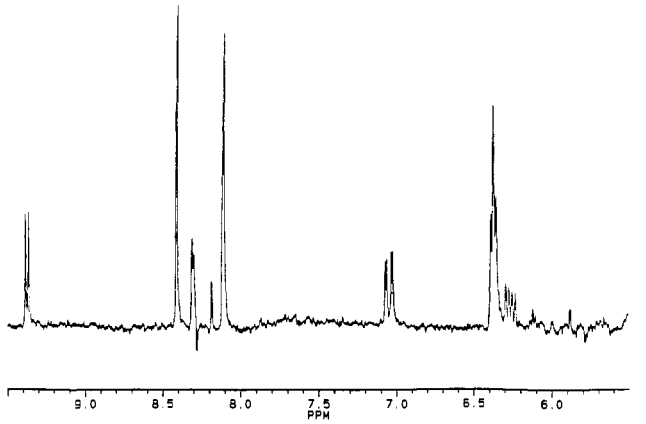
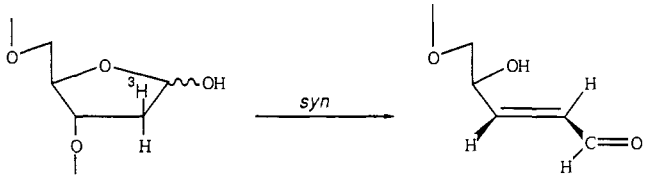


Figure 1. ^{1}H NMR spectrum (400 MHz) of the product of the UV endo V catalyzed degradation of polymer containing alternating deoxyadenosine and abasic site residues. The assignments of the α,β-unsaturated aldehyde are made in the text; the resonances at 8.41, 8.11, and 6.37 ppm are associated with the H_8, H_2, and $H_{1'}$ protons, respectively, of the deoxyadenosine portion of the product.

Scheme I



radioactivity, 44 800 cpm/μmol at 91% reaction). No ^{3}H was found in the solvent after bulb-to-bulb lyophilization. The polymer containing ^{3}H in the *pro-S* 2-hydrogen of the abasic site (specific radioactivity, 239 000 cpm/μmol) was converted by UV endo V into a nucleotide ester product which contained no radioactivity. However, at 22% reaction, the specific radioactivity of the unreacted abasic site was 266 000 cpm/μmol, and at 61% reaction, the specific radioactivity of the unreacted abasic site was 329 000 cpm/μmol. These increases in specific radioactivity correspond to tritium selection effects of 8 and 10, respectively.[8] UV endo V catalyzes the stereospecific abstraction of the *pro-S* 2-hydrogen of the abasic site to affect the β-elimination reaction (Scheme I). The significant isotope effect demonstrates that proton abstraction is rate determining.

Unlabeled poly(dA-dU) was treated with uracil-DNA glycosylase, and following removal of the uracil by gel filtration, this damaged polymer was fully degraded by UV endo V.[9] The 400-MHz ^{1}H NMR spectrum of the product is reproduced in Figure 1. The aldehydic H_1 of the enzymatic product (9.37 ppm) is coupled to the vinylic H_2 (6.24 ppm, $J_{1,2}$ = 8 Hz). H_2 is coupled to the vinylic H_3 (7.04 ppm, $J_{2,3}$ = 16 Hz), which is also coupled to H_4 ($J_{3,4}$ = 4 Hz). Since the chemical shifts and coupling constants for H_1, H_2, and H_3 of the enzymatic product are essentially identical with those of the analogous protons of (4*R*)-4,5-dihydroxy-*trans*-2-pentenal,[10] the trans geometry can be assigned to the enzymatic product. In support of this assignment, photoisomerization of both the enzymatic product and (4*R*)-4,5-dihydroxy-*trans*-2-pentenal yields anomeric mixtures of cyclic unsaturated hemiacetals.[11] On the basis of these properties, the UV endo V product is the 3'-ester of deoxyadenosine 3',5'-bisphosphate with the 5-hydroxyl group of (4*R*)-4,5-dihydroxy-*trans*-2-pentenal. The abstraction of the *pro-S* 2-hydrogen and the geometry of the product define the stereochemical course of the elimination reaction as syn (Scheme I). The identical stereochemical course is also followed with a double-stranded substrate [generated from poly(dA-dT,dU), where the dT:dU ratio is 8:1] (data not shown). Although all of the analogous enzyme catalyzed elimination reactions β to the carbonyls of ketones and thiolesters proceed with the same stereochemical course,[12] the relatively low pK_a of the phosphate monoester leaving group presumably would not require protonation by the conjugate acid of the base abstracting the 2-hydrogen.[13]

This stereochemical course requires that the β-elimination reaction proceed from an open-chain form of the abasic site whose predominant form in solution is a mixture of cyclic hemiacetals. Whether the acyclic substrate is the aldehyde itself or an activated derivative such as an imine remains to be elucidated.

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Supplementary Material Available: Synthesis of [2'-^{3}H]UTP used to prepare [2'(*S*)-^{3}H]dUTP, reaction conditions for various enzymatic reactions, ^{1}H NMR spectra comparing the UV endo V product with (4*R*)-4,5-dihydroxy-*trans*-2-pentenal, ^{1}H NMR spectra comparing the photoisomerized UV endo V product with photoisomerized (4*R*)-4,5-dihydroxy-*trans*-2-pentenal, and the ^{13}C NMR spectrum of photoisomerized (4*R*)-4,5-dihydroxy-*trans*-2-pentenal (10 pages). Ordering information is given on any current masthead page.

(7) The conditions for this UV endo V reaction are available in the supplementary material.
(8) Melander, M. *Isotope Effects on Reaction Rates*; Ronald Press: New York, 1960.
(9) The conditions for this UV endo V reaction are available in the supplementary material.
(10) Esterbauer, H.; Sanders, E. B.; Schubert, J. *Carbohydr. Res.* **1975**, *44*, 126-132.
(11) The photoisomerization was conducted in 5-mm NMR tubes by using flint-filtered light. The ^{1}H NMR spectra of the photoisomerized enzymatic product and unsaturated 2-deoxyribose are virtually identical. The ^{13}C NMR spectrum of the isomerized unsaturated 2-deoxyribose reveals the presence of two hemiacetal carbons as well as two resonances for each of the remaining carbon atoms. These spectra are available in the supplementary material.
(12) (a) Schwab, J. M.; Klassen, J. B.; Habib, A. *J. Chem. Soc., Chem. Commun.* **1986**, 357. (b) Widlanski, T.; Bender, S. L.; Knowles, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 1873-1875.
(13) Alternatively, the 3'-phosphodiester could act as the general base which catalyzes its own elimination: Widlanski, T.; Bender, S. L.; Knowles, J. R. *J. Am. Chem. Soc.* **1989**, *111*, 2299-2300.

Iron-Hydroperoxide-Induced Phenylselenization of Hydrocarbons (Fenton Chemistry)

Ceshing Sheu, Andrzej Sobkowiak, Li Zhang,
Nubar Ozbalik, Derek H. R. Barton, and Donald T. Sawyer*

Department of Chemistry, Texas A&M University
College Station, Texas 77843

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The Gif systems (iron catalyst, reduced dioxygen, py/HOAc) for the selective transformation of methylenic carbons to ketones,[1-3] when done in the presence of 1,2-diphenylselenide (PhSeSePh), yields PhSe derivatives of the hydrocarbon substrates at the expense of the ketonization process. A recent study[4] has characterized the use of iron(II) bis(picolinate) [Fe(PA)$_2$] as a catalyst to activate HOOH for the efficient, selective ketonization of methylenic carbons. Because the latter system closely parallels the substrate transformations of the Gif system,[2,3] we became curious as to the effect of PhSeSePh. Here we wish to report that the combination of Fe(PA)$_2$, HOOH, PhSeSePh, and a hydrocarbon substrate (e.g., c-C_6H_{12}) [2:2:1:100 mole ratio] in py/HOAc reacts stoichiometrically to give 2 equiv of the PhSe derivatives of the substrate [e.g., 2(c-C_6H_{11})-SePh].

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(3) Barton, D. H. R.; Boivin, J.; Motherwell, W. B.; Ozbalik, N.; Schwarzentruber, K. M.; Jankowski, K. *Nouv. J. Chim.* **1986**, *10*, 387.
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0002-7863/89/1511-8030$01.50/0

Table I. Phenylselenization of Hydrocarbons by a Fenton Chemistry [$Fe(PA)_2$ + (HOOH)]/PhSeSePh System[a]

A. Cyclohexane (1 M); 19 mM $Fe(PA)_2$, 19 mm HOOH, 10 mM PhSeSePh

conditions	reactn efficiency,[b] % (±4)	products,[c] % (±4) PhSe-(c-C_6H_{11})	PhSe-py	c-C_6H_{10}(O)	c-C_6H_{11}OH	(c-C_6H_{11})-py	(c-C_6H_{11})$_2$
py/HOAc (mole ratio, 1.8:1)	100[d]	93	4	3	0	0	0
controls (no PhSeSePH): [$Fe(PA)_2$] [HOOH]							
19 mM 19 mM	79	0	0	14	0	77	9
9 mM 9 mM	85	0	0	34	0	63	3
3.3 mM 56 mM	72	0	0	94	6	0	0
py	73	93	6	1	0	0	0
py/HOAc (mole ratio, 1:1)	89	92	5	3	0	0	0
DMF	20[e]	0	0	0	1	0	0
MeCN [100 mM c-C_6H_{12}, 10 mM $Fe(PA)_2$, 10 mM HOOH, and 5 mM PhSeSePh]	7	57	0	0	43	0	0
control (no PhSeSePh and 500 mM c-C_6H_{12})	51	0	0	33	65	0	2

B. Various Hydrocarbons (RH); 19 mM $Fe(PA)_2$, 19 mM HOOH, 10 mM PhSeSePh; py/HOAc (1.8:1)

RH (1 M)	reactn efficiency,[b] % (±4)	products,[c] % (±2) PhSe-R	[relative isomer abundance] (theor)	PhSe-py	R(O)
n-hexane	76	90	[12:43:45] (6/4/4)[f]	4	6
2-Me-butane	57	93	[17:8:35:40] (6/3/2/1)[g]	5	2
adamantane (0.1 M)	40[h]	69	[63:37] (12/4)	26	1
$PhCH_2CH_3$	48[i]	48	[32:68] (3/2)	5	14

[a] Substrate, $Fe(PA)_2$, and PhSeSePh combined in 3.5 mL of py/HOAc solvent (unless otherwise indicated), followed by slow addition (1–2 min) of 2–13 μL of 17.3 M HOOH (49%) in H_2O to give 9–56 mM HOOH. Reaction time and temperature; 10 min at 22 ± 2 °C. [b] 100% represents one substrate oxidation per HOOH [except for production of R(O), R–R, and R–py, which require 2HOOH]. Remainder of HOOH was consumed to produce PhSe(O)OH, $^1/_n$[pyOH]$_n$, or O_2. [c] The product solutions were analyzed by capillary-GC and GC-MS (direct injection of product solution or ether extract). [d] Addition of more HOOH to the product solution (after consumption of all PhSeSePh) only produced more c-C_6H_{10}(O). [e] Major product, (DMF)–SePh (two isomers, 79% and 20%). [f] Isomer order, $-CH_2$SePh and >CHSePh. [g] Isomer order, $-CH_2$SePh(2), $-CH_2$SePh(1), >CHSePh(1), and >CSePh(1). Authentic samples of PhSe–R were prepared from bromides (RBr) or mesylates or by reaction of R• with PhSeSePh. [h] About 4% of product was py-adamantane. [i] About 33% of product was R–R (five isomers).

Table I summarizes the reaction efficiencies and product profiles for cyclohexane with the $Fe(PA)_2$/HOOH system in the presence and absence of PhSeSePh for various solvents (the py/HOAc (1.8:1 mole ratio) matrix is optimal). The product profiles for four other hydrocarbon substrates with the relative abundance of the PhSe–R isomers is given in Table IB.

The results for the $Fe(PA)_2$/HOOH combination (1:1 mole ratio) with cyclohexane in the absence of PhSeSePh (Table IA) confirm that the primary step is Fenton chemistry[5] to produce one •OH per HOOH (eq 1).[6] The production of (c-C_6H_{11})-py

$$Fe(PA)_2 + HOOH \xrightarrow{k_1} (PA)_2Fe(OH) + {}^\bullet OH \qquad (1)$$

as the major product as well as the formation of significant amounts of (c-C_6H_{11})$_2$ (Table IA) are consistent with •OH radical chemistry.[5,7,8] Although carbon radicals (R•) are trapped by

$$^\bullet OH + RH \rightarrow R^\bullet + H_2O \qquad (2)$$

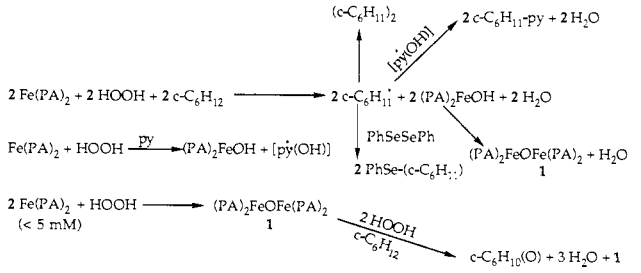
$$k_2, \sim 10^9\ M^{-1}\ s^{-1}$$

$$^\bullet OH + py \rightleftarrows [p\dot{y}(OH)] \rightarrow {}^1/_n[py(OH)]_n \qquad (3)$$

$$k_3, 3 \times 10^9\ M^{-1}\ s^{-1}$$

pyridine to give R–py,[10] the presence of substantial fluxes of [(pẏ(OH)] should favor radical/radical coupling (Scheme I). When the HOOH/$Fe(PA)_2$ ratio is large, the $Fe(PA)_2$ (at low concentration) is rapidly transformed to $(PA)_2FeOFe(PA)_2$, which activates the remaining HOOH for the ketonization of methylenic carbons (Table I and Scheme I)[4] and eliminates reduced iron for the Fenton process.

Scheme I



In the presence of PhSeSePh and excess hydrocarbon substrate the Fenton process [$Fe(PA)_2$/HOOH] produces carbon radicals (R•), which are trapped by PhSeSePh to give PhSe–R products (Table I and Scheme I). The distribution of PhSe–R isomers appears to reflect the isomer abundance for the R• radicals from the Fenton cycle (eq 1 and 2). For *n*-hexane and 2-Me-butane the R–SePh isomer distribution (Table IB) indicates that the relative reaction probabilities of •OH with a C–H bond in $-CH_3$, $>CH_2$, and >CH groups are 0.17, 1.00, and 2.29 (the respective C–H bond energies are 100, 96, and 93 kcal),[10] which are in accord with the relative values for aqueous •OH (0.21/1.00/2.1).[11] Thus,

(5) Walling, C. *Acc. Chem. Res.* **1975**, *8*, 125.

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(7) (a) Dorfman, L. F.; Adams, G. E. *Natl. Stand. Ref. Data Ser.* (*U.S., Natl. Bur. Stand.*) **1973**, NSRDS-NBS 46, 20 (SD catalog No. C13.48:46). (b) Buxton, G. V.; Greenstock, C. L.; Helman, W. D.; Ross, A. B. *J. Phys. Chem. Ref. Data* **1988**, *17*, 513.

(8) In the absence of other radicals or substrates [(pẏ(OH)] oligomerizes to a dark red solution or a brown-bronze solid.[5] Roberts, J. L., Jr.; Morrison, M. M.; Sawyer, D. T. *J. Am. Chem. Soc.* **1978**, *100*, 329.

(9) (a) Minisci, F.; Citterio, A.; Giordano, C. *Acc. Chem. Res.* **1983**, *16*, 27. (b) Minisci, F.; Citterio, A.; Vismara, E.; Giordano, C. *Tetrahedron* **1985**, *41*, 4157.

(10) *CRC Handbook of Chemistry and Physics*, 68th ed.; CRC: Boca Raton, FL, 1987; p F-178.

PhSeSePh provides the means to trap first-formed carbon radicals and thereby give insight to the mechanism of their generation.

The chemistry that is outlined in Scheme I yields phenylselenyl derivatives of C–H centers, which, upon subsequent elimination of PhSeH via oxygenation to $PhSe(O)OH$[3] yield the olefinic derivative of the substrate.[12]

With 1:1 $Fe(PA)_2$/HOOH Fenton chemistry is the dominant process, but when the mole ratio of $Fe(PA)_2$/HOOH is 1:10 or less (as well as under Gif^{III} or Gif^{IV} conditions),[1,13] the major part of the chemistry does not involve oxy radicals or reduced iron (Table IA).[4,13]

Acknowledgment. This work was supported by the National Science Foundation under Grant CHE-8516247 (D.T.S.), the Welch Foundation under Grant A-1042 (D.T.S.), the NIH (D.H.R.B.), and with a Robert A. Welch Graduate Fellowship (C.S.).

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(13) For definitions of these terms, see: Barton, D. H. R.; Halley, F.; Ozbalik, N.; Schmitt, M.; Young, E.; Balavoine, G. *J. Am. Chem. Soc.* **1989**, in press.

Investigations on Transition-State Geometry in the Aldol Condensation

Scott E. Denmark* and Brad R. Henke

Roger Adams Laboratory, Department of Chemistry
University of Illinois, Urbana, Illinois 61801

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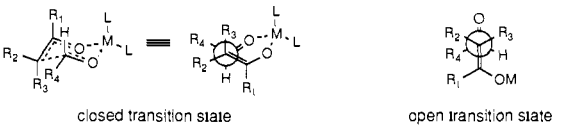
The aldol condensation has developed into one of the most important carbon–carbon bond-forming reactions used in organic synthesis today.[1] The synthetic utility of the aldol reaction stems from the high levels of internal[2] asymmetric induction that can be achieved under kinetic control. This diastereoselectivity is dependent upon the enolate geometry, metal counterion, and the bulk of the groups on the enolate and carbonyl moieties.[1c] Several transition-state hypotheses have been formulated to explain the stereochemical outcome. The most popular of these is the chairlike, chelated transition state first proposed by Zimmerman.[3-5] This hypothesis (Chart I) implies a synclinal orientation of enolate and carbonyl moieties. However, Lewis acid-catalyzed aldol reactions[1d,6] behave differently in that the product configuration is often independent of enolate geometry. In these cases open, nonchelated transition states with an antiperiplanar orientation of enolate and carbonyl moieties have been invoked (Chart I).[6]

The orientation of the enolate and carbonyl groups assumed in the transition-state hypotheses above is questionable since the intermolecular nature of these reactions makes it impossible to assign the disposition of the reactants unambiguously.[7] A

Chart I



Scheme I

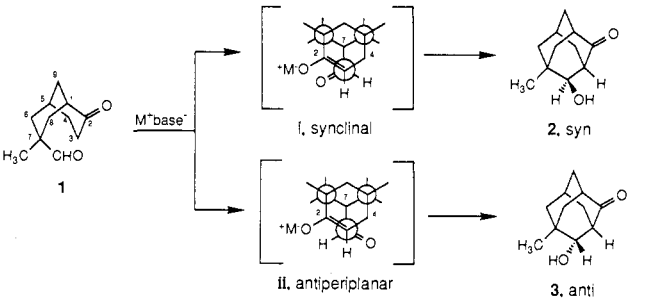
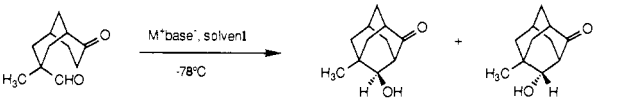


Table I. Effect of Metal Cation and Base Type in the Cyclization of **1**



entry[a]	M^+	base[b]	solvent	2/3[c,d]	yield,[d] %	$\Delta\Delta G^{\ddagger}$ (195 K)
1	K	HMDS	THF	59/41	73	0.14
2	Na	HMDS	THF	67/33	69	0.27
3	Li	HMDS	THF	87/13	87	0.74
4	MgBr	HMDS	THF	96/4	94	1.23
5	K	*t*-BuO	THF	65/35	89	0.24
6	Na	*t*-BuO	THF	67/33	91	0.27
7	Li	*t*-BuO	THF	83/17	99	0.62

[a] All cyclizations were performed with 1.1 equiv of base at −78 °C. [b] HMDS = hexamethyldisilazide. [c] Average of at least three runs within ±3%. [d] Ratios and yields were calculated based on independently determined response factors vs cyclododecane.

Table II. Effect of Solvent in the Cyclization of **1**

entry[a]	base	solvent	2/3[b,c]	yield,[c] %	$\Delta\Delta G^{\ddagger}$ (195 K)
1	$LiN(TMS)_2$	THF	87/13	87	0.74
2	$LiN(TMS)_2$	hexane	87/13	88	0.74
3	$LiN(TMS)_2$	toluene	87/13	84	0.74
4	$LiN(TMS)_2$	Et_2O	90/10	96	0.85
5	$LiN(TMS)_2$	DME	70/30	84	0.33
6	$KN(TMS)_2$	THF	59/41	73	0.14
7	$KN(TMS)_2$	toluene	89/11	90	0.81

[a] All reactions were performed with 1.1 equiv of base at −78 °C. [b] Average of at least three runs within ±3%. [c] Ratios and yields were calculated based on independently determined response factors vs cyclododecane.

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