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A Comparison of Reactivity of $(EtO)_2P(O)CH_2I$ with Related Non-Phosphorus-Containing Iodides in the Radical Iodine Atom Transfer Addition

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ABSTRACT: *Based on competitive reactions and ^1H NMR measurements, it was found that $(EtO)_2P(O)CH_2I$ is at least 2–3 orders of magnitude less reactive than other non-phosphorus iodides of the EWG-CH_2I type (EWG = NC, COOMe, 4-Br-C_6H_4CO). $MeSCH_2I$ turned out to be totally unreactive in the title reaction.* © 2003 Wiley Periodicals, Inc. Heteroatom Chem 14:186–188, 2003; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.10121

INTRODUCTION

Use of phosphonate reagents in synthesis of biologically active and natural products is well documented and has been recently reviewed [2]. Working on the development of new reagents and reactions in the phosphonate chemistry, we have recently elaborated experimental conditions for the new iodine atom transfer (**4**→**5**) addition reaction of 1-iodoalkylphosphonates **1** to alkenes and alkynes **3** leading to the modified 3-iodo-substituted phosphonates **5** [3,4] (Scheme 1).

This type of reaction was reviewed for various heteroatom donors which, however, did not possess phosphorus-containing groups [5–7]. The discussed reaction, because of the presence of the easily functionalizable iodine atom in the product **5**, gave greater synthetic perspectives than the related reaction that was previously elaborated by us [8] and carried out under reductive conditions. At this stage of investigations, a further progress in utilization of the iodine atom transfer reaction is not possible without a knowledge of the relative reactivity of diethyl 1-iodoalkylphosphonates (**1**) [9]. Therefore, in this paper we wish to report our results aimed at estimation of a reactivity of the phosphonate iodide **1** ($R^1 = H$) in relation to reactivities of iodides **6a–d** possessing other non-phosphorus-containing groups like COOMe, NC, 4-Br-$C_6H_4C(O)$, and SMe, based on competitive reactions of the corresponding electrophilic radicals **2** and **7a–d** with *n*-hexene as an electron-rich alkene standard (Scheme 2). The reactivity of **1** towards other alkenes is known and was demonstrated by us earlier [3]. The radical species **2** and **7** were generated via homolysis of the C—I bond in organic iodides **1** ($R^1 = H$) and **6a–d** using α,α'-azaisobutyronitrile (AIBN).

The iodide **1** ($R^1 = H$) was synthesized in the Arbuzov reaction of $P(OEt)_3$ with CH_2I_2 in 50% yield [10]. The remaining iodides **6a,c,d** were obtained in

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Phosphorus containing radicals. Part 11. For Part 10 see Ref. [1].

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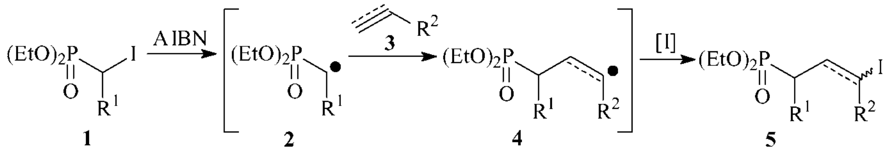


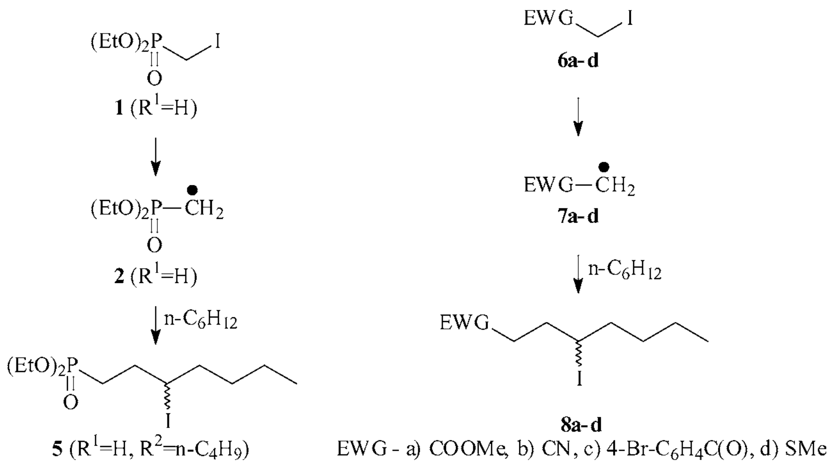
SCHEME 1 The iodine atom transfer (**4**→**5**) addition reaction of **1** to alkenes and alkynes.

the Finkelstein reaction of the corresponding chlorides or bromides with NaI in anhydrous acetone or CCl$_4$ (**6a**-Cl, 100%, acetone; **6c**-Br, 95%, acetone; **6d**-Cl, 90%, CCl$_4$) and the iodide **6b** was a commercial reagent. Before the competitive reactions were carried out, the corresponding iodine atom transfer addition reaction products **5** and **8a–d** as reference compounds were synthesized separately in the reaction of **2** (R^1 = H) and **7a–d**, respectively, with 10 equiv. of *n*-hexene and a stoichiometric amount of AIBN (benzene, 80°C; 7 h).

At the outset, it turned out that the iodide **6d** was totally unreactive towards *n*-hexene and a complex mixture in addition to the starting material was formed in this case as a result of destabilizing both steric and electronic effects of two sulfur electron pairs.

However, with the remaining iodides **2** (R^1 = H) and **6a–c**, the corresponding products **5** and **8a–c** were obtained in yields up to 83%. Fortunately, each of the isolated products **5, 8a–c**, and **10** displayed characteristic well-separated ^{1}H NMR signals, enabling observation of relative amounts of these products in a function of time during competitive reactions (**8a**-COO$\underline{Me}$ $\delta = 3.71$ ppm, **8b**-NC—C$\underline{H}_2$ $\delta = 2.62$ ppm, **8c**-4-Br-C$_6$H$_4$C(O)C$\underline{H}_2$ $\delta = 3.20$ ppm). The amount of **5**, which did not possess any characteristic and distinguishable signal in the ^{1}H NMR spectrum, was calculated from ^{31}P NMR spectra and was correlated with the amount of the unreacted **1** in the ^{1}H NMR spectra based on the P(O)CH$_2$I doublet. The competitive reactions were carried out by mixing all starting iodides **1** (R^1 = H) and **6a–c** (1 equiv. of each) with *n*-hexene (40 equiv.) and AIBN (4 equiv.) followed by refluxing of the resulting mixture in benzene for 7 h. ^{1}H NMR samples were collected after 0, 15, 30 min, and then after 1, 1.5, 2, 3, 4, 5, 6.5 h to give 10 measure points from which the most conclusive, first 6 points are taken into account in Fig. 1 (see also Experimental section). To test the reproducibility of the reaction with four substrates, the analogous reactions with two (**1** and **6a, 1** and **6c**) and three substrates (**1, 6a, 6c**) were also carried out.

It turned out that the compound **8b** was formed rapidly as the first product, yet before the benzene refluxing point was reached, i.e. within first 5–10 min. After less than 40 min the corresponding substrate **6b** was completely consumed. The least reactive iodide **1** (R^1 = H) gave **5** (R^1 = H, R^2 = *n*-Bu) in 4 and 21% yields after the 1- and 2-h reflux, respectively, when the remaining iodides were almost consumed. Because the yield of **5** in a noncompetitive reaction of **1** and *n*-hexene was 80%, such a big difference in reactivity between **1** and a group of the four remaining iodides **6a–d** could be useful for a



SCHEME 2 Synthesis of 3-iodo-substituted iodides **5** and **8a–d**.

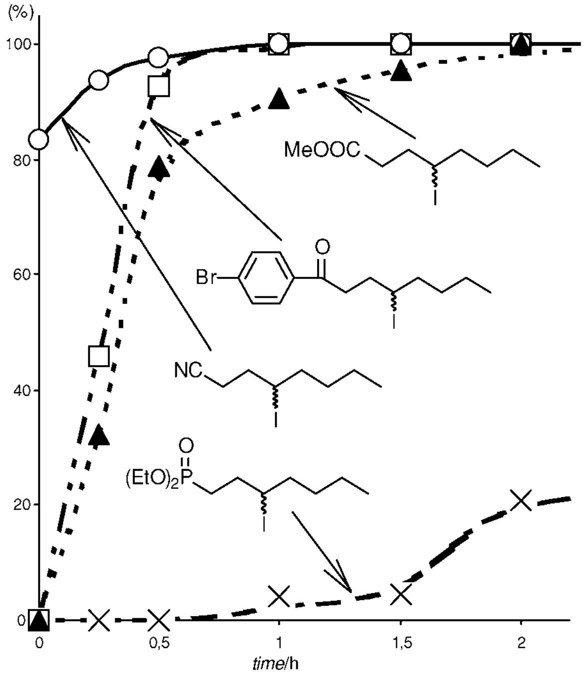


FIGURE 1 A comparison of relative rates of the products formation in the radical iodine atom transfer addition reaction of EWG-CH_2I to *n*-hexene.

rational design of synthetic schemes with the use of regioselective iodine atom transfer reactions. Based on ratios of increments of amounts of the products **5** and **8a–c**, in the first 15 min, when concentration changes were almost linear, this reactivity difference could be estimated to be at least 2–3 orders of magnitude.

EXPERIMENTAL

Competitive Reactions of Iodides **1** and **6a–c**

To a stirred solution of a mixture of starting iodides **1** (35 mg, 0.126 mmol), **6a** (25 mg, 0.126 mmol), **6b** (21 mg, 0.126 mmol), **6c** (41 mg, 0.126 mmol), and *n*-hexene (424 mg, 630 μl, 5.05 mmol) in benzene (12 ml), AIBN (83 mg, 0.505 mmol) was added and the resulting mixture was refluxed for almost 7 h. Each of 10 samples (0.7 ml) collected after 0, 15, and 30 min, then after 1, 1.5, 2, 3, 4, 5, and 6.5 h was evaporated and analyzed using ^{1}H NMR ($CDCl_3$, 200 and 500 MHz). The first sample (the starting zero point) was collected at 70–75°C, i.e. before the benzene boiling point was reached. The remaining nine samples (after 15 min, 30 min, etc. till 6.5 h) were collected during the reflux, without cooling the reaction mixture. The relative amounts of the obtained iodides **5** and **8a–c** based on the ^{1}H NMR spectra in a function of time are summarized in Fig. 1. Analogous competitive reactions were carried out with two (**1/6a, 1/6c**) and three substrate iodides (**1/6a/6c**).

REFERENCES

[1] Bałczewski, P.; Bialas, T.; Szadowiak, A.; Mikołajczyk, M. Phosphorus Sulfur Silicon 2002, 177, 1579–1582.

[2] Mikołajczyk, M.; Bałczewski, P. In Topics in Current Chemistry; Majoral, J. P. (Ed.); Springer-Verlag: Berlin, Heidelberg, 2002; Vol. 223, pp. 161–214.

[3] Bałczewski, P.; Białas, T.; Mikołajczyk, M. Tetrahedron Lett 2000, 41, 3687–3690.

[4] Bałczewski, P.; Mikołajczyk, M. New J Chem 2001, 25, 659–663. For other non phosphorus involving iodine atom transfer addition reactions see references therein.

[5] Giese, B. Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds; Pergamon Press: Oxford, 1986; pp. 77–86.

[6] Curran, D. P.; Porter, N. D.; Giese, B. Stereochemistry of Radical Reactions: Concepts, Guidelines and Synthetic Approaches, VCH Weinheim: New York, 1996, pp. 180–181.

[7] Curran, D. P. Synthesis 1988, 489–513, Part 2.

[8] Bałczewski, P.; Mikołajczyk, M. Rev Heteroat Chem 1998, 18, 37–59 and references cited therein.

[9] For reactivity of the chalcogen (S, Se, Te) groups with alkyl radicals see: Curran, D. P.; Martin-Esker, A. A.; Ko, S.-B.; Newcomb, M. J Org Chem 1993, 58, 4691.

[10] Bałczewski, P.; Mikołajczyk, M. Synthesis 1995, 392–396 and references cited therein.