Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2010, **20**, 145–147

Mendeleev
Communications

Alteration of the course of the Michaelis–Arbuzov reaction in imidazolium ionic liquids

Ekaterina V. Matveeva, Vladimir A. Kozlov and Irina L. Odinets*

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 499 135 5085; e-mail: odinets@ineos.ac.ru

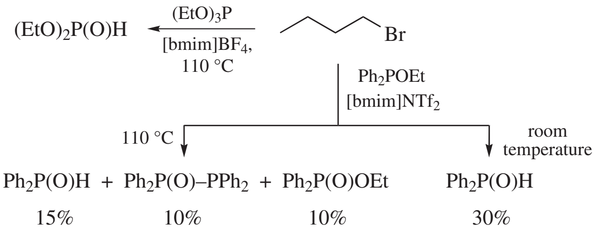
DOI: 10.1016/j.mencom.2010.05.007

Room-temperature imidazolium ionic liquids [Rmim][X] (X = Br, BF_4, NTf_2) as a reaction medium change the reaction course of phosphorus(III) acid esters with primary alkyl halides, aryl bromides, and propargyl bromide to afford hydrophosphoryl compounds, products of oxidation of the starting phosphorus substrates, and 2,3-bis(phosphoryl)prop-1-enes, respectively.

It is well known that ionic liquids (ILs) due to their ability to dissolve organic, inorganic and metal complex materials (they are often mentioned as supersolvents) and to promote a variety of chemical transformations as well as potential for recyclability, low toxicity, and non-volatile nature are currently in focus of synthetical chemistry in the search for green alternatives of traditional toxic, flammable and hazardous organic solvents.[1] The 'green' principles enter also organophosphorus chemistry and ionic liquids and water were found to accelerate some main reactions leading to the substances of practical and research importance.[2] Among those, the Michaelis–Arbuzov reaction is an important one of general value in the conversion of 3-coordinate phosphorus esters to 4-coordinate species with the formation of P–C bond. Recently, we demonstrated that room-temperature imidazolium ionic liquids (ILs) [Rmim][X] (X = Br, BF_4, PF_6, NTf_2) proved to be efficient recyclable media promoting the Michaelis–Arbuzov reaction in the case of activated alkyl halides such as ethyl bromoacetate, chloroacetonitrile, benzyl bromides, *etc*. In these cases the reactions can be performed under lower reaction temperature (even under ambient conditions) in a short period of time.[3] The best ionic liquid of choice depended on the starting phosphorus(III) ester, namely, for triethyl phosphite [bmim][NTf_2] demonstrated better results, while for ethyl diphenylphosphinite it was [hmim][Br]. In continuation of this study it was of undoubted interest to estimate the possibility of applying ILs as a promoting medium in the Michaelis–Arbuzov reaction with other types of alkyl halides.

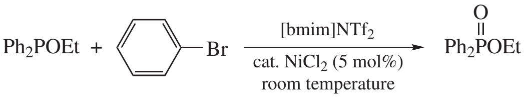
Here, we report on unusual results obtained in the reaction of phosphorus(III) acid esters with primary alkyl halides, aryl bromides, and propargyl bromide in the presence of ILs.

Under conditions which were advantageous for the Michaelis–Arbuzov reaction in the case of activated alkyl halides, the reactions of both triethylphosphite and ethyl diphenylphosphinite with butyl bromide proceeded mainly in ionic liquids as dealkylation of one ester group at the phosphorus atom to afford the corresponding hydrophosphoryl compounds.[†] Thus, according to the NMR data, the reaction of $(EtO)_3P$ with BuBr at 110 °C in [bmim]BF_4 yielded a mixture of $(EtO)_2P(O)H$ (*ca.* 50%) and unreacted phosphorus substrate (about 40%) (Scheme 1). Ethyl diphenylphosphinite was slightly more stable in ILs and approximately 65% of this compound remained unchangeable both at elevated temperature and under ambient conditions. In such a way, the reaction of Ph_2POEt with BuBr in [bmim]NTf_2 at 20 °C resulted in the mixture of the starting substrate and the product of its dealkylation in a 7:3 ratio while under elevated temperature it was accompanied by partial oxidation into corresponding phosphinate and tetraphenyldiphosphine monooxide (Scheme 1).



Scheme 1

The weak electrophiles such as aryl halides are known to react with P^{III}-acid esters according to the Arbuzov reaction course only under the catalytic action of metal salts among which nickel dichloride being the most effective (5–10 mol%, 150 °C, several hours).[4] However, when the reaction of Ph_2POEt with bromobenzene in the presence of $NiCl_2$ was performed in [bmim]NTf_2, it resulted in ethyl diphenylphosphinate due to oxidation (70% yield) (Scheme 2).



Scheme 2

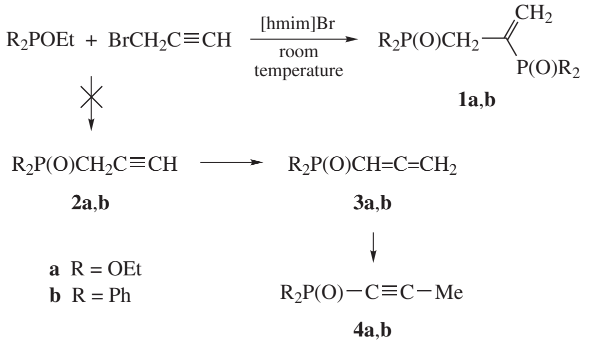
Anomalous reaction course was revealed also for the reaction of P^{III}-acid esters with propargyl bromide in ILs. Under typical reaction conditions this reaction, investigated mostly using trialkylphosphites as an example,[5] is usually accompanied by acetylene–allene–acetylene rearrangement to afford phosphorylacetylenes with the internal triple bond rather than the species with terminal triple bond (yields < 15%). Surprisingly, being performed in ILs, this reaction resulted in 2,3-bis(phosphoryl)-prop-1-enes **1a**,**b** instead of the expected products **2a**,**b** or the related compounds **4a**,**b** with internal triple bonds formed *via* the above rearrangement (Scheme 3). Using the ratio of the starting reactants equal to 2:1, the yields of propenes **1a**,**b** were *ca.* 45% for $(EtO)_3P$ ([bmim]NTf_2, 20 or 110 °C) and about 78% for

---

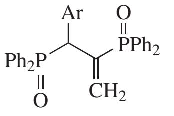
[†] Formation of hydrophosphoryl compounds was unambiguously confirmed by the ^{31}P NMR spectra of the corresponding reaction mixtures using the authentic additives: $(EtO)_2P(O)H$, δ_P 6.9 ppm ($^1J_{PH}$ 680 Hz); $Ph_2P(O)H$, δ_P 21.6 ppm ($^1J_{PH}$ 480 Hz).

Ph_2POEt ([hmim]Br, room temperature). After work-up, 2,3-bis(diphenylphosphoryl)prop-1-ene **1b** was isolated in 30% yield as an off-white solid while the yield of its analogue **1a** was only 12% (>90% purity) after distillation.[‡] However, in both cases the structures of propenes **1a**,**b** were unambiguously confirmed by the multinuclear NMR spectra. The compounds demonstrated two doublets in the ^{31}P NMR spectra (AB-system) at 17.55 and 25.31 ppm with the coupling constant $^3J_{PP}$ 32.0 Hz (for **1a**) and at 30.79 and 32.80 ppm with $^3J_{PP}$ 22.1 Hz (for **1b**) and the corresponding sets of signals in the ^{1}H and ^{13}C NMR spectra.

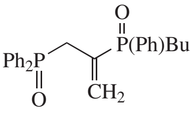
Previously, the products of the similar structure were obtained *via* double phosphorylation of α-aryl substituted propargylic alcohols with diphenylphosphine oxide catalyzed by thiolate-bridged diruthenium complex [Cp*RuCl(μ$_2$-SMe)$_2$-RuCp*Cl, (Cp* = 5-C$_5$Me$_5$)][6] (60 °C, 18 h, compound **5**), by thermal induced *tert*-butylphenylphosphine addition to (allenyl)diphenylphosphine oxide in refluxing toluene (48 h, compound **6**)[7] or by the Arbuzov reaction of trimethylphosphite with dimethyl (3-bromoprop-1-en-2-yl)phosphonate [110 °C, $(MeO)_3P$ as a solvent, compound **7**].[8] Note that the above-mentioned ruthenium catalyzed reaction was supposed to proceed *via* $Ph_2P(O)H$ addition either to the intermediate terminal acetylene $Ph_2P(O)CH(Ar)C{\equiv}CH$ or to the product of its acetylene-allene rearrangement.[6]



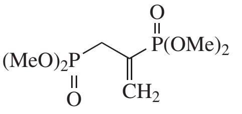
Scheme 3



5



6



7

Taking into account the formation of the corresponding hydrophosphoryl compound from starting P^{III}-esters, *i.e.*, diethylphosphite or diphenylphosphinous acid in ILs in the case of inactive alkyl and aryl halides, we suggested that formation of products **1a**,**b** can be attributed to the general reaction scheme similar to those for metal-catalyzed or thermally induced processes mentioned in refs. 6, 7. In other words, the reaction of phosphite or phosphinite with propargyl bromide in ILs according to Scheme 3 could initially result in the Arbuzov-type products **2a**,**b** with terminal triple bonds which may undergo further acetylene-allene rearrangement to afford allenes **3a**,**b**. The subsequent addition of the corresponding hydrophosphoryl compounds, formed under reaction conditions, to either of these intermediates could produce the final bisphosphorylated propenes **1a**,**b**. At that, ionic liquid could activate all steps of the process.

To verify this supposition, we performed the reactions of $Ph_2P(O)H$ with either of $Ph_2P(O)CH_2C{\equiv}CH$ and $Ph_2P(O)CH{=}C{=}CH_2$ in ILs. However, these test experiments revealed that $Ph_2P(O)H$ did not add to either of these compounds in [hmim][Br] or [bmim][NTf$_2$] even at prolonged reaction times. That means that the above reactions proceed *via* different reaction pathway.

To elucidate it, the reaction of ethyl diphenylphosphinite with propargyl bromide was performed in [bmim][BF$_4$] capable of stabilizing the intermediate phosphonium salts due to the presence of non-nucleophilic anion.[3] Under these conditions, the ^{31}P NMR spectra of the reaction mixture comprised two doublets at 44.9 and 61.8 ppm with the coupling constant equal to 73 Hz which slowly transformed into the signals of the final product **1b** (δ_{P1} 30.79 ppm, δ_{P2} 32.80 ppm, $^3J_{PP}$ 22.1 Hz). These data allow us to suggest that the above reaction involves the first attack of a phosphorus lone pair of diphenylphosphinite on the electrophilic carbon atom in propargyl bromide to form an intermediate salt **A** which can rearrange to the corresponding allenic intermediate **B**. The further addition of the second molecule of Ph_2POEt either to **A** or to **B** salts results in formation of the ^{31}P NMR detected intermediate **C** bearing phosphonuim and ylidic phosphorus atoms. In time, the intermediate **C** transforms into the final product **1b** by dealkylation and hydrolysis of ethoxy groups at phosphonium and ylidic phosphorus atoms, respectively (Scheme 4).

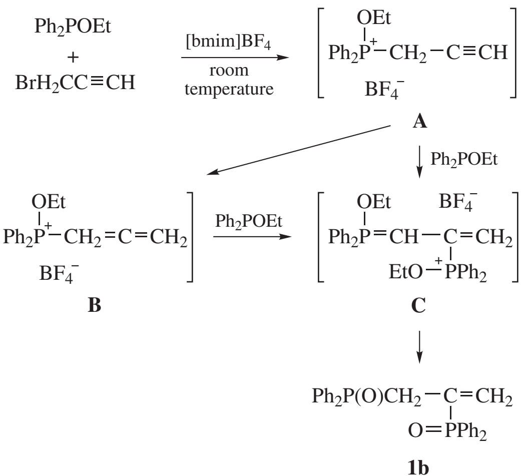
In conclusion, we have found that imidazolium ionic liquids as a reaction medium change the reaction course of phosphorus(III) acid esters with primary alkyl halides, aryl halides and propargyl bromide affording in hydrophosphoryl compounds, the products of oxidation of the starting phosphorus substrate, and 2,3-bis(phosphoryl)prop-1-enes, respectively, instead of the typical Arbuzov products. The procedure for the synthesis of 2,3-bis(phosphoryl)prop-1-enes in ionic liquids is advantageous over other known methods.

[‡] NMR spectra were recorded on a Bruker Avance-400 spectrometer and the chemical shifts (δ) were internally referenced by the residual solvent signals relative to TMS (^{1}H and ^{13}C) or externally to H_3PO_4 (^{31}P).

Diphenyl-1-propynylphosphine oxide[9] and diphenyl(1,2-propadienyl)phosphine oxide[10] were obtained according to the published procedures.

2,3-Bis(diethoxyphosphoryl)prop-1-ene **1a**. Triethylphosphite (0.02 mol) was added to a solution of propargyl bromide (0.011 mol) in [bmim]NTf$_2$ (5 g) at room temperature followed by stirring of the final mixture for 3 days. Then the reaction mixture was extracted with Et_2O (3×20 ml), the solvent was evaporated under reduced pressure and the residue was distilled in a vacuum to give 0.4 g (12%) of bisphosphorylated propene **1a** with 90% purity according to the spectral data. Bp 170–190 °C (20 Torr), ^{31}P NMR (162 MHz, $CDCl_3$): AB-system, 17.55 [P(1)], 25.31 [P(2), $^3J_{PP}$ 32 Hz]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.28–1.33 (m, 12H, Me), 2.75 [dd, 2H, $CH_2P(1)$, $^2J_{P(1)H}$ 21.4 Hz, $^3J_{P(2)H}$ 12.3 Hz], 4.05–4.14 (m, 8H, OCH_2), 6.24 (dd, 1H, H_A, $^3J_{P(2)H}$ 21.8 Hz, $^4J_{P(1)H}$ 4.9 Hz), 6.25 (dd, 1H, H_B, $^3J_{P(2)H}$ 47.4 Hz, $^4J_{P(1)H}$ 3.7 Hz).

2,3-Bis(diphenylphosphoryl)prop-1-ene **1b**. Ethyl diphenylphosphinite (2 mmol) was added to a solution of propargyl bromide (1 mmol) in [hmim]Br (0.5 g) at room temperature. After stirring (for 3.5 h, 69% of **1b**; 3 days, 78% of **1b**) water (1 ml) was added to the reaction mixture and this solution was extracted with CH_2Cl_2 (3×10 ml). The combined extracts were dried over Na_2SO_4. After evaporation of the solvent under reduced pressure, the residue was separated by column chromatography (SiO_2, CH_2Cl_2–methanol, 100:2) to afford propene **1b** as off-white solid. Yield 30%, mp 142 °C. ^{31}P NMR (162 MHz, $CDCl_3$): AB-system, 30.79 [P(1)], 32.80 [P(2), $^3J_{PP}$ 22.1 Hz]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.41 [dd, 2H, $CH_2P(1)$, $^2J_{P(1)H}$ 13.0 Hz, $^3J_{P(2)H}$ 8.3 Hz], 5.52 (dd, 1H, H_A, $^3J_{P(2)H}$ 21.0 Hz, $^4J_{P(1)H}$ 3.0 Hz), 6.77 (dd, 1H, H_B, $^3J_{P(2)H}$ 43.2 Hz, $^4J_{P(1)H}$ 2.3 Hz), 7.38–7.56, 7.72–7.79 (m, 20H, 4Ph). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 29.63 (dd, $^1J_{P(1)C}$ 67.0 Hz, $^2J_{P(2)C}$ 9.9 Hz), 128.60 (d, *meta*-C in Ph, $^3J_{PC}$ 11.5 Hz), 129.09 (d, *ipso*-C in Ph, $^1J_{P(1)C}$ 81.1 Hz), 130.97 (d, *ortho*-C in Ph, $^2J_{P(1)C}$ 9.9 Hz), 131.83 (s, *para*-C in Ph), 131.96 (d, *ortho*-C in Ph, $^2J_{P(2)C}$ 9.3 Hz), 132.15 (s, *para*-C in Ph), 132.59 (d, *ipso*-C in Ph, $^1J_{P(2)C}$ 81.5 Hz), 134.33 (appar. t, $=CH_2$, $^2J_{P(2)C} = {}^3J_{P(1)C} = 8.0$ Hz), 134.72 (dd, C=, $^1J_{P(2)C}$ 51.6 Hz, $^2J_{P(1)C}$ 7.4 Hz). IR (KBr, ν/cm^{-1}): 3055 ($C{=}CH_2$), 1198, 1174 (P=O). Found (%): C, 72.28; H, 5.27; P, 13.46. Calc. for $C_{27}H_{24}O_2P_2 \cdot 0.1CH_2Cl_2$ (%): C, 72.28; H, 5.41; P, 13.76.



Scheme 4

This work was supported by the Russian Foundation for Basic Research (grant no. 05-03-32692) and Deutsche Forschungsgemeinschaft (436 RUS 113/766/1-1).

References

1 (*a*) *Ionic Liquids as Green Solvents: Progress and Prospects*, eds. R. D. Rogers and K. R. Seddon, ASC Symposium Ser., Washington DC, 2003; (*b*) *Ionic Liquids in Synthesis*, eds. P. Wasserscheid and T. Welton, Wiley-VCH, Weinheim, 2003.

2 (*a*) G. Keglevich, Z. Baan, Z. Finta, I. Hermecz, T. Novak and I. L. Odinets, *Curr. Org. Chem.*, 2007, **11** (1), 107; (*b*) E. V. Matveeva and I. L. Odinets, *Curr. Org. Chem.*, 2010, **14** (12), in press.

3 (*a*) E. V. Matveeva, I. L. Odinets, V. A. Kozlov, A. S. Shaplov and T. A. Mastryukova, *Tetrahedron Lett.*, 2006, **47**, 7645; (*b*) I. L. Odinets, E. V. Matveeva, E. V. Sharova, O. I. Artyushin, V. A. Kozlov, D. V. Vorobyeva, S. N. Osipov, T. A. Mastryukova and G.-V. Röschenthaler, *Phosphorus Sulfur Silicon Relat. Elem.*, 2008, **183**, 383.

4 P. Tavs, *Chem. Ber.*, 1970, **103**, 2428.

5 (*a*) M. Gordon and C. E. Griffin, *J. Org. Chem.*, 1966, **31**, 333; (*b*) H. I. Jacobson, M. J. Griffin, S. Preis and E. V. Jensen, *J. Am. Chem. Soc.*, 1957, **79**, 2608.

6 M. D. Milton, G. Onodera, Y. Nishibayashi and S. Uemura, *Org. Lett.*, 2004, **6**, 3993.

7 T. Gati, A. Simon, F. Toth, A. Szmigielska, A. M. Maj, K. Pietrusiewicz, S. Moeller, D. Magiera and H. Duddeck, *Eur. J. Inorg. Chem.*, 2004, 2160.

8 I. E. Gurevich and J. C. Tebby, *J. Chem. Soc., Perkin Trans. 1*, 1995, 1259.

9 R. S. Macomber and E. Kennedy, *J. Org. Chem.*, 1976, **41**, 3191.

10 A. P. Boisselle and N. A. Meinhardt, *J. Org. Chem.*, 1962, **27**, 1828.

Received: 8th December 2009; Com. 09/3432