

## Wadsworth–Emmons reaction: the unique catalytic reaction by a solid base

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### Abstract

The near-stoichiometric amount of bases is used both in laboratory and industry in Wadsworth–Emmons (WE) reactions, since the by-product,  $(\text{EtO})_2\text{P}(\text{O})\text{OH}$ , formed in the reaction neutralizes the base into an inert salt. A strategy to design, develop, and evolve the recyclable Mg–Al–hydrotalcite– $\text{O}^t\text{Bu}$  (HT– $\text{O}^t\text{Bu}$ ) by the interaction of  $\text{KO}^t\text{Bu}$  with the calcined hydrotalcite that transforms a well-defined stoichiometric WE reaction into a catalytic one in an effort to minimize the quantum of effluents released and reduce the cost of the process is described here. HT– $\text{O}^t\text{Bu}$  is found to be an efficient solid base for WE reactions for the simple synthesis of  $\alpha$ ,  $\beta$ -unsaturated esters and nitriles for the first time. The HT– $\text{O}^t\text{Bu}$ , composed of various ratios of Mg/Al (i.e., 2, 2.5, and 3) and different contents of  $^t\text{BuO}^-$  (Mg/Al:3), and their precursors were prepared and well characterized to draw a correlation between structure and reactivity of the hydrotalcites in WE reactions.

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**Keywords:** Wadsworth–Emmons reaction; Hydrotalcite; Solid bases; Potassium *t*-butoxide

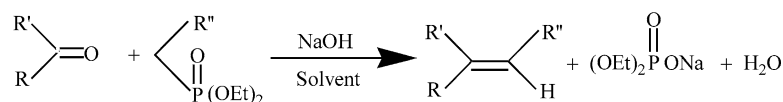
### 1. Introduction

The creativity and art of organic synthesis have reached an interesting phase of development, which aims to exert ultimate control over a chemical reaction to minimize pollution levels. With an ever-increasing level of global competition and environmental consciousness, there is an incentive to find new catalytic processes with higher atom utilization preferably close to theoretical values to eventually minimize pollution levels. Heterogeneous catalysis is particularly attractive because it allows the production and ready separation of large quantities of products using small amounts of catalysts. The versatile Wadsworth–Emmons reaction has numerous applications in the elegant synthesis of intermediates for fine chemicals such as perfumes, fragrances, analgesics, insecticides, carotenoids, pheromones, pharmaceuticals, and prostaglandins and is classically induced by bases under homogeneous conditions [1,2]. With

the inherent advantages such as the use of cheaper triethylphosphite as a starting material for the synthesis of phosphonate, easy separation of the water-soluble phosphate at the end of the reaction from the product, and faster reactivity of the phosphonate reagent, the Wadsworth–Emmons (WE) reaction has a greater scope of utility than the Wittig reaction. The condensation of an aldehyde or a ketone into an unsaturated nitrile or ester with a phosphonate is traditionally effected in the presence of strong soluble bases [3] such as KOH,  $\text{Ba}(\text{OH})_2$ , BuLi, and Triton B and NaH, KF,  $\text{Sn}(\text{OSO}_2\text{CF}_3)_2$ -*N*-ethylmorpholine,  $\text{K}_2\text{CO}_3$ -18crown-6,  $\text{KO}^t\text{Bu}$ , and NaOEt. There are a few reports available under the category of solid reagents [4] for WE reactions mediated particularly by KF/alumina, and MgO or ZnO. The problems encountered in the industrial application of these reactions include the generation of a large amount of effluents due to the use of equimolar amounts of base to the substrate and lower yields of the desired product arising due to moderate chemoselectivity prompted by the competing side reactions such as Knoevenagel or aldolisations. The base used in this condensation is transformed to an inert phosphonate salt during the reaction to render the

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Scheme 1. The Wadsworth–Emmons reaction using the soluble base.

process stoichiometric, while the use of incompatible basicity induces side reactions (Scheme 1). Design of a solid base to transform the WE reaction into a catalytic process that minimizes pollution levels offers a great challenge.

We believe that the hydroxalite (HT) [5] could be a material of choice for WE reactions in view of its specific properties as underlined. The structure of HT consists of brucite  $[\text{Mg}(\text{OH})_2]$ -type octahedral layers in which a part of the M(II) cations are isomorphously substituted by the M(III) cations. The excess positive charge of the octahedral layers resulting from this substitution is compensated by interstitial layers built of anions. These materials are represented by the general formula,  $[\text{M}(\text{II})_{(1-x)}\text{M}(\text{III})_x \cdot (\text{OH})_2]^{x+}[(\text{A}^{y-})_{x/y} \cdot n\text{H}_2\text{O}]^{x-}$ , where M(II) and M(III) are the divalent and trivalent cations, respectively,  $\text{A}^{y-}$  is the interlayer anion and the value of  $x$  is in the range of 0.1 to 0.33. The basicity and activity can be easily tuned up by choosing a set of hetero elements M(II)/M(III) and changing their ratio for brucite sheet, and/or by incorporating different anions in the interlayer of brucite from a pool of a wide range of multiple options [6]. The interesting characteristic of these materials is their anionic exchange ability, which makes them very useful as anion exchangers, adsorbents, and most importantly as catalysts. Upon thermal decomposition at about 723 K, HT transformed into a highly active homogeneous mixed-oxide phase for a variety of organic transformations [7]. The rehydrated HT [8] composed of hydroxyl anions displayed superior activity over the HTs composed of  $\text{Cl}^-$ ,  $\text{NO}_3^-$ , or  $\text{CO}_3^{2-}$  anions or calcined HTs. Later, we designed and developed the Mg–Al–HT– $\text{O}^t\text{Bu}$  (HT– $\text{O}^t\text{Bu}$ ), a solid base by an exchange of nitrate anion of HT with  $\text{KO}^t\text{Bu}$  for the first time in our laboratory that displayed manifold activity in various organic transformations [9]. The studies on the solid bases were hitherto confined to the improvement of the rate of the reaction for the established catalytic reactions.

In this paper, we devised a strategy to design, develop, and evolve the recyclable HT– $\text{O}^t\text{Bu}$  by the interaction of  $\text{KO}^t\text{Bu}$  with the calcined HT that transforms a well-defined stoichiometric Wadsworth–Emmons reaction into a catalytic one in an effort to minimize the quantum of effluents released and to reduce the cost of the process. We report the unique example of highly selective WE reactions in quantitative yields at a faster rate in the liquid phase using catalytic amounts of heterogeneous HT– $\text{O}^t\text{Bu}$  and also a correlation is drawn between the structure and the reactivity of the HT in transforming the stoichiometric reaction into a catalytic one for the first time.

## 2. Experimental

### 2.1. General

$\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ ,  $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ , and NaOH, purchased from Aldrich, and phosphonates, aldehydes, and  $\text{KO}^t\text{Bu}$ , purchased from Fluka, were used as such. All the other solvents (otherwise stated) and chemicals were obtained from commercial sources and used as such without further purification. Tetrahydrofuran (THF) and dimethylformamide (DMF) were distilled and dried by known procedures. All the reactions were conducted under an atmosphere of nitrogen. The workup of the catalysts was handled under nitrogen atmosphere in a glovebox. Proton nuclear magnetic resonance ( $^1\text{H}$  NMR) spectra were recorded on a Gemini Varian at 200 MHz, as solutions in  $\text{CDCl}_3$  at 298 K;  $\delta$  were in ppm down field from tetramethylsilane (TMS).  $^{27}\text{Al}$  MAS NMR was measured on a Gemini Varian at 400 MHz spectrometer using  $\text{Al}(\text{OH})_6^{3+}$  as reference. Mass spectra were obtained at an ionization potential of 70 eV, scanned on a VG 70-70H (micro mass). Infrared spectra were recorded on a Nicolet 740 FT-IR spectrometer either as neat liquids or KBr pellets. Thin-layer chromatography was performed on silica gel 60F<sub>254</sub> plates procured from E. Merck. ACME silica gel (60–120 mesh) was used for column chromatography. Thermogravimetric (TG), differential thermal analysis, and mass of the evolved gas during the thermal decomposition of catalyst were studied by means of a TG-DTA Mettler Toledo Star system and a Balzers thermostar GSD 300T, respectively, using open aluminum crucibles, containing samples weighing about 8–10 mg with a linear heating rate of  $10 \text{ K min}^{-1}$ . Nitrogen was used as a purge gas for all these measurements. X-ray powder diffraction (XRD) data were collected on a Siemens/D-5000 diffractometer using  $\text{Cu-K}\alpha$  radiation. The elemental analysis of the catalysts was determined by ICP mass and CHN analyzer on a Elementar Vario EL (Germany) instrument. The SEM (scanning electron microscopy) of the catalysts was done on a Hitachi SEM S-520, instrument. Isomer ratios (*E/Z*) were determined by  $^1\text{H}$  NMR spectroscopy. In case of nitriles only mixture of isomers were isolated. The yields were calculated based on the isolated product.

### 2.2. Preparation of catalysts

The preparation of HT– $\text{NO}_3$  (Mg/Al, 3/1) was based on a literature procedure [5]. HT– $\text{NO}_3$  was prepared in nitrogen atmosphere to avoid carbonation in air.  $\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$  (30.8 g, 0.12 mol) and  $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$  (15.0 g,

0.04 mol) were dissolved in deionized and decarbonated water (100 ml). The pH of the solution was adjusted to 10 by the addition of NaOH (2 M). The slurry was stirred for 2 h at room temperature, filtered, and then dried under vacuum at 353 K. HT-NO<sub>3</sub> (Mg/Al ratios, 2 and 2.5) were prepared similarly by taking appropriate ratios of Mg and Al nitrates.

### 2.3. HT-O<sup>t</sup>Bu: Using HT-NO<sub>3</sub> (cat. A)

HT-O<sup>t</sup>Bu was prepared from uncalcined HT-NO<sub>3</sub>. HT-NO<sub>3</sub> (1.214 g) was added to a solution of KO<sup>t</sup>Bu (0.1 M), prepared by dissolving KO<sup>t</sup>Bu (1.12 g, 10 mmol) in freshly dried THF (100 ml). The solution was stirred for 24 h in nitrogen atmosphere and then filtered under nitrogen. A white solid, HT-O<sup>t</sup>Bu (1.382 g), was obtained, which was washed with excess of THF (300 ml). <sup>t</sup>BuO<sup>-</sup> was exchanged to an extent of 7.6% as indicated by elemental analysis. All the catalysts were well dried under vacuum.

### 2.4. HT-O<sup>t</sup>Bu: using calcined HT (cat. B)

HT-NO<sub>3</sub> (Mg/Al, 3/1) was calcined at 723 K in a flow of air for 6 h (temperature raised 25 K min<sup>-1</sup>) and cooled to room temperature in a flow of dry nitrogen to obtain calcined HT. The calcined HT (1.214 g) was added to a solution of KO<sup>t</sup>Bu (0.1 M) prepared by dissolving KO<sup>t</sup>Bu (1.12 g, 10 mmol) in freshly dried THF (100 ml). The solution was stirred for 24 h in a nitrogen atmosphere and then filtered under nitrogen. A white solid, HT-O<sup>t</sup>Bu (cat. B, 1.432 g), which was obtained, was washed with excess of THF (300 ml admixed with 0.1% of decarbonated water). This protocol restores the partial layered structure of the HT. <sup>t</sup>BuO<sup>-</sup> was present to an extent of 7.4% as indicated by elemental analysis and rechecked with GC analysis of the desorbed anion. (To achieve economic viability, the mother liquor of the used KO<sup>t</sup>Bu solution could be recycled after adjusting its molar concentration in the preparation of cat. B.) Similarly, cat. B1 and B2 were prepared under similar conditions using 0.05 and 0.02 M KO<sup>t</sup>Bu solutions, respectively. The other HT catalysts comprising Mg/Al (2.5, 2) were also synthesized similarly by taking the appropriate calcined HT. The rehydrated HT-OH (cat. C) catalyst was obtained using a reported procedure [8b]. The HT-F (cat. D) catalyst was obtained using a reported procedure [6b].

### 2.5. KO<sup>t</sup>Bu impregnated on HT-NO<sub>3</sub>

A mixture of KO<sup>t</sup>Bu (0.011 g, 0.1 mmol) in THF (10 ml) and HT-NO<sub>3</sub> (100 mg) was stirred for 15 min and evaporated to dryness on rotavapor to give a solid, KO<sup>t</sup>Bu impregnated on HT-NO<sub>3</sub>.

### 2.6. General procedure for Wadsworth–Emmons reactions

In a two-necked glass flask were introduced dry DMF (10 ml), the carbonyl compound (1 mmol), and phospho-

nate (1 mmol). Then cat. B (Table 2, 0.025 g for 2a and 0.050 g for 2b, 2c, and 5) was charged and the mixture was refluxed under stirring to effect the condensation reaction of the carbonyl compound with phosphonate and the stirring was continued until the completion of the reaction, as monitored by thin-layer chromatography (TLC). After the completion of the reaction, the catalyst was filtered, water (10 ml × 4) was added to the filtrate, and then the final product of the reaction was extracted with ethyl acetate. The protocol involving addition of water followed by extraction with ethyl acetate is required to separate the by-product (EtO)<sub>2</sub>P(O)OH. The solvent was removed by rotavapor, and the crude product was purified by column chromatography using ethyl acetate/hexane (2/8) as an eluent.

### 2.7. Recycle studies

The reusability of the catalyst was carried out with 4-nitrobenzaldehyde and triethylphosphonoacetate in freshly distilled and dried DMF by adopting the following protocol under similar experimental conditions as described above. After the completion of reaction, the catalyst was allowed to settle and the supernatant solution was pumped out from the reaction flask. The catalyst was washed with dry DMF four times (4 × 10 ml), and allowed to settle and the supernatant DMF solution was pumped out. Fresh quantities of 4-nitrobenzaldehyde and triethylphosphonoacetate were introduced. The cat. B was thus reused for six cycles adopting the identical protocol.

## 3. Results and discussion

A detailed characterization of the HT-O<sup>t</sup>Bu (Mg/Al, 3/1) (cat. A and cat. B) in the WE reaction along with its precursors is provided here to draw a correlation between the structure and the reactivity of the HT.

### 3.1. Characterization of catalysts

Mg and Al and carbon contents of the samples were determined by inductively coupled plasma (ICP) analysis and CHN analyzer, respectively. The elemental analysis of the catalysts gives an Mg:Al ratio (2.83 for cat. A, 2.98 for cat. B), which is very close to the originally charged HT-NO<sub>3</sub> and calcined HT, respectively. Since this ratio does not vary upon exchange with <sup>t</sup>BuO<sup>-</sup> anion, it is suggested that no selective dissolution of metal (Mg or Al) takes place during the anion-exchange process [10].

### 3.2. Powder X-ray diffraction

The X-ray diffraction of the powder samples of cat. A and cat. B show a characteristic pattern of HT [11] (Fig. 1). The

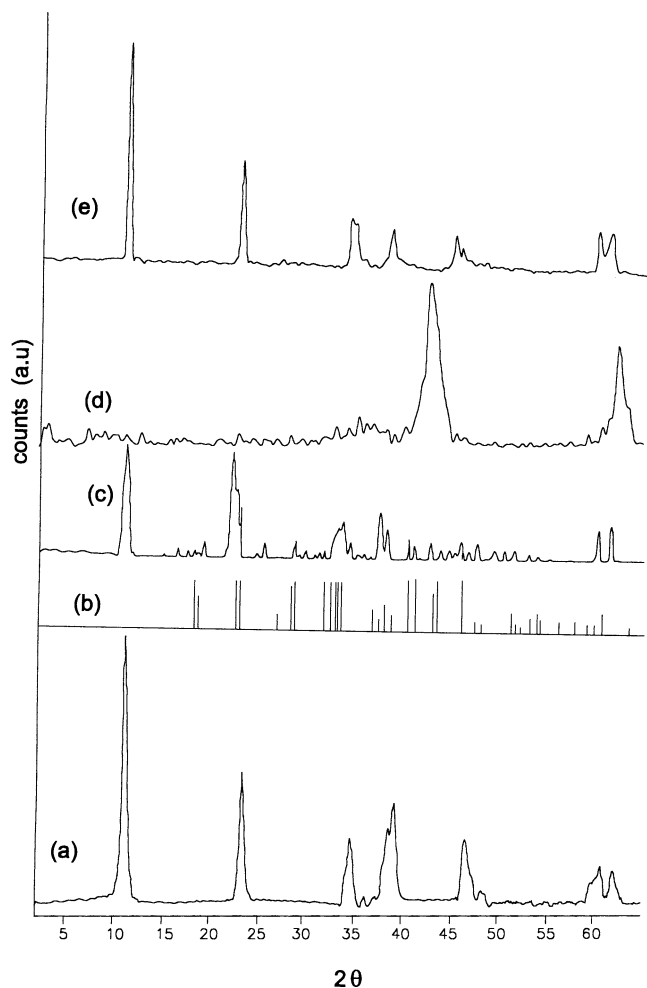


Fig. 1. X-ray powder-diffraction patterns of various hydrotalcite catalysts and  $\text{KNO}_3$ . (a) cat. **B**, (b)  $\text{KNO}_3$ , (c) cat. **A**, (d) calcined HT, (e)  $\text{HT-NO}_3$ .

X-ray powder diffraction patterns of the precursor HT material and the  $\text{HT-O}^t\text{Bu}$  (cat. **A** and cat. **B**) hardly differ in the range of  $2\theta = 3\text{--}65^\circ$ . The  $d_{003}$  reflection corresponds to the interlamellar distance plus the thickness of the mineral sheet (4.8 Å). In the case of  $\text{HT-NO}_3$ , cat. **A**, and cat. **B**, no change in the interlamellar distance is observed. Since no new phase is detected clearly in the XRD patterns, the intercalation must proceed inhomogeneously by local structural distortion of the layers, resulting in an irregular stacking of the individual layers within the crystal structure [10]. The XRD of cat. **A** shows other signals corresponding to  $\text{KNO}_3$  (Fig. 1b). The exchange of  $\text{NO}_3^-$  with  $^t\text{BuO}^-$  has thus been confirmed. The XRD pattern exhibits the impurity of  $\text{KNO}_3$  in cat. **A**, despite subjecting the catalyst to several washings with THF due to the insolubility of  $\text{KNO}_3$  in THF. In order to obtain a pure  $\text{HT-O}^t\text{Bu}$  (cat. **B**) devoid of  $\text{KNO}_3$  (Fig. 1b), calcined HT (723 K for 6 h in a flow of air) was used in place of  $\text{HT-NO}_3$  for the exchange of the  $^t\text{BuO}^-$  in THF. The regain of HT structure upon exchange of  $^t\text{BuO}^-$  on calcined HT is due to the hydration caused by the admixed water in THF solvent. The memory effect of HT is the well-accepted phenomenon in the HT chemistry [5a].

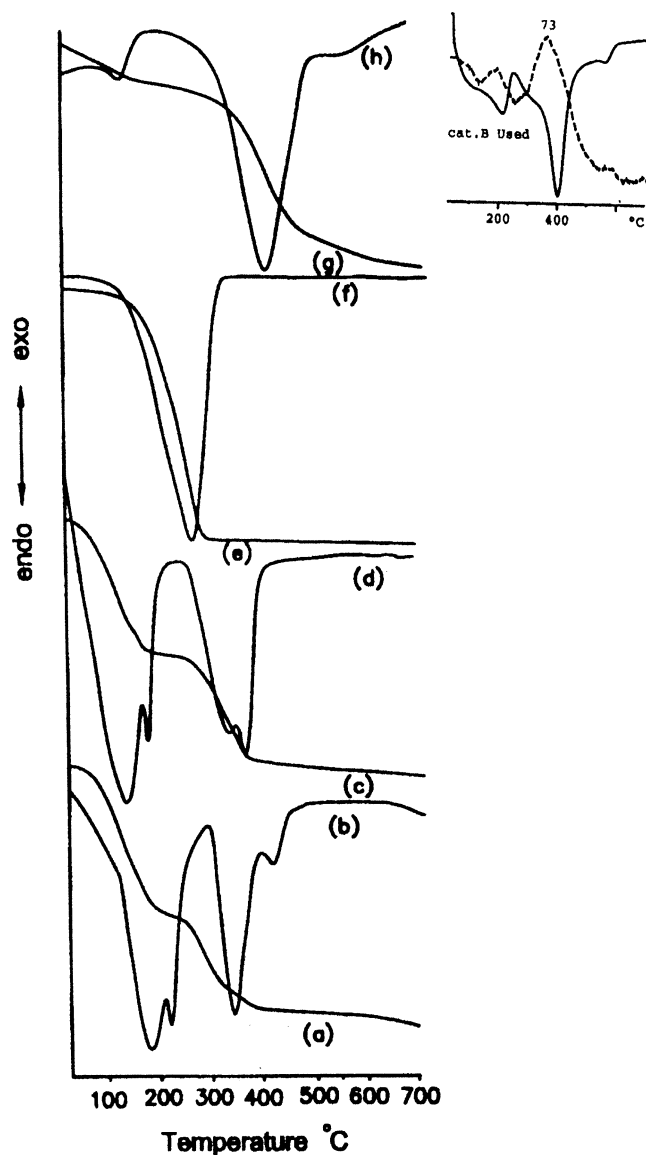


Fig. 2. TGA and DTA of various HT catalysts and their precursors. (a) TGA of cat. **A**, (b) DTA of cat. **A**, (c) TGA of cat. **B**, (d) DTA of cat. **B**, (e) TGA of  $\text{KO}^t\text{Bu}$ , (f) DTA of  $\text{KO}^t\text{Bu}$ , (g) TGA of  $\text{HT-NO}_3$ , (h) DTA of  $\text{HT-NO}_3$ . (The inset of the figure shows DTA-MS of the used cat. **B**.)

### 3.3. Thermal analysis

The profiles of thermogravimetric analysis and corresponding DTA of the samples (cat. **A**, **B**,  $\text{HT-NO}_3$ , calcined HT, and  $\text{KO}^t\text{Bu}$ ) are shown in Fig. 2. The DTA curves of all the HT samples resemble the hydrotalcite pattern as reported in the literature [5a]. The first endotherm of DTA below  $\sim 513$  K corresponds to the release of surface (physically absorbed) and interlayer water of the brucite. The second set of endotherm between 593 and 853 K is attributed to the structural dehydroxylation and decomposition of brucite layers. The loss of water for cat. **B** as is evident from DTA-MS is due to the hydration caused by the admixed water in THF solvent. In general, the weight loss around 743 K, that is, above the inflection point in the TG curves, may be

assigned to the elimination of  $\text{NO}_3^-$ . The DTA of a pure  $\text{KO}^t\text{Bu}$  shows a sharp curve at 559 K (Fig. 2f) is owing to its decomposition. The thermal decomposition experiments demonstrated that the decomposition of  $^t\text{BuO}^-$  anions is shifted to 604 K in cat. **A** and cat. **B** to indicate that the electrostatic interaction between  $^t\text{BuO}^-$  and positively charged brucite layer is stronger. The DTA-MS of cat. **A**, cat. **B**, and used catalyst show a loss of pyrolysis product ( $m/z$  73 amu) corresponding to the  $^t\text{BuO}^-$ . (The inset of the Fig. 2 shows DTA-MS of the used cat. **B**.)

### 3.4. FT-IR spectroscopy

The cat. **A** and cat. **B** were studied by FT-infrared spectroscopy to probe structural modifications before and after the anion-exchange process and are represented in Fig. 3. The cat. **A** and cat. **B** exhibit similar absorption bands at 1448 and 1388 and 1447 and 1385  $\text{cm}^{-1}$ , which are very close to that of the homogeneous analogue ( $\text{KO}^t\text{Bu}$ ) (Fig. 3d). These two absorption bands are assigned to the symmetric and asymmetric vibrations of a *tert*-butyl group. The molecular vibration of  $\text{NO}_3^-$  anion in cat. **A** (Fig. 3b), which is observed around 1384  $\text{cm}^{-1}$ , is very close to the value in the literature (1385  $\text{cm}^{-1}$ ). It can also be seen that

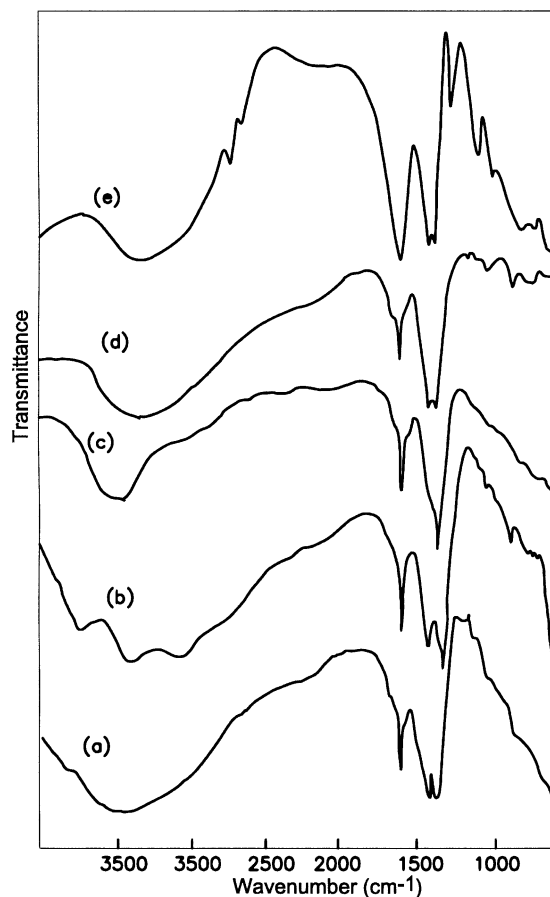


Fig. 3. FT-IR spectra of various hydrotalcite catalysts and their precursors. (a) cat. **B**, (b) cat. **A**, (c)  $\text{HT-NO}_3$ , (d)  $\text{KO}^t\text{Bu}$ , (e) used cat. **B**.

the cat. **A**, obtained from uncalcined  $\text{HT-NO}_3$  (Fig. 3c) via a simple exchange process, shows the peak at 1385  $\text{cm}^{-1}$  in elongated form to indicate the presence of unexchanged nitrates too. There is no such projection for the cat. **B** (Fig. 3a), since it is devoid of  $\text{NO}_3^-$ . The IR spectra showed strong absorption bands in the range 3400–3600  $\text{cm}^{-1}$  due to the hydroxyl (OH)-stretching vibration, and the corresponding deformation mode appeared around 1630  $\text{cm}^{-1}$  in all the samples of HT [12].

### 3.5. $^{27}\text{Al}$ MAS NMR studies

To understand in depth the change in coordination of Al during the exchange process, a solid-state  $^{27}\text{Al}$  MAS NMR study of the  $\text{HT-NO}_3$ , calcined HT, cat. **A**, and cat. **B** was undertaken. The  $^{27}\text{Al}$  MAS NMR of cat. **A** (Fig. 4b) and its precursor,  $\text{HT-NO}_3$  (Fig. 4d), show a single peak at  $\delta$  7 and 9 ppm, respectively, to indicate the presence of octahedral aluminum only, while cat. **B** (Fig. 4a) and its calcined precursor (Fig. 4c) exhibit two peaks centered at  $\delta$  7 and 69, 8 and 68 ppm, respectively, corresponding to both tetrahedral and octahedral Al. During the calcination, the  $\text{Al}^{3+}$  cations adopt a tetrahedral coordination due to dehydration [13].

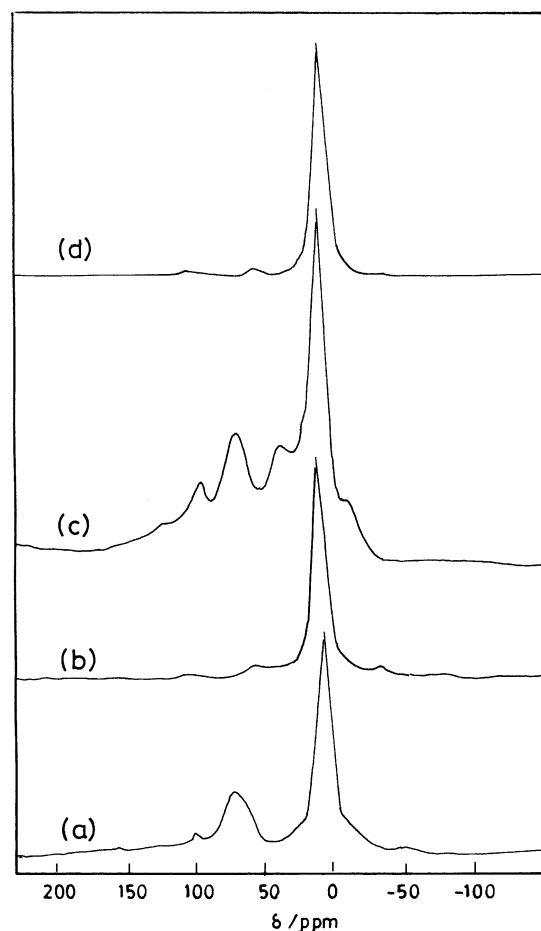


Fig. 4.  $^{27}\text{Al}$  MAS NMR spectra of various HT catalysts and their precursors. (a) cat. **B**, (b) cat. **A**, (c) calcined HT, (d)  $\text{HT-NO}_3$ .

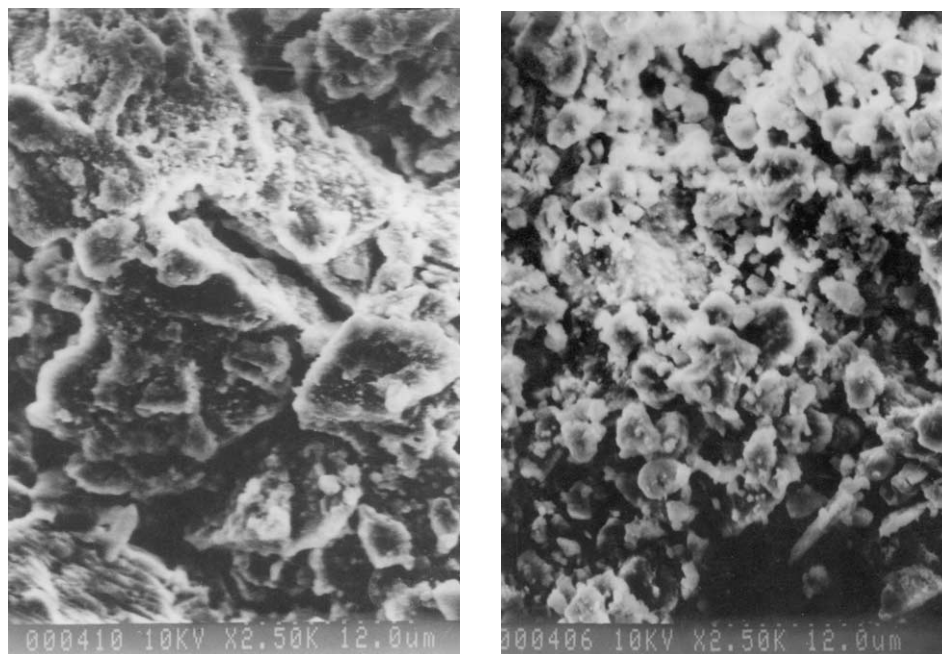


Fig. 5. Scanning electron micrographs of hydrotalcite catalysts. (a) cat. **A**, (b) cat. **B**.

### 3.6. Scanning electron microscopy

The cat. **A** and cat. **B** were subjected to scanning electron microscopy. The cat. **A** and cat. **B** samples are seen as agglomerates of platelets (Fig. 5).

### 3.7. HT-O<sup>t</sup>Bu for WE reaction

The HTs composed of various ratios of Mg/Al (i.e., 2, 2.5, and 3), different anions (i.e., OH<sup>-</sup>, F<sup>-</sup>, NO<sub>3</sub><sup>-</sup>, <sup>t</sup>BuO<sup>-</sup>), and different contents of <sup>t</sup>BuO<sup>-</sup> were evaluated in the WE reaction of 2-methoxybenzaldehyde with diethylcyanomethylphosphonate to 2-methoxycinnamitrile in DMF under reflux in an effort to develop the best catalyst system and the results are summarized in Table 1. The HTs (Mg/Al, 1/3) composed of <sup>t</sup>BuO<sup>-</sup> anions are found in general to be the superior catalysts in WE reactions. On the other hand, the reactions conducted with other HTs, comprising various anions such as NO<sub>3</sub><sup>-</sup>, OH<sup>-</sup>, and F<sup>-</sup> [6b], show poor activity. The catalytic activity of HTs comprising different anions is in the order of <sup>t</sup>BuO<sup>-</sup> ≫ OH<sup>-</sup> > F<sup>-</sup>, which is in consonance with the basicity of the anions. Despite the increased basic magnesium content, the activity in the WE reaction using HT-O<sup>t</sup>Bu (Mg/Al, 3/1) is slightly enhanced (Table 1 entries 2–4). Fig. 6 shows that the yield of the product is proportional to the content of <sup>t</sup>BuO<sup>-</sup> in the hydrotalcite. These results unambiguously demonstrate that the <sup>t</sup>BuO<sup>-</sup> anion is the sole contributory factor for activity in the WE reaction and rules out any diffusion. Further, the cat. **B** obtained from calcined HT exhibits higher activity over cat. **A** prepared from uncalcined hydrotalcite. The HT-NO<sub>3</sub>, the precursor for cat. **A**, is essentially inactive and the calcined HT, the precursor for cat. **B**, affords 5% of the prod-

Table 1

The catalytic Wadsworth–Emmons reaction between 2-methoxybenzaldehyde and diethylcyanomethylphosphonate using various HT catalysts and some homogeneous analogues<sup>a</sup>

Entry	Catalyst	Yield <sup>b</sup>
1	HT-O <sup>t</sup> Bu (3:1) (cat. <b>A</b> ) [7.6] <sup>c</sup>	92
2	HT-O <sup>t</sup> Bu (3:1) (cat. <b>B</b> ) [7.4]	96
3	HT-O <sup>t</sup> Bu (2.5:1) [7.5]	93
4	HT-O <sup>t</sup> Bu (2:1) [7.5]	92
5	Calcined HT	5
6	HT-OH (rehydrated) (cat. <b>C</b> )	18
7	HT-F (cat. <b>D</b> )	16
8	HT-NO <sub>3</sub>	NR <sup>d</sup>
9	KOH	18
10	NaOH	20
11	K <sub>2</sub> CO <sub>3</sub>	18
12	KF	17
13	KO <sup>t</sup> Bu	21
14	KO <sup>t</sup> Bu impregnated on hydrotalcite	30 <sup>e</sup>

<sup>a</sup> All reactions were carried out at 4 mmol scale and cat. **B** (100 mg, 0.1 mmol of <sup>t</sup>BuO<sup>-</sup>), 20 ml of DMF under reflux, and stirring for 2 h and work-up was carried out as detailed under Experimental; in case of HTs and soluble bases, HT (100 mg) or soluble base (0.1 mmol) was charged in place of cat. **B**.

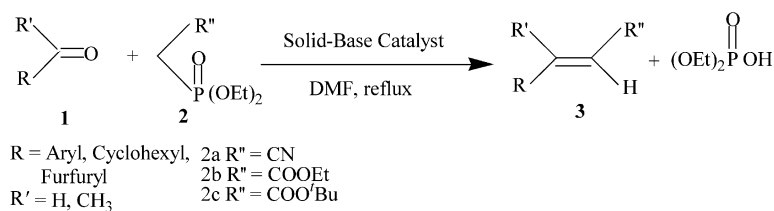
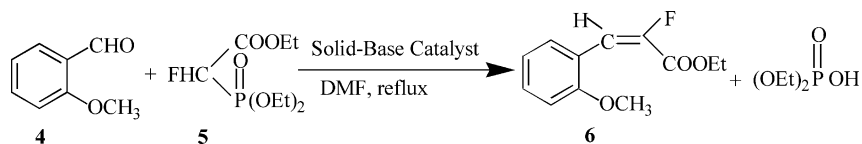
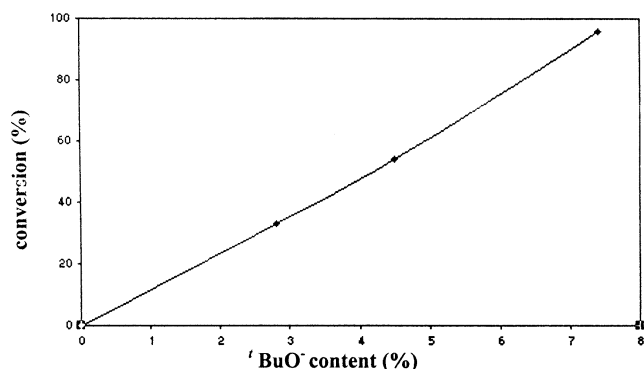
<sup>b</sup> Isolated yields.

<sup>c</sup> The values in the parentheses indicate the wt% of <sup>t</sup>BuO<sup>-</sup>.

<sup>d</sup> No reaction.

<sup>e</sup> 100 mg of HT impregnated with KO<sup>t</sup>Bu.

uct (Table 1, entries 5 and 8). Therefore, the contribution of HT matrix for the activity is insignificant, which reinforces the above hypothesis. Further, the efficacy of the <sup>t</sup>BuO<sup>-</sup> exchanged on cat. **A** and **B** is well demonstrated, when compared with the relatively poor yields obtained using the hydrotalcite impregnated with KO<sup>t</sup>Bu (Table 1, entry 14). The yields obtained with the various soluble bases such as KOH,

Scheme 2. The Wadsworth–Emmons reaction catalyzed by HT- $\text{O}^t\text{Bu}$  (cat. **B**).Scheme 3. The Wadsworth–Emmons reaction of 2-methoxybenzaldehyde with triethyl-2-fluoro-2-phosphonoacetate catalyzed by HT- $\text{O}^t\text{Bu}$  (cat. **B**).Fig. 6. WE reaction of 2-methoxybenzaldehyde with diethylcyanomethylphosphonate using varying  $t\text{BuO}^-$  contents on HT.

NaOH,  $\text{K}_2\text{CO}_3$ , KF, and  $\text{KO}^t\text{Bu}$  are 18, 20, 18, 17, and 21%, respectively, as against 92 and 96% with cat. **A** and **B**, respectively. It is thus unambiguously established that the nearly stoichiometric molar amount of soluble base to the substrate is required, while a catalytic amount of solid base (cat. **A** or **B**) is adequate for the accomplishment of the reaction. Low yields  $\sim 23\%$  were obtained using cat. **B**, when methanol was used as a solvent in place of DMF.

Buoyed with these results that established superiority of cat. **B**, we further carried out WE reactions with a variety of substrates in order to extend the scope of the reaction using cat. **B** (Scheme 2, Table 2). The novelty of the process is that the WE reaction can be made truly catalytic, selective, and very effective for aldehydes. No by-product prompted by aldolisation or Knoevenagel is noted. Secondary reactions are unfavored because the most acidic compound (the phosphonate) occupies the surface, so that there is no possibility for the activation of the aldehyde. However, the reactions with the ketones exhibit poor yields or no reaction (Table 2, entries 18 and 19). The interaction of carbonyls with phosphonates provides  $\alpha, \beta$ -unsaturated nitriles and esters with similar stereoselectivities as obtained using  $\text{KO}^t\text{Bu}$  under similar conditions [3]. The condensa-

Table 2

The Wadsworth–Emmons reaction of carbonyl compounds with various phosphonates catalyzed by HT- $\text{O}^t\text{Bu}$  (cat. **B**)

Entry	Carbonyl compound <i>R</i>	<i>R</i> '	Phosphonate (2)	Time (h)	Isolated yield ( <i>E/Z</i> ) <sup>a</sup> (3)
1	$\text{C}_6\text{H}_5$	H	2a	2.0	96 (75/25)
2	$\text{C}_6\text{H}_5$	H	2b	2.5	76 (99/1)
3	$\text{C}_6\text{H}_5$	H	2c	2.0	61 (94/6)
4	<i>o</i> - $\text{OMeC}_6\text{H}_4$	H	2a	2.0	96 (74/26)
5	<i>o</i> - $\text{OMeC}_6\text{H}_4$	H	2b	2.5	62 (99/1)
6	<i>p</i> - $\text{ClC}_6\text{H}_4$	H	2a	2.5	93 (55/45)
7	<i>p</i> - $\text{ClC}_6\text{H}_4$	H	2b	3.0	98 (99/1)
8	<i>p</i> - $\text{NO}_2\text{C}_6\text{H}_4$	H	2a	2.0	98 (78/22) 92 (76/24) <sup>c</sup>
9	<i>p</i> - $\text{NO}_2\text{C}_6\text{H}_4$	H	2b	2.5	90 (99/1)
10	$\text{C}_4\text{H}_3\text{O}$	H	2a	1.5	98 (75/25)
11	$\text{C}_4\text{H}_3\text{O}$	H	2b	2.0	86 (99/1)
12	$-\text{C}_6\text{H}_{11}-$	H	2a	2.5	95 (96/4)
13	$-\text{C}_6\text{H}_{11}-$	H	2b	3.0	80 (99/1)
14	$\text{C}_6\text{H}_4\text{CH}=\text{CHCH}_2$	H	2a	2.5	88 (66/34)
15	$\text{C}_6\text{H}_4\text{CH}=\text{CHCH}_2$	H	2b	3.0	50 (99/1)
16	$-\text{C}_5\text{H}_{10}-$	H	2a	2.5	98
17	$-\text{C}_5\text{H}_{10}-$	H	2b	3.0	90
18	$\text{C}_6\text{H}_5$	$\text{CH}_3$	2a	6.0	27 (67/33)
19	$\text{C}_6\text{H}_5$	$\text{CH}_3$	2b	10.0	NR <sup>b</sup>
20	<i>o</i> - $\text{OMeC}_6\text{H}_4$	H	5	3.5	90 (1/99) (6)

<sup>a</sup> All the reactions were carried out at 1 mmol scale; all products are known compounds and their spectra (NMR, mass, and IR) are in accordance with literature values; isomer distribution was determined by using  $^1\text{H}$  NMR spectroscopy.

<sup>b</sup> No reaction.

<sup>c</sup> Using cat. **A**.

tion of carbonyl compounds with triethylphosphonoacetate or *t*-butyl diethylphosphonoacetate offers *E:Z* ratios of near  $> 99$  under optimized conditions, whereas the diethylcyanomethylphosphonate gives a 75:25 to 50:50 ratio. The increase in *Z* isomer in the latter case is attributed to the lesser steric requirement of the linear cyano group [2a,2b]. No reaction occurred when the reaction was conducted with the filtrate of solid base treated with DMF, indicating that the active ingredient was not leached from the solid catalyst.

The reaction between 4-chlorobenzaldehyde and diethylcyanomethylphosphonate was carried out at 10 mmol scale, which gave near retention of stereo chemistry (Table 2, entry 6) under present reaction conditions.

The synthesis of ethyl 2-fluoro-3-(2-methoxyphenyl)-2-propenoate, a useful class of intermediate compound (**6**) in the synthesis of several biologically active fluorinated molecules such as retinoids, insect sex pheromones, and pyrethroids [3t,14], is also realized using the cat. **B** (Scheme 3, Table 2, entry 20).

The WE reaction indeed requires the use of molar quantities of soluble bases, since the base is neutralized with the by-product,  $(\text{EtO})_2\text{P}(\text{O})\text{OH}$ , to form inactive phosphonate salt. In order to devise a catalytic reaction, it is necessary to protect the used base from the neutralization with the generated phosphonic acid by-product during the reaction. HTs are basic in nature and the anions of HTs are highly ionized. The exchangeability with various anions is pH dependent. The IR (Fig. 3e) and DTA-MS (inset of Fig. 2) of the used catalyst show the retention of  $t\text{BuO}^-$  even after reaction, when the WE reaction was conducted in DMF. This result suggests that the pH 12.2–10.8 of the reaction medium noted during the reaction disallows the neutralization of  $\text{HT-O}^t\text{Bu}$  with the  $(\text{EtO})_2\text{P}(\text{O})\text{OH}$ . The neutralization could otherwise have made the catalyst inactive. This is indeed observed, when a separate reaction is conducted in methanol (at lower pH), which affords poor yields. These results are in consonance with the earlier observation that the exchange of phenylphosphonic acid with the intercalated nitrate of HT takes place at pH 6.5 to 7 [15].

The recyclability of cat. **A** and **B** was checked with 4-nitrobenzaldehyde and diethylcyanomethylphosphonate in freshly distilled and dried DMF (Table 2, entry 8, Fig. 7). The cat. **A** is deactivated faster, as is evident even in the second cycle (11%). The cat. **B** exhibits consistent activity and selectivity for three cycles and thereon the catalyst is slowly deactivated due to ingress of moisture of the air during recycle studies. The cat. **B** thus achieves high turnover number (TON)  $\cong 36$  for each cycle up to three cycles calculated based on the  $t\text{BuO}^-$  content (7.4%) of the solid catalyst and the total TON for all the 6 cycles amounts to  $\cong 182$ . The presence of tetrahedral Al in cat. **B** as is evident from NMR confirms that structurally it is more defective than the cat. **A** and also partially hydrated during exchange of  $t\text{BuO}^-$ . It is known that the calcined HT, a precursor for cat. **B**, which develops tetrahedral Al sites due to dehydration, has smaller crystallites and eventually larger surface area than the uncalcined HT [16]. The direct determination of the surface area for cat. **A** and **B** is difficult as the samples will undergo modification during the measurement. SEM analysis also reveals very different morphology of the samples with larger aggregates for cat. **A**. When a separate experiment was conducted introducing water (3 ml) into the reaction mixture, there was no reaction. This has substantiated the poisoning effect of water on the reaction. As the moisture is causing the deactivation, cat. **A** with the larger crystallites is deactivated faster

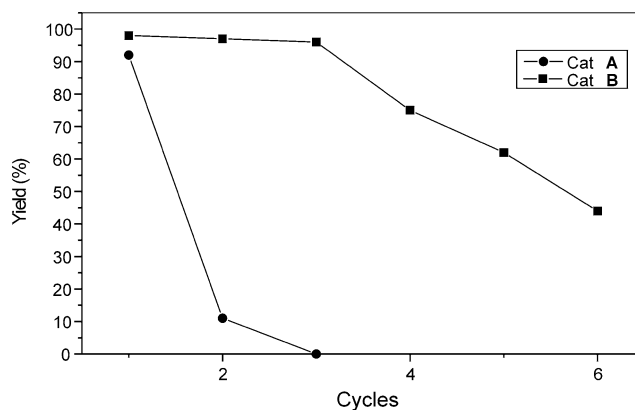


Fig. 7. Yields of 4-nitrocinnamitrile obtained in the multiple uses of cat. **A** and **B** in the Wadsworth–Emmons reaction of 4-nitrobenzaldehyde with diethylcyanomethylphosphonate.

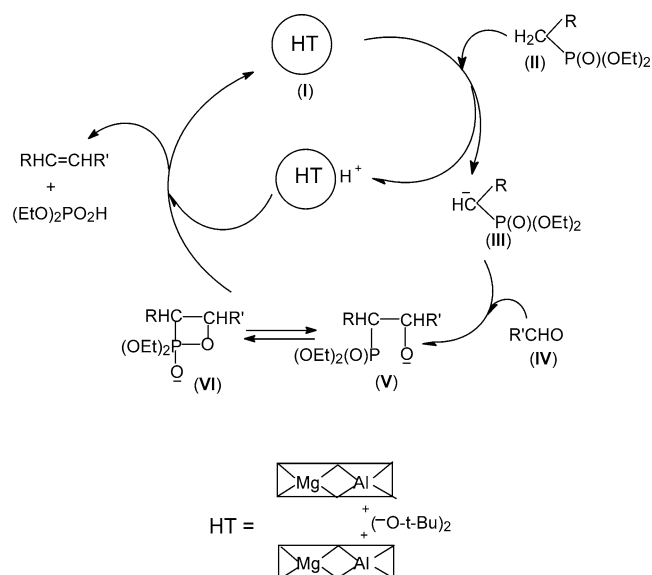
than cat. **B**. The larger surface area of cat. **B** retards the effect of poisoning. The display of higher activity and sustained recyclability by cat. **B** is ascribed to the smaller crystallites and larger surface area. This is in consonance with the observations made by Roelofs et al. [16a]. Hence, the highly reactive basic anion of the HT, adequately robust enough from deactivation with the  $(\text{EtO})_2\text{P}(\text{O})\text{OH}$ , is responsible for the origin and exposition of the sustained catalytic activity to achieve the high turnover number. All these results demonstrate that the WE reactions could be conducted with high atom utilization using solid base catalyst rather than soluble bases, which require near-stoichiometric quantities.

Although several proposals have been advanced based on the number of detailed mechanistic studies undertaken, the reaction mechanism of the WE reaction with soluble bases involving the reaction of phosphonate carbanions with aldehydes has not been fully established. The plausible mechanism for the WE reaction employing cat. **B** is likely to proceed in an almost identical path to the one observed in the soluble bases [2a,3a] since the ratio of the stereoisomers formed is the same in the both cases. The cat. **B** (**I**) abstracts the proton of the phosphonate (**II**) to form a phosphonate carbanion (**III**) as suggested in Scheme 4. The carbanion complex reacts with a carbonyl compound (**IV**) to form a betain anion (**V**) and then transforms into oxophosphetane anion (**VI**). The complex (**VI**) on interaction with the proton affords olefin and  $(\text{EtO})_2\text{P}(\text{O})\text{OH}$ . The regenerated cat. **B** (**I**) participates in another TON of the reaction.

#### 4. Conclusions

Thus, the display of unprecedented catalytic activity in the WE reaction using the  $\text{HT-O}^t\text{Bu}$  will find wider applications in both laboratory and industry for the preparation of  $\alpha, \beta$ -unsaturated nitriles or esters. The  $t\text{BuO}^-$  is found to be the sole contributory factor for activity in the WE reaction. The pH-dependent exchange property, the inherent characteristic of HTs, disallows the neutralization of  $\text{HT-O}^t\text{Bu}$





Scheme 4. The plausible mechanism for the Wadsworth–Emmons reaction catalyzed by HT–O<sup>t</sup>Bu (cat. **B**).

with the (EtO)<sub>2</sub>P(O)OH to manifest the catalytic activity. The higher activity and turnover number displayed by the cat. **B** is ascribed to the smaller crystallites and high surface area. All these results demonstrate that the WE reactions could be conducted with high atom utilization using solid base catalysts rather than soluble bases, which require near-stoichiometric quantities.

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