

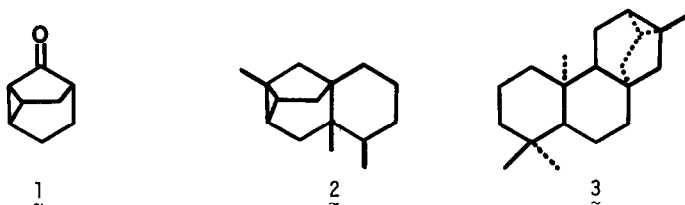
BICYCLOANNULATION A ONE-STEP SYNTHESIS OF  
TRICYCLO [3.2.1.0<sup>2,7</sup>] OCTAN-6-ONES.

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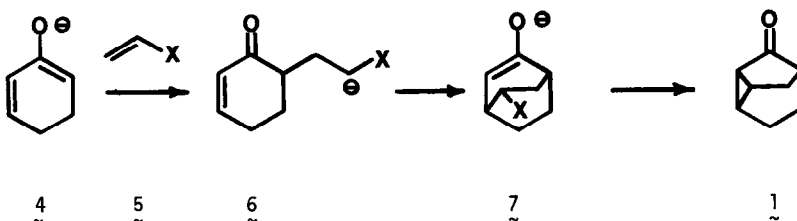
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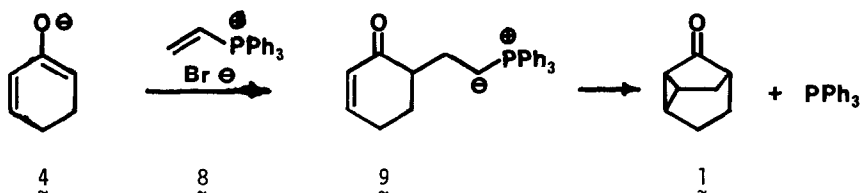
In recent years, a number of publications have appeared in which the tricyclo [3.2.1.0<sup>2,7</sup>] octan-6-one system (1) is utilized in synthetic intermediates as a convenient precursor of bicyclo [3.2.1] octane and bicyclo [2.2.2] octane systems.<sup>1</sup> All of these investigations have employed the copper-catalyzed intramolecular cyclization of cyclohexenyl diazomethyl ketones in the formation of the required tricyclic compounds. Our interest in this structure (1) derives from our planned syntheses of isshwarane and trachylobane terpenoids,<sup>2,3</sup> exemplified by the parent hydrocarbons 2 and 3 respectively. We expected that if the  $\alpha'$ -enolate (4) of an  $\alpha,8$ -cy-



clohexenone were generated and allowed to react with a Michael acceptor (5) in which the activating group (X) is also a good leaving group, the initial addition to form 6 and subsequent internal Michael attack<sup>4</sup> would be followed by an intramolecular nucleophilic displacement of the X group in 7 by the enolate.<sup>5</sup>

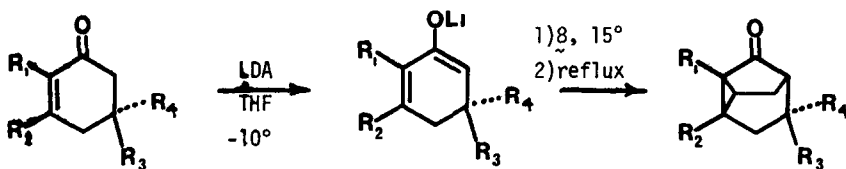


A reagent which appears to satisfy the requirements for 5 is vinyltriphenylphosphonium bromide (8) which is rendered all the more inviting because of its commercial availability. Not only has this salt been found to readily undergo conjugate addition with enolates,<sup>6</sup> but also the desired cyclopropane formation by the resulting ylide, 9, has analogy in its previously observed intermolecular counterpart.<sup>7</sup> Furthermore, 8 is a highly efficient dienophile in



the Diels-Alder reaction,<sup>8</sup> and the conversion of 4 to 7 ( $X = \text{PPh}_3^+$ ) is formally in the latter category

The realization of this proposal is shown below. The kinetically controlled generation of



10a  $R_1 = \text{CH}_3, R_2, R_3, R_4 = \text{H}$

11a 10% (gc)

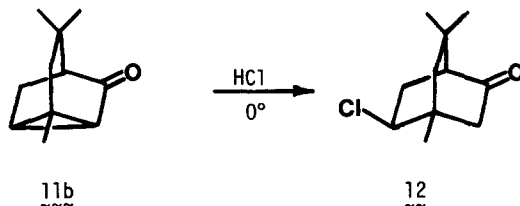
10b  $R_1 = \text{H}, R_2, R_3, R_4 = \text{CH}_3$

11b 22% (gc)

10c  $R_1 = \text{CH}_3; R_2, R_3 = \text{H}; R_4 = \begin{array}{c} \text{CH}_3 \\ | \\ \text{C}=\text{CH}_2 \end{array}$

11c 18% (isolated)

cross-conjugated dienolates by the use of lithium diisopropylamide (LDA) has been well documented.<sup>4,9</sup> Although the yields of final products are low, a complex strained ring system is formed from monocyclic precursors in one step, and only insignificant amounts of other volatile products were observed. The spectral data for 11a were identical to those reported by Scario and Licker<sup>3,10</sup> Analytical and spectral properties<sup>11</sup> of 11b and 11c were entirely consistent with the assigned structures. The exclusive formation of one stereoisomer (11c) from d-carvone (10c) should be noted. Addition of HCl to 11b proceeded smoothly to give 12 in quantitative yield<sup>11</sup> Similar reactivity has been noted for other compounds possessing the tricyclic system ]<sup>1a</sup>



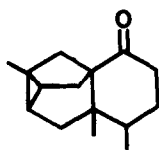
Since the overall process (10 + 11) results in the attachment of two new adjoining rings to an existing structure<sup>12</sup> we propose to classify this as a "bicycloannulation" reaction. A related bicycloannulation procedure has recently been reported by Dauben and Kozikowski<sup>13</sup> The ready availability of  $\alpha,\beta$ -unsaturated ketones makes this method more attractive than the one previously used<sup>1</sup> in many cases. In addition, compounds such as 11b and 11c are only attainable by the present procedure, which is therefore complimentary to previous methods.

We are optimistic that further work will improve the efficiency of this remarkable reaction, as no attempt to optimize conditions has yet been made. Experiments designed to trap and prove the existence of the assumed intermediate ylide 9 and enolate 7 ( $X = \text{PPh}_3$ ,  $\oplus$ ) are in progress.

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#### REFERENCES

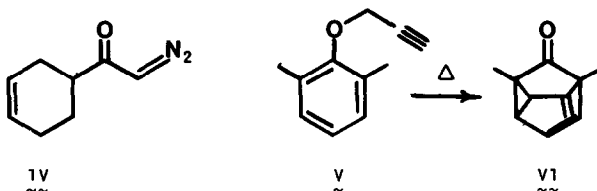
1. For leading references see: (a) H.O. House, S.G. Boots and V.K. Jones, J. Org. Chem., **30**, 2519 (1965), (b) W.F. Erman and L.C. Stone, J. Am. Chem. Soc., **93**, 2821 (1971); (c) P.N. Chakraborty, R. Dasgupta, S.K. Dasgupta, S R. Ghosh and U.R. Ghatak, Tetrahedron, **28**, 4653 (1972); (d) A. Tahara, M. Shimagaki, S. Ohara and T. Nakata, Tetrahedron Lett., 1701 (1973), (e) L.N. Mander, R.H. Prager and J.V. Turner, Aust. J. Chem., **27**, 2645 (1974), (f) D. Becker and H.J.E. Loewenthal, Israel J. Chem., **10**, 375 (1972).
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3. A recent attempt to synthesize ishwarone (1) via the diazoketone method failed:



1

D.L. Licker, Ph.D. Thesis, Iowa State University, 1973; C.J.V. Scanio and D L. Licker, Tetrahedron Lett. 1363 (1972).

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5. The ring closure of  $7$  ( $X = \text{OTs}$ ) to form  $1$  is a key step in one of the types of syntheses of ishwarane and trachylobane described in reference 2.
6. I Kawamoto, S. Muramatsu and Y. Yura, Tetrahedron Lett., 4223 (1974), and references therein
7. W.G. Dauben, D.J. Hart, J. Ipaktschi and A.P. Kozikowski, ibid., 4425 (1973), and references therein.
8. R.A. Ruden and R. Bonjouklian, ibid., 2095 (1974).
9. G. Stork, R.L. Danheiser and B. Ganem, J. Am. Chem. Soc., **95**, 3414 (1973)
10. Private communication from C.J.V. Scanio
11. Satisfactory nmr ( $^1\text{H}$  and  $^{13}\text{C}$ ), ir, and ms (including exact mass determinations) spectra were obtained for all new compounds. Details will be presented in the full paper.
12. Although two other methods for the construction of system  $1$  involve simultaneous double ring formation ( $1\text{v} \rightarrow 1^1$  and  $\text{v} \rightarrow \text{v}1^1$ ), these are cyclizations, rather than annulations.



13. W.G. Dauben and A.P. Kozikowski, Tetrahedron Lett., 3711 (1973).
14. N. Sarcevic, J. Zsindely and H. Schmid, Helv. Chim. Acta, **56**, 1457 (1973).