

Stereochemistry of a Michaelis–Arbusov Reaction: Alkylation of Optically Active Ethyl Trimethylsilyl Phenylphosphonite with Retention of Configuration

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Summary Ethylation of ethyl phenylphosphinate (I) *via* ethyl trimethylsilyl phenylphosphonite or *via* the corresponding trimethylstannyl ester, and free-radical addition of (I) to ethylene proceed with complete, or almost complete, retention of configuration.

WE report the formation of optically active ethyl alkylphenylphosphinates by means of a stereospecific Michaelis–Arbusov reaction† of optically active ethyl trimethylsilyl phenylphosphonite with alkyl iodides.

As shown in the Scheme, treatment of ethyl phenylphosphinate (I), $\alpha_D^{25} - 0.80^\circ$,‡ with a 50% excess of chlorotrimethylsilane–triethylamine in benzene under reflux, according to the procedure of Issleib and Walther,³ gave ethyl trimethylsilyl phenylphosphonite (II) in 88% yield after distillation (b.p. $53^\circ/0.05$ mm), $\alpha_D^{25} - 1.68^\circ$. The large negative value of the ³¹P n.m.r. chemical shift of (II) ($\delta^{31\text{P}} - 145$ p.p.m., neat, relative to external 85% H₃PO₄) is characteristic^{3,4} of its trivalent structure. Hydrolysis of (II), $\alpha_D^{25} - 1.68^\circ$, with 0.1 N-aqueous sulphuric acid,³ containing 3.75% H₂¹⁸O, produced (I) with unchanged optical activity ($\alpha_D^{25} - 0.80^\circ$) in 49% yield. Evidence for hydrolysis of (II) with exclusive fission of the silicon–oxygen bond, and hence with retention of configuration, was obtained from the mass spectrum of recovered (I), which showed that no detectable amount of ¹⁸O above natural abundance was incorporated. Consequently, the trimethylsilylation of (I) also proceeds with complete retention of configuration.

Alkylation of (II), $\alpha_D^{25} - 1.68^\circ$, with excess of methyl iodide in benzene at room temperature,³ followed by treatment with aqueous alkali, gave ethyl methylphenylphosphinate (VI; R = Me), $\alpha_D^{25} - 0.86^\circ$. Similarly, (VI; R = Et), $\alpha_D^{25} - 0.90^\circ$, was obtained from (II), $\alpha_D^{25} - 1.92^\circ$ [derived from (I), $\alpha_D^{25} - 0.86^\circ$], and ethyl iodide. Although we were not able to isolate pure ethyl trimethylstannyl phenylphosphonite (III) from the reaction of (I) with

diethylaminotrimethylstannane,³ the former intermediate was conveniently used *in situ* for a one-step, stereospecific alkylation of (I). Thus, a solution of (I), $\alpha_D^{25} - 1.45^\circ$, in ether was gradually added to a mixture of diethylaminotrimethylstannane and excess of ethyl iodide in ether at room temperature. After filtration of triethylamine hydroiodide and treatment with aqueous silver nitrate, distillation yielded (VI; R = Et) with $\alpha_D^{25} - 1.60^\circ$.§

In order to elucidate the stereochemistry of the Michaelis–Arbusov reactions of (II) and (III) with alkyl iodides, we have also investigated the Michaelis–Becker reaction of (I) with alkyl iodides. According to the procedure of Farnham *et al.*,⁵ the latter reaction is known to proceed with complete retention of configuration. Thus, alkylation of the sodium salt (IV) of ethyl phenylphosphinate [obtained from (I), $\alpha_D^{25} - 1.45^\circ$, optical purity 3.5%]² with methyl iodide in dimethylformamide⁵ gave (VI; R = Me), $\alpha_D^{25} - 1.58^\circ$, [$\alpha_D^{25} - 1.46^\circ$ (c 0.4, benzene), optical purity 3.4%].⁶ Apparently, this result confirms the complete, or almost complete, stereospecificity of the Michaelis–Becker reaction under the given experimental conditions.⁵ In a similar way, (I), $\alpha_D^{25} - 0.80^\circ$, was converted with ethyl iodide into (VI; R = Et), $\alpha_D^{25} - 0.89^\circ$. A comparison of the optical rotations of (–)-(I) with those of the products (–)-(VI; R = Me or Et), obtained by alkylation of the intermediates (–)-(II), (III), and (IV) with methyl and/or ethyl iodide shows that, within experimental error, these reactions proceed with the same degree of stereospecificity and with the same overall stereochemical course. Since alkylation of the anion (IV),^{5¶} as well as trimethylsilylation of (I) proceed with complete retention of configuration, it follows that the Michaelis–Arbusov reactions of (II) with methyl and ethyl iodide proceed with complete retention of configuration. By analogy, complete retention of configuration is also assumed for alkylation of the trimethylstannyl ester (III) with ethyl iodide.

Free-radical addition of (I), $\alpha_D^{25} - 1.45^\circ$, to ethylene under

† For a stereospecific Michaelis–Arbusov reaction of a geometric isomer of 2-methoxy-5-t-butyl-1,3,2-dioxaphosphorinan with methyl iodide, see ref. 1.

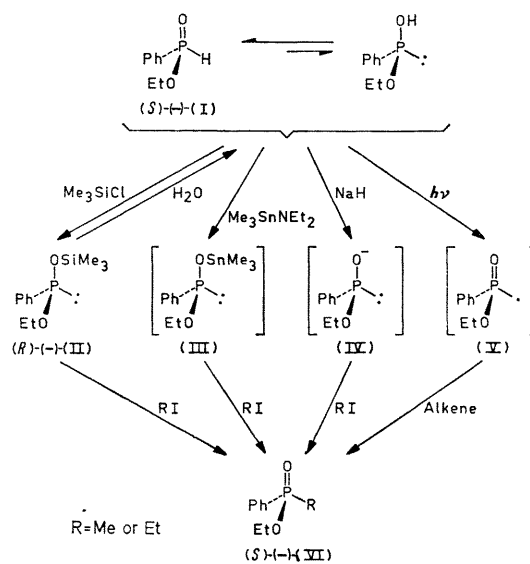
‡ In this paper, optical rotations refer to neat products (*l* = 1 dm), unless otherwise stated.

§ Iodotrimethylstannane (b.p. $62^\circ/15$ mm) and impure (–)-(VI; R = Et) are isolated from the reaction mixture, when the treatment with aqueous silver nitrate is omitted.

¶ Since (–)-(VI; R = Me) has the absolute configuration (S)_r (ref. 6), it follows that the absolute configuration of (–)-(I) is (S)_r.

the influence of a high-pressure u.v. lamp⁷ gave (VI; R = Et), $\alpha_D^{25} -1.54^\circ$. Consequently, the stereochemical course of this reaction, presumably with the phosphinyl radical (V) as one of the free-radical intermediates,⁷ is identical with that of alkylation of the intermediates (II), (III), and (IV), *i.e.* complete, or almost complete, retention of configuration. Previously, we have suggested⁷ that the free-radical additions of an optically pure epimer of menthyl methylphosphinate (m.p. 42°) to ethylene and cyclohexene proceed with inversion of configuration. However, alkylation of the anion of this epimer with ethyl iodide, according to the procedure of Farnham *et al.*,⁵ gave (*R*)_P-menthyl ethylmethylphosphinate {m.p. $79-80^\circ$, $[\alpha]_D^{25} -69.0^\circ$ (*c* 0.7, benzene)}, identical in all respects (mixed m.p., ³¹P and ¹H n.m.r. spectra) with the product obtained from the free-radical addition to ethylene. Based on the firmly established retention mechanism of the Michaelis-Becker reaction,⁵ it is concluded that the free-radical additions of menthyl methylphosphinate to ethylene and cyclohexene proceed with retention of configuration.⁸ Our erroneous evidence for an inversion mechanism of the free-radical alkylations was deduced from a reaction scheme,⁷ involving retention of configuration for the addition of sulphur to optically pure menthyl methylphosphinate (m.p. 42°) and inversion of configuration for the subsequent Grignard reaction of menthyl *S*-methyl methylphosphonothioate with phenylmagnesium bromide, which yielded (*R*)_P-menthyl methylphenylphosphinate. Our present results

show that the last two reactions proceed either both with inversion or both with retention of configuration.



SCHEME

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