Concurrent Primary and Secondary Deuterium Kinetic Isotope Effects

in Anilinolysis of O-Aryl Methyl Phosphonochloridothioates

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Experimental

(a) **Substrates.** The starting material, methyl phosphonothioic dichloride, phenols and triethylamine were G.R. grade and were used without further purification. Aryl methyl phosphonochloridothioates were prepared by reacting methyl phosphonothioic dichloride with phenols for 2 hrs in the presence of triethylamine in methylene chloride on an ice bath. Triethylamine hydrochloride salt was separated by filtration. The remaining product was treated with ether and water for workup. After workup, anhydrous MgSO₄ was added, and the solvent was evaporated under reduced pressure after filtration. The substrates were identified by TLC, IR, ¹H NMR, ¹³C NMR, ³¹P NMR, GC-MS and elemental analysis. The physical constants after column chromatography (silica gel/ethyl acetate + n-hexane) were as follows.

4-Methoxyphenyl methyl phosphonochloridothioate:^{1,2} liquid; IR (neat) 3006 (C-H, aromatic), 2833 (C-H, aliphatic), 1595, 1502, 1443, 1405 (POC₆H₄), 1301 (P-CH₃), 840 cm⁻¹ (P=S); ¹H NMR (400 MHz, CDCl₃) δ 6.89 (d, J = 8.8 Hz, 2H, phenyl), 7.18 (d, J = 8.8Hz, 4H, phenyl), 3.79 (s, 3H, OCH₃), 2.50 and 2.46 (two s, 3H, P-CH₃-H); ¹³C NMR (100 MHz, CDCl₃) δ 157.34, 142.89, 122.28, 114.48, (C=C, phenyl), 55.58 (OCH₃), 30.64 and 29.64 (P-CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 99.50 (s, 1P, P=S); m/z 236 (M⁺); Anal. Calcd for C₈H₁₀O₂PSCI: C, 40.6, H, 4.3. Found: C, 40.8; H, 4.5.

4-Methylphenyl methyl phosphonochloridothioate:^{2,3} liquid; IR (neat) 3028 (C-H, aromatic), 2919 (C-H, aliphatic), 1611, 1508, 1405, 1204 (POC₆H₄), 1301 (P-CH₃), 824 cm⁻¹ (P=S); ¹H NMR (400 MHz, CDCl₃) δ 7.18 (d, J = 7.2 Hz, 2H, phenyl), 7.14 (d, J = 7.2 Hz, 2H, phenyl), 2.47 and 2.51 (two s, 3H, P-CH₃-H), 2.35 (s, 3H, CH₃-H); ¹³C NMR (100 MHz, CDCl₃) δ 121.26, 121.37, 130.23, 130.27 (C=C, phenyl), 31.37 and 29.36 (P-CH₃), 20.39 (CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 98.65 (s, 1P, P=S); m/z 220 (M⁺); Anal. Calcd for C₈H₁₀OPSCI: C, 43.6; H, 4.6. Found: C, 43.5; H, 4.4.

Phenyl methyl phosphonochloridothioate:¹⁻⁵ liquid; IR (neat) 3001 (C-H, aromatic), 2925 (C-H, aliphatic), 1595, 1486, 1404, 1160 (POC₆H₄), 1307 (P-CH₃), 737 cm⁻¹ (P=S); ¹H NMR (400 MHz, CDCl₃) δ 7.40 (d, J = 9.2 Hz, 2H, phenyl), 7.28 (t, J = 9.2 Hz, 3H, phenyl), 2.57 and 2.50 (two s, 3H, P-CH₃-H); ¹³C NMR (100 MHz, CDCl₃) δ 149.54, 129.56, 126.04, 125.35, 121.50, (C=C, aromatic), 30.91 and 29.90 (P-CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 98.21 (s, 1P, P=S); m/z 206 (M⁺); Anal. Calcd for C₇H₈OPSCl: C, 40.7; H, 3.9. Found: C, 40.5; H, 3.8.

3-Chlorophenyl methyl phosphonochloridothioate:^{6,7} liquid; IR (neat) 3095 (C-H, aromatic), 2920 (C-H, aliphatic), 1592, 1487, 1410, 1200 (POC₆H₄), 1301 (P-CH₃), 843 cm⁻¹ (P=S); ¹H NMR (400 MHz, CDCl₃) δ 7.18–7.32 (m, 3H, phenyl), 7.35 (s, 1H, phenyl), 2.58 and 2.50 (two s, 3H, P-CH₃-H); ¹³C NMR (100 MHz, CDCl₃) δ 135.12, 129.85, 129.81, 123.08, 122.97, 118.12 (C=C, aromatic), 31.40 and 29.40 (P-CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 98.30 (s, 1P, P=S); m/z 241 (M⁺); Anal. Calcd for C₇H₇OPSCl₂: C, 34.9; H, 2.9. Found: C, 34.7; H, 2.8. **4-Cyanophenyl methyl phosphonochloridothioate:** liquid; IR (neat) 3103 (C-H, aromatic), 2920 (C-H, aliphatic), 2229 (C=N) 1604, 1495, 1410, 1231 (POC₆H₄), 1301 (P-CH₃), 851 cm⁻¹ (P=S); ¹H NMR (400 MHz, CDCl₃) δ 7.69–7.72 (d, *J* = 8.8 Hz, 2H, phenyl), 7.38–7.40 (d, *J* = 8.8 Hz, 2H, phenyl), 2.53 and 2.56 (two s, 3H, P-CH₃-H); ¹³C NMR (100 MHz, CDCl₃) δ 152.60, 133.91, 122.63, 117.95 (C=C, aromatic), 110.14 (C=N), 30.95 and 29.95 (P-CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 97.97 (s, 1P, P=S); m/z 232 (M⁺); Anal. Calcd for C₈H₇NOPSCI: C, 41.5; H, 3.1; N 6.1. Found: C, 41.7; H, 3.2; N 6.2. (b) Product analysis. 4-Methylphenyl methyl phosphonochloridothioate was reacted with excess 4-methoxy aniline for more than 15 half lives at 55.0 °C in acetonitrile. The 4-methoxy aniline hydrochloride salt was separated by filtration. Acetonitrile was evaporated under reduced pressure. The remaining product was isolated with ether by a workup process and dried over anhydrous MgSO₄. The product was isolated by evaporating the solvent under reduced pressure after filtration. The physical constants after column chromatography (silica gel/ethyl acetate + n-hexane) were:

(CH₃)(4-CH₃C₆H₄O)P(=S)NH-C₆H₄-4-CH₃O: yellowish solid; mp 96–98 °C; IR (nujol) 2943 (C-H, aromatic), 2826 (C-H, aliphatic), 1508, 1459, 1383 (POC₆H₄), 1286 (P-CH₃), 780 cm⁻¹ (P=S); ¹H NMR (400 MHz, CDCl₃) δ 7.06 (s, 4H, phenyl), 7.01 (d, *J* = 9.2 Hz, 2H, phenyl), 6.83 (d, *J* = 8.8 Hz, 2H, phenyl), 5.15 (1H, d, *J* = 9.2 Hz, NH-H), 3.76 (s, 3H, OCH₃-H), 2.27 (s, 3H, CH₃-H), 2.04 and 2.00 (two s, 3H, P-CH₃-H); ¹³C NMR (100 MHz, CDCl₃) δ 155.84, 147.94, 134.76, 132.78, 129.99, 121.18, 114.93 (C=C, aromatic), 55.53 (OCH₃), 20.78 and 20.40 (P-CH₃), 19.34 (CH₃); ³¹P NMR (162 MHz, CDCl₃) δ 82.66 (s, 1P, P=S); m/z 307 (M⁺); Anal. Calcd for C₁₅H₁₈NO₂PS: C, 58.62; H, 5.90; N, 4.56. Found: C, 58.39; H, 6.03; N, 4.46.

¹H NMR spectra

(a) ¹H NMR spectrum for 4-cyanophenyl methyl phosphonochloridothioate:



¹³C NMR spectrum for 4-cyanophenyl methyl phosphonochloridothioate:



(b) ¹H NMR spectrum for $(CH_3)(4-CH_3C_6H_4O)P(=S)NH-C_6H_4-4-CH_3O$:



13 C NMR spectrum for (CH₃)(4-CH₃C₆H₄O)P(=S)NH-C₆H₄-4-CH₃O:



31 P NMR spectrum for (CH₃)(4-CH₃C₆H₄O)P(=S)NH-C₆H₄-4-CH₃O:



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Figure S1. The Hammett plots of $\log k_{H(D)}$ vs σ_X for the reactions of Y-*O*-aryl methyl phosphonochloridothioates with XC₆H₄NH₂ (**1**) and XC₆H₄ND₂ (**2**) in MeCN at 55.0 °C.



Figure S2. The Hammett plots of $\log k_{H(D)}$ vs σ_Y for the reactions of Y-*O*-aryl methyl phosphonochloridothioates with XC₆H₄NH₂ (**1**) and XC₆H₄ND₂ (**2**) in MeCN at 55.0 °C.

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