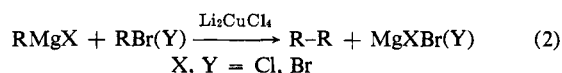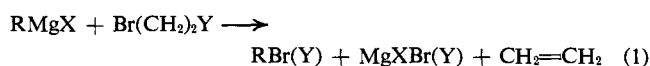3-Anteisotridecenoic acid and 3-isododecenoic acid are part of the fatty acid components of the peptide antibiotic amphomycin[11] and these are now easily synthesized by halopolycarbon homologating sec-butyl (or 2-methylbutyl) and isobutyl Grignard reagents, respectively.

With the ready availability of 1-chloro-3-bromopropane[12] and the homologous even-numbered alkyl alcohols and halides, the synthesis of the less accessible odd-numbered alkyl chlorides such as tridecyl and pentadecyl chlorides[13] is easily accomplished in excellent (80–90%) yield.

The application of the halopolycarbon homologation technique to the synthesis of long chain α,ω-dibromides is exemplified by the synthesis of 1,18-dibromooctadecane in 70–80% yield from 1,6-hexanedimagnesium chloride and 1,6-dibromohexane.

Halo dicarbon homologation does not occur[14] with ethylene chlorobromide or dibromide. Instead ethylene[15] (evolved as a gas and identified) and the alkyl halides (RX) are formed. The alkyl halides undergo further (coupling) reaction with the starting Grignard reagent to afford R–R′.

$$RMgX + Br(CH_2)_2Y \longrightarrow$$
$$RBr(Y) + MgXBr(Y) + CH_2=CH_2 \quad (1)$$

$$RMgX + RBr(Y) \xrightarrow{Li_2CuCl_4} R-R + MgXBr(Y) \quad (2)$$
$$X, Y = Cl, Br$$

Since approximately 50–60% of the dihaloethane was covered, it is apparent that reaction 2 is faster than 1.

Preliminary work indicates that the reaction of alkyl and aryl lithium reagents with α,ω-dibromoalkanes in the absence of Cu (I or II) but in the presence of TMEDA may be a useful alternative. In the absence

(11) (a) M. Bodanszky, G. F. Sigler, and A. Bodanszky, J. Amer. Chem. Soc., 95, 2352 (1973); M. Bodanszky, N. C. Chaturvedi, and J. A. Scozzie, J. Antibiot., 22, 399 (1969). (b) For more cumbersome alternative routes to the synthesis of iso and anteiso series of alcohols and acids see A. H. Milburn and E. V. Truter, J. Chem. Soc., 3344 (1954).

(12) (a) Dow Chemical Corporation, Michigan Chemical Corporation. Related reactions are the following. (b) Recently it was shown that vinyl copper(I) reagents prepared by addition of alkyl copper(I) to 1-alkynes selectively displaces iodide from 1-chloro-3-iodopropane. J. F. Normant, G. Cahiez, C. Chuitt, and J. Villieras, Tetrahedron Lett., 2407 (1973). (c) Chloroiodoethylene reacts selectively with alkynyl- and perfluoralkylcopper(I) to give the corresponding chlorovinyl derivatives. J. Burdon, P. L. Coe, C. R. Marsh, and J. C. Tatlow, J. Chem. Soc., Perkin Trans. 1, 639 (1972).

(13) These compounds (i.e., the corresponding bromides) are usually prepared from the commercially available fatty acids (C_{12}–C_{13}) via the Hunsdiecker reaction or the Cristol–Firth modification: S. J. Cristol and W. C. Firth, Jr., J. Org. Chem., 26, 280 (1961). Cf. A. Roedig in "Methoden der Organischen Chemie," Vol. 5, part 4, E. Müller, Ed., George Thieme Verlag, Stuttgart, 1960, p 488; C. V. Wilson, Org. React., 9, 332 (1957).

(14) On the other hand, 2-bromoethyl tosylate reacts selectively with lithium dibutyl cuprate at −78° to give hexyl bromide. At higher temperatures (−20°) dialkylation occurs, i.e., decane is the only product. C. R. Johnson and G. A. Dutra, J. Amer. Chem. Soc., 95, 7777 (1973). Uncomplexed organolithium cleaves alkyl tosylates via S–O scission. L. Friedman and R. J. Honour, unpublished results.

(15) The formation of olefins from the reaction of organometallic reagents (reductive elimination or dehalogenation) with vicinal dihalides is well established. M. Mousseron and F. Winternitz, Bull. Soc. Chim. Fr., 13, 604 (1946); L. Skattebol, Tetrahedron, 21, 1357 (1965); G. H. Posner and J. S. Ting, Syn Commun., 3, 281 (1973).

(16) For the parameters affecting the reaction of organolithium reagents and alkyl halides see R. J. Honour, Ph.D. Thesis, Case Western Reserve University, 1970.

of TMEDA extensive halogen–metal exchange occurs and the reaction has no synthetic value.[16]

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Application of Nonenzymic Biogenetic-Like Olefinic Cyclizations[1] to the Total Synthesis of dl-Serratenediol

Sir:

Serratenediol (1),[2] a member of a recently discovered class of pentacyclic triterpenoids having a seven-membered C ring.[2,3] contains nine asymmetric centers; hence a feasible total synthesis requires a plan involving a very high degree of stereoselectivity. We envisaged such a scheme based on the biogenetic-like cyclization of a tetraenic alcohol such as 2, which seemingly had

1

2
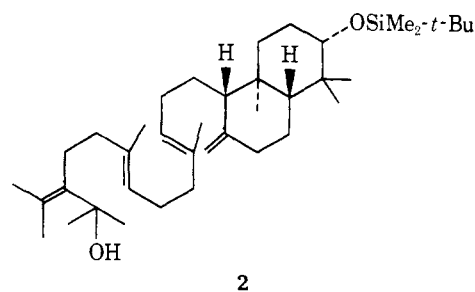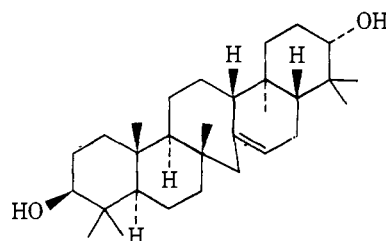
promise of leading to a substance, 15, having the complete serratene ring system. The present communication contains an account of the successful reduction of this plan to practice.

The cyclization substrate 2 was produced as follows. The known tricyclic ketone 8[4] was prepared by a new method (see Scheme I) based on the olefinic cyclization 6 → 7. The allylic alcohol 3,[5] obtained by reaction

(1) For a recent paper in this series see W. S. Johnson, K. Wiedhaup, S. F. Brady, and G. L. Olson, J. Amer. Chem. Soc., 96, 3979 (1974).

(2) (a) T. Ysuda, T. Sano, K. Kawaguchi, and Y. Inubushi, Tetrahedron Lett., 1279 (1964); (b) Y. Inubushi, Y. Tsuda, T. Sano, T. Knoita, S. Suzuki, H. Ageta, and Y. Otake, Chem. Pharm. Bull., 15, 1153 (1967).

(3) J. W. Rowe, Tetrahedron Lett., 2347 (1964).

(4) G. Stork, A. Meisels, and J. E. Davis, J. Amer. Chem. Soc., 85, 3419 (1963).

(5) The formulas depict only one enantiomer of a racemic pair. The nmr and ir spectra of all specimens were consistent with the assigned structures. Moreover, new compounds which could be distilled or crystallized gave satisfactory combustion analyses. Yields are reported for distilled, chromatographed, or recrystallized substances only.

Scheme I. Synthesis of Tricyclic Ketone 8[5,a]

3 → a → **4**

5 → c → **6** → d,e →

7, X = C(CH₃)₂
8, X = O

+

7a
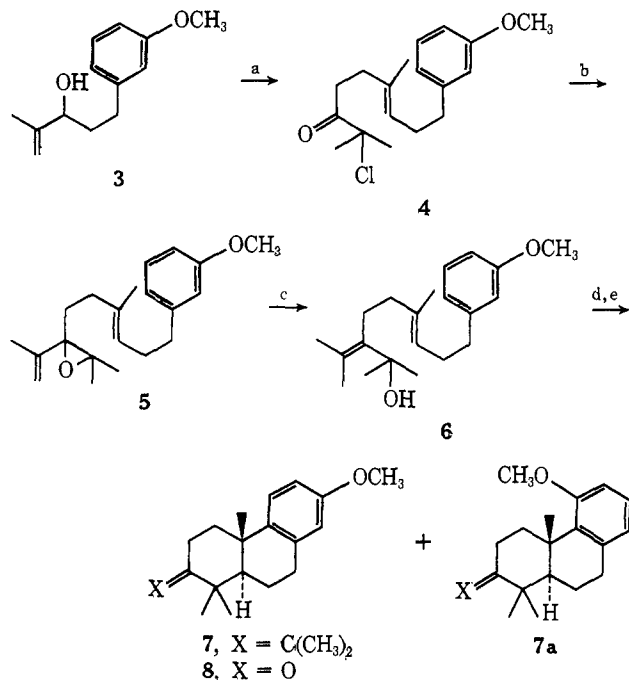
[a] (a) 3-Chloro-3-methyl-2,2-dimethoxybutane (3 quiv), xylene, 2,4-dinitrophenol (0.1 equiv), 120–125°, 6 hr. (b) Isopropenyl-lithium, Et₂O, −78°, 15 min; EtOH, −78 to 25°, 1 hr. (c) Li, NH₃–Et₂O (2:1), 1 hr; BrCH₂CH₂Br. (d) SnCl₄, CH₂Cl₂, −95°, 1 hr; Py, −95 to 25°. (e) O₃ (1.5 equiv), CH₂Cl₂–MeOH, −78°; Me₂S, −78° to 25°, 1 hr.

of 3-(m-methoxyphenyl)propanal[6] and isopropenyl-magnesium bromide in THF at −78°, was submitted to the chloro ketal Claisen reaction[7] and thus was converted into the chloro ketone **4** in 80% yield. This chloro ketone was transformed, according to a new method involving reaction with isopropenyllithium followed by reduction of the resulting allylic epoxide **5**,[8] into the substance **6**, containing the tetramethylallylic alcohol function which is known to be an excellent group for initiating cyclization.[9] Cyclization of the substrate **6**, under conditions reported[6] to favor cyclization para to the methoxyl group in the aromatic ring, afforded an 85:15 mixture of **7**:**7a**. A combination of crystallization and chromatography gave pure **7**, mp 103.5–104.5°, in 61% overall yield. Selective ozonolysis[10] of **7** afforded pure **8**, mp 73.5–74° (lit.[4] 56–58°)[11] in 77% yield (29% overall from m-methoxycinnamic acid). This synthesis of **8** provides improvements in both overall yield and stereospecificity[11] as compared with the previous approach.

Conversion of ketone **8** to the known keto acid **11** (see Scheme II) was accomplished using minor modifications of the reported procedures.[4] Reaction of **11**

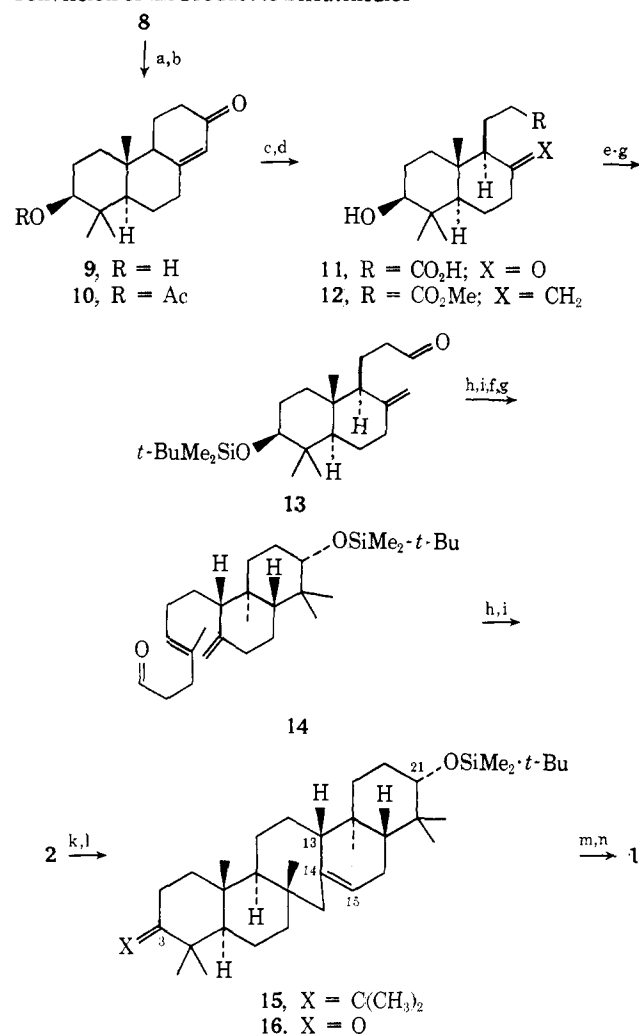(6) P. A. Bartlett and W. S. Johnson, *J. Amer. Chem. Soc.*, **95**, 7501 (1973).

(7) L. Werthemann and W. S. Johnson, *Proc. Nat. Acad. Sci. U. S.*, **67**, 1465 (1970).

(8) N. R. Hunter and W. S. Johnson, unpublished results.

(9) W. S. Johnson and T. K. Schaaf, *Chem. Commun.*, 611 (1969).

(10) M. B. Rubin, *J. Chem. Educ.*, **41**, 388 (1964).

(11) A comparison sample of **8**, mp 56–58°, kindly furnished by Professor Stork, showed two peaks of nearly equal intensity on glc, and the nmr spectrum indicated the presence of six angular methyl resonances. Our sample of **8** was homogeneous by glc and possessed only three angular methyl signals (δ 1.09, 1.13, 1.24). Birch reduction followed by acid hydrolysis led to hydroxyenone **9**, mp 149.5–150.5° (lit.[4] 151–152°).

Scheme II. Synthesis and Cyclization of **2** and Conversion of the Product to Serratenediol[5,a]

8 ↓ a,b

9, R = H
10, R = Ac

→ c,d →

11, R = CO₂H; X = O
12, R = CO₂Me; X = CH₂

→ e·g →

t-BuMe₂SiO **13** → h,i,f,g →

14 → h,i →

2 → k,l → **15**, X = C(CH₃)₂
16, X = O
→ m,n → **1**

[a] (a) Li, t-BuOH, THF, NH₃, −78°, 4 hr; H₃O⁺, MeOH. (b) Ac₂O, Py, 25°, 24 hr. (c) RuO₄, NaIO₄,H₂O, Me₂CO, 25°, 6 hr; OH⁻. (d) Ph₃P=CH₂ (10 equiv), DMSO (distilled from dimsyl sodium), 70°, 24 hr; OH⁻; CH₂N₂, Et₂O, 0°, 16 hr. (e) t-BuMe₂-SiCl (8 equiv), imidazole (17 equiv), DMF, 25°, 3 hr. (f) NaAlH₂-(OCH₂CH₂OCH₃)₂, THF–C₆H₆, 0°, 2 hr. (g) CrO₃·2Py, CH₂Cl₂, 25°, 0.2 hr. (h) Isopropenylmagnesium bromide, THF, −78°, then 25°, 1.5 hr. (i) CH₃C(OCH₃)₃, CH₃CH₂CO₂H (catalysis), 105°, 4 hr. (j) See steps a–c, Scheme I. (k) TFA (5 equiv), CH₂-Cl₂, −78°, 5 hr; aqueous NaHCO₃. (l) RuO₄, CCl₄ (1.6 equiv) −15 to 0°, 2 hr. (m) Li, NH₃, THF, t-BuOH, −33°, 0.5 hr. (n) NBu₄F, THF, 70°, 12 hr.

with methylenetriphenylphosphorane followed by esterification gave ester **12** in 58% overall yield from **9**. The hydroxyl group was then protected as the tert-butyldimethylsilyl ether.[12] Treatment of **12** with Red-Al[13] followed by modified Collins oxidation[14] provided aldehyde **13** in 91% yield from **12**. This aldehyde was then treated with isopropenylmagnesium bromide to give an allylic alcohol which was subjected to the ortho-acetate Claisen reaction.[15] The resulting dienic ester

(12) E. J. Corey and A. Venkateswarlu, *J. Amer. Chem. Soc.*, **94**, 6190 (1972).

(13) "Red-Al" is a 70% solution of NaAlH₂(OCH₂CH₂OCH₃) in benzene marketed by Aldrich Chemical Co.

(14) R. Rodehorst and R. Ratcliff, *J. Org. Chem.*, **35**, 4000 (1970).

(15) W. S. Johnson, L. Werthemann, W. R. Bartlett, T. J. Brocksom, T-t. Li, D. J. Faulkner, and M. R. Petersen, *J. Amer. Chem. Soc.*, **92**, 741 (1970).

was reduced and oxidized as described for ester **12** to give a new aldehyde **14** in 58% overall yield from **13**. Reaction of **14** with isopropenylmagnesium bromide gave an allylic alcohol which was transformed *via* the chloro ketal Claisen sequence (see above) into the tetraenic alcohol **2** in 48% overall yield from **14**. This polyolefinic precursor to the serratene skeleton was thus obtained in an overall yield of 3.1% from *m*-methoxycinnamic acid.

Cyclization of **2** with trifluoroacetic acid (TFA) in dichloromethane at $-78°$ gave the pentacyclic substance **15** (methyl resonances: δ 0.02 (6 H), 0.65 (3 H), 0.73 (3 H), 0.80 (6 H), 0.87 (12 H), 1.07 (3 H), 1.18 (3 H), 1.64 (3 H), 1.77 (3 H); vinyl proton, δ 5.32), in 20% yield. This product contained an isomeric substance (*ca.* 14% yield) which could be separated by chromatography. Based on its nearly identical mass spectrum and similar nmr spectrum, we tentatively regard it as having the constitution shown in formula **17**, which
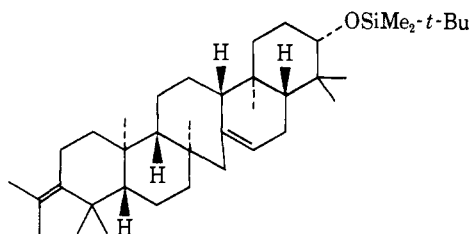
17

could arise by an alternative cyclization pathway in which ring C assumes a quasi-boat conformation.[16]

Selective ozonolysis of the isopropylidene group of **15** was unsuccessful, but the use of ruthenium tetroxide[17] effected the conversion to **16**, mp 208.5–210.5°, in 39% yield after purification by preparative tlc. The ketone was then reduced to the C-3 equatorial alcohol, mp 182–191°, and the C-21 hydroxyl protecting group was removed to give *dl*-serratenediol (**1**), mp 258.5–264.5° (reported for natural serratenediol,[2b] 282–284°) in 85% yield. The ir (CHCl₃), 100-MHz nmr, and mass spectrum of **1** were identical within experimental limits to the corresponding spectra of the naturally occurring material.[2,3] Moreover, the natural and synthetic materials had identical retention times on glc and identical R_f values on tlc. In addition, synthetic **1** was converted by oxidation and Wolff-Kishner reduction[2b] to the parent hydrocarbon, serratene. Acid isomerization gave a 3:1 equilibrium mixture of isoserratene (double bond at 13, 14) and serratene. These were identified by coinjection glc experiments with naturally derived materials. Thus, for the first time, totally synthetic serratenediol has been produced.[18]

Acknowledgments. This work was carried out in the laboratories of Professor William S. Johnson, to whom we are deeply indebted for encouragement and for his assistance in the preparation of this manuscript. We wish to thank the National Institutes of Health and National Science Foundation for grants (to W. S. J.) in support of this research. Finally, we are also grate-

(16) *Cf.* E. E. van Tamelen and R. J. Anderson, *J. Amer. Chem. Soc.*, **94**, 8225 (1972).

(17) H. Nakata, *Tetrahedron*, **19**, 1959 (1963).

(18) The reported conversion[2a] of naturally occurring α-onocerin, which has been totally synthesized,[4] into serratenediol, constitutes a formal total synthesis.

ful to Dr. John W. Rowe and Professor Yasuo Inubushi for generous gifts of natural serratenediol, serratene, and isoserratene, and to Professor Gilbert Stork for supplying a specimen of ketone **8**.

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Silicon–Carbon Multiple-Bonded (p_π–p_π) Intermediates. Evidence for Dipolar Character in Reactions with Trichlorosilane and Other Silicon Halides

Sir:

Pioneering studies concerning the generation and reactions of an unsaturated silicon–carbon reaction intermediate, $(CH_3)_2Si{=}CH_2$, led Gusel'nikov and Flowers to conclude that this reactive intermediate does not behave as a diradical (odd electron spins unpaired).[1] All of their evidence, quantitative and qualitative, was consistent with thermolytic generation of this intermediate as a p_π–p_π bonded species. In the absence of a suitable trapping agent, generation and reaction (in the gas phase) proceeds according to Scheme I.

Scheme I
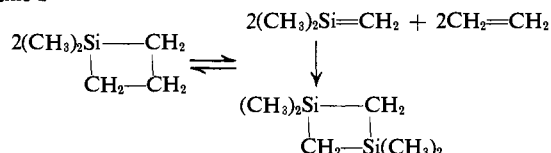
Absence of involatile products, an exact product ratio of 2:1 for ethylene:cyclodimer, and too high a preexponential factor, A, all disfavor a diradical structure (which would require electron spin unpairing during generation of $(CH_3)_2Si{-}\dot{C}H_2$) and favor a p_π–p_π bonding formulation, $(CH_3)_2Si{=}CH_2$.

During previous studies we formed and recorded the (largely unproven) conviction that silicon–carbon double bonds, generated thermolytically according to Scheme I, possessed considerable dipolar character.[2]

$$\overset{\delta+}{R_2Si}{=}\overset{\delta-}{CH_2}$$

1
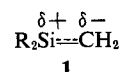
In the present work, bonding postulate **1** led us to undertake the first studies of the reactions of silicon–carbon double bonds with silicon chlorides and fluorides. Especially for the latter, the extremely high bond energy of the silicon–fluorine bond ($\sim$135 kcal/mol)[3]

(1) M. C. Flowers and L. E. Gusel'nikov, *J. Chem. Soc. B*, 419 (1968).

(2) (a) D. N. Roark and L. H. Sommer, *J. Chem. Soc., Chem. Commun.*, 167 (1973); (b) R. D. Bush, C. M. Golino, D. N. Roark, and L. H. Sommer, *J. Organometal. Chem.*, **59**, C17 (1973); (c) C. M. Golino, R. D. Bush, D. N. Roark, and L. H. Sommer, *J. Organometal. Chem.*, **66**, 29 (1974); (d) C. M. Golino, R. D. Bush, and L. H. Sommer, *J. Amer. Chem. Soc.*, **96**, 614 (1974); (e) R. D. Bush, C. M. Golino, G. D. Homer, and L. H. Sommer in press.

(3) T. Cottrell, "The Strength of Chemical Bonds," 2nd ed, Butterworths, London, 1958, pp 270–280.