

The Oxidation of Ketones with a Heteropolyacid, $H_5[PMo_{10}V_2O_{40}]$ and Dioxygen

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Substituted cycloalkanones, 1-phenylalkanones, and open-chain ketones are oxidatively cleaved by the title compound under very mild conditions.

The oxidative cleavage of ketones has been studied using several precursors¹ and has found important applications in industrial syntheses.² Metal-catalysed oxidation of ketones often occurs in acidic³ or basic⁴ media. These results and others concerning vanadium-based oxidizing systems^{5–7} have led us to design vanadium(v) catalyst precursors which are highly soluble in organic media.

In order to test one of the most powerful precursors, the heteropolyacid with the Keggin structure, $H_5[PMo_{10}V_2O_{40}] \cdot 30–36H_2O$, belonging to the series $H_{3+n}[PMo_{12-n}V_nO_{40}] \cdot \gamma H_2O$ or 'HPA-*n*' (*n* = 1–6),⁶ we considered several ketones: cycloalkanones, 1-phenylalkanones, and simple ketones. Moderate to good conversions were obtained under very mild conditions. The heteropolyacids HPA-*n* were prepared by standard methods.⁸

The results, for the reaction of the cycloalkanones depicted in Scheme 1, are presented in Table 1.† Each was subjected to the same oxidation conditions [60 °C; $p(O_2) \approx 10^5$ Pa; MeCN; 2 or 6 h] with HPA-2. Treatment of 2,4-dimethylcyclopentanone (**1**) for 2 h (run 1) gives 5-oxo-3-methylhexanoic acid (**9**) in high yield (94%). 2,6-Dimethylcyclohexanone (**2**) produces mainly 6-oxo-2-methylheptanoic acid (**10**), also in good yield (89%) (run 2). Most notably, other α -substituted cyclohexanones yield a single major product: e.g. (run 3); 2-phenylcyclohexanone (**3**) gives 6-phenyl-6-oxo-hexanoic acid (**11**). One important feature emerges from these results: oxidative cleavage of the resulting ketoacids does not occur under these

conditions. The emphasis in these processes is on the selective synthesis of linear (substituted) products (Scheme 1). By-products were observed, but they were always produced in low yield. Moreover, the substrate/HPA-*n* ratio in the 140–160 range and the high conversion and high selectivity clearly indicate that the HPA-2 is acting as a catalyst and is more efficient than the $FeCl_3$ catalyst described by Ito *et al.*⁹

HPA-2 can be used also in the oxidation of 1-phenylalkanones (Table 2). The oxidative cleavage of 1-phenylpropan-1-one (**4**) (60 °C; 24 h) proceeds to the extent of only 43% to give benzoic (**12**) and acetic (**15**) acids (run 4). Evidence is found for the formation of acetaldehyde, but the yield of this product cannot be measured under our conditions. Other phenylalkanones are converted in high yield; for instance, at room temperature 2-phenylacetophenone (**5**) gives benzaldehyde (**13**) and benzoic acid (**12**) which is a product of the direct oxidative cleavage of the substrate, and also of the diphenyl-ethanedione formed as an intermediate, and of benzaldehyde co-oxidation (run 5). 2-Hydroxy-2-phenylacetophenone (**6**) reacts similarly, the conversion (run 6) reaching 95% only in ethanol; other solvents cause inhibition. Benzaldehyde (**13**) and ethyl benzoate (**14**) are the only isolated products. All results are compatible with Scheme 2.

Oxidative cleavage of open-chain ketones has been studied by several groups and usually produced the customary intractable mixtures.¹ Pentan-3-one (**7**) and 4,4-dimethylpentan-2-one (**8**) react with HPA-2 and dioxygen without organic solvent to afford the corresponding carboxylic acids but the yields under these conditions are moderate to low (Table 3; runs 7–8). Methyl *n*-alkyl ketones are also oxidized (conversion $\leq 10\%$).

In conclusion, we have demonstrated that cycloalkanones, 1-phenylalkanones, and alkyl ketones undergo oxidative cleavage. Other experiments show that the efficiency of

Table 1. Oxidation of cycloalkanones by HPA-2 and O_2 .^a

Run	Substrate (mmol)	HPA-2 (mmol)	% Conversion ^b	Product	% Yield ^c
1	(1) (4.0)	0.025	99	(9)	94
2	(2) (11.0)	0.075	91	(10)	89
3	(3) (2.4)	0.015	96	(11)	90

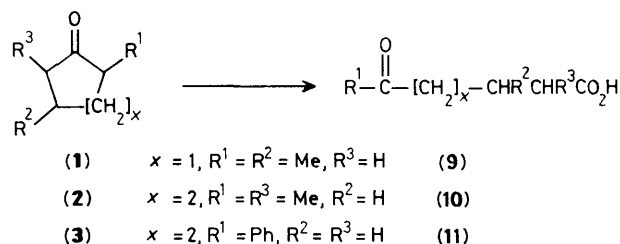
^a Reaction conditions: HPA-2 = $H_5[PMo_{10}V_2O_{40}] \cdot 30–36H_2O$; [HPA-2] $\approx 10^{-2}$ mol l⁻¹; solvent (MeCN): 2 cm³ (run 1) and 6 cm³ (runs 2 and 3); 60 °C; $p(O_2) \approx 10^5$ Pa; 2 h (run 1) and 6 h (runs 2 and 3).
^b % of substrate consumed. ^c Products analysed by coupled GC-MS (OV17 and OV105 columns); internal standard: heptanoic acid.

Table 2. Oxidation of 1-phenylalkanones by HPA-2 and O_2 .^a

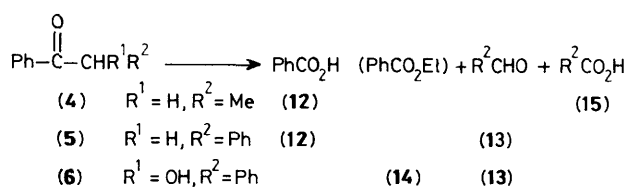
Run	Substrate (mmol)	HPA-2 (mmol)	Solvent (cm ³)	% Conversion ^a	Products (% Yields)
4	(4) (11.9)	0.2	MeCN (4.0)	43	(12) (40) (15) (32)
5	(5) (16.4)	0.2	MeCN (4.0)	86	(12) (102) (13) (41)
6	(6) (4.8)	0.05	EtOH (6.0)	95	(14) (91) (13) (93)

^a Reaction conditions: see Table 1; 60 °C, 24 h (run 4); 20 °C 6 h (runs 5 and 6); internal standard anisole.

† All compounds gave satisfactory ¹H n.m.r. spectra.



Scheme 1. Conditions: HPA-2, O_2 , 60 °C, MeCN.



Scheme 2. Conditions: HPA-2, O_2 , 20–60 °C, MeCN or EtOH.

Table 3. Oxidation of open-chain ketones^a by HPA-2 and O₂.

Run	Substrate (mmol)	HPA-2 (mmol)	% Conversion ^a	Products (% Yield)
7	Et ₂ CO (7) (9.45)	0.08	45	(15) (30) EtCO ₂ H (35)
8	Bu ^t CH ₂ COMe (8) (3.60)	0.05	42	(15) (16) Bu ^t CO ₂ H (20) Bu ^t CH ₂ CO ₂ H(20)

^a Reaction conditions: see Table 1; 60 °C, 24 h.

HPA-2 is related to the key role of vanadium(v) and to the large solubility of this 'acidic complex' in organic media. The results reported here may have potential application to more complex ketones as well as to other reaction types. It is noteworthy that aqueous acidic solutions of HPA-*n* (*n* = 4–6) have been used as cocatalysts in association with palladium(II) or rhodium(III) salts to oxidize unsaturated substrates to ketones.^{5,7} We believe that our observations set limits to the utility of these catalytic systems. Other substrates and complexes are being studied as are the mechanisms by which the reported processes take place.

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