Photocyclization of a portion of the mixture as described above for pure **7a** gave phenanthrene **8b** (20%) identical with material described above. Evaporation of the methanol-soluble portion and crystallization gave **9** (75%), mp 99–100 °C. The analytical sample of **9** was obtained by crystallization from cyclohexane: mp 102–103 °C; UV (methanol) 262 (8900), 271 (6900), 291 (1700), 303 (1600) nm; IR 1710, 2900, 3000 cm^{-1}; NMR δ 10.30 (2 H, disappeared upon addition of deuterium oxide), 7.30 (8 H), 2.90 (4 H), 2.2–2.8 (8 H), 1.3–2.0 (12 H); mass spectrum, *m/e* 410.2448 (M^+), 392, 374.

Anal. Calcd for $C_{26}H_{34}O_4$: C, 76.06; H, 8.34. Found: C, 76.23; H, 7.97.

The stilbene **7a** was recovered unchanged in 90% yield from treatment with zinc amalgam as described above.

Acknowledgment. We wish to acknowledge a useful discussion with Professor R. A. Raphael of Cambridge University.

Registry No. 1, 70161-78-3; *cis*-**2a**, 20657-42-5; *trans*-**2a**, 36888-18-3; **2b**, 56526-10-4; **2c**, 73049-16-8; **2d**, 73049-17-9; **3a**, 15815-47-1; **3b**, 73049-18-0; **3c**, 38378-77-7; **4**, 73049-19-1; **5**, 73049-20-4; **6a**, 73049-21-5; **6b**, 73049-22-6; **7a**, 73049-23-7; **7b**, 73049-24-8; **8a**, 73049-25-9; **8b**, 70161-79-4; **9**, 73049-26-0; **10**, 73061-94-6; **11**, 73049-27-1; **12**, 73049-28-2; 2-(*N*-morpholino)-1-cyclopentene, 936-52-7; *o*-phenylenediamine, 95-54-5.

Vinylphosphonium Bicycloannulation of Cyclohexenones and Its Use in a Stereoselective Synthesis of Trachyloban-19-oic Acid[1]

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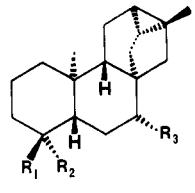
Tricyclo[3.2.1.$0^{2,7}$]octan-6-ones are prepared in a single step from α-cyclohexenones by reaction of the α' enolates of the latter with vinyl- or isopropenyltriphenylphosphonium bromide. The α-substituted vinylphosphonium salt generally gives higher yields and faster reaction rates than the parent compound. With 4,4-dimethylcyclohex-2-en-1-one, the major products result from the condensation of 2 mol of phosphonium salt per mol of enone; this anomaly can be ascribed to steric hindrance. In a model study, the ring system of the sesquiterpene ishwarane is constructed in one step from Δ^2-1-octalone and the isopropenyl salt. Podocarpic acid is converted to trachyloban-19-oic acid, the enantiomer of a sunflower diterpene, by using this bicycloannulation method as the key step.

The common sunflower (*Helianthus annuus* L.)[2] contains in its flower head,[3] roots,[4] and shoots[4] large amounts of *ent*-trachyloban-19-oic acid[5] (**1**), a member of the rare pentacyclic (trachylobane) diterpene class. Not long after Pyrek reported[3] the discovery of this natural product in 1970, the closely related derivative ciliaric acid (**2**) was found in two other sunflower species, *H. ciliaris*[6] and *H. laciniatus*,[7] and was correlated by conversion[6] to **1**. The trachylobane terpenes[8] as a whole are biogenetically important in that their carbon skeleton represents a deprotonated form of a key intermediate proposed[9] by Wenkert for the biosynthesis of the tetracyclic diterpenes, and the discovery[10] of this system in nature (trachylobanic acid **3**) helped to confirm his hypothesis.[11,12] The recent isolation[13] of trachylobane itself (**4**) together with all the basic types of tetracyclic diterpenes from one source, the monkey



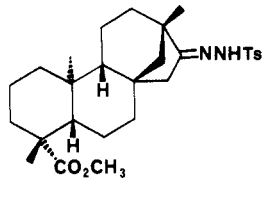
1 $R_1 = CH_3$, $R_2 = CO_2H$, $R_3 = H$

2 $R_1 = CH_3$, $R_2 = CO_2H$, $R_3 = OH$

3 $R_1 = CO_2H$, $R_2 = CH_3$, $R_3 = H$

4 $R_1 = R_2 = CH_3$, $R_3 = H$

5 $R_1 = CH_3$, $R_2 = CO_2CH_3$, $R_3 = H$



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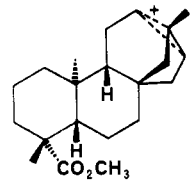

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(1) Bicycloannulation. 5. For the previous paper in this series, see R. M. Cory, L. P. J. Burton, and R. G. Pecherle, *Synth. Commun.*, **9**, 735 (1979).

(2) C. B. Heiser, "The Sunflower", University of Oklahoma Press, Norman, OK, 1976.

(3) (a) J. St. Pyrek, *Tetrahedron*, **26**, 5029 (1970); (b) O. Achmatowicz, Jr., A. Ejchart, L. Kozerski, and J. St. Pyrek, *J. Chem. Soc., Chem. Commun.*, 98 (1971).

(4) Z. Kasprzyk, W. Janiszewska, and M. Papaj, *Bull. Acad. Pol. Sci., Ser. Sci. Biol.*, **22**, 1 (1974).

(5) In the original name for this compound[3] the prefix ent was omitted.

(6) L. F. Bjeldanes and T. A. Geissman, *Phytochemistry*, 11, 327 (1972).

(7) A. Ortega, A. Ayala, C. Guerrero, and A. Romo de Vivar, *Rev. Soc. Quim. Mex.*, **16**, 191 (1972).

(8) J. R. Hanson in "Chemistry of Terpenes and Terpenoids", A. A. Newman, Ed., Academic Press, New York, 1972, Chapter 4, p 155; R. McCrindle and K. H. Overton in "Advances in Organic Chemistry, Methods and Results", Vol. 5, R. A. Raphael, E. C. Taylor, and H. Wynberg, Eds., Interscience, New York, 1965, p 47.

(9) E. Wenkert, *Chem. Ind. (London)*, 282 (1955).

(10) G. Hugel, L. Lods, J. M. Mellor, D. W. Theobald, and G. Ourisson, *Bull. Soc. Chim. Fr.*, 1974 (1963); 2882, 2888, 2894 (1965).

(11) A. C. Oehlschlager and G. Ourisson in "Terpenoids in Plants", J. B. Pridham, Ed., Academic Press, New York, 1967, Chapter 5, p 83.

(12) For further work in this area see: R. A. Appleton, A. J. McAlees, A. McCormick, R. McCrindle, and R. D. H. Murray, *J. Chem. Soc. C*, 2319 (1966); A. J. McAlees, R. McCrindle, and S. T. Murphy, *J. Chem. Soc., Perkin Trans. 1*, 1042 (1976); D. R. Robinson and C. A. West, *Biochemistry*, **9**, 70, 80 (1970); J. W. ApSimon and S. F. Hall, *Can. J. Chem.*, **56**, 2156 (1978).

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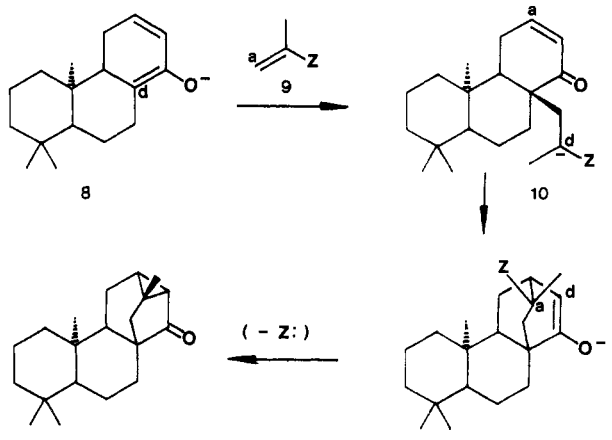
puzzle tree (*Araucaria araucana*), adds further credence to this view (modified somewhat to take into account our increased understanding of carbonium rearrangements since 1955). More recent biological interest in acid **1** stems from its larvicidal activity[14] towards several Lepidoptera species, including the sunflower moth (*Homeosoma electellum*), a major pest of the sunflower.

Our own interest in the trachylobanes is centered on the design of new synthetic methods for the construction of the CDE ring portion (tricyclo[3.2.1.$0^{2,7}$]octane) of their molecular framework.[15] One of the first approaches to this system involved the cyclization[16] of the methyl ester of isostevioltosylhydrazone (**6**) (beyerane ring system) to the methyl ester (**5**) of acid **1**, which must proceed via the formal biogenic intermediate cation **7**. Although **5** was formed only as a minor product along with three others, this 1968 study by Coates and Bertram represents one of the few examples of the synthesis of a natural product (as its methyl ester) *before* its discovery in nature. However, from a synthetic viewpoint, this task was considerably simplified by the fact that the C and D rings were already in place in the naturally derived starting material, isosteviol, leaving only the problem of the single cyclization to form the E (cyclopropane) ring.

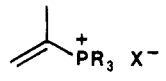
Our strategy can be described in terms of the symbolism developed[17] by Seebach for the donor (d)–acceptor (a) approach in synthetic methodology. With the realization that reactivity umpolung of synthon **9** can be achieved by heteroatom exchange or modification of the group Z,[18] the plan shown in Scheme I may be set out. Thus, it should be possible to design a reagent **9** which would react with a cross-conjugated enolate of type **8** in such a way that the entire construction of the DE ring system may be carried out in a single synthetic operation. The initial attack to give intermediate **10** is expected to occur stereoselectively from the α face of the enolate, dictated by the steric hindrance to α attack afforded by the (axial) angular methyl group.[19] Since the overall sequence results in the attachment of two new adjoining rings (a *bicyclic* ring system) to an existing structure, we termed such a process "bicycloannulation."[15a,20] In this case, of course, the two

Scheme I. Synthetic Strategy



new rings are added to an already extant six-membered ring to form a *tricyclic* system (aside from the uninvolved A and B rings).

A candidate for the bicycloannulation reagent **9** which seemed eminently suitable is the vinylphosphonium salt **11**, where the R_3P group has been chosen to perform the



11

functions of the group Z in Scheme I.[21] Vinylphosphonium salts, especially the commercially available vinyltriphenylphosphonium bromide (VTB, "Schweizer's reagent"), have been successfully employed in a variety of annulations in which the first step is conjugate addition of an enolate to give a keto ylide which then undergoes intramolecular Wittig condensation to a cycloalkene.[22] In addition, a large number of publications have described the analogous use of vinylphosphonium salts in the synthesis of heterocyclic compounds.[23] More closely related to Scheme I is the bicycloannulation method of Dauben and Kozikowski,[20f] which involves a vinylphosphonium enolate zwitterion as a intermediate. This latter study is also one of several in which the cyclopropanation of an α,β-unsaturated carbonyl compound by a phosphorus ylide was reported.[24] In fact, even an example of an intramo-

(13) L. H. Briggs and G. W. White, *Tetrahedron*, **31**, 1311 (1975). See also: B. R. Gonzales, S. Valverde, and J. M. Rocha, *An. Quim.*, **66**, 503 (1970); A. G. Gonzalez, J. L. Breton, B. M. Fraga, and J. G. Luis, *Tetrahedron Lett.*, 3097 (1971).

(14) A. C. Waiss, Jr., B. G. Chan, C. A. Elliger, and V. H. Garrett, *Naturwissenschaften*, **64**, 341 (1977); C. A. Elliger, D. F. Zinkel, B. G. Chan, and A. C. Waiss, Jr., *Experientia*, **32**, 1364 (1976).

(15) Preliminary papers: (a) R. M. Cory and D. M. T. Chan, *Tetrahedron Lett.*, 4441 (1975); (b) R. M. Cory, Y. M. A. Naguib, and M. H. Rasmussen, *J. Chem. Soc., Chem. Commun.*, 504 (1979).

(16) R. M. Coates and E. F. Bertram, *Tetrahedron Lett.*, 5145 (1968); *J. Org. Chem.*, **36**, 3722 (1971).

(17) D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **18**, 239 (1979).

(18) C. J. M. Stirling, *Acc. Chem. Res.*, **12**, 198 (1979).

(19) See, for example: R. B. Turner, K. H. Gänshirt, P. E. Shaw, and J. D. Tauber, *J. Am. Chem. Soc.*, **88**, 1776 (1966); K. Mori and M. Matsui, *Tetrahedron*, **24**, 3095 (1968).

(20) It should be noted that bicycloannulation as herein defined is only one type of double annulation and that the latter should be considered distinct from double cyclization, in which nothing is *added* to an existing structure in the formation of the rings. For earlier examples of bicycloannulation see: (a) C. F. Huebner, E. Donoghue, L. Dorfman, F. A. Stuber, N. Danieli, and E. Wenkert, *Tetrahedron Lett.*, 1185 (1966); (b) H. C. Brown and E. Negishi, *J. Am. Chem. Soc.*, **89**, 5478 (1967); H. C. Brown, "Organic Syntheses Via Boranes", Wiley, New York, 1975, pp 129–132, 158–68; (c) T. J. Katz and J. J. Cheung, *J. Am. Chem. Soc.*, **91**, 7772 (1969); T. J. Katz, E. J. Wang, and N. Acton, *ibid.*, **93**, 3782 (1971); I. Murata, T. Tatsuoka, and Y. Sugihara, *Tetrahedron Lett.*, 4261 (1973); U. Burger and F. Mazenod, *ibid.*, 2881 (1976); R. M. Pagni, M. Burnett, and A. C. Hazell, *J. Org. Chem.*, **43**, 2750 (1978); (d) S. Danishefsky, W. E. Hatch, M. Sax, E. Abola, and J. Pletcher, *J. Am. Chem. Soc.*, **95**, 2410 (1973); (e) P. W. Hickmott, H. Suschitzky, and R. Urbani, *J. Chem. Soc., Perkin Trans. 1*, 2063 (1973); (f) W. G. Dauben and A. P. Kozikowski, *Tetrahedron Lett.*, 3711 (1973).

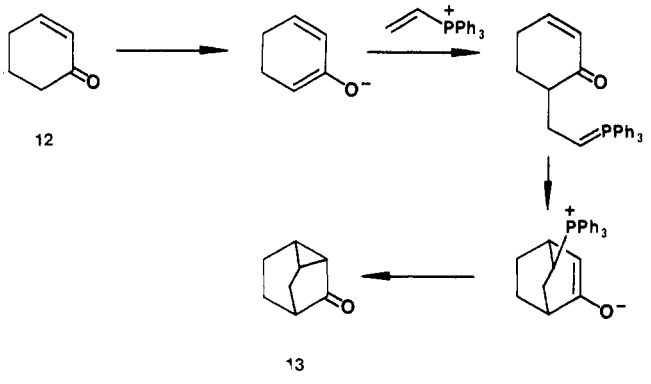
(21) For recent studies on the electronic structure of vinylphosphonium salts, see: T. A. Albright, W. J. Freeman, and E. E. Schweizer, *J. Am. Chem. Soc.*, **97**, 2946 (1975); T. A. Albright, S. V. de Voe, W. J. Freeman, and E. E. Schweizer, *J. Org. Chem.*, **40**, 1650 (1975).

(22) E. E. Schweizer and G. J. O'Neill, *J. Org. Chem.*, **30**, 2082 (1965); I. Kawamoto, S. Muramatsu, and Y. Yura, *Tetrahedron Lett.*, 4223 (1974); *Synth. Commun.*, **5**, 185 (1975); P. L. Fuchs, *Tetrahedron Lett.*, 4055 (1974); G. Büchi and M. Pawlak, *J. Org. Chem.*, **40**, 100 (1975); W. G. Dauben and J. D. Robbins, *Tetrahedron Lett.*, 151 (1975); A. T. Hewson, *ibid.*, 3267 (1978); S. F. Martin and S. R. Desai, *J. Org. Chem.*, **43**, 4673 (1978). An annulation sequence involving a Diels–Alder cycloaddition (with the vinylphosphonium salt acting as the dienophile) followed by a Wittig condensation has also been reported: R. Bonjouklian and R. A. Ruden, *J. Org. Chem.*, **42**, 4095 (1977).

(23) E. E. Schweizer, *J. Am. Chem. Soc.*, **86**, 2744 (1964); E. Zbiral, *Synthesis*, 775 (1974); M. E. Garst and T. A. Spencer, *J. Org. Chem.*, **39**, 585 (1974); W. Flitsch and E. R. Gesing, *Tetrahedron Lett.*, 1997 (1976); U. Widmer, N. Gakis, B. Arnet, H. Heimgartner, and H. Schmid, *Chimia*, **30**, 453 (1976); J. M. McIntosh and R. S. Steevensz, *Can. J. Chem.*, **55**, 2442 (1977); M. A. Calcagno and E. E. Schweizer, *J. Org. Chem.*, **43**, 4207 (1978).

(24) J. P. Freeman, *Chem. Ind. (London)*, 1254 (1959); *J. Org. Chem.*, **31**, 538 (1966); H. J. Bestmann and F. Seng, *Angew. Chem., Int. Ed. Engl.*, **1**, 116 (1962); P. A. Grieco and R. S. Finkelhor, *Tetrahedron Lett.*, 3781 (1972); W. G. Dauben, D. J. Hart, J. Ipaktschi, and A. P. Kosikowski, *ibid.*, 4425 (1973); R. F. Heldeweg, H. Hogeveen, and E. P. Schudde, *J. Org. Chem.*, **43**, 1912 (1978); M. J. Devos, J. N. Denis, and A. Krief, *Tetrahedron Lett.*, 1847 (1978); 1511, 1515 (1979).

Scheme II. Vinylphosphonium Bicycloannulation



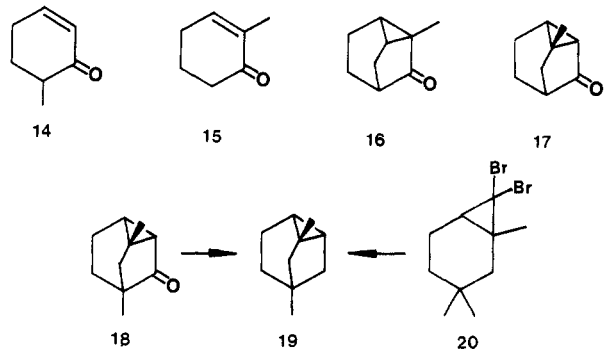
lecular cyclopropanation of the type proposed in Scheme I was known.[25] With regard to the last step in Scheme I, analogous transformations were involved in previous syntheses by Kelly[26] and Herz.[27]

The α' enolate 8 is expected to be kinetically preferred over the more stable γ enolate, and such cross-conjugated dienolates are readily formed by treatment of the corresponding α-cyclohexenones with an excess of a hindered strong base.[28] The first two steps in Scheme I have a very close analogy in the annulation of cyclohexenones by Michael acceptors.[29] Following publication of our initial paper,[15a] the bicycloannulation of cyclohexenones with methyl α-bromocrotonate was reported by Hagiwara and co-workers.[30] In this case, the activating group (CO_2CH_3) is *different* from the leaving group (Br), but the reaction is otherwise analogous to that shown in Scheme I. The successful use of vinylphosphonium salts in the bicycloannulation of cyclohexenones and the implementation of Scheme I by this method are now described in detail.[31,32]

Results and Discussion

Model Studies. Reduced to its simplest form, our initial objective was the observation of the reaction shown in Scheme II. A fairly large number of tricyclo-[3.2.1.$0^{2,7}$]octan-6-ones, of which **13** is the parent, have been prepared by copper-catalyzed cyclization of cyclohexenyl diazomethyl ketones.[33,34] Since the parent ketone **13** had been prepared in this manner[33a,b] and was therefore available for comparison purposes, the α' enolate of 2-cyclohexen-1-one (**12**) was prepared with lithium diisopropylamide (LDA) in THF and allowed to react with VTB at reflux. No volatile product was obtained, but the formation of the desired enolate was confirmed in a separate experiment by methylation[35] with methyl iodide, which gave a moderate yield of the monomethyl product **14** as the only volatile material isolated.

In contrast to the parent ketone **12**, however, 2-methyl-2-cyclohexen-1-one (**15**) gave a 9% yield of the desired tricyclic ketone **16** under the same conditions. The



structure of the product was assigned by comparison of its spectral data with those previously reported by Scanio and Lickei.[33d,34,36] Only 4% of the starting material was recovered, but no other volatile material was obtained. The large amount of brown intractable gum formed here and in the reaction with **12** indicated that a possible explanation for the consumption of most of the starting ketone without producing the desired product would be copolymerization of the enolate and the vinylphosphonium salt.

Since an isopropenyl (rather than unsubstituted vinyl) phosphonium salt (**11**) was required for the synthesis of the trachylobane system, it was important to also test the bicycloannulation method on isopropenyltriphenylphosphonium bromide (ITB, **11**, R = Ph, X = Br) and simple α-cyclohexenones. Surprisingly, reaction of ITB with the α' enolate from the parent enone **12**, which had failed to give any of the desired ketone **13** from VTB, led to a 17% yield of the expected tricyclic ketone **17**, the spectral properties of which were completely consistent with this structure. These included a ketone carbonyl absorption at 1712 cm^{-1} in the infrared spectrum, a methyl singlet at δ 1.32 in the ^1H NMR spectrum, which was further interpreted with the aid of a shift reagent (vide

(25) H. J. Bestmann and H. Morper, *Angew. Chem., Int. Ed. Engl.*, 6, 561 (1967).

(26) R. B. Kelly, J. Eber, and H.-K. Hung, *Can. J. Chem.*, 51, 2534 (1973); *J. Chem. Soc., Chem. Commun.*, 689 (1973); R. B. Kelly, B. A. Beckett, J. Eber, H.-K. Hung, and J. Zamecnik, *Can. J. Chem.*, 53, 143 (1975).

(27) W. Herz, R. N. Mirrington, and H. Young, *Tetrahedron Lett.*, 405 (1968); W. Herz, R. N. Mirrington, H. Young, and Y. Y. Lin, *J. Org. Chem.*, 33, 4210 (1968).

(28) J. d'Angelo, *Tetrahedron*, 32, 2979 (1976).

(29) (a) R. A. Lee, *Tetrahedron Lett.*, 3333 (1973); (b) H. Hagiwara, K. Nakayama, and H. Uda, *Bull. Chem. Soc. Jpn.*, 48, 3769 (1975); (c) K. B. White and W. Reusch, *Tetrahedron*, 34, 2439 (1978); (d) D. Spitzner, *Angew. Chem., Int. Ed. Engl.*, 17, 197 (1978); *Tetrahedron Lett.*, 3349 (1978). See also: R. K. Boeckman, Jr., J. P. Bershas, J. Clardy, and B. Solheim, *J. Org. Chem.*, 42, 3630 (1977); M. E. Jung and C. A. McCombs, *J. Am. Chem. Soc.*, 100, 5207 (1978).

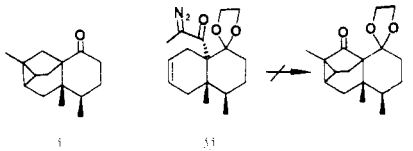
(30) H. Hagiwara, T. Kodawa, H. Kosugi, and H. Uda, *J. Chem. Soc., Chem. Commun.*, 413 (1976).

(31) For related heterocyclic bicycloannulations, see M. E. Garst, *J. Org. Chem.*, 44, 1578 (1979), and references therein.

(32) We have found two other classes of compounds which perform the work of reagent **9**; these studies will be reported in due course.

(33) (a) W. v. E. Doering, E. T. Fossel, and R. L. Kaye, *Tetrahedron*, 21, 25 (1965); (b) H. O. House, S. G. Boots and V. K. Jones, *J. Org. Chem.*, 30, 2519 (1965); (c) W. F. Erman and L. C. Stone, *J. Am. Chem. Soc.*, 93, 2821 (1971); (d) C. J. V. Scanio and D. L. Lickei, *Tetrahedron Lett.*, 1363 (1972); (e) D. Becker and H. J. E. Loewenthal, *Isr. J. Chem.*, 10, 375 (1972); (f) L. N. Mander, R. H. Prager, and J. V. Turner, *Aust. J. Chem.*, 27, 2645 (1974); (g) A. Tahara, M. Shimagaki, S. Ohara, T. Tanaka, and T. Nakata, *Chem. Pharm. Bull.*, 23, 2329 (1975); (h) U. R. Ghatak, S. K. Alam, P. C. Chakraborti, and B. C. Ranu, *J. Chem. Soc., Perkin Trans. 1*, 1669 (1976).

(34) Significantly, the attempted synthesis of ishwarone (i) via the diazo ketone ii met with failure: C. J. V. Scanio and D. L. Lickei, "Abstracts of Papers", 166th National Meeting of the American Chemical Society, Chicago, IL, Aug 1973, American Chemical Society, Washington, DC, 1973, No. AGFD 32; D. L. Lickei, Ph.D. Dissertation, Iowa State University, Ames, IA, 1973 [*Diss. Abstr.*, 34, 4880-B (1974)].



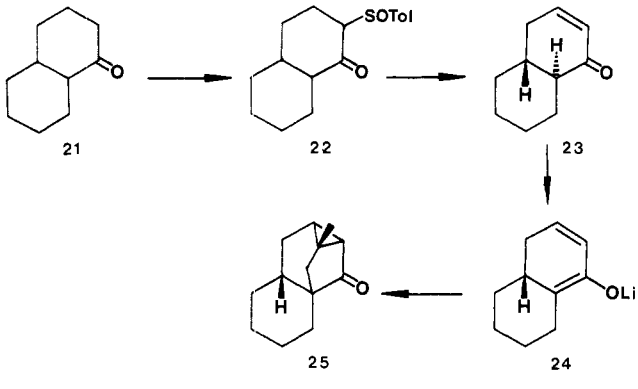
(35) R. A. Lee, C. McAndrews, K. M. Patel, and W. Reusch, *Tetrahedron Lett.*, 965 (1973); *J. Org. Chem.*, 40, 1504 (1975); M. Tanabe and D. F. Crowe, *J. Chem. Soc., Chem. Commun.*, 564 (1973); C. Agami, J. Levisalles, and B. LoCicero, *Tetrahedron*, 35, 961 (1979); C. Agami, M. Chauvin, and J. Levisalles, *Tetrahedron Lett.*, 1855 (1979); P. A. Grieco, S. Ferriño, and T. Oguri, *J. Org. Chem.*, 44, 2593 (1979).

(36) We are grateful to Dr. C. J. V. Scanio for a copy of the pertinent pages of D. L. Lickei's thesis.

infra), and the correct mass-to-charge ratio of the molecular ion in the mass spectrum. The ^{13}C NMR spectral data for this and all other polycyclic compounds described herein have already been published and were also very useful in their identification.[37] In addition to the fact that ITB gave the desired product while VTB did not with the same substrate, it was also interesting to note that the reaction with ITB proceeded at room temperature, whereas VTB required refluxing to force the reaction to completion in all cases in which it did give the desired product. Possible reasons for these results are discussed further on in this paper.

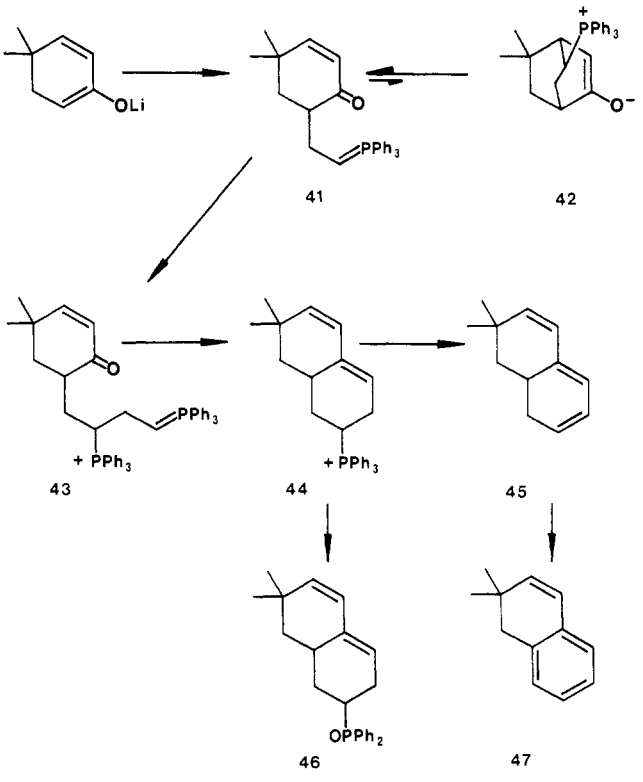
In order to study the reaction with a model somewhat closer in structure to the proposed trachylobane precursor 8, we treated the α' enolate of 6-methyl-2-cyclohexen-1-one (14), obtained as described above by methylation of 12, with VTB in refluxing THF, but only brown intractable material was obtained. Surprisingly, the same substrate on reaction with ITB at room temperature in THF gave a 44% yield of the desired tricyclooctanone 18. The structure was again inferred from spectral data, and further confirmation was procured by Wolff–Kishner reduction to the corresponding hydrocarbon, tricyclooctane 19. The latter was found to be identical with one of the products isolated[1] from reaction of the dibromocyclopropane 20 with methyllithium. In addition to aiding the structural assignments, this correlation served nicely to compare our two bicycloannulation methods and to show that either method can be used to synthesize the same compound in at least some cases.[38]

It was now apparent that we had in hand a powerful method for the construction of the trachylobane system in a single step, the efficiency of which, in terms of time and convenience, far out weighed any consideration of the low to moderate yields obtained. For a model structurally closer to Scheme I, octalone 23, which possesses the B- and C-ring portion of the projected trachylobane precursor 8, was synthesized from 1-decalone (21) by sulfinylation[39] and

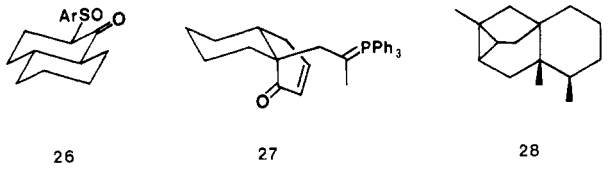


sulfoxide elimination.[40] The intermediate sulfoxide 22, prepared by reaction of 21 with methyl *p*-toluenesulfinate in the presence of sodium hydride,[39] appeared to be a mixture of diastereomers, but one of these could be separated by fractional crystallization. This pure diastereomer exhibited a doublet of doublets in its NMR spectrum at δ 3.38 with coupling constants of 8 and 11 Hz, indicating[41]

Scheme III. Reaction of VTB with 33



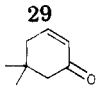
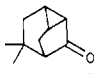
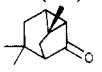
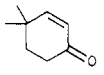
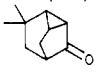
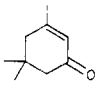
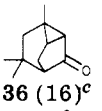
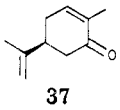
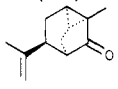
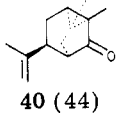
an equatorial configuration for the toluenesulfinyl group. The most likely structure for this isomer would have the more stable trans ring fusion as shown in 26, where the



configuration at sulfur is unknown. Even though the overall yield of octalone 23 was only about 20% from this two-step sequence, it was much more convenient than the previously reported preparation of this compound, which required more steps and gave a lower overall yield.[42] Treatment of the α' enolate (24) of this octalone with ITB smoothly produced, stereoselectively, the desired tetracyclic ketone 25 in 36% yield. The stereochemistry was deduced mainly by an NMR shift reagent study (vide infra) and was confirmed by ^{13}C NMR.[37] Thus, even without the help of the (axial) angular methyl group in enolate 8, the trachylobane stereochemistry obtains. In order to produce this result, initial attack by ITB must be from the α face of enolate 24 to give the *cis*-octalone 27. This preference for a cis ring junction has been observed in related alkylations and has been explained in terms of steric hindrance to approach from the α face (which gives the trans ring fusion).[43] With the very bulky reagent ITB, the stereoselectivity is apparently enhanced to the point of exclusion of the other possible diastereomer. The ketone 25 is also of interest in that it embodies the ring system of the sesquiterpene ishwarane (28) and points the way to

(37) R. M. Cory and J. B. Stothers, *Org. Magn. Reson.*, 11, 252 (1978).
(38) For syntheses of ishwarane (28) and ishwarone (i, ref 34) using our "carbon atom insertion" bicycloannulation, see respectively: R. M. Cory and F. R. McLaren, *J. Chem. Soc., Chem. Commun.*, 587 (1977); R. M. Cory, D. M. T. Chan, F. R. McLaren, M. H. Rasmussen, and R. M. Renneboog, *Tetrahedron Lett.*, 4133 (1979).
(39) R. M. Coates and H. D. Pigott, *Synthesis*, 319 (1975). See also H. J. Monteiro and J. P. de Souza, *Tetrahedron Lett.*, 921 (1975).
(40) B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Am. Chem. Soc.*, 98, 4887 (1976); B. M. Trost, *Chem. Rev.*, 78, 363 (1978).
(41) A. Casadevall, E. Casadevall, and M. Mion, *Bull. Soc. Chim. Fr.*, 4498 (1968); C. Cuvelier, R. Ottinger, and J. Reisse, *Tetrahedron Lett.*, 277 (1972).
(42) W. S. Johnson, J. D. Bass, and K. L. Williamson, *Tetrahedron*, 19, 861 (1963).
(43) H. O. House and B. M. Trost, *J. Org. Chem.*, 30, 2502 (1965); H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, Menlo Park, CA, 1972, pp 592–3.

Table I. Bicycloannulation of Cyclohexenones

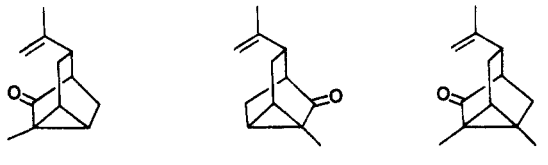
entry	substrate	reagent	procedure[a]	products (% yield)
1	12	VTB	A	nil[b]
2	12	ITB	D	17 (17)[c]
3	14	VTB	A	nil[b]
4	14	ITB	D	18 (44)[c]
5	15	VTB	A	16 (9)[c]
6	 29	VTB	C	nil[b]
7	 30	VTB	C	 31 (13)[c]
8	30	ITB	B	 32 (42)
9	 33	VTB	A	 + others[d] 34 (low)
10	 35	VTB	E	 + 35 (45)[c] 36 (16)[c]
11	 37	VTB	E	 + other[d] 38 (32)[c] 39 (2)[c]
12	37	VTB	A	(38 + 39) (18)
13	37	VTB	C	(38 + 39) (20)[c]
14	37	VTB	E + HMPA	(38 + 39) (35)[c]
15	37	ITB	B	 40 (44)
16	23	ITB	D	25 (36)[c]

[a] See Experimental Section. [b] No volatile products. [c] Determined by GC (internal standard). [d] See text.

a potential synthesis of this natural product as well.[38]

In order that the effect of cyclohexenone substituents on the bicycloannulation could be more fully evaluated, several additional substrates were subjected to our bicycloannulation procedure with VTB and ITB, and the results of these experiments are summarized in Table I, along with those discussed above. With two substituents at the 4(γ)-position (**33**), the second step in the presumed bicycloannulation mechanism, which involves attack by the ylide carbon (α to P) at the β-carbon of the enone, is almost completely blocked. As a result, although a small amount of impure product tentatively assigned the desired structure **34** was obtained, the major products were formed by condensation of *two* vinylphosphonium moieties with one enolate. A possible mechanistic scheme, shown in Scheme III, is that in which the equilibrium for the cyclization of the ylide **41** to the zwitterion **42** is unfavorable due to steric hindrance to attack at the β-position of the enone moiety in **41**, forcing the ylide to react with a second vinylphosphonium ion to give the 2:1 adduct **43**. The latter can then undergo an intramolecular Wittig condensation[22] to form phosphonium ion **44**. Under the strongly basic conditions of the reaction, **44** could then undergo E2 elimination of a proton and triphenylphosphine, and the resulting triene **45** apparently undergoes air oxidation on workup to give the aromatization product **47**, which had been previously described.[44] The remainder of the phosphonium salt **44** is evidently hydrolyzed[45] on workup with aqueous sodium bicarbonate to the phosphine oxide **46**, which was isolated in relatively large quantities. The latter was apparently a mixture of diastereomers and could not be purified by recrystallization, but spectral data were completely consistent with this structure.

The bicycloannulation of *d*-carvone (**37**) was especially interesting since it showed a strong stereoselectivity for the product formed by attack of the phosphonium ion on that face of the enolate opposite to the isopropenyl group. Logically, this selectivity is enhanced for the more bulky ITB over that for VTB, so that while a small percentage of minor product (**39**) was obtained from VTB, reaction



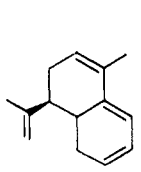
38 39 40

with ITB led exclusively to **40**. A third product, obtained in 13% yield, from the reaction of the α' enolate of carvone with VTB was the tetraene **48**, analogous to the triene **45** and presumably formed in the same way.

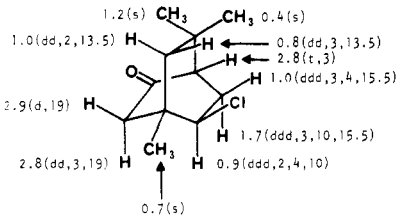
The conditions for the bicycloannulation were varied to some degree as the project evolved. At first the vinyl-

(44) A. Costantino, G. Linstrumelle, and S. Julia, *Bull. Soc. Chim. Fr.*, 912 (1970).

(45) S. Warren, *Acc. Chem. Res.*, 11, 401 (1978).



48

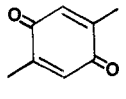


49

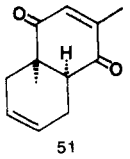
phosphonium salt was inconveniently added in solid form all at once (procedure A), but it was subsequently found that the moderate solubility of the salts in pyridine (procedures B and C) allowed them to be added dropwise in this solvent without affecting the yield (cf. Table I, entries 12 and 13).[46] Furthermore, switching from methyllithium in THF to *n*-butyllithium in *hexane*–THF for the formation of LDA from diisopropylamine led to greatly increased yields (cf. Table I, entries 13 and 11) and convenience (procedures D and E). Addition of hexamethylphosphoramide (HMPA) to the reaction mixture just before VTB had virtually no effect (cf. Table I, entries 11 and 14). This last observation is particularly interesting in view of a recent statement that HMPA is "essential" for the annulation of cyclohexenone α' enolates with α-phenylthio- and α-phenylsulfinylcrotonic esters.[29b]

The structure of the tricyclic product **36** was confirmed by addition of hydrogen chloride[33b] with cyclopropane ring opening to give the corresponding bicyclo[2.2.2]octanone **49**, shown with relative LIS (lanthanide induced shifts) induced by Eu(fod)$_3$ in the ^{1}H NMR spectrum and with multiplicities and coupling constants in parentheses assigned by decoupling.

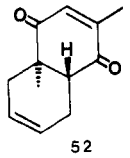
In connection with one of our projected routes[47] to trachylobane, we also had occasion to test the bicycloannulation method on the enedione **52**. This compound,



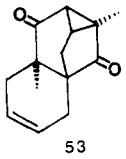
50



51



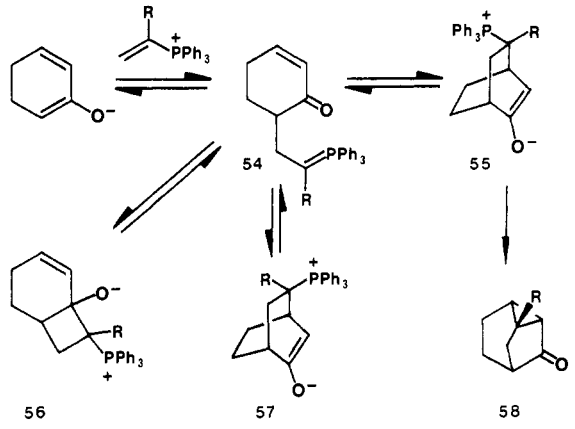
52



53

prepared by boron trifluoride catalyzed[48] Diels–Alder addition of the quinone **50** to 1,3-butadiene, is presumed to have been formed via the cis isomer **51**.[49] A closely related adduct has been reported to undergo epimerization under the same conditions.[50] Although bicycloannulation of **52** with VTB did give a low yield of the desired tetracyclic diketone **53**, it was insufficient to merit further pursuit of this idea. Although the angular methyl group should provide steric hindrance to attack from its side, this interpretation should be considered with a certain amount of caution, since Δ^6-1-octalones are alkylated at C-9 to give predominate trans ring fusion even without an angular (C-10) methyl group already present.[51]

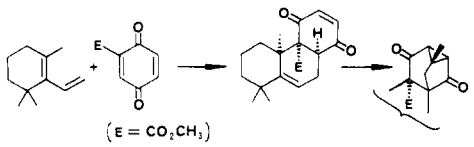
Scheme IV. Mechanism



Our mechanistic description of the processes occurring in the course of these bicycloannulation reactions is diagrammed in Scheme IV. With either of the vinylphosphonium salts, VTB (R = H) or ITB (R = Me), in the procedure (E or D, respectively) which gave the highest yields, the salt was added dropwise in pyrdine solution to a solution of the enolate in THF–hexane (containing excess LDA to ensure that the α' enolate did not equilibrate with the more stable γ enolate) at room temperature. At the end of the addition, the enolate was almost completely consumed, as judged by working up a small aliquot and subjecting it to GC analysis using an internal standard. In the case of ITB, the formation of the tricyclooctanone **58** (R = Me) was essentially complete at this point, and only 1 or 2 h at room temperature was required to finish it. After that, refluxing the mixture did not increase or decrease the yield of product. By contrast, the formation of **58** (R = H) from VTB was only partial at room temperature, and the yield of **58** was increased considerably by a few hours of reflux. Likewise, the addition of VTB to the enolate solution *at reflux* did not change the amount of **58** obtained. Thus, while the addition of the phosphonium salt is being carried out, conjugate attack by the enolate on the double bond of the salt occurs at room temperature to give the intermediate enone ylide **54**. The ylide could conceivably undergo 1,2-addition to the carbonyl group, forming betaine **56**, but this is presumably prohibited by strain. Consequently, it can add 1,4 to the enone system in two ways to give either the anti zwitterion **55** or the syn zwitterion **57**. It may also reverse to the enolate and vinylphosphonium salt, or it may initiate polymerization of the salt and/or the enolate. With ITB the entire sequence leading to the tricyclooctanone **58** (R = Me) is over fairly quickly at room temperature, but with VTB only a small portion of the ultimate yield of **58** (R = H) is obtained at room temperature. Thus, some of the material from reaction with VTB is held at an intermediate stage which does not give **58** until the mixture is heated to reflux.

(46) We are grateful to Professor J. M. McIntosh, University of Windsor, for the recommendation of the use of pyridine as solvent for the difficultly soluble phosphonium salts.

(47) This proposal involved the following sequence:



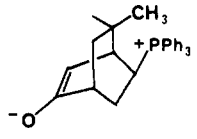
(48) Z. Stojanac, R. A. Dickinson, N. Stojanac, R. J. Woznow, and Z. Valenta, *Can. J. Chem.*, **53**, 616 (1975).

(49) L. F. Fieser and A. M. Seligman, *Chem. Ber.*, **68**, 1747 (1935). See also J. J. Sims and V. K. Honwad, *Tetrahedron Lett.*, 2155 (1973).

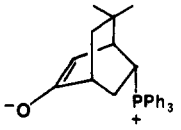
(50) F. Bohlmann, W. Mathar, and H. Schwarz, *Chem. Ber.*, **110**, 2028 (1977).

(51) W. S. Johnson, D. S. Allen, Jr., R. R. Hindersinn, G. H. Sansen, and R. Pappo, *J. Am. Chem. Soc.*, **84**, 2181 (1962); R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615, 1620 (1962).

The effect of two substituents on the 4-position of the cyclohexenone, as in the case of **33**, may be to prevent the formation of the required anti configuration **55** due to the fact that there would be a very strong steric repulsion between the large PPh_3 substituent and one of the methyl groups in this intermediate (**59**). While the syn isomer



59



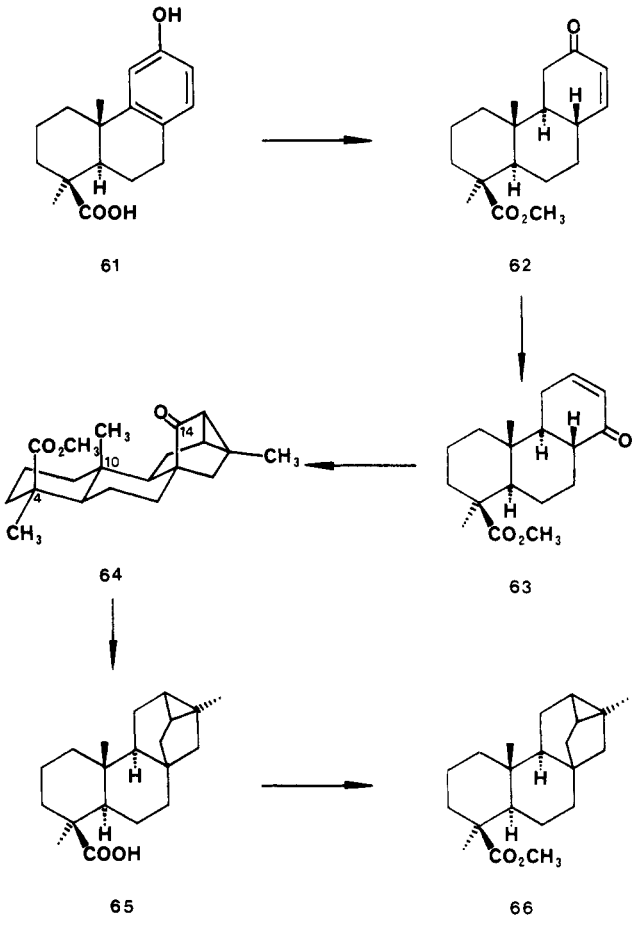
60

60 may be formed, it is expected to be easily reversible to the enone ylide corresponding to **54**, which then reacts as shown in Scheme II.

The fact that bicycloannulation with ITB was complete at room temperature and gave higher yields than that with VTB is one of the most intriguing of our findings. The better yields from ITB may be due, at least in part, to a decreased tendency of ITB to polymerize. However, the increased rate of formation of **58** (R = Me) from ITB may also be a result of faster displacement of PPh_3 from the zwitterion **55**. In this case, the greater steric repulsion between the leaving PPh_3 group and the tertiary alkyl center (R = Me) may be the determining factor. Alternatively, if all or some of the displacement is occurring via a diradical (electron-transfer) pathway,[52] even the syn zwitterion **57** could give **58** directly, and the tertiary radical intermediate would be more stable than the corresponding secondary one. This mechanism for substitution reactions, however, has been well established only for nitro compounds. The possibility that an S_N1i mechanism may obtain for the formation of **58** from **55** or **57** when R = Me but not when R = H cannot be ruled out at this time, but it does not seem likely.

Synthesis of Trachyloban-19-oic Acid. All considerations of mechanism aside, the model studies did serve to demonstrate that this bicycloannulation method was worthy of an assault on the trachylobane system. The most readily available precursor was the enone ester **63** which can be prepared from podocarpic acid (**61**) in a relatively straightforward manner[53] via the isomeric enone ester **62** (Scheme V). Podocarpic acid has been used to good advantage as the starting material for a variety of natural product syntheses,[54] and since it has itself been totally synthesized,[55] any synthesis of a natural product from naturally derived podocarpic acid constitutes a formal total synthesis. It will be noted, however, that **61** is related to the class of diterpenes *enantiomeric* to the corresponding diterpenes in the series to which the trachylobanes belong. Thus, **61** can only lead by synthetic modification to an enantiomer of a naturally occurring trachylobane diterpene. The use of the enone **63** would therefore be expected to provide trachyloban-19-oic acid (**65**), the *enantiomer* of *ent*-trachyloban-19-oic acid (**1**), upon vinylphosphonium bicycloannulation with ITB and

Scheme V. Synthesis of Trachyloban-19-oic Acid



61 62 64 63 65 66

reductive removal of the carbonyl oxygen.

Accordingly, enone **63** was prepared from podocarpic acid and was subjected to bicycloannulation with ITB. In consonance with the model studies, this reaction provided a 23% yield of the desired pentacyclic keto ester **64**, which was formed with complete stereoselectivity as predicted. The stereochemical configuration was deduced from spectral data, including ^{13}C NMR[37] and, most convincingly, ^1H NMR. In particular, the C-10 methyl group is strongly shielded both by the ester carbonyl and by the carbonyl group at C-14.[56] This is best seen by comparing its chemical shift at δ 0.53 with the corresponding methyl group in methyl trachyloban-19-oate (**66**) at δ 0.77 and in methyl trachylobanate at δ 0.97.[27] If the attack of ITB had been on the opposite (β) face of the enolate, giving the stereoisomeric keto ester **67**, no such shielding of the C-10

67 68

methyl would be expected. In fact, the analogous methyl group in the structurally similar keto ester **68** is *deshielded* relative to that in methyl trachylobanate.[27]

In any event, the structure assigned to the bicycloannulation product was confirmed by its successful con-

(52) N. Kornblum, *Angew. Chem., Int. Ed. Engl.*, **14**, 734 (1975); Z. V. Todres, *Russ. Chem. Rev. (Engl. Transl.)*, **47**, 148 (1978).

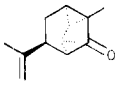
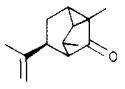
(53) R. C. Cambie and A. W. Missen, *Aust. J. Chem.*, **25**, 973 (1972). Our modification of this synthesis, presented in the Experimental Section, is based on a procedure reported by I. Wahlberg, K. Karlsson, and C. R. Enzell, *Org. Mass Spectrom.*, 162 (1975).

(54) (a) N. N. Girotra and L. H. Zalkow, *Tetrahedron*, **21**, 101 (1965); (b) T. A. Spenser, R. A. J. Smith, D. L. Storm, and R. M. Villarica, *J. Am. Chem. Soc.*, **93**, 4856 (1971); (c) D. M. S. Wheeler and P. R. Witt, *J. Org. Chem.*, **37**, 4211 (1972); (d) W. S. Hancock, L. N. Mander, and R. A. Massy-Westropp, *J. Org. Chem.*, **38**, 4090 (1973).

(55) T. A. Spenser, R. J. Friary, W. W. Schmiegel, J. F. Simeone, and D. S. Watt, *J. Org. Chem.*, **33**, 719 (1968), and references therein.

(56) This effect is well-known in the diterpene field. See, for example: W. A. Ayer, C. E. McDonald, and J. B. Stothers, *Can. J. Chem.*, **41**, 1113 (1963); P. A. Gunn, R. McCrindle, and R. G. Roy, *J. Chem. Soc. C*, 1018 (1971); J. C. Fairlie, A. J. McAlees, R. McCrindle, and E. Neidert, *Can. J. Chem.*, **52**, 706 (1974).

Table II. Relative[a] LIS[b] for Tricyclo[3.2.1.0^{2,7}]octan-6-ones

compd	H-1	H-2	H-4-anti[c]	H-4-syn[c]	H-5	H-7	H-8-syn[c]
16				1.7	3.0	(2.0)[d]	1.5
17	(0.8)				3.1	2.5	1.4
31	1.1		(1.0)	(2.1)	3.7	2.7	1.6
32	(0.6)	1.1	(0.9)	(1.9)	3.5	2.7	1.7
36	1.0	(0.7)	(0.9)	(2.2)	3.3	2.4	1.7
38	1.2	1.4	1.3	(1.0), 1.9,[e] 0.5[e]	3.1	(1.7)	1.3
40	(0.6)	1.4	1.3	(1.0), 1.8,[e] 0.5[e]	3.2	(1.7)	1.3
 71			1.1	(0.7), 1.6,[e] 0.4[e]	2.7	(1.2)	(0.9)
 72			(0.3), 0.5,[e] 0.3[e]	1.8	2.7	(1.7)	(1.0)

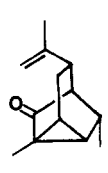
[a] H-8-anti LIS of 1.0. [b] Lanthanide induced shifts (downfield), extrapolated to a mole ratio of Eu(fod)$_3$/ketone of 1.0. [c] Anti and syn are with respect to the carbonyl bridge. [d] Numbers in parentheses are LIS for methyl protons. [e] LIS for vinyl protons.

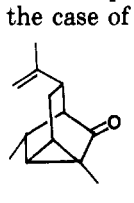
version to ester **66**. Thus, Wolff–Kishner reduction of the keto ester **64** proceeded with concomitant saponification to trachyloban-19-oic acid (**65**), the identity of which was inferred from its esterification by diazomethane to methyl trachyloban-19-oate (**66**) in ca. 30% overall yield from keto ester **64**. When compared with this synthetic material (**66**), an authentic sample of methyl *ent*-trachyloban-19-oate (**5**) kindly provided by Professor R. McCrindle of the University of Guelph showed identical ^{1}H and ^{13}C spectra and TLC and GC behavior. As expected, however, the ORD curve of the synthetic ester was the mirror image of that of the authentic ester derived from sunflower heads, the two enantiomers being dextrorotatory and levorotatory, respectively.

It is worthwhile to compare this one-step synthesis of the trachyloane system (**64**) from the ABC precursor **63** in 23% yield with the analogous (multistep) constructions previously reported. The total synthesis of trachylobane (**4**) by Kelly's group required some 12 steps and gave an 11% overall yield,[26] while the synthesis of methyl trachylobanate provided a 4% yield in nine steps, as reported earlier by Herz and co-workers.[27] Although these are somewhat imperfect comparisons, in that the starting materials are similar but not identical, they do give a rough idea of the great savings of time, effort, and materials afforded by the use of the bicycloannulation method described here. The most important advantage it offers, of course, is the fact that the preparation of a complex, strained tricyclic system, the fabrication of which would otherwise require a long sequence of synthetic transformations, can be effectiently accomplished in a single operation from a monocyclic precursor.[57] Furthermore, tricyclooctanones and derivatives thereof which were not available by previously known routes may be obtained easily by vinylphosphonium bicycloannulation.

Proton NMR Studies. The use of the shift reagent Eu(fod)$_3$ was extremely helpful in assigning the proton NMR resonances and hence the structures of the tricyclic ketones, as well as the tetracyclic ketones **25** and **53**. Although a quantitative evaluation of the data (Table II) was not possible,[58] the shifts are qualitatively what one would expect on the basis of the proximity of each proton to the carbonyl group.[59] Average shifts are presented in structure **73** (LIS for methyl protons in parentheses), in which the most striking feature is the very strong shift of the protons α to the carbonyl group relative to the others. Analogous behavior has been reported for related ketones.[58]

The stereochemistry of the isopropenyl group in the carvone products **38** and **40** is apparent from examination of the LIS for H-4 and the protons of the isopropenyl group. Thus, in each case a relatively small shift is seen for H-4, indicating an anti orientation, and the *syn*-vinyl proton is shifted 3.8 times farther than the *anti*-vinyl proton, an observation which is consistent only with a syn orientation for the isopropenyl group. This conclusion is confirmed by a comparison with the corresponding shifts for compounds **69** and **70**.[60] In the case of **70**, the H-4

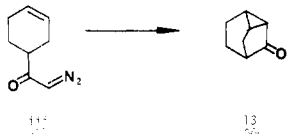

69


70

proton is shifted significantly farther than that in **69**, **40**, or **38**, and both of the vinyl protons show a very small shift as expected for an *anti*-isopropenyl group. Furthermore, the signal for the *methyl* protons of the isopropenyl group in **70** is shifted to a much smaller extent than the corresponding signals in **69**, **40**, and **38**.

Since no coupling was observed between H-8-anti and those vicinal to it at carbons 1 and 5, its absorption always

(57) While the copper-catalyzed cyclization of cyclohexenyl diazomethyl ketones[33] also does this in one step (e.g., iii → **13**), the diazo ketone must first be prepared, usually from the corresponding carboxylic acid chloride, which itself is not always readily available.



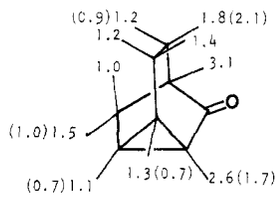
(58) We were unable to obtain agreement between the observed shifts and those calculated by means of the McConnell–Robertson equation. For a discussion of the problems involved, see H.-J. Schneider and E. F. Weigand, *Tetrahedron*, **31**, 2125 (1975). For recent studies of LIS of cyclopropyl ketones, see: (a) C. G. Andrieu, B. Lemarié, and D. Paquer, *Org. Magn. Reson.*, **6**, 479 (1972); (b) K. Hayakawa, H. Schmid, and G. Fráter, *Helv. Chim. Acta*, **60**, 561 (1977); (c) W. R. Dolbier, Jr., and O. T. Garza, *J. Org. Chem.*, **43**, 3848 (1978); (d) R. J. Abraham, D. J. Chadwick, and F. Sancassan, *Tetrahedron Lett.*, 265 (1979).

(59) R. M. Cory and A. Hassner, *Tetrahedron Lett.*, 1245 (1972); A. Hassner, R. M. Cory, and N. Sartoris, *J. Am. Chem. Soc.*, **98**, 7698 (1976).

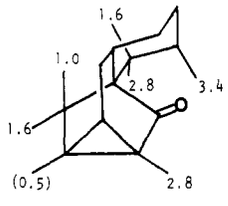
(60) The preparation of these compounds by P. C. Anderson in our laboratory will be reported separately.

appeared as a sharp doublet with a geminal coupling constant of 11–12 Hz (except in the case of compounds **69** and **70**). Other vicinal coupling constants (in hertz) are as follows (protons numbered in parentheses): 7 (1,2), 5–7 (1,7), 4 (1,8-syn), 2–3 (2,3-anti), 2–3 (2,3-syn), 8 (2,7), 14–15 (3-anti, 3-syn), 9–10 (3-anti, 4-anti), 8 (3-anti, 4-syn), 6 (3-syn, 4-anti), 8 (3-syn, 4-syn), 3 (4-anti, 5), 3 (4-syn, 5), 5–6 (5,8-syn). Long range (*W*) coupling was observed between H-4-syn and H-8-syn (2 Hz) and between H-5 and H-7 (1.5 Hz). All assignments were confirmed by selective decoupling, usually in the europium-shifted spectra.

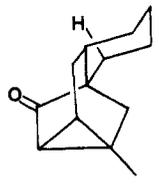
The LIS data (relative to H-8-anti) for the tetracyclic ketone **25** are shown in structure **74**. The signal shifted



73



74



75

farthest downfield (relative LIS of 3.4) appeared as a complex multiplet with $\sum J \simeq 50$ Hz. This total coupling could only arise from an axial proton flanked by two methylene groups, and it is thus assigned the position shown in **74**, which from a molecular model can be seen to be closest to the carbonyl oxygen. By contrast, the proton closest to the carbonyl oxygen in the stereoisomer **75** is that shown and would be expected to have a total coupling of only ca. 25 Hz, half that observed. The structure assigned to ketone **25** was also confirmed by ^{13}C NMR.[37]

Conclusions

Vinyl- and isopropenyltriphenylphosphonium bromide react with the α' enolates from a variety of α-cyclohexenones to give low to moderate yields of tricyclo[3.2.1.0^{2,7}]octan-6-ones. In spite of the 10–45% yields for this bicycloannulation procedure, the method is of great value because of its brevity, its convenience, and the general absence of volatile byproducts in most cases. ITB proved to be superior in efficiency, providing more of the desired bicycloannulation product and at a faster rate and lower temperature. In cases where a stereochemical duality is possible, the reaction is highly stereoselective, a fact attributable to the large bulk of the vinylphosphonium ions.

Since tricyclo[3.2.1.0^{2,7}]octane-6-ones have proven to be quite versatile in natural product synthesis,[33] the utility of vinylphosphonium bicycloannulation will certainly extend beyond synthesis of the trachylobane system. In addition, the fact that this method is capable of rapidly providing substituted tricyclooctanones not available by other means opens up new synthetic possibilities, some of which are currently under investigation in this laboratory. Finally, the general principles involved in the design of the vinylphosphonium salts as bicycloannulation reagents should not be limited to this class of compounds, and a search for other types of compounds with this ability may lead to even more powerful bicycloannulation methods.[32]

Experimental Section

All reactions were conducted under a positive pressure of argon. Ether, tetrahydrofuran, and dimethoxyethane were distilled from sodium–benzophenone, diisopropylamine was distilled from calcium hydride, pyridine was distilled from potassium hydroxide, and hexamethylphosphoramide was distilled from 13X molecular sieves. Preparative thick-layer chromatography was performed on precoated E. Merck silica gel GF (2 mm thick) on glass plates. Ethyl acetate was used to extract the separated components from the silica gel. Gas chromatography was carried out by using 1.5% OV-101 on Chromosorb G (100/120 mesh) in a 0.2 in. × 6 ft stainless-steel column with a helium flow rate of 60 mL/min unless otherwise noted.

Proton NMR spectra were recorded on a Varian HA-100 or XL-100 spectrometer, and chemical shifts are reported in parts per million downfield from internal tetramethylsilane. Infrared spectra were obtained on a Perkin-Elmer 621 spectrophotometer and are given in reciprocal centimeters. Mass spectra were determined on a Varian MAT-311A spectrometer employing an ionizing voltage of 70 eV. Melting and boiling points are uncorrected.

Methyllithium and *n*-butyllithium were obtained from Ventron as solutions in ether and hexane, respectively. They were titrated[61] with *sec*-butyl alcohol in xylene (bipyridyl indicator) before use.

6-Methyl-2-cyclohexen-1-one (14). To a solution of 2.4 mL (17.5 mmol) of diisopropylamine and ca. 2 mg of bipyridyl in 10 mL of THF at 0 °C was added dropwise 7.1 mL (14.9 mmol) of 2.1 M *n*-butyllithium in hexane. After the resulting red solution had been allowed to stir for 15 min at 0 °C, 1.2 g (12.5 mmol) of 2-cyclohexen-1-one (**12**) in 10 mL of THF was added dropwise. A further 30-min stirring at 0 °C was followed by rapid addition of 6 mL (130 mmol) of methyl iodide, which caused the color of the solution to change from red-purple to yellow. The ice bath was removed, and a white precipitate formed during 45 min of stirring at room temperature. The mixture was poured into 50 mL of saturated aqueous sodium bicarbonate and extracted with petroleum ether (bp 30–60 °C; 3 × 100 mL). The combined organic layers were washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, and concentrated by distillation of the solvent through a Vigreux column. At this point, GC showed only one peak in addition to that of the solvent and complete absence of the starting ketone. Short-path distillation afforded 0.77 g (56%) of pure **14** as a colorless liquid: bp 63–64 °C (9 mm) [lit.[62] bp 76–78 °C (15 mm)].

Bicycloannulation Procedure A. 7-Methyltricyclo[3.2.1.0^{2,7}]octan-6-one (16). About 2 mg of 2,2′-bipyridyl was dissolved in 6.6 mL (10.4 mmol) of 1.57 M ethereal methyllithium, and the bulk of the ether was evaporated under vacuum. After 10 mL of THF was added, the dark red solution was cooled to −65 °C, and 2.0 mL (14.1 mmol) of diisopropylamine was added. The mixture was stirred until evolution of methane had ceased and allowed to warm to −10 °C, and 0.846 g (7.69 mmol) of 2-methyl-2-cyclohexen-1-one[63] (**15**) in 5 mL of THF was added slowly dropwise. To the still dark red solution was then added 8 mL of THF, and, after the mixture had been allowed to warm to room temperature, 3.12 g (8.5 mmol) of VTB was added in one portion. The resulting reddish brown suspension was then heated to reflux, and the progress of the reaction was followed by GC. After 5 h of reflux no further change was noted, so the mixture was cooled to room temperature, poured into 50 mL of saturated aqueous sodium bicarbonate, and extracted with petroleum ether (bp 30–60 °C; 3 × 50 mL). The combined organic layers were washed with 50 mL of water and 50 mL of saturated aqueous

(61) S. C. Watson and J. F. Eastham, *J. Organomet. Chem.*, **9**, 165 (1967).

(62) H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975). For a related synthesis of **14**, see S. C. Goyal and S. M. Gupta, *Ann. Chim. (Paris)*, **2**, 57 (1977).

(63) E. W. Warnhoff, D. G. Martin, and W. S. Johnson, "Organic Syntheses", Collect. Vol. IV, Wiley, New York, 1963, p 162.

sodium chloride and dried over anhydrous sodium sulfate. GC analysis, using acetophenone as an internal standard, showed that 0.035 g (4%) of the starting ketone was recovered and that 0.095 g (9%) of the tricyclic ketone **16** was obtained. Evaporation of the solvent gave a yellowish brown oil which was subjected to bulb-to-bulb distillation. A light yellow liquid was collected at a bath temperature of 65–80 °C (0.1 mm), and pure **16** was separated from this by preparative GC on 5% Carbowax 20-M (programmed at 4 °C/min from 90 °C at injection). Spectral data were similar to those previously reported:[33d,34,36] IR (CCl_4) 1730 cm^{-1}; NMR (CCl_4) δ 1.16 (s, 3 H), 1.52 (m, 1 H), 1.76 (d, J = 11.5 Hz, 1 H), 1.8–2.3 (m, 7 H); MS m/e (relative intensity) 39 (35), 41 (30), 67 (43), 82 (51), 95 (99), 108 (41), 121 (4), 136 (100, M^+).

Bicycloannulation Procedure D. 1,5-Dimethyltricyclo[3.2.1.0^{2,7}]octan-6-one (18). To a solution of 0.94 mL (6.7 mmol) of diisopropylamine and 3 mg of bipyridyl in 5 mL of THF at 0 °C was added dropwise 2.8 mL (5.9 mmol) of 2.1 M *n*-butyllithium in hexane. After the resulting red solution had been allowed to stir for 15 min at 0 °C, 0.506 g (4.6 mmol) of **14** in 5 mL of THF was added dropwise over a period of 30 min, and the still reddish solution was stirred at 0 °C for 15 min. The ice bath was removed, and when the temperature of the solution had reached room temperature, 1.99 g (5.2 mmol) of ITB[67] in 15 mL of pyridine was added dropwise during 1 h. The mixture was stirred until GC showed no further increase in the product (2 h), poured into 50 mL of saturated aqueous sodium bicarbonate, and extracted with petroleum ether (3 × 50 mL). The combined organic layers were washed with cold 5% aqueous hydrochloric acid (3 × 50 mL), the combined HCl washes were back-washed with 50 mL of petroleum ether, and the combined petroleum ether solutions were washed with saturated aqueous sodium chloride and dried over anhydrous sodium sulfate. The solvent was removed by distillation through a Vigreux column, and bulb-to-bulb distillation [60–70 °C (0.1 mm)] gave **18** as a colorless liquid which was purified by preparative GC (115 °C). By GC analysis (biphenyl internal standard) the yield of **18** was 0.306 g (44%): IR (CCl_4) 1728 cm^{-1}; NMR ($CDCl_3$) δ 0.92 (s, 3 H), 1.30 (s, 3 H), 1.5–2.3 (m, 8 H); MS m/e (relative intensity) 39 (79), 41 (64), 67 (100), 79 (100), 94 (94), 108 (61), 122 (55), 135 (22), 150 (42, M^+). Anal. Calcd for $C_{10}H_{14}O$: m/e 150.1045. Found: m/e 150.1041.

1,5-Dimethyltricyclo[3.2.1.0^{2,7}]octane (19). A solution of 1.0 g of potassium hydroxide, 0.8 mL of 95% hydrazine, and 0.100 g of **18** in 4 mL of diethylene glycol was heated at 115 °C for 30 min. The mixture was then heated for 3 h at 180 °C, during which volatile material collected in an attached condenser. This was dissolved in pentane, washed with cold 1 M hydrochloric acid and saturated sodium chloride, dried over sodium sulfate, and concentrated by distillation of the solvent through a Vigreux column. Pure **19**, obtained from the residue by preparative GC (40 °C) was identical with a sample prepared from 1,5,5-trimethylcyclohexene by carbon atom insertion:[1] NMR ($CDCl_3$) δ 0.55 (dt, J = 8, 2.5 Hz, H-2), 0.87 (s, 3 H), 0.88 (m, H-7), 1.14 (s, 3 H), 1.37 (s, 2 H), 1.49 (d, J = 11 Hz, 1 H), 1.06–1.66 (m, 3 H), 1.89 (m, 2 H-3, $J_{2,3}$ = 2.5 Hz by double irradiation); MS m/e (relative intensity) 39 (13), 41 (15), 53 (9), 67 (12), 68 (11), 81 (24), 93 (47), 107 (100), 121 (22), 136 (45, M^+). Anal. Calcd for $C_{10}H_{16}$: m/e 136.1251. Found: m/e 136.1252.

1-Methyltricyclo[3.2.1.0^{2,7}]octan-6-one (17). Following procedure D, a yield of 52 mg (17%) of **17** was obtained (GC, biphenyl internal standard) from 0.21 g (2.3 mmol) of 2-cyclohexen-1-one (**12**) and 1.0 g (2.6 mmol) of ITB. Bulb-to-bulb distillation [75–80 °C (0.1 mm)] and GC (80 °C) gave pure **17** as a colorless liquid: IR ($CHCl_3$) 1712 cm^{-1}; NMR ($CDCl_3$) δ 1.32 (s, 3 H), 1.5–2.5 (m, 9 H); NMR ($CDCl_3$ plus 15 mol % of Eu(fod)$_3$) δ 1.64 (s, 3 H), 2.84 (ddd, J = 2, 6, 11.5 Hz, 1 H), 3.19 (dd, J = 1.5, 8 Hz, 1 H), 3.94 (m, 1 H); MS m/e (relative intensity) 36 (32), 39 (27), 54 (22), 67 (41), 68 (40), 77 (44), 79 (54), 91 (42), 93 (100), 95 (48), 108 (70), 121 (7), 136 (64, M^+). Anal. Calcd for $C_9H_{12}O$: m/e 136.0885. Found: m/e 136.0883.

2-(*p*-Toluenesulfinyl)-1-decalone (22). To a refluxing suspension of 0.58 g (24 mmol) of oil-free sodium hydride and 2.04 g (12 mmol) of methyl *p*-toluenesulfinate[64] in 25 mL of 2-methoxyethyl methyl ether (DME) was added 1.83 g (12 mmol) of 1-decalone (**21**) in 5 mL of DME in 5 min. The mixture was refluxed for 3 h, cooled, and filtered. The white solid thus collected was washed with ether and dissolved in 50 mL of 5% aqueous potassium hydroxide, which was then extracted with ether, acidified with 10% aqueous hydrochloric acid and extracted with ether (3 × 200 mL). The combined ether layers were washed with saturated aqueous sodium bicarbonate (2 × 100 mL), dried over anhydrous sodium sulfate, and evaporated to give oily white crystals which were recrystallized from 1:1 ethyl acetate–hexane to give 1.5 g (43%) of **22** as white crystals: mp 150–152 °C; IR ($CHCl_3$) 1709 cm^{-1}; NMR ($CDCl_3$) δ 0.8–2.3 (m, 14 H), 2.37 (s, 3 H), 3.38 (dd, J = 8, 11 Hz, 1 H), 7.27 (d, J = 8 Hz, 2 H), 7.54 (d, J = 8 Hz, 2 H); MS m/e (relative intensity) 68 (54), 81 (55), 91 (100), 108 (29), 124 (61), 133 (21), 139 (20), 151 (36), 274 (10), 290 (12, M^+). Anal. Calcd for $C_{17}H_{22}O_2S$: m/e 290.1340. Found: m/e 290.1348.

Δ^2-1-Octalone (23). A solution of 1.0 g (3.4 mmol) of **22** in 10 mL of carbon tetrachloride was refluxed for 5 h. The mixture was cooled and washed with saturated aqueous sodium bicarbonate, the aqueous layer was washed with ether, and the combined organic layers were washed with saturated aqueous sodium chloride, dried over sodium sulfate, and evaporated to an oil. Bulb-to-bulb distillation [70–80 °C (0.1 mm)] gave 0.21 g (41%) of white crystals, which were recrystallized from ethanol: mp 68–69 °C (lit.[42] mp 71–72 °C); NMR ($CDCl_3$) δ 0.5–2.7 (m, 12 H), 5.87 (dm, J = 9 Hz, 1 H), 6.82 (m, 1 H).

1α-Methyl-1,3,4,5,6,6aβ,7,7aα-octahydro-1,2a-methano-2a*H*-cyclopropa[*b*]naphthalen-2(1aα*H*)-one[65] (25). Procedure D and bulb-to-bulb distillation [80 °C (0.1 mm)] gave a colorless oil which was purified by preparative GC (15 °C). GC analysis (biphenyl internal standard) showed that the yield of **25** from 0.17 g (1.12 mmol) of **23** and 0.44 g (1.16 mmol) of ITB was 0.77 g (36%): IR ($CHCl_3$) 1710 cm^{-1}; NMR ($CDCl_3$) δ 0.7–2.2 (m, 14 H), 1.28 (s, 3 H), 2.38 (ddd, J = 2, 10, 13 Hz, 1 H); NMR ($CDCl_3$ plus 31 mol % of Eu(fod)$_3$) δ 2.24 (s, 3 H), 3.54 (d, J = 11 Hz, 1 H), 2.3–3.8 (m, 7 H), 3.88 (d, J = 8 Hz, 1 H), 4.01 (ddd, J = 2, 10, 13 Hz, 1 H), 4.5 (m, 1 H), 4.66 (d, J = 11 Hz, 1 H), 6.15 (br d, J = 13 Hz, 1 H), 6.34 (d, J = 8 Hz, 1 H), 7.10 (m, $\sum J$ = ~50 Hz, 1 H); MS m/e (relative intensity) 67 (56), 79 (58), 91 (82), 95 (100), 105 (69), 119 (48), 132 (33), 147 (43), 162 (84), 175 (20), 190 (69, M^+). Anal. Calcd for $C_{13}H_{18}O$: m/e 190.1358. Found: m/e 190.1360.

Bicycloannulation Procedure B. 1,4,4-Trimethyltricyclo[3.2.1.0^{2,7}]octan-6-one (32). A solution of LDA in THF was formed as in procedure A from 2.7 mL (4.05 mmol) of ethereal methyllithium, ca. 3 mg of bipyridyl, 4 mL of THF, and 0.65 mL (4.7 mmol) of diisopropylamine. To the dark red solution was added dropwise 0.387 g (3.1 mmol) of 5,5-dimethyl-2-cyclohexen-1-one[66] (**30**) in 5 mL of THF as the temperature of the mixture rose from −25 to 0 °C. The red solution was allowed to warm to room temperature and 1.393 g (3.6 mmol) of ITB in 17 mL of *pyridine* was added dropwise over a period of 1.8 h. By GC, most of the product formation was found to take place during this addition, and the reaction was complete within 2 h following the addition. The resulting clear orange-red solution was worked up as in procedure A. The majority of the solvent was removed from the petroleum ether extract by distillation through a Vigreux column, and the residue was bulb-to-bulb distilled [bath temperature 70–78 °C (0.02 mm)] to give 0.212 g (42%) of almost pure **32** as a colorless liquid. Samples for spectral analysis were obtained by preparative GC (150 °C) of this material: IR (CCl_4) 1727 cm^{-1}; NMR ($CDCl_3$) δ 0.88 (s, 3 H), 1.01 (s, 3 H), 1.30 (s, 3 H), 1.6 (m, 3 H), 1.9 (m, 4 H); NMR ($CDCl_3$ plus 17 mol % of Eu(fod)$_3$) δ 1.67 (s, 3 H), 1.73 (s, 3 H), 2.31 (s, 3 H), 2.42 (dt, J = 8, 3 Hz, 1 H), 2.60 (m, 2 H), 2.75 (d, J = 12 Hz, 1 H), 3.06 (dd, J = 5.5, 12 Hz, 1 H), 3.64 (dd, J = 1.5, 8 Hz, 1 H), 4.28 (d, J = 5.5 Hz, 1 H); MS m/e (relative intensity) 41 (14), 55 (9), 67 (26), 79 (31), 83 (28), 93 (100), 107 (33), 136 (26), 149 (12), 164 (88, M^+). Anal. Calcd for $C_{11}H_{16}O$: m/e 164.1201. Found: m/e 164.1205.

(64) J. W. Wilt, R. G. Stein, and W. J. Wagner, *J. Org. Chem.*, **32**, 2097 (1967).

(65) Alternatively: 1-methyltetracyclo[7.2.1.0^{2,11}.0^{4,9}]dodecan-10-one. The difficulty in denoting the stereochemistry makes this system less desirable.

(66) G. A. Hiegel and P. Burk, *J. Org. Chem.*, **38**, 3637 (1973).

(67) E. E. Schweizer, A. T. Wehman, and D. M. Mycz, *J. Org. Chem.*, **38**, 1583 (1973).

Bicycloannulation Procedure C. 4,4-Dimethyltricyclo[3.2.1.0^{2,7}]octan-6-one (31). Procedure B was followed except that after the addition of VTB, the mixture was refluxed until no further increase in the product peak was observed by GC (4 h). Workup as before and bulb-to-bulb distillation [80–90 °C (0.4 mm)] gave a light yellow liquid from which pure **31** was isolated by preparative GC (125 °C). By GC analysis (biphenyl internal standard) the yield of **31** from 0.969 g (7.8 mmol) of 5,5-dimethyl-2-cyclohexen-1-one[66] (**30**) and 3.049 g (8.3 mmol) of VTB was 0.155 g (13%): IR (CCl_4) 1716 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (s, 3 H), 1.02 (s, 3 H), 1.5 (m, 1 H), 1.7 (m, 4 H), 2.1 (m, 3 H); NMR ($CDCl_3$ plus 20 mol % of Eu(fod)$_3$) δ 1.68 (s, 3 H), 2.34 (s, 3 H), 2.80 (d, J = 12 Hz, 1 H), 2.92 (td, J = 6, 4 Hz, 1 H), 3.19 (ddd, J = 4, 5.5, 12 Hz, 1 H), 3.74 (br t, J = 6 Hz, 1 H), 4.12 (br d, J = 5.5 Hz, 1 H); MS m/e (relative intensity) 39 (100), 41 (74), 53 (87), 67 (48), 79 (96), 81 (78), 91 (57), 93 (48), 107 (35), 135 (12), 150 (31, M$^+$). Anal. Calcd for $C_{10}H_{14}O$: m/e 150.1045. Found: m/e 150.1042.

Attempted Bicycloannulation of 4,4-Dimethyl-2-cyclohexen-1-one (33). Following procedure A, the α' enolate from 0.980 g (7.9 mmol) of **33**[68] was treated with 3.51 g (9.5 mmol) of VTB. After 2.5 h of reflux, most of the starting ketone had been consumed (GC), but only a very small peak had appeared in its place. The mixture was cooled to room temperature, 10 mL of hexamethylphosphoramide (HMPA) was added, ca. 10 mL of THF was evaporated from the solution under vacuum, and the mixture was again heated to reflux. After 42 h at reflux no further increase in the product peaks was observed, and workup as before gave a petroleum ether extract. Upon evaporation of most of the solvent, a large quantity of orange-yellow crystalline solid precipitated. The latter, after several recrystallizations from chloroform–petroleum ether, became light yellow crystals, mp 177–182 °C, which were assigned the phosphine oxide structure **46**: IR ($CHCl_3$) 1440 (PPh), 1180 (P=O) cm^{-1}; NMR ($CDCl_3$) δ 0.94 (s, 3 H), 0.98 (s, 3 H), 1.1–2.9 (m, 8 H), 5.36 (d and m, J = 9 Hz, 2 H), 5.78 (d, J = 9 Hz, 1 H), 7.42 (m, 6 H), 7.75 (m, 4 H); MS m/e (relative intensity) 145 (53), 160 (100), 202 (62), 347 (26), 362 (34, M$^+$).

The filtrate from collection of the above-mentioned precipitate was evaporated to an orange oil which was subjected to bulb-to-bulb distillation [75–100 °C (0.3 mm)] and preparative GC (5% Carbowax 20-M, programmed at 2 °C/min from 70 to 200 °C). Four major peaks were observed at 17.5-, 19.4-, 21.8-, and 30.3-min retention times. The size of the peak at 21.8 min increased at the expense of the peak at 19.4 min with each subsequent injection. The 21.8-min compound had spectral data similar to those reported[44] for the aromatic hydrocarbon **47**: IR (CCl_4) 1660 cm^{-1}; NMR (CCl_4) δ 1.03 (s, 6 H), 2.66 (s, 2 H), 5.63 (d, J = 10 Hz, 1 H), 6.24 (d, J = 10 Hz, 1 H), 6.95 (br s, 4 H) [lit.[44] NMR δ 0.95 (s, 3 H), 2.57 (s, 2 H), 5.62 (d, J = 9.3 Hz, 1 H), 6.24 (d, J = 9.3 Hz, 1 H), 6.96 (br s, 4 H)]; MS m/e (relative intensity) 105 (10), 115 (12), 128 (37), 143 (100), 158 (34, M$^+$). The 30.3-min compound was tentatively assigned to the (impure) desired product, 3,3-dimethyltricyclo[3.2.1.0^{2,7}]octan-6-one (**34**): IR (CCl_4) 1734 cm^{-1}; NMR (CCl_4) δ 1.07 (s, 3 H), 1.18 (s, 3 H), 1.7 (m, 6 H), 2.1 (m, 2 H); MS m/e 150 (M$^+$).

Bicycloannulation Procedure E. 2,4,4-Trimethyltricyclo[3.2.1.0^{2,7}]octan-6-one (36). Procedure D was followed except that after the addition of VTB, the mixture was refluxed until no further increase in the product was observed by GC (2 h). Workup as before and short-path distillation gave fractions containing mostly starting isophorone (**35**) at 32–52 °C (0.3 mm) and mostly **36** at 52–100 °C (0.3 mm) as a light orange liquid from which pure **36** was isolated by preparative GC (130 °C). By GC analysis (triphenylmethane internal standard) the yield of **36** from 0.469 g (3.4 mmol) of isophorone and 1.50 g (4.1 mmol) of VTB was 0.087 g (16%), and 0.211 g (45%) of isophorone was recovered. Thus, the yield of **36** based on unrecovered isophorone was 28%. In addition, the yield of triphenylphosphine was determined to be 0.182 g (131% based on the amount of **36** produced; 17% based on VTB). Spectral data for **36**: IR (neat) 1722 cm^{-1}; NMR ($CDCl_3$, 220 MHz) δ 0.92 (s, 3 H), 1.04 (s, 3 H), 1.08 (s, 3 H), 1.53 (m, 2 H), 1.63 (d, J = 14 Hz, 1 H), 1.84 (d, J = 14 Hz, 1 H), 1.96 (m, 1 H), 2.03 (m, 2 H); NMR ($CDCl_3$ plus 44 mol % of Eu(fod)$_3$) δ 2.07 (s, 3 H), 2.58 (s, 3 H), 3.70 (s, 2 H), 3.83 (dd, J = 4,5 Hz, 1 H), 3.87 (d, J = 12 Hz, 1 H), 4.33 (s, 3 H), 4.77 (ddd, J = 4, 5.5, 12 Hz, 1 H), 5.82 (d, J = 5 Hz, 1 H), 7.64 (d, J = 5.5 Hz, 1 H); MS m/e (relative intensity) 39 (95), 41 (92), 53 (27), 67 (44), 79 (33), 93 (100), 107 (28), 121 (49), 136 (23), 149 (5), 164 (50, M$^+$). Anal. Calcd for $C_{11}H_{16}O$: m/e 164.1200. Found: m/e 164.1160.

4-Isopropenyl-7-methyltricyclo[3.2.1.0^{2,7}]octan-6-one (38). By use of procedure E, 0.203 g (34%) of **38** plus **39** was obtained (GC, naphthalene internal standard) from 0.509 g (3.39 mmol) of *d*-carvone (**37**) and 1.520 g (4.12 mmol) of VTB. By GC analysis, the ratio of **38** to **39** was found to be ca. 20:1. Bulb-to-bulb distillation [65–90 °C (0.1 mm)] and preparative GC (160 °C) gave pure **38** as a colorless liquid: IR (CCl_4) 1729, 1646 cm^{-1}; NMR ($CDCl_3$, 220 MHz) δ 1.21 (s, 7-CH_3), 1.68 (dt, J = 7, 2.5 Hz, 2-H), 1.69 (m, vinyl CH_3), 1.81 (d, J = 11.5 Hz, 8a-H), 1.99 (ddd, J = 2.5, 5.5, 14.5 Hz, 3s-H), 2.01 (dd, J = 3, 7 Hz, 1-H), 2.20 (dd, J = 3, 6 Hz, 5-H), 2.28 (ddd, J = 3, 6, 11.5 Hz, 8s-H), 2.32 (ddd, J = 2.5, 10, 14.5 Hz, 3a-H), 2.63 (ddd, J = 3, 5.5, 10 Hz, 4-H), 4.78 (m, 2 vinyl H); MS m/e (relative intensity) 41 (47), 53 (20), 67 (41), 82 (44), 95 (60), 109 (31), 122 (37), 133 (20), 143 (11), 147 (13), 161 (29), 176 (100, M$^+$). Anal. Calcd for $C_{12}H_{16}O$: m/e 176.1197. Found: m/e 176.1200. The minor ketone **39** could not be completely separated from **38**, but its ^{13}C NMR spectrum[37] was consistent with the structure assigned herein.

In addition, a yield of 0.082 g (13%) of 1-isopropenyl-4-methyl-1,2,8,8a-tetrahydronaphthalene (**48**) was determined by GC: IR ($CHCl_3$) 1640 cm^{-1}; NMR ($CDCl_3$) δ 1.7 (m, 3 H), 1.9 (m, 3 H), 2.2 (m, 6 H), 4.8 (m, 2 H), 5.8 (m, 4 H); MS m/e 52, 79, 91, 105, 115, 128, 143, 154, 155, 171, 176, 186 (M$^+$). Anal. Calcd for $C_{14}H_{18}$: m/e 186.1409. Found: m/e 186.1401.

1,7-Dimethyl-4-isopropenyltricyclo[3.2.1.0^{2,7}]octan-6-one (40). Procedure B and bulb-to-bulb distillation [70–80 °C (0.01 mm)] gave 0.267 g (44%) of nearly pure **40** from 0.487 g (3.24 mmol) of *d*-carvone (**37**) and 1.439 g (3.75 mmol) of ITB. Pure **40** was collected as a colorless liquid by preparative GC (10% Silicone APOLAR-10C on 100/120-mesh GAS-CHROM Q at 210 °C) for spectral analysis: IR (CCl_4) 1721, 1646 cm^{-1}; NMR ($CDCl_3$) δ 1.11 (s, 7-CH_3), 1.25 (s, 1-CH_3), 1.37 (t, J = 2.5 Hz, 2-H), 1.66 (m, vinyl CH_3), 1.79 (d, J = 11.5 Hz, 8a-H), 2.02 (dd, J = 6, 11.5 Hz, 8s-H), 2.14 (ddd, J = 2.5, 6, 14.5 Hz, 3s-H), 2.22 (dd, J = 2.5, 6 Hz, 5-H), 2.27 (ddd, J = 2.5, 9.5, 14.5 Hz, 3a-H), 2.58 (ddd, J = 2.5, 6, 9 Hz, 4-H), 4.76 (m, 2 vinyl H); MS m/e (relative intensity) 41 (48), 67 (52), 79 (100), 91 (83), 107 (91), 119 (48), 122 (61), 123 (61), 135 (65), 147 (43), 162 (48), 175 (56), 190 (61, M$^+$). Anal. Calcd for $C_{13}H_{18}O$: m/e 190.1358. Found: m/e 190.1364.

5-Chloro-4,7,7-trimethylbicyclo[2.2.2]octan-2-one (49). Into a solution of 40 mg of **40** in 0.3 mL of $CDCl_3$ in an NMR tube at 0 °C was passed a stream of HCl gas. After 35 min NMR showed that **36** had been quantitatively converted to **49**. The solution was poured into 30 mL of saturated aqueous sodium bicarbonate and 40 mL of petroleum ether. The petroleum ether phase was washed with water (2 × 40 ml), dried over anhydrous sodium sulfate, and concentrated in vacuo. Preparative GC (programmed at 10 °C/min from 100 to 240 °C) gave pure **49** as a colorless liquid: IR ($CHCl_3$) 1712 cm^{-1}; NMR ($CDCl_3$) δ 0.95 (s, 3 H), 1.02 (s, 3 H), 1.13 (dd, J = 3, 13.5 Hz, 1 H), 1.19 (s, 3 H), 2.0 (m, 4 H), 2.37 (m, 2 H), 3.88 (ddd, J = 2, 6.5, 8.5 Hz, 1 H); NMR ($CDCl_3$ plus 40 mol % of Eu(fod)$_3$) δ 1.52 (s, 3 H), 1.97 (s, 3 H), 2.23 (dd, J = 2, 13.5 Hz, 1 H), 2.43 (s, 3 H), 2.83 (dd, J = 3, 13.5 Hz, 1 H), 3.45 (ddd, J = 3, 4, 15.5 Hz, 1 H), 3.98 (ddd, J = 3, 10, 15.5 Hz, 1 H), 4.89 (ddd, J = 2, 4, 10 Hz, 1 H), 5.06 (dd, J = 3, 19 Hz, 1 H), 5.08 (t, J = 3 Hz, 1 H), 5.40 (d, J = 19 Hz, 1 H); MS m/e (relative intensity) 41 (100), 55 (68), 69 (34), 83 (36), 91 (35), 107 (83), 109 (32), 123 (49), 165 (18), 185 (65), 187 (22), 200 (80, M$^+$), 202 (27, M$^+$). Anal. Calcd for $C_{11}H_{17}ClO$: m/e 200.0968. Found: m/e 200.0969.

2,4aα-Dimethyl-5,8-dihydronaphthalene-1(8aβ*H*),4(4a*H*)-dione (52). 1,3-Butadiene was introduced through a gas-dispersion tube to a solution of 5.4 g of 2,5-dimethyl-*p*-benzoquinone[69] (**50**) and 5.4 mL of boron trifluoride etherate in 40 mL of toluene. The reaction was mildly exothermic at first, and, while the introduction of butadiene was continued over a

(68) E. L. Eliel and C. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957).

(69) D. Bryce-Smith and A. Gilbert, *J. Chem. Soc.*, 873 (1964).

period of 30 min, the flask was warmed intermittently. The cooled mixture was then poured into 100 mL of ice and stirred while sodium bicarbonate was added in small portions until foaming ceased. The aqueous layer was extracted twice with ether, and the combined organic layers were washed with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried over magnesium sulfate, and evaporated to a light orange oil. Short-path distillation [73–74 °C (0.01 mm)] and separation of the crystals from the oil by filtration gave 3.8 g (51%) of **52** as white crystals: mp 26–28 °C; IR (CCl_4) 1690 cm^{-1}; NMR ($CDCl_3$) δ 1.33 (s, 3 H), 1.77 (br d, J = 18 Hz, 1 H), 2.00 (d, J = 2 Hz, and m, 4 H), 2.3 (m, 1 H), 2.6 (m, 1 H), 2.9 (m, 1 H), 5.66 (m, 2 H), 6.50 (m, 1 H); MS m/e (relative intensity) 68 (64), 77 (41), 91 (40), 119 (28), 129 (34), 147 (85), 162 (100), 175 (26), 190 (21, M^+). Anal. Calcd for $C_{12}H_{14}O_2$: m/e 190.0994. Found: m/e 190.0998.

1aα,6aα-Dimethyl-1α,3,6,7aα-tetrahydro-1,2a-methano-2a*H*-cyclopropa[*b*]naphthalene-2(1a*H*),7(6a*H*)-dione (53). Procedure C gave, from **52**, a low yield of **53** as white crystals, mp 153–160 °C, after preparative TLC (7:3 ethyl acetate–cyclohexane) and GC (185 °C): IR ($CHCl_3$) 1736, 1703, 1650 cm^{-1}; NMR ($CDCl_3$) δ 0.90 (s, 3 H), 1.32 (s, 3 H), 1.63 (br d, J = 19 Hz, 1 H), 1.90 (dd, J = 3, 13 Hz, 1 H), 2.07 (m, 2 H), 2.18 (d, J = 13 Hz, 1 H), 2.27 (d, J = 7 Hz, 1 H), 2.53 (dd, J = 3, 7 Hz, 1 H), 2.63 (br d, J = 19 Hz, 1 H), 5.54 (m, 2 H); MS m/e (relative intensity) 53 (36), 65 (36), 77 (57), 91 (100), 105 (35), 109 (26), 115 (43), 128 (35), 145 (74), 155 (35), 159 (65), 173 (52), 183 (30), 201 (26), 216 (65, M^+). Anal. Calcd for $C_{14}H_{16}O_2$: m/e 216.1150. Found: m/e 216.1152.

Methyl 14-Oxopodocarp-12-en-19-oate (63). To a solution of 3.54 g of methyl 12-oxopodocarp-13-en-19-oate (**62**)[54b] in 80 mL of methanol at −10 °C were added 2.3 mL of 30% aqueous hydrogen peroxide and 3.3 mL of 1 M aqueous sodium hydroxide. The mixture was stirred for 1.5 h at 0 °C and 0.5 h at room temperature; it was then diluted with 1 L of water, acidified with dilute aqueous hydrochloric acid, and extracted with ether (3 × 200 mL). The combined ether extracts were washed with saturated aqueous sodium chloride, dried over anhydrous sodium sulfate, and evaporated to a yellow oil.

This crude mixture of α and β epoxides was dissolved in 40 mL of methanol and cooled in an ice bath, and 2.1 g of hydrazine hydrate and 0.187 g of glacial acetic were added. The mixture was stirred 0 °C for 15 min, allowed to warm to room temperature (0.5 h), and then heated gently with a 40 °C water bath until gas evolution ceased. After addition to 500 mL of water, the mixture was extracted with ether (3 × 200 mL), and the combined ether extracts were dried over anhydrous sodium sulfate and evaporated to 3.0 g of a yellow oil.

The entire crude mixture of α and β alcohols was dissolved in 15 mL of methylene chloride and added to a suspension of 4.8 g of pyridinium chlorochromate in 25 mL of methylene chloride. After the mixture had been stirred for 3 h, 60 mL of ether was added, and the solution was decanted from the resulting black gum, which was washed with ether (3 × 25 mL). The combined organic extracts were passed through a pad of Florisil, and the filtrate was evaporated to give 2.1 g of crude **63** as brown oil. Chromatography on 100 g of Florisil (1:4 ether–hexane) gave 0.71 g (20%) of enone ester **63**, which was recrystallized from petroleum ether (bp 30–60 °C): mp 102–103 °C (lit.[70] mp 101–103 °C); IR ($CHCl_3$) 1720, 1670, 980 cm^{-1} (lit.[70] identical); NMR ($CDCl_3$) δ 0.76 (s, 3 H), 1.20 (s, 3 H), 3.66 (s, 3 H), 5.96 (dm, J = 10 Hz, 1 H), 6.96 (ddd, J = 3, 6, 10 Hz, 1 H) [lit.[70] NMR δ 0.74 (s, 3 H), 1.20 (s, 3 H), 3.65 (s, 3 H), 5.97 (d, J = 10 Hz, 1 H), 6.96 (m, 1 H)]; MS m/e (relative intensity) 79 (48), 81 (48), 95 (65), 109 (71), 123 (100), 133 (50), 216 (75), 230 (25), 231 (27), 240 (18), 258 (92), 272 (16), 290 (40, M^+). Anal. Calcd for $C_{18}H_{26}O_3$: m/e 290.1882. Found: m/e 290.1882.

(70) R. C. Cambie and A. W. Missen, *Aust. J. Chem.*, **25**, 973 (1972).

Methyl 14-Oxotrachyloban-19-oate (64). Procedure D (substituting ether for petroleum ether) followed by preparative TLC (1:4 ethyl acetate–cyclohexane) gave 0.089 g (23%) of keto ester **64** from 0.336 g (1.16 mmol) of enone **63** and 0.465 g (1.21 mmol) of ITB. Recrystallization from petroleum ether (bp 30–60 °C) gave white crystals: mp 143–145 °C; IR ($CHCl_3$) 1720 cm^{-1}; NMR ($CDCl_3$) δ 0.53 (s, 3 H), 1.14 (s, 3 H), 1.25 (s, 3 H), 3.61 (s, 3 H); MS m/e (relative intensity) 43 (98), 57 (100), 71 (79), 90 (46), 95 (39), 105 (40), 121 (41), 147 (34), 161 (33), 205 (33), 270 (39), 290 (9), 298 (6), 312 (8), 330 (26, M^+). Anal. Calcd for $C_{21}H_{30}O_3$: m/e 330.2195. Found: m/e 330.2201.

Methyl Trachyloban-19-oate (66). Into a solution of 10 mg of keto ester **64** in 1 mL of a stock solution of sodium diethylene glycolate in diethylene glycol (11.5 mg of sodium/mL) was distilled 0.7 mL of anhydrous hydrazine[71] (prepared by refluxing 95% hydrazine over potassium hydroxide for 3 H). The mixture was heated to 140 °C and refluxed for 20 h. The excess hydrazine was then distilled off until the temperature of the mixture reached 210 °C, at which it was heated for 24 h. After the mixture had been allowed to cool to room temperature, it was diluted with ether, and the solution was washed with ice-cold 1 M aqueous hydrochloric acid, water, and saturated aqueous sodium chloride. The dried (anhydrous sodium sulfate) ethereal solution was then treated with an excess of ethereal diazomethane[72] for 5 h at room temperature. The solvent was evaporated, leaving a yellow oil which was subjected to preparative TLC (1:4 ethyl acetate–hexane). There was thus obtained 3 mg (ca 30%) of ester **66**, which displayed ^1H and ^{13}C NMR spectra and TLC and GC behavior identical with those of an authentic sample of methyl *ent*-trachyloban-19-oate (**5**) derived from sunflower heads: ^1H NMR ($CDCl_3$) δ 0.57 (dt, J = 8, 2.5 Hz), 0.77 (s, 3 H), 1.13 (s, 3 H), 1.14 (s, 3 H), 3.63 (s, 3 H) [lit.[3a] ^1H NMR δ 0.6 (m), 0.75 (s, 3 H), 1.12 (s, 6 H), 3.60 (s, 3 H)]; ^{13}C NMR (CD_2Cl_2) δ 12.5, 19.2, 20.0, 20.6, 21.0, 22.2, 22.7, 24.7, 28.8, 33.4, 38.5, 39.0, 39.6, 39.9, 41.1, 44.1, 50.7, 51.2, 53.1, 57.3 (C=O not determined).[73] The ORD curve of the synthetic ester (**66**, dextrorotatory) was the mirror image of that of the natural (ent) ester (levorotatory).

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