

Solvent-free mechanochemical synthesis of phosphonium salts†

Viktor P. Balema,* Jerzy W. Wiench, Marek Pruski and Vitalij K. Pecharsky*

Ames Laboratory, Iowa State University, Ames, IA 50011-3020, USA. E-mail: balema@ameslab.gov

Department of Materials Science and Engineering, Iowa State University, Ames, IA 50011, USA.

E-mail: vitkp@ameslab.gov

Received (in Corvallis, OR, USA) 17th December 2001, Accepted 7th February 2002

First published as an Advance Article on the web 6th March 2002

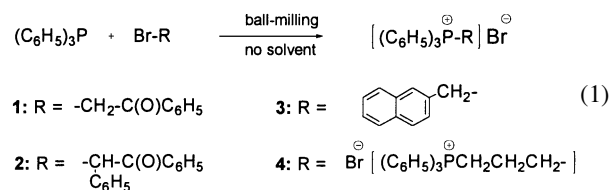
Phosphonium salts have been prepared during high-energy ball-milling of triphenylphosphine with solid organic bromides; the reactions occur at ambient conditions without a solvent; in the case of 2-bromo-2-phenylacetophenone the reaction in a solution usually produces a mixture containing both the C-phosphorylated and O-phosphorylated compounds, while the solvent-free mechanically induced transformation results in the thermodynamically favorable C-phosphorylated product; the occurrence of the observed transformations during mechanical processing of solid reactants is confirmed by the solid-state ^{31}P NMR spectroscopy and X-ray powder diffraction.

Mechanical processing (ball-milling) of solids is a scalable technique, which is routinely used in materials science^{1,2} and in the pharmaceutical industry.³ However, mechanical activation is seldom attempted in synthetic organic chemistry and when it is, mechanical treatment is carried out in the presence of a solvent or is followed by additional processing, *e.g.*, heating.⁴⁻⁶ Furthermore, as far as we are aware, mechanochemical transformations of organo-phosphorus compounds were previously unknown.

Here we report the solvent-free preparation of phosphonium salts during mechanical processing of solid reactants at ambient conditions. Traditionally, phosphonium salts are synthesized in organic solutions in a typical $\text{S}_{\text{N}}2$ quaternization reaction of ternary phosphines with organic halides.^{7,8} These transformations may be complicated by side-reactions, and thus become unsuitable for the synthesis of desired compounds. Especially unreliable are reactions of ternary phosphines with α -bromo ketones, where the alkylation of phosphines is accompanied by the formation of O-phosphorylated products and by the dehydrobromination of starting ketones.⁷⁻⁹

To explore the reactivity of triphenylphosphine with solid organic bromides during mechanical processing in a solvent-free environment, triphenylphosphine and 2-bromoacetophenone, taken in a 1 : 1 molar ratio, were sealed under helium in a hardened-steel vial with steel balls and milled for one hour in a Spex-8000 mill. Ball-milling for one hour was found to be sufficient for the completion of this reaction.‡ The obtained powder was analyzed by solid-state $^{31}\text{P}\{^1\text{H}\}$ cross polarization magic angle spinning nuclear magnetic resonance (CP MAS NMR) spectroscopy and X-ray powder diffraction. Commercial phenacyltriphenylphosphonium bromide **1** (Lancaster Synthesis) was used as a reference. The solid-state $^{31}\text{P}\{^1\text{H}\}$ CP MAS spectra of both the powder obtained after mechanical processing and commercial phosphonium salt, are shown in Fig. 1. They contain only one signal at $\delta^{31}\text{P} = 23$ ppm, indicating a complete transformation of triphenylphosphine ($\delta^{31}\text{P} = -5$ ppm) and 2-bromoacetophenone into salt **1** (eqn. (1)). Also, the X-ray powder diffraction pattern of the mechanochemically prepared compound **1**† is in an excellent agreement with that of the commercial phosphonium salt. For an additional purification, the mechanically prepared phosphonium bromide **1** was dissolved in hot water and isolated after crystallization in 90%

yield. Its ^1H and ^{31}P NMR spectra in CDCl_3 and the melting point¹⁰ were identical with those of the commercial product.



The success in the mechanochemical solid-state alkylation of triphenylphosphine with 2-bromoacetophenone encouraged us to study its mechanochemical reaction with 2-bromo-2-phenylacetophenone. It was reported previously that 2-bromo-2-phenylacetophenone reacts with triphenylphosphine in solution yielding a mixture of C- and O-phosphorylated reaction products.⁹ The mechanochemical reaction was carried out following the procedure used for the preparation of salt **1** (eqn. (1)). Again, the solid-state $^{31}\text{P}\{^1\text{H}\}$ CP MAS spectrum of the ball-milled sample contains only one peak centered at $\delta^{31}\text{P} = 26$ ppm (Fig. 1), consistent with the position of the signal in the NMR spectrum of pure (α -benzoyl- α -phenylmethylene)triphenylphosphonium bromide **2** (eqn. (1)). The latter was obtained in 99% yield, recrystallized from a methanol–diethyl ether solution and characterized by liquid-state ^1H , ^{31}P , and ^{13}C NMR spectroscopy and elemental analysis.¹⁰ The formation of the C-phosphorylated compound **2** in almost quantitative yield shows that the mechanochemical solvent-free technique clearly discriminates between the C- (Arbuzov) and O-phosphorylation (Perkow) pathways in favor of the more thermodynamically stable Arbuzov-type product. Using the same mechanochemical approach, we also succeeded in the preparation of two other phosphonium salts **3** and **4**, (eqn. (1)) from corresponding solid organic bromides. While 2-(naphthalenylmethyl)triphenylphosphonium bromide **3** easily forms during ball-milling of the reactants in hardened-steel equipment for one hour, the preparation of propane-1,3-diylbis(triphenylphosphonium) dibromide **4** requires mechanical processing in a tungsten carbide

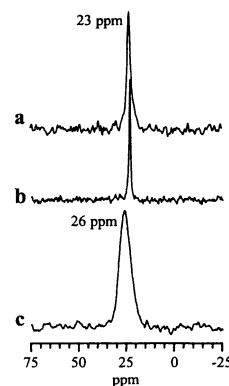


Fig. 1 The solid-state $^{31}\text{P}\{^1\text{H}\}$ CP MAS NMR spectra of the mechanochemically prepared bromide **1** (a), the commercial salt **1** (Lancaster Synthesis) (b) and the phosphonium bromide **2** prepared mechanochemically (c).

† Electronic supplementary information (ESI) available: X-ray diffraction patterns of **1**. See <http://www.rsc.org/suppdata/cc/b1/b111515d/>

vial with tungsten carbide balls for 12.5 h. In both cases, phosphonium salts were isolated in high, or moderate yields (3: 95%, 4:51%) and the comparison¹⁰ with the commercially available products confirmed their formation.

Several models describing mechanically induced reactions between triphenylphosphine and organic halides can be suggested. One of the probable mechanisms when low-melting halides react with triphenylphosphine is a local formation of low-melting eutectics in the triphenylphosphine–organic bromide systems during ball-milling. In this case, the reactions may occur in the melt, which forms locally and momentarily in the areas where the rapidly moving balls collide with both the walls of the reaction vial and with one other.

To verify the possibility of the eutectics formation in the triphenylphosphine–bromobenzophenone systems, we studied two mixtures: triphenylphosphine and 4'-bromobenzophenone (A), and triphenylphosphine, 4'-bromobenzophenone and salt 1(B), both in an equimolar ratio. Mixture A was ball-milled for one hour, or melted and then cooled to room temperature. Mixture B was ball-milled for one hour. Since both 2-bromoacetophenone and 4'-bromobenzophenone melt at nearly the same temperature, 48–50 and 50–52 °C, respectively, and the chemical structures of these bromoketones are almost identical, it is reasonable to expect that their eutectics with triphenylphosphine (mp 80–82 °C) will show similar melting behavior. Furthermore, while 2-bromoacetophenone immediately reacts with triphenylphosphine in the melt forming salt 1, 4'-bromobenzophenone is inert towards the same phosphine providing a good model for understanding of the temperature-induced phase transformations in the triphenylphosphine–2-bromoacetophenone system.

In the case of A the onset of the first endothermic (melting) event is observed at 36 °C, and the second melting event at ~50 °C. Therefore, a low-melting eutectic indeed exists in the binary triphenylphosphine–4'-bromobenzophenone system. The onset of melting in B (38 °C) is close to that of A, indicating that the presence of the reaction product should have a minor effect (if any) on the reactions described above.

The existing data on the local temperature rise in different types of mills during mechanical processing of inorganic solids¹ and our results¹¹ on mechanical treatment of LiAlH₄ are consistent with the 'localized melting' hypothesis. Based on the fact that prolonged ball-milling of pure LiAlH₄, which irreversibly loses hydrogen at 150 °C and above, does not result in noticeable change in this material,¹¹ the local temperature in a Spex-8000 mill cannot exceed 150 °C. The temperature in the vial, however, can locally reach ~35–40 °C, which is sufficient for the formation of liquid phases in some of the described processes.

The mechanochemical formation of the phosphonium salt 4 from high melting (mp 228–230 °C) 3-bromopropyl(triphenylphosphonium) bromide and triphenylphosphine is, however, difficult to explain by the localized melting mechanism¹² and, therefore, alternative scenarios should be also considered. One such possibility is that this chemical transformation proceeds in the solid-state during ball-milling. In this case, the mechanical treatment creates conditions sufficient for close contact and subsequent chemical interactions between reacting compounds and provides the mass transport required for the transformation to occur. Experiments to verify this hypothesis and establish possible activation periods are under way, and their results will be published elsewhere.

In summary, the results described above indicate that solvent-free mechanochemistry has a potential to become an alternative to conventional organic synthesis. Continuing research to establish the suitability of the mechanochemical synthesis to different reaction types may lead to the development of novel green technologies¹³ once its mechanism is better understood.

Ames Laboratory is operated by Iowa State University for the U.S. Department of Energy (DOE) under contract No. W-7405-ENG-82. Different aspects of this work were supported by the Office of Basic Energy Sciences, Materials Sciences

Division (VPB, and VKP) and Chemical Sciences Division (JWW and MP) of the U.S. DOE.

Notes and references

‡ The starting and reference compounds were purchased from Aldrich or Lancaster Synthesis. Solid-state ³¹P{¹H} CP MAS NMR spectra were collected on a Chemagnetics Infinity 400 MHz spectrometer equipped with a Chemagnetics MAS probe using a variable amplitude cross polarization scheme (contact time of 0.5 ms, relaxation delay of 5 s, and spinning rate of 20 kHz). ¹H, ¹³C and ³¹P NMR spectra in CDCl₃ or C₆D₆ were obtained using Varian VXR-300 and Varian VXR-400 spectrometers. Chemical shifts are reported with respect to the 85% solution of H₃PO₄ in water (³¹P) or TMS (¹H and ¹³C) as the external standards. Ball-milling (for 15 min to 12.5 h) of various quantities of materials, usually about 1.0 g total, was performed in a Spex-8000 mill using 21 g of steel balls in a hardened-steel vial, or 70 g of tungsten carbide balls in a tungsten carbide (CW) vial sealed under helium as protective atmosphere. Processing times under one hour usually resulted in lower yields. Chemical reactions described in this work do not continue after ball-milling has been stopped. Forced-air cooling of the vial was employed to prevent its heating during ball-milling experiments.

- 1 C. Suryanarayana, *Progr. Mater. Sci.*, 2001, **46**, 1.
- 2 V. P. Balema, K. W. Dennis and V. K. Pecharsky, *Chem. Commun.*, 2000, 1665.
- 3 T. P. Shakhshneider and V. V. Boldyrev, *Mol. Solid State*, 1999, **3**, 271.
- 4 F. Toda, *Acc. Chem. Res.*, 1995, **28**, 480.
- 5 V. D. Makhaev, A. P. Borisov and L. A. Petrova, *J. Organomet. Chem.*, 1999, **590**, 222.
- 6 M. Nüchter, B. Ondruschka and R. Trzetzki, *J. Prakt. Chem.*, 2000, **342**, 720.
- 7 W. A. Johnson, *Ylides and imines of phosphors*, John Wiley & Sons, Inc., New York, 1993.
- 8 *The Chemistry of Organophosphorus Compounds vol. 3, Phosphonium Salts, Ylides and Phosphoranes.*, ed. F. R. Hartley, John Wiley & Sons, Ltd, Chichester, New York, Brisbane, Toronto, Singapore, 1994.
- 9 J. Borowitz, P. E. Rusek and R. Virkhaus, *J. Org. Chem.*, 1969, **34**, 1995.
- 10 Mechanochemically prepared phosphonium compounds. **1**: yield 90%; solid-state ³¹P{¹H} CP MAS NMR: $\delta^{31}\text{P}$ (ppm): 23.0; liquid-state NMR (CDCl₃): $\delta^{31}\text{P}$ (ppm): 23.0; $\delta^1\text{H}/J_{\text{P-H}}$ (ppm/Hz): 8.38/7.4 (d, 2H, Ph), 8.01–7.90 (m, 6H, Ph), 7.67–7.74 (m, 4H, Ph), 7.67–7.54 (m, 6H, Ph), 7.52–7.45 (m, 2H, Ph), 6.40/12.2 (d, 2H, CH₂); mp 270–273 °C; **2**: yield 99%; solid-state ³¹P{¹H} CP MAS NMR: $\delta^{31}\text{P}$ (ppm): 26.0; liquid-state NMR (CDCl₃): $\delta^{31}\text{P}$ (ppm): 27.4; $\delta^1\text{H}/J_{\text{P-H}}$ (ppm/Hz): 9.30/12.4 (d, 1H, CH), 8.42 (m, 2H, Ph), 8.02–7.96 (m, 6H, Ph), 7.71–7.67 (m, 3H, Ph), 7.60–7.55 (m, 6H, Ph), 7.46–7.35 (m, 5H, Ph), 7.22–7.19 (m, 1H, Ph), 7.15–7.11 (m, 2H, Ph); $\delta^{13}\text{C}\{^1\text{H}\}/J_{\text{C-P}}$ (ppm/Hz): 195.36/3.6 (d, CO), 135.57/9.7 (d, Ph), 134.41 (m, Ph), 133.78/5.2 (d, Ph), 131.89/5.2 (d, Ph), 131.19 (s, Ph), 129.75/13.2 (d, Ph), 129.51/2 (d, Ph), 129.17/2 (d, Ph), 128.86 (s, Ph), 128.83/5.9 (d, Ph), 118.78/86.6 Hz (d, CP, Ph), 54.30/54.9 (d, CP). Found (%): C 70.74, H 5.19%. Calculated for C₃₂H₂₆OPBr (%): C 71.50, H 4.84%; mp 246–248 °C (decomposition); **3**: yield 95%; solid-state ³¹P{¹H} CP MAS NMR: $\delta^{31}\text{P}$ (ppm): 25.0; liquid-state NMR (CDCl₃): $\delta^{31}\text{P}$ (ppm): 24.4; $\delta^1\text{H}/J_{\text{P-H}}$ (ppm): 7.98–7.1 (m, 22H, Aryl), 5.6/12.4 (d, 2H, CH₂); mp 239–241 °C; **4**: yield 51%; liquid-state NMR (CDCl₃): $\delta^{31}\text{P}$ (ppm): 25.4; $\delta^1\text{H}$ (ppm): 7.87–7.83 (m, 10H, Ph), 7.71–7.57 (m, 20H, Ph), 4.64–4.55 (m, 4H, CH₂), 2.3–1.83 (m, 2H, CH₂) mp 355–360 °C (decomposition).
- 11 V. P. Balema, K. W. Dennis and V. K. Pecharsky, *J. Alloys Compd.*, 2000, **69**, 313.
- 12 The solvent-free preparation of **4** was achieved only after steel balls were replaced by heavier CW balls thereby increasing the input of mechanical energy into the system.¹ It is feasible that additional energy is required due to high melting temperatures of triphenylphosphine and 3-bromopropyl(triphenylphosphonium) bromide. However, the localized melting mechanism offers no explanation for the fact that after a prolonged ball-milling of these reactants in the presence of an excess of Ph₃P (which is the low melting component in this system) the starting bromide still remains in the reaction mixture.
- 13 Solvent-free mechanochemistry may appear to be an energy intensive technique when compared with the conventional solvent-based chemical synthesis. However, considering life cycles of both processes, e.g. the energy required to produce, deliver, collect and dispose the solvents, and restore the environment, the advantages of the mechanochemical approach are noteworthy.