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Solvent-free Wittig olefination with stabilized phosphoranes—scope and limitations†

Thies Thiemann,*[a] Masataka Watanabe,[b] Yasuko Tanaka[a] and Shuntaro Mataka[a]

[a] *Institute for Materials Chemistry and Engineering, Kyushu University, 6-1 Kasuga-koh-en, Kasuga-shi, Fukuoka 816-8580, Japan. E-mail: thies@cm.kyushu-u.ac.jp*
[b] *Interdisciplinary Graduate School of Engineering, Kyushu University, 6-1 Kasuga-koh-en, Kasuga-shi, Fukuoka 816-8580, Japan*

Received (in Montpellier, France) 24th September 2003, Accepted 5th January 2004
First published as an Advance Article on the web 24th March 2004

Neat mixtures of arene/hetarenecarbaldehydes, alkanals as well as alkenals with alkyl (triphenylphosphoranylidene)acetates react exothermally to furnish the corresponding alkenes. In certain cases, heating has to be provided externally. Reaction times are short and yields are generally very high. Neat mixtures of ketones and alkyl (triphenylphosphoranylidene)acetates react preferentially under microwave irradiation. The better stabilized phosphoranes do not react in the solid state with aldehydes or ketones under conventional heating, but necessitate microwave irradiation, although not all of the phosphoranes have been found to be stable under microwave irradiation at 500 W (2450 MHz).

Introduction

Because of environmental concerns, safety considerations and/or for cost containment reasons the reduction of solvents for reactions, with the phasing out of certain solvents such as some of the chlorinated hydrocarbons, has become of pressing interest.[1] Especially with the development of the use of microwave irradiation in organic reactions, syntheses in solventless systems are being increasingly studied.[2] Higher concentrations of the educts as well as the different polarity of the medium, as opposed to the same reaction in a solvent, can alter the distribution and yield of the products.

A limited number of reports have also appeared on Wittig olefination reactions in solventless systems.[3–7] For the most part, however, these have been limited to reactions for which microwave irradiation[5,6] has been used or phosphonium salts have been employed in the presence of a base and steel mills[7] or other special methods of stirring have been utilized. In the following it is shown that certain stabilized phosphoranes react exothermally when mixed with aldehydes. The reactions can be completed by heating the neat mixtures for 10 min; no stirring needs to be employed. The experiments were run on scales of 3.5–35 mmol of aldehyde with equal success. Undoubtedly, the procedure is applicable on an even wider scale range. The scope and limitations of this procedure will be discussed.

Results and discussion

Many phosphoranes, which exhibit extended pi-conjugation due to a carbonyl, a carboxyl or nitrile function neighboring the P=C moiety, are rather stable towards oxygen and moisture and may be kept as a pure substance without appreciable decomposition over long periods of time. Often they are sufficiently stable to be functionalized, thus offering opportunities to prepare libraries of phosphoranes from the parent phosphoranes themselves.[8] Nevertheless, they are often reactive enough to undergo Wittig olefinations with aldehydes and have been used very frequently as reagents in preparative synthesis. In the overwhelming number of cases the Wittig reactions have been carried out in solvents, either at room or elevated temperatures. Typical solvent systems that have been used include halogenated solvents such as chloroform,[9] dimethoxyethane (DME),[9] benzene or toluene.[10] At times, benzoic acid has been used as additive.[9b,11] Reaction times vary, but often these reactions are run for 1–4 h. In the following, it is noted that these reactions can be performed with short reaction times and with minimal efforts (microwave irradiation, stirring or inert atmosphere are not required) when alkyl (triphenylphosphoranylidene)acetates are reacted in solventless systems. Thus, a number of benzaldehydes undergo a Wittig olefination reaction when mixed with the stabilized phosphoranes **2a**/**2b** (Scheme 1). In some cases such as **1c** and **1i**, the reactions are exothermic and the heat generated is sufficient to drive the reaction to completion within 10 min without an external energy source. The reactions of **2a**/**2b** with the heterocyclic aldehydes, thienylcarbaldehydes **1a**, **1g** and **1s**, nicotinic aldehyde (**1m**) and furfural (**1f**) are exothermic. Here, simple mixing of the aldehydes with **2a**–**2d** generates temperatures of 60–70 °C. A number of Wittig reactions proceed only after initial warming of the mixture, but then proceed normally. A typical example is the reaction of *p*-anisylaldehyde (**1b**) and methyl (triphenylphosphoranylidene)acetate (**2a**). In many cases it has been found to be beneficial to submit the mixtures to an additional external, conventional heating (100 °C, 10 min).

In cases where the aldehydes have low melting points the heat evolved in the initial reaction is often sufficient to melt the aldehydes so that the phosphorane mixes ideally upon addition. Typical examples (see Scheme 2) in this regard are *o*-nitrobenzaldehyde (**1o**; mp. 43–46 °C for a commercially available sample) and *p*-bromobenzaldehyde (**1r**; mp. 55–58 °C for a commercially available sample). Aldehydes with higher melting points such as *p*-nitrobenzaldehyde (**1p**) have to be intimately mixed as a solid with the solid phosphorane. The mixture is then heated at 100 °C for 10 min. The resulting melt consists for the most part of product, triphenylphosphine oxide and unreacted phosphorane.

In all of the above reactions, the products are obtained as a mixture of *E* and *Z* isomers. As is usual for stabilized ylides,

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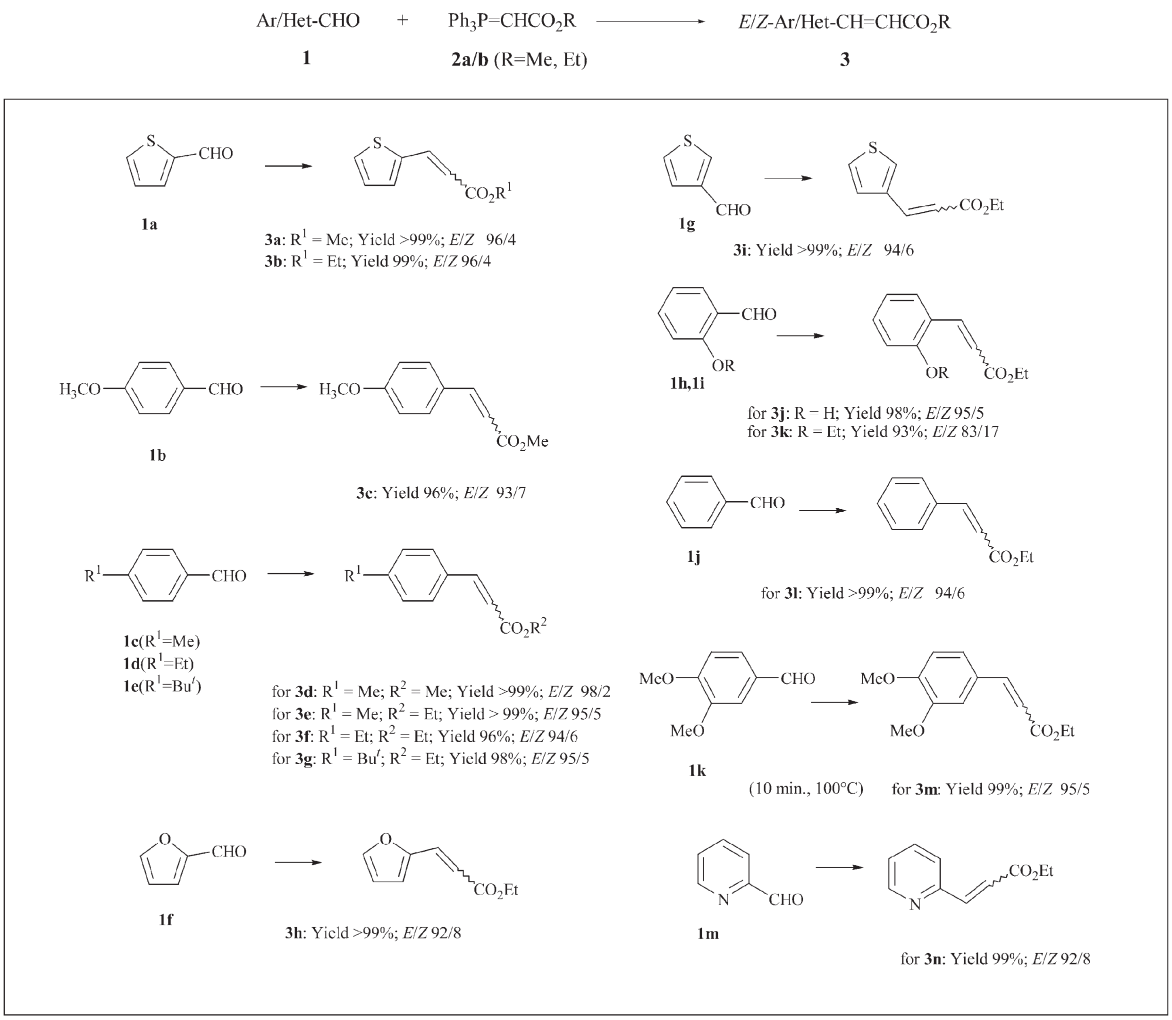
† This contribution is dedicated to Prof. Dr. Masashi Tashiro on the occasion of his 70th birthday.

DOI: 10.1039/b311894k

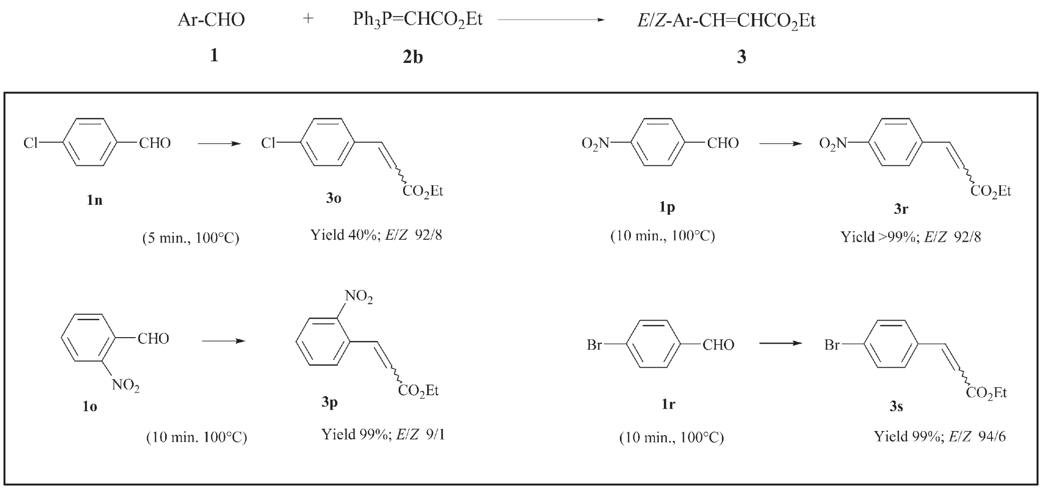


1a, **1c**, **1f**, **1g**, **1i** proceed to termination of the reaction without external heating; for all other entries heating has been applied (10 min., 100°C)

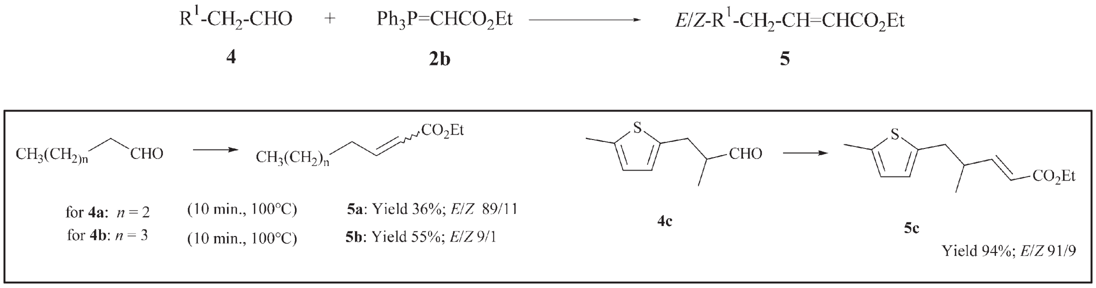
Scheme 1 Wittig olefination of heteroarenecarbaldehydes and arenecarbaldehydes with electron-donating substituents.

the *E* isomer is dominant.[12] The presence of ortho substituents in the aromatic aldehydes tend to increase the amount of *Z* isomer. For the most part, *E* and *Z* isomers can easily be separated by column chromatography.[13] When the *E* and *Z* isomers could not be separated, such as for **3f** and **3g**, the isomeric ratio was calculated from the integral in the ^{1}H NMR spectrum of the olefinic protons of the acrylate moiety, especially the proton at C2.[14]

2a/**2b** can also be reacted with alkanals (Scheme 3). Here, there is only a weak evolution of heat upon mixing the components. The reaction mixtures are submitted to conventional external heating (100 °C, 10 min). Pure alkanals give lower yields than the aromatic aldehydes. Initially, this was deemed to be an effect of the higher volatility of the alkanals in the reaction mixtures. Subsequently, it has been noticed, however, that incorporation of one or more aryl moities in the starting



Scheme 2 Wittig olefination of arenecarbaldehydes with electron-withdrawing substituents.



Scheme 3 Wittig olefination of alkanals.

materials increases the yield dramatically, such as for **4c**. It may be that an interaction of the aromatic units in the aldehyde component and the phosphorane facilitates the generation of a homogeneous melt and thus facilitates the reaction.

Generally, alkenals have been found to give good yields of alkenes in the reaction with **2a**/**2b** (Scheme 4). The estrane derivative **6a** must initially be mixed thoroughly with the phosphorane, but then forms a good melt upon heating to 100 °C.

The reaction of aldehydes with substituted alkyl (triphenylphosphoranylidene)acetates was also investigated. To compare the reactivity of different phosphoranes, the reaction with 5-methylthienyl-2-carbaldehyde (**1s**) was chosen. It was found that the methyl- and bromo-substituted phosphoranes, **2c** and **2d**, react in a way similar to the parent compounds (Scheme 5). Here again, the reaction with many of the aromatic and heteroaromatic aldehydes is exothermic.

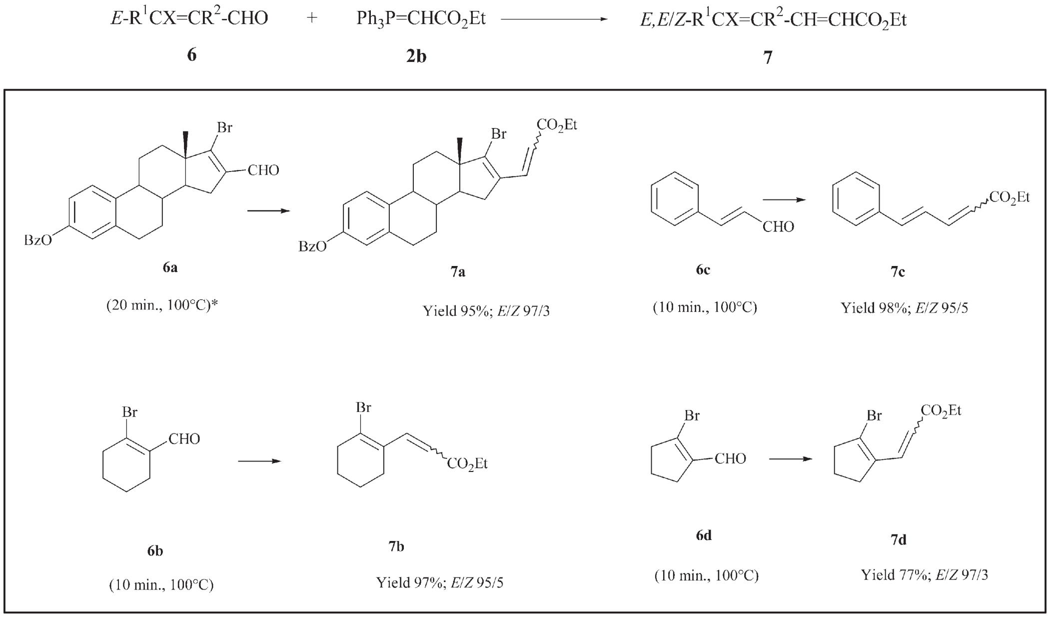
In solution, **2f** is known not to undergo Wittig olefination reactions successfully—only trichloroacetaldehyde has been reacted, albeit with a poor yield.[15] Unfortunately, **2f** also does not react under the conditions mentioned above. When **2f** and **1s** are mixed, no evolution of heat can be detected. Also, heating the mixture at 100 °C for up to 30 min does not yield an olefination product. Instead, triphenylphosphine is partly eliminated from the phosphorane.

Phosphorane **2e**, which is the alcoholysis product of **2f**,[15] reacts with **1s**, when the mixture is heated to 100 °C (10 min), in moderate yield. Here, also the *E* isomer predominates. No isomerization of the double bond to the maleate takes place.

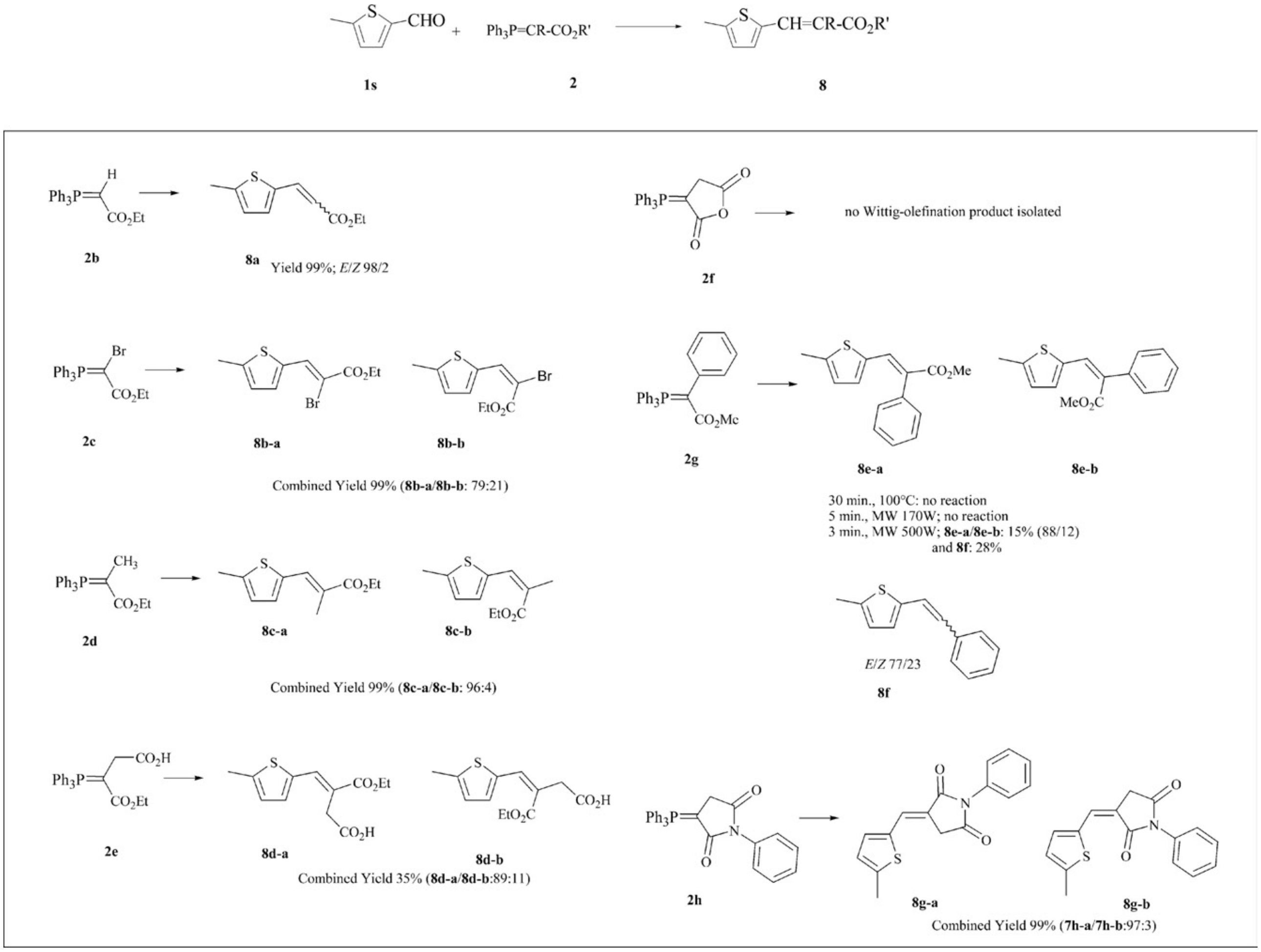
Methyl (triphenylphosphoranylidene)phenylacetates (**2g**) does not react when directly mixed with an aldehyde such as **1s**, even when heated at 100 °C for 30 min. Microwave irradiation of **2g** and **1s** (500 W, 2.5 min) gives a small amount of products **8e–a**/**8e–b**. Here, however, already a significant amount of side product **8f** is formed. As the phosphorane itself is stable under the conditions used and product **8e–a** [synthesized separately from phenylacetic acid (**12**) and 5-methylthienylcarbaldehyde (**1s**) analogous to a sequence by Cadogan *et al.*,[16] with subsequent esterification of the obtained acid with diazomethane (Scheme 6] was also found to be stable under these conditions (*i.e.*, even at 3 × 3 min; this involves iterative periods of 3 min irradiation at 500 W and 3 min resting phase), it can be assumed that a reaction intermediate such as the initial addition product of **2g** and **1s** is the unstable species.

2h, which has already been reacted with benzaldehyde under similar conditions,[17] undergoes smoothly the Wittig olefination with **1s**. The alkene can be precipitated from the solution by addition of methanol to the reaction mixture. The precipitate is exclusively the *E* isomer, **8g–a**. Column chromatography of the filtrate also yields a small amount of the *Z* isomer, **8g–b**, which had not been detected previously in the reaction of **2h** with other aldehydes under similar conditions. Although the reaction of **2h** with aromatic and heteroaromatic carbaldehydes is slightly exothermic, it is much less so than the reactions of **2a–2d**.

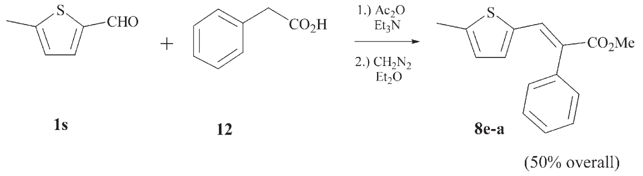
When mixed as a solid with ketones such as cyclohexanone at room temperature, **2b** does not react (Scheme 7). Even when heated at 100 °C for 30 min, only a small amount of ethyl cyclohexylideneacetate (10%) is formed.[18] Here again, microwave irradiation of a mixture of cyclohexanone and **2b** at



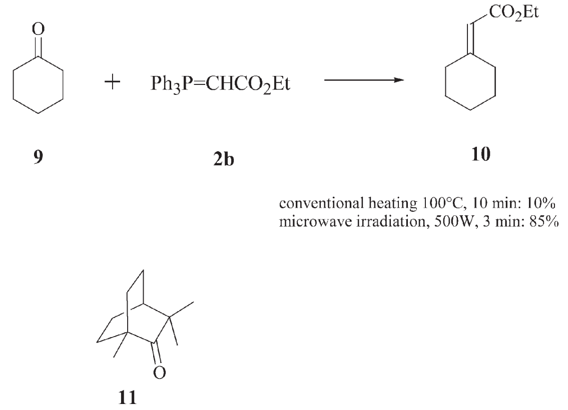
Scheme 4 Wittig olefination of alkenals.



Scheme 5 Wittig olefination with a variety of alkoxycarbonyl-substituted and related phosphoranes.



Scheme 6 Preparation of **8e–a**.



Scheme 7 Wittig olefination of ketones.

500 W/2450 MHz had a beneficial effect, yielding the Wittig olefination product in 85% yield within 3 min. The effect of using microwave irradiation in the reaction of ketones with stabilized phosphoranes has already been studied[6] to some extent, and thus a further presentation is not warranted. However, it is important to note that not all ketones undergo a Wittig olefination with **2b** under these conditions. Thus, fenchone [1,3,3-trimethyl-2-norbornanone, (**11**)] (Scheme 7) does not yield any product with **2b** even under microwave irradiation at 500 W.

Thus, the stability of the phosphoranes themselves under microwave irradiation was assessed (Fig. 1). Phosphoranes **2e**, **2f** and **2g** as powders are perfectly stable under microwave irradiation at 500 W (3 × min), while **2h** is not. Here, appreciable amounts of triphenylphosphine can be detected after irradiation. **2h** has also been reported to be unstable in solution at elevated temperatures.[19] After being wetted with a solvent such as chloroform and dried (RT, 15 Torr, 3 h), **2f** and **2g** remain stable even under prolonged microwave irradiation at 500 W (10 × 3 min), but **2e** is not stable. Again, triphenylphosphine can be detected and isolated from an irradiated sample of **2e**; monomethyl maleate can also be detected by ^{1}H NMR spectroscopy in the crude mixture after microwave irradiation.

Conclusion

Aromatic and heteroaromatic aldehydes, alkanals and alkenals undergo Wittig olefination reactions with alkyl (triphenylphosphoranylidene)acetates in absence of a solvent, when the neat components are simply mixed together. Many of the reactions are exothermic. In a few cases microwave irradiation is beneficial for the reaction outcome. While most of the phosphoranes utilized are stable under microwave irradiation, some, such as **2h**, are not.

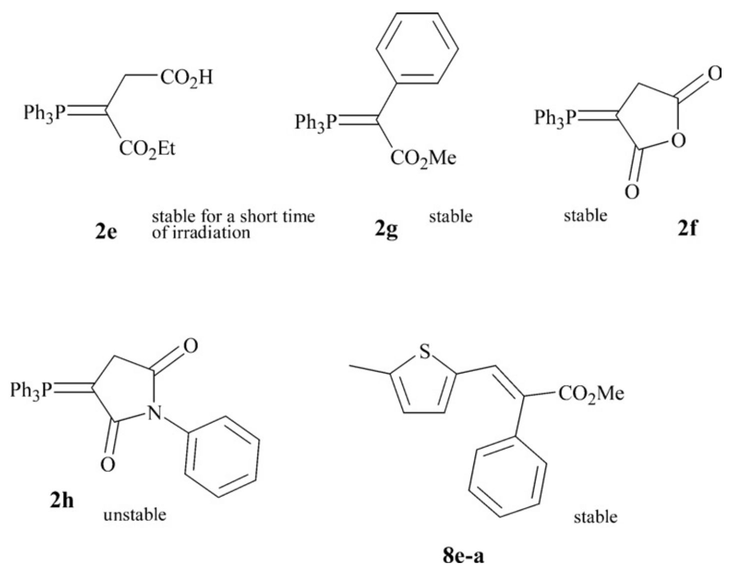


Fig. 1 List of compounds whose stability under microwave irradiation (500 W) was assessed.

Experimental

General methods and materials

Melting points were measured on a Yanaco microscopic hot-stage and are uncorrected. Infrared spectra were measured with a JASCO IR-700 machine. ^{1}H- (at 270 MHz) and ^{13}C-NMR (at 67.8 MHz) spectra were recorded with a JEOL EX-270 or with a JEOL GSX-270 spectrometer. The chemical shifts are relative to TMS (solvent $CDCl_3$). Partly the interpretation of the ^{13}C-NMR data was aided by DEPT (Distortionless Enhancement of Polarisation Transfer) experiments: (+) denoted primary and tertiary, (−) secondary and C_{quat} quaternary carbons. Mass spectra were measured with a JMS-01-SG-2 spectrometer (EI, 70 eV). Column chromatography was carried out on Wakogel 300.

For some of the heating experiments an electric oven, EYELA NDO-450N, preheated at 100 °C, was used. For microwave irradiation experiments a domestic microwave oven National NE-S12 (with power settings at 170 W/500 W and 750 W; 2450 MHz) was used. Narrow-mouthed Erlenmeyer flasks (borosilicate) topped with Saran-Wrap were employed through-out.

All aromatic and heteroaromatic aldehydes used as well as aldehydes **4a**, **4b** and **6c** have been obtained commercially. Thienylpropanal **4c**[20] was synthesized from 2-methylthiophene and methacrolein, and the bromoenaldehydes **6a**,[21] **6b**, and **6d** were prepared from the corresponding ketones by Arnold-Vilsmeier reaction. While commercially available, phosphoranes **2a**/**b** were prepared according to Dershowitz and Ramirez,[22] **2c** by bromination/dehydrobromination of **2b** analogous to a procedure by Osborne,[23] **2f**[15] and **2h**[17] by reaction of triphenylphosphine to maleic anhydride and *N*-phenylmaleimide, respectively, and **2e** by ethanolysis of **2f**.[15] **2d**[24] and **2g**[25] were also synthesized according to the literature.

Wittig olefination

Example of ethyl 2-bromo-3-(*E*)-(5′-methylthien-2′-yl)acrylate (8b–a). To 5-methylthienyl-2-carbaldehyde (**1s**; 874 mg, 6.9 mmol) was added within 5 min solid ethyl (triphenylphosphoranylidene)bromoacetate (**2c**; 4.16 g, 9.7 mmol). The mixture evolved heat and formed a melt. The flask was covered and was warmed to 100 °C for 10 min (oil bath, sand bath or electric oven). After cooling the mixture the melt was transferred and subjected to column chromatography on silica gel (ether–hexane, 1:5) to give ethyl 2-bromo-3-(*Z*)-(5′-methylthien-2′-yl)acrylate (**8b–b**; 394 mg, 21%) and ethyl 2-bromo-3-(*E*)-(5′-methylthien-2′-yl)acrylate (**8b–a**; 1.48 g, 79%) as colorless oils.

Further selected examples are given below.[13]

8b–b. IR (KBr) ν 3064, 2980, 2918, 1701, 1579, 1450, 1376, 1258, 1195, 1166, 1057, 1025, 797 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.38 (t, 3H, ^3J 7.2 Hz, OCH_2CH_3), 2.48 (s, 3H, CH_3), 4.34 (q, 2H, ^3J 7.2 Hz, OCH_2), 6.72 (d, 1H, ^3J 3.6 Hz), 7.11 (d, 1H, ^3J 3.6 Hz), 7.57 (s, 1H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.12, 15.56, 62.30, 105.10, 125.23, 134.90, 136.08, 137.96, 143.35, 163.56; MS (FAB, 3-nitrobenzyl alcohol) m/z (%) 277 ([^{81}Br]MH$^+$, 87), 276 ([^{81}Br]M$^+$, 92), 275 ([^{79}Br]MH$^+$, 100), 274 ([^{79}Br]M$^+$, 81), 231 ([^{81}Br]M$^+ - C_2H_5O$, 55), 229 ([^{79}Br]M$^+ - C_2H_5O$, 54), 195 (22). HR-MS (EI, 70 eV) found: 273.9665; calcd for $C_{10}H_{11}O^{79}{}_2BrS$: 273.9663.

8b–a. IR (neat) ν 2980, 1717, 1603, 1450, 1256, 1203, 1163, 1040, 801 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.37 (s, 3H, ^3J 7.2 Hz, OCH_2CH_3), 2.54 (s, 3H, CH_3), 4.33 (q, 2H, ^3J 7.2 Hz, OCH_2), 6.82 (d, 1H, ^3J 3.6 Hz), 7.36 (d, 1H, ^3J 3.6 Hz), 8.35 (s, 1H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.11, 15.78, 62.50, 108.21, 125.66, 134.77, 135.53, 135.69, 146.88, 163.45; MS (FAB, 3-nitrobenzyl alcohol) m/z (%) 276 ([^{81}Br]M$^+$, 100), 274 ([^{79}Br]M$^+$, 92), 231 ([^{81}Br]M$^+ - C_2H_5O$, 52), 229 ([^{79}Br]M$^+ - C_2H_5O$, 51), 195, 167, 149, 122. HR-MS found: 273.9665; calcd for $C_{10}H_{11}O_2{}^{79}BrS$: 273.9663.

(*E*)-Ethyl 5-(5′-methylthien-2′-yl)-4-methylpent-2-enoate (*E*-5c). A mixture of **4c** (1.0 g, 6.4 mmol) and **2b** (3.0 g, 8.3 mmol) was reacted (10 min, no further heating) to give, after purification by column chromatography on silica gel (hexane–ether 5:1), ***E*-5c** (1.3 g, 86%). IR (neat) ν 2974, 2920, 1720, 1652, 1450, 1367, 1271, 1179, 1037, 795 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.09 (d, 3H, ^3J 6.6 Hz, CH_3), 1.29 (t, 3H, ^3J 7.2 Hz, CH_3), 2.43 (s, 3H, CH_3), 2.59 (ddddq, 1H, ^3J 7.3 Hz, ^3J 7.3 Hz, ^3J 6.9 Hz, ^3J 6.6 Hz, ^4J 1.3 Hz), 2.73 (dd, 1H, ^2J 14.5 Hz, ^3J 7.3 Hz), 2.87 (dd, 1H, ^2J 14.5 Hz, ^3J 6.9 Hz), 4.18 (q, 2H, ^3J 7.2 Hz, OCH_2CH_3), 5.79 (dd, 1H, ^3J 15.5 Hz, ^4J 1.3 Hz), 6.54 (br s, 2H), 6.93 (dd, 1H, ^3J 15.5 Hz, ^3J 7.3 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.25, 15.28, 18.76, 36.46, 38.42, 60.22, 120.29, 124.67, 125.27, 137.99, 139.71, 152.96, 166.74; MS (EI, 70 eV) m/z (%) 238 (M$^+$, 10), 111 (100). HR-MS found: 238.1026; calcd for $C_{13}H_{18}O_2S$: 238.1028. Anal. calcd for: $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61; found: C. 65.63; H, 7.59%.

Ethyl 3-(2′-bromocyclohex-1′-enyl)acrylate (*E*-7b). **6b** (1.3 g, 6.9 mmol) and **2b** (3.0 g, 8.6 mmol) were reacted (100 °C, 10 min) to yield, after purification by column chromatography on silica gel (hexane–ether 4:1), ***E*-7b** (1.6[4] g, 92%). IR (neat) ν 3070, 2980, 1712, 1622, 1447, 1365, 1307, 1175, 1039, 978, 859, 652 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.31 (t, 3H, ^{3}J 6.9 Hz, OCH_2CH_3), 1.74 (m, 4H), 2.27 (m, 2H), 2.69 (m, 2H), 4.23 (q, 2H, ^{3}J 6.9 Hz, OCH_2), 5.91 (d, 1H, ^{3}J 15.8 Hz), 7.87 (d, 1H, ^{3}J 15.8 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.29, 21.82, 24.30, 27.17, 38.15, 60.41, 118.87, 131.21, 132.70, 144.29, 167.08; MS (EI, 70 eV) m/z (%) 260 ([^{81}Br]M^{+}, 14), 258 ([^{79}Br]M^{+}, 14), 215 ([^{81}Br]M$^{+} - C_2H_5O$, 10), 213 ([^{79}Br]M$^{+} - C_2H_5O$, 10), 179 (91), 151 (100). HR-MS found: 258.0253; calcd for $C_{11}H_{15}O^{79}{}_{2}Br$: 258.0255. Anal. calcd for: $C_{11}H_{15}O_2Br$: C, 50.98; H, 5.83; found: C. 50.95; H, 5.80%.

Ethyl 3-(2′-bromocyclopent-1′-enyl)acrylate (*E*-7d). 6d (1.02 g, 5.82 mmol) and **2b** (2.55 g, 7.31 mmol) were reacted (10 min, 100 °C) to yield, after purification by column chromatography on silica gel (hexane–ether 4:1), ***E*-7d** (1.07 g, 75%). IR (neat) ν 2976, 2848, 1712, 1628, 1365, 1304, 1167, 1083, 1040, 979, 858 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.32 (t, 3H, ^{3}J 7.2 Hz, CH_3), 2.00–2.06 (m, 2H), 2.45–2.52 (m, 2H), 2.79–2.84 (m, 2H), 4.23 (q, 2H, ^{3}J 7.2 Hz), 5.84 (d, 1H, ^{3}J 15.8 Hz), 7.57 (d, 1H, ^{3}J 15.8 Hz); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.23, 21.51, 31.00, 41.43, 60.47, 120.90, 130.03, 136.86, 137.74, 166.99; MS (EI, 70 eV) m/z (%) 246 [^{81}Br]M^{+}, 15), 244 ([^{79}Br] M^{+}, 15), 201 ([^{81}Br]M$^{+} - C_2H_5O$, 9), 199 ([^{79}Br]M$^{+} - C_2H_5O$, 11), 165 (48), 137 (100). HR-MS found: 244.0091; calcd for $C_{10}H_{13}O_2{}^{79}Br$: 244.0099.

(*Z*)- and (*E*)-3-ethoxycarbonyl-4-(5′-methylthien-2′-yl)but-3-enoic acid (8d–a and 8d–b). 1s (0.87 g, 6.9 mmol) and **2e** (3.49 g, 8.6 mmol) were reacted (100 °C, 15 min) to give, after purification by column chromatography (ether–$CHCl_3$ 2:1), **8d–a** (545 mg, 31%) and **8d–b** (68 mg, 4%).

8d–a. IR (KBr) ν 3500–2800, 1697 (v br), 1455, 1092, 930, 676, 574, 551, 517, 461 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.32 (t, 3H, ^{3}J 6.9 Hz, OCH_2CH_3), 2.51 (s, 3H, CH_3), 3.77 (s, 2H, CH_2), 4.27 (q, 2H, ^{3}J 6.9 Hz, OCH_2CH_3), 6.77 (d, 1H, ^{3}J 3.6 Hz), 7.13 (d, 1H, ^{3}J 3.6 Hz), 7.26 (s, 1H), 10.31 (br s, 1H, COO*H*); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.20, 15.58, 33.62, 61.22, 119.57, 126.15, 133.56, 134.79, 135.51, 145.44, 167.69, 176.66; MS (FAB, 3-nitrobenzyl alcohol) m/z (%) 255 (MH^{+}, 75), 209 (M$^{+} - C_2H_5O$, 100), 181 (62), 136 (34). HR-MS (FAB) found: 255.0689; calcd for $C_{12}H_{15}O_4S$ (MH^{+}): 255.0691.

8d–b. ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.27 (t, 3H, ^{3}J 7.2 Hz, OCH_2CH_3), 2.49 (s, 3H, CH_3), 3.43 (s, 2H), 4.15 (q, 2H, ^{3}J 7.2 Hz, OCH_2), 6.70 (d, 1H, ^{3}J 3.6 Hz), 6.96 (s, 1H), 7.13 (d, 1H, ^{3}J 3.6 Hz), 10.31 (br s, COOH); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 14.11, 15.51, 40.91, 60.83, 116.91, 124.87, 135.56, 136.28, 137.19, 146.90, 166.41, 171.50; MS (EI, 70 eV) m/z (%) 254 (M^{+}, 47), 210 (96), 181 (74), 136 (100). HR-MS found: 254.0607; calcd for $C_{12}H_{14}O_4S$: 254.0613.

(*E*)- and (*Z*)-3-(5′-methylthien-2′-ylmethylidene)-*N*-phenyl-(4*H*)-maleimide (8g-a and 8g–b). 1s (0.87 g, 6.9 mmol) and **2h** (3.75 g, 8.6 mmol) were reacted. While the reaction is exothermic, it was found beneficial to submit the melt to additional heating (10 min, 100 °C). Thereafter, methanol (20 mL) was added to the melt and precipitated **8g–a** (1.82 g) was filtered off. Thereafter the filtrate was concentrated *in vacuo* and the residue was submitted to column chromatography on silica gel (ether–$CHCl_3$ 2:1) to give additional **8g–a** (combined yield: 1.87 g, 96%) and **8g–b** (58 mg, 3%).

8g–a. IR (KBr) ν 1767, 1704, 1641, 1502, 1385, 1175, 898, 807, 699 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.58 (s, 3H, CH_3), 3.63 (d, 2H, ^{4}J 2.3 Hz), 6.85 (d, 1H, ^{3}J 3.6 Hz), 7.21 (d, 1H, ^{3}J 3.6 Hz), 7.33–7.51 (m, 5H), 7.83 (t, 1H, ^{4}J 2.3 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 15.87, 34.15, 118.95, 126.45, 126.91, 128.45, 129.09, 132.01, 132.16, 133.93, 136.41, 147.28, 172.90 (2 C=O); MS (EI, 70 eV) m/z (%) 283 (M^{+}, 85), 136 (100). HR-MS found: 283.0663; calcd for $C_{16}H_{13}O_2NS$: 283.0667. Anal. calcd for: $C_{16}H_{13}O_2NS$: C, 67.82; H, 4.62; N, 4.94; found: C. 68.12; H, 4.62; N, 4.89%.

8g–b. IR (KBr) ν 3064, 2916, 1764, 1699, 1633, 1495, 1391, 1161, 1135, 902, 803, 754, 698 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.51 (s, 3H, CH_3), 3.61 (d, 2H, ^{4}J 1.5 Hz), 6.78 (d, 1H, ^{3}J 3.7 Hz), 7.06 (d, 1H, ^{4}J 1.5 Hz), 7.33–7.52 (m, 6H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 15.58, 36.14, 115.67, 125.77, 126.60, 126.90, 128.33, 129.07, 132.35, 135.15, 136.91, 148.57, 172.83 (2 C=O); MS (EI, 70 eV) m/z (%) 283 (M^{+}, 69), 136 (100). HR-MS found: 283.0668; calcd for $C_{16}H_{13}O_2NS$: 283.0667.

Methyl 3-(*Z*)-(5′-methylthien-2′-yl)-2-phenylacrylate (8e–a). A mixture of **1s** (874 mg, 6.9 mmol) and **2g** (3.5 g, 8.5 mmol) was placed into a 30 mL Erlenmeyer flask (borosilicate, narrow-mouthed, top covered with Saran Wrap® [polyvinylidene chloride]) and was irradiated for 3 min in a microwave oven at 500 W. The mixture was transferred to silica gel and submitted to column chromatography (hexane–ether 3:1) to yield **8e–a** (0.23 g, 13%). IR (neat) ν 3058, 2948, 1707, 1612, 1450, 1206, 1165 cm^{-1};^{1}H NMR (270 MHz, $CDCl_3$) δ 2.24 (s, 3H, CH_3), 3.68 (s, 3H, $COOCH_3$), 6.52 (d, 1H, ^{3}J 3.6 Hz), 6.90 (d, 1H, ^{3}J 3.6 Hz), 7.17 (m, 2H), 7.36 (m, 3H), 7.89 (s, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 15.55, 52.20, 125.17, 127.67, 128.34, 129.00, 130.05, 134.11, 134.34, 135.38, 136.59, 146.04, 168.19; MS (EI, 70 eV) m/z (%) 258 (M^{+}, 100); 199 (M$^{+} - C_3H_7O$, 53); 184 (M$^{+} - C_3H_6O_2$, 31), 165 (14), 141 (33). HR-MS found: 258.0712; calcd for $C_{15}H_{14}O_2S$: 258.0715. Anal. calcd for: $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46; found: C. 69.56; H, 5.32%.

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