

Flash Vacuum Pyrolysis of α -Acyl-*o*-methoxybenzylidene-triphenylphosphoranes to give 2-Substituted Benzofurans

R. Alan Aitken

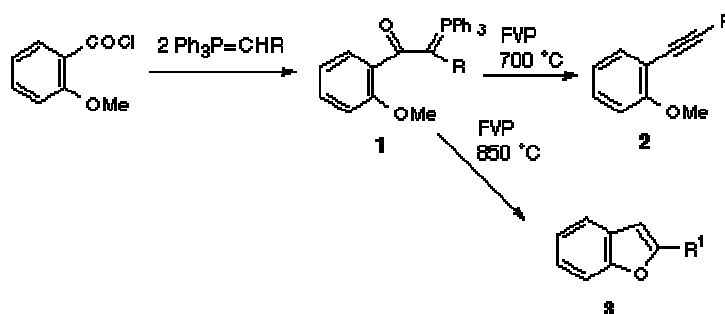
*School of Chemistry, University of St Andrews, North Haugh,
St Andrews, Fife, KY16 9ST, UK
E-mail: raa@st-andrews.ac.uk*

Dedicated to Otto Meth-Cohn on the occasion of his 65th birthday

Abstract

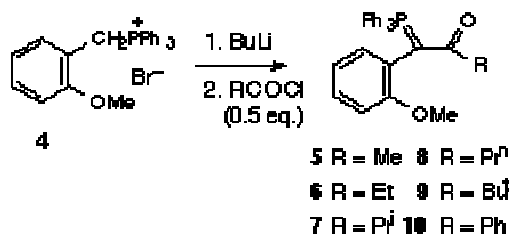
The title stabilised ylides, readily prepared in one step from acid chlorides, are converted upon FVP at 850 °C into 2-substituted benzofurans. When the acyl group is aromatic it appears unchanged as the 2-substituent in the product while for aliphatic examples degradation processes may lead to 2-alkenyl products.

Some time ago we reported that, while flash vacuum pyrolysis (FVP) of the 2-methoxybenzoyl substituted stabilised ylides **1** at 700 °C gave the expected alkynes **2** by extrusion of Ph_3PO , simply increasing the pyrolysis temperature to 850 °C resulted in loss of the OMe group and cyclisation of the resulting phenoxy radicals to give 2-substituted benzofurans **3**.¹ Depending on the nature of R, the products were formed with $\text{R}^1 = \text{Me}$ and Et (R = Me), $\text{R}^1 = \text{vinyl}$ (R = Et or Pr^i), $\text{R}^1 = \text{Me}$, Et and vinyl (R = Pr^n , Bu^n or Pent^n) and $\text{R}^1 = \text{Ph}$ (R = Ph). and these patterns could be accounted for by interaction of the initially formed benzofuran-3-yl radicals with the 2-alkyl group. As shown access to **1** was gained by reaction of 2-methoxybenzoyl chloride with an appropriate non-stabilised ylide.



We have subsequently extended this chemistry to construction of more complex systems by using groups R which can interact with the benzofuran-3-yl radical intermediate in a more constructive way leading to tri- and tetracyclic heterocyclic systems.² In the course of this work it has become apparent that it is sometimes advantageous to approach the key intermediates **2** by starting from an ylide bearing the 2-methoxyphenyl group and reacting it with a suitable acid chloride. In this paper we describe the preparation and pyrolytic behaviour of the isomeric ylides **5-10** which has remained unreported until now.

As shown these were readily prepared by treatment of 2-methoxybenzyltriphenylphosphonium bromide **4**³ with butyllithium followed by 0.5 equiv. of an acid chloride. The reaction takes place with transylidation to give the required ylides **5-10** and regenerate 0.5 equiv. of the quaternary phosphonium chloride.⁴



The products were stable pale yellow solids which showed the expected ³¹P NMR signals in the range $\delta_{\text{P}} +10.9\text{-}14.4$ and also had highly informative ¹³C NMR spectra with phosphorus coupling extending throughout the *P*-phenyl groups and to the first one or two carbons of both the acyl and 2-methoxyphenyl groups (Table 1).

When the ylides were subjected to FVP at 850 °C and 10⁻²-10⁻³ Torr using the previously described apparatus,⁵ Ph₃PO was obtained at the furnace exit and in the cold trap colourless liquids which proved to be the desired 2-substituted benzofurans.

As shown in Table 2, the nature and yield of the products closely paralleled those obtained from the isomeric ylides **1**. Thus, the acetyl ylide **5** gave a mixture of 2-methyl and 2-ethyl products **11** and **12**, the propionyl and isobutyryl ylides gave only 2-vinylbenzofuran **13**, the *n*-butyryl ylide gave a mixture of **11**, **12** and **13**, while the benzoyl ylide gave the phenyl product **15**. The mechanism for formation of these was fully described in our previous paper and the similar product distribution is of course to

be expected from the common intermediacy of **2**. One R group not previously investigated was *t*-butyl and the result from this was in accord with those for R = Et and Prⁱ where if only β (and no γ) hydrogens are present on the alkyl group, β -hydrogen abstraction occurs with loss of H[•] (R = Et) or Me[•] (R = Prⁱ) to give **13**. In the case of **9** a similar process occurred with loss of Me[•] to give 2-isopropenylbenzofuran **14** which showed excellent agreement with published spectroscopic data.

Table 1. ¹³C NMR Spectra of ylides **5–10**, δ_C (J_{P-C})

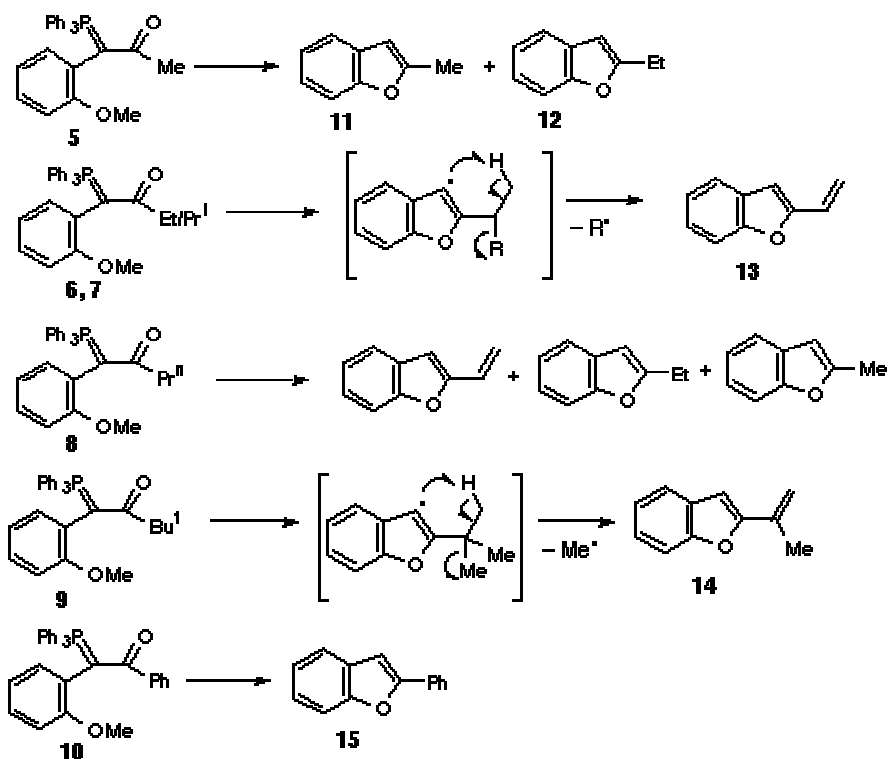
		P-Phenyl					
	R	CO	P=C	C-1	C-2	C-3	C-4
5	Me	187.9 (6)	65.0 (112)	127.4 (90)	133.6 (9)	128.0 (12)	131.1 (2)
6	Et	191.5 (5)	64.0 (111)	127.5 (87)	133.5(10)	128.0 (12)	131.0 (2)
7	Pr ⁱ	194.2 (4)	63.3 (111)	127.9 (90)	133.5 (10)	127.9 (12)	130.9 (2)
8	Pr ⁿ	190.4 (5)	65.1 (111)	127.6 (90)	133.6 (9)	128.0 (12)	131.0 (2)
9	Bu ^t	193.6 (2)	67.1 (113)	127.9 (91)	133.3 (7)	127.7 (11)	130.4 (<2)
10	Ph	184.1 (6)	67.1 (111)	127.6 (92)	133.5 (10)	128.1(12)	131.1 (2)

R signals	2-MeOC ₆ H ₄	
5	25.7 (10)	158.7 (3), 136.8(5), 128.0, 127.5, 120.1, 109.9, 54.3
6	30.6 (10), 10.9	158.7 (3), 136.9 (6), 127.9, 127.5, 120.0, 109.8, 54.3
7	33.5 (10), 20.0, 19.8	158.9 (3), 137.1 (5), 127.8, 127.45, 119.9, 109.8, 54.2
8	39.3 (9), 19.7, 14.2	158.8 (3), 137.0 (5), 127.48, 127.46, 120.0, 109.8, 54.3
9	40.8 (10), 28.8 (3 C)	159.3 (4), 138.6 (6), 127.84, 127.80, 119.3 (2), 109.4 (2), 54.3
10	142.0 (12), *	158.6 (3), 137.2 (6), 127.46, 127.43, 120.2, 109.8, 54.3

* additional signals 128.4(2 C), 127.9, 127.0 (2 C)

Table 2. Results of pyrolysis of ylides **5–10**

	R	Products from FVP of 5–10 (%)				Products from FVP of 1 (%) ¹			
		11	12	13	15	11	12	13	15
5	Me	7	19	-	-	8	20	-	-
6	Et	-	-	46	-	-	-	83	-
7	Pr ⁱ	-	-	49	-	-	-	60	-
8	Pr ⁿ	7	16	18	-	9	52	10	-
10	Ph	-	-	-	50	-	-	-	80



Experimental Section

General Melting points were determined using a Reichert hot-stage microscope and are uncorrected. Infra red spectra were recorded as nujol mulls on a Perkin Elmer 1420 instrument. NMR spectra were obtained for ¹H at 80 MHz using a Bruker WP80 instrument and for ¹³C and ³¹P at 75 MHz and 121 MHz respectively using a Varian Gemini 2000 instrument. All spectra were run on solutions in CDCl₃ with internal Me₄Si as reference for ¹H and ¹³C and external 85% H₃PO₄ as reference for ³¹P. Chemical shifts are reported in ppm to high frequency of the reference and coupling constants *J* are in Hz.

Mass spectra were obtained on an A. E. I. MS-902 spectrometer using electron impact at 70 eV.

Preparation of β -Oxoalkylidenetriphenylphosphoranes 5-10 A solution of 2-methoxybenzyltriphenylphosphonium bromide³ (10 g, 21.6 mmol) in dry THF (100 cm³) was stirred under N₂ while *n*-butyllithium in hexane (22 mmol) was added by syringe. After 15 min a solution of the appropriate acid chloride (10.8 mmol) in dry THF (10 cm³) was added dropwise and the resulting mixture stirred for 3 h. It was then added to water (250 cm³) and the mixture extracted with ether (2 x 100 cm³) and ethyl acetate (100 cm³). The combined extract was washed with water (2 x 100 cm³), dried over MgSO₄ and evaporated to give a pale yellow solid. This was recrystallised from ether / hexane to give the products as described below:

[(Acetyl)(2-methoxyphenyl)methylene]triphenylphosphorane 5 Reaction using acetyl chloride gave pale yellow crystals (1.70 g, 37%), mp 188-190 °C (Found: C, 78.9; H, 5.9. C₂₈H₂₅O₂P requires C, 79.2; H, 5.9%); ν_{\max} /cm⁻¹ 1577, 1524, 1438, 1272, 1250, 1120, 1072, 746 and 694; δ_{H} 7.9-7.25 (16 H, m), 7.2-6.45 (3 H, m), 3.38 (3 H, s) and 1.96 (3 H, s); δ_{C} see Table 1; δ_{P} +14.3; *m/z* 424 (M⁺, 0.5%), 409 (0.5), 393 (2), 277 (100), 262 (20), 201 (19), 199 (16) and 183 (24).

[(Propionyl)(2-methoxyphenyl)methylene]triphenylphosphorane 6 Reaction using propionyl chloride gave yellow crystals (2.55 g, 54%), mp 153-155 °C (Found: C, 79.1; H, 6.3. C₂₉H₂₇O₂P requires C, 79.4; H, 6.2%); ν_{\max} /cm⁻¹ 1601, 1582, 1273, 1123, 1073, 962, 789, 743 and 692; δ_{H} 7.9-7.25 (16 H, m), 7.2-6.45 (3 H, m), 3.38 (3 H, s), 2.24 (2 H, q, *J* 7) and 1.04 (3 H, t, *J* 7); δ_{C} see Table 1; δ_{P} +13.7; *m/z* 438 (M⁺, 48%), 409 (100), 406 (45), 379 (7), 337 (3), 277 (6), 262 (10) and 183 (12).

[(2-Methoxyphenyl)(2-methylpropionyl)methylene]triphenylphosphorane 7 Reaction using isobutyryl chloride gave yellow crystals (2.98 g, 61%), mp 154-157 °C (Found: C, 79.35; H, 6.5. C₃₀H₂₉O₂P requires C, 79.6; H, 6.5%); ν_{\max} /cm⁻¹ 1588, 1572, 1515, 1269, 1108, 1073, 971, 742, 715 and 692; δ_{H} 7.9-7.25 (16 H, m), 7.2-6.45 (3 H, m), 3.38 (3 H, s), 2.73 (1 H, septet, *J* 7), 1.05 (3 H, d, *J* 7) and 0.96 (3 H, d, *J* 7); δ_{C} see Table 1; δ_{P}

+13.4; m/z 452 (M^+ , 0.2%), 421 (0.2), 409 (3), 277 (100), 262 (2), 201 (20), 199 (16), 185 (10), 183 (14) and 152 (10).

[(Butyryl)(2-methoxyphenyl)methylene]triphenylphosphorane 8 Reaction using butyryl chloride gave yellow crystals (2.34 g, 48%), mp 138-141°C (Found: C, 79.75; H, 6.8. $C_{30}H_{29}O_2P$ requires C, 79.6; H, 6.5%); ν_{max} / cm^{-1} 1583, 1517, 1276, 1123, 1073, 972, 749 and 691; δ_H 7.9-7.25 (16 H, m), 7.2-6.45 (3 H, m), 3.38 (3 H, s), 2.22 (2 H, t, J 7), 1.60 (2 H, sextet, J 7) and 0.84 (3 H, t, J 7); δ_C see Table 1; δ_P +13.9; m/z 452 (M^+ , 40%), 421 (48), 409 (100), 277 (12), 262 (44), 183 (42) and 135 (72).

[(2-Methoxyphenyl)(2,2-dimethylpropionyl)methylene]triphenylphosphorane 9 Reaction using pivaloyl chloride gave pale yellow crystals (3.27 g, 65%), mp 200-202 °C (Found: C, 79.75; H, 6.8. $C_{31}H_{31}O_2P$ requires C, 79.8; H, 6.7%); ν_{max} / cm^{-1} 1590, 1572, 1288, 1177, 1108, 1016, 964, 742 and 692; δ_H 7.9-7.25 (16 H, m), 7.2-6.4 (3 H, m), 3.48 (3 H, s) and 1.05 (9 H, s); δ_C see Table 1; δ_P +10.9; m/z 466 (M^+ , 8%), 409 (100), 277 (2), 262 (6), 204 (2) and 183 (7).

[(Benzoyl)(2-methoxyphenyl)methylene]triphenylphosphorane 10 Reaction using benzoyl chloride gave pale yellow crystals (3.57 g, 68%), mp 224-226 °C (Found: C, 81.25; H, 5.5. $C_{33}H_{27}O_2P$ requires C, 81.5; H, 5.6%); ν_{max} / cm^{-1} 1580, 1507, 1433, 1282, 1254, 1135, 1030, 973, 756, 745, 719 and 690; δ_H 7.9-7.3 (15 H, m), 7.3-6.4 (11 H, m) and 3.30 (3 H, s); δ_C see Table 1; δ_P +14.4; m/z 486 (M^+ , 5%), 455 (5), 336 (12), 313 (6), 277 (25), 262 (13), 183 (18), 169 (70) and 84 (100).

FVP of ylides to give benzofurans

Flash vacuum pyrolysis was carried out using the previously described apparatus.⁵ A sample of the ylide was volatilised through a horizontal quartz tube heated externally to 850 °C and maintained at 10^{-2} - 10^{-3} Torr and the products collected in a liquid nitrogen-cooled cold trap. In the case of **5-9** the benzofuran products were collected in the cooler part of the cold trap separate from the Ph_3PO and were directly dissolved out with $CDCl_3$ for NMR analysis and estimation of the yield by adding an accurately known amount of CH_2Cl_2 and comparing integrals. In the case of **10** the less volatile product was collected

together with the Ph_3PO at the furnace exit and was dissolved out and isolated by preparative TLC.

FVP of **5** (200 mg) at 850 °C gave Ph_3PO at the furnace exit and in the cold trap a colourless liquid which proved to be mainly 2-methylbenzofuran (7%); δ_{H} 7.5-7.1 (4 H, m), 6.35 (1 H, q, J 1) and 2.18 (3 H, d, J 1) [lit.,⁶ (CCl_4) 7.07, 6.02 and 2.36], and 2-ethylbenzofuran (19%); δ_{H} 7.5-7.1 (4 H, m), 6.35 (1 H, t, J 1), 2.78 (2 H, q of d, J 7, 1) and 1.31 (3 H, t, J 7) [lit.,⁶ (CCl_4) 7.4-6.8, 6.3-6.17, 2.78 and 1.34].

FVP of **6** (100 mg) at 850 °C gave Ph_3PO at the furnace exit and in the cold trap a colourless liquid which proved to be mainly 2-vinylbenzofuran (46%); δ_{H} 7.55-7.1 (4 H, m), 6.61 (1 H, dd, J 17, 11), 6.54 (1 H, s), 5.92 (1 H, dd, J 17, 2) and 5.34 (1 H, J 11, 2) [lit.,⁷ 7.51-7.01, 6.59, 6.49, 5.95 and 5.31].

FVP of **7** (200 mg) at 850 °C gave Ph_3PO at the furnace exit and in the cold trap a colourless liquid which proved to be mainly 2-vinylbenzofuran (49%).

FVP of **8** (250 mg) at 850 °C gave Ph_3PO at the furnace exit and in the cold trap a colourless liquid which proved to be a mixture of 2-vinylbenzofuran (18%), 2-ethylbenzofuran (16%) and 2-methylbenzofuran (7%).

FVP of **9** (200 mg) at 850 °C gave Ph_3PO at the furnace exit and in the cold trap a colourless liquid which proved to be mainly 2-isopropenylbenzofuran (40%); δ_{H} 7.6-7.2 (4 H, m), 6.63 (1 H, s), 5.81 (1 H, m), 5.18 (1 H, m) and 2.12 (3 H, m) [lit.,⁸ 7.6-7.2, 6.68, 5.84, 5.22-5.20 and 2.12]; m/z 158 (M^+ , 100%), 143 (30), 131 (20), 128 (21) and 115 (50).

FVP of **10** (500 mg) at 850 °C gave a solid at the furnace exit shown by GCMS to consist mainly of Ph_3PO and 2-phenylbenzofuran. This was isolated by preparative TLC to give colourless crystals (50%), mp 118-120 °C (lit.,⁹ 120-121 °C); δ_{H} 7.9-7.2 (9 H, m) and 6.97 (1 H, s); δ_{C} 111.1 (C-7) and 101.3 (C-3) [lit.,⁸ 111.1 and 101.2].

References

1. Aitken, R. A.; Burns, G. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2455.
2. Aitken, R. A.; Burns, G.; Morrison, J. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3937.
3. Aitken, R. A.; Drysdale, M. J.; Ferguson, G.; Lough, A. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 875.
4. Bestmann, H. J.; Arnason, B. *Chem. Ber.* **1962**, 95, 1513.
5. Aitken, R. A.; Atherton, J. I. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1281.
6. Hosokawa, T.; Ohkata, H.; Moritani, I. *Bull. Chem. Soc. Jpn.* **1975**, 48, 1533.
7. Brewer, J. D.; Elix, J. A. *Aust. J. Chem.* **1975**, 28, 1059.
8. Kundu, N. G.; Pal, M.; Mahanty, J. S.; De, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2815.
9. Stoermer, R. *Ber. Dtsch. Chem. Ges.* **1903**, 36, 3979.