HALIDE- AND BASE-FREE WITTIG REACTION: PHOSPHONIUM METHYLCARBONATE SALTS AS YLIDE PRECURSORS

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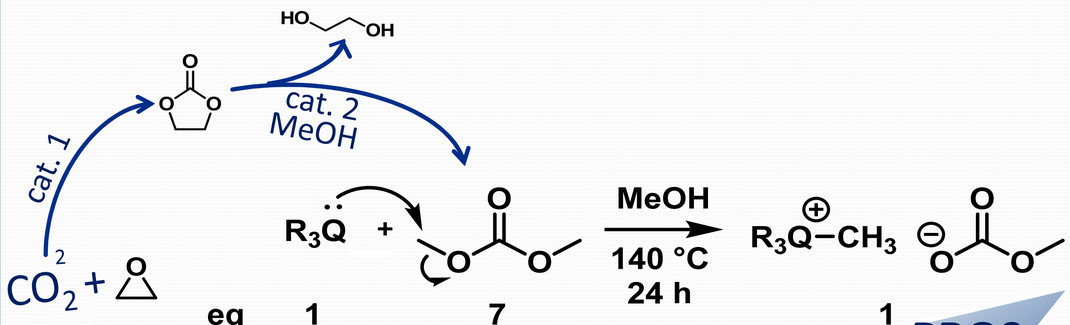
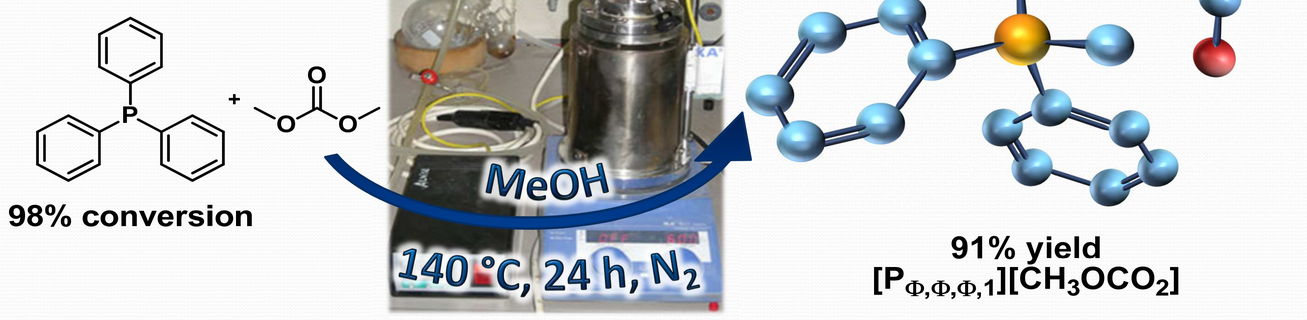
Synthesis of the ylide precursor

Quaternarization of amines and phosphines with DMC[1]



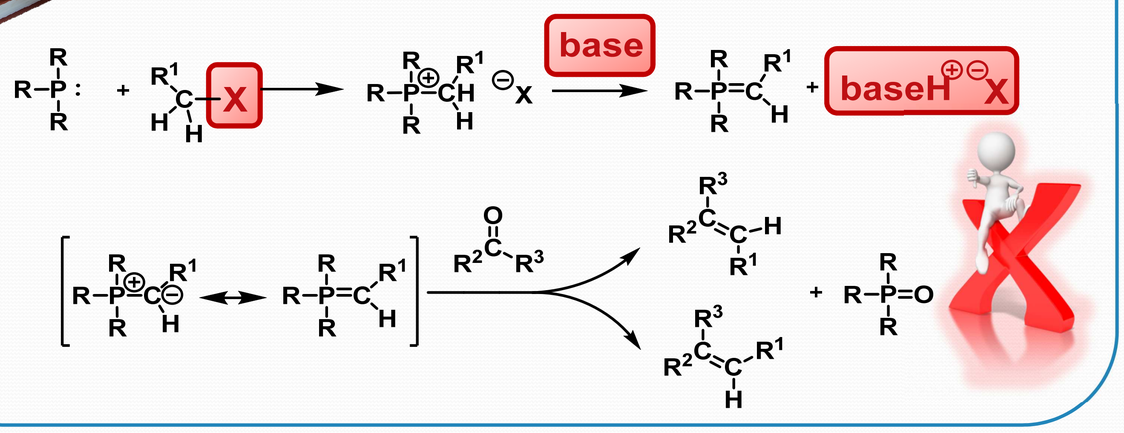
Q = N, P
R = alchyl

PROS
- 100% AE
- DMC[3] as alkylating agent
- Easy isolation of the ionic liquid
- Recovery of excess DMC and MeOH

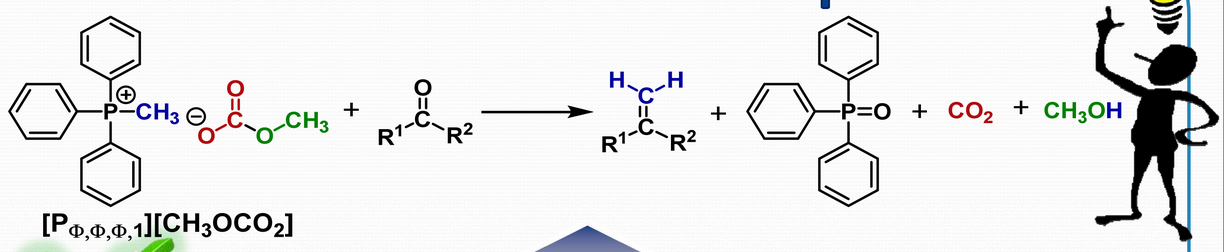


Small amounts (< 7%) of a by-product and residual TPP (< 2%) were removed by stirring the off-white solid with 8 equivalents of cyclohexane at 50 °C, for 1 h under N_2 atmosphere. Pure $[P_{\Phi,\Phi,\Phi,1}][CH_3OCO_2]$ was obtained in **83 % isolated yield**.

Traditional Wittig reaction[4]



Our halide- and base-free protocol



PROS
- Totally **halide-free** reaction
- **No added bases** are required to form the ylide
- triphenylphosphineoxide, CO_2 e CH_3OH are the only by-products of the reaction, **no saline** by-products are formed

Model reaction

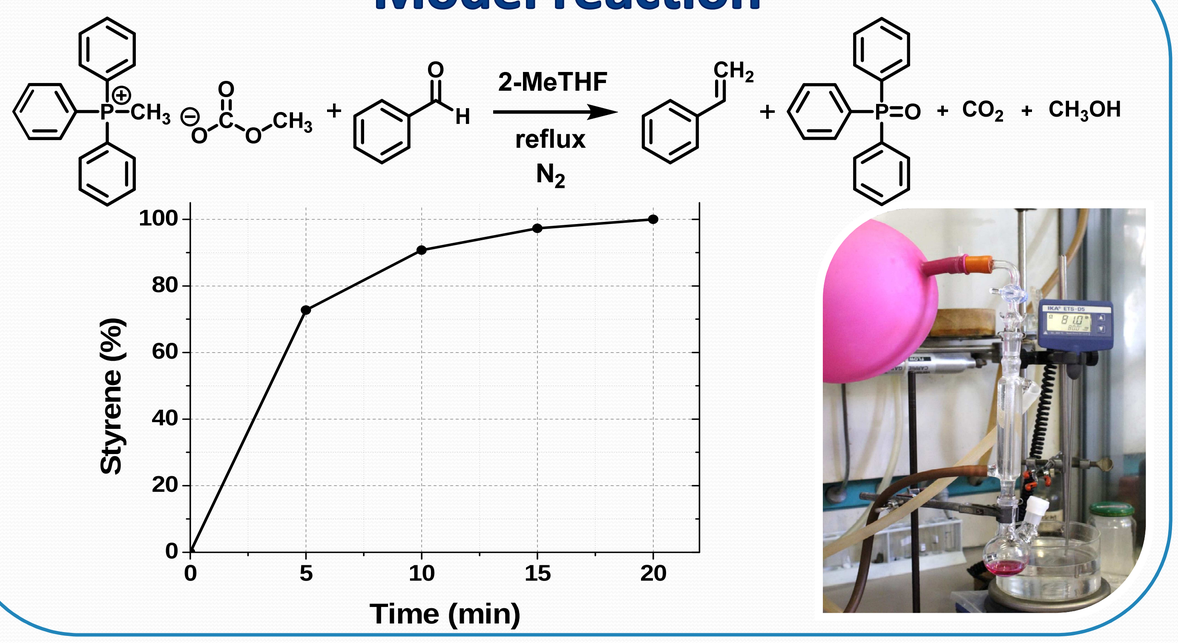
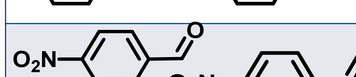
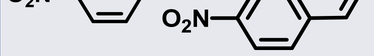
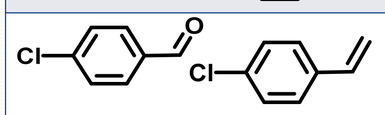
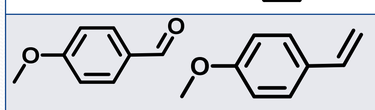
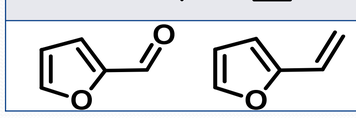
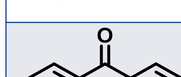
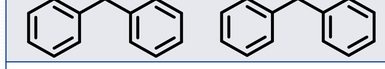
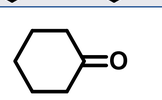


Table 1 Wittig reaction of $[P_{\Phi,\Phi,\Phi,1}]$ [MC] with different aldehydes[a]...			
Substrate	Product	Time (min)	Yield (%)
		40	100[c]
		5	94[d]
		20	100[c]
		125	78[c]
		60	100[c]

... and ketones[b]			
Substrate	Product	Time (h)	Yield (%)
		23	100[c]
		23	100[c]
		23	0[c]

[a] Reaction conditions: 80 °C, N_2 atm, phosphonium salt/aldehyde molar ratio=1.1; [b] phosphonium salt/ketones molar ratio=3; [c] GC-yield; [d] isolated yield.

Hydrogen-deuterium exchange: synthesis of labeled olefins

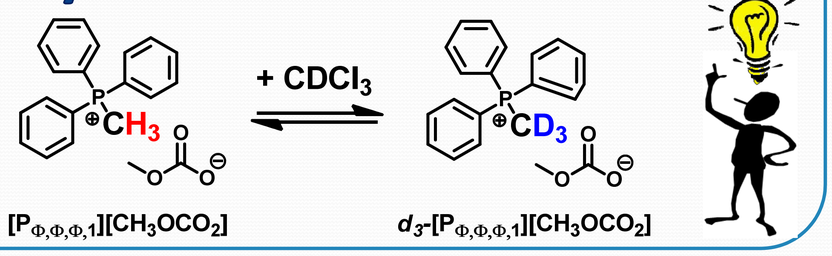
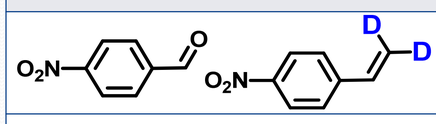


Table 2 Synthesis of labeled olefins[a]			
Substrate	Product	Time (min)	Yield (%)[b]
		5	47

[a] Reaction conditions: 80 °C, N_2 atm, phosphonium salt/aldehyde molar ratio=1.1; [b] isolated yield.

REFERENCES

[1] Fabris, M.; Lucchini, V.; Noe, M.; Perosa, A.; Selva, M. *Chem. Eur. J.* **2009,** *15* (45), 12273-12282.
[2] Sakakura, T. Choi, JC; Yasuda, H. *Chem. Rev.* **2007,** 107, 2365.
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[4] Wittig, G.; Geissler, G. *Justus Liebigs Ann. Chem.* **1953**, *580*, 44; El-Batta, A.; Jiang, C.; Zhao, W. et al. *J. Org. Chem*. **2007**, 72, 5244-5259; Byrne, P. A.; Gilheany, D. G. *Chem. Soc. Rev.* **2013**, *42*, 6670-6696.