Chemoselective Hydrogenation of α,β-Unsaturated Sulfones and Phosphonates via Palladium-Assisted Hydrogen Transfer by Ammonium Formate

Brindaban C. Ranu,* Sankar K. Guchhait, and Keya Ghosh

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta 700 032, India

Received January 26, 1998

The reduction of α,β-unsaturated sulfones and phosphonates to the corresponding saturated analogues constitutes a useful process as these compounds are of great importance in the studies of biological systems[1] as well as in synthetic strategy.[2] Surprisingly, there are only a few methods available in the literature for effecting the reduction of the carbon−carbon double bond in α,β-unsaturated sulfones and phosphonates. The most commonly used reagents for the reduction of sulfones are sodium borohydride,[3] lithium triethyl borohydride,[2] and (triphenylphosphine)copper hydride hexamer $[(PPh_3)CuH]_6$.[3] The yield in the $NaBH_4$ reaction is not always satisfactory,[3] while the use of $LiEt_3BH$ and $[(PPh_3)CuH]_6$ is not very economical. The reduction of phosphonates is usually carried out under high-pressure (50 psi) hydrogenation over palladium on activated carbon.[4] Recently, a binuclear palladium complex, $[(t\text{-}Bu_2PH)PdP\text{-}t\text{-}Bu_2]_2$, has been used for the hydrogenation of the double bond of α,β-unsaturated sulfones and phosphonates at 1 atm of hydrogen pressure, producing the saturated compound in 49−93% yield.[5] Although this method is quite satisfactory, the operation is not very straightforward and the reagent is costly and also not easily accessible. Thus, a simple and efficient method for this useful transformation is still in demand. The ammonium formate/Pd−C system is a versatile catalytic hydrogen-transfer agent,[6] and recently, we have utilized this reagent system for the regio- and stereoselective hydrogenation of conjugated carbonyl compounds.[7] We now wish to disclose that ammonium formate/Pd−C is also very efficient in the reduction of the C=C bond in α,β-unsaturated sulfones and phosphonates (Scheme 1).

In a typical experimental procedure. the conjugated sulfone or phosphonate was stirred with ammonium formate and 10% Pd−C in dry methanol at room temperature under argon for a certain period of time as required to complete the reaction (TLC). The catalyst was filtered through a short plug of silica gel, and the product was isolated by solvent evaporation and extraction of the residue with ether. The carbon−carbon double bond in several structurally varied sulfones and phosphonates underwent hydrogenation to give the corresponding saturated analogues in high yields by this procedure. The results are reported in Table 1. The reactions are very clean, and no chromatographic separation is required to obtain spectrally pure substances. No side products were isolated from any reaction. For the compounds in Table 1, the substituents on the aromatic ring apparently do not have any influence on the course of hydrogenation. The chloro and methoxy groups on the aromatic ring remain unaffected under these conditions. Moreover, ammonium formate/Pd−C system is a mild reagent and usually does not reduce nonconjugated double bonds.[6,7]

In summary, the mild conditions, high yields of products, operational simplicity, easy availability, and low cost of the reagent make this methodology a more useful and practical alternative to the existing methods for reduction of α,β-unsaturated sulfones and phosphonates. We believe that this method will find useful applications in the field of organic synthesis.

Scheme 1

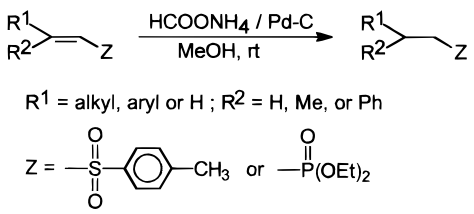
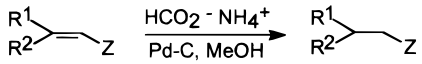


Table 1. Hydrogenation of α,β-Unsaturated Sulfones and Phosphonates by Ammonium Formate/Pd-C



entry	R^1	R^2	Z	time, h	yield[a] (%)
1	$Me_2CHCH_2CH(OH)$	H	SO_2-*p*-Tol	22	90
2	Ph	H	SO_2-*p*-Tol	18	92
3	*p*-$MeOC_6H_4$	H	SO_2-*p*-Tol	20	82
4	*p*-ClC_6H_4	H	SO_2-*p*-Tol	24	85
5	Ph	Me	SO_2-*p*-*Tol*	22	86
6	*p*-MeC_6H_4	Me	SO_2-*p*-Tol	20	82
7	Ph	Ph	SO_2-*p*-Tol	24	85
8	H	H	$PO(OEt)_2$	18	88
9	Ph	H	$PO(OEt)_2$	20	93
10	*m*-$MeOC_6H_4$	H	$PO(OEt)_2$	20	82
11	*p*-ClC_6H_4	H	$PO(OEt)_2$	24	90
12	Ph	Ph	$PO(OEt)_2$	24	83

[a] Yields refer to those of pure isolated products, fully characterized by spectral and analytical data.

Experimental Section

General Methods. Melting points were determined on a glass disk with an electrical bath (Reichert, Austria) and are uncorrected. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were run in $CDCl_3$ solutions. IR spectra of solid samples were taken as KBr plates, and those of liquid samples were run as thin films. Methanol was dried over magnesium and distilled before use. Ammonium formate and palladium−charcoal were

(1) (a) Schneider, K. C.; Benner, S. A. *Tetrahedron Lett.* **1990**, *31*, 335. (b) Musicki, B.; Widlanski, T. S. *J. Org. Chem.* **1990**, *55*, 4231.
(2) Ley, S. V.; Simpkins, N. S.; Whittle, A. J. *J. Chem. Soc., Chem. Commun.* **1983**, 503.
(3) (a) Musicki, B.; Widlanski, T. S. *Tetrahedron Lett.* **1991**, *32*, 1267. (b) Sakakibara, T.; Takai, I.; Yamamoto, A.; Iizuka, H.; Hirasawa, K.; Ishido, Y. *Tetrahedron Lett.* **1990**, *31*, 3749.
(4) Bigge, C. F.; Johnson, G.: Ortwine, D. F.; Drummond, J. T.; Retz, D. M.; Brahce, L. J.; Coughenour, L. L.; Marcoux, F. W.; Probert, A. W., Jr. *J. Med. Chem.* **1992**, *35*, 1371. (b) Francis, J. E.; Webb, R. L.; Ghai, G. R.; Hutchison, A. J.; Moskal, M. A.; deJesus, R.; Yokoyama, R.; Rovinski, S. L.; Contardo, N.; Dotson, R.; Barclay, B.; Stone, G. A.; Jarvis, M. F. *J. Med. Chem.* **1991**, *34*, 2570.
(5) Cho, I. S.; Alper, H. *J. Org. Chem.* **1994**, *59*, 4027 and references therein.
(6) Ram, S.; Ehrenkaufer, R. E. *Synthesis* **1988**, 91.
(7) Ranu, B. C.; Sarkar, A. *Tetrahedron Lett.* **1994**, *35*, 8649.

S0022-3263(98)00128-5 CCC: $15.00
Published on Web 07/08/1998

used as available commercially. The α,β-unsaturated sulfones and phosphonates were prepared following a literature procedure.[5,8−10] Some of these compounds have not been reported previously, and so their spectral (IR, ^{1}H NMR, and ^{13}C NMR) data are included in Supporting Information.

General Procedure for Reduction of α,β-Unsaturated Sulfones and Phosphonates. Representative Procedure. A mixture of (*E*)-styryl *p*-tolyl sulfone (258 mg, 1 mmol), ammonium formate (378 mg, 6 mmol), and palladium on charcoal (10%, 30 mg) in dry methanol (15 mL) was stirred at room temperature under argon for 18 h (monitored by TLC). The reaction mixture was then filtered through a short plug of silica gel. Methanol was stripped off from the filtrate under reduced pressure, and the residue was extracted with ether. The ether extract was washed with water, dried (Na_2SO_4), and evaporated to furnish the product, which was, though considerably pure (NMR), chromatographed over silica gel to provide analytically pure compound (240 mg, 92%). The product was easily characterized by comparison of its spectral results (IR, ^{1}H NMR, and ^{13}C NMR) with literature data.[5]

This procedure is followed for the reduction of other sulfones and phosphonates included in Table 1. Although the results reported in Table 1 were based on mmol-scale reactions, gram-scale reactions also afforded the corresponding products in analogously good yields.

Several of these reduced products were reported previously,[5] and the spectroscopic and analytical data of those that are new compounds are presented below.

3-Hydroxy-5-methylhexyl *p*-tolyl sulfone (Table 1, entry 1): IR (neat) 1140, 1300, 1410, 1450, 1470, 1600 cm^{-1}; ^{1}H NMR δ 0.88 (d, J = 6 Hz, 3H), 0.90 (d, J = 6 Hz, 3H), 1.18−1.43 (m, 2H), 1.67−1.78 (m, 2H), 1.90−1.96 (m, 2H), 2.45 (s, 3H), 3.16−3.34 (m, 2H), 3.73−3.80 (m, 1H), 7.36 (d, J = 8 Hz, 2H), 7.79 (d, J = 8 Hz, 2H); ^{13}C NMR δ 21.5 (CH), 21.9 (CH_3), 23.1 (CH_3), 24.5 (CH_3), 30.5 (CH_2), 46.6 (CH_2), 53.1 (CH_2), 68.0 (CH), 127.9 (2 CH), 129.8 (2 CH), 136.7 (C), 143.8 (C). Anal. Calcd for $C_{14}H_{22}O_3S$: C, 62.19; H, 8.20. Found: C, 62.36; H, 8.38.

2-(*p*-Methoxyphenyl)ethyl *p*-tolyl sulfone (Table 1, entry 3): mp 105 °C; IR 1610, 1515, 1300, 1250, 1150, 1090, 735 cm^{-1}; ^{1}H NMR δ 2.46 (3H, s), 2.94−3.00 (2H, m), 3.27−3.33 (2H, m), 3.76 (3H, s), 6.80 (2H, d, J = 9 Hz), 7.02 (2H, d, J = 9 Hz), 7.36 (2H, d, J = 9 Hz), 7.80 (2H, d, J = 9 Hz); ^{13}C NMR δ 21.6 (CH_3), 28.0 (CH_2), 55.4 (CH_3), 57.9 (CH_2), 114.2 (2 CH), 128.1 (2 CH), 129.3 (2 CH), 129.9 (2 CH), 130.3 (C), 136.1 (C), 144.7 (C), 158.5 (C). Anal. Calcd for $C_{16}H_{18}O_3S$: C, 66.18; H, 6.25. Found: C, 66.22; H, 6.45.

2-(*p*-Chlorophenylethyl p-tolyl sulfone (Table 1, entry 4): mp 86 °C; IR 1595, 1570, 1490, 1440, 1300 cm^{-1}; ^{1}H NMR δ 2.45 (3H, s), 2.97−3.05 (2H, m), 3.27−3.36 (2H, m), 7.03 (2H, d, J = 9 Hz), 7.21 (2H, d, J = 9 Hz), 7.35 (2H, d, J = 9 Hz), 7.78 (2H, d, J = 9 Hz); ^{13}C NMR δ 21.6 (CH_3), 28.2 (CH_2), 57.3 (CH_2), 128.0 (2 CH), 128.1 (C), 128.7 (C), 128.8 (2 CH), 129.6 (2 CH), 129.9 (2 CH), 135.9 (C), 144.2 (C). Anal. Calcd for $C_{15}H_{15}O_2SCl$: C, 61.12; H, 5.13. Found: C, 61.07; H, 5.08.

2-Methyl-2-*p*-tolylethyl p-tolyl sulfone (Table 1, entry 6): mp 90 °C; IR 1600, 1515, 1450, 1405, 1285, 1140, 1085 cm^{-1}; ^{1}H NMR δ 1.40 (3H, d, J = 6 Hz), 2.27 (3H, s), 2.41 (3H, s), 3.27−3.38 (3H, m), 6.94 (2H, d, J = 9 Hz), 7.01 (2H, d, J = 9 Hz), 7.24 (2H, d, J = 9 Hz), 7.66 (2H, d, J = 9 Hz); ^{13}C NMR δ 20.9 (CH_3), 21.5 (CH_3), 22.1 (CH_3), 34.6 (CH), 63.5 (CH_2), 126.5 (2 CH), 127.0 (C), 127.8 (2 CH), 129.2 (2 CH), 129.6 (2 CH), 136.3 (C), 141.1 (C), 144.3 (C). Anal. Calcd for $C_{17}H_{20}O_2S$: C, 70.8; H, 7.0. Found: C, 70.73; H, 6.98.

2,2-Diphenylethyl *p*-tolyl sulfone (Table 1, entry 7): mp 146 °C; IR 1600, 1570, 1490 cm^{-1}; ^{1}H NMR δ 2.38 (3H, s), 3.90 (2H, d, J = 6 Hz), 4.61 (1H, t, J = 6 Hz), 7.12−7.22 (12H, m), 7.53 (2H, d, J = 9 Hz); ^{13}C NMR δ 21.4 (CH_3), 46.1 (CH), 61.5 (CH_2), 126.7 (2 CH), 127.5 (4 CH), 128.1 (2 CH), 128.6 (4 CH), 129.4 (2 CH), 136.6 (C), 141.4 (2 C), 144.1 (C). Anal. Calcd for $C_{21}H_{20}O_2S$: C, 74.97; H, 6.00. Found: C, 74.78; H, 6.20.

Diethyl [2-(*m*-methoxyphenyl)ethyl]phosphonate (Table 1, entry 10): IR 1605, 1585, 1490, 1455, 1440 cm^{-1}; ^{1}H NMR δ 1.33 (6H, t, J = 6 Hz), 2.00−2.12 (2H, m), 2.85−2.94 (2H, m), 3.80 (3H, s), 4.06−4.16 (4H, 2 q, J = 6 Hz), 6.75−6.81 (1H, m), 7.19−7.27 (1H, m), 7.45−7.56 (1H, m), 7.64−7.71 (1H, m); ^{13}C NMR δ 16.43 (2 CH_3), 26.5 (CH_2), 28.5 (CH_2), 55.1 (CH_3), 61.6 (2 CH_2), 111.6 (CH), 113.7 (CH), 120.3 (CH), 129.5 (CH), 131.9 (C), 159.9 (C). Anal. Calcd for $C_{13}H_{21}O_4P$: C, 57.35; H, 7.77. Found: C, 57.61; H, 7.54.

Diethyl [2-(*p*-chlorophenyl)ethyl]phosphonate (Table 1, entry 11): IR 1605, 1500, 1455, 1440 cm^{-1}; ^{1}H NMR δ 1.31 (6H, t, J = 6 Hz), 2.00−2.11 (2H, m), 2.87−2.96 (2H, m), 4.12 (4H, 2 q, J = 6 Hz), 7.19−7.32 (4H, m); ^{13}C NMR δ 16.4 (2 CH_3), 26.5 (CH_2), 28.4 (CH_2), 61.6 (2 CH_2), 128.0 (2 CH), 128.5 (2 CH), 140.7 (C), 141.0 (C). Anal. Calcd for $C_{12}H_{18}O_3PCl$: C, 52.09; H, 6.56. Found: C, 52.38; H, 6.66.

Diethyl (2,2-diphenylethyl)phosphonate (Table 1, entry 12): IR 1605, 1450 cm^{-1}; ^{1}H NMR δ 1.10 (6H, t, J = 6 Hz), 2.58 (2H, dd, J = 6,18 Hz), 3.69−3.91 (4H, m), 4.40−4.49 (1H, m), 7.26−7.29 (10H, m); ^{13}C NMR δ 16.2 (2 CH_3), 29.7 (CH_2), 45.4 (CH), 61.4 (2 CH_2), 126.5 (2 CH), 127.6 (4 CH), 128.5 (4 CH), 144.0 (2 C). Anal. Calcd for $C_{18}H_{23}O_3P$: C, 67.89; H, 7.29. Found: C, 68.00; H, 7.45.

Acknowledgment. Financial support from CSIR, New Delhi [Grant No. 01(1364)/95)] is gratefully acknowledged. S.K.G. and K.G. also thank CSIR for their fellowships.

Supporting Information Available: Spectroscopic data for α,β-unsaturated sulfones (Table 1, entries 1, 3, 4 and 6) and phosphonates (Table 1, entries 10−12) (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO980128N

(8) Kamigata, N.; Sawada, H.; Kobayashi, M. *Chem. Lett.* **1979**, 159.
(9) Hirao, T.; Masunaga, T.; Ohshiro, Y.; Agawa, T. *Tetrahedron Lett.* **1980**, *21*, 3595.
(10) (*E*)-3-Hydroxy-5-methylhex-1-enyl-p-tolyl sulfone (Table 1 entry 1) was obtained from Dr. S. Sengupta, Jadavpur University, Calcutta, India, as a gift.