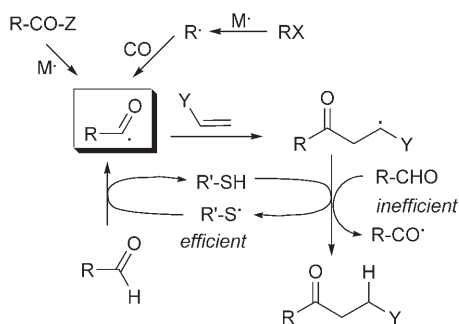


Acylation of Electrophilic Olefins through Decatungstate-Photocatalyzed Activation of Aldehydes**

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A useful synthesis of ketones involves the addition of acyl radicals to olefins or alkynes.^[1] These intermediates are generated either by group transfer from acyl selenides^[1] or by addition of alkyl radicals (from halides) to CO (usually at 70–90 atm).^[2] In both cases, activation requires the use of stannyl, or less usually silyl, radicals ($M^\bullet$, Scheme 1). The environ-



Scheme 1. Radical acylation of olefins.

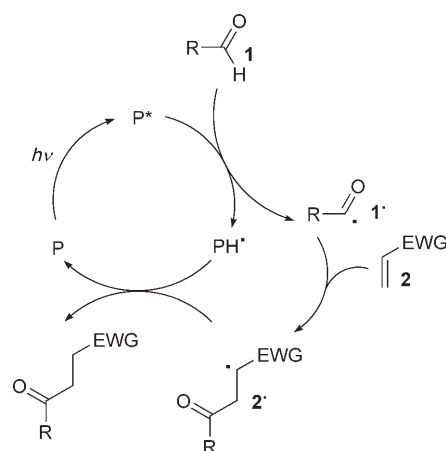
mental limitations to the use of organotin reagents has fostered the recent introduction of further radical precursors, such as acyl hydrazides,^[3a] acyl hydrazines,^[3b] and thiol esters.^[3c] However, the obvious breakthrough would be to generate acyl radicals directly from the corresponding aldehydes, doing so through a tin-free method and raising atom economy to 100%. The homolysis of the C(=O)–H bond by initiation by acetyl peroxides and UV light^[4] is limited by the inefficient hydrogen abstraction from R–CHO by the adduct radical, except in the case of alkenes bearing an electron-withdrawing substituent (Y in Scheme 1). An auxiliary reducing agent such as a thiol ($R'-SH$; *tert*-dodecylmer-

captane or thioglycolate) is often added^[1,5] to maintain active chain propagation.

The photogeneration of acyloxy radicals (e.g. *t*BuO•) is inconvenient owing to the low absorptivity of the precursor peroxides,^[6] whereas aromatic ketones absorb strongly and react similarly in their $n\pi^*$ triplet state.^[7] Accordingly, benzophenone was used with some success in the photochemical acylation of enones by acetaldehyde (40 equiv)^[8a] as well as of methoxynaphthoquinones (with about 8 equivalents of aldehyde),^[9] although benzophenone-derived by-products were also formed and their separation from the desired product was a serious drawback.^[8b]

Tetrabutylammonium decatungstate (TBADT) is known to abstract hydrogen atoms efficiently from simple aliphatic derivatives, including alkanes,^[10] and recently we demonstrated that this reagent could be applied to the alkylation of electrophilic alkenes.^[11] We surmised that TBADT photocatalysis may be the desired method for the activation of the C(=O)–H bond in aldehydes.

The process should be initiated by excited TBADT (P^* in Scheme 2) through hydrogen abstraction from aldehyde **1** and



Scheme 2. Decatungstate-photocatalyzed activation of aldehydes. P: $(nBu_4N)_4[W_{10}O_{32}]$ (photocatalyst); EWG: electron-withdrawing group.

terminated by back hydrogen transfer to adduct radical **2'**, thus closing the catalytic cycle.^[10] As an inorganic photocatalyst is used, the end products should be easily purified by elimination of the solvent and simple distillation of the crude photolyzed product. Previous experience with alkanes and alcohols had shown that TBADT could be used in a low amount (usually 2 mol% relative to the substrate).^[11]

A further limitation to be confronted is that most of the acylations reported to date involved an intramolecular, rather

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Table 1: Photocatalyzed acylation of electron-poor olefins.

$ \begin{array}{c} \text{R}-\text{C}(=\text{O})-\text{H} \\ \mathbf{1} \end{array} + \begin{array}{c} \text{CH}_2=\text{CH}-\text{EWG} \\ \mathbf{2} \end{array} \xrightarrow[\text{MeCN, } h\nu]{(n\text{Bu}_4\text{N})_4[\text{W}_{10}\text{O}_{32}]} \begin{array}{c} \text{R}-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{EWG} \\ \mathbf{3-10, 12, 15} \end{array} $				
Entry	Aldehyde 1	Olefin 2	Product(s)	Yield [%] ^[a]
1				63
2				57
3				56
4				60
5				58
6		2a		52
7		2c		60
8 ^[b]		2a		15:34
9 ^[c]		2a		40:5 ^[d]
10				45:25
11 ^[c]		2f		46: < 1 ^[d]
12		2a		70
13 ^[e]		2a		48:16 ^[d]

[a] Yield of the isolated product (following distillation of crude mixture). [b] Reaction carried out in a photochemical reactor at 21 °C. [c] Reaction carried out at –20 °C. [d] GC yields. [e] Reaction carried out at –50 °C in propionitrile.

than intermolecular, reaction.^[1] In fact, intermolecular reactions took place with a satisfactory yield only in the presence of a large excess of either of the reagents. An excess of the alkene lowered the competing decarbonylation of acyl radicals prior to acylation (see below), but led to a concom-

itant hydrostannylation when Bu₃SnH was used as the radical mediator.^[12] On the other hand, aldehydes were employed as the solvent in some cases.^[1,13]

With these points in mind, we investigated the photochemistry ($\lambda_{\text{irr}} = 310 \text{ nm}$, MeCN as solvent) of an equimolar

mixture (0.1M) of an aliphatic aldehyde (**1a–f**) and an electron-poor olefin (**2a–f**) in the presence of TBADT (2×10^{-3} M). To our delight, under these conditions heptaldehyde **1a** was found to acylate α,β -unsaturated esters, ketones, and nitriles (**2a–e**) in about the same irradiation time (ca. 24 h) to afford the corresponding functionalized ketones **3–7** in similar yields of the isolated product (ca. 60 % in all cases; see Table 1 and Supporting Information for details).

Thus, the carbonyl hydrogen atom was selectively abstracted. No reaction took place in the absence of TBADT, nor were the yields increased by using a larger amount of TBADT or by adding *tert*-dodecanthiol (5–10 mol %) to the reaction mixture.^[14]

The scope of the reaction was explored by studying a primary aldehyde hindered at the β position, namely 3,3-dimethylbutanal (**1b**). Acylation of dimethyl maleate took place in the same irradiation time as with **1a** and gave succinate **8** in a comparable yield. Likewise, the 1,4-diketone **9** was isolated in 60 % yield from the photocatalyzed reaction of a β -phenyl-substituted aldehyde, 3-phenylpropionaldehyde (**1c**), with cyclohexenone. On the contrary, acylation was ineffective when using aromatic aldehydes, as these absorbed light competitively and were consumed through different paths, or with electron-rich olefins such as 2,3-dimethylbutene or cyclohexene (even in the presence of the thiol).

An important issue in determining the scope of the reaction was the decarbonylation of acyl radicals. The literature shows that this process depends on the stability of the corresponding alkyl radicals, on the temperature, and on the solvent used.^[1,15,16] Decarbonylation is known to be decreased to some extent when using $(\text{Me}_3\text{Si})_3\text{SiH}/\text{Et}_3\text{B}$ as radical initiators^[17] and more effectively through an indirect approach recently proposed by Skrydstrup and co-workers through SmI_2 reduction of different radical precursors (*N*-acyl oxazolidinones) at temperatures below -40°C .^[18] In principle, the simple approach of lowering the temperature is suited to aldehydes owing to the lower activation energy of acylation versus the decarbonylation reaction.^[19] However, lowering the temperature is not an option thermally because it slowed down the rate of the chain reaction. In the present case, the photocatalyzed hydrogen-abstraction step was virtually independent of the temperature and application to easily fragmenting acyl radicals at a low temperature seemed possible.^[20]

We thus examined secondary aldehydes **1d** and **1e**. As expected, photolysis of 2-ethylbutyraldehyde (**1d**) in the presence of **2a** gave a mixture of acylsuccinate **10** (15 %) and alkylsuccinate **11** (34 %, see Table 1). At -20°C , however, ketone **10** was by far the main product (40 %) along with a small amount of **11** (ca. 5 %). Likewise, the photocatalyzed reaction between aldehyde **1e** and cyclopentenone (**2f**) at room temperature gave both 1,3-diketone **12** (45 %) and 3-cyclohexylcyclopentanone **13** (25 %), whereas at -20°C compound **12** was formed almost exclusively (46 %, with less than 1 % **13**). Prolonged irradiation led to significant consumption of both photoproducts.

Finally, the photolysis of an equimolar mixture of the tertiary aldehyde pivalaldehyde (**1f**) and maleate **2a** in the presence of TBADT was studied. At room temperature, no acylation was observed and *tert*-butylsuccinate **14** was formed

as the sole product (70 %). In an attempt to contrast the fast decarbonylation typical of tertiary acyl radicals,^[21] we repeated the reaction at -50°C using the lower melting propionitrile rather than acetonitrile as solvent. Under these conditions, compound **14** was again formed as the main product but was accompanied by ketodiester **15** (16 % yield).^[22] Although a reversal of the selectivity was not obtained in this case,^[23] a positive indication about the thermal control of decarbonylation was obtained; this was, to our knowledge, the first instance whereby addition of a tertiary acyl radical onto an alkene was obtained.^[24]

In conclusion, the photocatalyzed activation of aldehyde hydrogen atoms offered an easy access to acyl radicals and the synthesis of unsymmetrical ketones through trapping by electrophilic olefins. The method involves the use of TBADT in a low amount (2 mol %) and equimolar amounts of the reagents, does not require the use of foul-smelling auxiliaries, and qualifies as a “green” synthetic method. With tertiary aldehydes, a single process occurs, namely alkylation. As with other radical methods, decarbonylation and acylation processes compete when using secondary aldehydes at room temperature. However, photocatalysis is equally effective at a low temperature and allows acylation at -20°C with secondary aldehydes and a significant fraction of acylation with tertiary aldehydes.

Experimental Section

Typical procedure for the photochemical acylation of olefins: A solution of aldehyde (**1a–f**, 3 mmol, 0.1M), olefin (**2a–f**, 0.1M), and TBADT^[11b] (200 mg; 2×10^{-3} M) in MeCN (30 mL) was poured into two quartz tubes and purged for 10 min with argon. The tubes were then serum-capped and irradiated with six 15-W phosphor-coated lamps (emission centered at 310 nm). The photolyzed solution was concentrated under reduced pressure, and the products were purified by bulb-to-bulb distillation. When mixtures were formed, separation was carried out by column chromatography (on silica gel, with cyclohexane/ethyl acetate as eluants).

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- [23] The rate constants for the decarbonylation of aldehydes and for the addition of pivaloyl radical to acrylonitrile are known (with considerable uncertainty). In the hypothesis that these values roughly apply to the present reaction, the acylation/alkylation ratios are predicted to be 3.5 and 0.9 for secondary and tertiary aldehydes at 23 °C, and 0.005 and 0.02 at –20 °C. This prediction fits with the observed trend, although the $k_{\text{CO}}/k_{\text{add}}$ ratio is clearly larger in the present reactions, particularly for tertiary aldehydes.
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