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Reduction of diaryl alkenes by hypophosphorous acid–iodine in acetic acid

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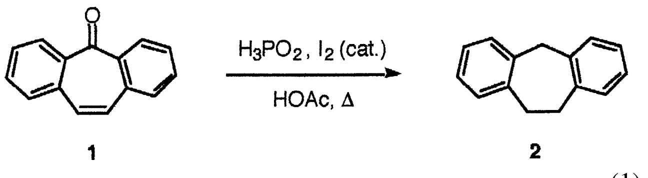
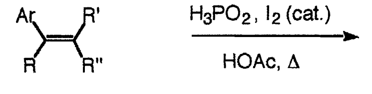
Abstract—A mixture of 50% aqueous H_3PO_2 and I_2 (in catalytic amount) in HOAc efficiently reduces aryl alkenes to the corresponding alkanes in high yield. Addition of acetic anhydride to the medium results in ring-acetylation (or *N*-acetylation in the case of amines). H_3PO_2 costs only one-fifth as much as hydriodic acid on a mole basis and one mole of H_3PO_2 produces four moles of HI, resulting in a 20-fold cost advantage for H_3PO_2/I_2 over aqueous HI as a source of HI. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

We reported earlier that hydrogen iodide, regenerated catalytically by a mixture of hypophosphorous acid and iodine, reduces diaryl ketones and diaryl carbinols to the corresponding diarylmethanes in high yield.[1,2] In the course of that work, we observed that the carbon–carbon double bond of dibenzosuberenone (**1**) is reduced, as well as its carbonyl group, to afford dibenzocycloheptane (**2**) (Eq. (1)).[1] Since the double bond of **1** is formally conjugated with the carbonyl group, and this system is also capable of reducing the carbon–carbon double bond of α,β-unsaturated ketones,[1,3] it was not clear whether other ethylenic double bonds would be reduced by this system. In the present study we report the reduction of a variety of aryl substituted ethylenic double bonds by H_3PO_2/I_2 in acetic acid (Eq. (2)).



(1)



3a, Ar = R'' = C_6H_5 ; R = R' = H
b, Ar = R'' = 4-$CF_3C_6H_4$; R = R' = H
c, Ar = C_6H_5 ; R'' = 2-thienyl ; R = R' = H
d, Ar = R = R' = C_6H_5 ; R'' = H
e, Ar = R = R' = R'' = C_6H_5
f, Ar = R'' = C_6H_5 ; R = CH_3 , R' = H
g, Ar = R = C_6H_5 ; R' = R'' = H
h, Ar = C_6H_5 ; R'' = 4-$Me_2NC_6H_4$; R = R' = H

4

(2)

2. Results and discussion

2.1. General

The alkenes examined in this study include *trans*-stilbene (**3a**), 4,4′-bis[trifluoromethyl]stilbene (**3b**), 1-phenyl-2-(2-thienyl)ethylene (**3c**), triphenylethylene (**3d**), tetraphenylethylene (**3e**), α-methylstilbene (**3f**), 1,1-diphenylethylene (**3g**), 4-dimethylaminostilbene (**3h**), acenaphthylene (**5**), dibenz[*c*,*f*]azepine (iminostilbene) (**6a**), and cyclooctene (**7**). Preliminary experiments showed that reduction of the ethylenic bond of **3a** does not take place in dimethylformamide or dimethylsulfoxide, but that the reduction takes place readily in hot acetic acid. A mixture containing 50% aqueous hypophosphorous acid, alkene, and iodine in ca. 20:5:4 molar proportion in acetic acid was refluxed for 24 h. Analysis was by GC-mass spectrometry (GC–MS) and ^{1}H NMR spectroscopy; it was possible in almost all cases to compare the spectra of the products and their GC–MS retention times with authentic samples. A few alkenes were reduced in deuterated medium by substituting D_3PO_2 and DOAc for their protio counterparts, and several experiments were carried out with added acetic anhydride to generate a non-aqueous medium. When acetic acid was completely replaced by acetic anhydride as solvent in the reduction of **3a**, a mixture containing bibenzyl (**4a**) (69%) and 1,2-diphenyl-3-butanone[4] (**8**) (31%) was produced (run 2); the identity of **8** was proved by comparison with a synthetic sample. Control experiments demonstrated that both hypophosphorous acid and either iodine or hydrogen iodide are required for reduction of the double bond, as we previously observed in a study of the reduction of benzophenones to diphenylmethanes.[1]

Keywords: hydrogen iodide; hypophosphorous acid; alkenes.

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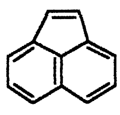

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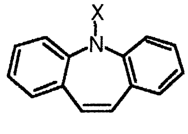
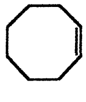


6a, X = H
b, X = Ac



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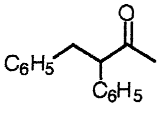

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Table 1. Reduction of aryl alkenes by hypophosphorous acid–iodine in acetic acid

Entry	Alkene	Aryl alkane (yield, %)	Other products (yield, %)
1	**3a**	99	
2	**3a**[a]	68	**8** (30)
3	**3b**	98	
4	**3c**	99	
5	**3d**	97	
6	**3e**	100[b]	
7	**3f**	98	
8	**3g**	96	
9	**3h**	0	Starting material (100)
10	**5**	98	
11	**5**[c]	52	**9a** (40); **9b** (3); **9c** (5)
12	**6**	8	**11** (92)
13	**6**[b]	47	**12** (20); **11** (18); **10b** (9); unk (4); unk (2)
14	7	0	Cyclooctyl iodide (100)

50% aq. HPO/I/alkene=20:5:4 in acetic acid at reflux for 24 h.

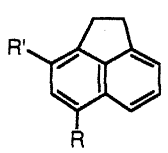
[a] Acetic anhydride as solvent.

[b] 96 h required for reduction.

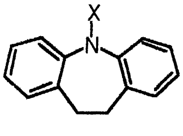
[c] Sufficient acetic anhydride added to reaction mixture to destroy all water.

The results (Table 1) demonstrate that the carbon–carbon double bond of most diarylethylenes is reduced in good yield by this reagent system. Runs 9 and 12 show that the presence of a basic nitrogen retards reduction, presumably by protonation by hydrogen iodide to produce a charged form of the substrate. Confirmation that electron-withdrawing substituents do indeed retard reduction was found in a competition experiment in which an equimolar mixture of **3a** and **b** was reduced at 100°C. A sample taken after 1 h showed 6% of **4a** but only a trace of **4b**; after 1.5 h, the ratio of **4a** to **b** was 27:7. Since even **3d** was reduced efficiently, the long reaction time required to reduce **3e** is probably due to its low solubility in the reaction medium. The failure of cyclooctene (**7**) to undergo reduction (run 14) demonstrates the need for aryl substitution for reduction to occur and is therefore mechanistically significant (see below). The fact that **3h** is not reduced (entry 9) probably arises because the dimethylamino group is protonated in this medium, making the group strongly electron-withdrawing.

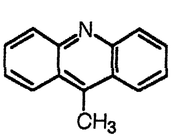
Inclusion of acetic anhydride in the medium resulted in acetylation (runs 2, 11, and 13). Thus, whereas reduction of the ethylenic bond of acenaphthylene (**5**) proceeds in quantitative yield under the standard conditions (run 10), addition of acetic anhydride to the reaction results in formation of substantial amounts of acetylacenaphthenes **9a** and **b** (run 11). A small amount of 5-ethylacenaphthene (**9c**) was also produced; we had previously observed that alkyl aryl ketones are reduced slowly under these conditions.[1] We assume that reduction of **5** precedes acylation. Formation of 5-acetylacenaphthene (**9a**) as the major regioisomer of acetylation is in accord with previous reports on the acylation of this substance.[5,6]



9a, R = Ac ; R' = H
b, R = H ; R' = Ac
c, R = Et ; R' = H



10a, X = H
b, X = Ac



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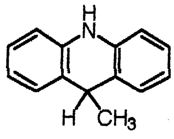

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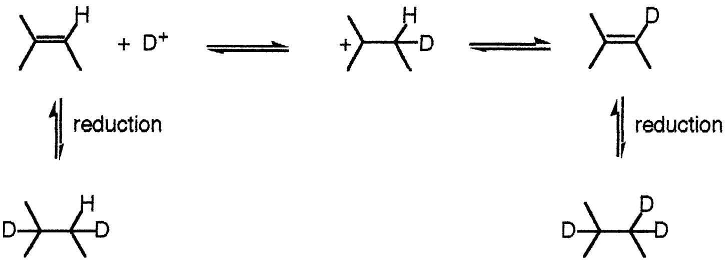
Dibenz[*c*,*f*]azepine (**6a**) represents the most complex chemistry observed in this study. When **6a** was subjected to the standard conditions, a mixture was produced consisting of dihydrodibenz[*c*,*f*]azepine (**10a**) (47%), 9-methylacridine (**11**) (18%), 9-methyl-9,10-dihydroacridine[7,8] (**12**) (20%), *N*-acetyldihydrodibenz[*c*,*f*]azepine (**10b**) (9%), and two compounds produced in too small amounts to isolate, of mass 223 (4%) and 221 (2%), respectively.

One series of experiments involved sampling the composition of the reaction mixture from the reduction of stilbene (**3a**) as a function of time. After 5 min, the mixture contained three components, bibenzyl (**4a**), unreacted **3a**, and α-iodobibenzyl (**13**) in a trace:95:5 ratio. After 15 min, the ratios **4a**/**3a**/**13** were trace:91:8. At 60 min, these ratios amounted to 15:49:36. At the end of 24 h, the only constituent of the mixture was **4a**.

2.2. Deuteration

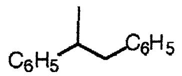
Experiments involving deuterated reagents proved to be quite informative. A reaction mixture containing stilbene in deuterated hypophosphorous acid (in D_2O) and acetic acid-*d* was sampled during reaction and analyzed by mass spectrometry. After 1 h the small amount of bibenzyl produced had mostly incorporated two deuterium atoms, with a small amount of d_3 content. However, after 6 h there was ca. 30–35% of d_3 and 4–5% of d_4 content in the bibenzyl. Likewise, stilbene present in the solution after 1 h consisted of mostly d_0 with ca. 20% d_1 material and 3–5% *2*, but after 6 h the isotopic content of the unreacted stilbene was approximately 40:40:20 $d_0/d_1,d_2$. Thus, though reduction should result in addition of two deuterium atoms across the double bond, as reaction proceeds the alkene incorporates an increasing amount of deuterium, resulting in overall addition of more than two deuteriums. As a matter of fact, ^{1}H NMR spectroscopy and



Scheme 1.

mass spectrometry showed that 1,1-diphenylethylene (**3g**) affords 1,1-diphenylethane containing four deuterium atoms per mole (**14**) when subjected to the same reaction conditions.

The first step in the reduction process is undoubtedly protonation of the carbon–carbon double bond. This hypothesis is supported by the fact that electron-withdrawing substituents retard reaction (the competition experiment between **3a** and **b** already referred to and also run 9, since the amino group of **3h** is undoubtedly largely protonated in our medium). Further suggestive evidence for protonation of the alkene comes from the deuterium exchange observed with deuterated reagents. As Scheme 1 demonstrates, the actual amount of deuterium incorporated into the alkane depends upon the relative rates of exchange and reduction. If reduction is slow relative to exchange, two deuterium atoms will be introduced into the product. This situation is approximated in the early stages of reduction of stilbene; however, as reaction proceeds the stilbene begins to incorporate significant amounts of deuterium and the resulting bibenzyl is deuterated to a correspondingly higher degree. On the other hand, alkenes which exchange deuterium rapidly compared to the rate of reduction should incorporate deuterium to the maximal degree. 1,1-Diphenylethylene (**3g**) exemplifies this situation; exchange is apparently fast because of the high stability of the doubly benzylic tertiary carbocation (**15**) produced by protonation of **3g**, and hence the product (**14**) is totally deuterated.



13

$(C_6H_5)_2CDCD_3$

14

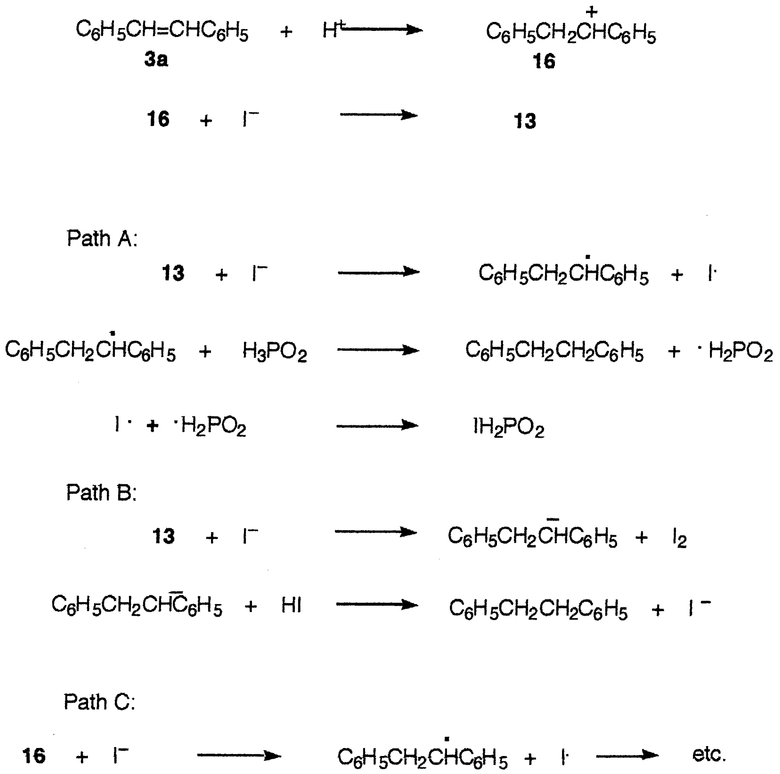
$(C_6H_5)_2C^+CH_3$

15

$C_6H_5CH^+CH_2C_6H_5$

16

Formation of iodide **13** as an intermediate during the reduction of stilbene, presumably by trapping of carbocation **16** by iodide, raises an intriguing mechanistic question: Is **13** on



$$\underset{\mathbf{3a}}{C_6H_5CH{=}CHC_6H_5} + H^+ \longrightarrow \underset{\mathbf{16}}{C_6H_5CH_2\overset{+}{C}HC_6H_5}$$

$$\mathbf{16} + I^- \longrightarrow \mathbf{13}$$

Path A:

$$\mathbf{13} + I^- \longrightarrow C_6H_5CH_2\dot{C}HC_6H_5 + I\cdot$$

$$C_6H_5CH_2\dot{C}HC_6H_5 + H_3PO_2 \longrightarrow C_6H_5CH_2CH_2C_6H_5 + \cdot H_2PO_2$$

$$I\cdot + \cdot H_2PO_2 \longrightarrow IH_2PO_2$$

Path B:

$$\mathbf{13} + I^- \longrightarrow C_6H_5CH_2\overset{-}{C}HC_6H_5 + I_2$$

$$C_6H_5CH_2CH\overset{-}{C}_6H_5 + HI \longrightarrow C_6H_5CH_2CH_2C_6H_5 + I^-$$

Path C:

$$\mathbf{16} + I^- \longrightarrow C_6H_5CH_2\dot{C}HC_6H_5 + I\cdot \longrightarrow \text{etc.}$$

Scheme 2.

the reaction path to alkane or is it simply involved in a side equilibrium off the main reduction route? Both possibilities are shown in Scheme 2. Iodide ion could reduce **13** by either an electron-transfer radical mechanism (path A) or by direct displacement on iodine to afford a carbanion which is subsequently protonated (path B). Alternatively, formation of **16** could be reversible and **16** itself could be the actual intermediate which is reduced. This could readily occur by electron transfer between iodide ion and **16** (path C), since iodide is readily oxidized and benzyl cations are relatively easily reduced.[9] The failure of cyclooctene (**7**) to be reduced could be understood in terms of any of these possibilities: it should be protonated less readily than the aryl alkenes and the resulting iodide would be both harder to reduce and less likely to reionize to the carbocation than a benzylic iodide[10,11] The formation of ketone **8** from the reduction of stilbene in the presence of acetic anhydride might be construed as evidence for a carbanion intermediate which attacks acetic anhydride nucleophilically. On the other hand it is possible that **8** is produced by electrophilic acylation of the carbon–carbon double bond of **3a**, followed by reduction of the double bond of the resulting α,β-unsaturated ketone by HI.

The conversion of dibenz[*c*,*f*]azepine (**6a**) to 9-methylacridine (**11**) (which is presumably then reduced to **12**), in which one of the vinyl carbons of **6** ultimately becomes a methyl group, is unusual but precedented. Both amine **6a** and its *N*-acyl derivative **6b** are converted into **11** when heated in acid[12,13] Amide **6b** is clearly unusual electronically: for example, it does not undergo hydrolysis to **6a** under conditions (acid or base) under which **10b** is readily hydrolyzed;[14] this and its UV spectrum[14] and crystal structure[15] all indicate that the electrons on nitrogen do not interact with the ring, probably because such overlap would produce a Hückel 8-electron antiaromatic system.

3. Conclusion

The results demonstrate that a mixture of hypophosphorous acid and iodine in acetic acid efficiently reduces aryl alkenes to the corresponding alkanes, which are obtained in high purity. Although the reaction is broadly applicable, reduction is slow in the presence of basic sites. Addition of acetic anhydride to the medium results in ring-acetylation (or N-acetylation in the case of amines). Although the actual reductant in these reactions is undoubtedly hydrogen iodide produced by reaction between the two, this reaction system has advantages over aqueous hydrogen iodide. Because of the lower water content, H_3PO_2/I_2 reductions generally proceed more rapidly than with aqueous HI,[1] and not only does aqueous HI cost five times as much as H_3PO_2, but one mole of H_3PO_2 produces four moles of HI,[1] resulting in a 20-fold cost advantage for H_3PO_2/I_2 over aqueous HI as a source of HI.

4. Experimental

4.1. General

^{1}H NMR spectra were recorded in $CDCl_3$ on a Varian 300 MHz spectrometer. GC-MS analysis was carried out on a Hewlett–Packard Model 5850 instrument. Flash chromatographic separations were carried out using Merck 230–400 mesh silica gel. Preparative scale thin layer chromatography was performed on 1000 μm silica gel plates. All products are known compounds and their NMR and mass spectra were compared with authentic commercial samples and/or with spectra in the literature.

4.1.1. 1-Phenyl-2-(2-thienyl)ethylene (3c).[16] To 1.2 g (2.4 mmol) of Aldrich 'Instant Ylide' (a benzyltriphenylphosphonium bromide–sodium amide dry mixture) was added 2 mL of dry THF. 2-Thiophenecarboxaldehyde (0.19 mL, 1.9 mmol) was added to the bright orange solution. After 15 min stirring, the mixture had turned to a light brown color. After quenching with 2.0 mL of 25% aq. NaOH and neutralization with 6.0 mL of 0.1 M HCl and extraction with ether, the ether was dried over Na_2SO_4 and evaporated. Flash chromatography removed triphenylphosphine oxide and afforded **3c** (0.22 g, 63%) as a 2:3 *cis*/*trans* mixture.

4.1.2. *trans*-4-Dimethylaminostilbene (3h).[17] Alkene **3h** was synthesized by the same procedure as in the preceding paragraph except for substitution of 4-dimethylaminobenzaldehyde. The product was isolated as bright orange crystals in 54% yield.

4.2. Representative procedure for reduction of alkenes

Iodine (1 g, 4 mmol) and stilbene (**3a**) (1.0 g, 5.56 mmol) were added to 25 mL of acetic acid and the solution was flushed with nitrogen. Hypophosphorous acid (50% aq., 2 mL, 19.3 mmol) was added and the solution was heated to reflux. After 24 h, the mixture was quenched with 50 mL water and extracted with benzene. The organic extracts were washed successively with aq. $NaHCO_3$ and aq. $NaHSO_3$, dried over $MgSO_4$, and evaporated. Analysis by GC–MS demonstrated that the colorless solid (0.99 g, 99%) consisted of bibenzyl (**4a**) in 100% purity.

4.3. Reduction of 3a in acetic anhydride

Reduction was carried out as in the preceding paragraph, except for substitution of acetic anhydride for acetic acid. Product analysis by GC–MS showed two products: bibenzyl (**4a**) (69%) and 1,2-diphenyl-3-butanone (**8**) (31%). A comparison sample of the latter substance was prepared by $K_2Cr_2O_7/H_2SO_4$ oxidation of 1-phenyl-2-propanol followed by phase-transfer benzylation of the resulting 1-phenyl-2-propanone by a literature procedure.[4]

Acknowledgements

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