## Photochemical Release of Aldehydes from $\alpha$ -Acetoxy Nitroveratryl Ethers

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## ABSTRACT

Photolabile aldehyde-releasing precursors ( $\alpha$ -acetoxy ethers) were prepared by reduction of the corresponding esters with DIBAL and quenching the intermediate aluminum hemiacetal with acetic anhydride. These species smoothly released aldehydes upon irradiation with UV light at 350 nm. Using this method, not only simple model aliphatic aldehydes were liberated but also specimens relevant for the flavor and fragrance industry (methional, phenylacetaldehyde, and (*R*)-citronellal).

Slow and controlled release of substances is of great interest in many applications. Chemical,<sup>1</sup> enzymatic,<sup>2</sup> and photochemical<sup>3</sup> liberation of various caged organic molecules have been achieved in the past decade. In the particular case of the fragrance industry, the slow photorelease of odorant aldehyde has been studied on many instances (e.g., by Norrish type II fragmentation).<sup>4</sup> The very recent report by Banerjee et al. on the photochemical liberation of ketones from enol ethers prompted us to disclose our progress in this field.<sup>5</sup>

Aldehydes and ketones are traditionally protected as acetals and ketals. The latter species offer good chemical resistance with respect to various conditions (basic, oxidizing, reducing, etc.), and we have exploited this feature introducing the photolabile bis(*o*-nitrophenyl)ethane-1,2-diol,<sup>6</sup> a symmetrical version of the glycol developed by Gravel et al.<sup>7</sup> On the other hand, when stability in solution is not a central issue,  $\alpha$ -acetoxy ethers could represent an attractive substitute to regular acetals, because their liberation is significantly less sensitive to the reaction medium (e.g., pH, water content) and for their inherently simpler structure.

2-Nitroveratrol **1** was acylated with acid chlorides  $2\mathbf{a}-\mathbf{h}$ in excellent yields using standard conditions (RCOCl, NEt<sub>3</sub>) in dichloromethane to give the esters  $3\mathbf{a}-\mathbf{i}$ . In one case, a carboxylic acid was used (citronellic acid  $2\mathbf{i}$ ) in combination with a classical DCC-mediated esterification. The  $\alpha$ -acetoxy



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ethers **4a**–**i** were then prepared by the procedure developed by Rychnovsky<sup>8</sup> and Rovis:<sup>9</sup> very slow addition of a solution of DIBAL in hexane at -78 °C was followed by the sequential addition of pyridine, DMAP in CH<sub>2</sub>Cl<sub>2</sub>, and finally acetic anhydride, while maintaining a careful control of temperature (Scheme 1, Table 1). The  $\alpha$ -acetoxy ethers

entry	2	R	$\operatorname{ester}^a$	$ether^a$
1	2a	Me	<b>3a</b> (89%)	<b>4a</b> (80%)
2	$2\mathbf{b}$	Et	<b>3b</b> (94%)	<b>4b</b> (81%)
3	2c	Pr	<b>3c</b> (96%)	<b>4c</b> (70%)
4	2d	n-C <sub>4</sub> H <sub>9</sub>	<b>3d</b> (96%)	<b>4d</b> (65%)
5	<b>2e</b>	n-C <sub>5</sub> H <sub>11</sub>	<b>3e</b> (94%)	<b>4e</b> (66%)
6	2f	n-C <sub>11</sub> H <sub>23</sub>	<b>3f</b> (74%)	<b>4f</b> (72%)
7	$2\mathbf{g}$	$CH_2Ph$	<b>3g</b> (89%)	4g (90%)
8	2h	$(CH_2)_2SMe$	<b>3h</b> (89%)	<b>4h</b> (77%)
9	<b>2i</b>	CH <sub>2</sub> CH(Me)(CH <sub>2</sub> ) <sub>2</sub> C=Me <sub>2</sub>	<b>3i</b> (48%) <sup>b</sup>	<b>4i</b> (71%)

 $^a$  Isolated yield.  $^b$  DCC-mediated esterification with (*R*)-citronellic acid **2i**.

showed a reasonable stability both in solution and as a wax. Purification by flash chromatography did not lead to significant degradation.

On the other hand, this protocol was not possible with cation-stabilizing substitutents (R = vinyl, phenyl), presumably because of the spontaneous ionization of the final  $\alpha$ -acetoxy ether. To study the thermal stability of these species, we submitted **4c** to thermolysis at 200 °C for 4 h. The corresponding enol ether **5** was cleanly obtained (51%) by elimination of acetic acid, as a 3:2 *Z/E* isomeric mixture (Scheme 2). The latter underwent the same type of photolysis



as its parent  $\alpha$ -acetoxy ether, i.e., releasing the aldehyde but avoiding the concomitant release of smelly acetic acid. This simple elimination reaction represent an interesting strategy to access photosensitive enol ethers, complementary to the one developed by Banerjee et al.<sup>5</sup>

Solutions of **4a**–**i** in acetonitrile were exposed to UV light in a Rayonet apparatus equipped with 16 RPR3500 lamps ( $\lambda_{max}$  350 nm). Not unexpectedly, aldehydes were smoothly



released, without traces of products other than the usual aromatic residues typical to the 2-nitroveratrol derivatives photolysis and acetic acid (Scheme 3, Table 2). Similar results were obtained even when oxygen was not strictly excluded, an important observation for potential applications in photosensitive materials.

 Table 2.
 Photochemical Liberation of Aldehydes 6a-i

entry	ether	R	reaction time (h)	aldehyde <sup>a</sup>
1	4a	Me	3	<b>6a</b> (58%)
<b>2</b>	<b>4b</b>	Et	4	<b>6b</b> (79%)
3	<b>4c</b>	Pr	4	<b>6c</b> (70%)
4	<b>4d</b>	n-C <sub>4</sub> H <sub>9</sub>	3	<b>6d</b> (74%)
5	<b>4e</b>	$n-C_5H_{11}$	4	<b>6e</b> (57%)
6	<b>4f</b>	$n-C_{11}H_{23}$	3	<b>6f</b> (69%)
7	4g	$CH_2Ph$	4	<b>6g</b> (62%)
8	<b>4h</b>	$(CH_2)_2SMe$	4	<b>6h</b> (53%)
9	<b>4i</b>	$CH_2CH(Me)(CH_2)_2C{=}Me_2$	3	<b>6i</b> (73%)

<sup>a</sup> Yield determined by <sup>1</sup>H NMR, using an internal standard. The photolyses were carried out in nondegassed acetonitrile at 350 nm.

As the purpose of this work is not a preparative method to generate aldehydes, they were not systematically isolated, but the very large chromatographic retention factor differences between the aldehyde and the side products make purification very easy. The aldehydes were, however, unambiguously characterized spectroscopically by comparison with pure samples prepared separately.<sup>10</sup> Noteworthy, aldehydes with specific odors were released, such as the sulfure-containing methional **6h** (potato), phenylacetaldehyde **6g** (fruity, honey-like), and (R)-citronellal **6i** (citrus green).

In summary, we were able to prepare photosensitive  $\alpha$ -acetoxy ethers, which could release aldehydes upon exposure to UV light. While not representing a preparative

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<sup>(10)</sup> All of the aldehydes 6a-i are commercially available.

method, this strategy is attractive in the perspective of smart materials, which respond chemically to external stimuli.<sup>3b</sup> Resin-bound photolabile linkers have been developed and used.<sup>3d,11</sup> Our progress in this direction will be reported in due course.

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**Supporting Information Available:** Detailed experimental procedures and spectral information for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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