Pergamon

Tetrahedron Letters, Vol. 38, No. 45, pp. 7871-7874, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10152-6

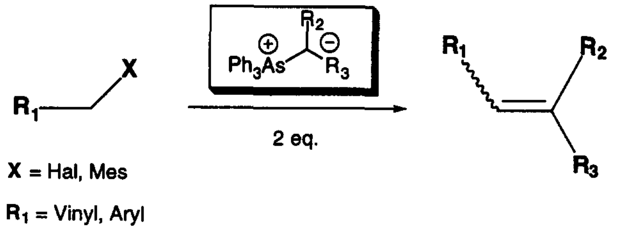
Olefination of Activated Halides and Mesylates using Arsonium Ylides

André Seyer, Lilian Alcaraz, C. Mioskowski*

Université Louis Pasteur, Laboratoire de Synthèse Bioorganique associé au *CNRS-URA 1386*,
Faculté de Pharmacie, 74 route du Rhin, BP 24, 67401 Illkirch, France.

Abstract: Alkyltriphenylarsonium ylides react with activated primary halides and mesylates to afford olefins in good yields and with high *E*-selectivity. © 1997 Elsevier Science Ltd.

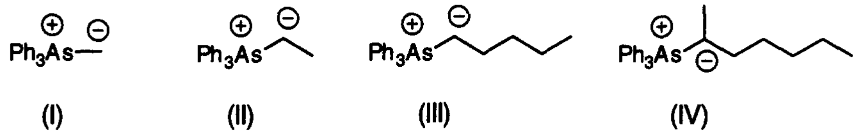
Ylides are useful reagents widely used to synthesize alkenes or epoxides from the corresponding aldehydes or ketones.[1-3] We recently reported the straightforward olefination of alkyl halides and mesylates by means of dimethylsulfonium methylide. Terminal olefins were obtained in high yields by a one-carbon homologation reaction.[4] To extend the scope of this process to the synthesis of polysubstituted olefins, we investigated the reaction of halides or mesylates with more substituted sulfonium ylides. Unfortunatly, diphenylsulfonium ethylide and tetrahydrothiophenium ethylide, were unreactive due, in part, to their poor stability under reaction conditions.[3,5] Phosphonium ylides were also not suitable for the preparation of substituted olefins. Alkylation of the phosphonium ylides was observed as previously reported.[6] Finally, we became interested in arsonium ylides and we found that they convert very efficiently activated bromides or mesylates into the desired substituted alkenes.[2] This original reactivity of arsonium ylides can be ascribed to their high nucleophilicity, required in the first step, and to their strong basicity needed in the second step of the transformation[7,8] (Schemes 1 and 3).



Scheme 1

Fax: +(33) 03 88 67 68 63; e-mail: mioskow@aspirine.u-strasbg.fr

Arsonium salts are obtained in good yields from triphenylarsine and alkyl iodides in refluxing acetonitrile.[2] The corresponding ylides were then easily generated by treatment with *n*-BuLi in THF/HMPA. In this paper, we would like to report the olefination reaction induced by four different non stabilized arsonium ylides I, II, III, IV (Scheme 2) with various halides and mesylates.

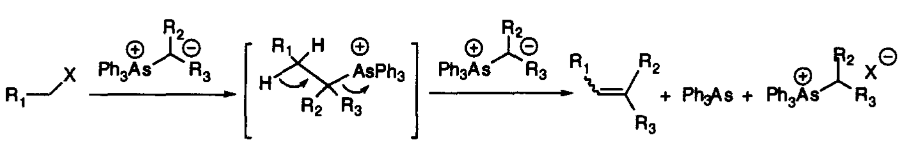


Scheme 2

The scope and the limitations of the reaction are summarized in Table 1. In contrast to dimethylsulfonium methylide, the analogous arsonium ylide I does not give terminal olefin in the presence of non activated primary bromides (entry 1), neither does ylide II (entry 2). Primary benzylic bromides react with ylide I to give the expected terminal olefin in a comparable yield to the one obtained with dimethylsulfonium methylide (entry 3). Di-substituted olefins were obtained with high *E* selectivity with ylides II and III (entries 4 and 5), whereas a 1/1 *E/Z* mixture of trisubstituted olefins is obtained with ylide IV (74% yield, entry 6). Secondary benzylic bromide react with ylide I to give mainly elimination of HBr and low yield of the desired olefin (entry 7). Geranyl mesylate was converted in excellent yields into conjugated dienes (entries 8, 9) with high *E* selectivity. Allylic chloride exhibited the same reactivity and gave mono-, di- and tri-substituted alkenes by treatment, respectively, with ylides I, II,I II and IV. High *E* selectivity was observed for 1,4 disubstituted dienes (entries 10, 11 and 12) and a 1/1 mixture for the 1,1',4 trisubstituted conjugated diene (entry 13). 1,3 Ene-ynes were obtained in high yields with propargylic bromide and ylides I and II (entries 14 and 15). Noteworthy is the formation of a 1/1 *E/Z* mixture with ylide II (entry 15) compared to the *E* selectivity observed with benzylic or allylic halides and mesylates (entries 7, 9, and 11).

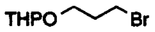
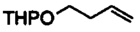
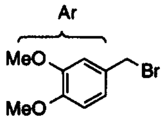
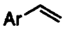
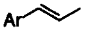
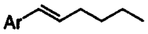
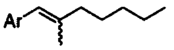
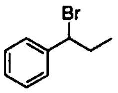
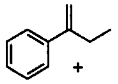
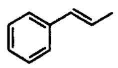
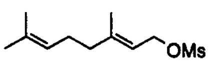
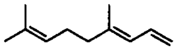
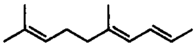
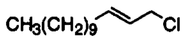
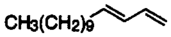
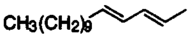
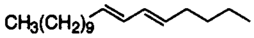
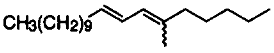
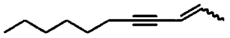
We also examined the reactivity of semi-stabilized arsonium ylides (triphenylarsonium benzylide or triphenylarsonium allylide) and stabilized arsonium ylides (triphenylarsonium ethylacethylide). Under the same reaction conditions, no olefin formation was observed.

The mechanism of the reaction is identical to the one proposed for dimethylsulfonium methylide olefination.[8] The first step is the alkylation of arsonium ylide, followed by β-elimination of triphenylarsine which is induced by a second ylide equivalent (Scheme 3).



Scheme 3

Table 1. Olefination of Activated Halides and Mesylates

Entry	Substrate	Ylide	Product	E/Z[a]	Yield[b] (%)
1		I		–	0
2		II		–	0
3		I		–	95
4		II		>98/2	92
5		III		>98/2	83
6		IV		1/1	74
7		I	 +	–	13
				–	85
8		I		–	91
9		II		>98/2	88
10		I		–	90
11		II		>98/2	86
12		III		>98/2	85
13		IV		1/1	75
14		I		–	88
15		II		1/1	84

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

[b] Based on isolated, chromatographically homogeneous material.[9]

In conclusion, we report here the first direct olefination of activated halides and mesylates to form substituted olefins. Non stabilized arsonium ylides were schown to be efficient to perform these very useful transformation leading to disubstituted alkenes with high *E* selectivity and to trisubstituted alkenes as a 1:1 mixture of E/Z isomers.

Typical experimental procedure : To a vigorously stirred suspension of alkyl-triphenylarsonium salt (3 equiv., 1.5 mmol), in anhydrous THF/HMPA at -40°C (9/1, 8 mL) was added dropwise *n*-BuLi in excess (3 equiv., 1.5 mmol, 0.94 mL of 1.6 M hexane solution). The mixture was allowed to warm to -20°C over a period of 30 minutes and then cooled back to -40°C. The electrophile (1 equiv., 0.5 mmol) in dry THF (1 mL) was then introduced and the reaction mixture was allowed to warm to room temperature. Stirring was maintained for an additional hour. The reaction mixture was then diluted with Et_2O and quenched with 30 mL of water and 10 mL of brine. The aqueous layer was extracted several times with ether, and the combined organic layers were dried over magnesium sulfate, filtered and concentrated under vacuum. Purification of the crude through a pad of silica gel gave the desired alkene in yields reported in Table 1.

Acknowledgments :

This work was supported in part by the Bio-Avenir Program (Rhône-Poulenc / CNRS) and ARC (France). We thank Alain Valleix for mass spectroscopy measurements and Eric Doris for reviewing the manuscript.

References and Notes :

1. Corey, E.J.; Chaykowsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353-1364. Maryanoff, B.E; Reitz, A.B. *Chem. Rev.* **1989**, *89*, 863-927.
2. Lloyd, D.; Gosney, I.; Ormiston, R.A. *Chem. Soc. Rev.* **1987**, *16*, 45-74.
3. Trost, B.M.; Melvin, L.S. *Sulfur Ylides - Emerging Synthetic Intermediates*, Academic Press: New-York, 1975.
4. Alcaraz, L.; Harnett, J.J.; Mioskowski, C.; Martel, J.P.; Le Gall, T.; Shin, D.S.; Falck, J.R *Tetrahedron Lett.* **1994**, *35*, 5453-5456.
5. Corey, E.J.; Oppolzer, W. *J. Am. Chem. Soc.* **1964**, *86*, 1899-1900. Trost, B.M.; Ziman, S.D. *J. Am. Chem. Soc.* **1971**, *93*, 3825-3827. Koval' I.V., *Russ. Chem. Rev.* **1994**, 63, 147-168.
6. Hercouet, A.; Le Corre, M. *Tetrahedron Lett.* **1979**, 2995-2998.
7. Johnson, A.W.; Amel, R.T. *Can. J. Chem.* **1968**, *46*, 461-463.
8. Ousset, J.B.; Mioskowski, C.; Solladié, G. *Synth. Commun.* **1983**, *13*, 1193-1196. Boubia, B.; Mioskowski, C.; Manna, S.; Falck, J.R. *Tetrahedron Lett.* **1989**, *30*, 6023-6026.
9. All compounds were fully characterized by NMR (^1H, ^{13}C), Mass Spectroscopy and Combustion Analysis.

(*Received in France* 3 *September* 1997; *accepted* 17 *September* 1997)