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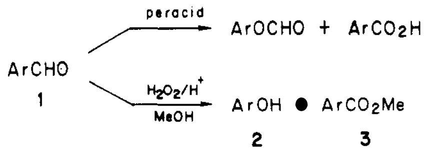
Acid-Catalyzed Oxidation of Benzaldehydes to Phenols by Hydrogen Peroxide

Summary: A wide variety of benzaldehydes were oxidized to phenols by hydrogen peroxide in acidic methanol.

Sir: The oxidation of benzaldehydes to phenols is one of the important synthons in organic synthesis and can be attained by means of Dakin reaction or Baeyer–Villiger reaction by peracids.[1,2] Dakin reaction is, in general, limited to use for the oxidation of hydroxylated benzaldehydes such as salicylaldehydes and *p*-hydroxybenzaldehydes.[2] On the other hand, Baeyer–Villiger reaction of benzaldehydes by peracids is widely applicable for the synthesis of aryl formates and/or benzoic acids. This oxidation is, however, unfavorable for substrates possessing functional groups labile to peracids.

We report here that these defects are overcome by acid-catalyzed oxidation of benzalhydes with hydrogen peroxide in methanol. The characteristic features of the present oxidation are as follows: (i) the reaction is achieved by the use of 30–35% aqueous hydrogen peroxide which is easy to handle, (ii) the oxidation products are phenols and/or methyl benzoates, while aryl formates and/or benzoic acids are the products in the Baeyer–Villiger oxidation by peracids, (iii) olefinic substituents in benzaldehydes are stable under the present reaction conditions, (iv) the reaction appears to proceed through peroxy hemiacetals.

When a solution of 2-methoxybenzaldehyde (**1a**) (5.0 g, 36.7 mmol) and 31% aqueous H_2O_2 (5.3 g, 48 mmol) in methanol (50 mL) was stirred with sulfuric acid (0.5 mL) at room temperature for 24 h, 2-methoxyphenol (**2a**) was produced in a 94% yield. Similarly, a wide variety of other



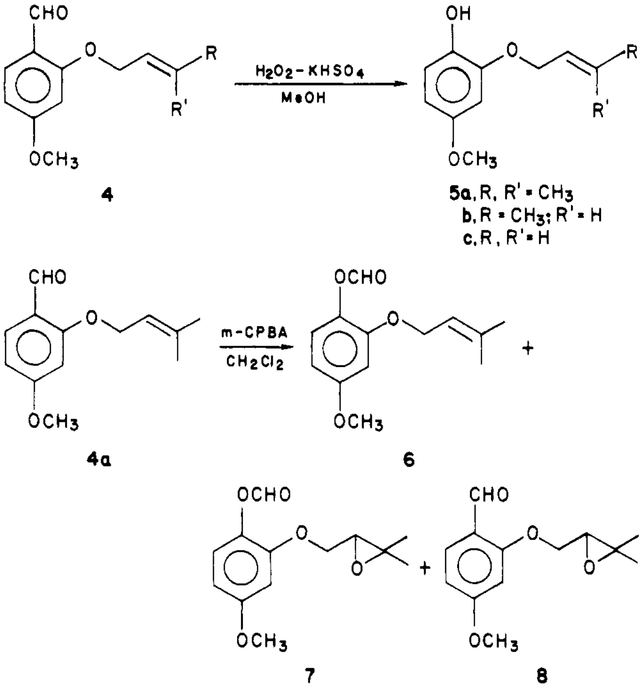
benzaldehydes **1** were oxidized to the corresponding phenols **2** and/or methyl benzoates **3** as cited in Table I. The results showed that, in most cases, the present system gave phenols **2** more selectively than the peracid oxidation, though the migratory aptitude of aryl groups compared with the hydrogen of the aldehyde function were similar to the conventional Baeyer–Villiger oxidation.[3-6]

Table I. Acid-Catalyzed Oxidation of Benzaldehydes by Hydrogen Peroxide[a]

run	benzaldehyde 1	reactn time, h	yield,[c,d] % phenol 2	yield,[c,d] % ester 3
a	2-methoxy	24	94 (60)[4]	
b	3-methoxy	68	(31)[4]	68
c	4-methoxy	24	90 (92)[4]	
d	2,3-dimethoxy	63	30	14
e	2,4-dimethoxy	14	90	
f	3,4-dimethoxy	5	60 (83)[4]	
g	2,3,4-trimethoxy	1	97 (83)[4]	
h	2,4,5-trimethoxy	4	89 (79)[4]	
i	2,4,6-trimethoxy	2	89 (63)[5]	
j	3,4-methylenedioxy	24	67 (58)[6]	8
k	4-methyl	24[b]	28	51
l	4-chloro	24[b]		87
m	4-nitro	12[b]		80

[a] Unless otherwise stated, benzaldehyde **1** (5 mmol) and 31% H_2O_2 (6.4 mmol) were stirred in the presence of H_2SO_4 (0.1 mL) in methanol (10 mL) under an argon atmosphere at room temperature. [b] The reaction mixture was heated at refluxing temperature. [c] All the products were isolated by chromatography (SiO_2). [d] Figures in parentheses are the yields of phenols by peracid oxidation of the corresponding benzaldehydes followed by hydrolysis.

The superiority of the present system was strikingly shown in the oxidation of 4-methoxy-2-(3-methyl-2-buten-1-yloxy)benzaldehyde (**4a**). Treatment of **4a** (0.75 g) with H_2O_2 (31%, 470 mg) in acidic methanol [$KHSO_4$ (70 mg), 7 mL] at room temperature for 4 h gave the corresponding phenol **5a** in a 80% yield. By contrast, the oxidation of **4a** with *m*-chloroperbenzoic acid gave a mixture of a formate **6** (18% yield) and epoxides **7** (30% yield) and **8** (40% yield). The other (allyloxy)benzaldehydes **4b** and **4c** were also selectively converted into phenols **5b** (97% yield) and **5c** (83% yield), respectively, by the H_2O_2/MeOH/H^+ oxidation.



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5a, R, R' = CH_3
b, R = CH_3; R' = H
c, R, R' = H

4a **6** **7** **8**

The present oxidation is a type of Baeyer–Villiger oxidation. To account for the formation of phenols **2** and/or

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(1) For a review, see: Hassall, C. H. "Organic Reactions"; Wiley: New York, 1967; Vol. 9, pp 73–106.

(2) For a review, see: Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 467. See also ref 1.

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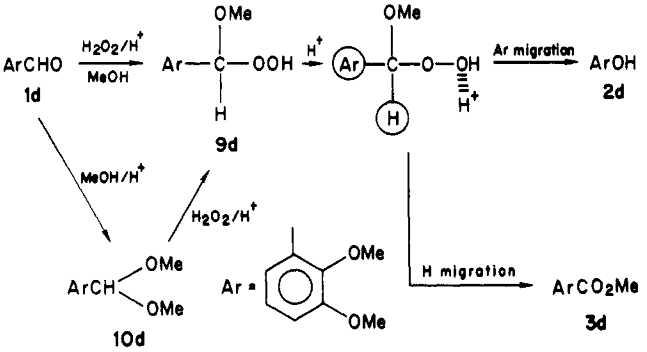
methyl benzoates **3** from benzaldehydes **1**, peroxy hemiacetals **9** have often been suggested as reactive intermediates. Thus, we tried to isolate the peroxide **9** from the reaction mixture and found that in certain cases **9** was isolable. As shown in Table I, the oxidation of 2,3-dimethoxybenzaldehyde (**1d**) required a long reaction time. When the reaction was quenched by weak base after 24 h, the reaction mixture was found to contain peroxy hemiacetal **9d** in addition to the phenol **2d** and the benzoate **3d**.

The peroxy hemiacetal **9d** was more conveniently prepared from dimethyl acetal **10d**; treatment of a solution of **10d** and concentrated H_2O_2 (~70%) in acidic methanol at room temperature for 24 h gave **9d** in a 69% yield together with a small amount of **2d** (12% yield) and **3d** (3% yield). The peroxide **9d** was isolated as a colorless oil[7] by chromatographic purification (SiO_2/CH_2Cl_2). To ascertain the intermediacy of **9d** in the oxidation of **1d** with H_2O_2 in acidic methanol, **9d** was treated with a catalytic amount of concentrated H_2SO_4 in tetrahydrofuran at room temperature for 24 h to yield the phenol **2d** (33% yield) and the benzoate **3d** (16.5% yield).[8] This product distribution was similar to the result cited in Table I (run d).



We have demonstrated a convenient oxidation of benzaldehydes to phenols (and/or benzoates) by hydrogen peroxide in acidic methanol. This reaction provides a synthetic method to use benzaldehydes as latent phenols and can be used for systems bearing functional groups such as the C=C double bond which are labile to peracids.

Registry No. **1a**, 135-02-4; **1b**, 591-31-1; **1c**, 123-11-5; **1d**, 86-51-1; **1e**, 613-45-6; **1f**, 120-14-9; **1g**, 2103-57-3; **1h**, 4460-86-0; **1i**, 830-79-5; **1j**, 120-57-0; **1k**, 104-87-0; **1l**, 104-88-1; **1m**, 555-16-8; **2a**, 90-05-1; **2c**, 150-76-5; **2d**, 5150-42-5; **2e**, 13330-65-9; **2f**, 2033-89-8; **2g**, 19676-64-3; **2h**, 20491-91-2; **2i**, 20491-92-3; **2j**, 533-31-3; **2k**, 106-44-5; **3b**, 5368-81-0; **3d**, 2150-42-7; **3j**, 326-56-7; **3k**, 99-75-2; **3l**, 1126-46-1; **3m**, 619-50-1; **4a**, 37761-51-6; **4b**, 92720-63-3; **4c**, 71186-58-8; **5a**, 92720-64-4; **5b**, 92720-65-5; **5c**, 71186-61-3; **6**, 92720-66-6; **7**, 92720-67-7; **8**, 92720-68-8; **9d**, 92720-69-9; **10d**, 59276-32-3; HOOH, 7722-84-1; $3\text{-ClC}_6H_4C(O)OOH$, 937-14-4.

Supplementary Material Available: Representative experimental procedures of **1** (1 page). Ordering information is given on any current masthead page.

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[7] NMR ($CDCl_3$) δ 3.55 (s, 3 H), 3.82 (s, 3 H), 3.85 (s, 3 H), 6.03 (s, 1 H), 6.8–7.1 (m, 3 H), 9.11 (br s, 1 H). IR (liquid film) 3400, 1595, 1490, 1270, 1070, 1005, and 795 cm^{-1}. Mass spectrum, m/z (relative intensity) 214 (7, M^+), 196 (60), 181 (87), 167 (33), 166 (83), 165 (81), 163 (74), 151 (39), 107 (51), 77 (76), 45 (100).

[8] The reaction of **9d** in methanol gave similar a result.

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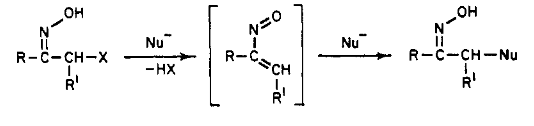
Intramolecular [4 + 2] Cycloadditions of Nitrosoalkenes with Olefins

Summary: The first examples of intramolecular capture of nitrosoalkenes generated by in situ 1,4-elimination of α-chloro silyl oximes are reported.

Sir: The intermediacy of nitrosoalkenes in the reactions of α-halo oximes with bases has been known for over 80 years.[1,2] The flash of blue color observed during these reactions has been unambiguously attributed to nitrosoalkenes by independent isolation,[3] spectroscopic characterization,[4] and kinetic and stereochemical studies.[5]

Nitrosoalkenes thus generated undergo rapid addition of a variety of nucleophiles resulting in an overall nucleophilic functionalization α to ketones[2] (eq 1). In the



$$R-\underset{}{C}(=N-OH)-CH(R^1)-X \xrightarrow[-HX]{Nu^-} \left[R-C(=N{=}O)=CH-R^1 \right] \xrightarrow{Nu^-} R-C(=N-OH)-CH(R^1)-Nu \qquad (1)$$

presence of dienes or dienophiles, nitrosoalkenes can undergo [4 + 2] cycloadditions as 2π or 4π components, respectively.[6] Recently Gilchrist,[7] Viehe,[4] and Iskanderl[8] have reported a number of examples of the latter process, i.e., nitrosoalkenes acting as 4π components. These studies reveal several limitations which hamper general application of the potentially useful reaction: (1) electron-withdrawing substituents (phenyl, carbonyl, trihalomethyl) on the nitrosoalkene are necessary, (2) only nucleophilic olefins give cycloadducts, (3) a 5–20-fold excess of olefin is required, and (4) reactions are not completely regioselective. *We report that the intramolecular variant of this reaction, Scheme I, offers a practical solution to these problems and is also stereospecific.*

Of primary concern in developing this reaction were (1) the ability to generate solutions of stable nitrosoalkenes and (2) the selection of a dienophilic appendage with sufficient proximity and reactivity. In a recently reported investigation with model substrates we demonstrated[9] that (1) nitrosoalkenes are efficiently generated from α-chlorosilyl ketoximes with fluoride ion, (2) the efficiency of generation of nitrosoalkenes was independent of silyl oxime geometry and disposition of the chlorine atom, (3) nitrosoalkenes capable of tautomerization were produced in lower concentration, and (4) dialkyl-substituted alkenes are not suitable dienophiles.

With these considerations in mind we prepared enol ether 4[10] from 3-bromo-2-cyclohexen-1-one[11] as shown in Scheme II. Two reactions in this scheme are noteworthy.

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