, 3641.
(23) Phillips, W. D.; Rowell, J. C.; Weissman, S. I. *J. Chem. Phys.* **1960**, *33*, 626.
(24) Johnson, C. S., Jr; Gutowsky, H. S. *J. Chem. Phys.* **1963**, *39*, 58.
(25) Strom, E. T.; Bluhm, A. L.; Weinstein, J. *J. Org. Chem.* **1967**, *32*, 3853.
(26) Cohen, S. G.; Chao, H. M. *J. Am. Chem. Soc.* **1968**, *90*, 165.
(27) Schenck, G. O.; Koltzenburg, G.; Roselins, E. *Z. Naturforsch B* **1969**, *24*, 222.
(28) Padwa, A.; Bergmark, W.; Pashayan, D. *J. Am. Chem. Soc.* **1969**, *91*, 2653.
(29) Mohammed, M.; Kosower, E. M. *J. Am. Chem. Soc.* **1971**, *93*, 2713.
(30) Norman, R. O. C.; Pritchett, R. J. *J. Chem. Soc. B* **1967**, *2*, 378.
(31) Hayon, E.; Simic, M. *Acc. Chem. Res.* **1974**, *7*, 114.
(32) Kosower, E. M.; Teuerstein, A.; Burrows, H. D.; Swallow, A. J. *J. Am. Chem. Soc.* **1978**, *100*, 5185.
(33) Bielski, B. H. J.; Chan, P. C. *J. Am. Chem. Soc.* **1980**, *102*, 1713.
(34) Gase, A. R.; Pandit, U. K. *J. Am. Chem. Soc.* **1979**, *101*, 7059.
(35) Ono, N.; Tamura, R.; Kaji, A. *J. Am. Chem. Soc.* **1980**, *102*, 2851.

reported in gauss. Varian Model 200 and 1700 gas chromatographs were used for preparative and analytical gas chromatography. Preparative liquid chromatography was performed by using a Chromatronix medium-pressure liquid chromatograph. Preparative ultraviolet irradiations were carried out in a Pyrex immersion well with a 450-W, medium-pressure, Hanovia, mercury arc lamp. Microanalyses were performed by Atlantic Microlab.

Preparation of Materials. 5,6-Dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) was prepared by the condensation of ethyl pyruvate and 2-amino-2-methylpropanol.[36] For kinetic experiments, **4** was further purified by preparative-scale gas chromatography using a 0.63 cm × 3.65 m column of 5% FS-1265 on 60/80-mesh Diatoport S at 160 °C (He flow rate 60 mL/min). A mixture of the meso and *dl* radical dimers (**2** and **3**) of the 3,5,5-trimethyl-2-morpholinon-3-yl radical was prepared by photoreductive dimerization of 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) in 2-propanol solvent.[6,36] 5,6-Dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (**6**) was prepared by the condensation of ethyl phenylglyoxalate with 2-amino-2-methylpropanol.[37] 4,5-Dihydro-4,4-dimethyl-2-phenyl-1,3-oxazin-6-one (**6a**) was prepared according to the procedure of Baker and Ollis.[38] 4-(Diphenylmethylene)-2,5-cyclohexadienone (fuchsone, **12a**) was prepared as described by Bistrzycki and Herbst.[39] 2-Benzoyl-4,4-dimethyl-2-oxazoline (**9**) was prepared according to the procedure of Hansen and Wang.[8] Further purification for kinetic experiments was accomplished by medium-pressure liquid chromatography using a 2.5 cm × 50 cm column of Woelm 32–63-μm silica gel eluted with 3% acetonitrile in benzene at 9.6 mL/min or by preparative gas chromatography using the FS-1265 column described above at 185 °C (He flow rate 50 mL/min). Dianisyloxoammonium perchlorate was prepared by using the procedure described by Meyer and Gottlieb-Billroth.[40] 4,4′-Dichlorobenzil (**17a**) was prepared via the benzoin condensation of 4-chlorobenzaldehyde[41] and subsequent oxidation of the intermediate benzoin with cupric sulfate–pyridine complex.[42]

5,5-Dimethyl-3-phenylmorpholin-2-one (8). 5,6-Dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (1.1 g, 0.055 mol) in 25 mL of ethyl acetate was hydrogenated at atmospheric pressure with 0.010 g of 10% palladium on carbon catalyst. This afforded a quantitative yield of 5,5-dimethyl-3-phenylmorpholin-2-one. An analytical sample was prepared by preparative GLC with a 0.63 cm × 2 m column of 5% FS-1265 on 60/80-mesh Diatoport S at 182 °C (He flow rate 50 mL/min), and the following spectral data were obtained: IR (neat) 3.02, 3.37, 5.76 μm; ^{1}H NMR ($CDCl_3$) δ 1.22 (s, 3 H), 1.39 (s, 3 H), 1.75 (br, 1 H), 4.11 (d, J = 10.5 Hz, 1 H), 4.32 (, J = 10.5 Hz, 1 H), 4.85 (s, 1 H), 7.47 (m, 5 H); mass spectrum (70 eV), m/e (relative intensity) 205 (2.1), 161 (93), 147 (64), 146 (55), 106 (base), 105 (30), 104 (66), 91 (52), 77 (28), 56 (29), 43 (31), 42 (22).

Anal. Calcd for $C_{12}H_{14}O_2N$: C, 70.22; H, 7.36. Found: C, 70.03; H, 7.39.

Methyl 2-Phenyl-2-(1,1-dimethyl-2-hydroxyethyl)aminoacetate. To a 100-mL, round-bottomed flask equipped with a condenser and drying tube were added 0.50 g (2.46 mmol) of 5,5-dimethyl-3-phenylmorpholin-2-one (**8**) and 50 mL of absolute methanol which had been distilled from magnesium methoxide and stored over 3A molecular sieves. The solution was refluxed for 20 h, and then the solvent was rotary evaporated, leaving a viscous, colorless oil. A ^{1}H NMR spectrum of the crude product indicated that a small amount of the starting material **8** was present plus the desired product, methyl 2-phenyl-2-(1,1-dimethyl-2-hydroxyethyl)aminoacetate. Attempts to isolate the acetate via preparative GLC and TLC were unsuccessful. Both methods caused the acetate to close to the morpholinone **8**. The ^{1}H NMR spectrum of the aminoacetate was assigned from the spectrum of the mixture as follows: NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.09 (s, 3 H), 2.40 (br, 2 H), 3.27 (s, 2 H), 3.70 (s, 3 H), 4.50 (s, 1 H), 7.40 (m, 5 H).

Partial Deuteration of a Mixture of Meso and *dl* Radical Dimers 2 and 3. To a 250-mL, round-bottomed flask equipped with a serum stopper with nitrogen gas inlet and outlet needles was added 1.66 g (5.85 mmol) of undeuterated radical dimers **2** and **3**. The flask was immersed in an ice–water bath, and to it was added 50 mL of argon-degassed chloroform. To the magnetically stirred, nitrogen-purged, chloroform solution was added 20 mL of 99.7% deuterium oxide. The two-phase mixture was then stirred vigorously under a nitrogen atmosphere for 1.5 h at 0 °C. The chloroform solution was separated with a separatory funnel, dried over magnesium sulfate, and rotary evaporated. A clean white solid (1.60 g, 5.61 mmol, 96%) was obtained. A ^{1}H NMR spectrum of the product was identical with that reported for **2** plus **3** minus some of the N–H absorption. The product was analyzed by EPR spectroscopy in chloroform solvent, and the ratio of *N*-deuterio-3,5,5-trimethyl-2-morpholinon-3-yl to 3,5,5-trimethyl-2-morpholinon-3-yl was approximately 50:50 (vide infra).

3,4-Dideuterio-3,5,5-trimethylmorpholin-2-one (5c). 5,6-Dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (1.00 g, 7.1 mmol) in 25 mL of ethyl acetate was reduced with deuterium at atmospheric pressure with 0.10 g of 10% palladium on carbon catalyst. Approximately 240 mL of deuterium gas reacted in 3 h at ambient temperature and a 630-mm presure. The reaction solution was filtered and the solvent rotary evaporated, giving a quantitative yield of a clear colorless oil. An ^{1}H NMR spectrum indicated that the product was a 70:30 mixture of 3,4-dideuterio-3,5,5-trimethylmorpholin-2-one and 3,5,5-trimethylmorpholin-2-one. This ratio was determined by comparison of the methylene AB pattern to the methine quartet. The ^{1}H NMR spectra of the deuterated and undeuterated morpholinones were identical except for the absence of the methine quartet and a broad singlet absorption for the 3-methyl substituent in the spectrum of the deuterated compound.

Reduction of 5,6-Dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (6) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). To a ^{1}H NMR sample tube, which had a 9-mm attachment for connection to a vacuum line, were added 100 mg (0.49 mmol) of 5,6-dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (**6**) and 70 mg (0.25 mmol) of a mixture of radical dimers **2** and **3**. To the tube was added 0.5 mL of deuteriochloroform, and the solution was quickly frozen in liquid nitrogen and freeze (−196 °C)–pump (10^{-5}/torr)–thaw (ambient temperature) degassed through five cycles and sealed at 10^{-5} torr. The sample tube was then thawed and allowed to sit at room temperature for 22 days. A ^{1}H NMR spectrum of the sample revealed that all of the radical dimers **2** and **3** and half of the phenyloxazinone **6** had reacted to give two products. The products were tentatively identified as 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) and 5,5-dimethyl-3-phenylmorpholin-2-one (**8**). The two products were isolated by preparative GLC on a 0.64 cm × 2 m column of 5% FS-1265 on 60/80-mesh Diatoport S at 150 °C (He flow rate 60 mL/min). The ^{1}H NMR spectra of the isolated products were compared with those of independently prepared samples to confirm the tentative structural assignment. The reduction of 5,6-dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (**6**) by 3,5,5-trimethyl-2-morpholinon-3-yl (**1**) was similar in methanol solvent except that the product 5,5-dimethyl-3-phenylmorpholin-2-one partially reacted with solvent to give methyl 2-phenyl-2-(1,1-dimethyl-2-hydroxyethyl)aminoacetate as described above.

Reduction of 2-Benzoyl-4,4-dimethyl-2-oxazoline (9) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). To a ^{1}H NMR sample tube were added 50.8 mg (0.25 mmol) of 2-benzoyl-4,4-dimethyl-2-oxazoline, 35.5 mg (0.125 mmol) of a mixture of **2** and **3**, and 0.50 mL of deuteriochloroform. The solution was freeze–pump–thaw degassed as described above and sealed. The sample was heated at 35 ± 0.1 °C for 15 days. The ^{1}H NMR spectrum indicated that the only products of the reaction were 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) and 2-(phenylhydroxymethyl)-4,4-dimethyl-2-oxazoline (**10**) in a ratio of 1:1, that all of the radical dimers reacted, and that half of the benzoyloxazoline reacted. The ^{1}H NMR spectral properties of the products were identical with those previously reported.[36,40] The composition of the product mixture was verified by GLC analysis using the FS-1265 on Diatoport S column described above.

Reduction of Benzil (17) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). A sample tube (15 × 200 mm) was charged with 150 mg (0.71 mmol) of benzil, 215 mg (0.75 mmol) of a mixture of radical dimers **2** and **3**, and 6 mL of dry chloroform. The reaction solution was freeze–pump–thaw degassed as described above through four cycles and sealed. The reaction mixture was heated at 50 ± 1 °C for 14 days. The product mixture was analyzed by GLC using a 0.63 cm × 3.65 m column of 5% FS-1265 on 60/80-mesh Diatoport S at 210 °C (He flow rate 60 mL/min). Only 68% of the benzil was reduced to benzoin, uncorrected for differences in molar response. The solvent was removed by rotary evaporation, and 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one was removed on a vacuum line at 10^{-3} torr. The resultant white solid was recrystallized from 95% ethanol, and 88 mg (59%) of benzoin was collected [mp 133.5–134.5 °C (lit.[43] mp 133 °C)]. Based upon benzil reacted, the yield was 86%. The benzoin had physical and spectral properties identical with those of an authentic sample. A byproduct of the reaction was 3,5,5-trimethyl-2-morpholinone resulting from some disproportionation of 3,5,5-trimethyl-2-morpholinon-3-yl. The ratio of 3,5,5-trimethyl-2-morpholinone to unreacted benzil was 1:1 as determined

(36) Koch, T. H.; Olesen, J. A.; DeNiro, J. *J. Org. Chem.* **1975**, *40*, 14.
(37) Biekert, E.; Sonnenbichler, J. *Chem. Ber.* **1961**, *94*, 2785.
(38) Baker, W.; Ollis, W. D. *J. Chem. Soc.* **1949**, 345.
(39) Bistrzycki, A.; Herbst, C. *Chem. Ber.* **1903**, *36*, 2333.
(40) Meyer, K.; Gottlieb-Billroth, H. *Chem. Ber.* **1919**, *52*, 1476.
(41) Leonard, N. J.; Rapala, R. T.; Herzog, H. L.; Blout, E. R. *J. Am. Chem. Soc.* **1949**, *71*, 2997.
(42) Clarke, H. T.; Dreger, E. E. In "Organic Syntheses"; Gilman, H., Blatt, A. H., Eds.; Wiley: New York, 1932; Collect. Vol. I, p 87.
(43) Arnold, R. T.; Fuson, R. C. *J. Am. Chem. Soc.* **1936**, *58*, 1295.

by GLC analysis using the FS-1265 column.

Reduction of 5,6-Dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (6) by *N*-Deuterio-3,5,5-trimethyl-2-morpholinon-3-yl (1a). To a ^{1}H NMR tube were added 25.4 mg (0.125 mmol) of **6** and 17.8 mg (0.063 mmol) of radical dimers **2** and **3**. Methanol-d_4 (0.50 mL) was added, and the sample was immediately frozen in liquid nitrogen, freeze–pump–thaw degassed as described above, and sealed at 10^{-5} torr. The sample was heated at 35 ± 0.1 °C for 5 days. The ^{1}H NMR spectrum of the reaction mixture indicated that the methine protons of 5,5-dimethyl-3-phenylmorpholin-2-one (**8**) and methyl 2-phenyl-2-(1,1-dimethyl-2-hydroxyethyl)aminoacetate were absent.

Reduction of 2-Benzoyl-4,4-dimethyl-2-oxazoline (9) by *N*-Deuterio-3,5,5-trimethyl-2-morpholinon-3-yl (1a). An ^{1}H NMR sample tube was charged with 20.3 mg (0.10 mmol) of 2-benzoyl-4,4-dimethyl-2-oxazoline (**9**) and 14.2 mg (0.040 mmol) of a mixture of the radical dimers (**2** and **3**). Then 0.50 mL of methanol-d_4 was added, and the sample was immediately frozen in liquid nitrogen, freeze–pump–thaw degassed as described above, and sealed at 10^{-5} torr. The sample was heated at 35 ± 0.1 °C for 5 days. The product mixture consisted of 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**), 2-(phenylhydroxymethyl)-4,4-dimethyl-2-oxazoline (**10**), and unreacted **9**. The absorption due to the methine proton of **10** was absent.

Disproportionation of *N*-Deuterio-3,5,5-trimethyl-2-morpholinon-3-yl (1a). To a ^{1}H NMR tube were added 100 mg of partially deuterated radical dimers **2** and **3** and 1.0 mL of methanol-d_4. The solution was freeze–pump–thaw degassed and sealed at 10^{-5} torr. The sample was heated at 70 ± 1 °C for 9.5 h. A ^{1}H NMR spectrum indicated that about 60% disproportionation had occurred and that the absorption due to the methine proton of 3,5,5-trimethylmorpholin-2-one (**5**) was absent.

Control Experiments in Methanol-d_4. Accompanying the above three experiments were control experiments in which 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) and the reduced molecules were dissolved in methanol-d_4 and subjected to the same reaction conditions. The methyl protons of **4** and the methine protons of 5,5-dimethyl-3-phenylmorpholin-2-one, 2-(phenylhydroxymethyl)-4,4-dimethyl-2-oxazoline, and 3,5,5-trimethylmorpholin-2-one were not exchanged for deuterium.

Reduction of 4-(Diphenylmethylene)-2,5-cyclohexadienone (12a) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). A ^{1}H NMR tube was charged with 129 mg (0.50 mmol) of **12a**, 145 mg (0.51 m mol) of a mixture of radical dimers **2** and **3**, and 0.50 mL of deuteriochloroform. The tube was freeze–pump–thaw degassed, sealed, and heated at 35 ± 0.1 °C. The reaction was monitored by ^{1}H NMR spectroscopy. The reaction was quantitative, and the only products formed were 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) and (*p*-hydroxyphenyl)diphenylmethane (**14a**). To a 15 × 210 mm tube with a 9-mm attachment for connection to a vacuum line were added 1.02 g (4.0 mmol) of **12a**, 1.12 g (3.94 mmol) of a mixture of the radical dimers **2** and **3**, and 5 mL of chloroform. The sample was freeze–pump–thaw degassed through three cycles and sealed at 10^{-5} torr. The sample was reacted at ambient temperature for 19 days. The tube was opened and the solvent rotary evaporated to give a yellow oil. The oil was purified by preparative silica gel TLC using 10% methanol/90% chloroform solvent as eluent. A bright yellow band was extracted with methylene chloride. The solvent was rotary evaporated to give 1.02 g of an oil which was shown by ^{1}H NMR spectroscopy to consist of a 3:1 mixture of **14a** and **4**. The oil was subjected to a second preparative silica gel TLC using 75% benzene/25% acetonitrile solvent as eluent. A yellow solid [0.50 g, 48%; mp 108–110 °C (lit.[44] mp 110)] was then collected and shown to be diphenyl(*p*-hydroxyphenyl)-methane (**14a**) by ^{1}H NMR and mass spectrometry. The product gave the following spectral absorptions: ^{1}H NMR ($CDCl_3$) δ 4.85 (br, 1 H), 5.45 (s, 1 H), 6.68 (d, J = 10.5 Hz, 2 H), 6.91 (d, J = 10.5 Hz, 2 H), 7.15 (m, 10 H); upon addition of deuterium oxide, the peak at δ 4.85 disappeared; mass spectrum (70 eV), *m/e* (relative intensity) 260 (base), 259 (24), 184 (58), 183 (16), 182 (22), 166 (15), 165 (31), 153 (10), 152 (15), 76 (13).

Reduction of 4-[Bis(4-hydroxyphenyl)methylene]-2,5-cyclohexadien-1-one (12b) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). A ^{1}H NMR tube was charged with 95.2 mg (0.330 mmol) of **12b**, 92.3 mg (0.330 mmol) of a mixture of radical dimers **2** and **3**, and 0.50 mL of dimethyl-d_6 sulfoxide. The tube was freeze–pump–thaw degassed, sealed, and heated at 50 ± 1 °C. A quantitative formation of tris(*p*-hydroxyphenyl)methane (**14b**) and 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**4**) was determined by ^{1}H NMR spectroscopy.

General Procedure for the Preparation of Samples for EPR Analysis. The substrate and radical dimers **2** and **3** were combined in a 1-dram sample vial fitted with a serum stopper. Solvent (1.00 mL) was then added via syringe, and the solution was degassed by a stream of argon for 10 min with syringe needles for the inlet and outlet. After the solution was degassed, 0.3–0.6 mL of the solution was transferred via syringe to a 5-mm quartz EPR sample tube which had also been degassed with argon.

Effect of Radical Dimer (2 and 3) and 5,6-Dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (6) Concentrations on the Concentration of 5,5-Dimethyl-3-phenyl-2-morpholinon-3-yl (7). Three methanol solutions containing the following quantities of a mixture of radical dimers **2** and **3** and phenyloxazinone (**6**), respectively, were prepared as described above: 75.6 mg (0.266 mmol) and 500 mg (2.46 mmol), 75.8 mg (0.267 mmol) and 253 mg (1.25 mmol), 37.5 mg (0.132 mmol) and 502 mg (2.47 mmol). The solutions were each analyzed for the relative concentration of **7** by EPR spectroscopy using the same sample tube by recording four successive scans over one of the largest peaks in the spectrum. The concentration of **7** was assumed to be proportional to the peak height. The peak heights were 238.4 ± 5.2, 159.8 ± 2.6, and 193.6 ± 2.9 mm, respectively.

Kinetic Measurement of the Reduction of 5,6-Dihydro-5,5-dimethyl-3-phenyl-1,4-oxazin-2-one (6) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). To an ^{1}H NMR sample tube were added 25.4 mg (0.125 mmol) of **6** and 17.8 mg (0.063 mmol) of a mixture of radical dimers **2** and **3**. Methanol-d_4 (0.50 mL) was added, and the sample was immediately frozen in liquid nitrogen. The sample was freeze–pump–thaw degassed through five cycles as described and sealed at 10^{-5} torr. After the sample was thawed, an initial ^{1}H NMR spectrum was recorded, and the sample tube was immersed in a thermostated water bath at 35 ± 0.1 °C. The progress of the reaction was monitored by periodically recording the NMR spectrum and obtaining three to five integrations for each spectrum. The time-dependent appearance of **4** was measured from the integration of the 3-methyl absorption of **4** vs. the integration of the 3(3')-methyl absorptions of the radical dimers **2** and **3**. The time-dependent appearance of the product **8** was measured from the integration of the aromatic protons of **6** present as an equilibrium mixture of **8** and methyl 2-phenyl-2-(1,1-dimethyl-2-hydroxyethyl)aminoacetate vs. an integration of the aromatic protons of unreacted **6**. These two methods for measuring the extent of reaction were identical within experimental error for most of the reaction. Near the end of the reaction, the measurement of the appearance of **4** became complicated by a significant amount of overlap of the N–H absorption of **8** with the 3-methyl absorption of **4**; so the kinetics of the reaction were analyzed from the measurements of the appearance of **8**. The time-dependent average concentrations of **6** are shown in Table I.

Kinetic Measurement of the reduction of 2-Benzoyl-4,4-dimethyl-2-oxazoline (9) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1) in the Presence of 5,6-Dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (4). To a ^{1}H NMR tube were added 50.8 mg (0.250 mmol) of **9**, 35.5 mg (0.125 mmol) of a mixture of **2** and **3**, and 35.3 mg (0.250 mmol) of **4**. Deuteriochloroform (0.50 mL) was added, and the sample was degassed, reacted, and monitored as described above. The results are reported in Table II.

Kinetic Measurement of the Reduction of Benzil (17) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). A ^{1}H NMR sample tube was charged with 16.8 mg (0.080 mmol) of benzil and 11.4 mg (0.0400 mmol) of a mixture of **2** and **3**. Then 0.50 mL of deuteriochloroform was added, and the sample was degassed as described above. The sample was heated at 50 ± 1 °C, and the reaction's progress was monitored by integration of the ^{1}H NMR absorptions of the 3-methyl substituents of **2**–**4**. The results are reported in Table III.

Kinetic Measurement of the Reduction of 4,4'-Dimethylbenzil (17b) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). A ^{1}H NMR sample tube was charged with 19.0 mg (0.080 mmol) of **17b** and 11.4 mg (0.040 mmol) of a mixture of **2** and **3**. Then 0.50 mL of deuteriochloroform was added, and the sample was degassed, reacted, and monitored as described for the reduction of benzil. The results are reported in Table III.

Kinetic Measurement of the Reduction of 4,4'-Dichlorobenzil (17a) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). A ^{1}H NMR sample tube was charged with 22.3 mg (0.080 mmol) of **17a** and 11.4 mg (0.040 mmol) of a mixture of **2** and **3**. Then 0.50 mL of deuteriochloroform was added, and the sample was degassed, reacted, and monitored as described for the reduction of benzil. The kinetic data are reported in Table III.

Kinetic Measurement of the Reduction of 4,4'-Dimethoxybenzil (17c) by 3,5,5-Trimethyl-2-morpholinon-3-yl (1). To a ^{1}H NMR sample tube were added 43.2 mg (0.160 mmol) of **17c** and 11.4 mg (0.040 mmol) of a mixture of **2** and **3**. Then 0.50 mL of deuteriochloroform was added, and the sample was degassed, reacted, and monitored as described for the reduction of benzil. The kinetic data are reported in Table III.

Measurement of the Deuterium Kinetic Isotope Effect for Disproportionation of 3,5,5-Trimethyl-2-morpholinon-3-yl (1). To a ^{1}H NMR sample tube was added 300 mg of partially deuterated radical dimers (**2** and **3**), which upon dissolution in 0.50 mL of deuteriochloroform gave a mixture of *N*-deuterio-3,5,5-trimethyl-2-morpholinon-3-yl and 3,5,5-trimethyl-2-morpholinon-3-yl in the ratio 49.8 ± 0.4:50.2 ± 0.4, re-

(44) Bistrzycki, A.; Herbst, C. *Chem. Ber.* **1902**, *35*, 3133.

spectively, as determined by EPR spectroscopy (vide supra). The sample was immediately immersed in liquid nitrogen, freeze–pump–thaw degassed as described through five cycles and sealed at 2×10^{-5} torr. The sample was heated at 72 ± 1 °C for 3 h. During this time 17% disproportionation of starting materials occurred. After the 3 h, five successive ^{1}H NMR spectra at expanded sweep width were recorded. The relative amounts of reduction products were determined by comparison of the area for the methylene protons with the area for the methine protons. The areas of the ^{1}H NMR absorptions were measured by cutting out the expanded peaks and weighing. The k_H/k_D from the five spectra, uncorrected for the difference between the radical ratio and 50:50, was 1.03 ± 0.09.

EPR Measurement of the Ratio of *N*-Deuterio-3,5,5-trimethyl-2-morpholinon-3-yl (1a) to 3,5,5-Trimethyl-2-morpholinon-3-yl (1) in the Deuterium Kinetic Isotope Experiment. An identical sample with the one described above was analyzed by EPR spectroscopy to determine the relative concentrations of **1** and **1a**. The radical ratio was measured by double integration of a region of the EPR spectrum of the mixture in which the absorptions of **1** and **1a** were distinct and equally intense. The double integration was accomplished by cutting out and weighing the appropriate peaks. The EPR measurement at 72 °C prior to reaction gave a ratio of **1a** to **1** of 49.8 ± 0.4:50.2 ± 0.4. After 17% disproportionation, another EPR measurement was made at 72 °C, and the ratio of **1a** to **1** was 53.3 ± 2.0:46.7 ± 2.0. Although the ratio at termination was close to the initial ratio, the change introduced a small error in the k_H/k_D measurement. The k_H/k_D for the disproportionation calculated as $1.03 \times (51.5/48.5) = 1.10 \pm 0.09$, where 51.5/48.5 was the average radical ratio.

Acknowledgment. We thank Professors Shelby Sherrod and Edward King for helpful discussions and Dr. Joseph Keute for the synthesis of fuchsone and dianisyloxoammonium perchlorate. Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. We thank the General Medical Institute (Grant No. GM-18349), the National Cancer Institute (Grant No. CA-24665), and the Biomedical Research Support Grant Program of the National Institutes of Health for financial assistance.

Catalysis Mechanism of Phosphonium Salts Supported on Silica Gel in Organic–Aqueous Two-Phase Systems

Pietro Tundo* and Paolo Venturello

Contribution from the Istituto di Chimica Organica della Università, I-10125 Torino, Italy.
Received May 29, 1980

Abstract: The mechanism of phase-transfer catalysis by phosphonium salts supported on silica gel in organic-aqueous two-phase systems has been studied in the kinetically convenient reaction *n*-BuBr → *n*-BuI without solvent. This catalysis is not controlled by the diffusion but, as with homogeneous catalysts, by the regeneration of the catalytic centers. However, unlike with soluble catalysts, with such systems the reaction proceeds rapidly even in the absence of stirring. The longer the alkyl chain between the catalytic centers and the matrix, the larger the ratio of the activity without stirring to the optimal activity (ranging from 0.3 to 0.7). The long alkyl chain acts as an anion pump between the aqueous and organic phases, both of which are present in the third solid phase.

In the classical mechanism of phase-transfer (PT) catalysis,[1] the nucleophilic substitution reaction (eq 1) occurs in the organic

$$RX(org) + Y^-(org) \xrightleftharpoons{k,\ [Q^+]} RY(org) + X^-(org) \quad (1)$$

$$X^-(org) + Y^-(aq) \xrightleftharpoons{K_a,\ [Q^+]} X^-(aq) + Y^-(org) \quad (2)$$

phase and is the rate-determining step. For most entering and leaving groups, catalyst regeneration by exchange between the aqueous (aq) and organic (org) phases (eq 2) is so rapid that it has no effect on reaction rates.

Starks[2] has shown that in exchange reactions between 1-chlorooctane and sodium cyanide catalyzed by hexadecyltributylphosphonium bromide (**5**), equilibrium a, with equilibrium constant K_a, becomes the fastest step at quite low stirring speeds (approximately 250 rpm). Therefore, since the nucleophile concentration in the organic phase remains constant, pseudo-first-order kinetics are always observed with k as the rate constant.

Moreover in all the studies reported in the literature of PT catalysts supported on polystyrene[3] or silica[4] resins, pseudo-first-order kinetics have been observed for S_N2 displacement and reduction reactions.

In the case of polymeric silica support, it has been shown that the first step is the adsorption of the organic substrate on the matrix, to which the nucleophile-containing aqueous phase is also present. On the other hand, for nonconditioned polystyrene matrices, Regen[5] has shown that the reaction rate is independent of the stirring speed. The observed data suggested that a diffusion-limited chemical reaction was the rate-controlling step.

With the aim of elucidating the factors controlling the catalysis and the nature of catalytic environment of phosphonium salts chemically bonded to silica gel, catalysts **1–4** were studied in a simple and kinetically convenient reaction: bromine–iodine exchange on an alkyl halide, run in a two-phase organic–aqueous KI system. This reaction proceeds to the iodo derivative within the limits of detectability of the bromide, and thus eq 1 is completely shifted to the right. Moreover, because of the nucleophile selected (I^-) and because of the analogy with free catalysts, equilibrium 2 decidedly favors the uptake of I^- by the polymer.[6]

(1) (a) Weber, W. P.; Gokel, G. W. "Phase Transfer Catalysis in Organic Synthesis"; Springer-Verlag: West Berlin, 1977. (b) Starks, C. M.; Liotta, C. "Phase Transfer Catalysis"; Academic Press: New York, 1978. (c) Dehmlow, E. V.; Dehmlow, S. S. "Phase Transfer Catalysis"; Verlag Chemie: Weinhein, 1980.

(2) Starks, C. M.; Owens, R. M. *J. Am. Chem. Soc.* **1973**, *95*, 3613.

(3) (a) Regen, S. L. *J. Am. Chem. Soc.* **1975**, *97*, 5956. (b) Cinquini, M.; Colonna, S.; Molinari, M.; Montanari, F.; Tundo, P. *J. Chem. Soc., Chem. Commun.* **1976**, 394. (c) Molinari, M.; Montanari, F.; Tundo, P. *Ibid.* **1977**, 639. (d) Molinari, M.; Montanari, F.; Quici, S.; Tundo, P. *J. Am. Chem. Soc.* **1979**, *101*, 3920. (e) Tundo, P. *Synthesis* 1978, 315. (f) Review: Regen, S. L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 421.

(4) (a) Tundo, P. *J. Chem. Soc., Chem. Commun.* **1977**, 641. (b) Tundo, P.; Venturello, P. *J. Am. Chem. Soc.* **1979**, *101*, 6606.

(5) Regen, S. L.; Besse, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 4059.

0002-7863/81/1503-856$01.00/0