Vanadium-catalysed Novel Oxidation of Arylacetic Esters for the Synthesis of Arylglyoxylic Esters†

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Direct synthesis of arylglyoxylic esters in excellent yields from inexpensive arylacetic esters is realised for the first time by the oxidation of activated methylene using vanadium pillared clay as the catalyst and *tert*-butylhydroperoxide as an oxidant.

Arylglyoxylic acids are important biosynthetic and synthetic precursors for several biologically active compounds such as α-amino acids and α-hydroxy acids.[1,2] Although the synthesis of arylglyoxylic acid is realised either by adopting the retrosynthetic route of the oxidation of α-amino acids,[3] and α-hydroxy acids[4] or the palladium-complex-catalysed double carbonylation of iodobenzene,[5] there is no direct methodology to obtain arylglyoxylic acids by the oxidation of arylacetic acids. The inherent disadvantages in these processes are the use of expensive starting materials, high pressures, or low yields.

The design and synthesis of the oxo-vanadium catalysts for biomimetic reactions is of current interest in view of the presence of vanadium in bromoperoxidase[6] and nitrogenase[7] enzymes. A recent report[8] of bromination of trimethoxybenzene possible by the liberated bromine obtained in the oxidation of bromides using hydrogen peroxide catalysed by dioxovanadium(v), an enzyme mimic of bromoperoxidase indicated a possible pathway for the biogenesis of halogenated marine natural products. In view of this, we have designed and attempted a direct oxidation of arylacetic esters to arylglyoxylic esters using vanadium as the catalyst. Here, we present the first simple and convenient method for direct oxidation of cheaply and readily available arylacetic esters to arylglyoxylic esters in excellent yields by vanadium pillared montmorillonite catalyst (V-PILC)[9] with *tert*-butylhydroperoxide (TBHP) as an oxidant (Scheme 1, Table 1). In addition, specific oxidation of methylene sandwiched between aryl and ester groups, in the presence of another methylene flanked by two phenyls in a specially designed and prepared substrate represents a remarkable example of selective catalysis (Table 1, entry 10).

Oxidation of methyl phenylacetate afforded 79% of methyl phenylglyoxylate (entry 1). It should be noted that the presence of electron-donating groups such as methoxy (entries 2 and 3), methyl (entry 4) and amino (entry 5) on the aromatic ring in arylacetic esters facilitates the oxidation reaction to

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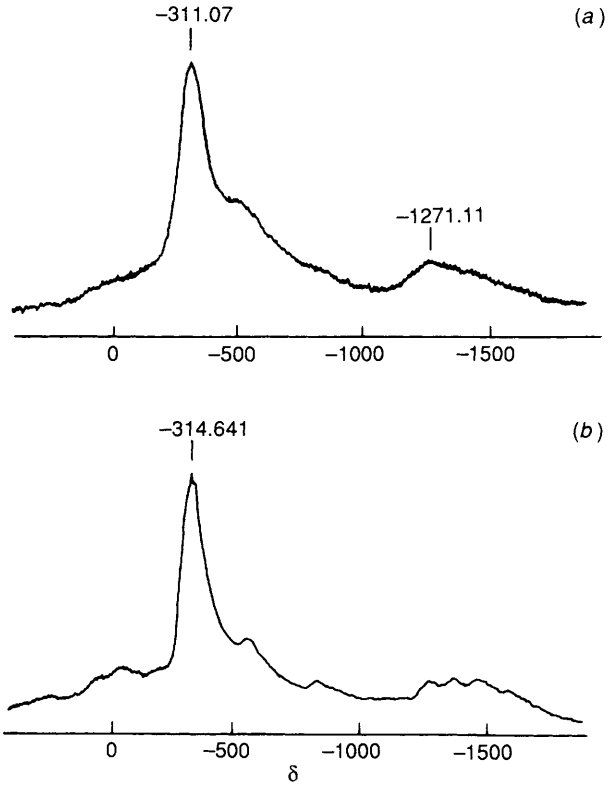
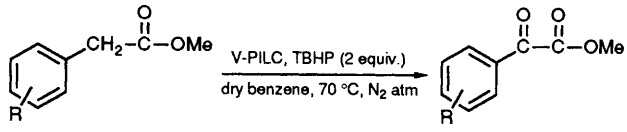


Fig. 1 Solid state ^{51}V NMR of (*a*) V-PILC (calcined) and (*b*) V_2O_5

Table 1 Selective oxidation of Ar–CH_2–C(O)–OMe to Ar–C(O)–C(O)–OMe

Entry	Substrate (Ar)	Reaction time/h	Isolated yield (%)
1	Ph	48	79
2	*o*-$MeOC_6H_4$	20	82
3	*p*-$MeOC_6H_4$	20	88
4	*p*-MeC_6H_4	48	76
5	*p*-$H_2NC_6H_4$	48	83[b]
6	*o*-$O_2NC_6H_4$	96	No reaction
7	*p*-$O_2NC_6H_4$	96	24
8	*o*-ClC_6H_4	48	71
9	*p*-ClC_6H_4	48	77
10	(*o*/*p*)-$PhCH_2$–C_6H_4	48	52

[a] All reactions were performed on 3 mmol substrate in 10 ml dry benzene using 75 mg of V-PILC (containing 0.1 mmol of vanadium) and 3 ml of azeotropically dried hydroperoxide (*ca.* 2.1 mol dm^{-3} in isooctane) at 70 °C under nitrogen atmosphere. [b] Reaction was carried out in dry methanol.



R = H, *p*-Me, *o*-MeO, *p*-MeO, *o*-NO_2, *p*-NO_2, *o*-Cl, *p*-Cl, *p*-NH_2, (*o*/*p*)-$PhCH_2$

Scheme 1 Oxidation of methyl arylacetate to methyl arylglyoxylate

afford arylglyoxylic esters in good yields, while the presence of electron-withdrawing groups such as nitro (entries 6 and 7) renders the reaction more difficult even on prolonged reaction time. *para*-Substituted substrates are found to give more α-keto ester than *ortho*-substituted ones. The reaction is very selective and specific towards the activated methylene sandwiched between aryl and ester group, unaffecting the substituents such as methyl and methoxy groups on aromatic ring. In the oxidation of ethylbenzene under similar conditions with V-PILC, the starting material was recovered as such even after 60 h. The inactivity of methylene in ethylbenzene prompted us to demonstrate specificity in the oxidation of methylene flanked by aryl and ester groups in the presence of methylene sandwiched in between two phenyl groups (entry 10). The reaction was applied for a variety of substrate systems such as methyl propionate, 4-chloro-2-methylphenoxyacetic ester and methyl hydrocinnamate as part of our study to understand the scope and applicability of the reaction, but the starting materials were recovered as such in each case.

V-PILC, both before and after calcination, was found to be effective for the oxidation of arylacetic esters to arylglyoxylic esters. Pillared clay before calcination composed of vanadium oxyhydroxy oligomer in its interlayer, which upon calcination at 400 °C formed polymeric V_2O_5 on dehydration. Solid state ^{51}V NMR spectroscopy (Fig. 1) of the calcined sample indicated the presence of pure crystalline V_2O_5, while the powder X-ray diffraction (XRD) showed retention of the basal expansion even upon calcination and thus thermal stability of the pillared clay catalyst.[9] V_2O_5/SiO_2 was also as effective as V-PILC under identical conditions in the oxidation reaction resulting in the formation of phenylglyoxylic ester. But, V_2O_5 was inactive under identical conditions. Thus, the enolate of the carboxylate, possibly formed owing to acidic sites of the support, chelated the vanadium and stabilised with the extended conjugation with aryl moiety. The chelated complex is thus vulnerable to facile oxidation by α-keto esters and responsible for the specific reactivity towards the activated methylene sandwiched between aryl and ester groups demonstrated here.

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