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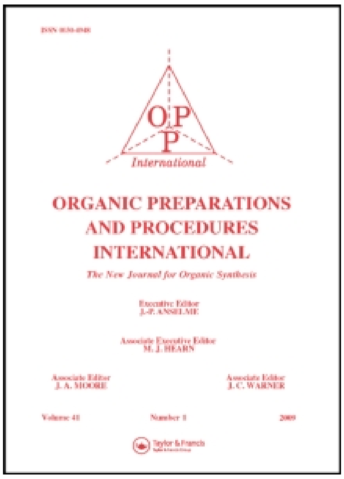

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A SIMPLE STEREOSELECTIVE METHOD FOR THE PREPARATION OF *(E)*-2,5-DIMETHYL-1,3,5-HEXATRIENE

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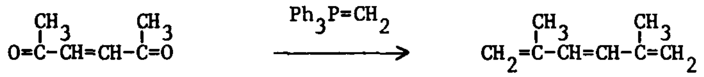
The four-step procedure of Hwa *et al.*[1] for the preparation of 1,3,5-hexatriene has been applied successfully in the synthesis of a variety of alkyl substituted hexatrienes[2,3], including *(E)*-2,5-dimethyl-1,3,5-hexatriene[3], *(E)*-I. However, for the preparation of isotopically substituted trienes, such as *(E)*-2,5-dimethyl-1,3,5-$(1,1,6,6\text{-}{}^{2}H_4)$hexatriene or its $(1,6\text{-}{}^{13}C_2)$ analogue (needed in these Laboratories for a study of the mechanism of formation of 1-methylene-2-isobutenylcyclopropane during the photolysis[3,4] of *(E)*-I and its *cis*-isomer, *(Z)*-I), the Hwa method appears less attractive, a major disadvantage being the necessary introduction of the label in an early stage in combination with low overall yield (~10%[3]). Moreover, the Hwa method in general produces a mixture of geometric isomers.

The present paper describes the preparation of *(E)*-I in 23% yield by a fully stereoselective single-step method requiring only bis-methylenation of the known[5] *(E)*-3-hexene-2,5-dione, *(E)*-II. The diketone is readily available from 2,5-dimethylfuran by the method of Levisalles.[5] Methylenation could be achieved with methylenetriphenylphosphorane under suitable



$$O{=}\overset{CH_3}{\underset{|}{C}}{-}CH{=}CH{-}\overset{CH_3}{\underset{|}{C}}{=}O \xrightarrow{Ph_3P{=}CH_2} CH_2{=}\overset{CH_3}{\underset{|}{C}}{-}CH{=}CH{-}\overset{CH_3}{\underset{|}{C}}{=}CH_2$$

II I

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reaction conditions (*vide* Experimental). The *(E)*-dimethylhexatriene obtained was shown (GC) to be uncontaminated with the *(Z)*-isomer.

With the use of isotopically modified reagents this method thus represents an unambiguous procedure for the preparation of the desired trienes with labels such as CD_2 or $^{13}CH_2$ at 1,6-positions in the olefins. The versatility of the Wittig reagent and the ease of preparation of substituted enediones from mono- and disubstituted furans[5] suggest extension of the method to the synthesis of other substituted trienes. One application of particular interest is the preparation of the *cis*-isomer, *(Z)*-I. However, attempts to methylenate the known[5] *(Z)*-3-hexene-2,5-dione, *(Z)*-II, under a variety of Wittig reaction conditions met with little success, the yield of the desired triene not exceeding 2%. Application of sodium bis-(trimethylsilyl)amide as a base for the generation of a lithium salt free solution of the phosphorane according to the general procedure of Bestmann *et al.*[6] was also unsuccessful in furnishing *(Z)*-I.

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EXPERIMENTAL

Mps are uncorrected. UV absorption spectra were measured with a Cary M14 spectrophotometer, IR spectra with a Beckman IR-10 instrument. ^{1}H-NMR spectra were recorded in $CDCl_3$ solutions on a Jeol JNM-PS 100 spectrometer; chemical shifts δ are reported in ppm downfield from TMS as internal standard. Gas chromatography was performed on a Hewlett-Packard F & M 5750 gas chromatograph using a WCOT glass capillary column coated with OV 101; temperature of injection port and column 150^o and 60^o, respectively.

(E)-3-Hexene-2,5-dione, *(E)*-II.- Prepared from 2,5-dimethylfuran in 42% yield according to the procedure reported by Levisalles.[5] One recrystallization of crude *(E)*-II, mp. 68^o, from cyclohexane (using Norit) furnished nearly white shining crystals, mp. 75^o, lit.[5] mp. $75-76^o$. UV (EtOH): ε_{228} 14400, ε_{324} 70; IR ($CHCl_3$): 1685 cm^{-1} (C=O).

(Z)-3-Hexene-2,5-dione, *(Z)*-II.- Prepared according to Levisalles[5] from 2,5-dimethylfuran *via* 2,5-dimethyl-2,5-dimethoxy-2,5-dihydrofuran in 48% yield, bp. 93-94°/18 mm, lit.[5] bp. 92°/16 mm. UV (EtOH): ε_{223} 6600, ε_{282} 170; IR (neat): 1690 cm^{-1} (C=O).

(E)-2,5-Dimethyl-1,3,5-hexatriene, *(E)*-I.- To a cooled (-20°) and vigorously stirred suspension of finely powdered methyltriphenylphosphonium iodide[7] (64.64 g, 0.16 mole) in dry tetrahydrofuran (200 ml, distilled from sodium, and again from $LiAlH_4$) in an atmosphere of dry nitrogen was added dropwise a 15% solution of butyllithium in hexane (Merck, 100 ml, 0.16 mole) in about 30 min. The resulting orange-red mixture was then stirred at room temperature (25°) for one hour, and cooled again to -10°. To this cooled and well stirred reaction mixture a solution of *(E)*-II (8.96 g, 0.08 mole) in dry tetrahydrofuran (50 ml) was added dropwise in an atmosphere of dry nitrogen in about 15 min. After the addition the mixture was warmed to room temperature and stirred for an additional period of two hours by which time all diketone *(E)*-II had reacted (as evidenced by TLC, ethyl acetate/benzene 1:1). The dark brown mixture was treated successively with aqueous methanol (1:1, 200 ml) and pentane (200 ml). The resulting mixture was then stirred at room temperature for three hours. The pentane layer was separated, and the aqueous layer was extracted with pentane (3 x 200 ml). The combined pentane solution was washed thoroughly with aqueous methanol (1:1, 3 x 100 ml), and dried. The pentane was removed by slow evaporation under reduced pressure (200 mm, bath temperature 35-40°; evaporation at lower pressure using a rotary evaporator results in considerable losses of dimethylhexatriene). The residual yellow liquid (2.2 g) was redissolved in pentane (25 ml) and passed through a column of silica gel (Merck Kieselgel 60, 0.063-0.200 mm, 100 g, column height 30 cm). Elution was carried out with pentane (1000 ml). The colourless pentane solution on evaporation

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under reduced pressure as above furnished an almost colourless liquid (2.1 g) which was further purified by distillation in an all glass tube oven (Büchi GKR-50) at 60°/20 mm. The distillate (2.0 g, 23%) upon GC analysis showed only two peaks, the major one (95%) corresponding to the peak of an authentic sample[4] of *(E)*-2,5-dimethyl-1,3,5-hexatriene, *(E)*-I. The retention time of the minor component (5%) proved to be different from that of an authentic sample[4] of *(Z)*-2,5-dimethyl-1,3,5-hexatriene, *(Z)*-I. The *(E)*-triene, if required, can easily be freed from the impurity by preparative GC[3]. Spectral data of *(E)*-I: UV (hexane): ε_{270} 33600, ε_{260} 44350, ε_{250} 31000; IR (neat): 3100, 3040, 3000-2860, 1780, 1620, 1455, 1440, 1375, 1315, 1260, 960, 885 cm^{-1}; NMR ($CDCl_3$): 1.84(s,6H), 5.01(s,4H), 6.25(s,2H).

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