(91%) of *p*-nitroaniline, mp 145–147°, and N-(*p*-nitrophenyl)-pyridinium bromide, 144 mg (106%). The salt was identified as its ferric chloride derivative, mp 146–147° (lit.[19] mp 149°).

Kinetic Studies. Rates of reaction of **1a–f** were determined in methanol solution at three different temperatures for each substrate. The methanol was dried by the method of Lund and Bjerrum[20] and was then distilled through an efficient fractionating column. In all cases rate studies were made on solutions containing sufficient triethylamine to convert all the iminium salt to free imine as indicated by uv spectral test. Rates were followed spectrophotometrically for disappearance of the imine using the appropriate wavelength for each substrate. Studies were made in a thermostated cell holder capable of maintaining the temperature at ±0.1° with a Cary Model 15 spectrophotometer. With each substrate studies at one temperature were made at several triethylamine concentrations to show the lack of dependence on base concentration. The rates were followed generally for *ca.* three half-lives and no deviation from first order was observed. The results are given in Table I, and typical runs for each substrate are illustrated in Figures 1 and 2.

(19) W. König, *J. Prakt. Chem.*, 70, 19 (1904).
(20) H. Lund and J. Bjerrum, *Ber.*, **64**, 210 (1931).

A General Approach to Cycloalkanone Synthesis.[1] Intramolecular Alkylation of 2-Chloro-1-olefins

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Abstract: Various cyclic ketones can be synthesized by incorporating allylic–vinylic dichlorides, *e.g.*, 2,3-dichloropropene, into reaction sequences originating with nucleophilic displacement at the allyl carbon. The relative inertness of vinyl chlorides allows various intervening chemical transformations of the adducts to be carried out, and minimizes the problem of haloalkene isomerization. Cycloalkanone formation is completed by intramolecular, electrophilic attack upon the "2-chloro-1-ene" side chain to produce a cyclic α-chlorocarbonium ion, which is then solvolyzed. Monocyclic C_5- to C_7-ketones, as well as *cis*-hydrindan-2-one and *trans*-2-decalone derivatives, have been synthesized in fair to good overall yield.

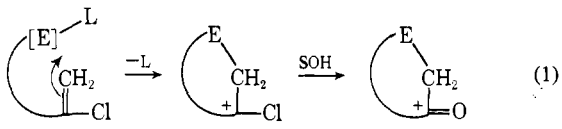
The construction of suitably functionalized cyclohexane units (*e.g.*, cyclohexenones and cyclohexanones) in polycyclic molecules has occupied a central position in the synthesis of natural products such as steroids,[3] terpenes,[4] and tetracyclines.[5] Most commonly, the key step in cyclohexanoid genesis is one of the following: (1) dissolving metal reduction of an aromatic ether[6] or pyridine[7] to produce ultimately a Δ^2-cyclohexenone; (2) Michael addition of an enolate ion[8] or enamine[9] to electrophilic olefins such as vinyl ketones or their equivalents (*e.g.*, 1,3-dichloro-2-butene or Mannich bases) followed by intramolecular aldol condensation or a second Michael reaction;[9d] (3) Diels–Alder cycloadditions;[3b] and (4) biogenetic-like 1,5-polyene cyclizations[10] which can produce even tetracyclic steroid-like molecules of "natural" stereochemistry from acyclic substrates in a single step.[11]

By comparison, cyclopentanoid rings are less readily produced directly, although the aldol condensation of 1,4-dicarbonyl compounds to Δ^2-cyclopentenones has some generality.[12] Quite often five-membered rings are obtained by ring contraction of a cyclohexanone derivative[13a] as in the synthesis of A-nor steroids[13b] and the normal D ring.[3b] Seven-membered rings are likewise often obtained indirectly by ring expansion of cyclohexanones with diazoalkanes.[14] The synthetic approach discussed in this paper allows for the creation of various monocyclic C_5–C_7 cyclanones, as well as fused and bridged analogs. Moreover, a variety of heteroatoms (*e.g.*, N, S) can be introduced into the ring.

The key step envisioned for producing a cyclanone involves intramolecular electrophilic attack upon a vinylic chloride;[15] in eq 1 and elsewhere, L signifies a

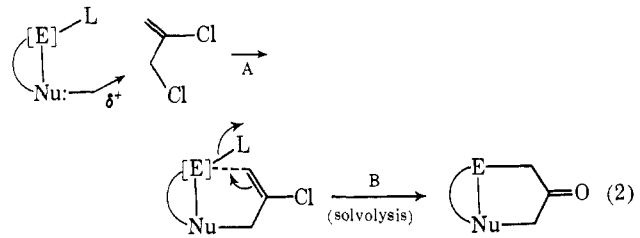
(1) Portions of this work appeared in preliminary reports: (a) P. T. Lansbury and E. J. Nienhouse, *J. Amer. Chem. Soc.*, **88**, 4290 (1966); (b) P. T. Lansbury, F. R. Hilfiker, and W. L. Armstrong, *ibid.*, 90, 534 (1968); (c) P. T. Lansbury and D. J. Scharf, *ibid.*, 90, 536 (1968).
(2) Samuel Silbert Predoctoral Research Fellow, 1968–1969.
(3) (a) L. Velluz, J. Valls, and G. Nomine, *Angew. Chem., Int. Ed. Engl.*, **4**, 181 (1965); (b) J. W. Cornforth, *Progr. Org. Chem.*, Vol. 3, J. W. Cook, Ed., Butterworths, London, 1955, pp 1–43.
(4) R. E. Ireland, "Organic Synthesis," Prentice-Hall, Englewood Cliffs, N. J., 1969, Chapters 4 and 5.
(5) (a) H. Muxfeldt, G. Hartmann, K. Kathawala, E. Vedejs, and J. B. Moobery, *J. Amer. Chem. Soc.*, 90, 6536 (1968); (b) J. J. Korst, J. D. Johnston, K. Butler, E. J. Biancs, L. H. Conover, and R. B. Woodward, *ibid.*, 90, 439 (1968).
(6) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, Chapter 3.
(7) S. Danishefsky and R. Cavanaugh, *J. Amer. Chem. Soc.*, 90, 520 (1968).
(8) E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. React.*, 10, 179 (1959).
(9) (a) R. V. Stevens and M. P. Wentland, *J. Amer. Chem. Soc.*, 90, 5580 (1968); (b) S. L. Keely, Jr., and F. C. Takh, *ibid.*, 90, 5584 (1968); (c) T. C. Curphey and H. L. Kim, *Tetrahedron Lett.*, 1441 (1968); (d) R. P. Nelson and R. G. Lawton, *J. Amer. Chem. Soc.*, 88, 3884 (1966).
(10) (a) W. S. Johnson, *Accounts Chem. Res.*, **1** 1 (1968); (b) E. E. van Tamelen, *ibid.*, 1, 111 (1968); (c) D. J. Goldsmith and C. F. Phillips, *J. Amer. Chem. Soc.*, 91, 5862 (1969), and earlier references cited therein.
(11) *Cf.* W. S. Johnson, *et al.*, *ibid.*, 90, 2994 (1968).
(12) (a) S. Coffey, Ed., "Rodd's Chemistry of Carbon Compounds," 2nd ed, Vol. II, part A, Elsevier, Amsterdam, 1967, pp 164–169, 180–183. (b) A. T. Nielsen and W. J. Houlihan, *Org. React.*, 16, 1 (1968).
(13) (a) *Cf.* W. G. Dauben, D. J. Ellis, and W. H. Templeton, *J. Org. Chem.*, 34, 2297 (1969); (b) C. Djerassi, Ed., "Steroid Reactions," Holden-Day, San Francisco, Calif., 1963, Chapter 11.
(14) *Cf.* J. B. Jones and P. Price, *Chem. Commun.*, 1478 (1969), and references cited therein.

leaving group and E refers to a potential (brackets) or actual electrophilic center during annelation. Al-



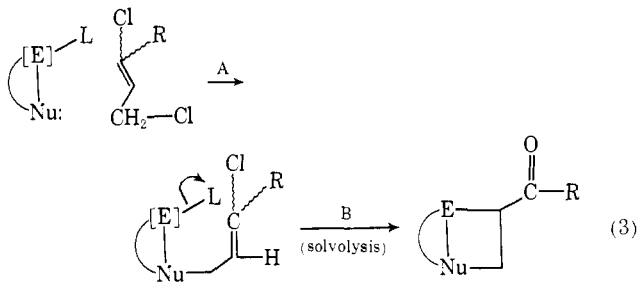
(1)

though chloroolefins have low nucleophilicity when compared with alkyl analogs, enol ethers, and enamines, etc., they are nevertheless more stable and survive unaltered during intervening synthetic operations which are necessary elsewhere in the molecule (*vide infra*). Moreover, their lack of anchimeric involvement at an incipient electrophilic center in the cyclization step allows chemical transformations, such as carbonium ion rearrangements, to occur *before* closure, which can also be of value in a well-planned synthesis. As a corollary, it becomes obvious that E (eq 1) must be quite stable (allowing SN1-like loss of L) to allow for successful closure. Finally, as these features of our scheme are elaborated upon, it will become clear that the cyclic chlorocarbonium ion initially formed shows little tendency to reopen or to isomerize further. Molecules with 2,3-dihaloallyl groupings,[16] exemplified by commercially available 2,3-dichloropropene (DCP), thus appeared to be suitable substrates for annelation because of their dual electrophilic and nucleophilic capabilities,[16] as illustrated in steps A and B, respectively. Similarly, 1,3-dihaloallyl units[16] are tailor made



(2)

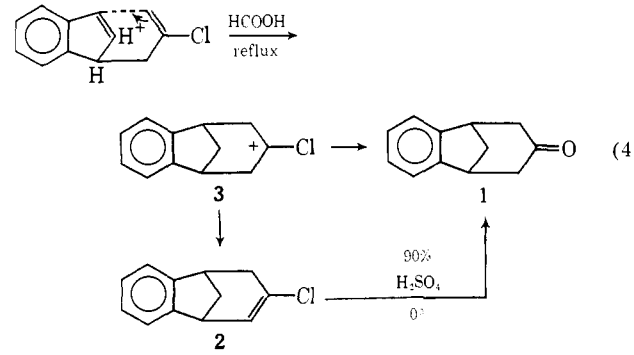
for cycloalkyl ketone synthesis (see eq 20), as we will report subsequently.[17] Although the above schemes



(3)

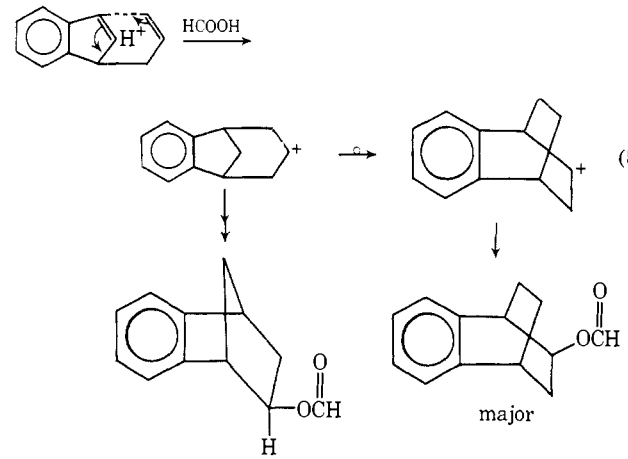
imply that Nu: and [E] are part of the same cyclic or acyclic molecule, these two portions of the final product can be introduced in different stages also.

The utilization of these ideas is illustrated by the synthesis of 3,5-(*o*-phenylene)cyclohexanone (**1**)[1a,18] which was required for a solvolysis study.[19] While other approaches to **1** were both time-consuming and inefficient,[20] we found that inverse addition of indenyl Grignard reagent to DCP (step A) proceeded in high yield and that formolysis of the resultant 1-(2-chloroallyl)indene (step B) gave **1** in *ca.* 60% yield.[1a] This was accompanied by *ca.* 30% of the bicyclic vinyl chloride (**2**), which itself hydrolyzed to **1** under appropriate conditions, thus raising the yield of **1**. As we had anti-



(4)

cipated, protonation of the diene occurred preferentially at C_2, producing the benzylic cation (E in our general scheme) that was required for intramolecular alkylation in the desired sense (→ **3**). Not only was **3** in the correct oxidation state for direct formation of **1**, but in addition unwanted skeletal rearrangement, which occurred during formolysis of 1-allylindene,[18,21] was now absent, *e.g.*



(5)

The fact that **1** could be synthesized in high yield, despite the presence of considerable ring strain led us

(15) K. Bott and H. Hellman, *Angew. Chem., Int. Ed. Engl.*, **5**, 870 (1966), have described the intermolecular reaction of 1,1-dichloroethylene and stable carbonium ions to give carboxylic acids *via* dichlorocarbonium ions.

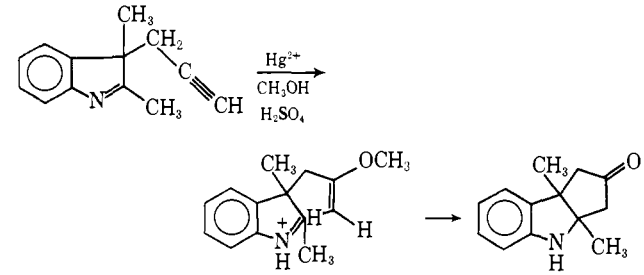
(16) The allylic halide structure is not essential; homoallylic halides are also suitable for nucleophilic displacement.

(17) P. T. Lansbury and P. C. Briggs, unpublished results. See Ph.D. Dissertation of P. C. Briggs, State University of New York at Buffalo, 1970.

(18) E. J. Nienhouse, Ph.D. Thesis, State University of New York at Buffalo, 1967.

(19) P. T. Lansbury and N. T. Boggs, *Chem. Commun.*, 1007 (1967).

(20) (a) N. T. Boggs, Ph.D. Thesis, State University of New York at Buffalo, 1967. Ketone **1** was originally prepared in several steps from benznorbornene. (b) Mercuric ion catalyzed hydrolysis of 1-propargylindene was completely unsuccessful, yielding only the indenylacetone derivative although cyclanone formation can occur in some cases, *e.g.*

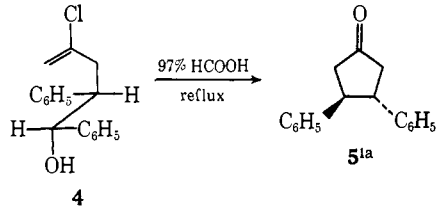


R. B. Woodward, Abstracts of 20th National Organic Chemistry Symposium, Burlington, Vt., June 1967, p 120.

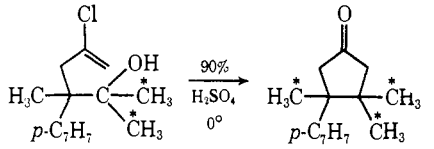
(21) P. T. Lansbury and E. J. Nienhouse, *Chem. Commun.*, 1008 (1967).

to explore[1] this annelation sequence in a variety of situations. Typical examples, which are summarized in eq 6–12, illustrate the possibilities for forming five- and six-membered monocyclic ketones from acyclic intermediates and their introduction into fused polycyclic systems from cyclic precursors. For convenience, only one of the enantiomeric forms is pictured throughout this paper to indicate the geometry of the racemate. Equations 8 and 9 illustrate the preparation

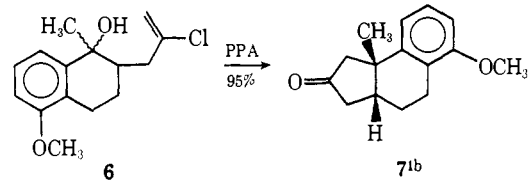
Cyclopentanone Syntheses



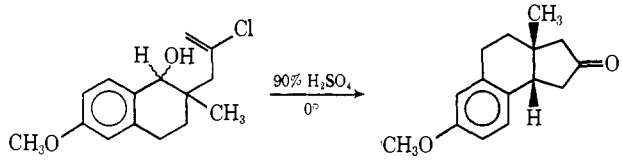
4 5[1a] (6)



10 (* indicates CD_3 label) 11 (7)



6 7[1b] (8)

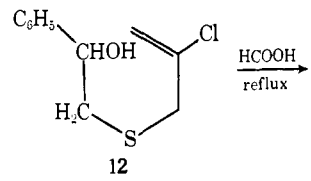


8 9[1b] (9)

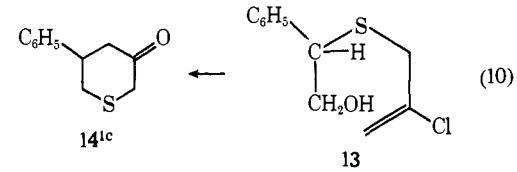
of potentially valuable tricyclic steroid intermediates, while eq 7 is the final step of a simple synthesis of the sesquiterpene β-cuparenone (11)[22] which has possible application for other related isoprenoids. Relatively stable cationic intermediates are seen to precede ring closure in the examples cited and these are sometimes a result of prior rearrangement. Thus, during conversion of **13** to **14**, an *epi*-sulfonium ion intermediate[23] intervenes in the ionization of the primary carbinol and this opens *via* the SN1 mechanism[23] to the benzylic cation directly accessible from **12**, which closes to **14**. Our inability to obtain 3-thianone (**23**) itself is understandable since the *epi*-sulfonium ion from **22** can only open by backside solvent attack.

Another instance where extensive rearrangement occurred prior to cyclization was in the synthesis of β-cuparenone (**11**). When two methyl groups in **10** were replaced by CD_3 (see asterisks in eq 7), the label in **11** was completely randomized among the three alkyl-bound methyls.[22] Being aware that ample opportunity for rapid aryl and alkyl shifts exists[24] allows one to plan

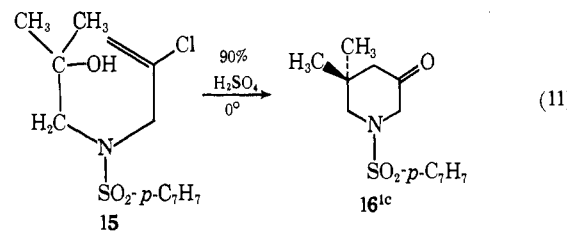
Cyclohexanone Syntheses



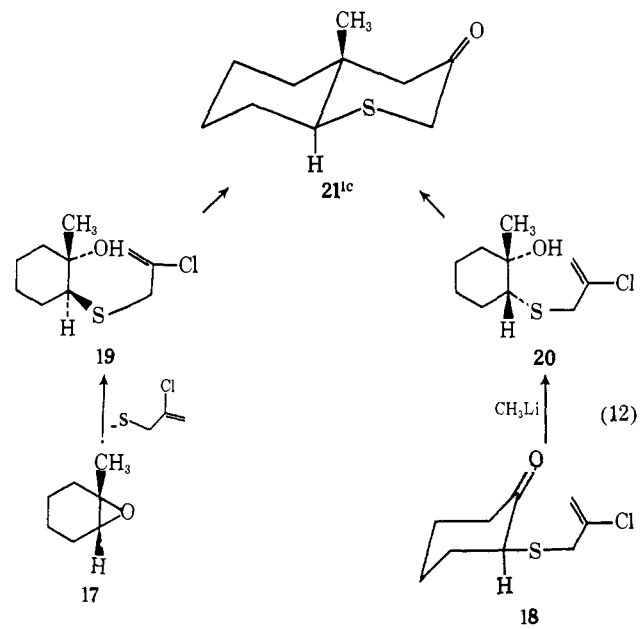
12



14[1c] 13 (10)



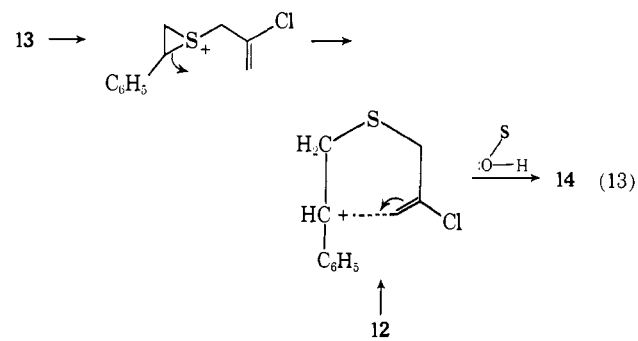
15 16[1c] (11)



(12)

syntheses of substituted cyclopentanones similar to β-cuparenone beginning with secondary carbinols that normally are unsuitable for cyclization.[25]

Nonstereospecificity in formation of polycyclic molecules is another consequence of nonconcerted ring clo-



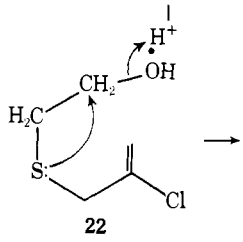
(13)

(22) (a) P. T. Lansbury and F. R. Hilfiker, *Chem. Commun.*, 619 (1969); (b) F. R. Hilfiker, Ph.D. Thesis, State University of New York at Buffalo, 1970.

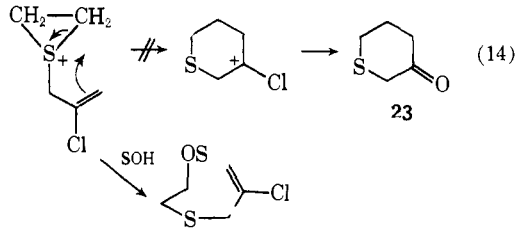
(23) W. H. Mueller, *Angew. Chem., Int. Ed. Engl.*, **8**, 482 (1969).

(24) G. Olah, M. B. Comisarow, and C. J. Kim, *J. Amer. Chem. Soc.*, **91**, 1458 (1969).

(25) Thus, 3-*p*-anisyl-3-(β-chloroallyl)-2-butyl alcohol cyclized in *ca.* 35% yield to 3,4-dimethyl-3-*p*-anisylcyclopentanone when allowed to react briefly in 90% sulfuric acid at 0°; P. T. Lansbury and F. R. Hilfiker, unpublished results.



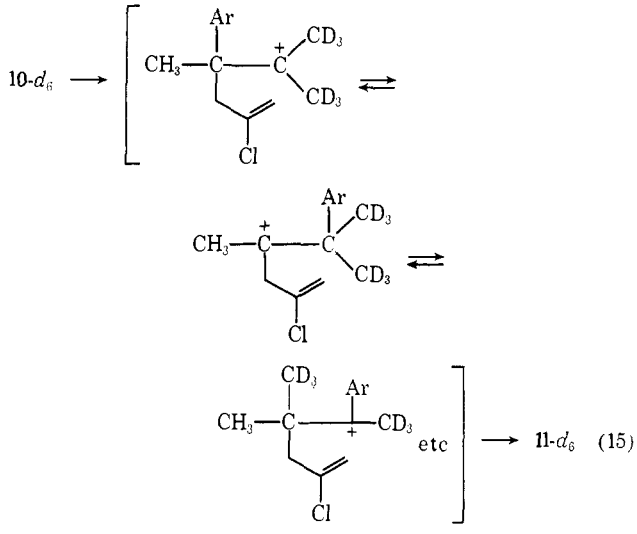
22



(14)

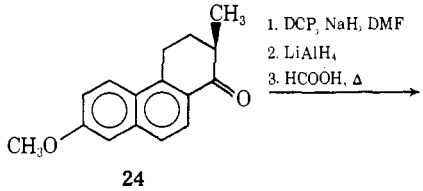
23

sure. Thus, *trans*-4-thia-9-methyl-2-decalone (**21**) was prepared from either **19** or **20**, as outlined above in eq 12, although in only 35–40% yield.[1c] Similarly, the construction of 8-methyl-2-hydrindanone deriv-

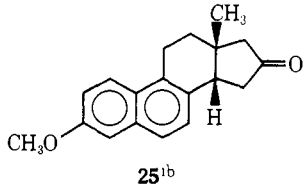


(15)

atives (eq 8 and 9) results in *cis*-ring fusions, as did the parent molecule,[1a] in spite of the fact that the precursors were mixtures of diastereomeric carbinols. A further illustration of this stereoselectivity is afforded by the synthesis of *cis*-16-equilenone methyl ether (**25**),[26] which required three steps beginning with **24**. The



24



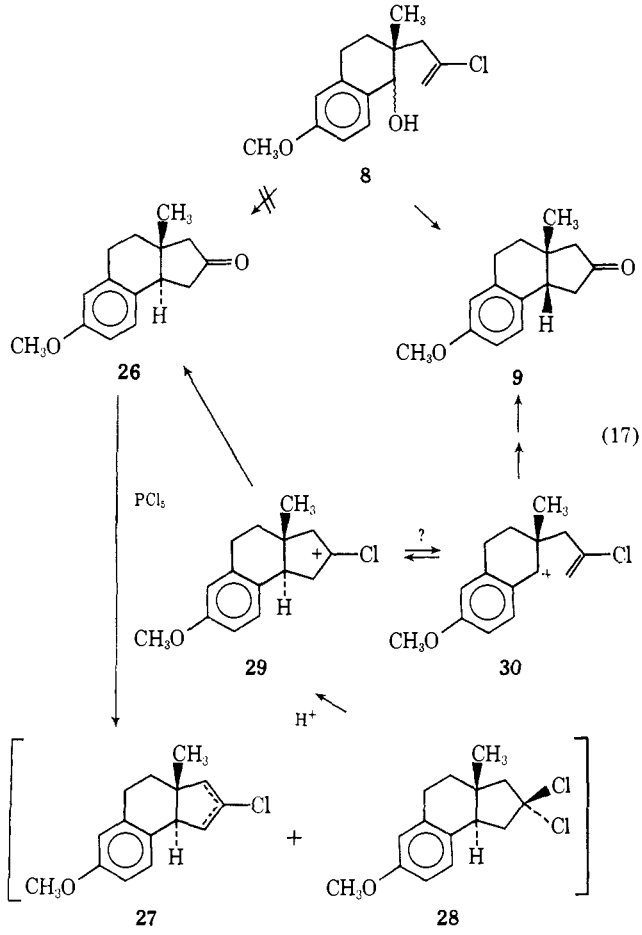
(16)

25[1b]

question of whether a *trans*-2-hydrindanone unit or the chlorocarbonium ion equivalent could be formed kinetically and revert to the more stable *cis* product

(26) A. L. Wilds, J. A. Johnson, and R. E. Sutton, *J. Amer. Chem. Soc.*, 72, 5524 (1950).

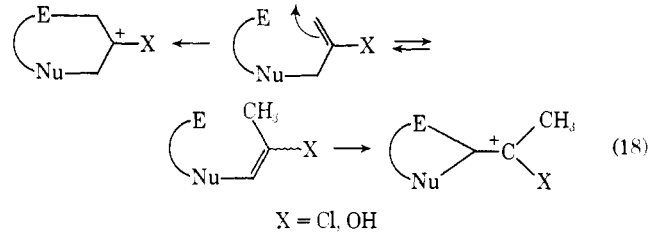
was tested in the following experiments. The *trans*-ketone **26**, which is isomeric but not interconvertible with the sole ketonic product of cyclization (**9**) in eq 9, was converted to a mixture of isomeric chloroolefins **27** and *gem*-dichloride **28** by phosphorus pentachloride; this was then allowed to react in 90% sulfuric acid at 0° (preferred cyclization conditions) with the reasonable expectation that all three chloro compounds would



(17)

give the *trans*-fused ion **29**. Any fragmentation of **29**, here particularly favored by relief of ring strain and formation of a *p*-anisyl carbonium ion (**30**), would result in formation of *cis*-ketone **9**. In the event, $\lesssim 5\%$ of **9** was isolated together with 85% of **26**. Thus it appears safe to say that the cyclization step (B) is largely irreversible and occurs *via* a transition state that resembles product, thus reflecting thermodynamic control.

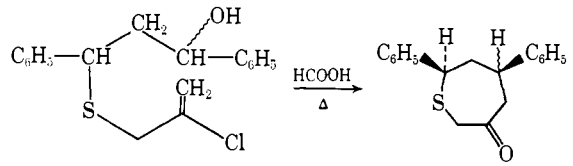
Brief mention should be made of initial efforts to synthesize seven-membered rings since the results pertain to the question of whether or not a chloroallyl group is isomerized to a more stable chloropropenyl one or even converted to a more nucleophilic enol for intramolecular alkylation. In those chloroallyl de-



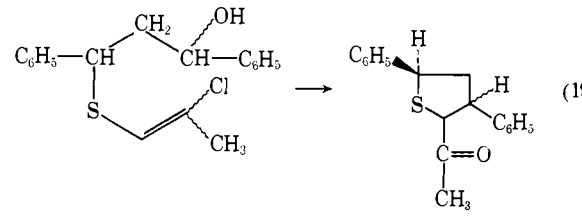
(18)

X = Cl, OH

rivatives constructed to yield five- and six-membered rings, the isomerized structure would be revealed by forming three- and four-membered cycloalkyl ketones, which is unlikely. However, a reaction designed to produce a cycloheptanone might easily be diverted to a cyclopentyl ketone[17] if the above isomerization (eq 18) were to occur under annelation conditions. Accordingly, the Michael adduct of chloroallyl mercaptan with benzalacetophenone was reduced to carbinol **31** (diastereomers) which was subjected to formolysis. A single ketone (**32**) was formed, albeit in only 20% yield; its cycloheptanone structure as formulated below was supported by infrared (carbonyl band at 5.89 μ) and nmr data, which simultaneously rule out the isomeric acetylthiophane **33**. Certainly if the β-chloro-



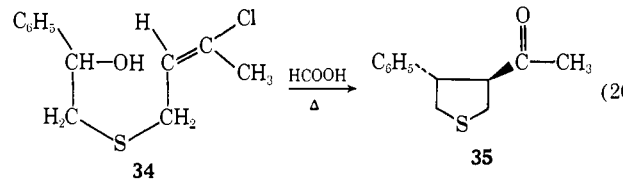
31 **32**



(19)

33

allyl group had isomerized to β-chloropropenyl, a high yield of **33** would have been anticipated. This assumption is fortified by the nearly quantitative cyclization observed in a similar system[17] (**34** → **35**), and

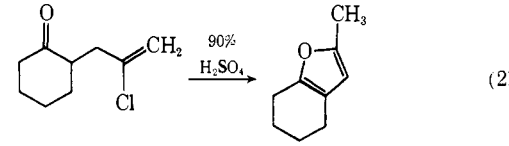


(20)

34 **35**

the general propensity for five- and six-membered rings to form more readily than seven- and larger-membered ones.[27] Fortunately, the relative inertness of vinyl chlorides to formic acid catalyzed isomerization (as shown in eq 19) allows compounds such as **31** to give **32** rather than **33**, which most certainly would result if we were dealing with the more nucleophilic enol ethers[28a] or enol acetates[28b] that are quite prone to isomerization.

We also wish to bring attention to the facile furanization of "masked" 1,4-diketones, such as 2-(β-chloroallyl)cyclohexanone,[18] which has been extended further by Nienhouse and coworkers.[29]



(21)

(27) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw Hill, New York, N. Y., 1962, pp 198–202.

(28) (a) G. Stork andP. F. Hudrlick, *J. Amer. Chem. Soc.*, **90**, 4462 (1968); (b) H. O. House, *Rec. Chem. Progr.*, **28**, 99 (1967).

As for optimum experimental conditions in cyclic ketone formation, we feel that these have to be worked out individually for the case in hand. From a good deal of experimentation, it can be generalized that hot 97% formic acid is the best medium in those cases where relatively stable cations are produced, since undesired attack on the chloroolefin is kept to a minimum. Where formolysis was unsuccessful, we found cold 90% aqueous sulfuric acid (v/v) for 5–30 min to work well, and in a few instances employed polyphosphoric acid. The Experimental Section gives some typical procedures.

Although the present work utilized only DCP among possible 2,3-dihaloallyl compounds, it is clear that many ramifications of this unit are worthy of further study. The same is true of 1,3-dihaloallyl compounds as precursors for cycloalkyl ketones.[17] We shall soon report on our results in these areas.

Experimental Section[30]

3,5-(*o*-Phenylene)cyclohexanone (1). Indenylmagnesium bromide (0.5 mol) was prepared in tetrahydrofuran (THF) by metalation of indene with ethylmagnesium bromide. The Grignard reagent was slowly added to a stirred, cold (−10°) solution of 55.5 g (0.5 mol) of 2,3-dichloropropene (DCP) in 60 ml of THF. After 0.5 hr, hydrolysis was accomplished with saturated ammonium chloride solution and the organic layer removed and dried over magnesium sulfate, together with THF washes of the inorganic residue. Distillation afforded 36.1 g (48% yield) of 1-(2-chloroallyl)indene, bp 79–80° (2.0 mm), showing infrared bands (neat) at 3.25, 3.41, 6.12, 6.85, 8.36, 8.92, 11.31, 12.92, 13.43, 13.80, and 14.04 μ. The nmr spectrum in CCl_4 showed aromatic protons centered at δ 7.16, the $C_2 + C_3$ protons at 6.71 and 6.38 (AB quartet), terminal $>C{=}CH_2$ at 5.19 and 5.04, the C_1 benzylic proton at 3.70, and the allylic methylene group at 2.48.

Anal. Calcd for $C_{12}H_{11}Cl$: C, 75.58; H, 5.77. Found: C, 75.43; H, 5.93.

To 900 ml of refluxing, stirred 97% formic acid was added dropwise 15.3 g of 1-(2-chloroallyl)indene. After an additional 1-hr reflux, the reaction was quenched in ice–water and the products were extracted into ether, washed with aqueous sodium bicarbonate, salt solution, and dried over magnesium sulfate. After solvent evaporation, the residual oil (14.1 g) was chromatographed over 300 g of alumina. Elution with low boiling petroleum ether gave 4.0 g (29%) of oily 1-chloro-3,5(*o*-phenylene)cyclohexene (**2**) which showed infrared bands at 3.39, 3.49, 6.12, 6.81, 6.87, 7.02, 9.69, 9.82, 10.36, 11.00, 11.14, 11.77, 12.27, 13.39, and 14.61 μ.

Anal. Calcd for $C_{12}H_{11}Cl$: C, 75.58; H, 5.77. Found: C, 75.49; H, 5.98.

Elution with 15% ether–petroleum ether afforded 8.1 g (59%) of ketone **1**, mp 64–66° (reported[20a] mp 66–68°), whose infrared

(29) E. J. Nienhouse, R. M. Irvin, and G. R. Finni, *J. Amer. Chem. Soc.*, **89**, 4557 (1967).

(30) Melting points were determined on a "Mel-Temp" capillary tube apparatus and are uncorrected; boiling points are also uncorrected. Infrared spectra were recorded on a Beckman IR-5A spectrophotometer and were calibrated using the 6.23 μ (1603 cm^{-1}) band of polystyrene film. Nuclear magnetic resonance spectra were obtained on Varian A-60 or HA-60 instruments, using carbon tetrachloride or chloroform-*d* as solvents, unless otherwise specified. Chemical shifts are recorded in δ units from internal tetramethylsilane. Mass spectra were run on a Perkin-Elmer RMU-6E mass spectrometer by Mr. Gary Herman. Vapor phase chromatography analyses were performed on Aerograph A-700 or F and M 720 instruments, using Apiezon M, Carbowax 20M Tide, or SE-30 silicone rubber columns (20% liquid phase on 60–80 mesh Chromosorb W) and helium as carrier gas. Column chromatography was performed using ether Merck chromatography-grade alumina or Will 60–200 mesh silica gel. Petroleum ether, frequently used as eluent, was the 30–60° bp fraction. Microanalyses were by Dr. A. Bernhardt and associates, Mullheim, Germany. The phrase "worked up as usual" signifies that after hydrolysis, the organic product(s) was taken up in ether, washed with sodium bicarbonate solution, followed by saturated aqueous sodium chloride and/or water, and then dried over anhydrous magnesium sulfate. Solvent was subsequently removed, using a rotary evaporator under reduced pressure, or the steam bath and the crude product purified by chromatography, recrystallization, or distillation as noted

(λ^{neat} >C=O 5.87 μ) and nmr spectra were identical with those of an independently prepared sample.[20a]

Anal. Calcd for $C_{12}H_{12}O$: C, 83.70; H, 7.01. Found: C, 83.69; H, 6.97.

Reaction of **1** with excess benzaldehyde and methanolic potassium hydroxide gave the dibenzylidene derivative as yellow needles (methanol–ethyl acetate), mp 128–129°.

Anal. Calcd for $C_{26}H_{20}O$: C, 89.62; H, 5.78. Found: C, 89.55; H, 5.89.

trans **- 3,4 - Diphenylcyclopentanone (5).** Equimolar quantities (0.1 mol) of ethanolic sodium ethoxide and desoxybenzoin, then dichloropropene were allowed to react for 3 hr at room temperature followed by 1-hr reflux. After the ethanol was removed by a rotary evaporator, hot water was added and the product allowed to crystallize. Filtration and recrystallization from methanol produced 21.7 g (80%) of α-(β-chloroallyl)desoxybenzoin, mp 66–68°; incorporation of the β-chloroallyl group was verified by infrared absorption (Nujol) at 6.10 and 11.12 μ and nmr peaks (CCl_4) at δ 5.09 and 5.01 (two 1 H broad "singlets") and 3.03 (AB portion of ABX spectrum, 2 H "octet" with $J_{AB} \sim 14.5$ Hz, $J_{AX} \simeq J_{BX} \simeq 7.5$ Hz, further broadened by allylic coupling).

Reduction of the ketone with excess lithium trimethoxyaluminum hydride[31] in tetrahydrofuran for 3 hr at 0°, followed by standard hydrolysis and work-up, gave crude product which was chromatographed on alumina. Elution with 20% ether–petroleum ether gave unreacted ketone, whereas pure ethyl ether eluted (±)-*erythro*-1,2-diphenyl-2-β-chloroallylethanol, mp 52–54°, in 65% yield; stereochemistry was assigned by applying Cram's rule.[32] Pertinent spectral data follow: ir (Nujol) OH at 2.92 and >=CH_2 at 6.12 and 11.32 μ; nmr (CCl_4) δ 2.60 (2 H doublet, $J \simeq 7.5$ Hz, broadened by allylic coupling), 3.32 (1 H, "quartet", $J \simeq 7.5$ Hz), 4.87 and 4.98 (two 1 H doublets, $J \simeq 2$ Hz).

A 5-mmol sample (1.35 g) of the above carbinol was added to 150 ml of refluxing 97% formic acid. After a 45-min reflux, the reaction mixture was quenched in ice water, extracted with ether, and worked up as usual. The crude product was recrystallized from methanol to provide 0.36 g (31%) of *trans*-3,4-diphenylcyclopentanone (**5**), mp 174–177° (reported[33] mp 177°), whose infrared spectrum (Nujol) showed cyclopentanone absorption at 5.73 μ. The 2,4-dinitrophenylhydrazone had mp 171–173°, again agreeing with the reported[33] value of 173°.

β-Cuparenone (11). Ethyl *p*-tolylacetate was prepared according to the procedure of Cope.[34] Alkylation of 30.7 g (0.116 mol) of this ester was accomplished with 1 equiv (0.118 mol) of sodamide in 400 ml of liquid ammonia and 40 ml of ether, to which was added 13.1 g (0.177 mol) of DCP in 30 ml of ether. After 90 min, a slight excess of ammonium chloride was added and the ammonia evaporated and replaced by ether. Water was added and the ether layer washed as usual, dried, and solvent was evaporated. Distillation gave 20.6 g (71% yield) of monoalkylated ester bp 116–118° (1 mm); M^+ at *m/e* 252; ir (neat) 3.31, 5.76, 6.10, 6.95, 7.49, 7.90, 8.14, 8.60, 8.90, 9.80, 11.30, and 12.25 μ.

Anal. Calcd for $C_{14}H_{17}ClO_2$: C, 66.54; H, 6.78. Found: C, 66.97; H, 6.90.

Seven grams (28 mmol) of the above ester was alkylated as above with methyl iodide in liquid ammonia–ether medium, then worked up in similar fashion. The product ester was obtained in 76% yield by distillation, bp 96–97° (0.15 mm); mass spectrum M^+ at *m/e* 266; ir (neat) 3.30, 5.80, 6.11, 6.87, 7.72, 8.12, 8.70, 9.14, 9.80, 11.30, 12.30, and 13.70 μ.

Anal. Calcd for $C_{15}H_{19}ClO_2$: C, 67.52; H, 7.18. Found: C, 67.78; H, 7.24.

Excess ethereal methyllithium was allowed to react (0° for 1 hr) with 5 g (19 mmol) of the dialkylated ester. After hydrolysis with ammonium chloride solution and standard washing and drying of the ether product layer, evaporation produced an oil which was chromatographed over alumina. Elution with ether–petroleum ether gave 3.76 g (80%) of oily alcohol **10**, whose infrared spectrum[22b] showed relevant bands at 2.82 (O–H), 6.11, and 11.35 μ (both >C=CH_2), and no carbonyl absorption. The confirmatory nmr spectrum[22b] showed *inter alia* the four methyl singlets required at δ 1.00, 1.18, 1.49, and 2.29 ($CDCl_3$).

Anal. Calcd for $C_{15}H_{21}ClO$: C, 71.26; H, 8.37. Found: C, 70.85; H, 8.34.

Dropwise addition of 2.12 g of **10** to 100 ml of cooled (−20°) 97% sulfuric acid produced a red solution which was stirred for 20 min, then hydrolyzed with excess ice water, and extracted with ether. After washing and drying the ether solution, solvent was stripped off and the residue chromatographed over alumina. After an initial olefin fraction, there was obtained 618 mg (34%) of (±)-β-cuparenone, showing carbonyl absorption at 5.73 μ and a fully consistent nmr spectrum,[35] showing methyl singlets at δ 0.73, 1.23, 1.42, and 2.25, a 2 H singlet at 2.12, a 2 H AB quartet at 2.58, and 4 ArHs at 7.08. The semicarbazone had mp 210–212.5° (reported[35] 213.5–215°).

cis-**6,7-(2-Methoxy)benzo-8-methyl-2-hydrindanone (7).** 5-Methoxy-1-tetralone (50 g, 0.283 mol) was alkylated,[36] using 650 ml of 2 *M* magnesium methyl carbonate in dimethylformamide and 100 g (0.90 mol) of DCP. After heating under N_2 at 65° for 14 hr, hydrolysis was accomplished with cold 10% hydrochloric acid, followed by several ether extractions and washing and drying of the combined extracts. Solvent removal and alumina chromatography of the residue led to 56.2 g (79% yield) of 2-(2-chlorallyl)-5-methoxy-1-tetralone, mp 54–56.5° (methanol): ir (Nujol) 3.40, 5.96, 6.11, 6.31, 7.00, 7.75, 7.93, 8.20, 9.50, 10.37, 11.25, 12.56, and 13.40 μ; nmr ($CDCl_3$) was consistent.[22b]

Anal. Calcd for $C_{14}H_{15}O_2Cl$: C, 67.05; H, 6.04. Found: C, 66.24; H, 6.33.

The above ketone (9.12 g) was treated with excess ethereal methylmagnesium iodide for *ca.* 4 hr at room temperature, then hydrolyzed with cold ammonium chloride solution. Extraction with ether, followed by washing, drying, and concentration led to a reddish oil (8.9 g) which was chromatographed on alumina. Elution with 10% ether–petroleum ether gave 7.65 g (78% yield) of white solid, mp 89–92° (prisms from hexane). Infrared (Nujol) showed O–H at 3.0 μ and –(Cl) C=CH_2 at 6.11 and 11.36 μ, and the nmr spectrum[22b] showed, *inter alia*, two methyl singlets at δ 1.27 and 1.55, corresponding to the two diastereomeric carbinols (**6**).

Anal. Calcd for $C_{15}H_{19}ClO_2$: C, 67.47; H, 7.16. Found: C, 67.58; H, 7.17.

Compound **6** (1 g) dissolved in *ca.* 1 ml of ether was gradually added to *ca.* 40 g of polyphosphoric acid at 96° under nitrogen. After 5 hr, the red mixture was cooled, poured into excess ice water, and worked up. Alumina chromatography of the dark oily product gave 356 mg (40% yield) of oily ketone **7** (eluted with 4% ether–petroleum ether), which was analyzed as the 2,4-dinitrophenylhydrazone, mp 233–234° (benzene).

Anal. Calcd for $C_{21}H_{22}N_4O_5$: C, 61.20; H, 5.47. Found: C, 60.95; H, 5.43.

The infrared spectrum[22b] of **7** confirmed the cyclopentanone structure, showing the carbonyl band at 5.75 μ and loss of OH and β-chloroallyl bands. Nmr ($CDCl_3$) showed 3 H singlet at 1.43 ($W_{H/2}$ = 1.3 Hz), 9 H multiplet at 1.6–3.04, 3 H singlet at 3.79 ($W_{H/2}$ = 1.0 Hz), and 3 aryl H's at 6.5–7.32. The half-height width of the angular methyl group (δ 1.43) indicated little "*W* coupling."

Other conditions for effecting the conversion of **6** to **7**, *e.g.*, sulfuric, formic, trifluoroacetic, and hydrofluoric acids, did not lead to improved yields of hydrindanone **7**.

cis-**4,5-(4-Methoxy)benzo-8-methyl-2-hydrindanone (9).** 6-Methoxy-1-tetralone (50 g) was alkylated with DCP by Stiles' method,[36] as above, providing 62 g (87%) of 2-(2-chloroallyl)-6-methoxy-1-tetralone, mp 55–56.5°, which displayed consistent infrared and nmr spectra.[22b]

Anal. Calcd for $C_{14}H_{15}O_2Cl$: C, 67.05; H, 6.04. Found: C, 66.82; H, 6.24.

Methylation of this ketone (4.6 g) was accomplished by using excess sodium hydride and methyl iodide in dimethylformamide. After 5 hr at room temperature, hydrolysis was effected with ice water and the product taken up in ether. After washing with water, salt solution and drying, the solution was evaporated and the residue chromatographed. Elution with 4% ether–petroleum ether yielded 4.04 g (85%) of oily 2-(2-chloroallyl)-2-methyl-6-methoxy-1-tetralone: ir (neat) 3.40, 5.99, 6.12, 6.24, 6.88, 7.45, 7.88, 7.95, 8.14, 9.17, 9.72, 11.32, and 12.95 μ; nmr ($CDCl_3$) *inter alia*, two methyl singlets at δ 1.22 and 3.80.

Lithium aluminum hydride reduction of the above tetralone (3.96 g) in ether occurred in 95% yield, giving an isomeric pair of carbinols (**8**) as evidenced by the appearance of two methyl singlets at δ 0.92 and 1.00 ($CDCl_3$) in the nmr spectrum.[22b] In-

(31) H. C. and C. J. Schoaf, *J. Amer. Chem. Soc.*, **86**, 1079 (1964).
(32) D. J. Cram and F. A. Abd Elhafez, *ibid.*, **74**, 5828 (1952).
(33) J. W. Lynn and J. English, Jr., *J. Org. Chem.*, **16**, 1546 (1951).
(34) A. C. Cope, P. A. Trumbull, and E. R. Trumbull, *J. Amer. Chem. Soc.*, **80**, 2844 (1958).
(35) G. L. Chetty and S. Dev, *Tetrahedron Lett.*, 73 (1964). We thank Professor Dev for providing us with copies of his infrared and nmr spectra, which were superimposable with ours.
(36) M. Stiles, *J. Amer. Chem. Soc.*, **85**, 621 (1963).

frared data (O–H at 2.90 μ, no carbonyl absorption) also supported the product, which had mp 90–94° (from petroleum ether).

Anal. Calcd for $C_{15}H_{19}O_2Cl$: C, 67.47; H, 7.16. Found: C, 67.16; H, 7.00.

The preferred cyclization medium for **8** appeared to be 90% sulfuric acid at 0° for *ca.* 10 min. From 2.04 g of **8** after hydrolysis and work-up there resulted 0.794 g (44%) of oily ketone **9**, which analyzed as the semicarbazone, mp 206–208° (ethanol).

Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.86; H, 7.38. Found: C, 66.78; H, 7.02.

Infrared (neat) 3.42, 5.75, 6.21, 6.65, 7.85, 8.04, 8.61, 8.72, 9.60, 11.76, 12.27, and 12.45 μ; nmr ($CDCl_3$) showed *inter alia* methyl singlets at 1.13 (C_8–CH_3) and 3.72 (OCH_3) whose $W_{H/2}$ values were 1.0 and 0.7 Hz, respectively.

***cis*-3-Methoxy-16-equilenone (25).** 1-Keto-2-methyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene (4.95 g) was treated with 2 equiv of sodium hydride in dimethylformamide at 55–60° for 17 hr (nitrogen atmosphere) and then treated with excess DCP for 5 hr at 65°. Solvent was then stripped *in vacuo* and the residue poured into ice water and worked up as usual. Chromatography over alumina (7% ether–petroleum ether) gave crystalline 1-keto-2-methyl-2-β-chloroallyl-7-methoxy-1,2,3,4-tetrahydrophenanthrene, mp 102–104.5° (methanol): ir (Nujol) 6.00, 6.16, and 11.21 μ (both β-chloroallyl): nmr ($CDCl_3$) δ 1.25 (3 H, singlet), 2.75 (2 H, AB quartet with J_{AB} = 14.2 Hz), 5.14 and 5.25 (two 1 H doublets, J = 1 Hz), these peaks confirming introduction of the C_2-β-chloroallyl group.

Lithium aluminum hydride reduction of the ketone in ether gave carbinol (95% yield of a diastereomeric mixture), mp 86–120° (hexane), whose infrared spectrum (Nujol) showed no carbonyl absorption and O–H at 3.02 μ; nmr ($CDCl_3$) confirmed the presence of isomeric carbinols with two methyl singlets appearing at δ 0.95 and 1.04.

A 900-mg sample of the above carbinols in 60 ml of 97% formic acid was refluxed for 30 min, then quenched in ice water, and worked up. Recrystallization of 650 mg of yellow-brown solid from methanol–acetone yielded 230 mg (30%) of pure **25**, mp 168.5–170° (reported[26] 171–172°) which was undepressed on admixture with authentic **25**. The infrared spectrum (KBr pellet) was superimposable with that of authentic **25**, showing peaks at 5.77, 6.16, 6.24, 6.63, 7.08, 7.31, 8.00, 8.08, 8.38, 8.50, 8.61, 9.67, 11.48, 12.15, and 2.24 μ.

***trans*-4,5-(4-Methoxy)benzo-8-methyl-2-hydrindanone (26).** The sequence for preparing **26** was patterned after that used by Wilds, *et al.*,[28] to synthesize *trans*-fused 16-keto steroids.

2-(2-Chloroallyl)-2-methyl-6-methoxy-1-tetralone (see above) was stirred for 10 min at 0° in 90% sulfuric acid. The red solution was then poured into excess ice water and worked up in the usual manner. Recrystallization of the crude product from methanol gave the pure diketone, mp 99–100°, showing infrared carbonyl absorption at 5.82 ($-CH_2C(=O)CH_3$) and 6.00 μ (p-$CH_3OC_6H_4C(=O)$) and a consistent nmr spectrum.[22b]

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.36. Found: C, 72.71; H, 6.92.

The diketone (5.5 g) was aldolized by refluxing under N_2 for 18 hr in aqueous methanolic potassium hydroxide. Upon dilution with water, extraction with ether, washing, drying, and solvent evaporation, there was obtained 5.0 g (90% yield) of the fused cyclopentenone, mp 97–98° (from hexane), showing infrared carbonyl absorption at 5.95 μ, a confirmatory nmr spectrum and M^+ at m/e 228.

Lithium aluminum hydride reduction of the cyclopentenone in refluxing ether (10 min), followed by conventional hydrolysis and work-up gave a mixture of stereoisomeric carbinols, mp 112–118°, whose nmr and infrared spectra were in accord with expectation. Hydrogenation (Pd–C in ethanol at 50 psig for 90 min) produced the saturated *trans*-fused cyclopentanol, mp 99.5–100.5° (from hexane–benzene), whose nmr spectrum showed no vinyl protons and was otherwise consistent.[22b] Oxidation of the saturated alcohol (939 mg) was performed by means of the Pfitzner–Moffatt reagent.[37] From alumina chromatography, there resulted 650 mg (63% yield) of the *trans*-fused tricyclic ketone **26**, mp 81–82° (from petroleum ether), which showed infrared carbonyl absorption at 5.73 μ, M^+ at m/e 230, and nmr chemical shifts at δ 0.73 (3 H, singlet), 1.70–3.40 (9 H, multiplet), 3.77 (3 H, singlet), and 6.50–7.00 (2 H, multiplet). The angular methyl peak at δ 0.73 had $W_{H/2}$ = 2.2 Hz, compared with the methoxyl peak, $W_{H/2}$ = 1.2 Hz, indicative of the *trans*-hydrindanone stereochemistry.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.22; H, 7.88. Found: C, 78.30; H, 7.94.

When ketone **26** was subjected to cold 90% sulfuric acid, as in the formation of **9**, and subsequently hydrolyzed and worked up, no detectable stereomutation (**26** → **9**) had occurred (vpc and infrared).

Attempted Interconversion of 9 and 26 *via* Chlorocarbonium Ions. A 530-mg (2.3 mmol) sample of *trans*-ketone **26** was refluxed for 40 hr with 528 mg (2.5 mmol) of phosphorus pentachloride in 5 ml of methylene chloride. Hydrolysis with ice water followed by ether extraction, washing, drying, and solvent evaporation gave an oil that was chromatographed over alumina. A mixture (243 mg) of carbonyl-free (infrared) chloroolefins (**27**) and *gem*-dichloride **28** was obtained; nmr showed *ca.* 0.7 vinyl Hs at δ 5.86 (due to **27**). This mixture was subjected to 90% sulfuric acid (as in synthesis of **9**) at 0° for 20 min, then hydrolyzed and worked up. Vpc analysis (6 ft Apiezon L column at 240° with He flow rate = 110 cc/min) showed the product to contain *ca.* 85% **26**, 5% **9** and *ca.* 10% recovered **27**.

5-Phenyl-3-thianone (14). 2-Chloroallyl mercaptan was prepared by refluxing molar quantities of DCP and thiourea in 500 ml of 95% ethanol for 16 hr. Sodium hydroxide (1 mol) in 300 ml of water was then added and reflux continued for 4 hr more. After stirring overnight, the crude mercaptan layer was separated and the basic aqueous layer acidified (10% sulfuric acid), then extracted with several portions of ether. The crude mercaptan and ether extracts were washed with water and dried over magnesium sulfate. Distillation *in vacuo* produced 35 g (32%) of mercaptan, bp 56–57° (70 mn), showing pertinent infrared bands at 3.9, 6.12, 7.15, 8.0, 8.25, 8.85, 11.24, 13.65, and 14.74 μ. The nmr spectrum (CCl_4 solvent) showed S–H at δ 2.02 (triplet, J = 8 Hz), $-CH_2-$ at 3.50 (doublet, J = 8 Hz), and $>C=CH_2$ at 5.30 and 5.49 (doublets with J = 2 Hz). The 2,4-dinitrophenyl thioether prepared from 2-chloroallyl mercaptan, mp 64–66°, was subjected to elemental analysis.

Anal. Calcd for $C_9H_7ClN_2O_4S$: C, 39.49; H, 2.60. Found: C, 39.59; H, 2.76.

A methanol solution of the sodium salt of 2-chloroallyl mercaptan was prepared from 9 mmol each of sodium methoxide and mercaptan. Thirty minutes later, an equivalent amount of styrene oxide in methanol was gradually added and the resultant solution stirred overnight at room temperature. Hydrolysis, ether extraction and work-up produced 2.1 g (99% yield) of a 2:1 mixture (by vpc analysis on a 4 ft Carbowax 20M column at 240°) of isomeric hydroxysulfides **12** and **13**, respectively. The pure, oily isomers were obtained by alumina chromatography, using 75% petroleum ether–25% ether as eluent, and their individual infrared and nmr spectra recorded[38] as well as obtaining separate elemental analyses.

Anal. Calcd for $C_{11}H_{13}ClOS$: C, 57.50; H, 5.68. Found for **12**: C, 57.31; H, 5.37. Found for **13**: C, 57.17; H, 5.42.

Either **12** or **13** (or a mixture) (1 g) was refluxed in 30 ml of 97% formic acid for 1.5 hr and the dark red solution then cooled, diluted with water, and extracted with ether. The ether extract was worked up as usual and the oily product (410 mg, 50%) purified by preparative vpc on a 4-ft Carbowax 20M column at 230°, providing crystalline **14**, mp 58–60°.

Anal. Calcd for $C_{11}H_{12}OS$: C, 68.60; H, 6.25. Found: C, 68.46; H, 6.16.

The infrared spectrum (neat) of **14** showed a carbonyl peak at 5.85 μ and the nmr spectrum plus that of the tetradeuterated derivative, was fully consistent with the assigned structure.

A 400-mg sample of **14** was oxidized with peracetic acid in 65% yield to the sulfone, mp 139–140°. The infrared spectrum was identical with that of an authentic sample,[39] mp 140°, and the mixture melting point was undepressed.

5,5-Dimethyl-3-thianone[1c] was prepared from the carbinol in cold 90% sulfuric acid as above, using isobutylene oxide rather than styrene oxide:[38] bp 49–50° (1 mm); ir λ_{max}^{film} 5.84, 6.83, 7.05, 7.63, 8.00, 8.61, 8.94, 9.39, 10.05, 10.82, and 13.15 μ; nmr (CCl_4) δ 1.13 (6 H, singlet) and three 2 H singlets at 2.17, 2.60, and 3.03. For analysis, the 2,4-dinitrophenylhydrazone was prepared, mp 129–131°.

(37) K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, 87, 5670 (1965).

(38) D. J. Scharf, Ph.D. Dissertation, State University of New York at Buffalo, 1969.

(39) Kindly furnished by Dr. G. A. Pagani, University of Milan.

Anal. Calcd for $C_{13}H_{16}N_4O_4S$: C, 48.10; H, 4.94. Found: C, 48.02; H, 5.33.

4-Thia-9-methyl-2-decalone (21). Using the same procedure as with styrene oxide, 10 g (89 mmol) of 1-methylcyclohexene oxide (**17**)[40] and 9.68 g (89 mmol) of 2-chloroallylmercaptan were allowed to react to give 19.5 g (98%) of the *trans*-alcohol **19**: bp 110–112° (1.25 mm); ir λ_{max}^{film} 2.90, 6.12, 6.91, 7.09, 7.26, 7.5, 8.30, 8.90, 10.28, 11.23, 12.41, 13.15, and 14.79 μ; nmr (CCl_4) δ 1.10 (3 H, singlet), 1.30–2.25 (4 H, multiplet), 2.60 (1 H, doublet of doublets), 2.74 (OH), 3.40 (2 H, $-CH_2-S$, broad singlet), 5.21, and 5.38 (pair of doublets, J = 1 Hz).

Anal. Calcd for $C_{10}H_{17}ClOS$. C, 54.21; H, 7.70. Found: C, 54.03; H, 7.60.

Cyclization of **19** (1 g) was carried out in 30 ml of 90% aqueous sulfuric acid under nitrogen at 5° for 20 min. After hydrolysis with ice water and extraction into ether, the product extract was washed, dried, and evaporated. The residue was chromatographed over silica gel; elution with 10% ether–petroleum ether provided 258 mg (35%) of oily ketone **21**: ir (film) 5.86, 6.89, 7.06, 7.23, and 8.0 μ; nmr (CCl_4) δ 1.20 (CH_3 singlet), 1.35–2.2 (multiplet $-(CH_2)_4-$), 2.4–2.7 (doublet of doublets, CH–S), 2.23 (AB quartet, J_{AB} = 14 Hz, $\Delta\nu_{AB}$ = 49 Hz, $-CH_2-C=O$), 3.07 (AB quartet, J_{AB} = 13 Hz, $\Delta\nu_{AB}$ = 29 Hz, $S-CH_2C=O$). Elemental analysis of **21** was carried on the semicarbazone: mp 215–216° (ethanol).

Anal. Calcd for $C_{11}H_{19}N_3OS$: C, 54.89; H, 7.90. Found: C, 55.19; H, 7.77.

The nmr methyl signal in **21** at δ 1.20 had $W_{H/2}$ = 1.6 Hz, when internal TMS had $W_{H/2}$ = 0.6 Hz, indicative of *trans* stereochemistry.

Hydrogenolysis of 400 mg of **21** with 10 g of Raney nickel[41] in refluxing dioxane for 3 hr, followed by filtration, solvent removal, and alumina chromatography produced 190 mg (57%) of (1-methylcyclohexyl)acetone: ir (film) 5.82, 6.89, and 7.37 μ; nmr (CCl_4) δ 1.0 ($>C-CH_3$), 1.42 (ring CH_2), 2.05 ($CH_3C(=O)$ 2.29 ($-C-CH_2-$). The semicarbazone, mp 180–181°, was analyzed.

Anal. Calcd for $C_{11}H_{21}N_3O$: C, 62.56; H, 9.96. Found: C, 62.56; H, 10.15.

The alternate route to **21** involved cyclizing carbinol **20**, the diastereomer of **19**, which was synthesized by the Grignard route. A methanol solution of the sodium salt of 2-chloroallyl mercaptan (28.2 mmol) was prepared as usual. This was gradually added to 5 g (28.2 mmol) of 2-bromocyclohexanone[42] in 50 ml of methanol. After 16 hr at room temperature, the mixture was diluted with water, extracted with ether, and worked up as usual. Distillation afforded 2.9 g (51%) of 2-(2-chloroallylthia)cyclohexanone: bp 99° (0.5 mm); ir (film) 5.87, 6.12, 7.0, 8.92, and 11.25 μ; nmr (CCl_4) δ 1.50–3.08 (multiplet, $-(CH_2)_4-$), 3.3 ($-S-CH_2$), 3.2–3.62 (multiplet, –S–CH), 5.28, and 5.4 ($=CH_2$). For analysis, the 2,4-dinitrophenylhydrazone was prepared, mp 120–122°.

Anal. Calcd for $C_{15}H_{17}ClN_4O_4S$: C, 46.95; H, 4.44. Found: C, 47.03; H, 4.66.

Excess methylmagnesium iodide was treated with 4 g (19 mmol) of the above cyclohexanone. After 1 hr, the Grignard mixture was hydrolyzed with saturated ammonium chloride solution and worked up as usual. Distillation provided 4.25 g (90%) of *cis*-alcohol **20**: bp 89–90° (0.4 mm); ir (film) 2.88, 6.12, 6.90, 7.08, 7.30, 7.50, 8.29, 9.09, 9.91, 10.41, 10.84, 11.25, 11.70, 13.16, and 14.78 μ; nmr (CCl_4) δ 1.29 ($-CH_3$), 1.35–2.0 (multiplet, $-(CH_2)_4-$), 2.35–2.70 (singlet and multiplet, OH and CH–S), 3.41 ($S-CH_2-$) 5.28, and 5.40 (doublets, J = 1 Hz, $>C=CH_2$).

Anal. Calcd for $C_{10}H_{17}ClOS$: C, 54.21; H, 7.70. Found: C, 53.98; H, 7.72.

Cyclization of **20** was carried out exactly as with **19**, yielding ketone **21**, in 35% yield.

5,5-Dimethyl-3-(N-*p*-toluenesulfonyl)piperidone (16). Equimolar quantities (70 mmol) of sodium hydride and *p*-toluenesulfonamide were treated in 350 ml of dimethylformamide (DMF) at 60° for 1.5 hr. The solution was then cooled to room temperature and 7 g (97 mmol) of isobutylene oxide in 50 ml of DMF added during 30 min. After 2 hr at 100°, the reaction was cooled and 20 ml of water added; the DMF solvent was then removed by distillation (50°/min) and the residue dissolved in 200 ml of 20% aqueous sodium hydroxide. After ether extraction, the basic solution was neutralized with 5% aqueous hydrochloric acid and then saturated with sodium chloride. This was now extracted with several portions of ether, which were combined, washed and dried, then solvent removed. Alumina chromatography of the crude product, eluting with ether–petroleum ether (increasing the proportion of ether gradually), gave 10 g (59%) of N-(2-methyl-2-hydroxypropyl)-*p*-toluenesulfonamide: mp 57–59° (carbon tetrachloride); ir (film) 2.85–3.05, 6.23, 7.6, 8.61, 9.13, 10.90, and 12.30 μ; nmr (acetone-d_6) δ 1.16 (*gem*-CH_3s), 2.31 ($Ar-CH_3$), 2.82 (doublet, J = 7 Hz, $HN-CH_2$), 3.70 (OH), 6.23 (triplet, J = 7 Hz, NH), 7.52 (AB quartet, J_{AB} = 9 Hz).

Anal. Calcd for $C_{11}H_{17}NO_3S$: C, 54.00; H, 7.00. Found: C, 54.04; H, 6.92.

Following the same procedure as above, 22-mmol quantities of sodium hydride, the above amide, and then DCP were allowed to react (overnight at room temperature, then 100° for 1 hr) in 350 ml of DMF solvent. After stripping off DMF, hydrolysis with 20% aqueous sodium hydroxide and ether extraction, followed by work-up gave 2.86 g (41%) of sulfonamide **15**: mp 72–74° (ethanol–water); ir (film) 2.83, 6.12, 6.23, 6.93, 7.49, 8.63, 9.15, 9.42, 11.09, 12.3, 13.05, 14.16, and 15.2 μ; nmr (CCl_4) δ 1.20 (*gem*-CH_3s), 2.41 ($Ar-CH_3$), 2.85 (OH), 3.23 ($N-CH_2$), 4.22 ($>N-CH_2-C\lesssim$), 5.25, and 5.31 (doublets, J = 1 Hz, $>C=CH_2$), 7.5 (AB quartet, J_{AB} = 9 Hz).

Anal. Calcd for $C_{14}H_{20}ClNO_3S$: C, 53.01; H, 6.41. Found: C, 52.96; H, 6.42.

N-(2-Hydroxy-2-methylpropyl)-*p*-toluenesulfonamide (2 g, 40% recovery) was recovered from the alkaline solution after acidification, etc.

Cyclization of **15** (700 mg) was carried out in 30 ml of 90% aqueous sulfuric acid for 25 min at 0–5°; the solution was then quenched on crushed ice and worked up as usual. Recrystallization (ether–pentane) of the solid product gave 600 mg (~90%) of 5,5-dimethyl-1-*p*-toluenesulfonyl-3-piperidone (**16**), mp 109–110° (reported[43] mp 110°), whose 2,4-dinitrophenylhydrazone had mp 186–188° (reported[43] mp 190°). Spectral properties for **16** were as follows: ir (Nujol mull) 5.77, 7.45, 8.60, 9.15, 10.25, 12.20, 13.08, and 15.03 μ; nmr (CCl_4) δ 0.99 (*gem*-CH_3s) 2.01 ($CH_2-C=O$), 2.34 ($Ar-CH_3$), 2.85 ($N-CH_2$), 3.30 ($N-CH_2-C=O$), 7.35 (AB quartet, J_{AB} = 8 Hz).

Compound **15** was also prepared by alkylating *p*-toluenesulfonamide first with DCP and then with isobutylene oxide.[38]

4,6-Diphenyl-3-thiacycloheptanone (32). 2-Chloroallyl mercaptan (1 g, 9.2 mmol) was added to 50 ml of methanol containing 150 mg (catalytic amount) of sodium methoxide. An equivalent quantity (1.91 g) of benzalacetophenone in 25 ml of methanol was added and the reaction mixture refluxed for 10 days. On cooling, excess water was added and the product taken up in ether and worked up conventionally. Alumina chromatography, with petroleum ether as eluent, provided *ca.* 20% recovered benzalacetophenone first and then 2.2 g (80%) of 3-(2-chloroallylthia)-3-phenylpropiophenone: mp 49–51° (ethanol–water); ir (Nujol mull) 5.91, 6.12, 6.23, 6.69, 7.50, 8.23, 8.96, 9.82, 10.20, 11.30, 13.40, and 14.50 μ; nmr (CCl_4) δ 2.94 ($S-CH_2$), 3.25 (doublet, J = 7 Hz, $-CH_2-C-$), 4.36 (triplet, J = 7 Hz, C_6H_5-CHs), 5.0 and 5.10 (doublets, J = 1 Hz $>C=CH_2$), and 6.8–7.5 (aromatic multiplet).

Anal. Calcd for $C_{18}H_{17}ClOS$: C, 68.05; H, 5.38. Found: C, 67.78; H, 5.48.

Reduction of the above ketone was carried out by ethereal lithium aluminum hydride, followed by conventional hydrolysis and work-up. Alumina chromatography, with 1:1 ether–petroleum ether eluent, afforded 3.0 g (~95%) of oily diastereomeric alcohols **31** which could not be separated, hence the vacuum-dried oil was analyzed directly: ir (film), 2.85, 6.12, 6.23, 6.69, 6.88, 7.10, 8.32, 8.95, 9.47, 11.30, 13.30, and 14.35 μ.

Anal. Calcd for $C_{18}H_{19}ClOS$: C, 67.70; H, 5.96. Found: C, 67.58; H, 5.89.

Cyclization of 1.9 g of **31** in 60 ml of refluxing 97% formic acid (4 hr) followed by hydrolysis, ether extraction, and work-up as usual provided 1.7 g of red oil. Chromatography on silica gel gave *ca.* 550 mg of dehydration product (eluted with petroleum ether) and 354 mg (21%) of ketone **32**: mp 110–112° dec (carbon tetrachloride); ir (Nujol) 5.89, 6.70, 7.95, 12.20, and 14.36 μ; nmr

(40) R. Filler, B. R. Camara, and S. M. Nagir, *J. Amer. Chem. Soc.*, **81**, 658 (1959).
(41) A. A. Pavlic and H. Adkins, *ibid.*, **68**, 1471 (1946).
(42) S. Trippett, *J. Chem. Soc.*, 419 (1957).
(43) R. F. C. Brown, V. M. Clark, and Lord A. Todd, *ibid.*, 2105 (1959).

(CCl_4) δ 2.1–4.0 (multiplet, 8 aliphatic H), 7.17 (broad singlet, 10 aromatic H).

Anal. Calcd for $C_{18}H_{18}OS$: C, 76.50; H, 6.37. Found: C, 75.30; H, 6.17.

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Total Synthesis of (±)-Calarene[1]

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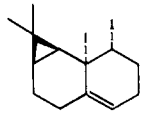
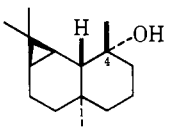
Abstract: A stereochemically defined synthetic route to the tricyclic sesquiterpene calarene (**1**) is described. The key intermediates, *cis*- and *trans*-4,4a-dimethyl-4,4a,7,8-tetrahydronaphthalene-2,5(3H,6H)-dione (**3a** and **3b**), were prepared by annulation of 2-methylcyclohexane-1,3-dione as its monopyrrolidine enamine (**6**) with 3-penten-2-one (**4**). The stereochemistry of **3b** was established by independent chemical and spectroscopic evidence. Pyrolysis of the 2-pyrazolines derived separately from *cis*- and *trans*-2(3H)-isopropylidene-8,8a-dimethyl-4,6,7,8-tetrahydronaphthalene-1(8aH)-one (**20** and **22**) by reaction with hydrazine served as an efficient means for introducing the fused dimethylcyclopropane ring. (±)-Calarene was obtained stereoselectively from **20**, whereas two stereoisomers (**25** and **26**), both distinctly different from calarene, were formed from **22**.

The naturally occurring hydrocarbon calarene (**1**) is one member of a small group of tricyclic sesquiterpenes which contain a dimethylcyclopropane ring fused to the nonisoprenoid octalin nucleus of the eremophilone family.[3] Structure **1** was first proposed by Büchi, Greuter, and Tokoroyama as the result of an extensive chemical study[4] and their conclusion was confirmed by concurrent investigations in other laboratories.[5] The structural and stereochemical assignment was supported by a correlation with 4-epimaaliol (**2**),[4] a synthetic isomer of the well-known natural sesquiterpene alcohol maaliol.[6] In this paper we describe a total synthesis of (±)-calarene which fully confirms the proposed structure and provides independent evidence regarding the relative stereochemistry depicted in **1**.[7,8]

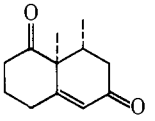


1

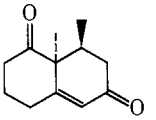


2

Our synthetic plan involved the initial preparation of the *cis*-unsaturated bicyclic ketone **3a**.[9] This substance not only appeared well suited for transformation into calarene, but also could serve as an intermediate in the total synthesis of other sesquiterpenes in the eremophilone family.[10] It seemed likely that the two carbonyl groups in **3a** could be chemically distinguished since the *peri*-like secondary methyl group sterically hinders the nonconjugated ketone. Furthermore, the angular methyl group might enable stereochemical control in reactions introducing the three-membered ring, or possibly other functionality.



3a



3b

A variant of the Robinson annulation reaction with 3-penten-2-one **4** in place of methyl vinyl ketone was used to prepare the requisite dimethyl octalone derivative.[11] Although a successful annulation reaction with **4** had been previously reported,[12] the stereochemistry of the product was not determined. Attempts to effect the annulation of 2-methylcyclohexane-1,3-

(1) Taken in part from the Ph.D. Thesis of J. E. S., University of Illinois, 1969.

(2) National Science Foundation Trainee, 1965–1969.

(3) For a recent review see A. R. Pinder, *Perfum. Essent. Oil. Rec.*, **59**, 645 (1968).

(4) G. Büchi, F. Greuter, and T. Tokoroyama, *Tetrahedron Lett.*, 827 (1962).

(5) (a) J. Vrkoč, J. Krepinsky, V. Herout, and F. Sorm, *Collect. Czech. Chem. Commun.*, **29**, 795 (1964); (b) P. Pesnelle and G. Ourisson, *Bull. Soc. Chim. Fr.*, 912 (1963); (c) J. Streith, P. Pesnelle, and G. Ourisson, *ibid.*, 518 (1963).

(6) (a) Structure: G. Büchi, M. Schach, M. Schach v. Wittenau, and D. M. White, *J. Amer. Chem. Soc.*, **81**, 1968 (1959); (b) total synthesis: R. B. Bates, G. Büchi, T. Matsuura, and B. R. Schaffer, *ibid.*, **82**, 2327 (1960).

(7) Portions of this investigation have been briefly reported: R. M. Coates and J. E. Shaw, *Chem. Commun.*, **47**, 515 (1968).

(8) For recent syntheses of the closely related sesquiterpene ketone aristolone see (a) C. Berger, M. Franck-Neumann, and G. Ourisson, *Tetrahedron Lett.*, 3451 (1968); (b) E. Piers, R. W. Britton, and W. de Wall, *Can. J. Chem.*, **47**, 831 (1969).

(9) All structural formulae except **1**, **2**, and **14** designate only one enantiomorph of a racemic mixture.

(10) (a) R. M. Coates and J. E. Shaw, *Tetrahedron Lett.*, 5405 (1968); (b) "Symposium on the Chemistry of Essential Oils," 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, Abstract 46; (c) *J. Org. Chem.*, **35**, 2597 (1970).

(11) This synthetic approach toward sesquiterpenoids of the eremophilone family has been employed in several recent investigations: (a) J. A. Marshall, H. Faubl, and T. M. Warne, Jr., *Chem. Commun.*, 753 (1967); (b) H. C. Odom and A. R. Pinder, *ibid.*, 26 (1969); (c) R. L. Hale and L. H. Zalkow, *ibid.*, 1249 (1968); (d) L. W. Piszkiewicz, Ph.D. Thesis, California Institute of Technology, 1967; *Diss. Abstr. B*, **27**, 3865 (1967); (e) C. J. V. Scanio, "Symposium on the Chemistry of Essential Oils," 158th National Meeting of the American Chemical Society, New York, N. Y., Sept 1969, Abstracts, AGFD 47.

(12) W. S. Rapson, *J. Chem. Soc.*, 1626 (1936).