Alkanes to nitriles and α-iminoesters. Polyoxotungstate photocatalytic radical chain initiation

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Irradiation of $W_{10}O_{32}^{4-}$ or $PW_{12}O_{40}^{3-}$, alkanes and methyl cyanoformate in CH_3CN solution produces either the corresponding nitriles or α-iminoesters with high selectivity, depending on the temperature, *via* a mechanism involving two roles for the polyoxotungstate.

While a host of C–H bond activation or functionalization methods developed in the last few years have provided a wealth of mechanistic information and some unusual or unprecedented transformations, few of the reactions have been of significant synthetic value. Organometallic systems that activate C–H bonds rarely lead to functionalization and are usually not catalytic in the metal complex,[1–5] while more conventional radical and electrophilic systems usually have selectivity or compatibility difficulties.[4,5] We report here the first catalytic conversion of unactivated C–H bonds to two desirable groups in high selectivity: nitriles and α-imino-acetic acid esters (henceforth iminoesters) *via* polyoxotungstate photocatalysis.[6,7] Nitriles are widely used in synthesis,[8] and α-ketoesters (or acids), readily derived from hydrolysis of the iminoesters, have a rich photochemistry and could be used to render hydrocarbon materials, including polyethylene, sunlight degradable and biodegradable.[9] Nitriles have been generated in moderate to good yields *via* organic radicals generated from conventional precursors (not generated catalytically by alkane C–H bond cleavage), by trapping with *tert*-butylisocyanide,[10] or with aryl and alkylsulfonyl cyanides.[11] Alkanes photolyzed in the presence of ClCN[12] or heated with consumption of considerable conventional radical initiator (10–24 mol% benzoyl peroxide) in the presence of methyl cyanoformate also yield nitriles.[13] The latter reaction forms some iminoester but yields were not given. There appear to be no good routes to iminoesters from unactivated C–H bonds.

Irradiation (λ > 280 nm) of CH_3CN solutions of $W_{10}O_{32}^{4-}$ or $PW_{12}O_{40}^{3-}$ containing one of a variety of alkanes and methyl cyanoformate (MCF) produces the corresponding nitriles at T = 90 °C and iminoesters at T = 22 °C. Significantly, the selectivities for these products and turnovers of the polyoxotungstate vary inversely with the concentration of the polyoxometalate and selectivities approach quantitative values at [polyoxotungstate] < 0.05 mM. Table 1 gives the products from many reactions using 1.5 mM polyoxotungstate, a concentration not optimal for selectivity but one permitting by-product quantification needed for mechanism elucidation. At low [polyoxotungstate], the selectivities for nitriles (high T) and iminoesters (low T) exceed those of all literature reactions. Significantly, as both nitriles and iminoesters are of comparable or lower reactivity than the alkanes themselves, these reactions may be of preparative value. For example, the iminoesters derived from 2,3-dimethylbutane and *cis*-1,2-dimethylcyclohexane were isolated in 59 and 67% yields respectively (at 28 and 61% conversions of alkane).

$$P_{ox} \xrightarrow{h\nu} P_{ox}^* \qquad (1)$$

$$RH + P_{ox}^* \longrightarrow R\bullet + H^+(P_{red}) \qquad (2)$$

$$R\bullet + NCCO_2CH_3 \longrightarrow RC(=N\bullet)CO_2CH_3 \qquad (3)$$

$$RC(=N\bullet)CO_2CH_3 + RH \longrightarrow RC(=NH)CO_2CH_3 + R\bullet \qquad (4)$$

$$RC(=N\bullet)CO_2CH_3 + H^+(P_{red}) \longrightarrow RC(=NH)CO_2CH_3 + P_{ox} \qquad (5)$$

$$RC(=N\bullet)CO_2CH_3 \longrightarrow RCN + CO_2 + CH_3\bullet \qquad (6)$$

$$CH_3\bullet + RH \longrightarrow CH_4 + R\bullet \qquad (7)$$

$$CH_3\bullet + NCCO_2CH_3 \longrightarrow CH_3C(=N\bullet)CO_2CH_3 \qquad (8)$$

$$CH_3C(=N\bullet)CO_2CH_3 + RH \longrightarrow CH_3C(=NH)CO_2CH_3 + R\bullet \qquad (9)$$

$$CH_3C(=N\bullet)CO_2CH_3 \longrightarrow CH_3CN + CH_4 + CO_2 \qquad (10)$$

$$RC(=NH)CO_2CH_3 \xrightarrow[\text{conditions}]{\text{under rxn}}\!\!\!\!\!\!\!\!\!\!/\!\!/\;\; RCN \qquad (11)$$

(P_{ox} and P_{red} are oxidised and reduced polyoxotungstate, respectively.)

These and other data discussed below rule out many mechanisms and are consistent with eqn. (1)–(10) for this chemistry. Previous studies (product, kinetics, spectroscopic and others) establish that the oxygen-to-tungsten charge-transfer excited states of polyoxotungstates abstract hydrogen atoms, eqn. (1) and (2).[6,7] The chemoselectivities and regioselectivities exhibited by the products in Table 1 indicate the same dominant C–H bond cleaving species is operable in the presence of MCF: (1) the tertiary/primary (3°/1°) C–H cleavage ratios (> 200 for 2,3-dimethylbutane and *cis*-1,2-dimethylcyclohexane), (2) the lack of reactivity of *tert*-butylbenzene (all primary C–H) and (3) the loss of stereochemistry during functionalization of *cis*-1,2-dimethylcyclohexane. The coupling and disproportionation (alkene only detectable) products in Table 1 are more consistent with radicals than other organic intermediates. Three lines of evidence indicate the title processes, unlike most polyoxotungstate photocatalyzed alkane functionalizations, involve radical chains. First, there is significant inhibition by radical inhibitors. This is seen for production of both reduced polyoxotungstate and organic products. For example, the ratio of rates for production of iminoester from 2,3-dimethylbutane using $W_{10}O_{32}^{4-}$, without and with 2.0 mM hydroquinone (HQ) inhibitor, $k_{\text{no HQ}}/k_{\text{with HQ}}$ > 100. This ratio without and with 2.0 mM 2,6-di-*tert*-butylphenol (BHT), $k_{\text{no BHT}}/k_{\text{with BHT}} = 5.7 \pm 0.2$. For HQ and BHT, respectively, *ca*. 10 and < 2% of the light is absorbed by the inhibitor; the rest by $W_{10}O_{32}^{4-}$. Second, the quantum yields for both nitrile and iminoester reactions exceed 1.0 when [polyoxotungstate] < 0.05 mM. Third, $W_{10}O_{32}^{4-}$ inhibits iminoester formation at high [$W_{10}O_{32}^{4-}$]. In contrast, photocatalytic C–H cleavage by $W_{10}O_{32}^{4-}$ generally exhibits conventional kinetics (reaction first order in $W_{10}O_{32}^{4-}$ and in alkane).[6,7]

Inhibition at high [$W_{10}O_{32}^{4-}$] most likely reflects redox capture of radical by polyoxotungstate.[6]

The two propagation steps, eqn. (3) and (4), both of which are precedented in studies involving conventionally generated radicals,[12] sum to the net reaction for production of iminoester. Several additional experiments establish that the mechanism for nitrile formation is eqn. (1)–(3), (6) and (7) [eqn. (8)–(10) are minor processes]: first, quantification of CO_2 (*via* $BaCO_3$) and CH_4 (*via* GC/TCD) products indicates that [nitrile] ~ [CO_2] ~ [CH_4]; second, when the reactions are run in *N,N*-dimethylacetamide (DMA), PhCN, or PhCl *versus* CH_3CN, very little CH_3CN [eqn. (10)] and little or no methyl pyruvate derivatives [eqn. (9)] are formed; third, negligible CH_3CH_3 from coupling of $CH_3\cdot$ is observed in CH_3CN (interestingly [CH_3CH_3]/[CH_4] ~ 1 in DMA). Control experiments demonstrated that reduced

Table 1 Functionalization of alkanes with methyl cyanoformate *via* polyoxometalate photocatalysis[a]

Polyoxo-tungstate[b]	Substrate	*t*/h; T/°C[c]	Organic product (%) of detected products[d] (turnovers, based on P_{ox})[e]			
	1		**1a**	**1b**		
$Na_4W_{10}O_{32}$		16; 22	< 1	75 (27)		
$Q_4W_{10}O_{32}$		16; 22	< 1	90 (9.1)		
$Q_3PW_{12}O_{40}$		16; 22	< 1	99 (0.3)		
$Na_4W_{10}O_{32}$		8; 90	78 (11)	6 (0.9)		
$Q_4W_{10}O_{32}$		8; 90	61 (5.3)	21 (1.8)		
	2		**2a**	**2b**	**2c**	
$Na_4W_{10}O_{32}$		16; 22	< 1	51 (8.4)	11 (1.9)	
$Q_4W_{10}O_{32}$		16; 22	< 1	51 (5.6)	< 1	
$Na_4W_{10}O_{32}$		8; 90	78 (20)	3 (0.8)	< 1	
$Q_4W_{10}O_{32}$		8; 90	59 (3.0)	20 (1.0)	< 1	
	3		**3a**	**3b**	**3c**	**3d**
$Na_4W_{10}O_{32}$		16; 22	2 (1.0)	75 (36)	< 1	2 (1.0)
$Q_4W_{10}O_{32}$		16; 22	< 1	80 (25)	< 1	2 (1.9)
$Q_3PW_{12}O_{40}$		16; 22	< 1	50 (0.4)	50 (0.4)	< 1
	4		**4a**	**4b**	**4c**	
$Na_4W_{10}O_{32}$		16; 22	< 1	51 (8.4)	11 (1.9)	
$Q_4W_{10}O_{32}$		16; 22	< 1	51 (5.6)	< 1	
$Na_4W_{10}O_{32}$		8; 90	76 (18)	2 (0.5)	< 1	
$Q_4W_{10}O_{32}$		8; 90	71 (9.2)	16 (2.0)	< 1	
	5		**5a**			
$Na_4W_{10}O_{32}$		8; 90	100 (1.0)			
	6		**6a**			
$Na_4W_{10}O_{32}$		8; 90	100 (0.5)			
	7					
$Na_4W_{10}O_{32}$		8; 90	No reaction			

[a] Acetonitrile solutions of polyoxotungstate (1.5 mM) and alkane (0.5 M) and MCF (0.25 M) were irradiated (550 W medium-pressure Hg lamp; Pyrex filter, $\lambda > 280$ nm). The average conversion (based on MCF) was 15% to simplify product distributions for mechanism elucidation. [b] Q = tetra-*n*-butylammonium. [c] t = irradiation time. [d] All new compounds were purified and their compositions and purities (> 98%) confirmed by ^{1}H NMR, high resolution MS, and elemental analysis. Moles of indicated product/moles of total organic products as determined by GC. [e] Turnovers = moles of indicated product/moles of polyoxotungstate.

$W_{10}O_{32}^{4-}$ does not react with either MCF (no CN^- is formed) or organic products (iminoester or nitrile). Finally, the yields of iminoester and nitrile correlate strongly (inversely) with each other between 22 and 90 °C, and iminoester does not convert to nitrile under the reaction conditions [eqn. (11) is not operative]. These 2 points suggest that both products derive from a common intermediate, most likely the iminyl radical, $RC(=N\cdot)CO_2CH_3$.

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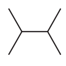
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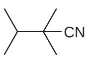
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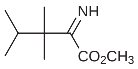

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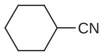

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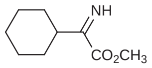

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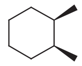
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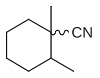

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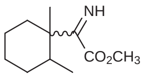

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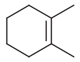
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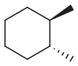
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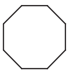
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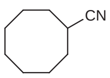

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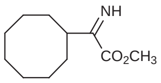

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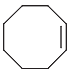
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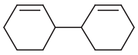
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$PhCH_3$ **6**

$PhCH_2CH_2Ph$ **6a**

$PhC(CH_3)_3$ **7**

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