

MICROWAVE INDUCED REACTION OF H-DIMETHYLPHOSPHONATE WITH STYRENE OXIDE

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ABSTRACT

The reaction of a neat mixture of styrene oxide and H-dimethyl-phosphonate under microwave catalysis and without any solvent for six minutes furnished a complex mixture containing dimethyl methylphosphonate, trimethylphosphate, phenylacetaldehyde, 1-methoxy-2-phenylethanol, 1-phenylethleneglycol, cis- and trans-1, 3-diphenylcyclobutanes, hydrogen 1-(2-phenylethyl)methylphosphinate, (1-phenylethyl)dimethylphosphonate and (1-phenylethyl)-dimethylphosphonate via free radical processes. The mechanism of formation of the said compounds and their GC-MS characterization are described herein.

INTRODUCTION

Oxiranes comprise an extremely versatile group of intermediates and as such have attracted considerable attention [1]. Because of their ready availability and exceptional reactivity, the epoxides have found varied applications as a versatile functional group in synthetic organic chemistry. The oxirane ring can be opened under almost all conditions: electrophilic, nucleophilic, neutral, gas-phase, thermal and free radical conditions (Fig. 1) [1a]. An excellent review on the preparation and synthetic applications of the oxiranes has appeared [1f]. Recently we investigated the free radical cleavage of styrene oxide with trifluoromethylthiocopper and reported the formation of products arising from the C – C and C – O bond fission [2]. However, their reaction with phosphorus compounds has found only a limited application including their routine use in the Michaelis-Becker reaction to prepare phosphinates [3, 4]. Tri-coordinated pentavalent phosphorus compounds or *in situ* generated intermediates have been found to react with oxiranes [3, 4]. Thus, phosphorus azide reacted with propylene oxide to furnish cyclic oxazaphoranes as well as acyclic compounds [5]. Also, the *in situ* formed highly reactive metaphosphates have been described to open the oxirane ring to yield isomeric 1, 3, 2-dioxaphospholane-2-oxide derivatives [6].

The *in situ* generated electrical energy from microwaves has been used to thermally catalyze chemical reactions. This type of energy transformation depends on the molecular properties of the reacting chemicals [7]. Since the advent of commercially available microwave cookers, the microwave thermal process is finding increasing and interesting applications in synthetic organic chemistry [8]. The popularity of the microwave-induced chemistry appears to rest primarily on

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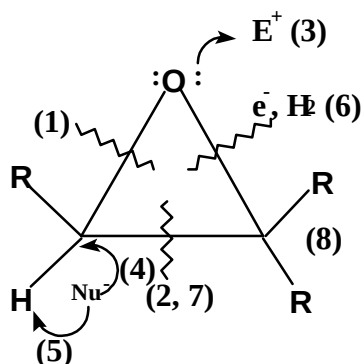


Figure 1. Types of Oxirane Cleavages and Reactions.

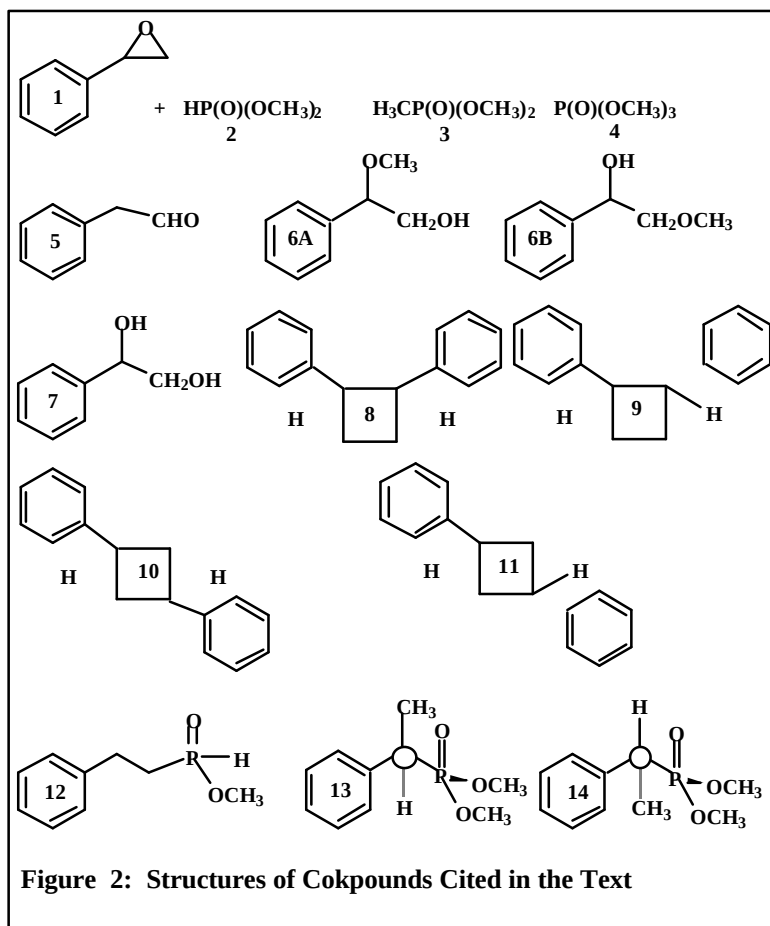
- (1, 2) Homolytic cleavages (free radical, photolytic, thermal)
- (3) Electrophilic attack on the ring oxygen
- (4) Nucleophilic attack on the ring carbon
- (5) Nucleophilic attack on the ring hydrogen
- (6) Reactions with electrons and surface reactions
- (7) Cycloadditions
- (8) Reactions of the substituent

its dramatic reduction of the reaction time and the possibility of carrying out neat reactions in “dry media” (solid phase). In fact, the latter appears to have significantly contributed to its enhanced usage [9]. The use of dielectric solvents seems to facilitate the transfer of the *in situ* generated thermal energy to chemical reactants [9b]. We became interested in adopting microwave chemistry for two reasons, namely the possibility of micro-scale chemistry and elimination of the hazardous waste thus generated during the normal work-up and its consequent disposal problems. In continuation of our interest in the chemistry of the oxirane cleavage reactions [10], the microwave catalyzed oxirane ring opening in the presence of hydrogen dimethylphosphonate has been examined and observed to lead to the formation of unusual products. This paper describes the probable mechanism of the formation of the novel compounds formed during the said reaction and their GC-MS characterization.

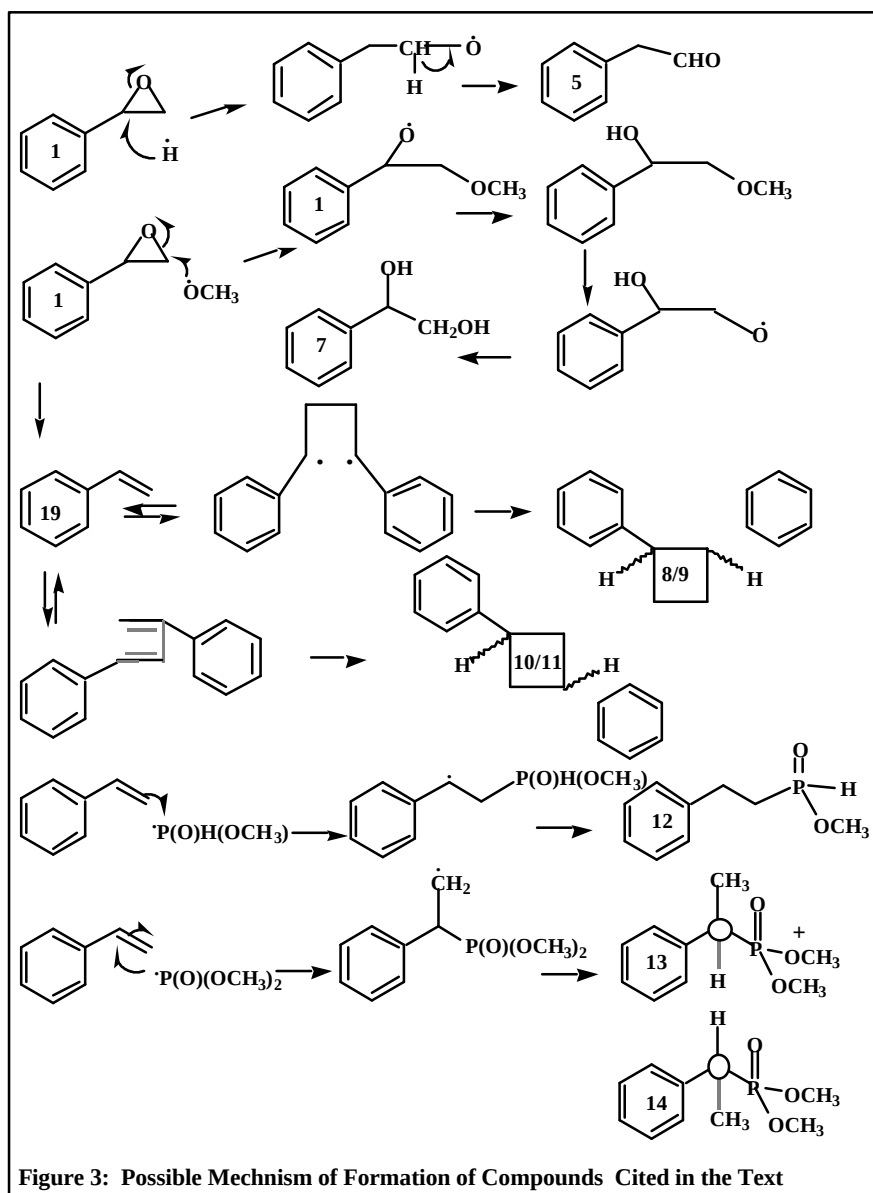
RESULTS AND DISCUSSION

Recently, H-phosphonates have attracted considerable attention and have found useful applications in phosphorylation reactions [11]. Microwave induced reaction of styrene oxide (1) with hydrogen dimethylphosphonate (2) has been found to furnish ten compounds excluding the starting materials (**Fig. 2**). Hydrogen dimethylphosphonate (2) itself gives two compounds, namely trimethylphosphonate (3) and trimethylphosphate (4). There is nothing unusual about this, for these compounds are usually formed during the oxidation and/ or free radical reaction of hydrogen dimethylphosphonate (2). The presence of the readily removable hydrogen at the phosphorus center of the H-phosphonates appears to be the genesis of its reactivity [12]. Among other things, H-phosphonates are known to be involved in the addition to: (i) multiple bonds [13a] and (ii) carbonyl group [13b] and (iii) in trans-esterifications [13c]. Dealkylations [13b], as well as P – O and C – O bond cleavages [13d] have been observed. Methyl radicals have been stated to react with trimethylphosphite, albeit sluggishly, to give trimethylphosphonate [14].

What is unusual about the reaction described here is the non-specific radical formation from H-dimethylphosphonate.



Deoxygenation of organic peroxides with phosphites has been described [15]. However, epoxides have also been said to remain unaffected in the presence of phosphites [16]. It has also been stated that phosphites [17a] and phosphines [17b] deoxygenate epoxides to furnish alkenes. Thus, there seems to be some contradiction as regards the reaction of epoxides with phosphorus compounds. Phosphorus stabilized carbanions are said to give various products on reacting with oxiranes. Thus, the formation of alkenes, cyclopropanes and ketones has been rationalized [18a]. Significant formation of the ketones was observed via hydrogen migration [18b]. However, the treatment of styrene oxide with benzylidene trimethylphosphorane yielded (2-phenylethyl)ketone as the minor product and cis trans 1,3-diphenylpropene as the major product [18b]. With methylenetriphenylphosphorane, styrene oxide has been reported to give a ketone and triphenylphosphine. With strongly basic ylides, cyclic ethers have been reported [18c]. The reaction of styrene oxide with ethoxycarbonyl triphenylphosphorane has been reported to give cyclopropanoids [18d-e].



The microwave catalyzed reaction of styrene oxide (**1**) with H-dimethylphosphonate (**2**) yields ten compounds. Of these, two are derived from the oxidation H-dimethylphosphonate (**2**) and the remaining have their origin in styrene oxide (**1**). It appears that the compounds identified herein are formed via the free radical processes. **Fig. 3** attempts to describe the probable mechanism of the formation of the compounds described in the narrative.

EXPERIMENTAL

Stoichiometric amounts of the respective reagents were mixed in glass vials or 5 ml ground joint round bottom flasks and stoppered, vigorously shaken on a vibro-mixer and heated in the microwave oven for a specified period. The reaction mixture was allowed to come to ambient temperature, the cooled product was first analyzed by gas chromatography and then subjected to GC-MS analysis.

Mass Spectral Fragmentation of Compounds Cited in the Text

1. Styrene oxide (**1**): $M^+=120$ (r.t.=4.83 min, 57.8%); 105 (M - CH₃); 93 (M - C₂H₃); 91 (C₇H₇, 100%); 89 (C₇H₅); 77 (C₆H₅); 65 (C₅H₅); and 51 (C₄H₃).
2. Hydrogen dimethylphosphonate (**2**): $M^+=110$ (r.t.=2.47 min, 31.9%); 109 (M - H); 95 (M - CH₃); 93 (M - OH); 80 (95 - CH₃, 100%); 79 (M - OCH₃); 65 (80 - CH₃); 63 (PO₂); 49 (PH₂O) and 47 (PO).
3. Trimethylphosphonate (**3**): $M^+=124$ (r.t.=2.98 min, 0.2%); 109 (M - H); 109 (M - CH₃); 94 (109 - CH₃, 100%); 79 (94 - CH₃); 79 (M - OCH₃); 65 (PH₂O₂); 63 (PO₂); 49 (PH₂O) and 47 (PO).
4. Trimethylphosphate (**4**): $M^+=140$ (r.t.=3.4 min, 0.6%); 110 (M - OCH₂, 100%); 109 (M - OCH₃); 95 (110 - CH₃, 100%); 79 [P(O)H (OCH₃)]; 79 (M - OCH₃); 65 (PH₂O₂) and 47 (PO).
5. Phenylacetaldehyde (**5**): $M^+=120$ (r.t.=4.58 min, 3.4%); 91 (C₇H₇, 100%); 65 (C₅H₅); and 51 (C₄H₃).
6. 1-Methoxy-2-phenyl-2-ethanol (**6B**): $M^+=152$ (r.t.=6.29 min, 1.6%); 105 (C₆H₅CO); 103 (121 - H₂O); 93 (121 - C₂H₄); 91 (C₇H₇); 78 (C₆H₆); 77 (C₆H₅); 65 (C₅H₅); and 51 (C₄H₃).
7. 1-Phenylethylene glycol (**7**): $M^+=138$ (r.t.=7.25 min, 0.9%); 107 (M - CH₂OH, 100%); 105 (C₆H₅CO); 91 (C₇H₇); 79 (C₆H₇); 77 (C₆H₆); 65 (C₅H₅); and 51 (C₄H₃).
8. 1, 2-(cis/trans)-diphenylcyclobutane (**8**) and 1, 2-(91 (C₇H₇))-diphenylcyclobutane (**9**): $M^+=208$ (not seen in both cases); (r.t.=8.34 min, 0.3%/ r.t.=8.48 min, 0.7%); 104 (C₈H₈, 100%); 91 (C₇H₇); 77 (C₆H₆) and 51 (C₄H₃).
9. 1, 3-(cis/trans)-diphenylcyclobutane (**10**) and 1, 3-diphenylcyclobutane (**11**): $M^+=208$ (not seen in both cases); (r.t.=8.34 min, 0.3%/ r.t.=8.48 min, 0.7%); 104 (C₈H₈, 100%); 91 (C₇H₇); 77 (C₆H₆) and 51 (C₄H₃).
10. Hydrogen (2-phenylethyl)methylphosphonate (**12**): $M^+=184$ (r.t.=10.32 min, 2.2%); 169 (M - CH₃); 153 (M - OCH₃); 136 (M - PHO); 134 (C₈H₇OCH₃); 121 (136 - CH₃, 100%); 105 (C₆H₅C₂H₄); 91 (C₇H₇); 79 [PH(O)(OCH₃)]; 77 (C₆H₆); 65 (C₅H₅) and 51 (C₄H₃).
11. Hydrogen (1-phenyl)ethyl-1-dimethylphosphinate (**13**): $M^+=214$ (r.t.=10.83 min, 7.8%); 199 (M - CH₃); 169 [199 - (OCH₂)]; 153 (M - OCH₃ - OCH₂); 136 [C₆H₅(OH) (OCH₃)CH₂]; 121 (136 - CH₃); 119 (C₈H₇O); 105 [M - P (O) (OCH₃)₂]; 102 (C₈H₆, 100%); 95 [P(O)(OH)-(OCH₃)]; 91 (C₇H₇); 79 [PH(O)(OCH₃)]; 77 (C₆H₆); 65 (C₅H₅) and 51 (C₄H₃).
12. Hydrogen (1-phenyl)ethyl dimethylphosphinate (**14**): $M^+=214$ (r.t.=11.0 min, 0.2%); 199 (M - CH₃); 169 [199 - (OCH₂)]; 153 (M - OCH₃ - OCH₂); 136 [C₂H₃P(O)(OCH₃)₂]; 121 (136 - CH₃); 119 (C₆H₅COCH₂); 105 [M - P (O) (OCH₃)₂]; 102 (C₈H₆, 100%); 95 [P(O)(OH)-(OCH₃)]; 91 (C₇H₇); 79 [PH(O)(OCH₃)]; 77 (C₆H₆); 65 (C₅H₅) and 51 (C₄H₃).

Mass spectra were obtained using a Finnigan TSQ-7000 GC/MS/MS equipped with a 30 m x 0.25 mm. i.d. DB-5 capillary column (J and W Scientific, Folsom, CA) or a Finnigan 5100 GC/MS equipped with a 15 m x 0.25 mm. i.d. Rtx-5 capillary column (Restek, Bellefonte, PA). The conditions on 5100 were: oven temperature 60-270° C at 10° C/min, injection temperature was 210°, interface temperature 230° C, electron energy 70 eV, emission current 500 µA and

scan time 1 sec. The conditions on the TSQ-7000 were: oven temperature 60-270° C at 15° C/min, injection temperature 220°, interface temperature 250° C, source temperature 150°, electron energy 70 eV (EI) or 200 eV (CI) and emission current 400 μ A (EI) or 300 μ A (CI) and scan time 0.7 sec. Data was obtained in both the electron ionization mode (range 45-450 da) and chemical ionization mode (mass range 60-450 da). Ultrahigh purity methane was used as the CI agent gas with a source pressure of 0.5 Torr (5100) or 4 Torr (TSQ-7100). Routine GC analyses were accomplished with a Hewlett-Packard 5890A gas chromatograph equipped with a J and W Scientific 30 m x 0.53 mm i.d. DB-5 column (J and W Scientific, Folsom, CA). The NMR spectra (^1H and ^{13}C) were recorded in CDCl_3 with TMS as the internal standard on a Varian VXR-400S spectrometer at 100 MHz and 376 MHz respectively.

Microwave Catalyzed Reaction of Styrene oxide (1) with H-Dimethylphosphonate (2): Stoichiometric amounts of styrene oxide (**1**, 0.22 g., 2 mmol) and H-dimethylphosphonate (**2**, 0.22 g., 2 mmol) were mixed in a glass vial or glass joint round bottom flask (5 ml), the mixture was shaken for a few minutes using the vibro-mixer and then heated in a table top microwave oven for two minutes. The reaction mixture after cooling to ambient temperature was analyzed by gas chromatography. Then, it was heated again for two minutes and reanalyzed. This process was repeated one more time to a total of six minutes of microwave heating. When no additional peaks appeared in the g. c. chromatogram, it was then subjected to GC-MS analysis. Thus, the following compounds were characterized based on their mass spectral fragmentation behavior: (1) dimethyl methylphosphonate (**3**), (2) trimethylphosphate (**4**), (3) phenylacetaldehyde (**5**), (4) 1-methoxy-2-phenylethanol (**6B**), (5) 1-phenylethleneglycol (**7**), (6) cis- and trans-1,3-diphenylcyclobutanes (**10-11**), (7) hydrogen 1-(2-phenylethyl)methylphosphinate (**12**), (8) (1-phenylethyl)dimethylphosphonate (**11**) and (1-phenylethyl)dimethylphosphonate (**12**). Their retention times, percentages of the yields of the compounds and mass spectral fragmentation are described in **Table 1**.

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