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LETTERS

Wittig reaction using perfluorinated ylides

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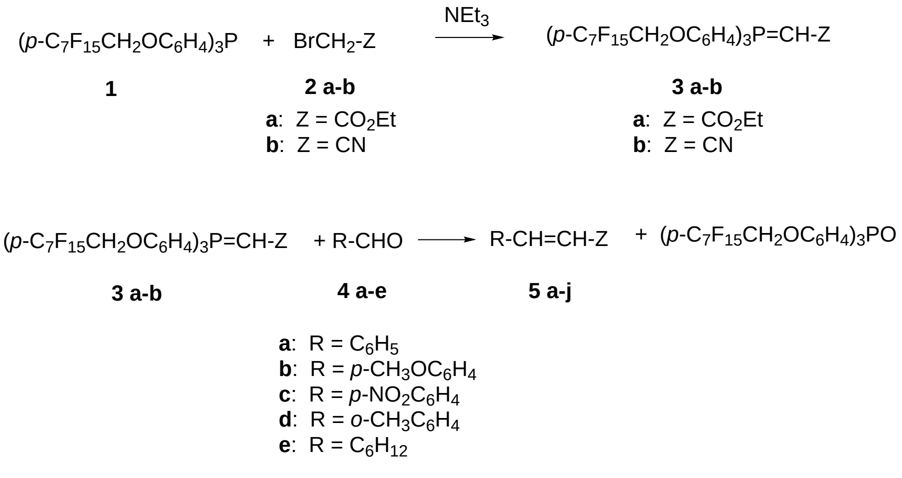
Abstract—Wittig reactions could be performed in perfluorosolvents using perfluorinated ylides, allowing both a very easy separation of the alkene from the phosphine oxide and a re-use of the latter by simple reduction of the crude oxide. © 2001 Elsevier Science Ltd. All rights reserved.

In 1994, Horvàth and Ràbai introduced the concept of fluorous biphasic system in catalysis,[1] followed in 1998 by Curran's concept of an 'ideal purification'.[2] In these concepts, the product(s) of the reaction is(are) separated into a different phase from everything else present in the mixture.[3] Since fluorous biphasic catalysis is becoming increasingly important during recent years, the use of fluorous organic reagents is also rapidly developing, since they allow an easy purification or removal of the fluorous compound from organic ones by simple liquid–liquid extraction techniques. A number of fluorous reagents (tin hydrides,[4] allyltin reagents,[5] allyl stannanes,[6] organoselenium reagent[7]) and protecting groups[8] have been introduced recently in organic synthesis.

The Wittig reaction is one of the most used methodology for C=C bond formation,[9] giving good to excellent stereoselectivities. However, one of the problems is the separation of the formed alkene from the by-product Ph_3PO, which is usually done by chromatography or by recrystallization. Recently an easy separation of alkenes from the phosphine oxide was performed using water-soluble phosphonium salts[10] or ionic salt as the solvent.[11]

In this communication, we demonstrate the usefulness of perfluorinated ylides in this coupling reaction, allowing the reaction to be performed in perfluorinated solvents, and most importantly an easy separation of perfluorinated phosphine oxide from the formed alkene.



$$(p\text{-}C_7F_{15}CH_2OC_6H_4)_3P + BrCH_2\text{-}Z \xrightarrow{NEt_3} (p\text{-}C_7F_{15}CH_2OC_6H_4)_3P{=}CH\text{-}Z$$

1 **2 a-b** **3 a-b**

a: $Z = CO_2Et$
b: $Z = CN$

$$(p\text{-}C_7F_{15}CH_2OC_6H_4)_3P{=}CH\text{-}Z + R\text{-}CHO \longrightarrow R\text{-}CH{=}CH\text{-}Z + (p\text{-}C_7F_{15}CH_2OC_6H_4)_3PO$$

3 a-b **4 a-e** **5 a-j**

a: $R = C_6H_5$
b: $R = p\text{-}CH_3OC_6H_4$
c: $R = p\text{-}NO_2C_6H_4$
d: $R = o\text{-}CH_3C_6H_4$
e: $R = C_6H_{12}$

Scheme 1.

Keywords: perfluorinated ylides; Wittig reaction; perfluorinated solvents; recycling.

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Table 1. Wittig reactions of ylides **3** with aldehydes **4**

Entry	Aldehyde	Bromide	Time (h)	Conversion of **4** (%)[a]	Yield olefin **5** (%)[b]	E/Z[c]
1	**4a**	**2a**	3	79	**5a** (66)	95/5
2	**4b**	**2a**	17	76	**5b** (64)	96/4
3	**4c**	**2a**	4.5	84	**5c** (80)	92/8
4	**4d**	**2a**	15	88	**5d** (65)	95/5
5	**4e**	**2a**	13	84	**5e** (61)	97/3
6	**4a**	**2b**	22	73	**5f** (50)	77/23
7	**4b**	**2b**	28	70	**5g** (41)	73/27
8	**4c**	**2b**	19	91	**5h** (56)	68/32
9	**4d**	**2b**	17	75	**5i** (56)	69/31
10	**4e**	**2b**	13	77	**5j** (51)	84/16

[a] Determined by GC and ^{1}H NMR.

[b] Yield based on the product obtained by extraction after elimination of the aldehyde.

[c] Determined by GC and ^{1}H NMR.

Benzaldehyde **4a** and phosphorane **3a** were selected as the model to develop this methodology (Scheme 1). The phosphorane **3a** was prepared in situ in a mixture of perfluorosolvent D-100 and toluene starting from perfluorophosphine **1**[12] and ethyl bromoacetate. At the end of the reaction, the obtained alkene was extracted with diethyl ether and the perfluorocompounds with perfluorosolvent.[13] Evaporation of the organic solvent gave the alkene **5a** as a mixture of the E/Z isomers in a 95/5 ratio in 66% yield (Table 1, entry 1), without any trace of phosphine oxide detected by ^{31}P NMR. Other aldehydes were used in this reaction. *p*-Methoxy and *p*-nitrobenzaldehyde **4b** and **4c** bearing an electron-donating and withdrawing group, respectively, reacted under these conditions to give the corresponding alkenes **5b** and **5c** in 64 and 80% yield, respectively (Table 1, entries 2 and 3). It is also the case for a sterically hindered benzaldehyde such as *o*-methylbenzaldehyde **4e**, which gave the olefin **5e** in 65% yield (Table 1, entry 4).

The Wittig reaction was extended to another ylide **3b**. Although the reaction proceeded sluggishly and so required longer reaction times, the expected alkenes **5g**–**5i** were also obtained in good yields as a mixture of the E/Z isomers in a ratio closed to those obtained in homogeneous conditions (Table 1, entries 6–9).

Aliphatic aldehydes can also be used in this Wittig reaction. Cyclohexane carboxaldehyde **4e** reacted with these two ylids **3a** and **3b** to give the corresponding alkenes **5e** and **5j** in 61 and 51% yield, respectively (Table 1, entries 5 and 10).

It should be noted that the procedure has not been optimized, and the chemical yields could probably be improved in the future.

Another advantage of this new methodology is the very easy separation of the perfluorophosphine oxide from the products of the reaction. Effectively the perfluorocompounds were quantitatively extracted using perfluorosolvents, and they were reduced to perfluorophosphine using trichlorosilane in toluene in quite good yield.[12]

In conclusion, Wittig reactions of stabilized perfluorinated ylides with aldehydes are easily performed in perfluorosolvents. This method offers an attractive possibility for an easy separation of the alkene and the phosphine oxide. Moreover, the phosphine oxide could be easily reduced and recycled. Work is in progress in order to improve this reaction and to extend it to other reactions using perfluorinated triphenylphosphine as reactant.

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13. *Experimental procedure*: In a Schlenk tube under argon were added the perfluorophosphine (300 mg, 0.2 mmol) in D-100 (2 mL) and ethyl bromoacetate (33.4 mg, 0.2 mmol) in toluene (2 mL). After being stirred for 1 h at 80°C, NEt_3 (21.2 mg, 0.21 mmol) was added and the solution was stirred for 0.5 h at 80°C. The aldehyde (0.19 mmol) was added and the mixture stirred for the desired time. At the end of the reaction, water (2 mL) and diethyl ether (2 mL) were added, and the different phases were separated. The aqueous and organic phases were extracted with D-100 (2×2 mL) and the aqueous phase with diethyl ether (2×2 mL). Evaporation of the fluorous phase gave the perfluorophosphine oxide, although evaporation of the organic phase gave the alkene together with the unreacted aldehyde.