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A convenient method for the synthesis of electron-rich phosphonates☆

Shijun Zheng, Stephen Barlow, Timothy C. Parker and Seth R. Marder*

Department of Chemistry, University of Arizona, Tucson, AZ 85721-0041, USA[†]

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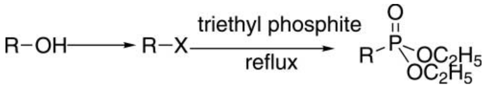
Abstract—Very electron-rich benzylic-type phosphonates can be prepared by treating the corresponding alcohols in triethyl phosphite with one equivalent of iodine at an appropriate temperature in a general one-pot process.

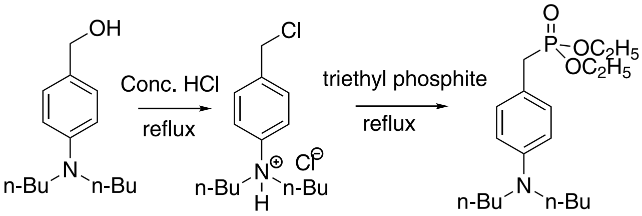
The growing interest in organic materials for nonlinear-optical, electronic and opto-electronic applications has led to the development of many new π-conjugated molecules.[1] One of the most important reactions utilized to synthesize these types of molecules is the Horner–Emmons condensation of an aldehyde with a phosphonate to form an alkene with exclusively *trans* stereochemistry.[2] The general method to synthesize a phosphonate from the corresponding alcohol typically involves two steps: (i) conversion of the alcohol to a halide; (ii) the Michaelis–Arbuzov reaction of the halide with a trialkyl phosphite for several hours at high temperature (Scheme 1).[3] This two-step procedure has drawbacks for very electron-rich benzylic-type alcohols such as 4-(diarylamino)benzyl alcohols and metallocenyl alcohols, which are potentially useful building blocks for electron-rich conjugated molecules. In particular, preparation of the halides can be complicated by oxidative or electrophilic side-reactions, and isolation of halides can be complicated by covalent/ionic equilibria.

These complications can be avoided in some cases by rendering the aromatic ring electron deficient through protonation. A method has been described for conversion of 4-(dialkylamino)-benzylic alcohols to the corresponding 4-(dialkylamino)-benzyl chloride hydrochloride salts by refluxing the alcohol in concentrated aqueous HCl; reflux of this product in triethyl phosphite gives the corresponding phosphonate (Scheme 2).[4] However, this method is unsuccessful with 4-(diarylamino)benzylic alcohols, which are extremely weak Brønsted bases at the nitrogen center. The method is also not applicable to ferrocenylmethanol and octamethylferrocenylmethanol; under acidic conditions these are converted to the corresponding carbocations which then readily undergo dimerization reactions.[5]

We have found a very simple general one-pot method to convert electron-rich benzylic-type alcohols to phos-



Scheme 1.



Scheme 2.

☆ Supplementary data associated with this article can be found at doi:10.1016/j.tetlet.2003.08.110

* Corresponding author. Tel.: 404-385-6048; fax: 404-894-7452; e-mail: seth.marder@chemistry.gatech.edu

[†] Current address: School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA 30332-0400, USA.

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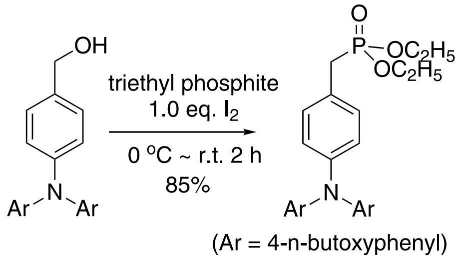

Scheme 3.

phonates by treating the alcohols in triethyl phosphite with one equivalent of iodine at an appropriate temperature (Scheme 3). Presumably $[(EtO)_3PI]^+[I]^-$ and/or $(EtO)_2P(O)I$ are intermediates, since triethyl phosphite is known to form these species rapidly on reaction with iodine, even at low temperatures.[6]

The scope of the method was tested by examination of a broad range of substrates (Table 1). This method not only renders the preparation of entries 1 and 5 possible (the preparation of these types of phosphonates has not been reported in literature) and provides a more convenient route to **4b**,[7] but also has the advantage that this one-pot reaction often proceeds at room temperature, which is useful for the synthesis of more complex electron-rich benzylic phosphonates that might not be stable at the elevated temperatures required for typical Michaelis–Arbuzov reactions. The rates of these reactions are highly dependent on the electron-richness of the substrates and their solubility in triethyl phosphite. For the less electron-rich benzylic alcohols (entries 8 and 9) the present method does not show significant advantages over the traditional method of Scheme 1; the substitution of the presumed iodide intermediate with triethyl phosphite does not appear to proceed as rapidly at room temperature as for the more electron-rich examples.

An example of the application of the electron-rich phosphonates, synthesized by the method described here, to the synthesis of conjugated materials is illustrated in Scheme 4. Compound **12** has a structural motif that is anticipated to show interesting two-photon absorbing properties.[8]

In summary, we have discovered a convenient high-yielding method for making very electron-rich benzylic-type phosphonates, which are otherwise difficult to make.

Supporting information available. Experimental procedures, and characterizing data for entries 1–11 and for the preparation of compounds **12** and **13**.

Acknowledgements

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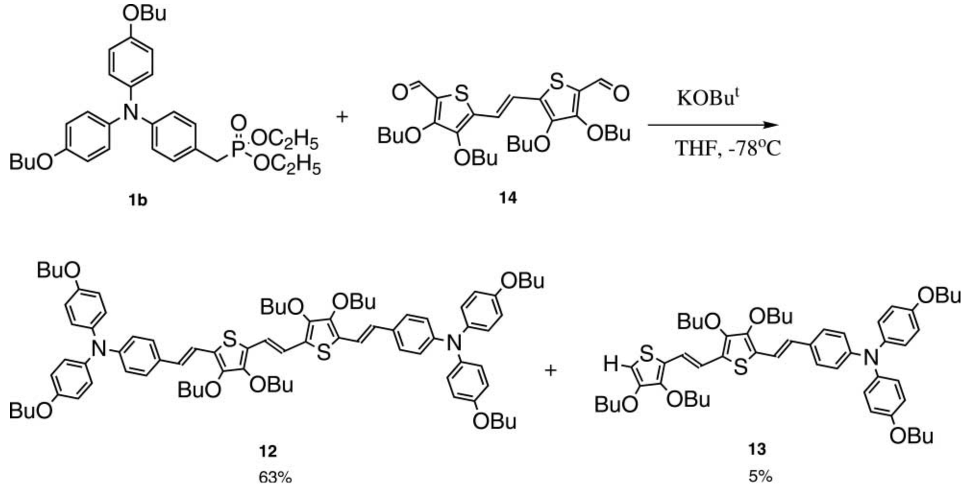
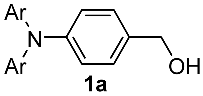
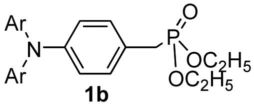
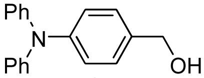
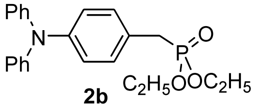
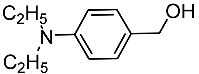
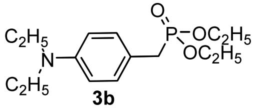
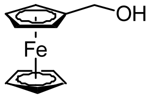
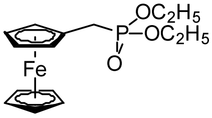
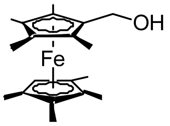
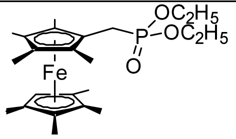
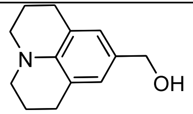
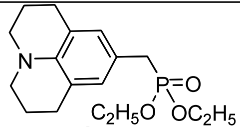
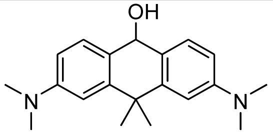
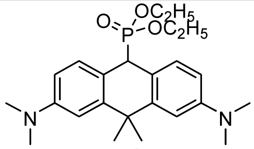
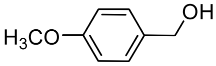
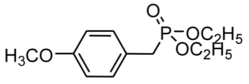
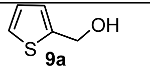
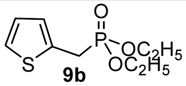
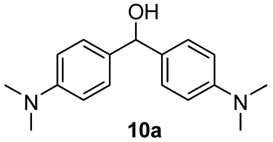
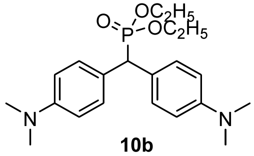
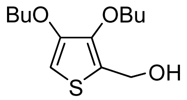
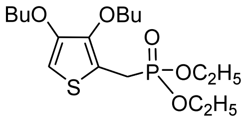


Scheme 4.

Table 1. Summary of the applicability of the method

Entry	Reactants	Products	Conditions	Yield/%
1	 **1a** Ar = 4-*n*-butoxyphenyl	 **1b** Ar = 4-*n*-butoxyphenyl	0°C → r.t. 2 h	85%
2	 **2a**	 **2b**	0°C → r.t. 12 h	69%
3	 **3a**	 **3b**	0°C → r.t. 2 h	61%
4	 **4a**	 **4b**	0°C → r.t. 2 h	74%
5	 **5a**	 **5b**	0°C → r.t. 12 h	69%
6	 **6a**	 **6b**	0°C → r.t. 12 h	73%
7	 **7a**	 **7b**	0°C → r.t. 24 h	70%
8	 **8a**	 **8b**	0°C→150° C 5h	78%
9	 **9a**	 **9b**	0°C→125° C 12h	40%
10	 **10a**	 **10b**	0°C→r.t. 12 h	77%
11	 **11a**	 **11b**	0°C→r.t. 24 h	55%

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7. **4b** has previously been obtained by reaction of $[FcCH_2NMe_3]^+[I]^-$ with $P(OEt)_3$ (Boev, V. I. *Zh. Obshch. Khim.* **1978**, *48*, 1594) and from the reaction of FcLi with $P(O)Cl(OEt)_2$ (Alley, S. R.; Henderson, W. *J. Organomet. Chem.* **2001**, *637–639*, 216).
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