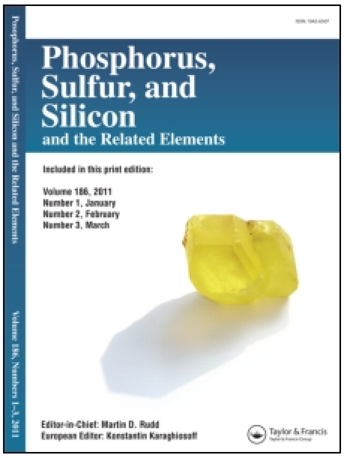

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Synthesis of Alkyl 6-(2-Alkoxy-2-oxoethyl)dibenzo[*d,f*][1,3]dioxepine-6-carboxylates from Stabilized Phosphorus Ylides

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*Protonation of the highly reactive 1:1 intermediates, produced in the reaction between triphenylphosphine and dialkyl acetylenedicarboxylates, by biphenyl-2,2′-diol leads to vinyltriphenylphosphonium salts, which undergo a Michael addition reaction with a conjugate base to produce the corresponding stabilized phosphorus ylides. Magnesium oxide powder was found to catalyze the conversion of the stabilized phosphorus ylides to alkyl 6-(2-alkoxy-2-oxoethyl)dibenzo[*d,f*]*[1,3]dioxepine-6-carboxylates in solvent-free conditions under microwave (0.5 KW, 3 min) and thermal (90 °C, 60 min) conditions.*

Keywords Acetylenic esters; biphenyl-2,2′-diol; [1,3]dioxepine; magnesium oxide; Michael addition; microwave irradiation; vinyltriphenylphosphonium salt

INTRODUCTION

Organophosphorus compounds have been extensively employed in organic synthesis[1–16] as useful reagents as well as ligands in a number of transition metal catalysts.[17] β-Addition of nucleophiles to the vinyl group of vinylic phosphonium salts leading to the formation of new alkylidenephosphoranes has attracted much attention as a very convenient and synthetically useful method in organic synthesis.[18–30] Phosphorus ylides are important reagents in synthetic organic chemistry, especially in the synthesis of naturally occurring products and compounds with biological and pharmacological activity.[6] Phosphorus ylides are a class of a special type of zwitterion, which bear strongly nucleophilic, electron-rich carbanions. The electron distribution around

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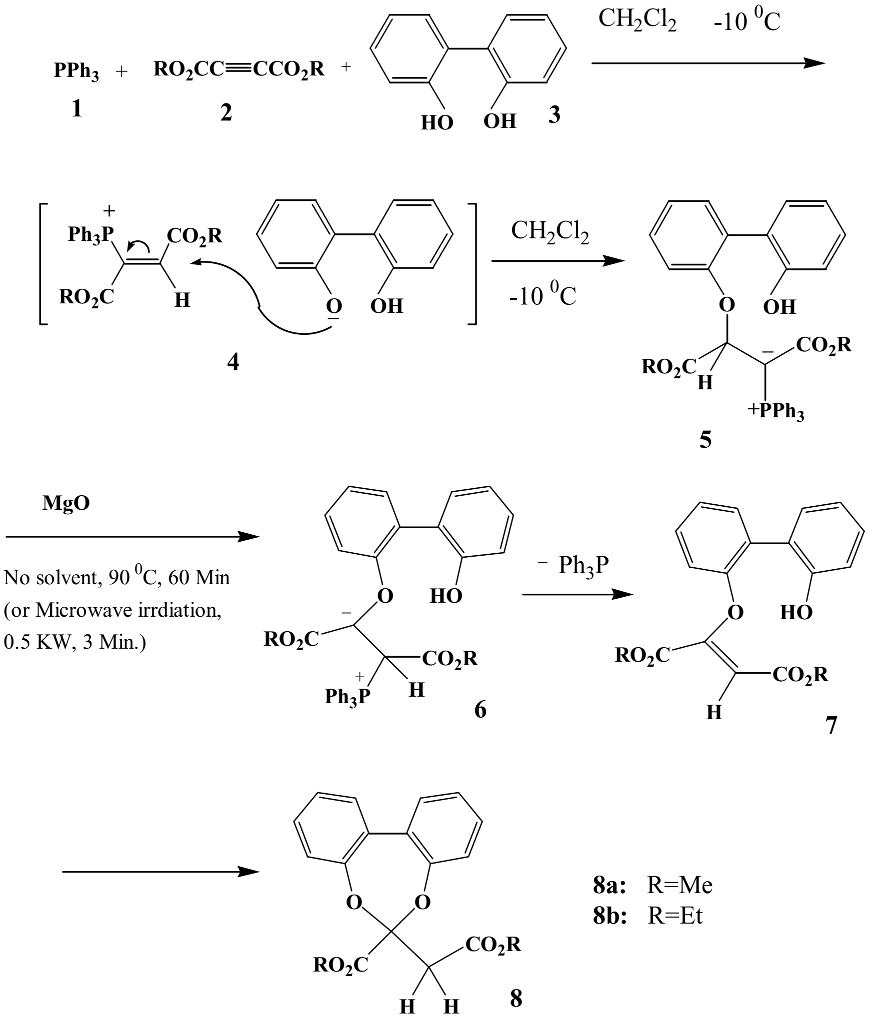
the $P^+–C^-$ bond and its consequent chemical implications has been probed and assessed through theoretical, spectroscopic, and crystallographic investigations.[30] Proton affinity of these ylides can be used as a molecular guide to assess their utility as synthetic reagents and their function as ligands in coordination and organometallic chemistry.[17,30] The nucleophilicity at the ylidic carbon is a factor of essential mechanistic importance in the use of these ylides as Wittig reagents.

Waste prevention and environmental protection are major requirements in an overcrowded world of increasing demands. Synthetic chemistry continues to develop various techniques for obtaining better products with less environmental impact. One of the more promising approaches is solvent-free organic synthesis.[31] In this regard, solvent free catalytic organic reaction has received tremendous attention in recent times.[32] In the past, we have established a convenient one-pot method for preparing stabilized phosphorus ylides utilizing *in situ* generation of the phosphonium salts.[18–28] [1,3]Dioxepine skeleton compounds are important heterocycles in organic, medicinal, and natural product chemistry.[33–35] Several methods have been reported for the preparation of [1,3]dioxepine skeleton compounds.[33–35] In this article, we report on the catalytic role of magnesium oxide powder in the conversion of stabilized phosphorus ylides to alkyl 6-(2-alkoxy-2-oxoethyl)dibenzo[*d,f*][1,3]dioxepine-6-carboxylates in solvent-free conditions[36,37] under microwave (0.5 KW, 3 min) and thermal (90°C, 60 min) conditions (Scheme 1).

RESULTS AND DISCUSSION

The ylide (**5**) may result from the initial addition of triphenylphosphine **1** to the acetylenic ester **2**, and concomitant protonation of the 1:1 adduct by biphenyl-2,2′-diol leads to vinyltriphenylphosphonium salts **4**, which undergo Michael addition reaction with a conjugate base to produce stabilized phosphorus ylide (**5**). TLC indicated the formation of ylides **5** in CH_2Cl_2. Magnesium oxide powder was found to catalyze the conversion of the stabilized phosphorus ylide (**5**) to alkyl 6-(2-alkoxy-2-oxoethyl)dibenzo[*d,f*][1,3]dioxepine-6-carboxylates (**8**) in solvent-free conditions[36] under microwave (0.5 KW, 3 min) and thermal (90°C, 60 min.) conditions. We have also used SiO_2, KH_2PO_4, K_2HPO_4, and $(NH_4)H_2PO_4$ in this reaction, but the yield of the product was very low, and in some cases decomposition and several products were observed. In the absence of the MgO powder, the powdered ylide **5** was not reactive under microwave irradiation at microwave power 0.5 KW after 3 min or under thermal (90°C, 60 min) conditions, and decomposition of



SCHEME 1

the starting materials were observed. The reaction also did not occur in dichloromethane solutions even after several days. The mechanism of the reaction has not been established experimentally. However, a possible explanation is proposed in Scheme 1. The structures of the products were deduced from their IR, ^{1}H NMR, and ^{13}C NMR spectra (See Experimental section).

CONCLUSION

In summary, we have found a new and efficient method for the preparation of alkyl 6-(2-alkoxy-2-oxoethyl)dibenzo[*d, f*][1,3]dioxepine-6-carboxylates (**8**) from stabilized phosphorus ylides (**5**) in the presence of magnesium oxide powder in solvent-free conditions (Scheme 1). We believe the reported method offers a simple and efficient route for the preparation of substituted [1,3]dioxepine derivatives **8** (Scheme 1). Its ease of workup and fairly good yields make it a useful addition to modern synthetic methodologies. Other aspects of this process are under investigation.

EXPERIMENTAL

A commercial oven (Butane M245) was used for microwave irradiation. IR spectra were recorded on a Shimadzu IR-460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a Bruker DRX-500 Avance spectrometer at 500 and 125 MHz, respectively.

General Procedure for the Preparation of Ylides 5 and Compounds 8a–b

To a magnetically stirred solution of triphenylphosphine **1** (1 mmol, 0.262 g) and biphenyl-2,2′-diol **3** (1 mmol, 0.186 g) in CH_2Cl_2 (4 mL), a mixture of **2** (1 mmol, 0.130 mL) in CH_2Cl_2 (3 mL) at –10°C was added dropwise over 15 min. The mixture was allowed to warm up to room temperature. Magnesium oxide powder (37 mmol, 1.5 g) was added and the solvent was evaporated. Dry magnesium oxide and the residue were heated (yield for **8a**, 47.3%; yield for **8b**, 41.0%) for 90 min at 60°C (or irradiated in microwave oven for 3 min at microwave power 0.5 KW; yield for **8a**, 46%; yield for **8b**, 41%) and then placed over a column of silica gel powder (12 g). The column chromatography was washed using ethyl acetate–light petroleum ether (1:10) as eluent. The solvent was removed under reduced pressure, and products were obtained as viscous yellow oils (**8a–b**) (Scheme 1). The characterization data of the compounds (**8a–b**) are given below.

Methyl 6-(2-methoxy-2-oxoethyl)dibenzo[d,f][1,3]dioxepine-6-carboxylate (8a)

Viscous yellow oil; IR (neat) (ν_{max}, cm^{-1}): 3070, 3000, 2954 and 2854 (C–H); 1751 (C=O, ester); 1604 (C=C , arom). ^{1}H NMR ($CDCl_3$)δ: 3.30 (2 H, s, CH_2), 3.77 and 3.86 (6 H, 2 s, 2 OCH_3); 7.23 (2 H, d, $^3J_{HH} = 7.7$ Hz, C3, C3′, arom); 7.35 (4 H, m, C4, C4′ and C5, C5′, arom); 7.51 (2 H, d, ${}^3J_{HH} = 7.2$ Hz, C6, C6′, arom). ^{13}C NMR ($CDCl_3$)δ: 41.04 (CH_2), 52.24 and 53.01 (2 OCH_3); 110.83 (O–C–O), 123.02, 126.23, 128.49, 129.14, 132.37 and 150.59 (12 C, arom); 167.03 and 168.42 (2 C=O).

Ethyl 6-(2-ethoxy-2-oxoethyl)dibenzo[d,f][1,3]dioxepine-6-carboxylate (8b)

Viscous yellow oil; IR (neat) (ν_{max}, cm^{-1}): 3070, 2985 and 2908 (C-H); 1743 (C —O, ester); 1604 (C=C, arom).^{1}H NMR ($CDCl_3$)δ: 1.31 (3 H, t, ${}^3J_{HH} = 7.1$ Hz, CH_3); 1.33 (3 H, t, ${}^3J_{HH} = 7.1$ Hz, CH_3); 3.28 (2 H, s, CH_2), 4.24 (2 H, q, ${}^3J_{HH} = 7.1$ Hz, OCH_2); 4.33 (2 H, q, ${}^3J_{HH} = 7.1$ Hz, OCH_2); 7.23 (2 H, d, ${}^3J_{HH} = 7.5$ Hz, C3, C3′, arom); 7.34 (4 H, m, C4, C4′ and C5, C5′, arom); 7.50 (2 H, d, ${}^3J_{HH} = 7.3$ Hz, C6, C6′, arom).^{13}C NMR ($CDCl_3$)δ: 14.11 and 14.14 (2 CH_3); 41.26 (CH_2), 61.11 and 62.23 (2 OCH_2); 110.79(O—C—O), 123.14, 126.10, 128.44, 129.00, 132.42 and 150.73 (12 C, arom); 166.44 and 167.91 (2 C=O).

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