



Hypophosphorous acid–iodine: a novel reducing system. Part 2: Reduction of benzhydrols to diarylmethylene derivatives

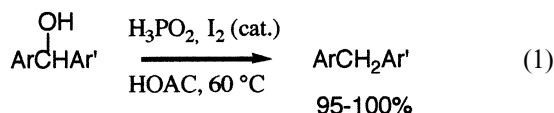
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Abstract—A mixture of hypophosphorous acid (H_3PO_2) and iodine in acetic acid reduces a variety of substituted benzhydrols to the corresponding methylene derivatives in very high yields. The active reducing agent is hydrogen iodide generated by reaction between iodine and hypophosphorous acid. © 2001 Elsevier Science Ltd. All rights reserved.

Apart from its use as for reductive deazonylation of diazonium ions,¹ there are few reports of the use of hypophosphorous acid (H_3PO_2) as a reagent in organic chemistry.² By the same token, there are not many reports of hydrogen iodide as a reducing agent for organic compounds.^{3–8} We recently reported that a mixture of hypophosphorous acid and iodine (the latter in catalytic amounts) in refluxing acetic acid is an efficient reducing agent for diaryl ketones.⁹ Fluorenone, dibenzosuberone, and a variety of substituted benzophenones were reduced to the corresponding methylene derivatives in 97–100% yield. We now report that a wide variety of benzhydrols bearing both electron-withdrawing and electron-supplying groups are reduced to the corresponding diarylmethylene derivatives very cleanly and in high yield (Table 1) (Eq. (1)) by this reagent system.



The diarylmethylenes are isolated in pure form (NMR and GC–MS analysis) after a simple workup. This procedure is competitive in terms of ease, cost, and yield with previous methods for deoxygenation of benzhydrols, including lithium–ammonia,¹⁰ $\text{Fe}(\text{CO})_5$,¹¹ diiododimethylsilane,¹² zinc iodide–sodium cyanoborohydride,¹³ triphenylsilane in trifluoroacetic acid–methylene chloride,¹⁴ sodium borohydride–trifluoroacetic acid,¹⁵ iodine–acetic acid–red phosphorus,¹⁶ and lithium alu-

minum hydride–aluminum chloride.¹⁷ Acetic acid is the preferred solvent for these conversions: reduction was slow or negligible in chloroform or benzene, and conversion of the benzhydrol to the corresponding methyl ether was observed in methanol. The ether was however slowly converted to diphenylmethane upon continued reaction. Reduction occurred in quantitative yield in almost every case. 4-Methoxybenzhydrol underwent cleavage of the *O*-methyl group and partial esterification of the phenolic group under the reaction conditions (run 3); similar behavior was observed previously with 4-methoxybenzophenone.⁹ Hydrogenolysis of halogen atoms was observed during reduction of 4,4-diiodobenzhydrol (run 12), but not with 4-bromo- or 4-chlorobenzhydrol or 4,4'-dichlorobenzhydrol. Benzhydrols containing nitro or ester groups were not investigated; it is known that nitro compounds are reduced by hydrogen iodide¹⁸ and we have found that esters are hydrolyzed (not reduced) under our experimental conditions. We are exploring methods to avoid this.

The actual intermediate in these reductions is probably the carbocation formed by protonation of the alcohol. Consistent with this hypothesis, benzhydrols bearing strongly electron-withdrawing groups are reduced noticeably more slowly than benzhydrols bearing electron-supplying substituents (runs 6, 7, 12, and 13). However, sampling of a 1:1 mixture of 4-methyl- and 4-bromobenzhydrol over a period of time showed that the two substances were reduced at about the same rate. The tertiary alcohols triphenylcarbinol and 1,1-diphenylethanol were reduced more readily than benzhydrol, which is also consistent with the rate of carbocation formation being the key factor in ease of reduction.

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A competing reaction during the attempted reduction of 4,4'-bis[dimethylamino]benzhydrol was cleavage to a mixture of 4-dimethylaminobenzaldehyde and dimethylaniline (run 8), presumably by hydrogen iodide; an old report showed that the same cleavage can be effected by hydrogen bromide.¹⁹ The reaction is curious in that it is most readily understood as proceeding through initial ring protonation of **1**, presumably facilitated by the *para*-dimethylamino group (Scheme 1).

Selectivity: We previously reported that reduction of substituted benzophenones to the corresponding diaryl-methanes can be effected in high yield by this same mixture of hypophosphorous acid and iodine in refluxing acetic acid.⁹ We hypothesized that those reductions take place via the benzhydrol as an intermediate. However, benzhydrols were never observed when the reactions were sampled throughout their progress. The reason for this is now clear: benzhydrols are reduced much faster than benzophenones and can in fact be reduced at much lower temperature. When an equimolar mixture of benzophenone and 3,4-dimethylbenzhydrol was allowed to react for as long as 72 h at 60°C, the alcohol was completely converted to 3,4-dimethyldiphenylmethane without any detectable reduction of benzophenone to diphenylmethane! Similar results were obtained using mixtures of benzophenone with 4,4'-di-X-benzhydrol, where X is chloro, methoxy, or dimethylamino. Reduction of substituted benzhydrols can be carried out at temperatures as low as 40°C, although at the expense of longer reaction times.

Reduction of 4-methylbenzhydrol (representative reaction): Iodine (1.00 g; 4.0 mmol), 4-methylbenzhydrol (0.79 g; 4.03 mmol), and acetic acid (25 mL) were stirred under nitrogen in a flask equipped with condenser. Hypophosphorous acid (50% aq.; 2 mL; 19.3 mmol) was added and the mixture was heated to 60°C. The mixture was stirred for 24 h, diluted with water, and extracted with hexane. The hexane was dried over MgSO₄ and removed under reduced pressure. Analysis by GC-MS showed only a single constituent, 4-methyldiphenylmethane,²⁰ produced in 100% yield. ¹H NMR (300 MHz, CDCl₃): δ 2.49 (s, 3H), 4.12 (s, 2H), 7.15–7.54 (m, 9H).

All of the diphenylmethanes prepared in this study are known compounds except for 3,4'-bis-[trifluoromethyl]-diphenylmethane (mp 41–42°C), which exhibited the following spectral properties: ¹H NMR (CDCl₃) δ 7.3–7.6 (m, 8H), 4.18 (s, 2H); MS (EI) *m/z* 304 (M⁺), 285 (M-F), 264 (M-2F), 235 (M-CF₃, 100), 215, 165. Anal. calcd for C₁₅H₁₅F: C, 59.22; H, 3.31; F, 37.47. Found: C, 59.08; H, 3.39; F, 37.18.

Acknowledgements

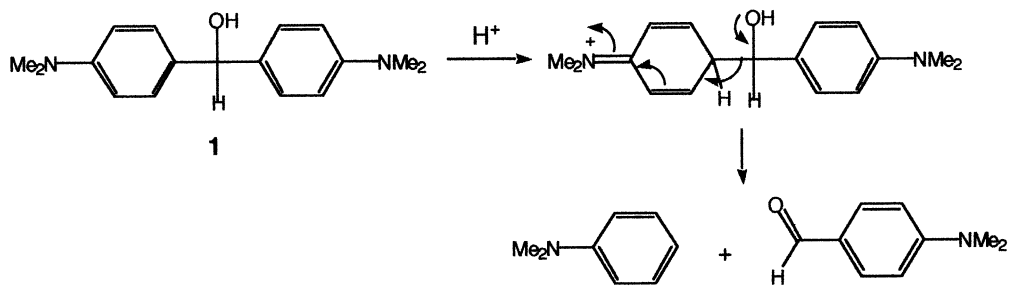
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Table 1. Reduction of aryl carbinols with hypophosphorous acid-iodine in acetic acid^a

Run	Alcohol	Product(s), yield
1	Benzhydrol	Diphenylmethane, 100%
2	4-Methylbenzhydrol	4-Methyldiphenylmethane, 100%
3	4-Methoxybenzhydrol	4-Hydroxydiphenylmethane, 95%; 4-acetoxydiphenylmethane, 5%
4	4-Bromobenzhydrol	4-Bromodiphenylmethane, 100%
5	4-Chlorobenzhydrol	4-Chlorodiphenylmethane, 100%
6 ^b	3-Trifluoromethylbenzhydrol	3-Trifluoromethyldiphenylmethane, 100%
7 ^b	4-Trifluoromethylbenzhydrol	4-Trifluoromethyldiphenylmethane, 100%
8	4,4'-Bis[dimethylamino]-benzhydrol	4,4'-Bis[dimethylamino]diphenylmethane, 50%; 4-dimethylaminobenzaldehyde, 50%
9	3,4-Dimethylbenzhydrol	3,4-Dimethyldiphenylmethane, 100%
10	4,4'-Dimethoxybenzhydrol	4,4'-Dimethoxydiphenylmethane, 100%
11	4,4'-Dichlorobenzhydrol	4,4'-Dichlorodiphenylmethane, 100%
12	4,4'-Diiodobenzhydrol	Diphenylmethane, 65%; 4-iododiphenylmethane, 19%; 4,4'-diiododiphenylmethane, 8%; benzhydrol, 3.5%; 4-iodobenzhydrol, 3.5%; 4,4'-diiodobenzhydrol, 1%
13 ^b	3,3'-Bis[trifluoromethyl]-benzhydrol	3,3'-Bis[trifluoromethyl]diphenylmethane, 100%
14 ^b	3,4'-Bis[trifluoromethyl]-benzhydrol	3,4'-Bis[trifluoromethyl]diphenylmethane, 100%
15	4,4'-Dimethylbenzhydrol	4,4'-Dimethyldiphenylmethane, 100%
16	Triphenylmethanol	Triphenylmethane, 100%
17	1,1-Diphenylethanol	1,1-Diphenylethane, 100%

^a Alcohol (4.0 mmol), iodine (0.4 mmol), 50% aq. hypophosphorous acid (19.3 mmol), acetic acid (25 mL), 24 h under nitrogen at 60°C.

^b Complete reaction required 48–72 h.



Scheme 1.

References

- Su, D.; Menger, F. M. *Tetrahedron Lett.* **1997**, 38, 1485.
- Marie, C. *Compt. Rend.* **1901**, 133, 219, 818.
- Meyers, C. Y.; Hou, Y.; Lutfi, H. G.; Saft, H. L. *J. Org. Chem.* **1999**, 64, 9444.
- Konieczny, M.; Harvey, R. G. *J. Org. Chem.* **1980**, 45, 1308.
- Konieczny, M.; Harvey, R. G. *J. Org. Chem.* **1979**, 44, 4813.
- Harvey, R. G.; Leyba, C.; Konieczny, M.; Fu, P. P.; Sukumaran, K. B. *J. Org. Chem.* **1978**, 43, 3423.
- Platt, K. L.; Oesch, F. *J. Org. Chem.* **1981**, 46, 2601.
- Rakhit, S.; Gut, M. *J. Org. Chem.* **1968**, 33, 1196.
- Hicks, L. D.; Han, J. K.; Fry, A. J. *Tetrahedron Lett.* **2000**, 41, 7817.
- Small, G. H.; Minnella, A. E.; Hall, S. S. *J. Org. Chem.* **1975**, 40, 3151.
- Alper, H.; Salisova, M. *J. Org. Chem.* **1980**, 21, 801.
- Ando, W.; Ikeno, M. *Tetrahedron Lett.* **1979**, 1979.
- Lau, C. K.; Dufresne, C.; Belanger, P. C.; Pietre, S.; Scheigetz, J. *J. Org. Chem.* **1986**, 51, 3038.
- Olah, G. A.; Tremper, H. S. *J. Am. Chem. Soc.* **1968**, 90, 2578.
- Gribble, G. W.; Leese, R. M.; Evans, B. E. *Synthesis* **1977**, 763.
- Marvel, C. S.; Hager, F. D.; Caudle, E. C. *Org. Syn. Coll. Vol. I*, 1941; 2nd ed., p. 224.
- Blackwell, J.; Hickinbottom, W. J. *J. Chem. Soc.* **1961**, 1405.
- Krasnec, L. Z. *Chem.* **1971**, 11, 110.
- Esselen, G. J.; Clarke, L. *J. Am. Chem. Soc.* **1914**, 36, 308.
- Chowdhury, S.; Georghiou, P. E. *Tetrahedron Lett.* **1999**, 40, 7599.