

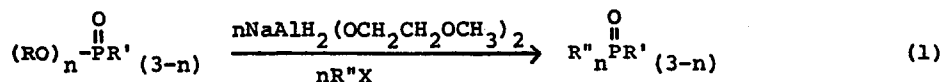
ANOMALY IN THE REACTION OF DIALKYL (2'-BROMOMETHYL)BENZYLPHOSPHONATE WITH
SODIUM BIS(2-METHOXYETHOXY)ALUMINIUM HYDRIDE

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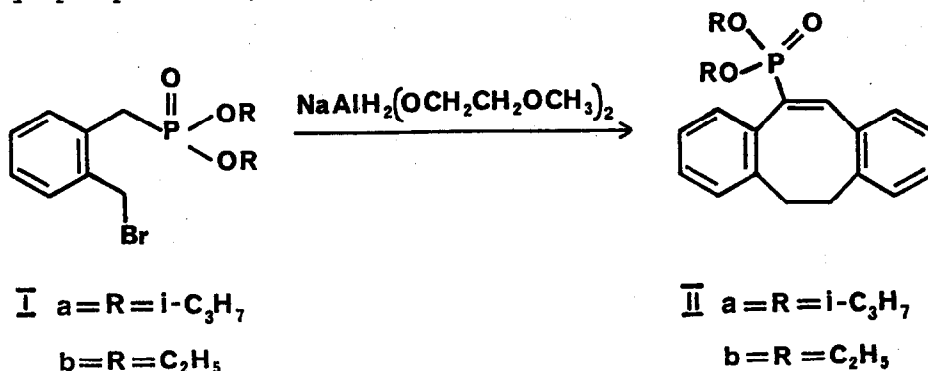
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Recently, the reaction¹ of a phosphorus ester with an alkyl halide in the presence of sodium bis(2-methoxyethoxy)aluminium hydride² to form new carbon-phosphorus bonds (Equation 1) was reported and proved to be a convenient procedure. We have applied this synthetic method to the preparation of macrocyclic biphosphines³ and isophosphindolines.⁴



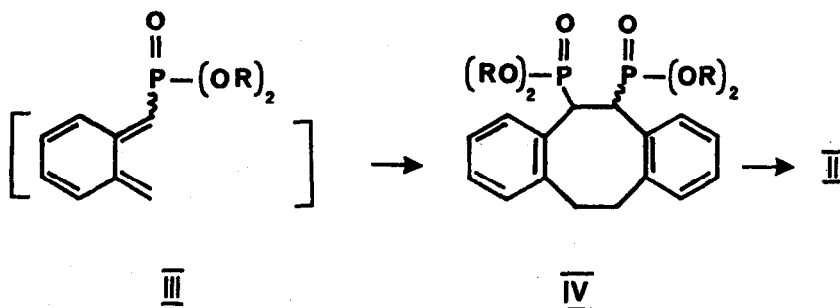
Anomaly occurred however in the reaction of dialkyl (2'-bromomethyl)-benzylphosphonate (I) with sodium bis(2-methoxyethoxy)aluminium hydride. The dialkyl phosphonates (Ia and b) were obtained



by the Arbuzov reaction of *o*-xylylene dibromide with equal mole of the appropriate trialkylphosphite at controlled temperature.^{5,6} When 300 mg Ia was

treated with 1.5 moles of $\text{NaAlH}_2(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2$ in diglyme at 135° for 48 h, the product, on working up, gave only one major component (~ 100 mg) after preparative layer chromatography. It was assigned to structure IIa on the basis of its spectroscopic data.⁶ The mass spectrum of IIa showed a molecular ion at $m/e = 370$. The other prominent peaks were at $m/e = 328$ (M-42) and $m/e = 286$ (M-42-42) which may arise from successive loss of $\text{CH}_3\text{CH}=\text{CH}_2$ through McLafferty rearrangement. The other strong peaks were at $m/e = 204$ ($\text{C}_{16}\text{H}_{12}^+$) and at $\frac{m}{e} = 91$ (C_7H_7^+). The nmr (CDCl_3) spectrum of IIa was equally informative. It gave signals at δ 8.0 (1H, vinyl proton, d, $J_{\text{P-H}} = 24$ Hz); 7.1-7.5 (8H, aromatic protons, m); 4.8 (2H, methine protons, m) 3.2 (4H, methylene protons, s) and 1.1-1.5 (12H, methyl protons, 2d). The IR spectrum of IIa showed a band at 1240 cm^{-1} (P=O stretching). I Ib was similarly obtained from Ib and had spectroscopic data consistent with its structure.^{6,7}

It appears that II may be formed from the dimerization of an unstable o-xilylenyl intermediate III⁸ to give IV followed by β -elimination of one of the phosphoryl groups.⁹

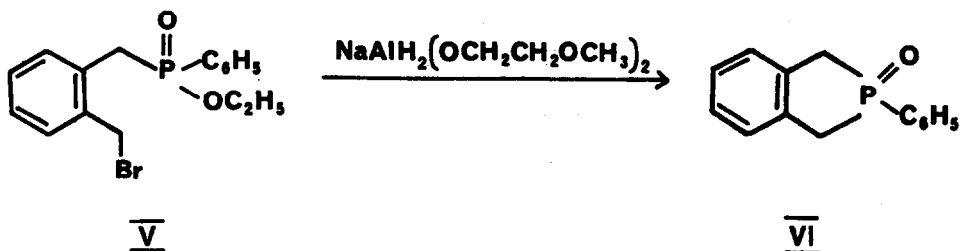


Support for the intermediary of IV was gained by carrying out the reaction of Ia with $\text{NaAlH}_2(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2$ at a lower temperature (125° for 30 h). Under these conditions, IIa was not formed, but instead, a new compound was obtained after preparative layer chromatography. Its spectroscopic data are compatible with structure IVa.⁶ Its mass spectrum showed a molecular ion at $\frac{m}{e} = 536$, followed by successive peaks at 494; 452; 410 and 368. This indicated the

presence of four isopropoxy groups. The nmr spectrum was in agreement with a head-to-head dimeric structure.^{10,11} It gave signals at δ 7.1-7.4 (8H, m, aromatic); 4.5-4.8 (4H, m, isopropylmethine); 3.7 (2H, A_2B_2 , benzylic), 3.4 (2H, s, benzylic), 3.3 (2H, d, $J_{P-H} = 20$ Hz) and 1.0-1.6 (24H, 2d, methyl). The compound is thus an equal mixture of cis- and trans-isomers. IIa could be obtained from IVa if the reaction temperature was increased to 135° for another 48 h.

Sodium bis(2-methoxyethoxy)aluminium hydride served therefore as a base to cause the elimination of hydrogen bromide from I. One may expect other strong bases to effect the same transformation. Indeed, when Ia was heated with potassium t-butoxide in diglyme at 110° for 24 h, IVa was formed, albeit in lower yield. Attempts to trap III with various dienophiles¹² were unsuccessful due to complicated side reactions of the dienophiles with potassium t-butoxide or sodium bis(2-methoxyethoxy)aluminium hydride.

The behavior of the dialkyl phosphonates (Ia and b) should be contrasted with that of ethyl (2'-bromomethyl)benzylphenylphosphinate (V). The reaction of V with $NaAlH_2(OCH_2CH_2OCH_3)_2$ gave the expected 2-phenylisophosphindoline 2-oxide (VI) as the only product⁴ (equation 4).

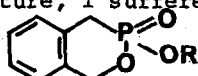


The delicate balance between proton abstraction to give III and hydride substitution at phosphorus is thus affected greatly by subtle structural modification.

References and Notes

1. R. B. Wetzel and G. L. Kenyon, *J. Amer. Chem. Soc.*, **94**, 1774 (1972).
2. The reagent is available commercially under the name vitride.
3. T. H. Chan and B. S. Ong, to be published.
4. T. H. Chan and K. T. Nwe, *Phosphorus*, in press.
5. Ia: n.m.r. δ 7.2-7.7 (4H, aromatic protons, m), 4.9 (2H, methylene protons, s), 4.7 (2H, methine protons, m), 3.4 (2H, methylene protons, d, $J_{P-H} = 24$ Hz), 1.3 (12H, methyl protons, m).
Ib: n.m.r. δ 7.3-7.8 (4H, aromatic protons, m), 4.9 (2H, methylene protons, s), 4.3 (4H, methylene protons, q) 3.5 (2H, methylene protons, d, $J_{P-H} = 24$ Hz), 1.4 (6H, methyl protons, t).

Under higher temperature, I suffered intramolecular cyclization to give



6. Consistent elemental analyses were obtained for all new compounds.
7. Iib: Mass Spectrum: $m/e = 342$ (M); $m/e = 314$ (M-28); $m/e = 286$ (M-28-28); $m/e = 204$ ($C_{16}H_{12}^+$); $m/e = 91$ ($C_7H_7^+$).
n.m.r. δ 8.0 (1H, vinyl proton, d, $J_{P-H} = 24$ Hz), 7.1-7.5 (8H, aromatic protons, m); 4.3 (4H, methylene protons, q); 3.2 (4H, methylene protons, s); 1.3 (6H, methyl protons, t).
8. O-Xylylene intermediate has been invoked by M. P. Cava and A. A. Deana, *J. Amer. Chem. Soc.*, **81**, 4266 (1959).
9. β -Elimination of similar kind has recently been examined. P. Haake and C. E. Diebert, *J. Amer. Chem. Soc.*, **93**, 6931 (1971).
10. The methylene protons are expected to couple with phosphorus in the head-to-tail dimer.
11. The head-to-head dimeric structure eliminates intermolecular S_N2 reaction for the formation of IV.
12. Dienophiles used were dimethyl maleate, dimethyl acetylenedicarboxylate and anthracene.