

A FACILE SYNTHESIS OF SUBSTITUTED CONJUGATED CYCLOHEXADIENES.<sup>1</sup>

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(Received in USA 29 August 1973; received in UK for publication 25 September 1973)

We wish to report a general method for the preparation of cyclohexadienes having structure  $\lambda$ . Previous procedures suffer from lack of specificity and difficulty of execution.<sup>2</sup> Our earlier findings that allylidetriphenylphos-



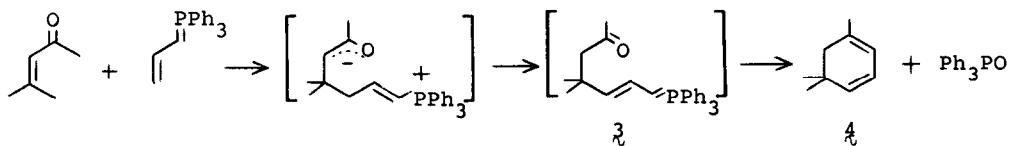
$\lambda$ , R<sub>1</sub> = alkyl; R<sub>2</sub>-R<sub>5</sub> = alkyl or H       $\zeta$ , n = 1,2,3,4

phoranes add in a conjugate fashion to cyclic enones of type  $\zeta^3$  led us to investigate their reaction with acyclic and semicyclic enones for the preparation of compounds of type  $\lambda$ .<sup>4</sup>

When mesityl oxide was treated with allylidetriphenylphosphorane in ether, 1,5,5-trimethylcyclohexa-1,3-diene ( $\lambda$ )<sup>5</sup> was obtained in 50% yield. In such a reaction, it has been shown that the addition of the  $\gamma$ -position of the ylid to the  $\beta$ -carbon of the enone occurs first, followed by proton transfer to generate ylid  $\zeta$  which then undergoes an intramolecular Wittig condensation to produce  $\lambda$ .<sup>3,4</sup>

(Scheme I).

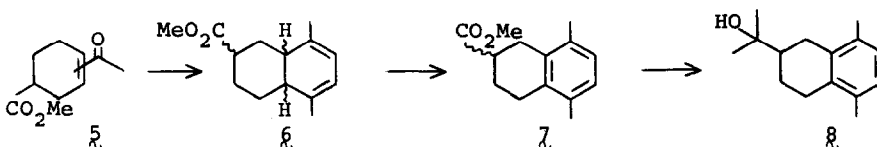
Scheme I



A variety of  $\alpha,\beta$ -unsaturated ketones were treated in a similar fashion to afford the dienes outlined in Table I.<sup>6</sup>

Application of this diene preparation to the synthesis of the sesquiterpene occidol (**8**) is outlined in Scheme II. The carbomethoxyacetylcyclohexene **5**, prepared by the Friedel-Crafts acylation of methyl cyclohex-3-enecarboxylate,<sup>8</sup> was

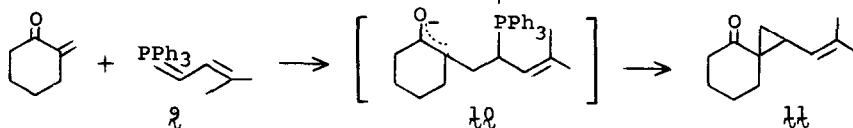
Scheme II



converted to **6** by treatment with 2-butenylidene triphenylphosphorane in refluxing THF for 4 hr in 30% yield. Subsequent sulphur dehydrogenation of **6** followed by treatment of the crude **7** with ethereal methyllithium afforded racemic occidol<sup>10</sup> in 70% overall yield from **6**.


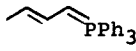


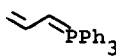


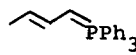
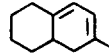
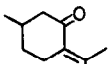
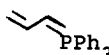
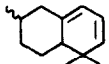

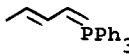
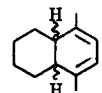

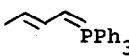
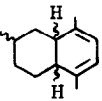

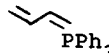
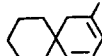
If the starting ylid is disubstituted at the  $\gamma$ -position, regeneration of the type **3** is not possible. In one case, when mesityl oxide was condensed with 3-methyl-2-butenylidene triphenylphosphorane (**9**), normal 1,2-addition occurred to give a mixture of the corresponding isomeric triene. With 2-methylenecyclohexanone, on the other hand, which is known to be a rather unusually reactive Michael acceptor, conjugate addition of the Wittig reagent **9** still occurs; now, however, from the  $\alpha$ -position of the ylid to give the betaine **10**, which subsequently closes to the cyclopropane **11**, (Scheme III). Infrared absorption at  $1700\text{ cm}^{-1}$ , nmr ( $\text{CCl}_4$ )  $\delta$  4.73 (br d, 1), 1.55-2.40 (m, 16), 0.40 (m, 1), uv  $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$  237 nm ( $\epsilon = 5500$ ), and parent ion 178 support the assigned structure **11**. A few cases of cyclopropane formation have been reported for the addition of simple methylenetriphenylphosphoranes with unsaturated carbonyl compounds.<sup>11</sup> This result is, however, in contrast to a similar condensation of 2-methylenecyclohexanone with (2-cyclohexylidene-ethylidene) triphenylphosphorane, which was reported to give

Scheme III



1-(1-cyclohexen-1-yl)-3-cyclohexylidenepropene via a [1,3]-hydrogen shift.<sup>12</sup>

Table I. Products and Yields of Ylid Reactions.

Enone	Ylid <sup>a</sup>	Diene Product <sup>b</sup>	Conditions <sup>c</sup>	Yield, % <sup>d</sup>
			Ether, 25°, 30 hr	62
			Ether, 25°, 30 hr	50 <sup>e</sup>
			THF, 25°, 18 hr	25 <sup>f</sup>
			THF, 25°, 16 hr	41 <sup>g</sup>
			THF, reflux, 30 hr	(25) <sup>h</sup>
			THF, reflux, 4 hr	(30) <sup>i</sup>
			Ether, 25°, 12 hr	32

a) Ylids generated from phosphonium bromides with *n*-butyllithium. b) Spectra and elemental analyses were consistent with the assigned structures. The dienes were the only volatile products obtained unless indicated otherwise. c) At least a 15% excess of ylid was used. For the volatile dienes ether was chosen to facilitate product isolation. d) Figures in parentheses refer to vpc yields; other figures refer to isolated yields. Yields were not optimized. e) Yield was 83% based on recovered starting material. f) The yield was low as a result of dimerization of the 2-methylenecyclohexanone. g) Pulgenone dimer accounted for the remainder of the starting material. h) Two isomeric trienes were also obtained in yields of 26 and 16%. i) A 60% yield of volatile product was obtained. Vpc analysis indicates five products and nmr analysis showed that some trienes were present.

## REFERENCES

- 1) This work was supported in part by Grant No. AM-00709, National Institute of Arthritis and Metabolic Diseases, U. S. Public Health Service.
- 2) a) H. Pines and R. H. Kozlowski, J. Amer. Chem. Soc., **78**, 3776 (1956). b) S. Coffey (Editor), Rodd's Chemistry of Carbon Compounds, 2nd Edition, Vol II B, p. 25, Elsevier Publishing Co., Amsterdam, (1968).
- 3) W. G. Dauben and J. Ipaktschi, J. Amer. Chem. Soc., **95**, 5088 (1973).
- 4) Previously, G. Büchi and H. Wüest (Helv. Chim. Acta, **54**, 1767 (1971)) reported the preparation of a substituted 1,3-cyclohexadiene by conjugate addition to an extremely electron deficient acyclic enone.
- 5) Identical with a sample prepared by S. W. Staley and F. L. Wiseman, Jrs., J. Org. Chem., **35**, 3868 (1970).
- 6) It is interesting to note that the only previously reported example of 1,2-addition in the reaction allylidenetriphenylphosphoranes with  $\alpha,\beta$ -unsaturated ketones is that of benzalacetophenone and cinnamylidenetriphenylphosphorane (F. Bohlmann, Chem. Ber., **89**, 2191 (1956)).
- 7) C. Mannich, Chem. Ber., **74**, 554 (1941).
- 8) The enone mixture, prepared by the method of Pishnamazzade and Guseinov, Dokl. Acad. Nauk. Azerb. SSR, **25**, 24 (1969), was shown by nmr to be a 3:1 mixture of the 3- and 4-acetyl isomers respectively.
- 9) L. G. Jupp, G. A. R. Kon, E. H. Lockton, J. Chem. Soc., 1638 (1928).
- 10) Previously prepared via a nine step sequence in an overall yield of 2.7% by Y. Hirose and T. Nakatsuka, Bull. Agri. Chem. Soc., Japan, **23**, 253 (1959).
- 11) a) J. P. Freeman, J. Org. Chem., **31**, 538 (1966); b) P. A. Grieco and R. S. Finkelhor, Tetrahedron Lett., 3781 (1972).
- 12) H. H. Inhoffen, K. Brückner, G. F. Domagk, and H. Erdmann, Chem. Ber., **88**, 1415 (1955).
- 13) Stipendiat der Deutsche Forschungsgemeinschaft.
- 14) National Science Foundation Predoctoral Fellow, 1971 - present.