

Synthesis of biaryls by intramolecular radical transfer: use of phosphinates

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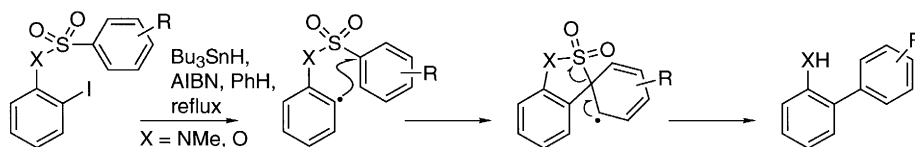
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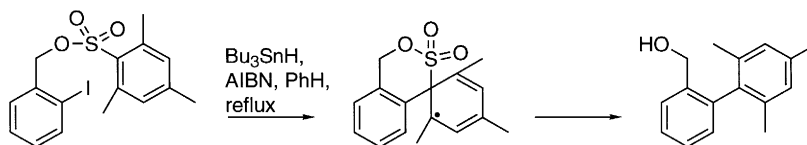
Abstract

Phosphinates **4a–13a** give biaryls **4b–13b** on heating with stannanes in the presence of a radical initiator. © 2000 Elsevier Science Ltd. All rights reserved.

Intramolecular transfer of aryl groups by a radical mechanism has been known for a long time,¹ but has recently attracted special attention with a view to evaluating the synthetic possibilities of the process. Much of the latest work has involved the formation of biaryls,^{2–4} and has usually been based on the -SO₂- group as a tether between two aromatic rings that are subsequently linked. Reactions such as those summarized in Scheme 1^{2a,b} are typical, and have been studied in detail. The transfer occurs by *ipso* substitution, followed by expulsion of the tether.⁵ In certain cases^{2a,c,3} (for example, Scheme 2^{2c} and Scheme 3³), the initial *ipso* attack can be of the 6-*exo* type.

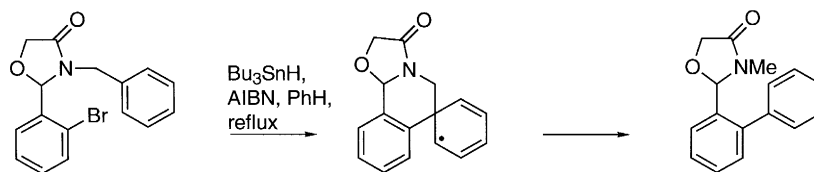


Scheme 1.



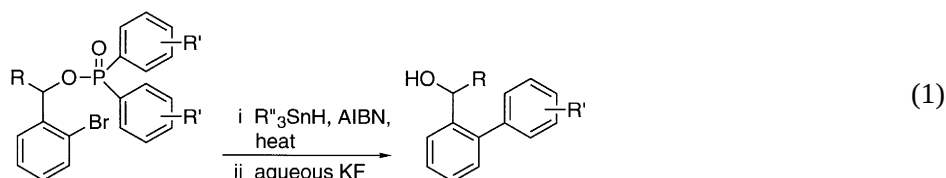
Scheme 2.

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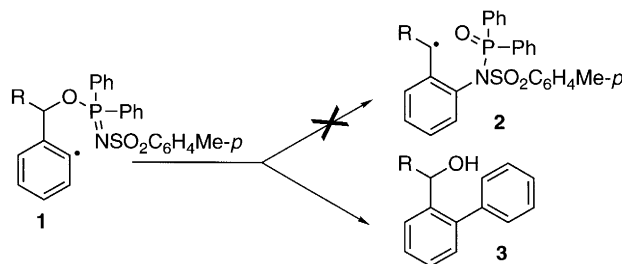
Scheme 3.

We report the transfer of aromatic units within the phosphinate compound class, according to Eq. (1).



(1)

Our initial experiments involved generation of radicals of type **1** (Scheme 4, R=H, Me, Ph), in order to establish⁶ if they would rearrange (**1**→**2**), by analogy to the well-known⁷ β-(phosphatoxy)alkyl and β-(acyloxy)alkyl radical rearrangements. In the event, the products isolated were of type **3** (R=H, 45%; R=Me, 50%, R=Ph, ca. 15%). It was quickly established that the presence of the nitrogen subunit is not essential, and that the reaction is a general one of phosphinates (see Eq. (1) and Table 1).



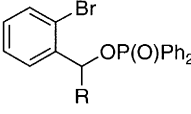
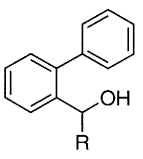
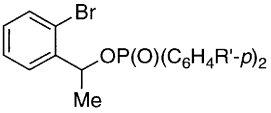
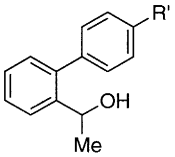
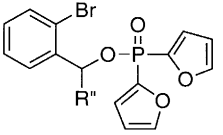
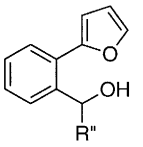
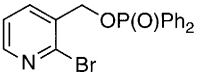
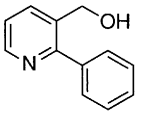
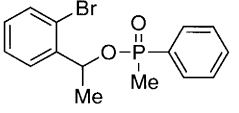
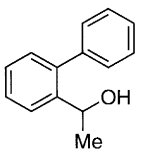
Scheme 4.

The starting phosphinates are available by acylation of the parent alcohol with the appropriate diarylphosphinic chloride [$\text{Ar}_2\text{P}(\text{O})\text{Cl}$,⁹ Et_3N , DMAP, CH_2Cl_2 , room temperature, ca. 1 h], and our general procedure for the radical rearrangement involves slow addition of a solution of stannane (0.03 M, 2 mmol) and AIBN (0.0075 M, 0.5 mmol) to a refluxing solution of the phosphinate (0.015 M, 1 mmol). We found that reactions done in xylene give better yields than those in lower-boiling hydrocarbons (toluene or benzene), at least as judged by experiments with **5a**, and so we generally used this solvent. Our preferred workup involves stirring the product mixture with saturated aqueous potassium fluoride, followed by chromatography.

As shown in Table 1, the presence of electron-withdrawing (CO_2Me) or electron-donating (OMe , Me) substituents is tolerated. The starting alcohol can be primary or secondary. In addition, we have tested heteroaromatic groups (see Table 1); they undergo the aryl transfer (cf. **10a**, **11a**) and can also serve as the location of the initial radical (cf. **12a**). The conversion of **13a** (which is a mixture of diastereoisomers) into **13b** shows that the phosphinate can carry an alkyl group on phosphorus.

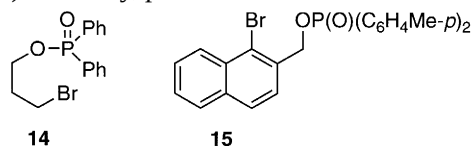
Attempts to extend the process to a primary alkyl radical (derived from **14**) were unsatisfactory, as the major product was that of simple reduction, and the desired phenyl transfer occurred only to a small

Table 1

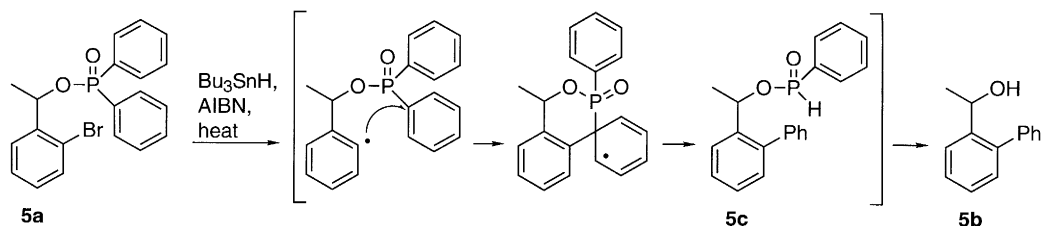
Starting phosphinate	Aryl transfer product	Conditions; workup
 4a R = H, 85% ^a 5a R = Me, 88% 6a R = Ph, 59%	 4b R = H, 58% 5b R = Me, 64% 6b R = Ph, 46%	Ph ₃ SnH, xylene; K ₂ CO ₃ -MeOH Ph ₃ SnH, xylene; K ₂ CO ₃ -MeOH Ph ₃ SnH, xylene; K ₂ CO ₃ -MeOH
 7a R' = Me, 84% 8a R' = OMe, 96% 9a R' = CO ₂ Me, 67%	 7b R' = Me, 63% 8b R' = OMe, 52% 9b R' = CO ₂ Me, 54%	Ph ₃ SnH, xylene; KF-water Ph ₃ SnH, xylene; KF-water Bu ₃ SnH, toluene; KF-water
 10a R'' = H, 94% 11a R'' = Me, 67%	 10b R'' = H, 44% ^b 11b R'' = Me, 17%	Ph ₃ SnH, xylene; NaCNBH ₃ ^c Ph ₃ SnH, xylene; NaCNBH ₃
 12a 76%	 12b 41%	Bu ₃ SnH, xylene; KF-water
 13a 79%	 13b 73%	Bu ₃ SnH, toluene; KF-water

^aYield from the parent alcohol. ^bThe simple reduction product (H instead of Br in **10a**) was isolated in 19% yield. ^cSee reference 8.

extent (transfer:reduction 1:2¹⁰).¹¹ With the naphthalene derivative **15**, only the reduction product (H instead of Br) was isolated (74%). Possibly, *peri* interactions hinder the desired process in this case.



Mechanistically, it is reasonable to assume that the early stages of the reaction involve the steps



Scheme 5.

shown in Scheme 5, with the initial radical transfer occurring via a six-membered transition state. In this preliminary work, however, we have not established the mechanism(s) by which **5b** is finally liberated. The suggested precursor **5c**,¹² made independently, is stable to the workup conditions but, on heating in xylene (overnight), it affords alcohol **5b** (ca. 42%), which can be detected (TLC¹³) before workup. In refluxing benzene or toluene (ca. 12 h), **5c** is stable but gives **5b** (ca. 46%) in benzene (toluene was not tested) in the presence of tributylstannane and AIBN.

All new compounds were characterized by spectroscopic measurements, including accurate mass measurement.

Acknowledgements

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