J. Braz. Chem. Soc., Vol. 13, No. 5, 687-691, 2002.
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0103 - 5053 $6.00+0.00

Short Report

On the Reactivity of α-(Triphenylphosphoranylidene)-benzylphenylketene with Nitrogen Compounds. Synthetic and Mechanistic Implications

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A reatividade do ilídeo de fósforo estabilizado derivado da difenilciclopropenona, o α-(trifenilfosforanilideno)-benzilfenilceteno, frente a compostos nitrogenados polifuncionalizados foi investigada. Em particular, a reação do α-(trifenilfosforanilideno)-benzilfenilceteno com o azodicarboxilato de etila pode se constituir como um novo método de síntese de *N*-acil-carbamatos densamente substituidos.

The reactivity of α-(triphenylphosphoranylidene)-benzylphenylketene, a stabilized phosphorus ylide derived from diphenylcyclopropenone, toward nitrogen compounds was investigated. Particularly, the reaction of diethyl azodicarboxylate with α-(triphenylphosphoranylidene)-benzylphenylketene provides a new route to polysubstituted *N*-acyl carbamates.

Keywords: α-(triphenylphosphoranylidene)-benzylphenylketene, phosphorus ylides, diphenylcyclopropenone, acyl carbamate

Introduction

While the reactivity of diphenylcyclopropenone (**1**) with nucleophiles has been well documented,[1] studies of the behavior of its derivative α-(Triphenylphosphoranylidene)-benzylphenylketene (**2**, α-TPBPK) with such reagents are scarce.[2] Otherwise, phosphorus ylides have been intensively used in organic synthesis, mainly in olefination reactions.[3] Stabilized triphenylphosphonium ylides have attracted attention and new methods of preparation,[4] their behavior under pyrolysis conditions[5] and structural elucidation[6] still demand investigation. When carrying out a transformation with stabilized triphenylphosphonium ylides their nucleophilicity has been the prime consideration.[7]

Recently, we reported the study of the reaction of triphenylphosphoranylidenesuccinic anhydride with a broad spectrum of nitrogen nucleophiles and a new method of synthesis of phosphonioum salts was described.[8] Our continued interest in the chemistry of cyclopropenones and their derivatives[1] as well as in the reactivity of phosphorus ylides stabilized by electrophilic functions[8] prompted us to study the behavior of α-TPBPK toward nitrogen compounds. In this work we present our results concerning the reactivity of α-TPBPK with such derivatives with emphasis on synthetic and mechanistic implications.

Results and Discussion

The ambiphilic α-TPBPK **2** is readily prepared by the reaction of diphenylcyclopropenone with triphenylphosphine. As expected, this solid is stable only under anhydrous conditions, but alternatively it can be generated *in situ*.[2] Thus, equimolar amounts of triphenylphosphine and diphenylcyclopropenone (**1**) were reacted under inert atmosphere and then the nucleophile was introduced (see Experimental). Among the broad spectrum of nitrogen nucleophiles available, we selected ones whose reactivity toward diphenylcyclopropenone was known. Thus, we began our study with 2-amino-4-methylpyridine **3**,[9] pyridinium *N*-imine 4[10] and *N*-benzoylacetamidine **5**[1] (examples of reactivity towards **1** are shown in Scheme 1).

α-TPBPK reacted with 2-amino-4-methylpyridine (**3**) to afford a crystalline solid along with almost quantitative recovery of triphenylphosphine. Although the IR spectrum of the product suggested the presence of amide NH and C=O groups, and proton NMR integration indicated that this material was a 1:1 adduct, the chemical shifts of the pyridinic ring ruled out the formation of **6** (δ H_3 6.15, δ H_5 6.37 and δ H_6 7.60, and 8.30, 6.80 and 8.10 for **6**,

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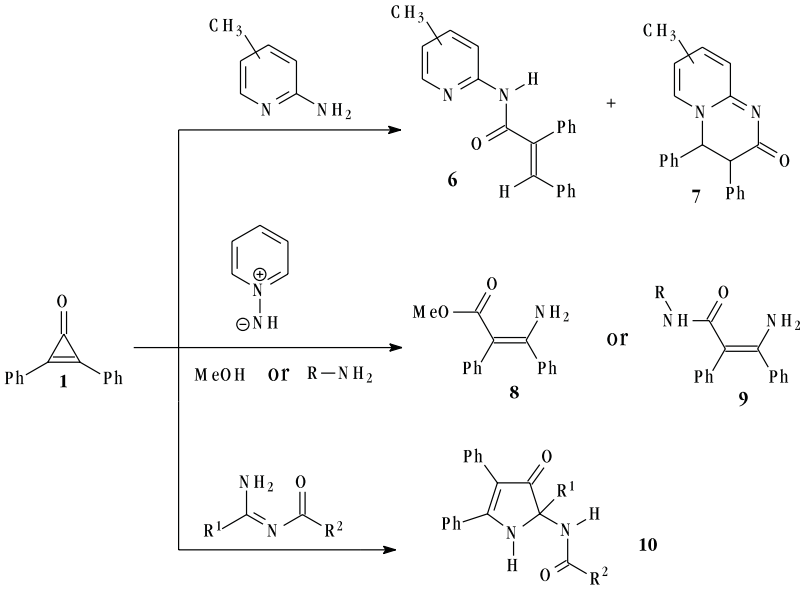


Scheme 1.

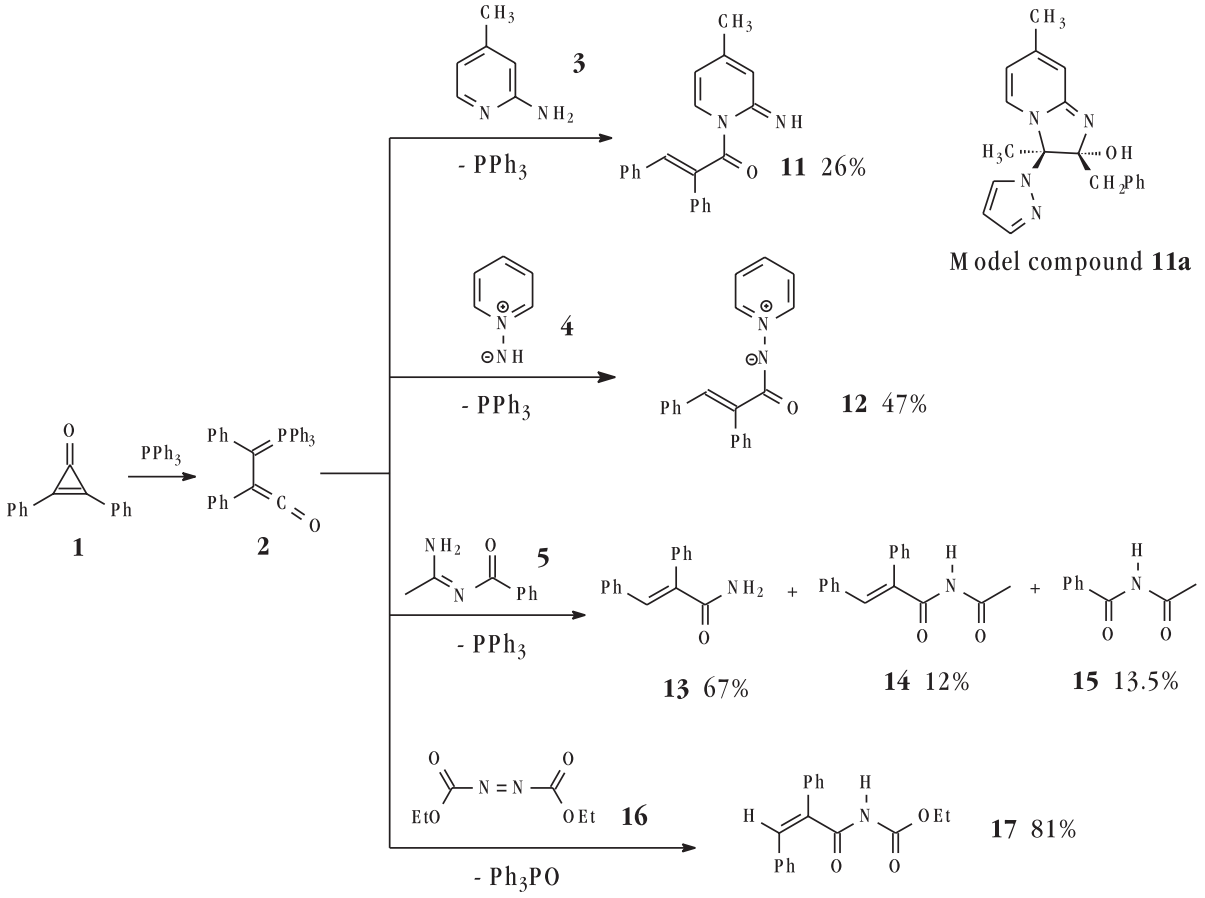
respectively[9]). Additionally, the NMR spectrum contained a low field N-H proton (δ10.20, D_2O exchangeable) as a broad signal and an olefinic proton as a sharp singlet at δ 7.82, indicating a *cis* relationship of the phenyl groups as in **6**, where this absorption appears at δ 8.0.[9] To accommodate these spectral features structure **11** was proposed (Scheme 2). Also, the hydrogen chemical shifts mentioned above for the nitrogen-containing ring of **11** with an exocyclic carbon-nitrogen double bond are in agreement with a model compound previously reported by us (**11a**, Scheme 2), whose X-ray structure was obtained.[11] It should be pointed out that **11** is not converted into **6** under reflux in chloroform or nitromethane. Under basic conditions (K_2CO_3), α-phenylcinnamic acid is the sole isolated compound.

When α-TPBPK was reacted with pyridinium *N*-imine (**4**), generated *in situ* by reaction of *N*-aminopyridinium iodide[12] with K_2CO_3, compound **12** was isolated in modest yield (Scheme 2). The pyridinium ring[13] and the *N*-α-phenylcinnamoyl moiety[9] in **12** could be defined by comparison with analogues described in the literature. We next studied the reaction of **2** with *N*-benzoylacetamidine (**5**). In this case, a mixture of products **13-15** was obtained in contrast to the reaction of this nucleophile[1] with **1**. As in the reaction of **2** with **3**, triphenylphosphine was recovered in the reaction of **2** with **4** and **5**. From a mechanistic viewpoint, the formation of **11-15** may be visualized as occurring through attack of the nitrogen nucleophile at the electrophilic carbon of the ketene portion of **2**, followed by triphenylphosphine elimination and proton transfer (Scheme 3).

To provide insight into the behavior of α-TPBPK toward nitrogen compounds without transferable hydrogen, **2** was treated with azobenzene and *N*-(*p*-methoxyphenyl)-benzaldimine, but only complex mixtures were formed. However, with diethyl azodicarboxylate **16** a clean reaction took place, wherein the *N*-acyl carbamate (**17**) was formed in excellent yield. This is a very interesting result since densely substituted *N*-acyl carbamates are versatile intermediates in the synthesis of nucleoside analogues and their preparation is not a trivial task.[14]

Contrary to the other reactions described above, triphenylphosphine oxide was the co-product, and the phenyl groups are positioned *trans* in **17**, as indicated by the chemical shift of the olefinic hydrogen as a sharp singlet at δ 7.20 (in **6**,[9] **11** and **12** the phenyl groups are positioned *cis* and the olefinic proton appears at δ 8.0, δ 7.82 and δ 7.82, respectively). However, the formation of **17** is not well understood and its mechanism is under study.

The results of the present work, together with those obtained previously with triphenylphosphoranylidenesuccinic anhydride,[8] provide an interesting spectrum of reactivity for phosphorus ylides stabilized by electrophilic functions, and also expand the frontiers of applications of cyclopropenone derivatives in synthesis. Particularly, the formation of **17** provides a new route to polysubstituted *N*-acyl carbamates. Studies involving the preparation of unsymmetrical cyclopropenones and their reactions with diethyl azodicarboxylate are under investigation to establish the mechanism, scope and limitations of this new synthetic protocol.

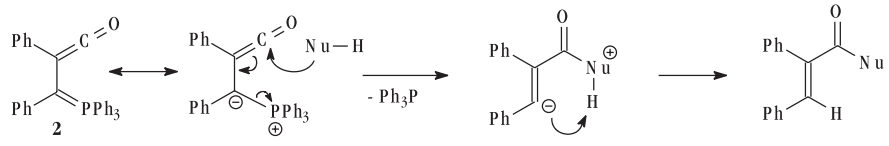


Scheme 2.

Experimental

Melting points were measured on a Hoover-Unimelt apparatus and are uncorrected. Infrared spectra were recorded as KBr discs on a Perkin Elmer FT-IR 1600 instrument. NMR spectra were obtained for ^{1}H at 300 MHz and for ^{13}C at 75 MHz using a Varian Gemini 300 or a Bruker AC300P spectrometer. Unless otherwise stated, all spectra were run in $CDCl_3$ solutions. Chemical shifts are reported in δ (ppm) units downfield from reference. Elemental analyses were performed on a Perkin Elmer 2401 Elemental Analysis by Instituto de Química, Universidade Estadual de Campinas, Brazil. *N*-aminopyridinium iodide,[12] *N*-benzoylacetamidine[15] and diphenylcyclopropenone[16] were prepared according to known procedures. All reactions were performed under a positive pressure of argon with oven-dried glassware (120 °C). Benzene and CH_2Cl_2 were distilled from Na-benzophenone and CaH_2, respectively.

*Reaction of α-TPBPK with 2-amino-4-methylpyridine (**3**).* A solution of 265.7mg (1.3 mmol) of diphenylcyclopropenone (**1**) and 345.6 mg (1.3 mmol) of triphenylphosphine in 5.0 cm^3 of benzene in a two-necked round-bottom flask was left at room temperature with stirring for



Scheme 3.

2 h. To the orange solution was added via syringe 141.3 mg (1.3 mmol) of 2-amino-4-methylpyridine (**3**) in 3.0 cm^3 of benzene. The solution turned yellow and was left stirring for 18 h, after which time the solvent was removed under reduced pressure. The residual solid was triturated with ethyl ether yielding 105.8 mg (26%) of **11** as a colorless solid, mp 131-132 °C. IR (KBr): ν_{max}/cm^{-1} 3349, 1676, 1646. ^{1}H NMR: 2.19 (s, 3H), 6.15 (s, 1H), 6.37 (d, ^3J 6Hz,1H), 7.01-7.09 (m, 2H); 7.10-7.14 (m, 3H); 7.26-7.37 (m, 5H), 7.60 (d, ^3J 6Hz, 1H), 7.82 (s, 1H), 10.20 (b, 1H). ^{13}C NMR: 21.5 (CH_3), 111.4 (CH), 113.7 (CH), 127.1 (CH), 128.0 (CH), 128.4 (CH), 129.8 (CH), 130.3 (CH), 135.8 (C), 137.2 (CH), 137.4 (C), 138.3 (C), 138.8 (CH), 152.9 (C), 156.6 (C), 174.3 (C). Anal. Calcd. for $C_{21}H_{18}N_2O$: C, 80.25%; H, 5.73%; N, 8.92%. Found: C, 80.35%; H, 5.71%; N, 8.99%.

*Reaction of α-TPBPK with pyridinium N-imine (**4**).* A solution of 410.0 mg (2.0 mmol) of diphenylcyclopropenone (**1**) and 533.5 mg (2.0 mmol) of triphenylphosphine in 8.0 cm^3 of CH_2Cl_2 in a two-necked round-bottom flask was left at room temperature with stirring for 1.5 h. To the orange solution was added successively 284.0 mg (2.1 mmol) of anhydrous K_2CO_3 and 222.0 mg (1.0 mmol) of *N*-aminopyridinium iodine. The reaction mixture was left stirring for 15 h, after which time was filtered and the solvent was removed under reduced pressure. The residue was triturated with petroleum ether and them purified by column chromatography (Florisil®, chloroform as eluent) to afford a solid witch was recrystallized from CH_2Cl_2/petroleum ether yielding 141.9 mg (47%) of **12** as a pale yellow solid, mp 154-156 °C. IR (KBr): ν_{max}/cm^{-1} 1638, 1557, 1470, 1301. ^{1}H NMR: 7.02 (m, 2H), 7.11 (m, 3H), 7.26- 7.36 (m, 5H), 7.60 (t, ^3J 7.1Hz, 2H), 7.82 (s, 1H), 7.86 (t, ^3J 7.1Hz, 1H), 8.63 (d, ^3J 5.6Hz, 2H). ^{13}C NMR: 125.7 (CH), 126.8 (CH), 127.4 (CH), 127.8 (CH), 128.2 (CH), 129.9 (CH), 130.1 (CH), 134.1 (CH), 136.3 (C), 137.0 (CH), 138.7 (C), 139.1 (C), 143.4 (CH), 172.4 (C). Anal. Calcd. for $C_{20}H_{16}N_2O$: C, 80.00%; H, 5.33%; N, 9.33%. Found: C, 79.79%; H, 5.20%; N, 9.21%.

*Reaction of α-TPBPK with N-benzoylacetamidine (**5**).* A solution of 105.0 mg (0.5 mmol) of diphenylcyclopropenone (**1**) and 134.3 mg (0.5 mmol) of triphenylphosphine in 8.0 cm^3 of benzene in a two-necked round-bottom flask was left at room temperature with stirring for 2 h. To the orange solution was added 83.2 mg (0.5 mmol) of *N*-benzoylacetamidine (**5**). The solution turned yellow and was left stirring for 24 h. After this time the solvent was removed under reduced pressure and the residue was purified by column chromatography (Florisil®) affording 15.7 mg (12%) of **14** (benzene/ethyl acetate 5%), 28.1 mg (13.5%) of **15**[17] (benzene/ethyl acetate 5%) and 76.5 mg (67%) of α-phenylcinnamamide (**13**)[18] (benzene/ethyl acetate 10%). **14**: IR (KBr): ν_{max}/cm^{-1} 3274, 1706, 1690, 1610. ^{1}H NMR: 2.57 (s, 3H), 7.01 (d, ^3J 7.3Hz, 2H), 7.15-7.37 (m, 5H), 7.49-7.52 (m, 3H), 7.83 (sl, 1H), 7.96 (s, 1H). ^{13}C NMR: 25.4 (CH_3), 128.6 (CH), 129.6 (CH), 129.8 (CH), 129.9 (CH), 130.4 (CH), 131.0 (CH), 133.5 (C), 134.7 (C), 134.9 (C), 141.3 (CH), 165.7 (C), 173.3 (C).

*Reaction of a-TPBPK with diethyl azodicarboxylate (**16**).* A solution of 314.4mg (1.5 mmol) of diphenylcyclopropenone (**1**) and 396.8 mg (1.5 mmol) of triphenylphosphine in 5.0 cm^3 of benzene in a two-necked round-bottom flask was left at room temperature with stirring for 2 h. To the orange solution was added via syringe 170.7 mg (1.0 mmol) of diethyl azodicarboxylate (**16**) in 4.0 cm^3 of benzene. The solution turned yellow and was left stirring for 18 h. After this time the solvent was removed under reduced pressure and the residue was triturated with petroleum ether. Purification by column chromatography (Florisil®, hexane/ethyl acetate 30%) afforded 233.6 mg (81%) of **17** as a colorless solid, mp 154-156 °C. IR (KBr): ν_{max}/cm^{-1} 1762, 1705. ^{1}H NMR (CCl_4): 1.18 (t, ^3J 7.1Hz, 3H), 4.14 (q, ^3J 7.1Hz, 2H), 7.09 (m, 5H), 7.20 (s, 1H), 7.21-7.25 (m, 3H), 7.35-7.39 (m, 2H). ^{13}C NMR (CCl_4): 14.0 (CH_3), 63.2 (CH_2), 127.7 (CH), 127.8 (CH), 127.9 (CH), 128.0 (CH), 129.7 (CH), 129.8 (CH), 134.3 (CH), 134.5 (C), 134.8 (C), 136.1 (C), 151.3 (C), 168.3 (C). Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.22%; H, 5.76%; N, 4.75%. Found: C, 73.57%; H, 6.01%; N, 4.33%.

Acknowledgments

The authors thank the Conselho Nacional de Densenvolvimento Científico e Tecnológico (CNPq) for a fellowship to SC.

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Received: November 11, 2001
Published on the web: July 16, 2002

FAPESP helped in meeting the publication costs of this article.