

The Facile Synthesis of a Very Hindered Phenol by Ligand Coupling

Derek H. R. Barton,^{*a} Dervilla M. X. Donnelly,^b Patrick J. Guiry,^{a,b} and Joseph H. Reibenspies^a

^a Department of Chemistry, Texas A & M University, College Station, TX 77843-3255, USA

^b Department of Chemistry, University College, Dublin 4, Ireland

The reaction of 2,4,6-trimethoxyphenyl-lead triacetate (**4**) with 3,5-di-*t*-butylphenol (**1**) at room temperature afforded the very hindered phenol (**5**) in good (87%) yield; acetylation gave the acetate (**7**) which was fully characterised, including an *X*-ray determination.

The concept of ligand coupling was originally due to Trost¹ and to Oae.² It implies that two groups attached to an atom couple together in a concerted manner without separating into radicals or ions. The expression 'reductive elimination,' much used in organometallic chemistry, designates the same overall transformation, but without specifying the mechanism involved.³

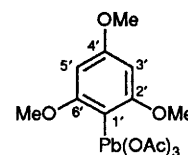
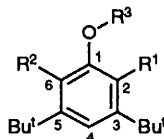
Ligand coupling is much in evidence in the arylation reactions promoted by Bi^V. One of the most striking aspects of ligand coupling, especially in Bi^V chemistry,⁴ is the ease of synthesis of very hindered compounds under mild conditions. For example, phenylation of (**1**) with Ph₃BiCl₂ under basic conditions afforded the diphenyl derivative (**2**) (77%). The intermediate (**3**) was isolated and fully characterised.⁵

We agree with Oae³ that ligand coupling will be seen with many other elements. We have demonstrated⁶ this for Bi^{III}, Sb^V, Te^{IV}, and Pb^{IV}. The ligand coupling chemistry of aryl-lead triacetates, a class of Pb^{IV} reagents, has been extensively studied and exploited by Pinhey.⁷ We have recently employed these in the synthesis of 3-aryl-4-hydroxy coumarins⁸ and the copper-catalysed *N*-arylation of amines.⁹ In both cases very hindered compounds were easily prepared.

Aryl-lead triacetates have the advantage of using their sole aryl group in the formation of the desired carbon-carbon bond. In addition, it is easy to prepare electron rich aryl-lead triacetates either by plumbylation¹⁰ or by tin-lead exchange.¹¹ In contrast, electron rich arylbismuth(V) compounds are not easily prepared and several aryl groups are wasted in each arylation reaction. We decided, therefore, to test the limits of ligand coupling using the phenol (**1**) and the lead reagent¹² (**4**). The phenol (**1**) (0.30 mmol) was reacted for 24 h with three equivalents of (**4**) and ten equivalents of dry pyridine in dry chloroform (1.0 ml). Homogeneity was maintained by adding a second ml of chloroform and after stirring for a further 24 h we obtained (**5**) (87%) and the monoarylated derivative (**6**) (10%). Compound (**5**), recrystallised as needles from hexane,[†] is one of the most sterically hindered phenols yet prepared¹³ and its facile synthesis in such a high yield is notable. Oxidation of (**5**) using benzeneseleninic acid¹⁴ and

O-phenylation of (**5**) by Ph₃Bi(OAc)₂ under copper catalysis¹⁵ were unsuccessful, presumably owing to the steric hindrance of the substrate in both cases. Acetylation of (**5**) by pyridine-acetic anhydride required drastic conditions (reflux, 140 °C for 24 h), as (**5**) is inert at room temperature, and thus we obtained the corresponding acetate (**7**) (94%), which recrystallised as plates from methanol.[‡]

From the ¹H and ¹³C NMR data it is clear that this acetate (**7**) is symmetrical. Compound (**7**) crystallised in the space group *P* $\bar{1}$ with two discrete molecules (**7a**) and (**7b**) per UNIQUE volume of the unit cell.[‡] No unusual bond lengths or angles for either molecule were seen. The conformations of (**7a**) and (**7b**) are similar and differ only in the torsion angles of the terminal methoxy and *t*-butyl groups. The central benzene rings of molecules (**7a**) and (**7b**) are planar [mean deviation from plane: 0.010 Å for (**7a**) and 0.005 Å for (**7b**)] and are nearly perpendicular to the terminal trimethoxyphenyl rings [intersection of the normals to the plane of the benzene ring and the trimethoxyphenyl rings for (**7a**): 82.2 and 81.6°, for (**7b**): 78.3 and 80.6°]. A ball and stick plot of (**7a**) is shown in Figure 1.



- (1) R¹ = R² = R³ = H
 (2) R¹ = R² = Ph, R³ = H
 (3) R¹ = R² = H, R³ = BiPh₃Cl
 (5) R¹ = R² = 2', 4', 6'-trimethoxyphenyl, R³ = H
 (6) R¹ = R³ = H, R² = 2', 4', 6'-trimethoxyphenyl
 (7) R¹ = R² = 2', 4', 6'-trimethoxyphenyl, R³ = Ac

[†] Crystal data for (**7**): C₃₄H₄₄O₈, colourless plate, 0.06 × 0.36 × 0.40 mm³, *M* = 580.7, triclinic, space group *P* $\bar{1}$ (No. 2), *a* = 13.416(5), *b* = 13.863(4), *c* = 19.753(4) Å, α = 73.05(2), β = 79.10(2), γ = 75.30(2)°, *U* = 3372.6(17) Å³, *Z* = 4, *D*_x = 1.14 cm⁻³, *F*(000) = 1248, μ = 0.75 cm⁻¹, 8859 reflections were collected at -80 °C on a Nicolet R3m diffractometer using graphite monochromated Mo-Kα (λ = 0.71073 Å) radiation with θ/2θ scans (4.00 ≤ 2θ ≤ 50.00°) of which 4858 were observed [*I* ≥ 2.0σ(*I*)]. The structure was solved by direct methods (SHELXS-86, G. M. Sheldrick, University of Göttingen, 1986, on FPS superminicomputer) and refined by full-matrix least-squares (SHELXTL-PLUS, G. M. Sheldrick, University of Göttingen, 1988, on μVaxII minicomputer) to *R* = 0.106, *wR* = 0.090, *S* = 2.80 [quantity minimized = Σw(*F*_o - *F*_c)², *w*⁻¹ = σ²(*F*) + 0.0001 *F*², 638 parameters]. Hydrogens were placed at idealised positions. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

[‡] Selected data for (**5**): m.p. 216.5–218 °C; *m/z* 538.2906 (*M*⁺) [C₃₂H₄₂O₇ requires *m/z* 538.2930 (*M*⁺)]; λ_{max} (MeOH) 215.5 and 279 nm (ε 59 919 and 5956 dm³ mol⁻¹ cm⁻¹); ν_{max} (CHCl₃) 3014 (m), 1598 (w), 1206 (s), 779 (s), and 665 (s) cm⁻¹; δ_H (200 MHz, CDCl₃) 7.26 (1H, s, 4-H), 6.18 (4H, s, 2 × 3'-H, 5'-H), 4.57 (1H, s, OH), 3.83 (6H, s, 2 × 4'-OCH₃), 3.66 (12H, s, 2 × 2'-OCH₃, 6'-OCH₃), and 1.17 (18H, s, 2 × *t*-C₄H₉); δ_C (50 MHz, CDCl₃) 161.72 (4'-C), 159.72 (2'-C, 6'-C), 152.11 (1-C), 148.51 (3-C, 5-C), 117.75 (4-C), 116.65 (2-C, 6-C), 109.24 (1'-C), 91.70 (3'-C, 5'-C), 55.78 (2'-OCH₃, 6'-OCH₃), 55.46 (4'-OCH₃), 36.65 [C(CH₃)₃], and 31.46 [C(CH₃)₃]; *m/z* (EIMS) 538 (*M*⁺, 4%), 368 (5), 353 (2), 256 (7), 227 (4), 185 (4), 207 (3), 129 (12), 109 (14), 98 (58), 83 (39), 69 (62), 57 (80), 56 (40), 55 (100), and 41 (95). For (**7**): 265–256 °C; *m/z* 580.3042 (*M*⁺) [C₃₄H₄₄O₈ requires *m/z* 580.3036 (*M*⁺)]; λ_{max} (MeOH) 218 nm (40 580 dm³ mol⁻¹ cm⁻¹); ν_{max} (CHCl₃) 2947 (m), 1751 (s), 1597 (w) 1450 (m), 1134 (s), and 756 (m) cm⁻¹; δ_H (200 MHz, CDCl₃) 7.59 (1H, s, 4-H), 6.10 (4H, s, 2 × 3'-H, 5'-H), 3.82 (6H, s, 2 × 4'-CH₃), 3.6 (12H, s, 2 × 2'-OCH₃, 6'-OCH₃), 1.29 (3H, s, CH₃), and 1.21 (18H, s, 2 × *t*-C₄H₉); δ_C (50 MHz, CDCl₃) 167.27 (C=O), 160.76 (4'-C) 158.86 (2'-C, 6'-C), 149.44 (1-C), 148.65 (3-C, 5-C), 123.94 (4-C), 123.59 (2-C, 6-C), 110.33 (1'-C), 90.63 (3'-C, 5'-C), 55.54 (4'-OCH₃, 55.25 (2'-OCH₃, 6'-OCH₃), 36.89 [C(CH₃)₃], 31.57 [C(CH₃)₃], and 19.56 (CH₃).

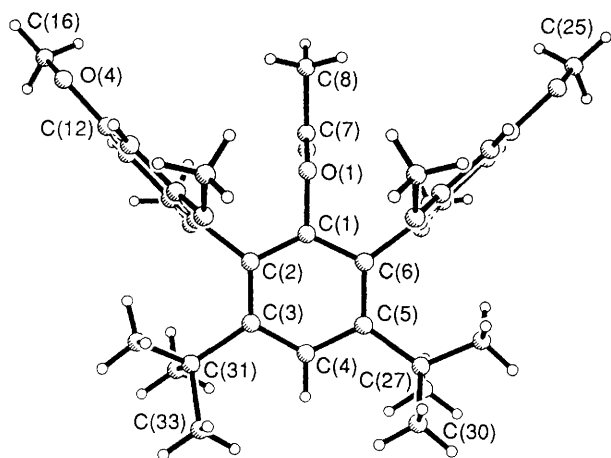


Figure 1. Ball and stick plot of compound (7a).

Thus, well-defined intermediates can be detected in the phenylation of phenols using Bi^{IV} reagents. Since the Pb^{IV} arylation reaction gives the same regioselectivity (*ortho* substitution) as observed with Bi^V reagents and also makes very hindered compounds without involving radicals,⁶ we believe that the mechanism is the same. However, although we have searched diligently, we have not yet been able to detect a Pb^{IV} intermediate. Of course, this may simply mean that it couples very rapidly once formed.¹⁶

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