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A SOLVOLYSIS ROUTE TO A MACROBICYCLIC ALLENE

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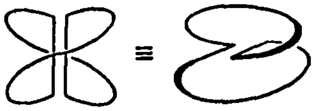
Abstract: One of our objectives was to develop further access to large bicyclic tetrasubstituted olefins by cationic rearrangement. Among other things, such olefins can serve as valuable precursors to bicyclic tetrasubstituted allenes, and we report one such conversion by a new route that provided the first symmetrical member of this rare class of compounds. We synthesized the bicyclic trisubstituted olefins (*Z*)-bicyclo[10.5.0]heptadec-1(17)-ene (**11**) and (*Z*)-bicyclo[10.6.0]octadec-1(18)-ene (**17**) via an intramolecular Wittig reaction and a titanium mediated intramolecular reductive coupling, respectively. Olefins **11** and **17** were isomerized under acidic conditions to their tetrasubstituted counterparts (*Z*)-bicyclo[10.5.0]heptadec-1(12)-ene (**12**) and (*Z*)-bicyclo[10.6.0]octatadec-1(12)-ene (**18**), respectively. The previously reported tetrasubstituted olefin (*Z*)-bicyclo[11.11.0]tetracos-1(13)-ene (**19**) was further elaborated in a three step sequence to the allene bicyclo[11.11.0]pentacosa-1(25),13(25)-diene (**22**). Our approach involved dichlorocyclopropanation of olefin **19** to cyclopropyl adduct 25,25-dichloro-tricyclo[11.11.1.0]pentacosane (**20**), silver assisted solvolysis of **20** to 25-chloro-1-methoxy-bicyclo[11.11.1]pentacos-13(25)-ene (**21**), and reductive elimination of **21** with zinc to allene **22**.

Introduction

Several research groups[1-5,7] have been interested in the synthesis and properties of π systems sterically shielded by bridging alkyl chains. Bicyclic *trans*-olefins, typified by **1** ("betweenanenes"), are the most thoroughly explored of such systems. Short or medium length methylene chains "encapsulate" the π bond, thereby greatly diminishing its reactivity.[1-3] Naturally, the concept of steric shielding of functionality by methylene chains is not confined to simple olefins. For example, a doubly bridged allene such as **2** is a conceivable structural analogue. Molecular models of such bicyclic allenes (**2**, a = b = 6 to 11) indicate that the bridging alkyl chains partially shield the central allenic carbon but not the termini. The extent of steric shielding should depend to a large degree on the lengths of the bridging chains as well as on their conformational flexibility. This shielding might also be enhanced by appropriate substitution on the chains (e.g., branching), or it might be diminished by replacement of ring methylenes by heteroatoms (e.g., O, N, S). Thus, normal allenic reactivity may be substantially altered by incorporation of the allenic system within such a bicyclic framework.



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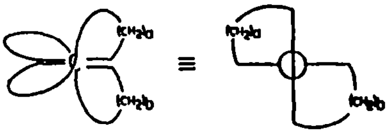

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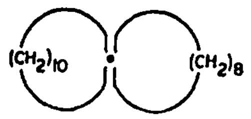
This bicyclic allene class of compounds was first conceptualized by Cahn, Ingold, and Prelog,[6] and only one hydrocarbon representative (**3**) has been reported by Nakazaki.[7a,b] (Very recently, Marshall[7c] synthesized two heterocyclic members (**4a,b**) of this doubly bridged allene family by starting with a preformed monocyclic allene and then closing the second ring.) Nakazaki used a precursor of type **5**, but unfortunately his route is not general for the hydrocarbon series in that it failed in three of four attempted applications (two by Nakazaki, one by us). Consequently, additional options to hydrocarbon bicyclic allenes (**2**) from bicyclic olefins of type **5** are needed. We now report a new method and apply it to the synthesis of one such allene

(22), the first symmetrical representative of this rare class of compounds. Our expectation is that this symmetry will facilitate future study of its chemical behavior. We also report the sytheses of two unsymmetrical bicyclic *cis*-olefins (5), which could serve as key precursors to bicyclic *trans*-olefins (1) or to bicyclic allenes (2).



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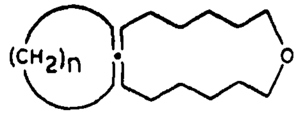
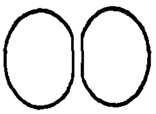


4a, n = 9
b, n = 12



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Results and Discussion

Bicyclic *cis*-olefins (5) assume pivotal importance in our projected allene synthesis. Much of our effort was therefore devoted to developing methodology for preparation of olefins of this type. The synthesis of one such system (19), by a scheme that is limited to symmetrical homologues, has been previously described in detail.[3] Our routes to two new and unsymmetrical bicyclic *cis*-olefins and to a symmetrical bicyclic allene are described below.

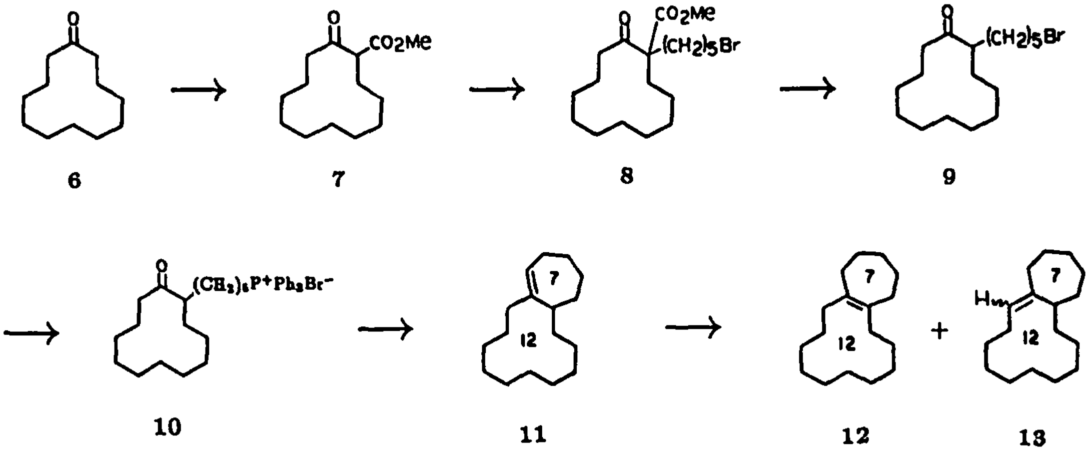
A. Bicyclo [10.5.0] System. We prepared the requisite bromoketone 9 from cyclododecanone (6) according to the sequence depicted in Scheme 1.[9] Ketone 6 gave the known[10] 2-carbomethoxy derivative 7 by condensation with dimethyl carbonate. Alkylation with 1,5-dibromopentane provided 8, which gave bromoketone 9 after hydrolysis and decarboxylation. Treatment of 9 with one equivalent of triphenylphosphine afforded phosphonium salt 10. The crude salt was characterized only by ^{1}H NMR, and was merely dried over P_2O_5 under vacuum prior to use.

We gained access to the bicyclo [10.5.0] system via an intramolecular Wittig reaction. Our experiment was closely modeled on a general method reported by Becker,[11] who observed that the yield dropped off dramatically (19%) for the formation of seven-membered rings. Our yield of olefin 11 was comparable (16%) and no traces of isomeric olefins could be detected. As it is well known that *trans*-cycloheptenes are thermally unstable,[14-18] we can be certain that the double bond in 11 is cis within the seven-membered ring. The IR was rather featureless except for a weak C=C stretch at 1655 cm^{-1}. A triplet at δ 5.45 in the ^{1}H NMR demonstrated the lone vinyl hydrogen; and a proton decoupled ^{13}C spectrum showed the requisite seventeen signals, including those at 124.98 and 146.63 ppm for the two sp^2 carbons.

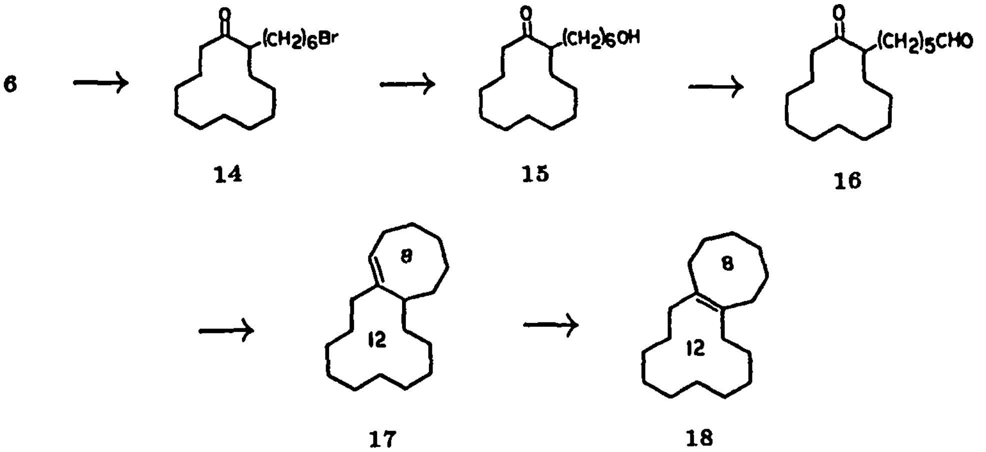
Initially, our efforts to obtain the target tetrasubstituted *cis*-olefin 12 via acid catalyzed (e.g., HCl, BF_3 etherate) isomerization of 11 gave intractable mixtures. Eventually, we found that gentle heating of 11 with the monohydrate of *p*-toluene sulfonic acid in benzene afforded desired isomer 12 in 40% yield (by GC). Starting olefin was completely consumed, and isomer 12 was accompanied by virtually only two other isomers (13 *E* + *Z*, 58% of the mixture by GC). This three component mixture could be partially separated by $AgNO_3$-silica preparative thin layer chromatography. Eventually, we found that preparative high pressure liquid chromatography (HPLC) was less costly and gave superior separations. Routinely, we used C18 reversed phase columns with acetonitrile as the mobile phase.

As expected, the IR of tetrasubstituted olefin 12 did not show a C=C stretch. In accord with molecular symmetry, nine signals were observed in the proton decoupled ^{13}C NMR, and a resonance at 137.42 ppm was assigned to the two equivalent sp^2 carbons. The UV showed a maximum at 203 nm (ε = 9600, heptane). The ^{1}H NMR showed an eight proton multiplet in the allylic region, and most of the remaining methylene hydrogens appeared as a broad envelope in the aliphatic region. We also observed a well defined quintet centered at δ 1.70. Tentatively, we attribute this resonance to the C15 methylene hydrogens in the cycloheptyl ring.

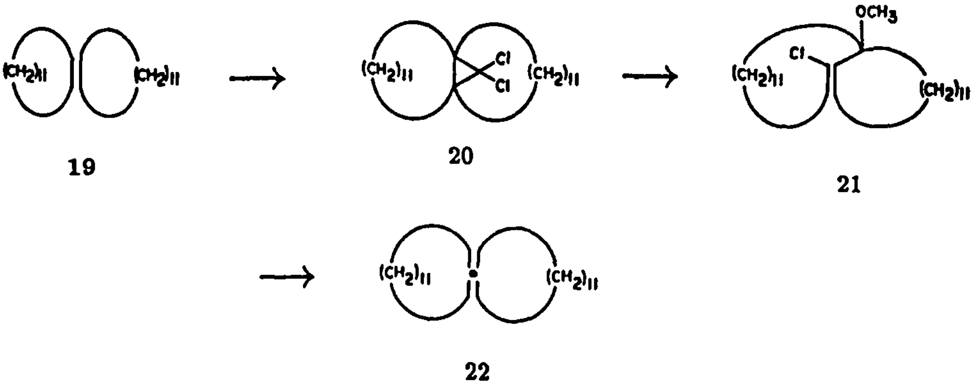
Scheme 1.



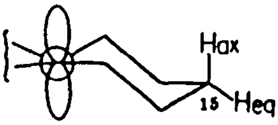
Scheme 2.



Scheme 3.



On the basis of dynamic ^{1}H NMR[19] as well as a number of force field[20] and quantum mechanics[21] calculations, *cis*-cycloheptene is believed to adopt a symmetrical chair-like conformation. Thus, the pseudo-axial H of C15 in **12** is expected to lie near the nodal plane of the double bond and conceivably close enough to experience a slight deshielding effect. However, ring inversion ($\Delta G^{\ddagger}$ = 5.4 kcal/mol; 22.6 kJ/mol) should be quite fast at room temperature relative to the NMR time scale. Consequently, the pseudo-axial and pseudo-equatorial hydrogens at C15 should experience an averaged magnetic environment at room temperature. Indeed the well defined quintet (δ 1.70) observed at 23 °C began to broaden and lose this multiplicity at -18 °C. Hence, we suggest that the averaged C15 methylene hydrogens are close enough to the deshielding region of the π system to experience this through-space effect.



HPLC also afforded the *E,Z* isomers of trisubstituted olefin **13**. Because we cannot unambiguously assign their stereochemistry, we designate these isomers *EZ* 1 and *EZ* 2 (36 and 22% of the isomer mixture, respectively). Both were characterized only by ^{1}H NMR, and each isomer exhibits an ABX pattern for the vinyl hydrogen because of the magnetic inequivalence of the vicinal methylene hydrogens. Isomer *EZ* 1 showed a one proton doublet of doublets (J = 10.7 and 4.3 Hz) centered at δ 5.17, whereas isomer *EZ* 2 showed a one proton doublet of doublets (J = 11.6 and 3.9 Hz) centered at δ 5.25.

B. Bicyclo [10.6.0] System. In Scheme 1 we used an intramolecular Wittig reaction for entry into the [10.5.0] system. Although the yield was low, the Wittig gave isomerically pure olefin **11**. Since the reason for the low yield was probably entropically related, we had little hope for successful intra-Wittig closure to give the eight-membered ring in **17**. Thus we opted for McMurry's[22] titanium-mediated intramolecular coupling methodology, and we required keto aldehyde **16** for this purpose. Scheme 2 outlines our approach.

Alkylation of cyclododecanone (**6**) with 1,6-dibromohexane gave bromoketone **14** (40%). Keto alcohol **15** was prepared from **14** by silver assisted solvolysis in aqueous acetone (83%). The reaction was quite clean, and the crude keto alcohol was pure enough for use directly in the next step. We found that $AgClO_4$ worked best in this solvolytic process, and that $AgNO_3$ gave a mixture containing the primary nitrate along with the desired alcohol **15**. Application of the Corey-Suggs[23] oxidation method with pyridinium chlorochromate gave the requisite keto aldehyde **16** from alcohol **15** in 74% yield after distillation.

We cyclized **16** to the trisubstituted olefin **17** by McMurry's titanium-mediated carbonyl coupling methodology.[22] With careful attention to experimental detail, we obtained (at best) a sixteen component mixture of hydrocarbons in which the desired trisubstituted olefin **17** predominated to the extent of 75% (GC). The minor components ranged from 0.7 to 4.8% in concentration. These figures correspond to a 24% yield of olefin **17** from the keto bromide **14**. For characterization purposes only, we isolated **17** from a combination of $AgNO_3$ preparative TLC and preparative HPLC. The ^{1}H NMR showed a definitive triplet for the lone vinyl H (δ 5.63). A lack of molecular symmetry dictates that all eighteen carbons should have been observed in the proton decoupled ^{13}C spectrum. We observed only seventeen, but a broad signal at 25.40 ppm showed a shoulder, which suggested the presence of the required additional signal. Also, signals at 126.43 and 140.40 ppm clearly indicated the two distinct sp^2 carbons of the trisubstituted double bond. Spectroscopically, the material appeared isomerically pure. Since it is unlikely that a *trans*-cyclooctenyl system would have been stable under the reaction conditions,[24-27] we believe that the double bond in **17** is cis relative to the eight-membered ring.

Earlier experience with the [10.5.0] system facilitated our efforts to isomerize **17** to the target tetrasubstituted *cis*-olefin **18**. Even though it complicated eventual isolation of **18**, we found it expedient to use the multi-component mixture containing 75% **17** for these isomerizations. As with the homologous [10.5.0] system, *p*-toluene sulfonic acid in benzene proved effective. Although a reaction temperature of 56 °C was adequate for the [10.5.0] system, a higher temperature (80 °C) was required to induce double bond migration in this [10.6.0] skeleton. Thus, we obtained a sixteen component mixture containing 53% *cis*-isomer **18** when the mixture containing 75% olefin **17** was subjected to these conditions.

We pursued only the target isomer **18**, and isolated it by a combination of preparative $AgNO_3$-TLC and HPLC. The ^1H NMR showed only allylic and aliphatic hydrogens in the expected relative ratios. As dictated by molecular symmetry, we observed nine signals in the proton decoupled ^{13}C spectrum, including a signal at 133.73 ppm for the two symmetry equivalent sp^2 carbons. The UV gave a maximum at 201.5 nm (ε = 12700, heptane). Since the *trans*-bicyclic isomers ("betweenanenes") do not appear accessible from acid catalyzed isomerization of their cis counterparts,[3, 28, 29] we believe that the double bond in **18** is cis relative to both rings.

C. Allene Synthesis. Of the three bicyclic *cis*-olefins available to us (**12**, **18**, **19**[3]) we selected **19** for further elaboration to an allene (Scheme 3). The target allene **22** would be unstrained and symmetrical, and we expected that these features would facilitate isolation and unambiguous characterization. Accordingly, we introduced the required additional carbon by the action of dichlorocarbene on olefin **19**. Conversion of olefins to dichlorocyclopropyl adducts under phase transfer catalysis conditions with chloroform and sodium hydroxide is well precedented.[30] In our case, **19** gave an adduct (**20**) that showed only a broad envelope in the aliphatic region of the ^1H NMR. Proton decoupled ^{13}C NMR showed only eight signals, including one at 80.07 ppm indicative of the dichlorinated cyclopropyl carbon.[31] We attempted Nakazaki's route for direct conversion of adduct **20** to allene **22** with methyllithium,[7a,b] but obtained only an unidentified mixture of hydrocarbons from which no allene could be isolated. This approach was abandoned in favor of a more promising avenue involving solvolytic ring-opening and subsequent reductive elimination to allene.

The silver-assisted solvolysis of dihalocyclopropyl compounds to give ring-opened vinyl halides is well documented.[32-34] As hoped, the reaction of dichloride **20** with a large excess of silver nitrate in methanol afforded vinyl chloride **21** (28%, not optimized) after chromatography. Proton decoupled ^{13}C NMR showed only twenty-five of the expected twenty-six signals. Yet, one of the signals (26.12 ppm) was quite broad and probably constituted two overlapping signals. Resonances at 48.44 (OCH_3), 89.50 (tertiary C-O), 130.73 (sp^2 C), and 141.92 (sp^2 C) ppm support our structural assignment for **21**.

We hoped to obtain the target allene **22** by the action of highly active zinc powder[35] on **21**. Our decision to use zinc was prompted by the well known use of this metal to effect eliminations of vinyl allyl dihalides to allenes and of halohydrin derivatives to olefins.[36, 37] In fact, we succeeded in converting vinyl chloride **21** to allene **22** with zinc in 1,2-dimethoxyethane, albeit in somewhat erratic yield. In the best of two trials, allene was the only product isolated (86%) and starting material was completely consumed. We found that this allene was unstable to overnight storage at 0 °C in $CDCl_3$ (Aldrich 100.0 atom % D). Reexamination of the sample by ^1H NMR showed previously unobserved signals in the vinyl H region as well as changes in the allylic region; no allenic signals remained. This outcome suggested that traces of acid in the $CDCl_3$ caused rearrangement of the initial allene. We did not pursue the structures of these rearrangement products.

Allene **22** was isolated and fully characterized. Only end absorption was observed in the UV, but at 200 nm, the ε is 12600. For the unsymmetrical [10.8] allene **3**, Nakazaki[7] reported a maximum of 213.5 nm (ε = 9400). In accord with our structural assignment, the ^1H NMR of **22** showed only allylic-type signals and a broad envelope for the remaining ring methylenes. Molecular symmetry in **22** requires eight signals for proton decoupled ^{13}C NMR, but we were unable to detect the central allenic sp carbon, which normally appears at approximately 200 ppm. The absence of this signal was probably due to the small sample size (only 400 mg), as well as an expected long relaxation time (T_1) for this sp carbon nucleus.[31] However, the terminal carbons of an allene also resonate at frequencies that are highly characteristic.[31] Indeed, a signal at 102.30 ppm for the two symmetry equivalent sp^2 allenic termini underscores our structural assignment for **22**.

EXPERIMENTAL

General. Melting points are uncorrected and were determined on a Thomas-Hoover apparatus in open capillaries. In two cases where limited amounts of sample were available, micro melting points were obtained on a Kofler Micro Hot Stage with a Model BPH Phase Microscope and are uncorrected. All boiling points are uncorrected. Infrared (IR) spectra were obtained with a Perkin-Elmer Model 457A or Model 599B spectrophotometer as solutions in $CHCl_3$ or CCl_4 ; or as neat films on NaCl plates; or as solids in anhydrous KBr disks. The 1601 cm^{-1} band of polystyrene film was used as an external calibration standard. Proton nuclear magnetic resonance (^1H NMR) spectra were determined for $CDCl_3$ solutions (unless otherwise specified) at 80 MHz on a Varian Model CFT-20; or at 300 MHz on a Bruker Model WM-300; or at 400 MHz on a Varian Model XL-400 spectrometer. Chemical shifts are reported in d units and were routinely referenced to the signal from residual H in the perdeuterated solvent used (δ 7.27 for $CDCl_3$, δ 7.15 for C_6D_6). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were determined for $CDCl_3$ solutions (unless otherwise specified) at 75 MHz on a Bruker Model WM-300 or at 100 MHz on a Varian Model XL-400 spectrometer with full proton broad-band noise decoupling. Carbon shifts are reported in parts per million (ppm) and were routinely referenced to the solvent carbon signal (77.0 ppm for $CDCl_3$ and 128.0 ppm for C_6D_6). UV-VIS data were obtained in heptane (Burdick and Jackson spectrophotometric grade) on a Cary Model 219 direct ratio recording double beam spectrometer with a wavelength accuracy of ±0.2 nm. Elemental microanalyses were performed by Galbraith Laboratories Inc., Knoxville, Tennessee, and by MicAnal Organic Microanalysis, Tuscon, Arizona. The term GC refers to gas chromatography with a Perkin-Elmer Model 900 instrument equipped with a Perkin-Elmer Sigma 10 Chromatography Data Station. Helium was the carrier gas. Columns used included: 4', 1/8" O.D., 2.5% BBBT on Chromosorb W-HP, 100/200 mesh; 9', 1/8" O.D., 1.5% SE-30 on Chromosorb W-HMDS; and 100', 0.02" I.D., FFAP capillary. The term HPLC refers to high pressure liquid chromatography on a Waters Associates instrument equipped with a Model U6K Universal Injector, Model 600A Solvent Delivery System, Model 450 Variable Wavelength UV Detector, Series R-400 Differential Refractometer Detector, and Omniscribe Model D50000 Chart Recorder. Analyses were routinely performed in the reversed-phase mode with acetonitrile (Burdick and Jackson) as solvent. Analytical separations were performed on an Altex Ultrasphere-ODS column (dp = 5 m, 4.6 mm I.D., 25 cm length). Preparative separations were performed on a Regis-ODS II column (dp = 5 m, 10 mm I.D., 50 cm length). The term TLC refers to thin layer chromatography. All plates were from Analtech Incorporated. The term $AgNO_3$-TLC refers to silver nitrate-impregnated silica chromatography. We accomplished vizualization by spraying with 50% (v/v) aqueous H_2SO_4 and then charring. Preparative $AgNO_3$-TLC was performed on 20 X 20 cm glass plates coated with 15 or 20% $AgNO_3$/silica gel GF (500, 1000, or 2000 m thickness). Column chromatography was performed on Brinkmann silica gel-60 (70-230 mesh) or J. T. Baker silica gel-60 (25-40 mesh).

25,25-Dichloro-tricyclo[11.11.1.0]pentacosane (20). This method was based on a close analogy from Nakazaki.[2c] The *cis*-olefin **19** (1.0 g, 3.0 x 10^{-3}) and cetyltrimethylammonium bromide (Aldrich, 95%, 0.08 g, 2.2 x 10^{-4}) were dissolved in $CHCl_3$ (baker, reagent grade, 23.6 mL). After addition of 50% (w/w) aqueous NaOH (17.6 mL), the heterogeneous mixture was stirred at a gentle reflux for 3 h. The mixture was partitioned between H_2O and $CHCl_3$, dried over Na_2SO_4, and filtered. Solvent removal gave 1.75 g of a glassy yellow solid, which was taken up in heptane. Passage through a short column of silica afforded 0.80 g of a colorless viscous oil, which contained at least two components by TLC. Crystallization from heptane (2x) afforded 0.66 g (53%) of colorless dichlorocarbene adduct **20**, m.p. 95.5-97.8 °C. GC (BBBT, 215 °C, 44 psi) indicated 99% purity. IR (CCl_4) 1470, 1445, 1350, 8555, 845 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.18-1.65 (m, 40 H), 1.67-1.81 (m, 4 H). ^{13}C NMR ($CDCl_3$) 24.46, 24.80, 24.93, 25.37, 26.55, 29.49, 37.52, 80.07 (cyclopropyl CCl_2) ppm. Anal. Calcd. for $C_{25}H_{44}Cl_2$ (416.36): C, 72.09; H, 10.65. Found: C, 72.42; H, 10.59.

25-Chloro-1-methoxy-bicyclo[11.11.1]pentacos-13(25)-ene (21). This procedure is based on similar chemistry reported by Baird.[34] Dichlorocarbene adduct **20** (0.16 g, 3.8 x 10^{-3} mmol) in anhydrous methanol (Omnisolv, 110 mL) with $AgNO_3$ (Aldrich, 99+%, 2.4 g, 1.4 x 10^{-2} mmol) was gently refluxed (no reaction without heating) for 3 h. The mixture was partitioned between H_2O and hexane, and the organic layer was dried over Na_2SO_4. Filtration and solvent removal gave 0.18 g of a colorless immobile oil. The pure vinyl chloro ether **21** was obtained as a colorless oil by a combination of preparative TLC, HPLC, and distillation bulb to bulb (ca. 195 °C, 0.4 torr, 44 mg, 28%). IR ($CHCl_3$) 1600, 1460, 1230, 1200, 1080, 930, 800, 710, 680 cm^{-1}. ^{1}H NMR (C_6D_6) δ 1.01-1.71 (m, 42.6 H), 1.71-1.85 (m, 2.2 H), 1.86-1.94 (m, 0.1 H), 1.95-2.10 (m, 2.1 H, allylic), 2.14-2.23 (m, 0.2 H, allylic), 2.38-2.48 (m, 0.2 H, allylic), 2.86 (s, 3.1 H, OCH_3), 3.04-3.14 (m, 1 H, allylic), 3.18 (s, 0.3 H, OCH_3), 3.41-3.50 (m, 1 H, allylic). Fractional H integrals indicate the presence of two isomers (conformers?). Note especially the two methoxyl signals, which suggest a ratio of 10.3 : 1. ^{13}C NMR (C_6D_6) 23.71, 23.76, 23.99, 24.24, 25.46, 25.55, 26.12 (broad s, probably two overlapping signals), 26.77, 26.88, 27.02, 27.11, 27.16, 27.30, 27.56, 28.22, 28.38, 29.56, 31.79, 33.12, 34.82, 36.47, 48.44 (OCH_3), 89.50 (tertiary C-O), 130.73 (sp^2 C), 141.92 (sp^2 C) ppm. Anal. Calcd. for $C_{26}H_{47}ClO$ (411.12): C, 75.96; H, 11.52. Found: C, 75.98; H, 11.64.

Bicyclo[11.11.1]pentacosa-1(25),13(25)-diene (22). This procedure was based on chemistry developed by Gustavson,[36] by House,[39] and by Rieke.[35] The reaction was conducted under argon (prepurified, < 4 ppm O_2) and rigorously anhydrous conditions. Potassium metal was handled under heptane, and anhydrous $ZnCl_2$ (Aldrich, 99.999+%) was handled in a glove box. 1,2-Dimethoxyethane (DME) was distilled from sodium/benzophenone. The $ZnCl_2$ (670 mg, 4.94 mmol) was weighed into a three-neck flask fitted with a condenser. Dry DME (5.0 mL) was added via syringe. One neck of the vessel was opened briefly to permit rapid introduction of potassium (ca. 390 mg, 4.94 mmol). [*CAUTION*: The reduction is very exothermic and extreme care must be exercised during the initial stage.] Without being stirred, the reduction mixture was very gradually warmed to 70 °C with occasional hand agitation. The mixture was stirred after most of the material had reacted, and reflux was continued for an additional 3 h. The substrate vinyl chloro ether **21** (20 mg, 4.94 x 10^{-2} mmol) in DME (2.0 mL) was transferred via cannula to the refluxing activated zinc suspension. In this particular trial, the reaction stopped short of completion and no further progress was observed after 20 min reaction time. The cooled mixture was filtered through celite and solvent was evaporated. The resultant oil was taken up in hexane and passed through silica to give 15 mg of a colorless immobile oil (ca. 3 : 1 starting material and allene, respectively, by ^{1}H NMR). Pure allene **22** was obtained from a portion of the crude product as a white solid, micro m.p. 68.9 °C (400 mg) after preparative HPLC and sublimation at 60 °C, 0.3 torr. IR (CCl_4 passed through neutral alumina) 2930, 2850, 1460 cm^{-1}. ^{1}H NMR (C_6D_6) δ 1.18-1.63 (m, 36 H), 1.93-2.04 (m, 4 H, allylic), 2.07-2.19 (m, 4 H, allylic). ^{13}C NMR (C_6D_6) d 25.75, 25.83, 25.89, 26.33, 27.23, 31.52, 102.30 (sp^2 C) ppm. UV (heptane) no maximum observed above 194 nm, but at 200 nm, ε = 12600. High-Resolution MS, obsd m/z 344.3426, $C_{25}H_{44}$ requires 344.3442.

2-(5-Bromopentyl)-2-methoxycarbonylcyclododecanone (8). The 2-methoxycarbonyl cyclododecanone[5a] (7, 16.6 g, 0.07 mol) in dry THF (250 mL) was added over 3 h to a stirred slurry of NaH (1.75 g, 0.073 mol) in dry THF (150 mL). This anionic mixture was added during 3.5 h to a refluxing solution of 1,5-dibromopentane (15.9 g, 0.07 mol, Aldrich 99% pure) in dry THF (150 mL). After 18 h at reflux the mixture was cooled and acidified with acetic acid/water (2 : 1, v/v). Removal of solvent left a semi-solid, which was extracted with petroleum ether. Evaporation of the solvent left **8** as an oil (21.1 g, 78%), which could be used directly in the next step. For characterization, a separate sample was purified by preparative TLC (silica taper plate, 10% v/v ethyl acetate/hexane) and subsequent bulb-to-bulb distillation (190-195 °C, 0.4 torr) of the colorless viscous oil. IR (neat) 1740, 1725, 1705, 1470, 1445, 1290, 1260, 1245, 1220, 1195, 1155, 1130 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 0.83-1.05 (m, 1 H), 1.05-1.54 (m, 17 H), 1.59 (d, J = 3.2 Hz, 1 H), 1.76-1.92 (m, 5 H), 1.97-2.21 (m, 3 H), 2.83-2.97 (m, 1 H), 3.39 (t, J = 7.0 Hz, 3 H, CH_2Br), 3.72 (s, 3 H, OCH_3). Anal. Calcd. for $C_{19}H_{33}BrO_3$ (389.37): C, 58.61; H, 8.54. Found: C, 58.42; H, 8.50.

2-(5-Bromopentyl)cyclododecanone (9). A mixture of crude keto ester **8** (21.1 g, 0.054 mol), aqueous 48% HBr (200 mL) and powdered clay (21 g, from an ordinary clay pot used for plants) was heated 30 h at 140 °C. The cooled mixture was diluted with water and extracted with ether. After a $NaCO_3$ extraction, the derived product was fractionally distilled (b.p. 190-210 °C, 1 torr) to give an oil (6.32 g, 35%) that solidified on storage at room temperature. Recrystallization from ethanol/water gave m.p. 43-44 °C. IR (neat) 2930, 2850, 1700, 1465, 1440 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ 1.30 (broad m), 1.51-2.15 (m), 2.32-2.75 (m, $CH_2C{=}O$), 3.40 (t, 2 H, CH_2Br). Anal. Calcd. for $C_{17}H_{31}BrO$ (331.34): C, 61.62; H, 9.43. Found: C, 62.00; H, 9.53.

2-[5-(Triphenylphosphonio)pentyl]cyclododecanone bromide (10). Becker's[11] general method was used. Diethyl ether was distilled from lithium aluminum hydride shortly before use. The keto bromide **9** (4.48 g, 1.46 x 10^{-2} mol) and triphenylphosphine (Aldrich, 99%, 3.84 g, 1.46 x 10^{-2} mol) in dry diethyl ether (12.0 mL) were sealed in a thick-walled pyrex tube, and heated at 130 °C for 94 h. The insoluble product oiled out of solution during the course of reaction. The product was taken up in methylene chloride, transferred, and solvent removed. Vacuum drying over P_2O_5 for 24 h afforded the phosphonium salt **10** (7.95 g, 92%) as a glassy solid which was characterized only by ^{1}H NMR and used without further purification. ^{1}H NMR ($CDCl_3$) δ 0.76-1.90 (m, 26 H), 2.25-2.75 (m, 3 H, a-carbonyl), 3.40-4.05 (br m, 2 H, $CH_2P^+Ph_3Br^-$), 7.35-8.05 (m, 15 H, aromatic).

Intramolecular Wittig. *Z*-Bicyclo[10.5.0]heptadec-1(17)-ene (11). This procedure was also based on a method by Becker[11] with modification. The reaction was conducted under argon and strictly anhydrous conditions. Dimethyl sulfoxide (DMSO) was distilled from CaH_2 onto molecular sieves (4Å) and stored under argon. A dimsyl sodium (DMSO anion) solution was prepared. Sodium hydride (Aldrich, 60% dispersion in mineral oil, 2.00 g) was washed with pentane. Dry DMSO (23.2 mL) was added, and the mixture was stirred and heated at 80 °C for 1 h (solution ca. 2.12 **M** in dimsyl sodium). In a separate vessel, the phosphonium salt **10** (7.95 g, 1.34×10^{-2} mol) was dissolved in dry DMSO (30.0 mL) and was added dropwise over a period of 20 min at room temperature. The mixture was stirred and heated at 76 °C for 10 min, then at 56 °C for 32 h. The cooled mixture was partitioned between H_2O and hexane. The organic extracts were dried over $MgSO_4$, and passed through a short column of silica to give the desired olefin **11** (0.49 g, 16%) as a colorless liquid which was pure (99%) by GC (FFAP, 170 °C, 14 psi). IR (neat) 2930, 2860, 1655 (w), 1465, 1445, 1345 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.05-1.32 (m, 24 H), 1.32-2.61 (m, 5 H, allylic), 5.45 (t, J = 6.2 Hz, 1 H, olefinic). ^{13}C NMR ($CDCl_3$) 23.38, 23.45, 23.79, 24.28, 24.36, 24.73, 24.97, 25.53, 25.88, 26.87, 27.37, 27.67, 35.78, 38.55, 38 68, 124.98 (sp^2 C), 146.63 (sp^2 C) ppm. Anal. Calcd. for $C_{17}H_{30}$ (234.43): C, 87.10; H, 12.90. Found· C, 87 28; H, 13.00.

Z-Bicyclo[10.5.0]heptadec-1(12)-ene (12). *E+Z*-Bicyclo[10.5.0]heptadec-1(2)-ene (13). The trisubstituted olefin **11** (126 mg, 5.35×10^{-1} mmol), *p*-toluene sulfonic acid (Baker, monohydrate, 99%, 82 mg, 4.30×10^{-1} mmol), and benzene (Baker, reagent grade, 10.3 mL) were stirred and heated at 57 °C for 12 h in a sealed ampoule. Evaporation of solvent and passage of the hexane solubles through silica provided 124 mg of a colorless liquid comprised of three main components (40 : 36 : 22) by GC (FFAP, 170 °C, 14 psi). Preparative TLC (hexane/20% $AgNO_3$-silica) afforded the tetrasubstituted olefin **12** (40% GC yield, 32 mg, 26% isolated yield) as a colorless liquid (96.3% pure by GC). The two minor isomers could be obtained only as a mixture by preparative TLC. Olefin **12** was obtained in higher purity (99% by GC) from preparative HPLC. IR (neat) 2915, 2840, 1470, 1445 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.04-1.66 (m, 20 H), 1.66-1.78 (quintet, J = 6 Hz, 2 H), 1.92-2 28 (m, 8 H, allylic). ^{13}C NMR (CD_2Cl_2) 23 26, 25.15, 25.68, 26.08, 27.72, 31.58, 33.24, 33.88, 137.42 (sp^2 C) ppm. UV (heptane) l_{max}203 nm (ε = 9600). Anal. Calcd. for $C_{17}H_{30}$ (234.43): C, 87.10; H, 12.90. Found: C, 87.04; H, 12.72.

The two remaining isomers **13** (36 and 22% by GC, denoted *EZ* 1 and *EZ* 2, respectively) could also be obtained pure (99% by GC) from preparative HPLC, and were characterized only by ^1H NMR. For **13** (*EZ* 1), ^1H NMR ($CDCl_3$) δ 0.86-1 93 (m, 25 H), 1.93-2.25 (m, 3 H, allylic), 2.30-2.48 (m, 1 H, allylic), 5.17 (dd, J = 10.7 and 4.3 Hz, 1 H, olefinic). For **13** (*EZ* 2), ^1H NMR ($CDCl_3$) δ 1.01-2 12 (m, 27 H), 2.25-2 45 (m, 1 H, allylic), 2.67-2.87 (m, 1 H, allylic), 5.25 (dd, J = 11 6 and 3.9 Hz, 1 H, olefinic).

2-(6-Bromohexyl)cyclododecanone (14) The solvent 1,2-dimethoxyethane (DME) was purified by distillation from sodium/benzophenone, and the reaction was conducted under argon and anhydrous conditions. Cyclododecanone (Aldrich, 97%, 17.0 g, 9.3×10^{-2} mol) in dry DME (85 mL) was added to a NaH dispersion (Aldrich, 60% dispersion in mineral oil, 2.8 g, 7.0×10^{-2} mol), and the mixture was gently refluxed for 6 h. The alkylating agent, 1,6-dibromohexane (Aldrich, 97%, 21.4 mL, 34 0 g, 1.4×10^{-1} mol), was added to the refluxing slurry as rapidly as possible. After 2 h reflux, the mixture was cooled, quenched with H_2O (ca. 25 mL), then partitioned between H_2O and diethyl ether The organic layer was dried over Na_2SO_4 and filtered, and the solvent was removed to afford 49.9 g of a slightly yellow liquid. Undesired material was removed by distillation (81-110 °C, 0.45 torr) to leave 21.9 g of a yellow, viscous liquid rich in desired bromoketone. The mixture was column (5 cm O.D., 54 cm length) chromatographed on silica (Baker, 450 g) with 2% ethyl acetate/hexane to afford 9.7 g (40%) of bromoketone **14** as a colorless and viscous liquid. Bulb-to-bulb distillation (185-215 °C, 0.3 torr) gave the analytical sample. IR (neat) 1701, 1470, 1250,732 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.91-1.89 (m, 28 H), 2.28-2.60 (m, 3 H, a to carbonyl), 3 38 (t, 2 H, CH_2Br). Anal. Calcd. for $C_{18}H_{33}BrO$ (345.36): C, 62.60; H, 9.63. Found: C, 62.59, H, 9.63.

2-(6-Hydroxyhexyl)cyclododecanone (15). The ketobromide **14** (1.0 g, 2.9×10^{-3} mol) and silver perchlorate (Alfa, 99%, 6.2 g, $3\ 0 \times 10^{-2}$ mol) in 10% (v/v) aqueous acetone (250 mL) were refluxed for 16 h. The mixture was partitioned between H_2O and diethyl ether. The organic phase was dried over Na_2SO_4 and filtered, and the solvent was removed to provide 0.87 g of a colorless oil that was pure enough to be used directly in the next step. For characterization, the material was column (3.5 cm O.D., 53 cm length) chromatographed on silica (Baker, 200 g) with 25% ethyl acetate/hexane, which gave 0.68 g (83%) of the alcohol **15**. Analytically pure colorless oil was obtained by bulb-to-bulb distillation (195-200 °C, 0.4 torr). IR (CCl_4) 3610, 3590-3120, 1706, 1251, 1160 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.95-1.80 (m, 29 H), 2.32-2.54 (m, 3 H, a to carbonyl), 3.58 (t, 2 H, CH_2-O). Anal. Calcd. for $C_{18}H_{34}O_2$ (282 47): C, 76.54; H, 12.13. Found: C, 76.27; H, 12.19.

2-(6-Oxohexyl)cyclododecanone (16). The Corey-Suggs oxidation method[23] was used. Methylene chloride was purified by distillation from P_2O_5 Pyridinium chlorochromate (PCC) was dried over P_2O_5 under vacuum prior to use, and the reaction was conducted under argon and anhydrous conditions. Keto alcohol

15 (0.30 g, 1.1 x 10^{-3} mol) in dry CH_2Cl_2 (5.0 mL) was rapidly added to a suspension of PCC (Aldrich, 98%, 0.34 g, 1.6 x 10^{-3} mol, 1.5 equivalent) in dry CH_2Cl_2 (4.0 mL). The mixture was stirred at room temperature for 3 h, then diluted with diethyl ether (anhydrous, ca. 15 mL) and filtered through Florisil. Evaporation of solvent afforded a colorless oil, which was adequately pure for the next step. Bulb-to-bulb distillation (160-180 °C, 0.25 torr) gave analytically pure keto aldehyde 16 (0.22 g, 74%) as a colorless, viscous oil. IR ($CDCl_3$) 2730, 1720, 1700 cm^{-1}. ^1H NMR ($CDCl_3$) δ 0.90-1.84 (m, 26 H), 2.34-2.61 (m, 5 H, a to carbonyls), 9.75 (t, 1 H, aldehydic). Anal. Calcd. for $C_{18}H_{32}O_2$ (280.46): C, 77.09; H, 11.50. Found: C, 77.25; H,11.82.

Intramolecular Coupling to Bicyclo[10.6.0]octadec-1(18)-ene (17). We followed McMurry's[22] general procedure. We prepared the zinc-copper couple by adding zinc dust (Fisher Scientific, 9.81 g, 1.5 x 10^{-1} mol) in one portion to $CuSO_4$ (Baker, 0.75 g, 4.7 x 10^{-3} mol) in deoxygenated H_2O with vigorous stirring. After 10 min, the mixture was filtered under argon and washed with deoxygenated acetone and diethyl ether. DME was purified by distillation from sodium/benzophenone, and $TiCl_3$ was handled in a glove box. The reaction was conducted under rigorously anhydrous and oxygen-free conditions. $TiCl_3$ (Aldrich, 25.1 g, 1.63 x 10^{-1} mol) and freshly prepared Zn-Cu couple (31.7 g, 4.9 x 10^{-1} mol) in DME (500 mL) were refluxed for 4.6 h. The color changed from an initial purple to blue, green, brown, and then to a final brownish-black. Crude keto aldehyde 16 (5.13 g, 1.83 x 10^{-2} mol) in DME (700 mL) was added via syringe pump (Sage Instruments, Model 355) to the refluxing suspension over a period of 25.5 h. Reflux was continued for 5.8 h after addition. The cooled suspension was filtered through celite, and the filtrate was partitioned between H_2O and hexane. The hexane layer was dried over $MgSO_4$ and filtered, and solvent was removed to give 1.60 g of a colorless liquid containing sixteen components by GC (FFAP, 185 °C, 14 psi). The major component (75.3%) proved to be the desired trisubstituted olefin 17 and the remaining unidentified minor components ranged from 0.7 to 4.8% in concentration. Analytically pure 17 was obtained from a combination of preparative $AgNO_3$-TLC, HPLC, and distillation (150-160 °C, 0.4 torr) as a colorless liquid. IR (neat) 2920, 2875, 1468, 1445 cm^{-1}. ^1H NMR ($CDCl_3$) δ 1.09-1.93 (m, 27 H), 1.96-2.12 (m, 2 H, allylic), 2.69-2.82 (m, 1 H, allylic), 5.64 (m, 1 H, olefinic). ^{13}C NMR (C_6D_6) 23.66, 24.43, 24.63, 24.97, 25.29, 25.40 (broad, probably two overlapping signals), 25.83, 25.90, 27.44, 27.76, 28.37, 31.54, 31.69, 36.02, 38.58, 126.43 (sp^2 C), 140.40 (sp^2 C) ppm. Anal. Calcd. for $C_{18}H_{32}$ (248.46): C, 87.02; H, 12.98. Found: C, 87.17; H, 13.02.

***Z*-Bicyclo[10.6.0]octadec-1(12)-ene (18).** A product mixture (0.55 g) from the coupling experiment described above (75% in olefin 17, ca. 1.7 x 10^{-3} mol), and *p*-toluene sulfonic acid monohydrate (Baker, 99%, 0.24 g, 1.3 x 10^{-3} mol) in benzene (Baker, reagent grade, 20.0 mL) were heated at 80 °C for 24 h. The solvent was removed and the hexane solubles were passed through silica to afford 0.49 g of a colorless liquid comprised of at least sixteen components by GC (FFAP, 185 °C, 14 psi). The major component (53%) proved to be the desired tetrasubstituted olefin 18. Purification of a portion of this material by a combination of preparative $AgNO_3$-TLC, HPLC, and distillation (140-150 °C, 0.45 torr) gave analytically pure olefin 18 as a liquid, which crystallized on standing at -20 °C, micro m.p. 42.4 °C. IR (neat) 2915, 2845, 1470, 1448 cm^{-1}. ^1H NMR (C_6D_6) δ 1.21-1.62 (m, 24 H), 1.96-2.13 (m, 4 H, allylic), 2.13-2.25 (m, 4 H, allylic). ^{13}C NMR ($CDCl_3$) 22.58, 24.74, 25.49, 26.00, 26.89, 27.94, 29.27, 29.70, 133.73 (sp^2 C) ppm. UV (heptane) λ_{max}202 nm ($\varepsilon = 12800$). Anal. Calcd. for $C_{18}H_{32}$ (248.46): C, 87.02; H, 12.98. Found: C, 87.06; H, 12.79.

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REFERENCES AND NOTES

(1) (a) Marshall, J. A.; Lewellyn, M. *J. Am. Chem. Soc.* **1977**, *99*, 3508-3510. (b) Marshall, J. A.; Chung, K. H. *J. Org. Chem.* **1979**, *44*, 1566-1567. (c) Marshall, J. A.; Constantino, M.; Black, T. H. *Synth. Commun.* **1980**, *10*, 689-692. (d) Marshall, J. A.; Black, T. H. *J. Am. Chem. Soc.* **1980**, *102*, 7581-7583. (e) Marshall, J. A.; Flynn, K. E. *J. Am. Chem. Soc.* **1983**, *105*, 3360-3362.

(2) (a) Nakazaki, M.; Yamamoto, K.; Yanagi, J. *J. Chem. Soc., Chem. Commun.* **1977**, 346-347. (b) Nakazaki, M.; Yamamoto, K.; Maeda, M. *J. Chem. Soc., Chem. Commun.* **1980**, 294-295. (c) Nakazaki, M.; Yamamoto, K.; Yanagi, J. *J. Am. Chem. Soc.* **1979**, *101*, 147-151.

(3) (a) Nickon, A.; Zurer, P. S. *Tetrahedron Lett.* **1980**, 3527-3530. (b) Nickon, A.; Zurer, P. S.; Hrnjez, B.; Tino, J.*Tetrahedron* **1983**, *39*, 2679-2690.

(4) (a) Ceve, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Org. Chem.* **1981**, *46*, 486-490. (b) Ceve, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *J. Chem. Soc., Chem. Commun.* **1980**, 755-756.

(5) (a) Nickon, A.; Rodriguez, A. D.; Ganguly, R.; Shirhatti, V. *J. Org. Chem.* **1985**, *50*, 2767-2777. (b) Nickon, A.; Rodriguez, A. D.; Shirhatti, V.; Ganguly, R. *Tetrahedron Lett.* **1984**, 3555-3558.

(6) Cahn, R. S.; Ingold, C.; Prelog, V. *Angew. Chem. Int. Ed. Eng.* **1966**, *4*, 385-416.

(7) (a) Nakazaki, M.; Yamamoto, K.; Maeda, M. *Chem. Lett.* **1981**, 1035-1036. (b) Nakazaki, M.; Yamamoto, K.; Maeda, M.; Sato, O.; Tsutsui, T. *J. Org. Chem.* **1982**, *47*, 1435-1438. (c) Marshall, J. A.; Rothenberger, S. D. *Tetrahedron Lett.* **1986**, 4845-4848.

(8) (a) Doering, W. von E., La Flamme, P. M. *Tetrahedron* **1958**, *2*, 74-79. (b) Logan, T. J. *Tetrahedron Lett.* **1961**, 173-175. (c) Moore, W. R.; Ward, H. R. *J. Org. Chem.* **1962**, *27*, 4179-4181. (e) Skattbol, L. *Acta Chem. Scand.* **1963**, *17*, 1683-1693.

(9) The conversion of 7 to 9 was developed initially in our laboratory by Dr. V. Shirhatti, who also kindly supplied us with some material for our experiments. Additional details are described in Rodriguez, A. D., Ph.D. Dissertation, The Johns Hopkins University, Baltimore, MD, 1983.

(10) Torri, S., Okamoto, T.; Veno, N. *J. Chem. Soc., Chem. Commun.* **1978**, 293-294.

(11) Becker, K. B. *Helv. Chim. Acta* **1977**, *60*, 68-80

(12) March, J. "Advanced Organic Chemistry;" McGraw-Hill: New York, 1977, p 192-193.

(13) Greenwald, R.; Chayovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128-1129.

(14) Inoue, Y.; Ueoka, T.; Hakushi, T. *J. Chem. Soc. Perkin Trans. II* **1983**, 983-988.

(15) Kropp, P. J. in "Organic Photochemistry," Padwa, A., Ed., Marcel Decker, Inc.: New York, 1979, Vol. IV, p 1-142.

(16) Corey, E. J.; Tada, M.; La Mahieu, R.; Libit, L. *J. Am. Chem. Soc.* **1965**, *87*, 2052-2054.

(17) Eaton, P. E.; Lin, K. *J. Am. Chem. Soc.* **1965**, *87*, 2051-2052.

(18) Bonneau, R.; Joussot-Dubien, J.; Yarwood, J.; Pereyre, J. *Tetrahedron Lett.* **1977**, 235-238.

(19) St. Jaques, M.; Vaziri, C. *Can. J. Chem.* **1971**, *49*, 1256.

(20) (a) Allinger, N L.; Spague, J. T. *J. Am. Chem. Soc.* **1972**, *94*, 5734. (b)Ermer, O.; Lifson, S. *J. Am. Chem. Soc.* **1973**, *95*, 4121. (c) White, D. N. J.; Bouill, M. J. *J. Chem. Soc., Perkin Trans. 2* **1977**, *13*, 1610.

(21) Favini, G.; Nava, A. *Theor. Chim. Acta* **1973**, *31*, 261.

(22) McMurry, J. E.; Fleming, M. P.; Kees, K. L.; Krepski, L. R. *J. Org. Chem.* **1978**, *48*, 3255-3266, and references therein.

(23) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647-2650.

(24) Shea, K. *Tetrahedron* **1980**, *36*, 1683-1715.

(25) Cope, A. C.; Pike, R. A.; Spencer, C. F. *J. Am. Chem. Soc.* **1953**, *75*, 3212-3215.

(26) Ermer, O. *Angew. Chem. Int. Ed. Eng.* **1974**, *13*, 604-606.

(27) Rogers, D. W.; Voitkenberg, H.; Allinger, N. L. *J. Org. Chem.* **1978**, *43*, 360-361. See also reference 20.

(28) Marshall, J. A.; Biernbaum, R. E.; Chung, K. -H. *Tetrahedron Lett.* **1979**, 2081-2084.

(29) Marshall, J. A.; Black, T. H.; Shone, R. L. *Tetrahedron Lett.* **1979**, 4737-4740.

(30) Starks, C. M.; Liotta, C. "Phase Transfer Catalysis;" Academic Press; New York, 1978.

(31) Levy, G. C.; Lichter, R. L ; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance Spectroscopy;" Wiley; New York, 1980.

(32) Moore, W. R.; Hill, J. B. *Tetrahedron Lett.* **1970**, 4553-4556.

(33) (a) Moore, W. R.; Hill, J. B. *Tetrahedron Lett.* **1970**, 4343-4346. (b) Brown, D. W.; Hendrick, M. E.; Jones, M. *Tetrahedron Lett.* **1973**, 3951-3954. (c) Warner, P.; Chang, S. -C.; Powell, D. R.; Jacobson, R. A. *Tetrahedron Lett.* **1981**, 533-536. (d) Paquette, L. A.; Chamot, E.; Browne, A. R. *J. Am. Chem. Soc.* **1980**, *102*, 637-643. (e) Paquette, L. A.; Browne, A. R.; Chamot, E.; Blount, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 643-651.

(34) Baird, M. S.; Nethercott, Reese, C. B. *J. Chem. Soc., Chem. Commun.* **1982**, 224-225.

(35) (a) Rieke, R. D. *Acc. Chem. Res.* **1977**, *10*, 301-306. (b) Rieke, R. D.; Uhm, S. J. *Synthesis* **1975**, 452-453.

(36) Gustavson, G. G. *J. Russ. Chem. Soc.* **1888**, *20*, 615.

(37) Cripps, H. N.; Kiefer, E. F. *Org. Syn.* **1962**, *42*, 12-14.

(38) Sugita, T.; Nishimoto, K.; Ichikawa, K. *Chem. Lett.* **1973**, 607-610.

(39) House, H. O.; Ro, R. S. *J. Am. Chem. Soc.* **1953**, *80*, 182-187.