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Cheletropic Reactions of Fluorocarbenes with Norbornadienes

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Abstract: The reaction of difluorocarbene (generated at 20–25 °C) with norbornadiene (**1**) and its 7-methyl derivative (**6**) proceeds initially to give the 1:1 adducts arising from exo and endo 1,2 addition and more importantly from homo-1,4 addition. From an investigation of the thermal behavior of the 1,2 adducts, it is established that the homo-1,4 adducts arise directly from linear cheletropic reaction, thereby constituting an unprecedented example. The 1,2 adducts are cis-fused cyclopropanes and exhibit two mechanistically different types of rearrangement on heating. At 80 °C the endo 1,2 difluorocarbene adduct of **1** smoothly epimerizes to the exo 1,2 adduct. The latter on stronger heating at 225 °C undergoes intramolecular cycloaddition in two steps to give the corresponding tetracyclic structure. The 1,2 adducts derived from fluorochlorocarbene and **1** display an unusual dichotomy of thermal behavior which depends on the configuration of the halogen substituents. Both exo and endo *Z* adducts (**12** and **15**), the more congested isomers, undergo spontaneously the cyclopropyl-allylic rearrangement in which the chlorine substituent migrates. Isomer **12** gives *exo*-4-chloro-3-fluorobicyclo[3.2.1]octa-2,6-diene (**13**), whereas **15** gives the endo ring enlarged product (**16**). In contrast, the exo and endo *E* adducts (**11** and **14**) are more thermally resistant, but at 200 and 100 °C they give stereospecifically **16** and **13**, respectively. This latter behavior is interpreted in terms of an initial stereomutation of the cyclopropane ring which puts the electronically better chlorine substituent in the correct configuration for electrocyclic ring opening. A discussion of the cheletropic reactions and the rearrangements of the cyclopropane adducts is presented. The different requirements for cyclopropane stereomutation and intramolecular cycloaddition are analyzed and discussed.

Introduction

We reported recently that the reaction of difluoro- and fluorochlorocarbene with norbornadiene gave sizable amounts of the endo homo-1,4 adducts.[1] The novelty and mechanistic importance of these results resides in the possibility that they constitute singular and unprecedented examples of linear cheletropic reactions of σ^2 carbenes. In this paper we now demonstrate that the homo-1,4 adducts arise directly and do not derive from any of the 1,2 adducts. By examining the individual thermal behavior of the 1,2 adducts, we elucidate the stereochemical course of their rearrangement and further show that the presence and configuration of the fluorine substituent exert a subtle control over the ease and manner of the opening of the cis-fused cyclopropane ring.

Our chief reason for choosing difluorocarbene was based on the primitive notion that, as difluorocarbene is less electrophilic than the other halocarbenes, the chances were good that reaction with a suitable conjugated diene would reveal some 1,4 addition.[2] It was assumed that the 1,2 and 1,4 additions would be in formal competition, but for different parts of the diene (Figure 1).[3] Both theoretical and experimental studies amply attest to the electrophilic behavior of σ^2 halocarbenes on 1,2 addition.[2,4] Indeed, the best description of the transition state for cyclopropanation is the one in which the carbene with its ligands projecting forward makes a lateral approach to the midpoint of the double bond so that overall C_s symmetry is maintained.[5] The corollary is that the p_z orbital of the carbene is engaged with the π system of the olefin in a nonlinear approach (Figure 2). Consequently any feature in the carbene, or in the substrate for that matter, which would disfavor this particular mode, could call forth 1,4 addition. Moreover, a concerted 1,4 addition, as it is a linear cheletropic reaction, will necessarily entail the simultaneous involvement of the empty and doubly occupied orbitals of the carbenic carbon atom. In this mechanistic context the terms electrophilic and nucleophilic become redundant; thus a carbene, less electrophilic with respect to 1,2 addition, might reveal greater potential for 1,4 addition.

Subsidiary, but nonetheless important, considerations which indicated difluorocarbene were the strength of the carbon–fluorine bond, the small size of the fluorine substituent and its spectroscopic visibility.[6] Difluorocarbene should experience little steric discrimination on approach to an obstructed olefin and once attached, it should stay intact as such and act as a structure probe by virtue of its ^{19}F nuclear magnetic resonance spectrum.

The choice of norbornadiene, a fortunate one as it turned out, was dictated by its suitability as a simple, rigid homoconjugated diene and by its proven ability to undergo [2 + 2 + 2] cycloadditions.[7]

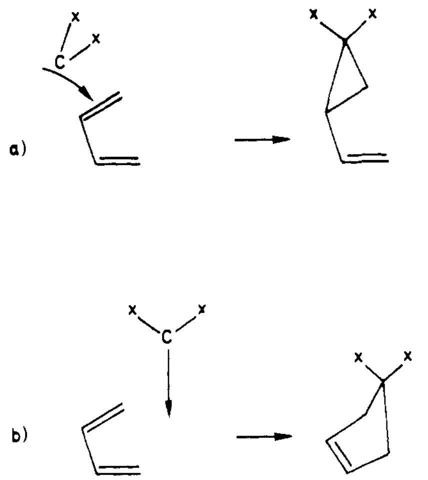
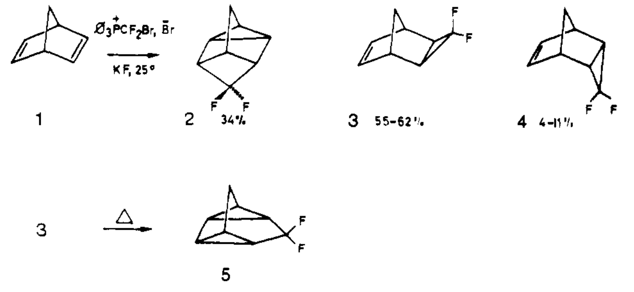


Figure 1. Alternative, competing 1,2 (a) and 1,4 (b) additions of a σ^2 carbene to cisoid butadiene.

Results

The generation of difluorocarbene from phenyl(trifluoromethyl)mercury and sodium difluorochloroacetate at 80 and 140 °C, respectively, in the presence of norbornadiene (**1**) gave just two 1:1 adducts, identified as the homo-1,4 adduct **2** and the exo 1,2 adduct **3**. Initially it was thought that, under these drastic conditions, either the exo or the unobserved endo 1,2 adduct could have been precursors for the mechanistically interesting homo-1,4 adduct **2**.[1b] With the advent of new and milder methods for producing difluorocarbene, it was possible to carry out the addition at room temperature. When triphenyl(bromodifluoromethyl)phosphonium bromide in the presence of potassium fluoride was used as reagent,[8] the adducts **2** and **3** were obtained as before (in relative yields of 34 and 55–62%), but this time the hitherto elusive endo 1,2 adduct **4** was obtained as well in yields of 4 to 11% (Scheme I). All adducts, **2**, **3**, and **4** were separated, correctly identified, and individually subjected to controlled heating. The homo-1,4 adduct **2** remained unchanged and emerged unscathed even on heating to 300 °C. In contrast, the endo 1,2 adduct **4** proved to be extraordinarily labile. At moderate temperatures, 60 to 80 °C, conversion proceeded smoothly and completely to the exo adduct **3**. Stereomutation was a first-order reaction with an activation energy of 28.2 kcal/mol at 25 °C. As the half-life of **4** at 80 °C is 9.2 h, it is easy to understand why it escaped detection in experiments run over many hours at 80 and 140 °C.

Scheme I



The exo adduct **3**, in its turn, on heating, underwent a clean transformation to its tetracyclic isomer **5**. A higher temperature, 225 °C, was required to bring about this change. Clearly this is not an easy affair as evidenced by the value of 39.0 kcal/mol found for the energy of activation.

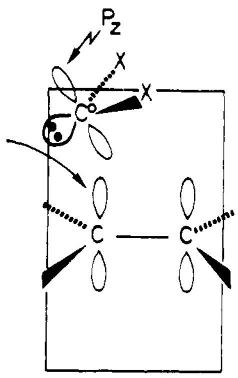
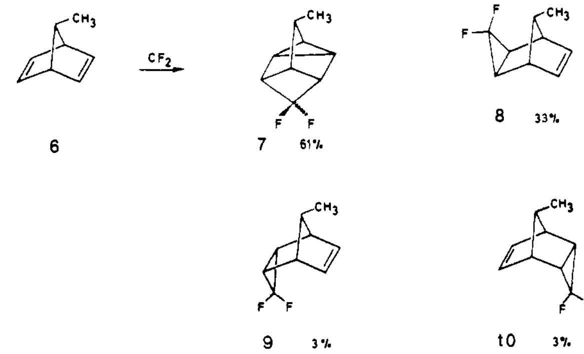


Figure 2. Nonlinear cheletropic reaction of a σ^2 carbene with an ethylene fragment.

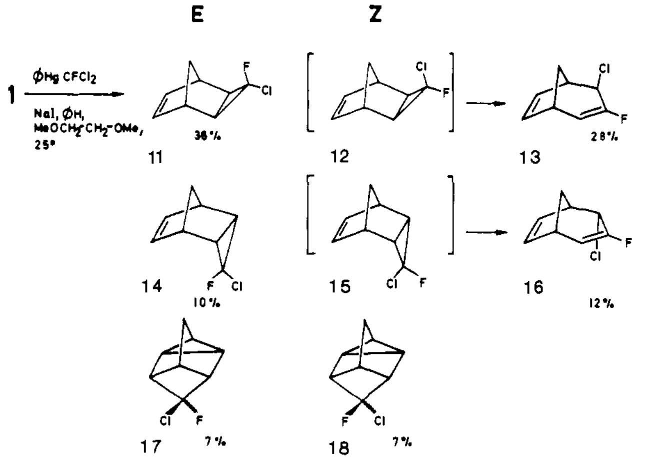
A nice confirmation of the reactivity of norbornadiene was provided by its 7-methyl derivative (**6**).[9] Addition of difluorocarbene at 25 °C gave four 1:1 adducts; the homo-1,4 **7** (61%), a single exo **8** (33%), and two endo 1,2 adducts **9** and **10** (3 and 3% relative yields) (Scheme II). Apart from the significantly large proportion of **7**, the endo 1,2 adducts displayed a net difference in their thermal behavior. Adduct **9** epimerized to **8** at moderate temperatures (70–80 °C), whereas adduct **10** remained intact up to 120 °C, thanks to the potential obstruction afforded by the syn-disposed methyl group.

Scheme II



Fluorochlorocarbene, on account of its C_s symmetry, in principle, ought to experience twice the number of addition modes displayed by difluorocarbene. A possible complication, making a full interpretation difficult, is that the adducts may spontaneously rearrange as they bear a good leaving group, chlorine. This expectation was realized earlier,[1b] when the carbene was prepared by base treatment[10] of fluorodichloromethane at 140 °C. However, recourse to the recently reported mild procedure in which phenyl(fluorodichloromethyl)mercury is allowed to decompose at 25 °C permitted a clarification of the total reaction.[11] Both sets of adducts (of *E* and *Z* configurations) arising from the three different modes of addition were obtained (Scheme III). Aside from the mechanistically significant homo 1,4 adducts (**17** and **18**), the adduct which constitutes the essential clue to a complete understanding of the reaction scheme is the previously unobserved endo *E* 1,2 adduct **14**. Clearly, its isolability is linked to its inherent thermal instability. To remove all doubt, both the endo *E* and exo *E* 1,2 adducts **14** and **11** were separated, and their thermal behavior was elucidated. At 100 °C the endo *E* adduct **14** underwent smooth rearrangement to *exo*-4-chloro-3-fluorobicyclo[3.2.1]octa-2,6-diene (**13**). With lesser facility, but with equal stereospecificity, the exo *E* adduct **11** on heating to 200 °C rearranged to the endo 4-chloro epimer **16**. Of course, both these rearranged products, **13** and **16**, were

Scheme III



originally present in the reaction mixture, and in this instance they undoubtedly arose from the spontaneous rearrangement of the unobserved *Z* 1,2 adducts **12** and **15.**

Discussion

Addition Process. The formation of the bishomoprismane structures **2, 7, 17,** and **18,** from the reaction of the fluorocarbenes, regardless of their source, strongly suggests that they are created in a single step. The best support for such a one-step process is the absence of any viable alternative two-step process. In fact, there is no passage from any of the exo or endo cyclopropane adducts to homo-1,4 products. Therefore one is on safe ground in concluding that the latter are primary products and not the artifacts of some rearrangement. It is significant that when higher reaction temperatures are used to generate the carbene, similar ratios for homo-1,4 and 1,2 additions were obtained, which is a good indication that there is competition for a common reactive intermediate, namely the free carbene in solution. These results are not only unprecedented, but reveal a new facet of carbene reactivity.

Although the addition of carbenes to olefins has been under active investigation for about 20 years, very few 1,4 additions have been reported.[12] It now appears that most of them are two-step processes.[13] Either a cyclopropane adduct is initially formed, which subsequently undergoes a vinylcyclopropane rearrangement, or the carbene has undergone relaxation to the triplet state, which on combination with the diene furnishes an allylic diradical which closes to 1,2 and 1,4 adducts. In any event, even 1,4 additions of triplet carbenes are rare enough.[13e,h] The absence of such behavior for singlet carbenes may be due to the high-entropy requirement. Normally the low degree of molecular order needed for the competing nonlinear 1,2 addition is pre-emptive. Evidently, norbornadiene possesses special properties which permit linear cheletropic reaction. However, the choice of carbene seems to be important. Bis(carbomethoxy)carbenes,[13j] in their singlet or triplet states, are reported to simply give the endo and exo 1,2 adducts with norbornadiene. The same behavior is apparently observed with dichloro- and dibromocarbenes.[14] Many products are formed, but they are supposed to derive from 1,2 addition on the exo and endo sides in a ratio of 8:1. The question immediately arises: are difluoro- and fluorochlorocarbenes qualitatively different in their chemical behavior to dichloro and dibromocarbene? The answer is probably no. Nevertheless, it is remarkable that fluorochlorocarbene shows more cyclopropanation at the expense of homo-1,4 addition than does difluorocarbene. This difference could be attributed either to the greater electrophilic character of fluorochlorocarbene or to its greater bulk and to its diminished capability of fulfilling the steric requirements for homo-1,4 addition. Obviously, the entropy is favorable for both fluorocarbenes to execute the necessary maneuver for homo-1,4 addition. However, it has to be realized that norbornadiene, like norbornene, possesses an unusual skeleton, especially with respect to the different steric requirements for exo and endo addition.[15] This aspect has already been dramatically illustrated by the suppression of exo attack to the advantage of endo addition when a methyl group is substituted at C-7 (cf. reactivity of **1** and **6**). Although the exo face of norbornadiene is generally regarded as being less encumbered than the endo face, a σ^2 carbene, like fluorochlorocarbene, is obliged to negotiate entry through a laterally disposed window, pushing its ligands through first. The inescapable consequence is 1,2 addition, but with a preference for the less hindered approach (*E*/*Z* product ratio = 1.3) (Figure 3a). The endo side, despite its greater congestion paradoxically permits more freedom of movement to an approaching carbene (vide infra). Two limiting approaches are possible, both of which can be productive. If the carbene approaches with its ligands in front, then the monoene element will be electronically selected provided a lateral approach is adopted. The 1,2 adduct forms (Figure 3b). If the carbene has its ligands trailing behind, then the pursuit of a linear approach by the reagent in the plane m bisecting the bridgehead and methylene carbon atoms, will necessarily engage the homo-diene portion and logically lead to the homo-1,4 adduct (Figure 3c). Both endo 1,2 and homo-1,4 approaches evoke little steric discrimination by the halogen ligands (*E*/*Z* ratio = 1.0).

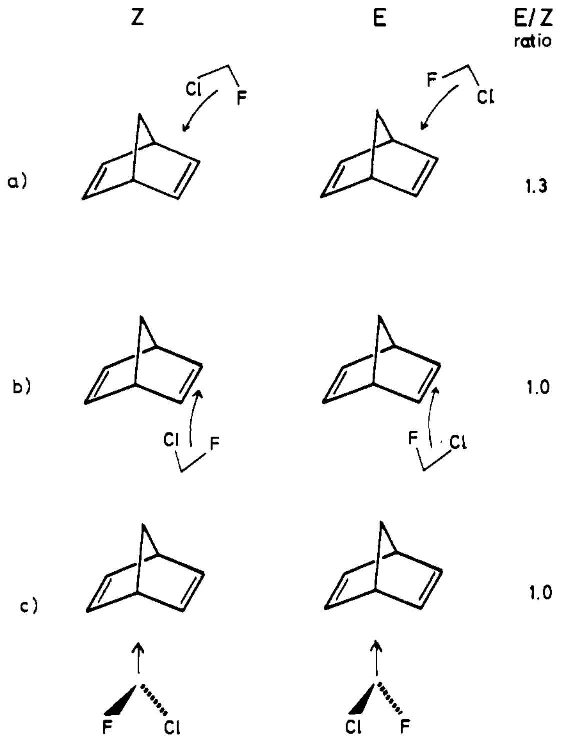


Figure 3. Cheletropic reactions of σ^2 fluorochlorocarbene with norbornadiene to give (a) exo 1,2 adducts, (b) endo 1,2 adducts, and (c) homo-1,4 adducts.

A more detailed picture of the homo-1,4 addition, a first example of a linear homocheletropic reaction of a σ^2 carbene, may be obtained by looking at the exchange interaction of the reacting partners.[16] The electronic structure of difluorocarbene has been the subject of much theoretical and experimental study,[2] and there is agreement that the ground-state species is a singlet, it is bent (FCF angle

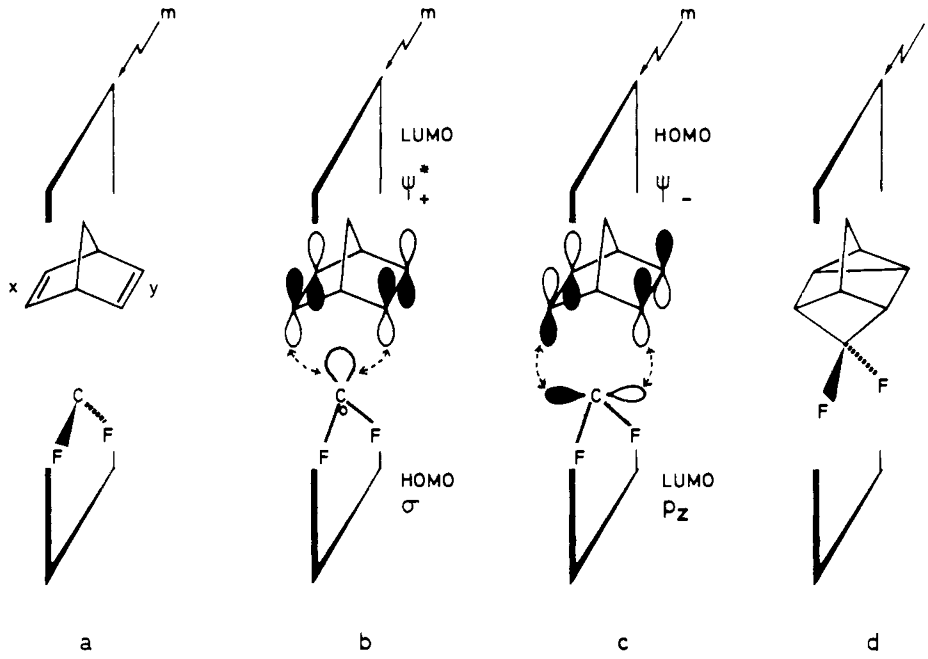


Figure 4. Linear approach (a) of σ^2 difluorocarbene to the endo side of norbornadiene with ensuing cheletropic reaction (b, c) to give the homo-1,4 adduct (d).

105°), and the highest doubly occupied MO is σ symmetric (Figure 4b). On the other hand, the lowest unoccupied orbital is of the π type and is antisymmetric with respect to the plane m (Figure 4c).

Norbornadiene is the classic example of a homoconjugated diene; the energy sequence and the symmetry characteristics of the π-type molecular orbitals are known from MINDO/2, EHT calculations,[17] and photon-electron spectroscopy.[18] It turns out that the through-space interaction of the two semi-localized π bonds (x and y) is more important than the through-bond interaction, with the result that the bonding combination

$$\psi_+ = \frac{1}{\sqrt{2}}(\pi_x + \pi_y)$$

lies at a lower energy than the anti-bonding combination

$$\psi_- = \frac{1}{\sqrt{2}}(\pi_x - \pi_y)$$

The latter, the HOMO, can mix with the LUMO of the carbene partner as both are antisymmetric with respect to the mirror plane m (Figure 4c). Similarly, the bonding combination of the π^* orbitals ($\psi_+{}^* = (1/\sqrt{2})(\pi_x{}^* + \pi_y{}^*)$), the LUMO of norbornadiene, because it is symmetric with respect to plane m, can mix in complementary fashion with the HOMO of the carbene (Figure 4b). The linear approach of the carbene to the homo-diene to form the bishomoprismane skeleton is consequently an allowed one-step process. The skeletal adjustments are minor, and the two pairs of carbon termini bend together in a concerted disrotatory movement to form the new bonds.

Rearrangement Process. Ring Inversion and Intramolecular Cycloaddition. The thermal properties of the endo and exo difluorocarbene adducts **4** and **3** provide invaluable information on the mechanisms of two separate and uniquely different processes peculiar to the cis-fused cyclopropane moiety. The isomerization of the endo to the exo adduct is noteworthy for its ease and its apparent stereospecificity. Not only is the activation energy low, $\Delta G^{\ddagger}{}_{25}$ = 28.2 kcal/mol, but the tiny value of the entropy of activation, $\Delta S^{\ddagger}{}_{25}$ = −2.2 eu, indicates that there is almost no loss of atomic ordering. The stereomutation of the cyclopropane ring must be reversible, and the exclusive formation of the exo isomer is dictated by its greater thermodynamic stability.[19] What is significant is that the clean sweep of the C-3 atom from the endo to the exo side (and vice versa) engenders no intermediate or state which can undergo intramolecular cycloaddition (Figure 5). The latter process therefore must entail an entirely different skeletal movement. In fact, the substantially higher energy and entropy of activation ($\Delta G^{\ddagger}{}_{25}$ = 39.0 kcal/mol; $\Delta S^{\ddagger}{}_{25}$ = −7.6 eu) needed for the quantitative conversion of the exo adduct **3** to the tetracyclic structure **5** confirms that a more drastic molecular distortion is required. As **3** and **5** both belong to the same point group (C_s), it follows that the intervening transition state or states cannot have the same symmetry. Since the C-2–C-4 σ bond of the cyclopropane ring in **3** is implicated in both stereomutation and the intramolecular cycloaddition, differentiation of its role can only be expressed by different conformations.

In order to appreciate how skeletal constraints in **3** (and **4**) can affect the orbital symmetry properties of the reacting bonds, a consideration of the intramolecular (2 + 2) exchange reaction is instructive. In molecules **3** and **4**, there can be discerned three potentially interacting fragments; the double bond at C-6–C-7, the cyclopropane σ bond between C-2 and C-4, and the *gem*-difluoromethylene group at C-3 (Figure 5). In the bent molecules **3** and **4** there is negligibly little interaction between any two of these three fragments. However, as soon as C-3 in **4** is displaced towards the exo side, but in the mirror plane m, then two interactions progressively become potentially important. The first of these is the hyperconjugative mixing of the doubly occupied π type orbital of the CF_2 group with the developing p orbitals on C-2 and C-4; although the symmetry is good, interaction is feeble due to the low-lying energy of the former (vide infra). The result is that the σ bond between C-2 and C-4 is smoothly transformed into a π bond in a disrotatory motion. The electron pair stays in a symmetric orbital throughout. However, with progressive disrotation the p orbitals at C-2 and C-4 now develop better overlap properties with the p orbitals at C-6 and C-7. A second exchange reaction arises (Figure 6). However, as long as C_s molecular symmetry is conserved, a double site interaction

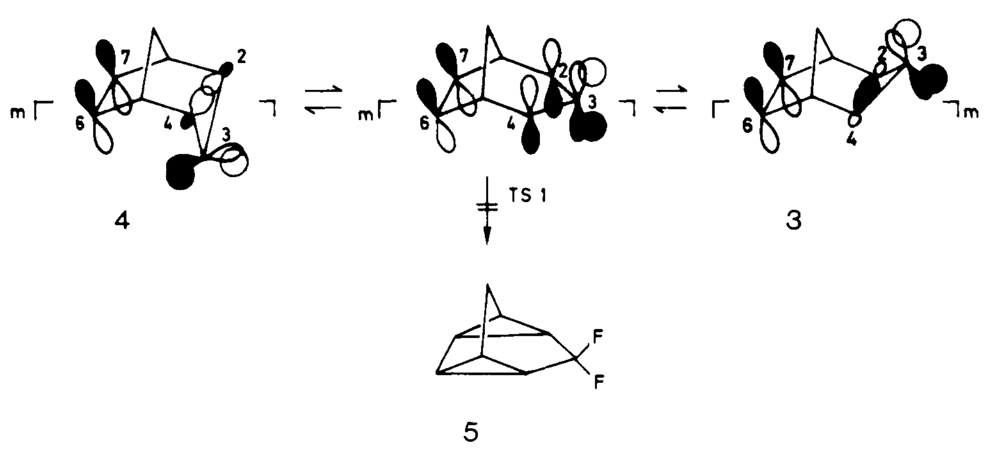


Figure 5. Epimerization of **4** to **3** by disrotatory rupture of the C-2–C-4 σ bond to create a π bond which does not undergo $[2_\pi + 2_\pi]$ addition to give **5**. Sets of orbitals on fragments C-3, C-2–C-4, and C-6–C-7 are all doubly occupied.

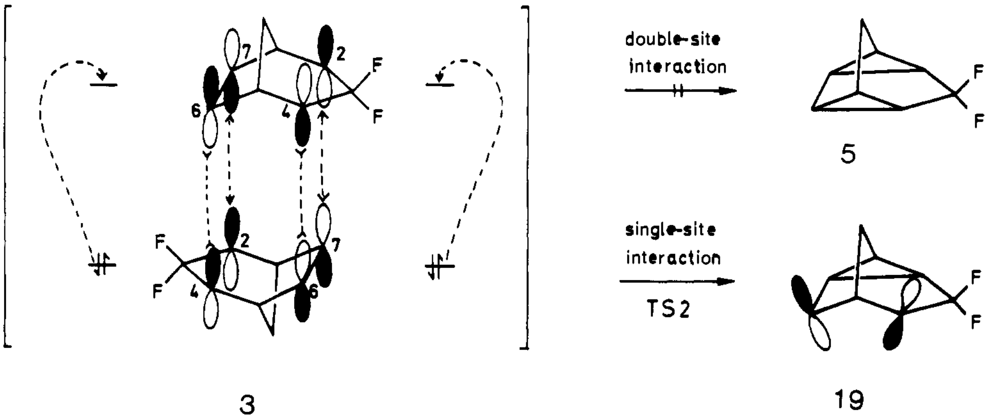


Figure 6. Interaction of HOMO's on fragments C-6–C-7 and C-2–C-4 with LUMO's on fragments C-2–C-4 and C-6–C-7, respectively, within molecule **3**. Double-site interaction fails to give **5**, but single-site interaction gives the intermediate **19** (symbolism of G. Klopman used, see ref 16b).

is compelled which cannot lead to the concerted formation of the two new bonds necessary to produce **5**. This is because there is mismatching between the stereodirecting orbitals of the two fragments (Figure 6). In resume, the flattened molecule midway between **3** and **4** is essentially a symmetric singlet and corresponds to the transition state (TS 1) for epimerization (Figure 7). This situation constitutes an experimental verification of the prediction made for the hypothetical ring flip of 5,5-difluorobicyclo[2.1.0]pentane.[20] Not only is the barrier to stereomutation low in both cases, partly due to the predicted weakening of the central cyclopropane bond by the *gem*-difluoro grouping,[21] but the hyperconjugative effect of the latter does not set up any additional barrier in the form of an inversion of the natural order of the cyclopropane σ–π bonding and antibonding levels.[22,23]

Intramolecular cycloaddition in **3** requires a departure from C_s symmetry. To do this, the skeleton needs to buckle so that C-2 and C-7 are pushed together to favor mixing at the matching ends of the occupied symmetric and vacant antisymmetric orbitals. Atoms C-4 and C-6 splay apart to minimize overlap at the nonmatching lobes.[24] This single-site interaction generates one new bond (TS 2) and furnishes the singlet intermediate **19** (Figure 6). Subsequent collapse of **19** via an undefined transition state (TS 3) produces the tetracyclic structure **5** (Figure 7).

Ring Inversion and Trapping of Epimers by Cyclopropyl-Allylic Rearrangement. The rearrangement behavior of the adducts obtained from fluorochlorocarbene and norbornadiene provides a nice proof of the existence of the reversibility of the cyclopropane stereomutation and a clear illustra-

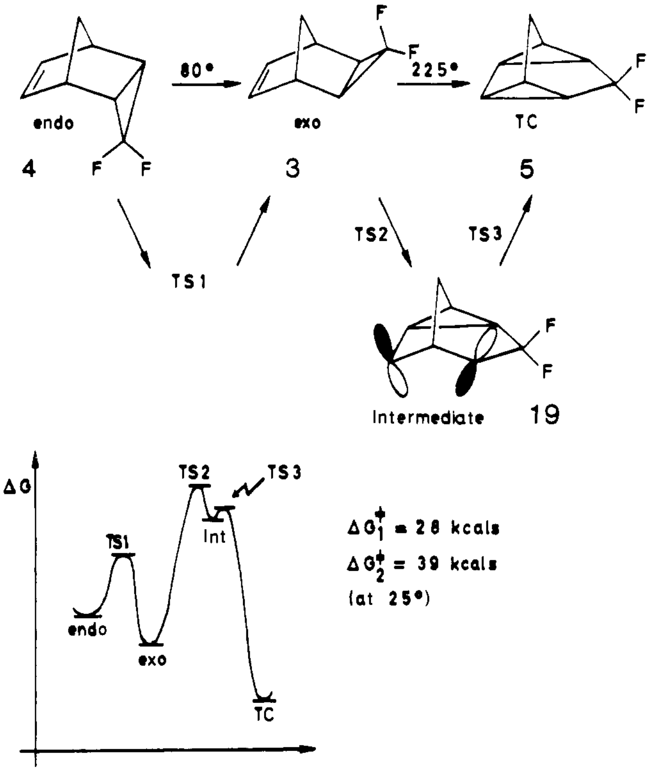
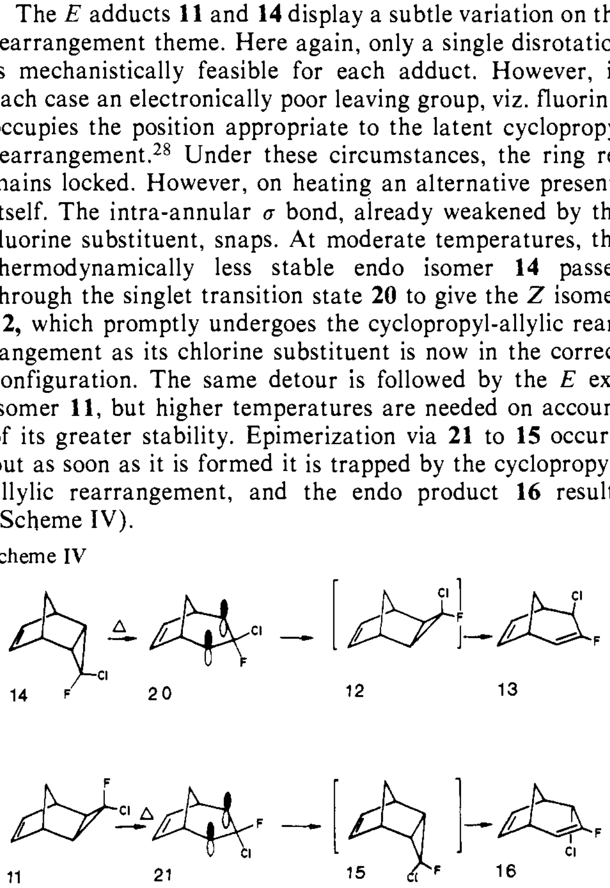


Figure 7. Thermal conversion of endo and exo difluorocarbene adducts (**4** and **3**) to the tetracyclic isomer **5** by passage through three transition states (TS 1, 2, and 3).

tion of how the configuration of the halogen substituents determine the choice of rearrangement course. First, it should be pointed out that for the exo and endo adducts only one disrotation is geometrically permitted in each case. For the *Z* adducts **12** and **15**, it so happens that a good leaving group, namely chlorine, is conveniently disposed so that its departure coincides with the disrotatory flattening of the molecular portion containing the C-3 atom.[25] Rearrangement takes place either within the compass of an ion pair where chloride immediately transfers from C-3 to the allylic positions C-2 or C-4 or by a non-ionic diplotropic shift similar to a 1,3 sigmatropic shift.[26] Unfortunately, rearrangement itself of **12** and **15** to the exo and endo 2-chloro products **13** and **16** is too rapid to be observed under the conditions of the addition (Scheme III). Nonetheless, good precedent exists in support of this supposition.[27]

The *E* adducts **11** and **14** display a subtle variation on the rearrangement theme. Here again, only a single disrotation is mechanistically feasible for each adduct. However, in each case an electronically poor leaving group, viz. fluorine, occupies the position appropriate to the latent cyclopropyl rearrangement.[28] Under these circumstances, the ring remains locked. However, on heating an alternative presents itself. The intra-annular σ bond, already weakened by the fluorine substituent, snaps. At moderate temperatures, the thermodynamically less stable endo isomer **14** passes through the singlet transition state **20** to give the *Z* isomer **12**, which promptly undergoes the cyclopropyl-allylic rearrangement as its chlorine substituent is now in the correct configuration. The same detour is followed by the *E* exo isomer **11**, but higher temperatures are needed on account of its greater stability. Epimerization via **21** to **15** occurs, but as soon as it is formed it is trapped by the cyclopropyl-allylic rearrangement, and the endo product **16** results (Scheme IV).

Scheme IV



Epilogue

These findings are of fundamental importance for two reasons. Firstly, an unprecedented linear homocheletropic reaction has been demonstrated. The limits of this reaction now remain to be defined, by varying the diene and carbene partners, as well as by testing the suitability of other electron-deficient species such as nitrenes. Secondly, the first example of a thermal epimerization in the tricyclo[3.2.1.0^{2,4}]oct-6-ene skeleton has been uncovered in which the intramolecular cycloaddition facility is kept mechanistically apart. This is due to the fortunate choice and beneficial presence of the *gem*-difluoro grouping on C-3 which lowers the energy of activation for the ring flip and yet ensures that the breaking C-2–C-4 bond remains as a symmetric and therefore unreactive singlet as long as the epimerizing molecule conserves its C_s symmetry.

We have already pointed out[29] that the Diels-Alder reaction of 1,2-bis(trifluoromethyl)-3,3-difluorocyclopropene with cyclopentadiene proceeds normally.[30] The endo adduct is obtained, which at 65 °C subsequently epimerizes to the exo isomer, and that it is the latter which on strong heating at 200 °C gives the tetracyclic isomer.[31]

A comparative examination of the effects of the *gem*-difluoro vs. the parent methylene group in similar systems should prove rewarding.[32] In particular a reconsideration of the thermal behavior of the exo and endo isomers of tricyclo[3.2.1.0^{2,4}]oct-6-ene and related structures is warranted.[33]

Experimental Section

Starting Materials. Commercial bicyclo[2.2.1]heptadiene-2,5 (**1**) and its 7-methyl derivative (**6**)[9] were purified by distillation from sodium prior to use. Triphenylphosphine was recrystallized from ethanol and converted to triphenyl(bromodifluoromethyl)-phosphonium bromide[8] by reaction with commercial dibromodifluoromethane immediately before use. Commercial potassium fluoride was dried by heating in a crucible over a free flame and allowing it to cool in a desiccator. Sodium iodide was dried in vacuo at 150 °C for 24 h. Phenyl(dichlorofluoromethyl)mercury was prepared and used without purification.[11] Triglyme and benzene were distilled from sodium and stored under nitrogen.

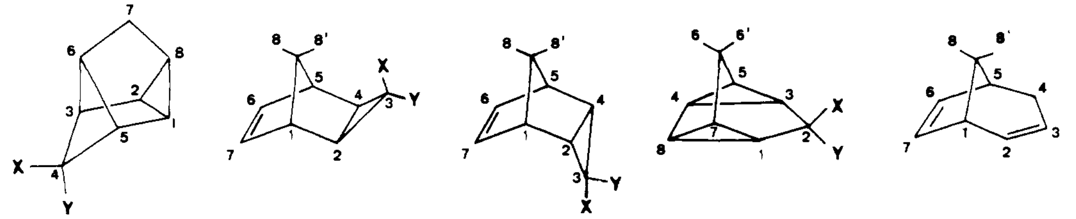
Chromatographic and Spectroscopic Methods. Analytical and preparative gas-liquid chromatography (GLC) were performed on Perkin-Elmer Model F11 and F21 instruments. Correct molecular weights for all new compounds were obtained by mass spectrometry performed on a Varian Model SM-1-B instrument. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded on a Varian Model XL-100 spectrometer. Absolute and relative product yields, if not indicated otherwise, were obtained from ^{19}F NMR integrals relative to hexafluorobenzene as internal integral standard.

Reaction of Triphenyl(bromodifluoromethyl)phosphonium Bromide with Norbornadiene (1). To a solution of 2.32 g (10 mmol) of triphenylphosphine in 10 ml of triglyme was added 2.6 g (11 mmol) of dibromodifluoromethane. After the rapid exothermic formation of the phosphonium salt, stirring was continued for 30 min. Next was added 0.92 g (10 mmol) of bicyclo[2.2.1]heptadiene and 2.4 g (41 mmol) of potassium fluoride, stirring was maintained at room temperature for 48 h, whereupon a dark-brown suspension resulted. The crude mixture was distilled under high vacuum at room temperature, and the products were isolated by preparative GLC (3 m, FFAP 20% on Chromosorb W, 100 °C). The exo 1,2 adduct **3**, the bishomoprismane **2**, and the endo 1,2 adduct **4** were separated in order of increasing retention times. Typical relative yields prior to GLC separation (average of four additions) are given in Scheme I. The overall yield varied between **54** and 62%. The structures of the adducts were unambiguously characterized by the ^{1}H and ^{19}F NMR parameters (Tables I-III).

Reaction of Triphenyl(bromodifluoromethyl)phosphonium Bromide with 7-Methylnorbornadiene (6). In a similar experiment, 2.32 g (10 mmol) of triphenylphosphine in 10 ml of triglyme was allowed to react with 2.6 g (11 mmol) of dibromodifluoromethane, 1.06 g (10 mmol) of **6**, and 2.4 g (41 mmol) of potassium fluoride for 48 h. Relative yields after partial purification by distillation in vacuo at room temperature are shown in Scheme II. The overall yield at this stage was 25%. Isolation was achieved by preparative GLC (3 m, FFAP 20% on Chromosorb W, 100 °C). The exo 1,2 adduct **8**, the bishomoprismane **7**, and the two endo 1,2 adducts **10** and **9** were separated in order of longer retention times. Structure elucidation was made from the ^{1}H and ^{19}F NMR data (Tables I-III).

Reaction of Phenyl(fluorodichloromethyl)mercury with 1. A solution of 3.31 g (36 mmol) of **1** in 24 ml of benzene and 0.3 ml of 1,2-dimethoxyethane was stirred with 4.41 g (12 mmol) of the organomercurial[11] and 3.6 g (14.4 mmol) of sodium iodide at 20 ± 0.5 °C under argon for 60 h. The mixture was prepurified by high-vacuum distillation at room temperature. The total yield of products based on the amount of organomercurial consumed was found to be 48%. Separation by preparative GLC (3 m, FFAP 5% on Chromosorb G, 100 °C) gave the exo 1,2 adduct **11**, the pair of bishomoprismanes **17** and **18**, the endo 1,2 adduct **14**, and the rearranged exo and endo epimers **13** and **16** in order of increasing retention times. Structures were determined from the NMR data (Tables I-III and ref 1b). Relative yields are the average of four experiments (Scheme III).

Table I. ^{1}H NMR Chemical Shifts δ (ppm) in $DCCl_3$ at 100.1 MHz Relative to Internal Me_4Si



	2	3	4	5	7	8	9	10	11	13	14	16
H-1	~1.5	3.20	3.22	~1.7	1.45	2.93	2.92	2,89	3.28	2.90	3.24	2.90
H-2	~1.5	1.66	2.26		1.45	1.64	2.26	2,20	1.72	~5.8	2.30	5.88
H-3	2.64			~1.7	2.68							
H-4		1.66	2.26	~1.2		1,64	2.26	2.20	1.72	4.25	2.30	4.80
H-5	2.64	3.20	3.22	~1.6	2.68	2.93	2.92	2.89	3.28	3.16	3.24	3.30
H-6	2.30	6.50	6.10	~1.9	2.0	6.30	5.92	6.08	6.56	5.8	6.06	6.00
H-6'				~1.7								
H-7	~1.5	6.50	6.10	~1.6	2.03	6.30	5.92	6.08	6.56	6.61	6.06	6.50
H-8	1.90	1.58	~1.9	~1.2	1.80				1.62	1.92	1.89 or	2.00
H-8'		0.98	~1.5			2.34			1.06	2.10	2.01	1.84
CH_3					0.81	0,74	0.95	0.95				

Table II. Characteristic Homo- and Heteronuclear Coupling Constants (in Hz)

	2	3	4	5	7	8	9	10	11	13	14	16
${}^2J_{HH}$		H-8, H-8' 10								H-4, H-5 2.0 H-6, H-7 5.5 H-8, H-8' 10	H-8, H-8' 7	H-4, H-5 6.0 H-6, H-7 5.5 H-8, H-8' 10
${}^3J_{HH}$						H-8, CH_3 6.4						
${}^3J_{HF}$		H-2, F(*y*) 14	H-2, F(*y*) 15.8			H-2, F(*y*) 14.2	H-2, F(*y*) 16.1	H-2, F(*y*) 15.8	H-2, F <1.5	H-4, F 2.0	H-2, F 1.4	H-2, F 12 H-4, F <0.5
${}^5J_{HF}$	H-8, F(*x*) 9.8		H-8, F(*y*) 8.5		H-8, F(*x*) 9.8			H-8, F(*y*) 8.4			H-6, F 3.0	
${}^2J_{FF}$	160.0	157.0	154.0	238.0	162.0	156.5	156.0	152.0				

Table III. ^{19}F NMR Chemical Shifts in δ (ppm)[a] in $DCCl_3$ at 94.1 MHz Relative to Internal $CFCl_3$

Compd	2	3	4	5	7	8	9	10	11	13	14	16
F(*x*)	118.9	139.1	148.2	109.6	119.1	144.0	143.1	139.9	147.0	113.8	156.2	116.0
F(*y*)	100.0	100.6	94.2	82,1	100.9	99.0	97.0					

[a] All values are at high field from the reference.

Thermal Rearrangements and Kinetics. Formation of *exo*-3,3-Difluorotricyclo[3.2.1.0^{2,4}]oct-6-ene (3) from *endo*-3,3-Difluorotricyclo[3.2.1.0^{2,4}]oct-6-ene (4). Heating a sample of **4** in $DCCl_3$ in a sealed NMR tube for 20 h at 80 °C resulted in quantitative conversion to **3**. The identity of the product with authentic **3** was established by ^{19}F NMR, ^{1}H NMR, and double injection on GLC. In order to obtain the Eyring parameters for isomerization, 0.3 M solutions of **4** in $DCCl_3$ with chlorobenzene as integral standard were heated in a micro-autoclave at 80, 90, and 100 °C. The reaction was followed by periodical GLC analysis (3 m, FFAP 20% on Chromosorb W, 90 °C) through four half-lives. Using the LEASQFIT program[34] (least-squares method) the following rates for the first-order process were obtained: $k_{80} = 1.257 \times 10^{-3}$ min^{-1}; $k_{90} = 3.783 \times 10^{-3}$ min^{-1}; $k_{100} = 10.80 \times 10^{-3}$ min. The activation parameters, $\Delta G^{\ddagger}{}_{25} = 28.2$ kcal/mol, and $\Delta S^{\ddagger}{}_{25} = -2.2$ eu, were obtained from the ACTIVEN program.[34]

Formation of 2,2-Difluorotetracyclo[5.1.0.0^{2,5}.0^{4,8}]octane (5) from *exo*-3,3-Difluorotricyclo[3.2.1.0^{2,4}]oct-6-ene (3). Heating a sample of **3** in acid-free benzene-d_6 at 225 °C resulted in its quantitative conversion to **5** after 3 h. Our preliminary report[1b] that **3** is thermally stable is therefore in error. Compound **3** was characterized after GLC purification (3 m, FFAP 20% Chromosorb W, 100 °C) by MS, ^{1}H and ^{19}F NMR (Tables I–III). Solutions of **3** in benzene-d_6 (0.3 M) with chlorobenzene as integral standard were heated in a micro-autoclave at 215, 225, and 230 °C. Periodical GLC analysis (3 m, FFAP 20% on Chromosorb W, 90 °C) up to four half-lives led to the following rate values: $k_{215} = 8.40 \times 10^{-3}$ min^{-1}, $k_{225} = 21.5 \times 10^{-3}$ min^{-1}, $k_{230} = 29.8 \times 10^{-3}$ min^{-1}. The Eyring parameters, $\Delta G^{\ddagger}{}_{25} = 39.0$ kcal/mol and $\Delta S^{\ddagger}{}_{25} = -7.6$ eu were calculated with the ACTIVEN program.

***exo*-3,3-Difluoro-*anti*-8-methyltricyclo[3.2.1.0^{2,4}]oct-6-ene (8) from Its Endo Isomer 9.** A solution of **9** and its epimer **10** in $DCCl_3$ was heated in a sealed NMR tube to 80 °C. ^{19}F NMR analysis at intervals revealed the growing appearance of **8** at the expense of **9**, whereas the concentration of **10** remained unchanged even up to 120 °C. From the integration of the ^{19}F signals, the half-life of **9** was estimated as 8 h at 80 °C. Identity of the thermally obtained product with the first-formed sample of **8** was established by ^{19}F, ^{1}H NMR, and double injection on GLC.

***exo*-4-Chloro-3-fluorobicyclo[3.2.1]octa-2,6-diene (13) from 3-*syn*-Fluoro-3-*anti*-chloro-*endo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (14).** Heating a sample of **14** in benzene-d_6 at 100 °C resulted in its disappearance with a half-life of about 50 min to give quantitatively **13**. The identity of **13** was proved by double injection on GLC and from its ^{1}H and ^{19}F NMR data.

***endo*-4-Chloro-3-fluorobicyclo[3.2.1]octa-2,6-diene (16) from 3-*syn*-Fluoro-3-*anti*-chloro-*exo*-tricyclo[3.2.1.0^{2,4}]oct-6-ene (11).** In a similar experiment **11** was heated in a sealed NMR tube in acid-

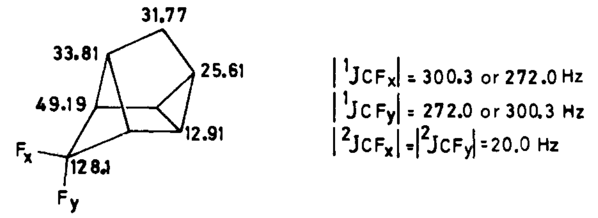


Figure 8. ^{13}C chemical shifts of **2** (in ppm) downfield from internal Me_4Si in $DCCl_3$ at 25.2 MHz.

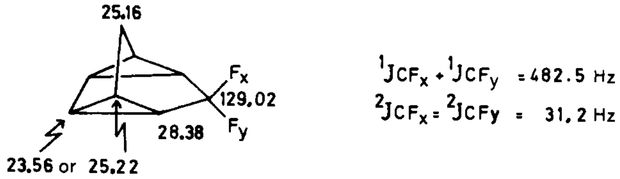


Figure 9. ^{13}C chemical shifts of **5** (in ppm) downfield from internal Me_4Si in C_6D_6 at 25.2 MHz.

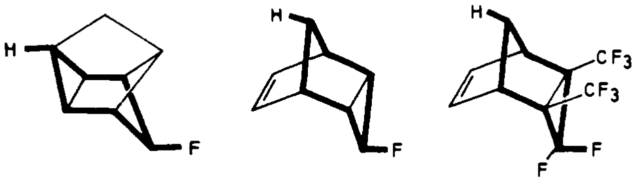


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Figure 10. Double zig-zag motif for $^5J_{HF}$ coupling.

free perchlorobutadiene at 200 °C. According to the ^1H and ^{19}F NMR spectra, **16** appeared as the sole product of rearrangement. The half-life of **11** was about 5 h. The identity of **16** was confirmed by its ^1H and ^{19}F NMR data and double injection on GLC.

Remarks on Features of the NMR Data. ^{13}C Shifts. A preliminary presentation of the ^{13}C-FT NMR spectrum of the key compound **2** has already been given.[1b] Owing to the absence of nuclear Overhauser enhancement and an apparently long relaxation time, no information was available at the time on the fluorine-bearing carbon atom C-4. Accumulation of 200 000 free induction decays after 10-deg pulses now reveals the ^{13}C-4 resonance. The chemical shift of C-4 in $DCCl_3$ lies at $\delta|\text{ppm}|$ 128.1. Moreover, the two fluorine atoms couple to sizably different extents with the ^{13}C-4 nucleus, viz. $^1J_{CF} = 300.3$ Hz and $^1J_{CF'} = 272.0$ Hz. No assignment of $^1J_{CF}$ to F_x or F_y is made (Figure 8). The structure of **5** was further confirmed by its ^{13}C shifts; there are just five (Figure 9).

Heteronuclear Coupling. Most of the NMR data compiled in Tables I–III requires no special comment as it is in full agreement with common knowledge. Attention however should be directed to significant proton–fluorine couplings over five σ bonds. All the tricyclic molecules of this series bearing the double zig-zag arrangement of fluorine and hydrogen, viz. **2**, **4**, **7**, and **10**, exhibit a large value of 8.4–10.0 Hz for $^5J_{HF}$ (Figure 10), whereas when the double zig-zag motif is absent, the value does not exceed 2.5–3.5 Hz (5th row, Table II). Interestingly enough the main product arising from the Diels–Alder reaction of 1,2-bis(trifluoromethyl)-3,3-difluorocyclopropene with cyclopentadiene shows a value of 8.5 Hz for $^5J_{HF}$. Accordingly we have assigned to it the endo configuration (**22**)[29] instead of the exo configuration originally proposed.[30]

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β-Epimerization and γ-Hydrogen Abstraction via Homoenolate Ions[1]

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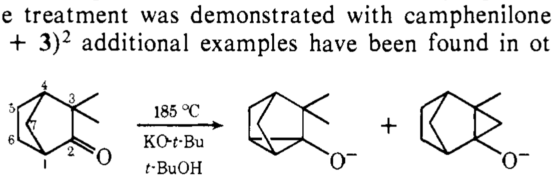
Abstract: Our objective was to study homoenolate ion formation in ketones with enolizable as well as homoenolizable centers, and in other systems having special structural features. Our substrates were camphor, *exo*- and *endo*-isocamphanone, 1-acetoxytricyclane, 2,2,4,4-tetramethylcyclobutanone, norbornan-7-one, cyclodecanone, 2,2,10,10-tetramethylcyclodecanone, cyclododecanone, and 2,2,12-trimethylcyclododecanone. At 185–250 °C in KO-*t*-Bu/*t*-BuOH for prolonged periods camphor, *exo*-isocamphanone, and *endo*-isocamphanone are interconvertible, and the camphor skeleton is favored. The exo $\rightleftharpoons$ endo isomerization in the isocamphanones illustrates epimerization at a homoenolic site. The tertiary *exo*-H in *endo*-isocamphanone is abstracted and recaptured more readily than is the *endo*-H in *exo*-isocamphanone. The homoenolate ion liberated from 1-acetoxytricyclane at room temperature partitions differently in proton capture than does the homoenolate generated from the isocamphanones at 185–250 °C. In deuterated medium at high temperature camphor incorporated label at sites other than at C-3 (enolic) and C-6 (homoenolic) as evidenced by species containing d_5 and d_6. Camphor-*10*-d_1 was synthesized and was shown to lose some of its deuterium when homoenolized in nondeuterated medium, thus establishing that hydrogens at C-10 are exchangeable. After an exchange of camphor in *t*-BuOD ^{1}H NMR studies showed that label is incorporated at C-8 and C-10 to comparable extents. Exchange at C-8 reveals that rigid C–H orientation is not a requirement for γ-hydrogen abstraction. D assay of mass spectral fragment ions confirmed that camphor exchanges at C-6, C-8, and C-10 in addition to the enolic site C-3. Exchange at C-6 in camphor proved more difficult than at C-6 in camphenilone, probably because camphor has competitive enolization as well as steric hindrance by methyl groups. At 185 °C in KO-*t*-Bu/*t*-BuOD, 2,2,4,4-tetramethylcyclobutanone exchanges at the methylene and at the methyl positions, but much of the ketone is cleaved to 2,2,4-trimethylpentanoic acid. When similarly treated, norbornan-7-one undergoes α-bridgehead exchange but no homoenolic exchange; most of the ketone is cleaved to cyclohexanecarboxylic acid. Cyclodecanone and cyclododecanone undergo enolic exchange (and some loss, probably by aldol condensations) but there is no homoenolic exchange or product that would indicate transannular interactions in these medium-ring ketones. Cyclodecanone was tetramethylated by repeated alkylations with $NaNH_2/CH_3I$, but cyclododecanone could only be trimethylated. These methylated ketones incorporated deuterium slightly at homoenolic sites.

Ever since generation of homoenolate ions by vigorous alkaline treatment was demonstrated with camphenilone (**1** → **2** + **3**)[2] additional examples have been found in other polycyclic ketones.[3] Homoenolic species have also been recognized as intermediates in a variety of reactions, including those of open-chain systems.[4] Hydrogens α to carbonyl groups are ordinarily much more acidic than more distant ones, and invariably homoenolizations have been explored with substrates that either lacked α protons or whose α protons were at bridgeheads and could not enolize readily because of Bredt's rule.[5] For studies of the reverse process (homoketonization), the homoenolate species are conveniently generated from cyclopropyl alcohols or cyclopropyl acetates and allowed to protonate under irreversible conditions.[6] The scope of homoenolization would be broadened considerably if remote proton abstractions could occur in substrates that also possess enolic hydrogens. One of our present objectives was to examine ketones that had α and β hydrogens to learn if enolate formation could lastingly prevent generation of homoenolate ions. We also wanted to learn whether remote chiral centers could be epimerized via homoenolate ions and, via deuterium exchange, to explore homoenolization in a variety of ring structures.



1 **2** **3**

Our ketonic substrates were camphor (**4**), *endo*-isocamphanone (**7**),[7] and *exo*-isocamphanone (**8**),[7] each of which has enolizable α hydrogens as well as potentially homoenolic hydrogens. We hoped that the enolates would be sufficiently hindered by the methyl groups to prevent excessive loss by aldol condensations and other side reactions. Abstraction from C-6 in camphor produces the delocalized homoenolate ion depicted by the single resonance structure **6**. Proton recapture can either revert it to camphor or can produce the isocamphanones **7** and **8** by exo and endo protonation, respectively. Therefore alkali-induced isomerization of camphor to the isocamphanones or vice versa would establish homoenolate intermediates, and exo-endo interconversion of the two isocamphanones would demonstrate remote epimerization. Our study also included homoketonization of

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