Transannular Cyclizations of 6-Substituted Cyclodecynes[1]

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A series of 6-substituted cyclodecynes has been synthesized and the transannular cyclizations of these compounds were studied. The observed transannular cyclizations were highly stereoselective and give products containing the bicyclo[4.4.0]decane skeleton.

Une série de cyclodécynes substitués en position 6 a été synthétisée et les cyclisations *trans*-annulaires de ces composés ont été étudiées. Les cyclisations *trans*-annulaires observées sont très stéréosélectives et conduisent à des produits contenant le squelette du bicyclo[4.4.0] décane.

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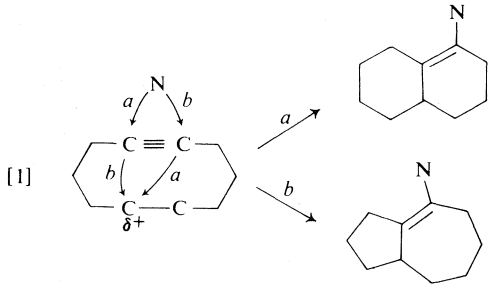
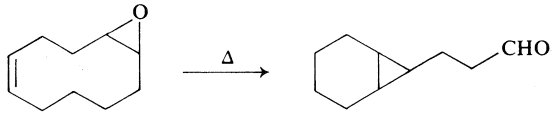
Transannular reactions in medium-sized rings have been an area of extensive study for the past 15 years (1). We were interested in the transannular cyclizations of suitably substituted ten-membered rings as a new synthetic route to bicyclo[4.4.0]decanes and/or bicyclo[5.3.0]decanes. In particular we hoped to take advantage of the known susceptibility of the acetylenic bond to both electrophilic and nucleophilic attack (2). This is summarized in eq. 1. Most transannular



[1]

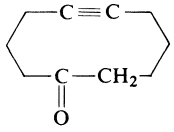
reactions in ten-membered rings appear to favor transition states involving six-membered rings (1, 3). However, the decomposition of cyclodecyl tosylhydrazone in an aprotic solvent yielded bicyclo[5.3.0]decane as the major product (4) and the peracid oxidation of cyclodecyne yielded *cis*-bicyclo[5.3.0]decan-2-one (5). Pyrolysis of epoxide **1** gave the aldehyde **2** (6). A transannular



1 **2**

cyclization to a bicyclo[5.3.0]decane has been proposed for this and other related rearrangements of sesquiterpene epoxides (6, 7). On the other hand the solvolysis of *cis*- and *trans*-cyclodec-5-en-1-yl tosylates gave products containing the bicyclo[4.4.0]decane skeleton only (1, 8), indicating that these transannular reactions occur via six-membered ring transition states. The report that the solvolysis of 6-octyn-2-yl tosylate in trifluoroacetic acid proceeded preferentially to products containing a cyclopentane ring (9) suggested that the related 6-substituted cyclodecynes may undergo transannular cyclizations to bicyclo[5.3.0]decanes. However, solvolysis of cyclodec-5-yn-1-yl tosylate has recently been found to yield predominantly *cis*- and *trans*-decalone-1 together with small amounts of bicyclo[5.3.0]decanone-2 (10).

Our initial studies were concerned with cyclodecyn-6-one **3** (11).[3] Ketone **3** was stable to



3

treatment with aqueous base. However, on treatment with aqueous acid the acetylenic ketone **3** gave an isomeric α,β-unsaturated ketone in high yield. It was quickly ascertained that this product was the octalone **4** by comparison of the spectroscopic properties and the v.p.c.

[1]A preliminary communication of a portion of this work has appeared. See ref. 27.

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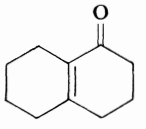
[3]We are grateful to Dr. Tanabe for a reference sample of **3** and spectral data as well as the details for the preparation of **3**.

retention times of the two materials. A sample of ketone **5** was prepared (12) and compared to the product from **3** and an authentic sample of **4**.



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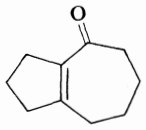

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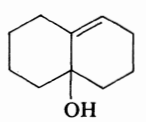
The ketones **4** and **5** could be clearly separated by v.p.c. and they had several differences in their i.r. spectra. When we carefully scrutinized the crude reaction mixture from the acid treatment of **3**, we could not find any trace of **5**. Several proton acids were found to be efficient catalysts in the isomerization of **3** to **4**. Lewis acids in aprotic solvents were also effective, for example, treatment of **3** with $BF_3 \cdot Et_2O$ in methylene chloride gave **4** in *ca.* 60% yield. We also studied the effect of solvent polarity on this isomerization. Although the isomerization was slower in nonpolar solvents, the yields of product **4** isolated were good (60–95%). One of the better procedures involves treating **3** with HCl in aqueous methanol to yield 95% **4**. In all of the above experiments we examined the crude reaction product for ketone **5** and in no case could any trace of **5** be detected in the reaction mixture. Furthermore, it was easy to show that ketone **5** is stable under these reaction conditions. All attempts to ketalize **3** gave only **4** and further reaction products of **4**.

The Birch reduction of open-chain γ-ethinyl ketones has been found to give only five-membered ring products (13). Hence we were interested in the course of this reduction of cyclodecyn-6-one **3**, since it is a cyclic γ-ethinyl ketone. On treatment with lithium in ammonia–tetrahydrofuran (13) **3** gave a mixture of the allylic alcohols **6** and **7** in the ratio of *ca.* 25:1 (*vide infra*) in excellent yield. These alcohols



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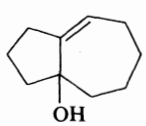

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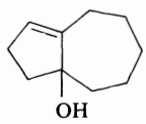
were rather prone to decompose and hence they were difficult to separate and fully characterize. For this reason these alcohols were oxidized in ethyl ether with aqueous chromic acid (14) to yield a mixture of **4** and **5** which could be readily separated and identified. This oxidative transformation and the spectral data of the alcohol **6** fully confirmed the structure of the major reduction product from **3**. A slight ambiguity existed in the case of the minor reduction product since structure **8** could be consistent with the spectral properties of this product.



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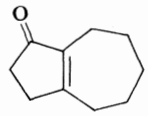

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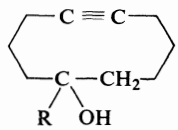
However, we rejected structure **8** by the fact that formation of **8** from **3** was unlikely on mechanistic grounds (13 and *vide infra*) and that the oxidative rearrangement of **8** to **5** was also unlikely. Alcohol **8** would be expected to give ketone **9** on oxidation. As the ketones **4** and **5** were separable by v.p.c. we used the ratio of **4**:**5** to estimate the ratio of alcohols in the reduction product from **3** since the alcohols themselves were not separable by the usual chromatographic techniques. Again the transannular cyclization of a cyclodecyne had occurred predominantly through a six-membered ring transition state; although in this case we did obtain a detectable amount of product arising from a five- (or seven-) membered transition state. This was consistent with the other transannular reactions of **3** but markedly different from the analogous reduction of open-chain compounds (13).

Reduction of cyclodecyn-6-one (**3**) with lithium aluminum hydride or sodium borohydride gave cyclodecyn-6-ol (**10**) in high yield.

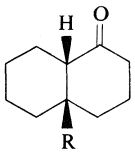


10 R = H
11 R = Me

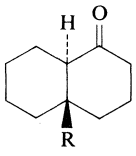
Treatment of **3** with methyllithium or methylmagnesium bromide gave the alcohol **11**. No transannular products could be detected either spectroscopically or chromatographically. Therefore the carbonyl group in **3** is more nucleophilic in hydride reduction than the acetylenic

group. In fact we have not found a nucleophilic H, C, N, or O which will add to the triple bond in **3** before it attacks the carbonyl group. On treatment with excess dimethyllithium cuprate ketone **3** was recovered unchanged.

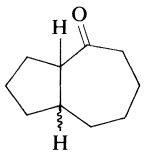
Treatment of cyclodecyn-6-ol (**10**) with refluxing methanolic HCl gave a good yield of *cis*- and *trans*-decalone-1 (**12** and **13**). We could not detect any of the isomeric bicyclo[5.3.0]decanone-2 (**14**) by v.p.c. The results differ slightly from the



12 R = H
18 R = Me



13 R = H
19 R = Me



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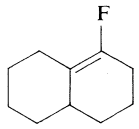
solvolysis and acetolysis of the tosylate from **10** which gave **12** and **13** as well as small amounts of *cis* and *trans*-**14** or either enol acetates (10). Since variation in solvent polarity did not effect the formation of **14** in the solvolysis experiments we cannot ascribe the difference between the solvolysis experiment (10) and the acid treatment of **10** to solvent effects.

When alcohol **10** was treated with $BF_3 \cdot Et_2O$ in methylene chloride a single very volatile product was obtained in good yield. The material was homogenous by t.l.c. and v.p.c., and no other product could be detected chromatographically or spectroscopically. Initially the spectroscopic data was confusing because of the presence of a band at 1705 cm^{-1} in the i.r. spectrum of the product. The molecular formula of this compound was established as $C_{10}H_{15}F$ by high resolution mass spectroscopy. The ^1H n.m.r. spectrum has a broad absorption between δ 1–3 and no other signals. The ^{19}F n.m.r. of the product has a relatively sharp singlet at 111 p.p.m. upfield from CCl_3F. These n.m.r. data are consistent with an olefinic fluorine (15) and the i.r. band at 1705 cm^{-1} is assigned to the double bond stretch of the fluoro olefin (15*b*, 16). The spectral data favor structure **15** for the fluoro olefin but they do not totally eliminate structure **16**. The ^{19}F n.m.r. data for a series of 1-fluorocycloalkenes are given in Table 1 (15*b*). Comparing the ^{19}F chemical shift and the J_{CH_2-CF} in the fluoro olefin from **10** with the data for the simple systems leads to the conclusion that these



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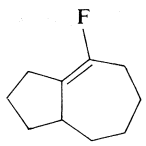
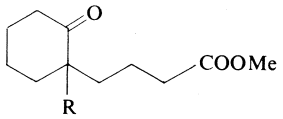


16

n.m.r. parameters favor the structure with the double bond in the smaller ring (15) for the fluoro olefin. This is further evidence of the homogeneity of the fluoro olefin, since **15** and **16** would be expected to show markedly shifted ^{19}F resonances.

To prove which structure was correct, **15** or **16**, we degraded the fluoro olefin in the following manner. The olefin was ozonized and the ozonide was worked-up oxidatively to give a keto acid with i.r. bands at 1705 and 1725 cm^{-1}. This is not consistent with a substituted cyclopentanone. In addition the acid was esterified to yield an ester with i.r. bands at 1705 and 1735 cm^{-1}. This ester was compared with an authentic sample of methyl 2-oxocyclohexylbutyrate **17** (17) which was prepared by the alkylation of the enamine from cyclohexanone



17 R = H
24 R = Me

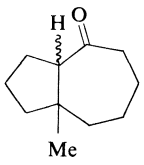
with methyl γ-iodobutyrate. The two compounds were identical by spectroscopic data, v.p.c. retention times, and m.p. and mixed m.p. of their 2,4-DNP derivatives. Thus the fluoro olefin must have structure **15**. The chromatographic properties of **17** from the degradation of **15** again indicated that the fluoro olefin was a single compound.

The tertiary alcohol **11** was also treated with refluxing methanolic HCl and a mixture of ketones was isolated in reasonable yield. This

TABLE 1. The ^{19}F n.m.r. data for 1-fluorocycloalkenes (15*b*)

Compound	F(p.p.m.)*	$J_{CH_2-CF=C}$ (Hz)
1-Fluorocyclopentene	122.7	Small
1-Fluorocyclohexene	101.7	?
1-Fluorocycloheptene	91.1	11.5

*The ^{19}F chemical shifts are p.p.m. from CCl_3F.

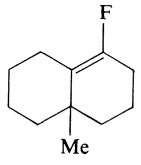


20 *cis*
21 *trans*

mixture consisted of **18**, **19**, **20**, and **21**. All four compounds could not be separated by v.p.c.; but by using a combination of v.p.c. and n.m.r. we were able to measure the relative amount of each isomer in the mixture. This transannular cyclization again was quite clean and free from side reactions. The ratios of **18**:**19** and **20**:**21** may be equilibrium values since they did not appear to change on prolonged acid treatment. We have not, as yet, investigated the reaction mixture at short reaction times to determine if the cyclization leads to a preference of either *cis* or *trans* isomer.

An authentic sample of the *cis* and *trans* isomers, **18** and **19**, was prepared by the conjugate addition of lithium dimethylcopper to the octalone **4** (18).[4] The conjugate addition yielded a predominance of the *cis* isomer **18**. These isomers could be equilibrated by acid or base and the *cis*–*trans* mixture was separable by v.p.c. The *cis* isomer **18** has an n.m.r. singlet at δ 1.02 and the *trans* isomer **19** has an n.m.r. singlet at δ 0.77 due to the angular methyl group. These assignments are in accord with n.m.r. signals for the C-19 methyl group in 5β-androstanone-4 (δ 1.12) and 5α-androstanone-4 (δ 0.74) (19). A sample of the *cis* and *trans* isomers, **20** and **21**, was prepared by the conjugate addition of lithium dimethylcopper to $\Delta^{1,7}$-bicyclo[5.3.0]-decanone-2 (**5**). These two isomers could also be separated by v.p.c. The *cis* isomer **20** has an n.m.r. singlet at δ 1.18 and the *trans* isomer **21** has an n.m.r. singlet at δ 0.72 due to the angular methyl group. All four isomers **18**–**21** could not be separated by v.p.c., however, by using a combination of v.p.c. and the intensity of the n.m.r. signals assigned to the angular methyl group in **18**–**21** we have found that the ratio of **18**:**19**:**20**:**21** from the acid-catalyzed cyclization of **11** was 1.0:1.4:0.1:0.25. This is the only example of transannular reactions of cyclodecynes in which we have found a significant amount of product resulting from cyclization through a five-membered ring transition state.

When alcohol **11** was treated with $BF_3 \cdot Et_2O$ in methylene chloride we again isolated a fluoro olefin in high yield. The product was homogeneous by a variety of chromatographic and spectroscopic techniques. The ^1H n.m.r. of this product has no vinyl protons but it does have a singlet at δ 1.05 due to the angular methyl group. The ^{19}F n.m.r. shows a relatively sharp singlet 110 p.p.m. upfield from CCl_3F. There is an i.r. absorption at 1700 cm^{-1} which is assigned to a monofluoro tetrasubstituted double bond stretching (*vide supra*). Again in this case there are two possible structures for the fluoro olefin, either **22** or **23**. The spectral data and our



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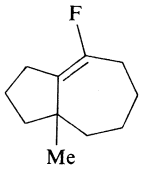
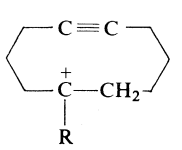


23

previous results led us to favor structure **22**. That is in fact the correct structure as proven by an oxidative sequence similar to that for compound **15**. Thus ozonolysis of the fluoro olefin from **11** and oxidative work-up gave a keto acid with a broad i.r. band at 1705 cm^{-1}. Esterification yielded methyl 1-methyl-2-oxocyclohexylbutyrate **24** which has i.r. bands at 1700 and 1730 cm^{-1}. No trace of the isomeric cyclopentanone which would arise from **23** could be found from the i.r. spectra of the keto acid and ester or from the v.p.c. of the ester.



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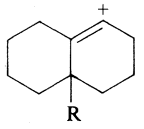

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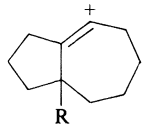
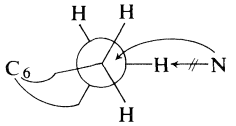


27

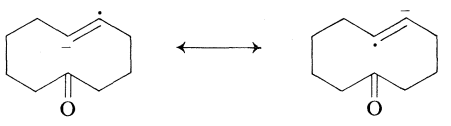
[4]We are grateful to Professor E. Piers and Miss W. M. Phillips for samples of **18** and **19**, and for their detailed experimental procedures.

If these cyclizations were to proceed via a free carbonium ion, **25**, then we would expect a preference for formation of **27** since the intermediary linear vinyl cation (9) should be more readily accommodated in a seven-membered ring (**27**) than a six-membered ring (**26**). It could be argued that **27** may be formed initially, and subsequently it rearranges entirely to **26**. However, recent evidence indicates that in fact **26** (R = H) rearranges to **27** (R = H) (20). Those reactions most likely to yield carbonium ions, for example, the solvolysis of the tosylate from **10** and acid treatment of **11** did lead to products which can be considered to arise from **27**. An examination of a molecular model of **3** or **10** suggests that C-1 and -2 are very nearly equidistant from C-6 and hence we might expect mixture of bicyclo[4.4.0]decanes and bicyclo-[5.3.0]decanes. However, we have found that there is a very strong preference for transannular cyclizations which proceed via a six-membered ring transition state. We feel that these cyclizations are essentially concerted, that is, the acetylene is simultaneously attacked by the electrophilic C-6 and an external nucleophile. Assuming that carbon atoms 1 and 2 approach sp^2 hybridization in the transition state for cyclization, then it appears, from models, that the transition state leading to the bicyclo[4.4.0]-decane skeleton has less steric interference and less torsional strain (21) than the transition state leading to the bicyclo[5.3.0]decane skeleton. Structure **28** is a Newman projection along



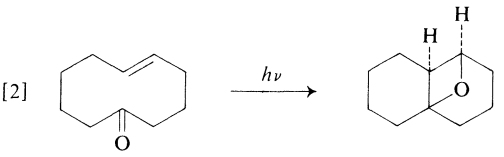
28

C-10, -1, -2, and -3. For *trans* coplanar addition of C-6 and a nucleophile to the triple bond it can be seen that one of the hydrogens on C-10 will sterically hinder the addition of the nucleophile to C-1; however, the nucleophile can add to C-2 with the two hydrogens on C-3 staggering it. This would explain the almost exclusive formation of products with a bicyclo[4.4.0]decane skeleton. Of course this does not explain the preponderance of **6** in the Birch reduction of **3**. Stork *et al.* (13*a*) have suggested that the Birch reduction of γ-ethinyl ketones involves a non-



29

linear vinyl radical anion as an intermediate. Assuming that the analogous reduction of **3** involves a similar intermediate **29** then inspection of models of **29** shows a clear preference for formation of the six-membered ring product **6**. A related radical cyclization may be involved in the photochemical closure shown in eq. 2 (22).



Experimental

Melting points were determined on a Kofler hot stage and are uncorrected. The i.r. spectra were recorded on a Perkin–Elmer model 700 and were calibrated using the 1601 cm^{-1} band of polystyrene. The ^1H n.m.r. spectra were recorded on either a Varian T-60 or Varian HA-100 and the ^{19}F n.m.r. spectra were recorded on a Varian T-60 equipped with a T-6-18 wide sweep module using CCl_3F as an internal standard. The mass spectra were obtained using an AEI MS-9 operating at 70 eV. Microanalyses were performed by Mr. Peter Borda, University of British Columbia. The v.p.c. analyses were performed with a Varian Aerograph 90-P-3 using column A, 5 ft × ¼ in. column of 3% SE 30 on Chromosorb W, and column B, 5 ft × ¼ in. column of 10% FFAP on Chromosorb W, or with a Perkin–Elmer Model 900 using column C, 5 ft × ⅛ in. column of 10% FFAP on Chromosorb W.

$\Delta^{1,7}$-Bicyclo[5.3.0]decenone-2 (5)

Compound **5** was prepared from $\Delta^{9,10}$-octalin by the method of Anderson and Nelson (12) to yield a product b.p. 114°/10 mm (lit. b.p. 126–128°/15 mm (12)).

Cyclodecyn-6-one (3)

A solution of 1.0 g (0.07 mol) of enone **5** in 20 ml of methanol was cooled in a water bath at 10° and treated with 10 ml of 30% hydrogen peroxide with stirring. A solution of 2 ml of 6 *N* sodium hydroxide in 5 ml of methanol was added dropwise over a period of ½ h and the resulting solution was stirred for an additional 15 h. The methanolic solution was diluted with 50 ml of water and extracted three times with methylene chloride. The extracts were combined, washed with brine solution until neutral, dried over anhydrous sodium sulfate, filtered, and the solvents were removed under reduced pressure. The residue was distilled at bath temperature 100°/0.6 mm to yield 0.82 g (74%) of 1,7-oxido-bicyclo[5.3.0]decanone-2.

A 1.61 g (0.097 mol) sample of the above epoxide was treated with tosylhydrazone under the conditions of

Schreiber *et al.* (11*b*) to yield cyclodecyn-6-one (**3**) which was distilled at a bath temperature of 55°/0.02 mm.

Acid Isomerization of Cyclodecyn-6-one (3)

(i) Methanolic Hydrochloric Acid

A 79 mg (0.53 mmol) sample of cyclodecyn-6-one (**3**) was dissolved in 1.5 ml of methanol containing one drop of concentrated hydrochloric acid and the solution was allowed to stand at room temperature for 12 h. Methanol was removed under reduced pressure, then the residue was dissolved in ether and washed with sodium bicarbonate solution. The organic extracts were dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure. The residue was distilled at bath temperature of 70–80°/0.2 mm to yield 75 mg (95%) of octalone **4** which was compared by i.r. and v.p.c., column B, to an authentic sample of **4** prepared by the method of House and Thompson (23).

Compounds **4** and **5** were separated by v.p.c., column B, and no trace of **5** could be detected in crude reaction product above or in the sample of distilled **4**.

(ii) Boron Trifluoride Etherate in Methylene Chloride

A solution of 225 mg (1.5 mmol) of **3** in 10 ml of methylene chloride was treated with *ca.* 0.5 ml of boron trifluoride etherate. The solution was stirred and it turned dark green. After 10 min, the reaction mixture was washed with saturated aqueous sodium bicarbonate until the organic layer was colorless. The organic extracts were dried over anhydrous sodium sulfate, filtered, and the solvent removed under reduced pressure. The v.p.c. analysis, column B, showed only **4** to be present in the crude residue. This residue was distilled at bath temperature of 70–80°/0.2 mm to yield 133 mg (59%) of pure **4**.

(iii) Additional Conditions for Isomerization

The following conditions were also found to be effective in the isomerization of **3** to **4**: hydrochloric, hydrobromic, or perchloric acid in methanol, dioxane, or hexane at room temperature; refluxing acetic acid and zinc; *p*-toluenesulfonic acid in refluxing benzene; and mercuric chloride in refluxing methanol.

Attempted Ketalization of 3

A solution of 80 mg of **3**, 0.5 ml of ethylene glycol and a few crystals of *p*-toluenesulfonic acid in 50 ml of benzene was refluxed for 16 h. The benzene solution was washed with aqueous brine, dried over anhydrous sodium sulfate, filtered, and the solvent was removed under reduced pressure. A v.p.c., column B, and t.l.c. analysis indicated that the major component of the mixture was **4** and a small amount of unreacted **3**.

Birch Reduction of Cyclodecyn-6-one (3)

A solution of 165 mg (1.1 mmol) of **3** in 1 ml of dry tetrahydrofuran was added to 100 ml of liquid ammonia. The solution was stirred and very small pieces of lithium wire were added until a blue color persisted. Ammonium chloride was quickly added to render the solution colorless and the ammonia was allowed to evaporate. Water was added to the residue and the mixture was extracted with ethyl ether. The extracts were combined, washed with aqueous sodium chloride solution until neutral, dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure to yield 168 mg of crude product. This semisolid showed no carbonyl absorption in the i.r. and it was sublimed at 25°/0.005 mm to give quantitative yield of product m.p. 61–69°; ν_{max} (CH_2Cl_2) 3580, 1605 cm^{-1}; δ (CCl_4) 5.4 (m, 1H), 1.2–2.6 (m, 15H); *m/e* calcd. for $C_{10}H_{16}O$: 152.1201; found: 152.1198; 152 (15%), 134 (58%), 119 (40%), 105 (52%), 91 (100%).

Oxidation of Alcohols from Birch Reduction of 3

The solution of the above alcohols from **3** (10 mg) in ethyl ether was added to an ice cold solution of 100 mg of chromium trioxide in 5 ml of water and 0.5 ml of concentrated sulfuric acid. The mixture was stirred for 2.5 h at 0° and then the ether layer was washed with water until neutral. The ether solution was dried over anhydrous sodium sulfate, filtered, and the solvent removed under reduced pressure to give an oily residue, ν_{max} ($CHCl_3$) 1650, 1630 cm^{-1}. This was analyzed by v.p.c., column C, and was found to contain **4** and **5** in the ratio of 25:1.

Cyclodecyn-6-ol (10)

Following the procedure of Hanack and Heumann (10) 15.2 mg (1.01 mmol) of **3** was reduced with lithium aluminum hydride (15 mg) in 10 ml of refluxing ethyl ether for 1½ h. The reaction mixture was cooled, treated with 5 ml of a saturated aqueous solution of potassium sodium tartrate, and the resulting mixture was stirred for 5 min. The aqueous layer was extracted with 2 × 20 ml of ethyl ether. The extracts were combined, dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure. The residue was distilled at bath temperature of 85–90°/0.5 mm to yield 145 mg (94%) of **10**, ν_{max} (CH_2Cl_2) 3360 cm^{-1}; δ (CCl_4) 1.2–1.9 (m, 10H), 1.94 (b.s, 1H, exchangeable in D_2O), 2–2.4 (m, 4H), 4.2 (m, 1H).

6-Methylcyclodecyn-6-ol (11)

A solution of 1.7 g (0.011 mol) of **3** in dry tetrahydrofuran was treated dropwise with 7 ml of 2.3 *M* solution of methyllithium under nitrogen. After addition of methyllithium the solution was stirred for an additional 3½ h at room temperature. Excess methyllithium was decomposed with water. The aqueous layer was saturated with sodium chloride and extracted with ethyl ether. The extracts were combined, dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure to yield an oily residue. This was purified by silica gel column chromatography using benzene – ethyl acetate (95:5 to 50:50) as eluant to give 500 mg (27%) of **11**. Due to its lability **11** could not be purified for combustion analysis; ν_{max} (film) 3390 cm^{-1}; δ ($CDCl_3$) 1.04 (s, 3H), 1.27 (s, 1H, exchangeable with D_2O), 1.2–1.8 (m, 10H), 1.9–2.4 (m, 4H); *m/e* 166 (8%), 151 (30%), 148 (26%), 133 (50%), 105 (52%), 91 (100%).

Acid Treatment of 10

A solution of 56 mg (3.71 mmol) of cyclodecyn-6-ol (**10**) and 2 drops of concentrated hydrochloric acid in 2 ml of methanol was refluxed for 3.5 h. The reaction mixture was poured into 30 ml of water and extracted with 30 ml of benzene – ethyl ether (1:1). The extracts were washed with 20 ml of saturated sodium bicarbonate solution and 20 ml of saturated sodium chloride, then dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure. The residual oil was purified by preparative t.l.c. (silica gel – benzene – ethyl acetate, 9:1) to yield 8 mg of **10** and 42 mg (87%

based on unrecovered starting material) of decalones **12** and **13**. These were shown to be identical to authentic **12** and **13** by v.p.c., column C.

*cis- and trans-Decalone-1 (**12** and **13**)*

A mixture of **12** and **13** (24) was prepared by Birch reduction (Li, NH_3, NH_4Cl) of $\Delta^{9,10}$-octalone-1 (**4**) followed by Jones oxidation (25) of the 1-decol to **12** and **13**. The mixture so obtained was equilibrated as follows. A solution of 15 mg of **12** and **13** from above in 2 ml of methanol and 2 drops of 1 *N* sodium hydroxide was heated on a steam bath for 5 min and then diluted with 20 ml of water. The organic material was extracted with 20 ml of ethyl ether and the extracts were washed with saturated aqueous sodium chloride solution until the washings were neutral to litmus. These ketones were cleanly separable by v.p.c. on column B or C.

*cis- and trans-Bicyclo[5.3.0]decanone-2 (**14**)*

Birch reduction followed by Jones oxidation (25) of $\Delta^{1,7}$-bicyclo[5.3.0]decenone-2 (**5**) gave a mixture of isomers **14** which are equilibrated as above for **12** and **13**. Again the isomers **14** were separable by v.p.c. on column B or C.

*Treatment of **10** with Boron Trifluoride Etherate*

A solution of 190 mg (1.26 mmol) of cyclodecyn-6-ol (**10**) in 20 ml of dry methylene chloride was treated with 0.5 ml of boron trifluoride etherate and stirred at room temperature for 15 min. The brown reaction mixture was washed with saturated aqueous sodium bicarbonate until the organic layer became colorless. The methylene chloride solution then was dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure. The very volatile residue was purified by preparative t.l.c. (silica gel – benzene) to yield 163 mg (85%) of fluoroalkene **15** which was homogeneous by v.p.c., columns B and C; ν_{max} (film) 1705 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 1–3 (m); ^{19}F n.m.r. δ_{CCl_3F} (CCl_4) 111; *m/e* calcd. for $C_{10}H_{15}F$: 154.1158; found: 154.1102; 154 (10%), 135 (100%).

*Ozonolysis of **15***

A solution of 100 mg of **15** dissolved in 2 ml of methanol was cooled in a Dry Ice – acetone bath and ozone was passed through the solution until a light blue color appeared. The excess ozone was removed under reduced pressure. The ozonide solution was treated with 0.5 ml of 30% hydrogen peroxide and refluxed on a steam bath for 15 min. The reaction mixture was poured into 25 ml of water and extracted with 3 × 20 ml of ethyl ether. The extracts were combined, dried over anhydrous sodium sulfate, and the solvents removed under reduced pressure to yield crude 2-oxocyclohexylbutyric acid; ν_{max} ($CHCl_3$) 1705, 1725 cm^{-1}.

The crude acid was esterified with diazomethane and the resulting keto ester **17** was purified by t.l.c. (silica gel – chloroform) to give pure **17**; ν_{max} ($CHCl_3$) 1705, 1735 cm^{-1}. This was converted to its 2,4-DNP derivative m.p. 109–111°, mixed m.p. with 2,4-DNP of authentic **17** 108–111° (lit. m.p. 112° (17)).

*Methyl 2-Oxocyclohexylbutyrate (**17**)*

A 10.6 g (70 mmol) sample of the pyrrolidine enamine of cyclohexanone (26) was dissolved in 100 ml of dry ethanol and treated with 7.6 g (33.6 mmol) of methyl γ-iodobutyrate. This mixture was refluxed under nitrogen for 20 h. Then the solvent was removed under reduced pressure. The residue was stirred (5 min) with 20 ml of water and extracted with 50 ml of ethyl ether. The ethereal solution was washed with 3 × 10 ml of saturated sodium chloride solution (neutral to litmus), dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure. The residue was distilled to yield 4 gm (60%) of **17** b.p. 60°/0.2 mm; ν_{max} ($CHCl_3$) 1710, 1730 cm^{-1}. A small portion was converted to its 2,4-DNP derivative, m.p. 110–113° (lit. m.p. 112° (17)).

*Acid Treatment of **11***

6-Methylcyclodecyn-6-ol (**11**) (20 mg) was dissolved in 2 ml of methanol containing one drop of concentrated hydrochloric acid and refluxed for 3.5 h. The mixture was diluted with 20 ml of water and extracted with 3 × 10 ml of ethyl ether. The extracts were combined, washed with 20 ml of saturated sodium bicarbonate solution, and 20 ml of saturated sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure. The residue was distilled, bath temperature of 85°/0.2 mm, to yield 13 mg (65%) of a mixture of ketones **18**, **19**, **20**, and **21** (v.p.c., columns B and C); ν_{max} ($CHCl_3$) 1705 cm^{-1}, no —OH stretch; δ (CCl_4) 0.72 (s), 0.77 (s), 1.03 (s), 1.20 (s).

*cis- and trans-7-Methylbicyclo[5.3.0]decanone-2 (**20** and **21**)*

Dimethyllithium cuprate was prepared from 571 mg (3.0 mmol) of dry cuprous iodide and *ca.* 4 ml of 2.3 *M* methyllithium in 100 ml of ethyl ether at 0°. A solution of 450 mg (3.0 mmol) of $\Delta^{1,7}$-bicyclo[5.3.0]decanone-2 (**5**) in 2 ml of dry ether was added dropwise under nitrogen to the cooled solution of dimethyllithium cuprate. After the addition was complete, the solution was stirred at 0° for an additional 2 h. The copper complex was decomposed with a saturated ammonium chloride solution and this mixture was stirred at room temperature for 1 h. The ether layer was separated, washed with saturated aqueous sodium chloride solution, dried over anhydrous sodium sulfate, filtered, and the solvents removed under reduced pressure. The residue was purified by preparative t.l.c. (silica gel – benzene) to yield 350 mg (70%) of **20** and **21**. This mixture of isomers was separated by v.p.c., column B; to give *cis*-7-methylbicyclo[5.3.0]decanone-2 (**20**) which distilled at bath temperature of 80°/0.2 mm; ν_{max} ($CHCl_3$) 1695 cm^{-1}; δ (CCl_4) 1.18 (s, 3H).

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.48; H, 10.83.

trans-7-Methylbicyclo[5.3.0]decanone-2 (**21**) was also obtained pure by v.p.c. This compound distilled at bath temperature of 82°/0.2 mm; ν_{max} ($CHCl_3$) 1695 cm^{-1}; δ (CCl_4) 0.72 (s, 3H).

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.47; H, 10.91. Found: C, 79.43; H, 10.80.

*Treatment of **11** with Boron Trifluoride Etherate*

A solution of 222 mg (1.34 mmol) of 6-methylcyclodecyn-6-ol (**11**) and 0.5 ml of boron trifluoride etherate in 20 ml of dry methylene chloride was stirred at room temperature for 15 min. The resulting brown solution was washed with saturated aqueous sodium bicarbonate until the organic layer became colorless. Then the organic layer was dried over anhydrous sodium sulfate, filtered

and the solvents removed under reduced pressure. The volatile residue was purified by preparative t.l.c. (silica gel – benzene) to yield 191 mg (86%) of fluoroalkene **22**; ν_{max} (film) 1700 cm^{-1}; ^1H n.m.r. δ (CCl_4) 1.05 (s, 3H), 1.2–2 (m, 12H), 2.05 (d, $J \simeq 6$ Hz, 1H), 2.7 (d, $J \simeq 12$ Hz, 1H); ^{19}F n.m.r. δ_{CCl_3F} (CCl_4) 110; *m/e* calcd. for $C_{11}H_{17}F$: 168.1314; found: 168.1314; 168 (35%), 153 (100%), 149 (40%).

Ozonolysis of ***22***

A solution of 100 mg of **22** was ozonized under the same conditions as **15** above to yield crude 1-methyl-2-oxocyclohexylbutyric acid ν_{max} ($CHCl_3$) 1705 cm^{-1} (br).

The crude acid was esterified with diazomethane and purified by t.l.c. (silica gel – chloroform) to yield pure **24**; ν_{max} ($CHCl_3$) 1700, 1730 cm^{-1}; δ ($CDCl_3$) 1.0 (s, 3H), 1.1–1.9 (m, 10H), 2.3 (m, 4H), 3.6 (s, 3H); *m/e* 212 (5%), 181 (5%), 152 (5%), 112 (90%), 55 (100%).

A small portion of **24** was converted to its 2,4-DNP derivative, m.p. 99–100°.

Anal. Calcd. for $C_{18}H_{24}N_4O_6$: C, 55.10; H, 6.16; N, 14.28. Found: C, 54.93; H, 6.11; N, 14.56.

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