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Reaction of Lithium Diphenylphosphonium Di(methylide) with Carbonic Acid Derivatives. A Novel Access to Polyfunctional Unsaturated Esters and Amides

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ABSTRACT

The lithium diphenylphosphonium di(methylide) $Ph_2P(CH_2)_2Li$ **1** *readily attacks cyclic carbonates, carbamates, and thiocarbamates, resulting in "pseudo-acylation" products, after a ring-opening step. Thus, new stabilized ylides are prepared, which can be used in situ as carbonyl olefination reagents towards aldehydes. This procedure is a new one-pot method for the synthesis of (E)-vinylic esters and amides, bearing a free ω-hydroxyl group. When a thiocarbamate is the initial substrate for* **1**, *a Michael-type cyclization occurs, following the Wittig olefination, resulting in the one-pot preparation of 7-membered heterocycles.*

INTRODUCTION

Doubly anionized phosphonium salts are more nucleophilic than ordinary ones. The second anionic center may be generated at the original ylide center, affording an α-lithio phosphorus ylide **3** [1]. Alternatively, a phosphonium salt having at least two alkyl substituents can be deprotonated twice at two different α-sites. The first example of such a phosphorus and lithium di(ylide) [not yldiid nor bis-ylide!] **2** (M = nonalkaline cations) have been extensively investigated in coordination chemistry since 1965 by H. Schmidbaur and coworkers [3], particularly as bidentate ligands for metal coordination, whereas only little has been done on their use as synthetic reagents [2b, c]. Then, our initial work on lithium phosphonium diylides in Organic Chemistry [4] showed their potential synthetic value, broader to classical ylides, due essentially to a greater nucleophilicity. This was followed by B. J. Walker's [5a–c] and C. Mioskowski's [5d] results on the stereochemistry of the Wittig reaction of semi-stabilized and stabilized diylides with aldehydes and ketones.

The enhanced nucleophilic reactivity of nonstabilized lithium phosphonium diylides (4:R = H, alkyl), as shown by our results concerning hindered ketones [4b], then esters and amides [4c], prompted us to study their behavior towards other moderately or weakly electrophilic carbonyl substrates, such as carbonates [4a]. We report here the results of the addition of **1** to various cyclic substrates derived from carbonic acid: carbonates, a carbamate and a thiocarbamate. We first wanted to demonstrate the ability of the diylide **1** to react with these compounds, according to an expected "pseudo-acylation" process, similar to the case of ethyl benzoate [4c], and to show its advantage over the corresponding monoylides. Moreover, we intended to study the synthetic value of such reactions for in situ carbonyl olefination.

Dedicated to Professor Dr. Leopold Horner on the occasion of his eightieth birthday.

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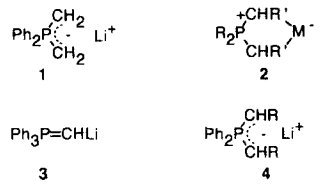
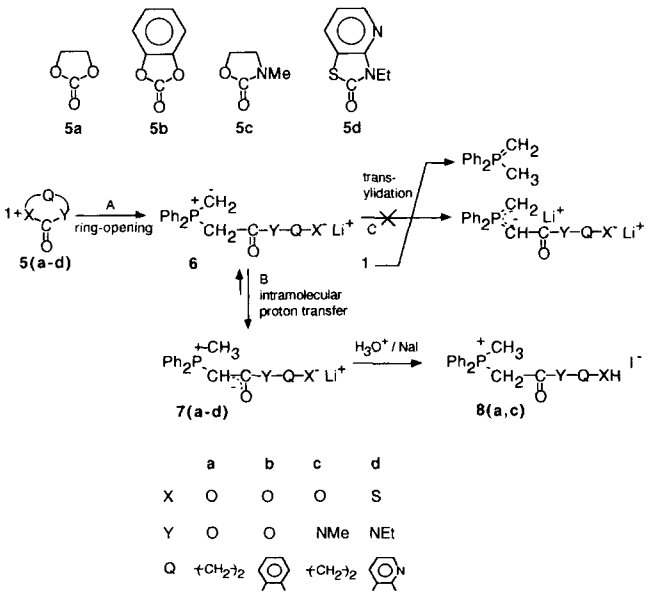


FIGURE 1

RESULTS AND DISCUSSION

We have previously referred briefly to our first results in this field, on acylation of **1** via a ring-opening process of cyclic aliphatic carbonates [4a], and in this study we investigate further the developments and new results obtained with cyclic substrates **5**; of a different nature (Q) = aliphatic or aromatic chain) and electrophilicity (X, Y = O, N, S): Scheme 1. The diylide **1** has a strong enough nucleophilicity to react with the carbonyl site of such low electrophilic substrates as aliphatic or aromatic cyclic carbonates **5a–b** or (thio)carbamates **5c–d**. Such substrates appear to be inert towards monoylides, as the only reported reaction of this type concerns a noncyclic activated carbonate: diphenyl carbonate [6].

The reaction pathway involves a ring-opening step (scheme 1, step A), and the acylation product **7** is then obtained from **6** owing to a propitious intramolecular proton transfer (path B), which prevents any transylidation (path C). This is rather important, as no loss of the initial phosphorus reagent **1** occurs by transylidation, as it is usually the case for a nonstabilized monoylide when an acylation reaction is carried out (for the case of a carbonate, see [6]), decreasing the theoretical yield to 50%.



SCHEME 1: Reaction of Diylide **1** with carbonic acid derivatives.

Experimental conditions for the condensation of the diylide **1** with cyclic substrates **5** are quite mild, as ring-opening occurs at room temperature (20–25°C; 3–4 hr) in the case of carbonates **5a–b**, and refluxing THF (66°C; half a day) is sufficient in the case of (thio)carbamates **5c–d**. We first showed the possibility of isolating in good yields the phosphonium salts **8** resulting from direct acidification of **7**, using either a carbonate or a carbamate (see Table 1: run 1, 6).

Then, we tried to use in situ these new stabilized ylides **7**, in a one-pot procedure without any purification, as new Wittig olefination reagents towards aldehydes (scheme 2). The efficiency of such a procedure has been probed with several aldehydes (Table 1).

The different experimental results (see Table 1) show an excellent transformation ratio of the substrates **5**. Thus, we have in hand an easy preparative route for new stabilized ylides **7**, bearing a free alkoxide, phenoxide or thiolate function. Moreover, the synthesis of analogous functionalized triphenylphosphonium ylides by classical methods [7] would have been more complicated, requiring protection-deprotection steps of the OH or SH groups.

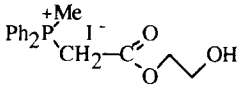
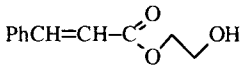
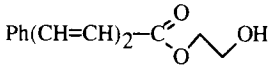
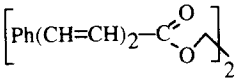
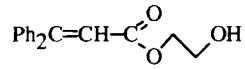
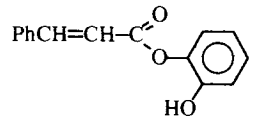
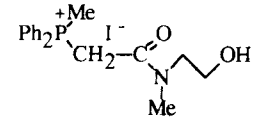
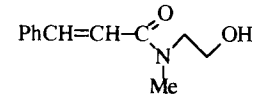
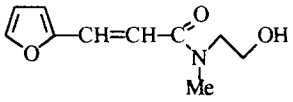
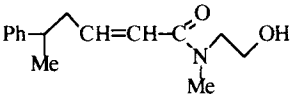
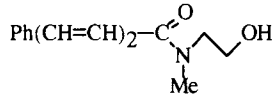
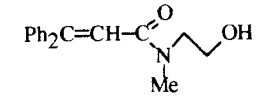
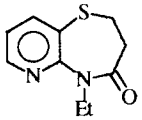
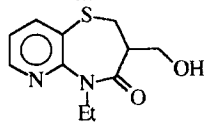
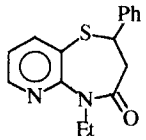
The use of 7 prepared in situ allowed the preparation of different α,β-unsaturated ω-functionalized esters or amides **9**, with an excellent E-stereoselectivity (higher than 92%), and good to excellent yields when aldehydes are used as Wittig substrates (run 2–4, 7–10). Due to the stabilized nature of the intermediate ylide **7**, no reaction occurs with benzophenone (run 4, 11) [8].

A by-product is obtained in one case (run 3), which results from a trans-esterification process of the Wittig product before acidic work-up. Even with changing the reaction conditions, this phenomenon was shown to be always predominant, and could not be easily related to the reaction conditions or to the transformation ratio.

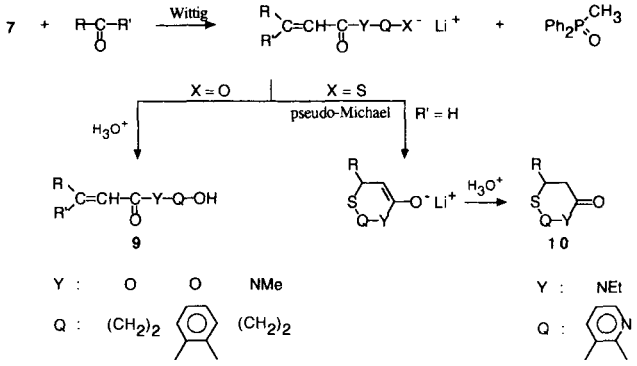
The lowest yield was observed with 3-phenylbutyraldehyde (run 9), an aliphatic substrate, probably explained by its partial enolization due to the presence of the free alkoxide group in **7**. In the case of the aromatic carbonate **5b**, the isolation in 45% yield of pyrocatechol after work-up and chromatography, and also the well known fragility of the obtained α,β-unsaturated pyrocatechol monoester towards hydrolysis [9], could explain the rather low yield of the Wittig product isolated.

When the in situ formed stabilized ylide **7** carries a thiolate group, the Wittig product undergoes a pseudo-Michael intramolecular cyclization, due to the soft character of this group: α,β-unsaturated amides are not detected after acidic work-up, but the corresponding 7-membered heterocycles are isolated in moderate to good yields (run 12, 13). In the case of formaldehyde, the use of a large excess

TABLE 1 One-pot preparation of phosphonium salts **8**, α, β-unsaturated esters and amides **9**, and heterocycles **10**, by reaction of **1** with **5**.

Run	*Substrate Scheme 1*	*Substrate Scheme 2*	*Isolated Products* **8, 9, 10**		*Isolated yields (%) (Z / E)*
1	**5a**	none	**8a**		80 (91% purity)
2	**5a**	PhCHO	**9a**		98 (9 / 91)[a]
3	**5a**	PhCH=CH—CHO	**9b**		10 (1 / 99)[a]
			9 b		86 (0 / 100)[b]
4	**5a**	Ph_2CO	**9c**		0
5	**5b**	PhCHO	**9d**		50 (0 / 100)[b]
6	**5c**	none	**8b**		85 (91% purity)
7	**5c**	PhCHO	**9e**		95 (5 / 95)[a]
8	**5c**	1-Furyl-CHO	**9f**		65 (0 / 100)[a]
9	**5c**	Ph(Me)CH—CH_2CHO	**9g**		32 (c)
10	**5c**	PhCH=CH—CHO	**9h**		75 (2 / 98)[a]
11	**5c**	Ph_2CO	**9i**		traces
12	**5c**	H_2CO (trimer)	**10a**		29
			11		35
13	**5d**	PhCHO	**10b**		47

[a] GC / MS
[b] ^{1}H-NMR
[c] not determined
[d] t.r. = 88%



SCHEME 2 Wittig reaction of the new stabilized ylides **7** with carbonyl compounds.

of this substrate resulted in the isolation of a corresponding aldolisation product **11**. Bearing in mind the easy reversibility of such a process, the actual yield of heterocycle **10a** may be considered to be 64%.

No formation of a 7-membered heterocycle was detected when the ylide **7** bore a phenoxide group, whose soft character seems to be insufficient to induce a pseudo-Michael cyclization. Until now, our attempts to react the diylide **1** with an urea, N,N-dimethylimidazolidine-2-one were unsuccessful, even at 100–150°C (diylide is destroyed) or with tBuOK activation.

EXPERIMENTAL SECTION

All reactions were performed in a dry, oxygen-free nitrogen atmosphere, using standard Schlenk techniques. THF was dried by refluxing over, and distilling from sodium benzophenone ketyl under N_2, and stored over sodium. The commercially available starting compounds were dried over P_2O_5 under 0.1 mm Hg if solid, and distilled under N_2 if liquid. Trans-cinnamaldehyde and furfural were distilled just before use. Dimethyldiphenylphosphonium iodide and pyrocatechol carbonate were prepared according to the literature (for the phosphonium salt, see [10]). We thank *Rhône-Poulenc Agrochimie* for supplying us with thiocarbamate **5d**.

^{1}H-NMR spectra were run at 60 or 250 MHz, respectively, on a Varian EM 360 and a BRUKER AC-250 (chemical shifts from internal or external TMS, given in ppm; coupling constants J given in Hertz). ^{31}P-{^{1}H}-NMR spectra were recorded at 32 MHz on a BRUKER WP-80, with external H_3PO_4 85% as a standard. IR spectra were taken on a PERKIN-ELMER 377 spectrometer, ν given in cm^{-1}. GC/MS measurements were carried out on a HEWLETT-PACKARD CPV 5890 instrument (column: OV17 or OV1; 1 = 25 or 30 m; d = 0,25 mm; argon) linked to a mass detector 5970 A (EI pos. mode at 70 eV). Mass Spectra were obtained on a JEOL JMS-DX 300 (FAB pos. or EI pos. (70 eV) modes). Melting points were carried out on a METTLER FP 5 or a LEITZ 350 apparatus, for recrystallized products.

Formation of Diylide **1**

Diylide **1** was obtained by a double deprotonation of the corresponding phosphonium salt, with two equivalents of n-butyllithium in hexane (commercial 1.6 N) or diethylether (prepared according to the literature [11]: 1.6 N) titrated [11] just before use.

To a suspension of 1.71 g (5.0 mmol) dimethyldiphenylphosphonium iodide in 50 to 100 ml THF, was added dropwise below −50°C, 10.0 mmol nBuLi. The resulting colourless suspension was maintained for 15 min at −50°C, then allowed to warm slowly to 0°C, and maintained for 1 hour. At about −20°C, the solid disappeared and the limpid solution took a yellow-green colour, without further change (^{31}P-NMR: δ = 30.9).

Usual Work-Up

After acidic hydrolysis of the mixture with HCl (0.5 N) the usual work-up was as follows: THF evaporation under reduced pressure, residual phase extraction with CH_2Cl_2 or $CHCl_3$, organic extract drying over Na_2SO_4, solvent evaporation. When necessary, elimination or purification of the remaining phosphonium salts was achieved by precipitation of the residue in 0.5–1 L dry Et_2O, after dissolving in a minimum of CH_2Cl_2. The solid thus formed was filtered off and washed with Et_2O. The filtrate was concentrated for further separation of the other organic products by silica gel or alumina column chromatography.

NOTE: Obtention of the phosphonium salts as iodides sometimes required anion exchange, effected by repeated washing of a solution of phosphonium salts in CH_2Cl_2 or $CHCl_3$, with aqueous solutions of NaI. This operation will not be cited again below.

REACTION OF **1** *WITH ETHYLENE CARBONATE* **5A** (*SCHEME 1: STEPS A,B*):

General Procedure: Preparation of Ylide **7a**:

To 4.2 mmol **1** in 50 ml THF was added dropwise at room temperature 0.31 ml (4.7 mmol) **5a** dissolved in 10 ml THF. A solid appeared during the addition, which then turned oily, whereas the liquid phase became colourless. Stirring was maintained for 4 hours.

Preparation of O-(2-hydroxyethyl) diphenylmethylphosphonioacetate iodide **8a** *(Table 1: run 1)*:

4.2 mmol ylide **7a** were prepared as above, and after 13 hours of additional stirring, the reaction mixture was hydrolysed by rapid addition of 20 ml HCl (0.5 N). Usual work-up and purification of the salt by a double precipitation in dry Et_2O produced 1.63 g (80% yield; 91% purity: by-product = dimethyldiphenylphosphonium iodide) phosphonium salt **8a**, as a very hygroscopic beige solid.

8a: H-NMR ($CDCl_3$) δ 2.97 (d, J = 14.0, 3H, P-Me), 3.66 (m, 2H, CH_2O) and 6.13 (m, 2H, CH_2OCO): A_2B_2 system, 3.87 (s broad, 1H, OH), 4.91 (d, J = 13.5, 2H, P-CH_2), 7.50–8.33 (m, 10H, aromatics). ^{31}P-NMR (CH_2Cl_2) δ 20.56 (s). IR ($CHCl_3$) (0.5 N) 1730 (C=O ester). MS (FAB) (glycerol) 303 (M^+): $PH_2MeP^+CH_2CO_2$-CH_2CH_2OH.

Reaction of **7a** *with Benzaldehyde (Table 1: Run 2)*:

To 5.0 mmol **7a** prepared as above, was added rapidly 0.53 g (5.0 mmol) benzaldehyde. The mixture was stirred for 12 hours at room temperature and, after hydrolysis with HCl (0.5 N), usual work-up and alumina column chromatography (eluent: hexane/$CHCl_3$: 1/1), 0.94 g (4.9 mmol; 98% yield; Z/E = 91/9) 2-hydroxyethyl cinnamate **9a** was obtained.

9a [12]: ^{1}H-NMR ($CDCl_3$) δ 2.23 (s, 1H, OH), 3.9 (m, 2H, CH_2O), 4.4 (m, 2H, CH_2O), 7.15 (AB system, δ_A 6.51, δ_B 7.78, J = 16, 2H, CH=CH), 7.3–7.65 (m, 5H, aromatics). IR (CCl_4) 1716 (C=O ester), 988–969 d. m (CH=CH trans). GC/MS (E.I.) 162 (M^+).

Reaction of **7a** *with Trans-Cinnamaldehyde (Table 1: Run 3)*:

To 5.3 mmol **7a** prepared as above in 125 ml THF was added dropwise 0.53 ml (4.2 mmol) trans-cinnamaldehyde in 25 ml THF. The mixture was stirred for 17 hours at room temperature; after hydrolysis with 20 ml HCl (0.5 N), usual work-up and purification by silica gel column chromatography (eluents: CH_2Cl_2/hexane 8/2 to 10/0; CH_2Cl_2 + 0–3% MeOH) gave successively 0.68 g (1.8 mmol; 86% yield; Z/E = 0/100) bis (5-phenyl 2,4-pentadienoate) glycol ethylene diester **9'b**, and 0.09 g (0.47 mmole; 10% yield; Z/E = 1/99) 5-phenyl 2,4-pentadienoate glycol ethylene monoester **9b**.

9'b: mp 121–122°C (CH_2Cl_2/hexane) (colourless thin needles). Anal. calcd: C 76.98, H 5.92; found: C 76.82, H 5.79. ^{1}H-NMR ($CDCl_3$) δ 4.45 (s, 4H, $O(CH_2)_2O$), 6.04 (part of AB system, J = 15.7, 2H, =CHCO (trans)), 6.82–6.97 (m, 4H, Ph—CH=CH), 7.25–7.54 (m, 12H, aromatics and CH=C—CO). IR (KBr) 1705 (C=O ester). M.S. (E.I.) 374 (M^+).

9b: (colourless oil): ^{1}H-NMR ($CDCl_3$) δ 3.23 (s broad, 1H, OH), 3.67–4.57 (A_2B_2 system, 4H, $O(CH_2)_2O$), 6.67 (AB system, δ_A 6.15, δ_B 7.19, J = 15.5, 2H, CH=CH (trans)), 6.77–7.87 (m, 8H, PhCH=CH—CH). GC/MS (E.I.) 218 (M^+).

Reaction of **7a** *with Benzophenone (Table 1: Run 4)*:

To 5.0 mmol **7a** prepared as above in 125 ml THF was added dropwise at room temperature, a solution of 2.74 g (15.0 mmol) benzophenone and 0.74 g (6.1 mmol; taking into account the neutralisation of 0.3 mmole residual basicity) benzoic acid in 25 ml THF. A thick solid appeared and the mixture was warmed 70 hours at refluxing THF. After hydrolysis at room temperature with 7 ml HCl (0.5 N) and usual treatment, the initial amount of benzophenone is recovered quantitatively by chromatography on silica gel column.

REACTION OF **1** *WITH PYROCATECHOL CARBONATE* **5b** *(SCHEME 1: STEPS A, B); FURTHER REACTION WITH BENZALDEHYDE (TABLE 1: RUN 5; SCHEME 2)*

To 5.1 mmol **1** in 100 ml THF was added dropwise at 10°C, a solution of 0.77 g (5.7 mmol) **5b** in 25 ml THF. A sudden decolouration was observed at the end of the addition, when a powdery solid appeared After 3 hours at room temperature, 0.63 ml (6.2 mmol) benzaldehyde in 25 ml THF was added. After 40 hours stirring, the mixture was rapidly hydrolysed with 15 ml HCl (0.5 N), and after usual work-up, reaction products were separated by chromatography on silica gel column (eluents: CH_2Cl_2 + 0 to 3% MeOH; rapid elution), to obtain 0.61 g (2.5 mmol; 50% yield) o-hydroxyphenyl cinnamate **9d**, and 0.28 g (2.5 mmol; 45% yield) pyrocatechol.

9d: mp 139.3°C (lit. [13]: 140–141°C). ^{1}H-NMR ($CDCl_3$): δ 5.72 (s broad, 1H, OH), 7.30 (AB system, δ_A 6.68, δ_B 7.92, J = 16.0, 2H, CH=CH (trans)), 6.99 (m, 2H) and 7.15 (m, 2H) and 7.59 (m, 2H): aromatics. IR (KBr) 1710 (C=O ester). M.S. (E.I.) 240 (M^+).

REACTION OF **1** *WITH CARBAMATE* **5c** *(SCHEME 1: STEPS A, B)*:

General Procedure: Preparation of Ylide **7c**:

To 5.0 mmol **1** in 50 to 100 ml THF was added dropwise at room temperature, 0.34 ml (4.3 mmol) to 0.47 ml (5.5 mmol) **5c** in 10 ml THF, and stir-

ring was maintained at refluxing THF for 14 hours. The mixture became colourless and a beige solid appeared.

Preparation of N-(2-hydroxyethyl) N-methyldiphenylmethylphosphonioacetamide iodide **8b** *(Table 1: Run 6):*

4.1 mmol **7c** prepared as above in 60 ml THF (stoichiometry **1 / 5c** = 1.0/1.1) were quickly hydrolysed by addition of 20 ml HCl (0.5 N), then classical work-up was performed and the phosphonium salts were purified by a double precipitation in dry Et_2O. We obtained 1.49 g (85% yield; 91% purity: by product = dimethyldiphenylphosphonium iodide) **8b**, as a very hygroscopic beige solid.

8b: ^{1}H-NMR ($CDCl_3$) δ 2.85 (d, J = 14.0, 3H, PMe), 2.88 (s broad, 3H, NMe) 3.17–3.93 (m 3.37, m 3.70, 5H, $N(CH_2)_2OH$), 5.07 (d, J = 13.0, 2H, PCH_2), 7.37–8.33 (m, 10H, aromatics). ^{31}P-NMR (CH_2Cl_2) δ 20.65 (s), 20.96 (s): ratio 35/65, conformers. IR ($CHCl_3$, 0.3 N) 1935 (C=O amide). M. S. (FAB) 316 (M^+): Ph_2MeP^+-$CH_2CON(Me)CH_2CH_2OH$.

Reaction of **7c** *with Benzaldehyde (Table 1: Run 7):*

To 5.0 mmol ylide **7c** prepared as above in 100 ml THF (stoichiometry **1 / 5c** = 1.0/1.0), was added at room temperature 0.53 g (5.0 mmol) benzaldehyde, and the mixture was allowed to react for 12 hours. After hydrolysis with HCl (0.5 N) and usual work-up, alumina column chromatography separation led to the obtainment of 0.97 g (4.7 mmol; 95% yield; Z/E = 5/95) N-(2-hydroxyethyl)-N-methylcinnamide **9e**.

9e: mp 77–78°C (lit. [14] 79–81°C). ^{1}H-NMR ($CDCl_3$) δ 3.00–3.25 (m, 3H, NMe), 3.5–4.0 (m, 5H, $N(CH_2)_2OH$), 6.8–7.9 (m, 7H, CH=CH and aromatics). IR (KBr) 1641 (Band I C=O amide), 1587 (band II C=O amide), 990–980 d.m (CH=CH trans). GC/MS (E.I.) 205 (M^+) Z/E = 5/95.

Reaction of **7c** *with Furfural (Table 1: Run 8):*

To 4.6 mmol ylide **7c** prepared as above in 125 ml THF (stoichiometry **1 / 5c** = 1.0/1.1) was added dropwise at room temperature 0.42 ml (5.0 mmol) furfural in 25 ml THF. The mixture was stirred for 28 hours. After hydrolysis with 16 ml HCl (0.5 N) (pH = 2–3) and usual work-up, purification of the reaction product by silica gel column chromatography led to 0.58 g (3.0 mmol; 65% yield; Z/E = 0/100) 3-(2-furyl)-N-(2-hydroxyethyl)-N-methylpropenamide **9f**.

9f: Colourless oil, rapid degradation pure or in solution. ^{1}H-NMR ($CDCl_3$) δ 3.1 and 3.25 (s broad and s broad, 3 H, NMe two conformers), 3.4–4.0 (m, 4H, $N(CH_2)_2O$), 4.39 (s, dilution displaced, 1H, OH), 6.27–6.67 (m, 2H, $H_\beta H_{\beta'}$ furyl), 6.82 (part of AB system, (δ_{A1} 6.81, δ_{A2} 6.91, J = 15.0, 1H, =CH—CO (trans) of the two conformers), 7.43 (d, part of AB system, J = 15.0, 1H, HC=C—CO (trans)), 7.47 (s broad, 1H, H_α furyl), GC/MS (E.I.) 195 (M^+) (Z/E = 0/100).

Reaction of **7c** *with 3-Phenylbutyraldehyde (Table 1: Run 9):*

To 5.0 mmol ylide **7c** prepared as above in 130 ml THF (stoichiometry **1 / 5c** = 1.0/1.1) was added dropwise at room temperature 0.82 ml (5.5 mmol) 3-phenylbutyraldehyde in 30 ml THF. The mixture was stirred for 26 hours. After hydrolysis with HCl 0.5 N (until pH = 4), usual work-up and silica gel column chromatography (eluents: $CHCl_3$; $CHCl_3$ + 2 to 5% MeOH), 0.40 g (1.6 mmol; 32% yield) N-(2-hydroxyethyl)-N-methyl-5-phenyl-2-hexenamide **9g** was obtained.

9g: yellow oil. ^{1}H-NMR (CCl_4) δ 1.22 (d, 2H, J = 6.5, CH_3C), 2.20–2.75 (m, 2H, C—CH_2—C), 2.87 (d broad, 3H, N-Me), 3.35–3.80 (m, 5H, CH—Ph and $N(CH_2)_2O$), 4.20 (s broad, 1H, OH), 5.7–7.0 (m, 2H, CH=CH), 7.17 (s, 5H, aromatics).

Reaction of **7c** *with Trans-Cinnamaldehyde (Table 1: Run 10):*

To 8.0 mmol ylide **7c** prepared as above in 250 ml THF (stoichiometry **1 / 5c** = 1.0/0.8) was added dropwise in 1 hour at room temperature 1.90 ml (15.0 mmol) cinnamaldehyde in 50 ml THF, and the mixture was stirred for 22 hr. The medium was hydrolysed with 27 ml HCl (0.5 N), treated in the usual manner, and the reaction product was precipitated in a mixture Et_2O/hexane, after elimination of the residual phosphonium salts. We obtained 1.39 g (6.0 mmol; 75% yield) N-(2-hydroxyethyl)-N-methyl-5-phenyl-2,4-pentadienamide **9h**.

9h: mp 120.4°C (CH_2Cl_2/Hexane). White-yellow brilliant needles. Anal. calcd: C 72.70, H 7.41, N 6.06; found: C 72.65, H 7.54, N 6.10. ^{1}H-NMR ($CDCl_3$) δ 3.03 and 3.16 (s and s, ratio 45/55), 3H, N-Me two conformers), 3.52 and 3.62 (t and t (ratio 46/54), J = 5.1 and 5.2, 2H, CH_2N two conformers), 3.80 (t, J = 5.2, 2H, CH_2O), 3.87 (s broad, dilution displaced, 1H, OH), 6.43 and 6.58 (d and d (ratio 55/45, part of AB system, J = 14.7, 1H, =CH—CO (trans) two conformers), 6.78–6.97 (m, 2H, PhCH), 7.25–7.50 (m, 6H, Ph and CH=C—CO). ^{13}C-NMR ($CDCl_3$) δ 52.3 (Me), 60.5 (CH_2N), 61.9 (CH_2O), (120.5, 121.6, 127.1, 129.1, 136.7, 140.1, 142.9, 143.8): (PhCH=CH—CH=CH), 168.9 (C=O). IR (KBr) 1630 (Band I C=O amide), 1580 (Band II C=O amide). GC/MS (E.I.) 231 (M^+) (Z/E = 2/98).

Reaction of **7c** *with Benzophenone (Table 2: Run 11)*

Method 1:

To 5.0 mmol ylide **7c** prepared as above in 125 ml THF (stoichiometry **1** / **5c** = 1.0/1.0) was added 0.92 g (5.0 mmol) benzophenone in 25 mL THF. The mixture was stirred for 4 days at room temperature and 1 d at reflux. The medium was then hydrolysed with 19 ml HCl (0.5 N), usual treatment being carried out and after silica gel column chromatography (eluents: Hexane/$CHCl_3$: 10/0 to 0/10; $CHCl_3$ + 3% MeOH) 0.07 g (0.39 mmole; 8% yield) 1,1-diphenylethylene, 0.83 g (4.5 mmol; 91% yield) recovered benzophenone and traces of N-(2-hydroxyethyl)-N-methyl-3-phenylcinnamide **9i** were obtained.

9i: mixture with other compounds. GC/MS (E.I.) 281 (M^+).

Method 2:

To 5.1 mmol ylide **7c** prepared as above in 130 ml THF (stoichiometry **1** / **5c** = 1.0/1.0) were added quickly at room temperature 2.98 g (16.4 mmol) benzophenone and 0.81 g (6.6 mmol; taken into account the neutralisation of residual basicity) benzoic acid. The mixture was allowed to evolve 6 days at refluxing THF, then 11 d at room temperature. After hydrolysis with HCl (0.5 N) and usual work-up, silica gel column chromatography led to the obtainment of 2.97 g (5.1 mmol; 100% yield) benzophenone.

REACTION OF **1** *WITH THIOCARBAMATE* **5d** *(SCHEME 1: STEPS A,B)*:

General Procedure: *Preparation of Ylide* **7d**:

To 4.0 mmol **1** in 50 to 100 ml THF was added quickly at room temperature 0.75 g (4.2 mmol) **5d** pure or dissolved in 20 ml THF. The mixture was stirred at refluxing THF for 14 to 18 hours, and became colourless, with the appearance of a fine beige solid.

Reaction of **7d** *with Formaldehyde (Table 1: Run 12)*:

To 3.1 mmol ylide **7d** prepared as above in 50 ml THF was added dropwise at room temperature 0.34 g (11.4 mmol formaldehyde) trioxymethylene, and the mixture was stirred for 2 days. After hydrolysis with HCl (0.5 N) until pH = 7, usual work-up and chromatography on a silica gel column (eluents: CH_2Cl_2 + 0 to 0.5% MeOH), 0.08 g (0.44 mmole; 16% yield) remaining **5d**, 0.19 g (0.9 mmole; 29% yield) 7-membered heterocycle **10a**, and 0.26 g (1.1 mmole; 35% yield) 7-membered heterocycle **11** were isolated.

10a: mp 92–93°C ($CHCl_3$/Hexane) colourless needles. Anal. calcd: C 57.67, H 5.81, N 13.45; found: C 57.48, H 5.81, N 13.61. ^{1}H-NMR ($CDCl_3$) δ 1.18 (t, J = 7.1, 3H, Me), 2.60 (t, J = 6.85, 2H, CH_2S), 3.45 (t, J = 6.85, 2H, CH_2CO), 4.09 (q, J = 7.1, CH_2N), 7.11 (dd, J = 7.6, J′ = 4.8, 1H, H_β pyrido), 7.93 (dd, J = 7.6, J′ = 1.9, 1H, H_γ pyrido), 8.48 (dd, J = 4.8, J′ = 1.8, 1H, H_α pyrido). IR (CCl_4) 1655 (Band I C=O amide), 1560 (Band II C=O amide). GC/MS (E.I.) 208 (M^+). **11**: mp 74–75°C white powder. Anal. calcd: C 55.44, H 5.92, N 11.76; found: C 55.62, H 6.03, N 11.72. ^{1}H-NMR ($CDCl_3$) δ 1.17 (t, J = 7.0, 3H, Me), 2.64 (m, 1H, CH—CO), 2.70–3.25 (s broad, dilution displaced, 1H, OH), 3.48 (AB system (with double A part), δ_A 3.44, δ_B 3.52, J_{AB} = 10.4 or 12.1 (bands 2 and 4 divided into two), J'_A = 6.6, 2H, CH_2O), 3.75 (d of AB system, δ_A 3.54, δ_B 3.93, J = 11.5, J'_A = 4.5, J'_B = 2.7, 2H, CH_2S), 4.11 (q of AB system, δ_A 4.02, δ_B 4.19, J_{AB} = 12.8 or 13.9 (bands 2 and 4 divided into two), J = 6.7, 2H, $C\underline{H}_2OH$), 7.14 (dd, J = 7.7, J′ = 1.8, 1H, H_γ pyrido), 8.50 (dd, J = 4.8, J′ = 1.8, 1H, H_α pyrido). IR ($CHCl_3$, 0.07 N) 1645 (band I C=O amide), 1560 (band II C=O amide). GC/MS (E.I.) 238 (M^+).

Reaction of **7d** *with Benzaldehyde (Table 1: Run 13)*:

To 4.0 mmol ylide **7d** prepared as above in 100 ml THF was added dropwise at room temperature 0.45 ml (4.4 mmol) benzaldehyde in 20 ml THF, and the mixture was stirred for 3 days. After hydrolysis with HCl (0.5 N) until pH = 7, usual work-up and chromatography on silica gel column (eluents: CH_2Cl_2/hexane 3/5 to 10/0; CH_2Cl_2 + 0.5% MeOH), 0.53 g (1.9 mmol; 47% yield) 7-membered heterocycle **10b** was obtained.

10b: mp 119–120°C (CH_2Cl_2/Hexane). Cottony beige needles. Anal. Calcd: C 67.58, H 5.67, N 9.85; found: C 67.75, H 5.62, N 9.67. ^{1}H-NMR ($CDCl_3$) δ 1.26 (t, J = 7.0, 3H, Me), 2.70 (dd, J = 14.1, J′ = 9.9, 1H, CHS), 3.28 (dd, J = 14.1, J′ = 5.3, 1H, CH_a—CO), 3.68 (dd, J = 9.8, J′ = 5.3, 1H, CH_b—CO), 4.28 (q of AB system, J = 7.0, 2H, CH_2N), 6.92 (dd, J = 7.6, J′ = 4.8, 1H, H_β pyrido), 7.11–7.34 (m, 5H, ph), 7.60 (dd, J = 7.6, J′ = 1.6, 1H, H_γ pyrido), 8.28 (dd, J = 4.8, J′ = 1.6, H_α pyrido). IR (KBr) 1655–1650 (d), 1570 (amide bands). GC/MS (E.I.) 284 (M^+).

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[7] The two classical synthesis methods of $Ph_3P{=}CH{-}Z$ ($Z{=}CO_2R$, $C(O)NR_2$, $C(O)R$, ...) are the following: a. Acylation of $Ph_3P{=}CH_2$ by X-Z, with the transylidation process decreasing the yields. b. Alkylation of Ph_3P by $Cl{-}CH_2{-}Z$ and further deprotonation, with a side reaction of direct attack of Cl instead of Z by Ph_3P. In our case, the $Cl{-}Z$ and $Cl{-}CH_2{-}Z$ acylation and alkylation reagents are functional: $Cl{-}C(O){-}X{-}Q{-}YH$ and $ClCH_2{-}C(O)\,X{-}Q{-}YH$.

[8] Initially, we expected an increase of the nucleophilic reactivity of the ylide **7**, because of a possible strong interaction between the X^- function and the phosphorus atom, decreasing its positive charge. Moreover, an acidic catalysis with 20% excess benzoic acid was unsuccessful (for ref. see: C. Ruchardt, S. Eichler, *Angew. Chem. Internat. Ed., 2* (10), 1963, 619).

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