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SYNTHESIS OF PROPELLANES BY "EXOCYCLIC" TRANSANNULAR CYCLOADDITION OF OLEFINIC METHYLENECYCLOPROPANES

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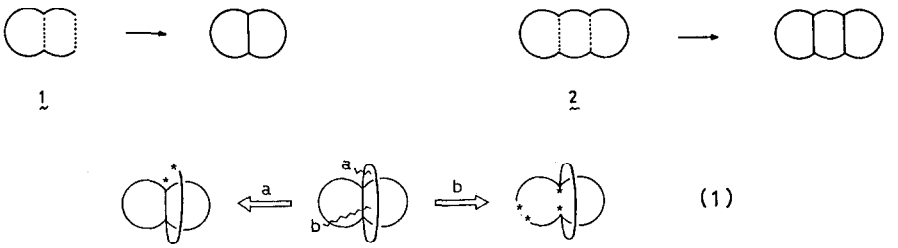
Abstract: Olefinic methylenecyclopropanes undergo quantitative transannular ring closure under Group 10 metal catalysis to give [3.3.3]propellanes through cycloaddition of trimethylenemethane-like intermediate.

Intramolecular cycloaddition has proven to be a highly useful tool for formation of a bicyclic structure from an acyclic molecule (**1**). It was suggested sometime ago[1] that an "endocyclic" transannular internal cycloaddition (**2**) of medium- or macrocyclic ring would help synthetic chemists to achieve even higher degree of efficiency and control in the synthesis of fused cyclic molecules. This suggestion was materialized very recently by two groups though the use of internal Diels-Alder reaction,[2,3] which resulted in a brilliant synthesis of a steroid nucleus.[3] We have in turn demonstrated recently the synthetic potential of "exocyclic" transannular cycloaddition,[4] providing a concise strategy for the synthesis of propellanes (eq 1, route b). In this paper, we detail the synthesis of propellanes through such "exocyclic" transannular cycloadditions.



(1)

Propellane continues to attract the interest of chemists of various disciplines.[5] Since the discovery of the unique sesquiterpene modhephene (**3**)[6,7] and 13-acetoxymodhepene (**4**),[8] the [3.3.3]propellane (**5**) has been a target of special interest.

3 X = H
4 X = OAc

5

The majority of synthetic approaches to propellanes rely on a strategy to form a third ring onto a preformed bicyclo[3.3.0]octane skeleton (eq 1, route a).[7] A more fascinating route b, however, in which both the central bond and a peripheral one are formed in a single step by "exocyclic" transannular cycloaddition is so far unexplored. In view of strong transannular interaction in an eight-membered ring, we envisioned that installation of suitable cycloaddition partners at both 1- and 5-positions of cyclooctane (cf. **7**) followed by internal, five-membered ring forming cycloaddition of these functional groups would result in a single-step construction of a [3.3.3]propellane **8**. A few previous examples of photochemical transannular four-membered ring closure[9] gave us a positive support to the plan.

(2)

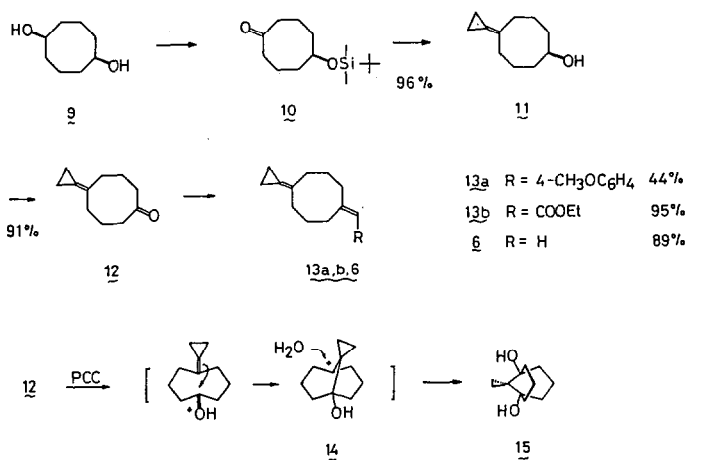
6 7 8

Stimulated by our current interests in the chemistry of functionalized strained rings,[10] we have decided to study a metal-catalyzed intramolecular cycloaddition between a methylenecyclopropane and an olefin (**6**).[11] We also expected that this reaction would shed some light to the mechanism of this cycloaddition, which has been considered to proceed through a trimethylenemethane-like intermediate (**7**). The formation of a methylenecyclopentane **8** made this propellane synthesis relevant to the modhephene problem, since the methylenecyclopentane **8** should readily isomerize to its endocyclic double-bond isomer.

Results and Discussion

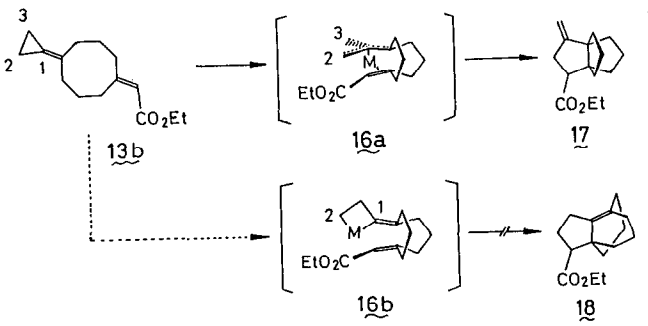
The olefinic methylenecyclopropanes **6** and **13a,b** were prepared in a straightfoward manner as illustrated in Scheme I. Mono-protection (and recycling) of cyclooctane-1,5-diol **9** followed by oxidation gave **10** in excellent yield, which was smoothly converted to methylenecyclopropane **11**. Use of $NaNH_2$ as a base[12] for the Wittig olefination with cyclopropylidene phosphorane[13] gave an excellent result. Pyridinium chlorochromate (PCC) oxidation of **11** gave an unexpected major product **15** with its characteristically high degree of symmetry. The acidity of the oxidant is undoubtedly responsible for the formation of this bridged product through transannular cationic cyclization of **12**. Retention of the cyclopropane ring during the transformation of a cationic intermediate **14** to **15** must be due to the orthogonality of the cation orbital and the cyclopropyl C-C bond in **14**. Swern oxidation of **11** on the other hand gave the desired **12**, which was then converted to the target methylenecyclopropanes either by the Wittig reaction (for **6** and **13a**) or by the Peterson reaction (**13b**).

Scheme I



Cycloaddition of methylenecyclopropane with an activated olefin under the catalysis of Group 10 metals is a reaction of considerable generality. The reaction however shows quite complex regiochemical behavior depending on the substitution of the substrate and the catalyst,[11] which has been interpreted through the intermediacy of both trimethylenemethane/metal complex (**16a**) and a metalacyclobutane (**16b**).[14a] Although the mechanism is obscure, the intermolecular precedents predict that no conditions would be available for the cyclization of the present substrate **13b** to propellane **17**. A nickel catalyst would mainly cleave the 2,3-bond in **13b**[14] to generate an

intermediate **16b** topologically incapable of cyclization (cf. **1i**). A palladium catalyst, on the other hand, would cleave the 3,4-bond[15] to form the desired trimethylenemethane-like intermediate (**16a**), the regiochemistry of cycloaddition of which would however be opposite to that suitable for the formation of **17**. Namely, precedents predict that either of the less substituted ends, C(3) or C(4), reacts in a Michael-like manner with the enoate moiety rather than the C(1) end required for the propellane formation.



(3)

Despite such prediction, $Ni(COD)_2$ (COD = 1,5-cyclooctadiene) in the presence of 0.5 equiv of PPh_3 effected clean cyclization of **13b** to **17** solely in the desired manner in excellent yield (Table 1, entry 1). The PPh_3/Ni ratio larger than 0.5 considerably slowed down the reaction rate (entry 2). A Ni(0) catalyst generated conveniently from $Ni(acac)_2$ and diisobutylaluminum hydride (Dibal) was also effective catalyst (entry 3). Palladium catalyst proved much more suitable than nickel catalyst. The reaction of **13b** in the presence of a Pd(0)-PPh_3 catalyst afforded **17** in 98% yield of isolated product (entry 4).

The cycloaddition of methylenecyclopropane to simple olefin has been little explored,[16] because of the destruction of the latter under the reaction conditions. However, the transannular cyclization of the prototype substrate **6** also proceeded cleanly to give the [3.3.3]propellane (**8**) as a volatile solid (entry 5).

Table 1. Synthesis of Propellanes 6 by Transannular Cyclization of Methylenecyclopropanes 4.

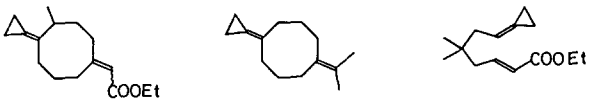
entry	substrate/ product	catalyst (mol%)	metal: Ph_3P	temp °C	%yield
1	**13b/17**	$Ni(COD)_2/Ph_3P$ (20)	1:0.5	110	74[a](94)[b]
2	**13b/17**	$Ni(COD)_2/Ph_3P$ (20)	1:1	110	18[a](78)[b]
3	**13b/17**	$Ni(acac)_2$/Dibal/Ph_3P (20)	1:0.5	90	91[a]
4	**13b/17**	$PdCl_2(Ph_3P)_2$/Dibal (10)	1:2	130	98[c]
5	**6/8**	$PdCl_2(Ph_3P)_2$/Dibal (20)	1:2	90	74[a]

[a]Yield determined by capillary g.l.c. [b]Yield based on conversion. [c]Yield based on pure isolated material.

The extremely facility of the internal cycloaddition either in the presence of a Ni or a Pd catalyst necessitates modification of the previous mechanistic picture of the reaction. It is important to note that the internal reaction proceeded through a single regiochemical course which is totally against the normal ones observed in intermolecular cases. The diverse reaction pathways recorded for the latter cases therefore does not reflect the fundamental mechanistic requirements.

The relative geometrical relationship between the two reaction sites and the metal atom appears very crucial for the cyclization. Attempted cyclization of the substrates **19-21** under a variety of conditions completely failed. The failure with the compound **19**, which differs from **13b** only for its single extra methyl group was particularly surprising since inspection of the mole-

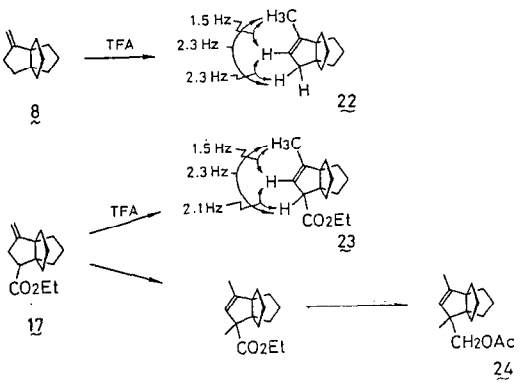
cular model did not reveal any serious effects of this methyl group. The extremely high sensitivity of the transannular cycloaddition has also been noted in the "endocyclic" counterparts,[2,4] which in turn comprises of the origin of the very high stereocontrol in successful applications.



19 20 21

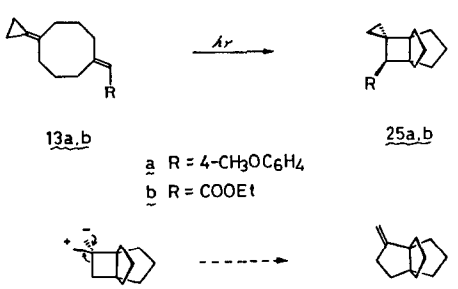
The propellane (**8**) possesses a highly symmetrical structure, whose ^{13}C NMR spectrum showed only five methylene carbon signals. The more complex analogue **17** shares similar NMR characteristics, and also showed a two-dimensional NMR spectrum in accordance with the assigned structure. Acid treatment (trifluoroacetic acid, room temp) of **8** and **17** quantitatively produced an endo-olefinic isomer **22** and **23** respectively, the ^1H NMR of which indicated the presence of an isolated $CH_2CH{=}CCH_3$ structure expected for the assigned structure (Scheme 2). It was converted to 12-nor-13-acetoxymodhephene (**24**) through several high-yield, standard transformations [(1)LDA/MeI, (2) TFA, (3) $LiAlH_4$, (4) Ac_2O], the spectra of which were similar to those of natural 13-acetoxy-modhephene (**4**).

Scheme 2



8 22 23 17 24

As an alternative approach to [3.3.3]propellanes, we considered a transannular [2+2]-photocycloaddition[9] of **13** to a spiro[3.3.2]propellane, which would produce the desired [3.3.3]propellane through an appropriate a rearrangement reaction. Despite the extremely strained nature of the product, the photoaddition reaction proceeded very smoothly. Both direct and sensitized reaction of **13a** and **13b** in acetonitrile for 2-2.5h at room temperature proceeded to give **25a** and **25b** in 86% and 90% yield, respectively. Various attempts to effect metal catalyzed rearrangement of the spiro[3.4]hexane ring to a cyclopentane, as illustrated in eq 4[18] however were unsuccessful.



13a,b 25a,b

a R = 4-$CH_3OC_6H_4$
b R = COOEt

(4)

In summary, the "exocyclic" transannular ring closure of an olefinic methylenecyclopropane not only provides a viable route to propellanes, but exhibits unique regioselectivity not observed with its intermolecular counterparts. In addition, the extreme facility of the cyclization

suggests that oxidative cleavage of peripheral bonds in propellanes such as **21**, **22**, and **23**, will serve as an attractive route to functionalized fused bicyclic systems.

Acknowledgment. We thank Professors S. Yamamura and Y. Shizuri for assistance in some structural assignments, and the Ministry of Education, Science, and Culture (#6370013) and the CIBA-GEIGY Foundation for the Promotion of Science for financial support.

Experimental

General Data. All reactions using air and moisture sensitive compounds were carried out in a dry reaction vessel under nitrogen. Routine chromatography was performed on silica gel using a mixture of ethyl acetate and hexane as eluent.

^1H NMR spectra was taken at 200 MHz on a JEOL FX-200 instrument, which was also used for ^{13}C NMR spectra at 50 MHz. Spectra are reported in part per million from internal tetramethylsilane. IR spectra were recorded on a Hitachi 260-10 or a JASCO IR-800 instrument; absorptions are reported in cm^{-1}. GC-MS analysis was performed on a Shimazu 9020-DF equipped with an OV-1 (7 m) capillary column. Microanalyses were performed on a Perkin-Elmer 240 instrument. Photochemical reactions were carried out with a 400 W high pressure mercury lamp (Ricoh Kagaku Co. Model UVL 400-P) in pyrex test tubes placed around the lamp. Ethereal solvents were distilled from benzophenone ketyl immediately before use. Toluene, acetonitlile, and methylenechloride were distilled from CaH_2 and stored under molecular sieves. All commercially available reagents were either distilled or recrystallization before use.

1-(tert-Butyldimethylsiloxy)cyclooctan-5-ol. To a refluxing solution of the diol **9** (7.2 g, 50 mmol), triethylamine (5.7 mL, 70 mmol), and 4-dimethylaminopyridine (0.5 g, 4 mmol) in 50 mL of THF was added a solution of tert-butyldimethylsilyl chloride (3.78 g, 25 mmol) in 25 mL of THF over 2 h. The resulting solution was stirred for an additional hour and was filtered. The crude product was purified by chromatography to obtain the title compound (4.22 g, 64 %), **9** (3.98 g, 55% recovery), and the bissilylated product (0.83 g, 9 %): IR (neat) 3380, 1250; ^1H NMR (CCl_4) -0.03 (s, 6 H), 0.82 (s, 9 H), 1.36-1.77 (m, 13 H), 3.32-3.87 (m, 2 H).

Anal. Calcd for $C_{14}H_{30}O_2Si$: C, 65.05; H, 11.70. Found: C, 64.78; H, 11.46.

5-(tert-Butyldimethylsiloxy)cyclooctan-1-one (10). To a suspension of PCC (13.6 g, 63 mmol) and alumina (ca. 30 g) in 40 mL of CH_2Cl_2 was added a solution of 1-(tert-butyldimethylsiloxy)cyclooctan-5-ol (11.3 g, 42 mmol) in 40 mL of CH_2Cl_2 at room temperature. The resulting suspension was stirred for 1h, and was poured into 200 mL of anhydrous ether. The mixture were passed through a short column of alumina, and the crude product was purified by chromatography (AcOEt/hexane 10 %) to obtain 9.8 g (88 %) of the title compound: IR (neat) 1697, 1250, 1065, 835, 770; ^1H NMR (CCl_4) -0.03 (s, 6 H), 0.83 (s, 9 H), 1.13-2.83 (series of m, 12 H), 3.60 (m, 1 H).

Anal. Calcd for $C_{14}H_{28}O_2Si$: C, 65.57; H, 11.00. Found: C, 65.35; H, 11.00.

1-(Cyclopropylidene)cyclooctan-5-ol (11). A stirred suspension of sodium amide (0.78 g, 20 mmol) and cyclopropyltriphenylphosphonium bromide (7.67 g, 20 mmol) in 30 mL of toluene was heated at 70 °C for 1.5 h. To this solution was added a solution of the ketone **10** (2.04 g, 7.7 mmol) in 2 mL of toluene, and the resulting mixture was heated at 80 °C for 12 h. Bulk of solvent was removed in vacuo, and hexane was added. Precipitate was removed by filtration, and the solvent was removed in vacuo to obtain crude oily material (3.19 g). To this was added a solution of 5 % HF in aqueous acetonitrile, and the resulting solution was stirred for 3.5 h. Sat. $NaHCO_3$ was added and the organic layer was extracted with ether. The combined organic layer was washed with brine, dried over $MgSO_4$. The crude product was purified by chromatography (elution with AcOEt/hexane 20 %) afforded 1.23 g (96 %) of the title compound: IR (neat) 3310, 3025, 1435; ^1H NMR (CCl_4) 0.98 (br d, J = 1 Hz, 4 H), 1.42-1.79 (m including a singnal at 1.60, 9 H), 2.00-2.44 (m, 4 H), 3.43-3.77 (m, 1 H).

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.45; H, 11.00.

1-(Cyclopropylidene)cyclooctan-5-one (12). To a stirred solution of oxalyl chloride (0.48 mL, 5.5 mmol) in 12 mL of CH_2Cl_2 at -60 °C was added a solution of dimethylsulfoxide (0.78 mL, 11 mmol) dissolved in 5 mL of CH_2Cl_2 over 2 min, and the resulting mixture was stirring for 2 min. To this solution was added a solution of **11** (831 mg, 5.5 mmol) in 10 mL of CH_2Cl_2, and the mixture was stirred for 0.5h. Triethylamine (3.5 mL, 25 mmol) was added, and the resulting solution was warmed to room temperature and was quenched by water. The mixture was extracted with CH_2Cl_2, and the combined organic extracts were dried over Na_2SO_4. The crude product was chromatographed (AcOEt/hexane 15 %) to obtain afforded 818 mg (91 %) of **12**: IR (CCl_4) 1690; ^1H NMR ($CDCl_3$) 0.87 (s, 4 H), 1.94-2.10 (m, 4 H), 2.20-2.36 (m including signals at 2.27, 2.28, and 2.31, 8 H).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.21; H, 9.85.

Preparation of 13a. To a suspension of (4-methoxyphenylmethyl)triphenylphosphonium bromide (1.22 g, 2.92 mmol) in 6 mL THF was added butyllithium (1.9 mL, 2.92 mmol, 1.56 M in hexane). The resulting mixture was stirred for 10 min and then cooled to -72 °C. To this was added a solution of the ketone **12** (371 mg, 2.26 mmol) in 0.8 mL of THF, and the solution was warmed to room temperature and then heated to reflux for 9 h. Bulk of the solvent was removed in vacuo, hexane was added, and precipitate was removed by filtration. The crude product was chromatographed (AcOEt/hexane 1 %) to obtain 265 mg (44 %) of **13a**: IR (CCl_4) 1600, 1535, 1500, 1395, 1245; ^1H NMR (CCl_4) 0.74 (br s, 4 H), 1.60-2.07 (m, 4 H), 2.07-2.57 (m, 8H), 3.86 (s, 3 H), 6.00 (s, 1 H), 6.63 (d, J = 8.6 Hz, 2 H), 6.93 (d, J = 8.6 Hz, 2 H); GC-MS (EI) m/e 268 (M^+, 49.1%), 239 (100%), 225, 159, 121, 91.

Anal. Calcd for $C_{19}H_{24}O$: C, 85.02; H, 9.01. Found: C, 85.21; H, 9.00.

Preparation of 13b. To a solution of diisopropylamine (1.7 mL, 12.0 mmol) in 35 mL of THF at -72 °C was added a solution of butyllithium (7.7 mL, 12 mmol, 1.56 M in hexane), and the solution was warmed to 0 °C and was stirred for 30 min. The mixture was cooled to -72 °C, and ethyl trimethylsilyl acetate (2.2 mL, 12.0 mmol) was added. The ketone **12** (0.98 g, 6.0 mmol) was added after 15 min. The resulting solution was stirred for 1 h at this temperature, 1 h at -23 °C, and 1 h at room temperature, and was quenched with water. The organic layer was extracted with ether, and the combined organic layer was washed with brine, and dried over Na_2SO_4. The crude product was chromatographed (AcOEt/hexane 2%) to obtain 1.34 g (95%) of **13b**: IR (neat) 3040, 1705, 1625, 1095, 1045; ^1H NMR ($CDCl_3$) 0.76 (s, 4 H), 1.24 (t, J = 2.0 Hz, 3 H), 1.80-2.06 (m, 4 H), 2.26 (br s having 4 shoulders, 6 H), 2.68 (distorted t, J = 5.9 Hz, 2 H), 4.05 (q, J = 2.0 Hz, 2 H), 5.43 (s, 1 H); GC-MS (EI) m/e 234 (M^+, 35.9%), 161, 119, 105, 91 (100%), 79, 41.

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.47. Found: C, 76.72; H, 9.44.

Preparation of 6. A stirred suspension of sodium amide (219 mg, 5.6 mmol) and methyltriphenylphosphonium tetrafluoroborate (1.53 g, 5.6 mmol) in 4 mL of benzene was heated at 60 °C for 1 h. To this solution, ketone **12** was added and the resulting solution was stirred for 5 h at 65 °C. After removal of the solvent in vacuo, hexane was added and the precipitate was removed by filtration, and hexane was removed in vacuo. The resulting oil was chromatographed (hexane) to obtain 453 mg (89%) of **6**: IR (CCl_4) 3011, 3007, 980, 875; ^1H NMR ($CDCl_3$) 0.80 (dd, J = 2.1, 1.1 Hz, 4 H), 1.69-1.89 (m, 4 H), 2.07-2.20 (m, 4 H), 2.20-2.35 (m, 4 H), 4.50 (d, J = 1.1 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 1.64 (t), 27.51 (t), 33.93 (t), 35.30 (t), 108.43 (t), 116.45 (s), 128.50 (s), 151.40 (s).

Anal. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.18. Found: C, 88.55; H, 11.02.

General Procedure of Transition Metal Catalyzed Reaction of 13. To a suspension of $PdCl_2(PPh_3)_2$ (14.0 mg, 0.02 mmol) in 1.7 mL of degassed toluene was added diisobutylaluminum hydride (0.04 mL, 0.04 mmol, 1.0 M in hexane) and **13b** (0.23 mL, 0.2 mmol, 0.88 M in toluene) at -72 °C. The reaction vessel was sealed, and heated for 11 h at 130 °C. The black metallic solid formed during the reaction was filtered through silica gel, and the filtrate was concentrated in vacuo. The resulting oil was chromatographed (AcOEt/hexane 3 %) to obtain 46.1 mg (98 %) of **17**: IR (neat) 3060, 1723, 1240, 1162, 880; ^1H NMR ($CDCl_3$) 1.26 (t, J = 7.4 Hz, 3 H), 1.21-1.37 (m, 4 H),

1.37-1.44 (m, 3 H), 1.44-1.74 (m, 3 H), 2.03 (distorted d, J = 7.6 Hz, 1 H), 2.11 (distorted d, J = 6.7 Hz, 1 H), 2.28-2.38 (m, 2 H), 3.36 (tt, J = 13.4, 3.4 Hz, 1 H), 4.06-4.46 (m, 2 H), 4.78 (dd, J = 4.6, 2.7 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 14.53 (q), 25.09 (t), 25.64 (t), 35.33 (t), 35.80 (t), 39.50 (t), 40.14 (t), 41.81 (t), 50.70 (d), 60.15 (t), 64.12 (s), 64.53 (s), 103,15 (t), 158.31 (s) (carbonyl carbon could not be located); the C-H COSY spectrum also confirmed the structural assignment. . GC-MS (EI) m/e 234 (M^+, 8.8 %), 189, 161 (100%), 119, 105, 91.

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.47. Found: C, 77.10; H, 9.45.

[3.3.3]Propellane 8. IR (CCl_4) 1625, 1220; ^1H NMR ($CDCl_3$) 1.43 (t, J = 7.4 Hz, 2 H), 1.28-2.72 (m involving br s at 1.47 and 1.48, 12 H), 2.29 (dt, J = 7.4, 1.7 Hz, 2 H), 4.72 (dd, J = 3.6, 1.7 Hz, 2 H); ^{13}C NMR (toluene-d_8) 27.00 (t), 34.94 (t), 38.38 (t), 41.79 (t), 41.91 (t), 62.65 (s), 64.86 (s), 103.08 (t), 114.92 (s); GC-MS (EI) m/e 162 (M^+, 26.8 %), 147, 134 (100%), 119, 105, 91, 79.

Propellane 22. To a solution of **17** (13.1 mg, 56 micro mol) in 0.4 mL of $CDCl_3$ was added trifluoroacetic acid (50 micro L, 0.65 mmol), and the resulting solution was quenched by sat. $NaHCO_3$ after 4 h. The mixture was extracted with ether, and the combined organic phase was washed with brine, dried over $MgSO_4$. The crude product was chromatographed (AcOEt/hexane 2.5 %) to obtain 11.6 mg (89 %) of **23.** IR (CCl_4) 1720, 1170; ^1H NMR ($CDCl_3$) 1.31 (t, J = 7.2 Hz, 3 H), 1.67 (dd, J = 3.3, 1.5 Hz, 3 H), 1.16-1.92 (series of m, 12 H), 3.26 (dd, J = 2.1, 1.5 Hz, 1 H), 4.19 (dq, J = 7.2, 1.9 Hz, 2 H), 5.00 (dd, J = 3.3, 2.1 Hz, 1 H); GC-MS (EI) m/e 234 (M^+, 4.5 %), 161 (100%), 133, 119, 117, 105, 91.

Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.47. Found: C, 76.60; H, 9.20.

[3.3.3]Propellane 221. IR (CCl_4) 2930, 2850, 1401; ^{1} NMR ($CDCl_3$) 1.34-1.60 (m, 12 H), 1.62 (dt, J = 2.3, 1.5 Hz, 3 H), 2.16 (quint, J = 2.3 Hz, 2 H), 5.04 (dq, J = 2.3, 1.5 Hz, 1 H); GC-MS (EI) 162 (M^+, 29.8 %), 147, 133 (100%), 105, 91.

Methylation of Propellane 17. To a stirred solution of diisopropylamine (10.9 micro L, 78 micro mol) and hexamethylphosphoramide (13.6 micro L, 78 micro mol) in 0.05 mL of THF at 0 °C was added to n-butyllithium (0.05 mL, 78 micro mol, 1.66 M in hexane), and the solution was stirred an additional 0.5 h and was cooled to -72 °C. To this solution was added a solution of **17** (12.3 mg, 52 micro mol) in 0.03 mL of THF, and the resulting solution was gradually warmed over to -30 °C, and then cooled again to -72 °C. To this solution was added iodomethane (16.2 micro L, 260 micro mol), and the solution was gradually raised to room temperature over 2 h. The reaction mixture was quenched by sat. ammonium chloride and was extracted with ether. The organic layer was washed with sat. $NaHCO_3$ and brine, and was dried over Na_2SO_4. The crude product was purified by silica gel chromatography (elution with AcOEt/hexane 2.5 %) to obtain 9.5 mg (74 %) of the methylated product: IR (CCl_4) 1730, 1220, 1150, 1120; ^1H NMR ($CDCl_3$) 1.14 (d, J = 0.7 Hz, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 1.1-1.8 (series of m, 10 H), 2.05 (d, J = 15.4 Hz, 1 H), 1.94-2.12 (m, 1 H), 2.17-2.34 (m, 1 H), 3.03 (br d, J = 15.4 Hz, 1 H), 4.13 (dq, J = 7.1, 1.9 Hz, 2 H), 4.77 (br d, J = 2.1 Hz, 1 H), 4.79 (br d, J = 2.5 Hz, 1 H); GC-MS (EI) 248 (M^+, 5.5 %), 233, 219, 205, 175 (100%), 174.

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.22; H, 9.86.

12-Nor-13-acetoxymodhephene (24). To a solution of the above methylated product (5.5 mg, 22 micro mol) in 0.4 mL of $CDCl_3$ was added trifluoroacetic acid (50 micro L), and the resulting solution was quenched with sat. $NaHCO_3$ after 3 h. The mixture was extracted with ether, the combined organic layer washed with brine, and dried over Na_2SO_4. The solvent was removed in vacuo to obtain 8.1 mg of a colorless oil. The oil was dissolved in 0.1 mL of ether, and added to an ethereal solution of ca. 10 mg of LAH. The resulting suspension was stirred for 2 h, and quenched with 1N aq. HCl. The mixture was extracted with ether, and the organic layer was washed with sat. $NaHCO_3$ and brine, and dried over $MgSO_4$. The solvent was removed in vacuo to obtain 4.7 mg of a colorless oil, which was used without further purification. To the crude product in 15 micro L of pyridine was added 5 micro L of acetic anhydride, and the resulting solution was stirred for 2 h. The crude product was purified by silica gel chromatography to obtain 3.5 mg (64 %) of **24**: IR

(CCl_4) 1742, 1245, 1132; 1H NMR ($CDCl_3$) 1.05 (s, 3 H), 1.11-2.04 (series of m, 12 H), 1.61 (d, J = 6.7 Hz, 3 H), 2.06 (s, 3 H), 3.86 (d, J = 3.6 Hz, 1 H), 3.99 (d, J= 3.6 Hz, 1 H), 5.82 (d, J = 1.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 13.83 (q), 21.24 (q), 22.49 (q), 26.90 (t), 27.19 (t), 36.96 (t), 37.72 (t), 37.81 (t), 38.04 (t), 50.03 (s), 71.32 (t), 72.35 (s), 72.67 (s), 129.37 (d), 138.24 (s).

Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.37; H, 9.74. Found: C, 77.10; H, 9.74.

General Procedure of Photocyclization of 13. A solution of **13b** (24.7 micro L, 0.1 mmol) in degassed 2 mL of acetonitrile in a Pyrex test tube was irradiated for 2.5 h. The organic solvent was removed in vacuo, and the resulting oil was chromatographed (AcOEt/hexane 2 %) afforded 21.0 mg (90 %) of **25b**. IR (CCl_4) 1720, 1155, 1045; ^1H NMR ($CDCl_3$) 0.31-0.34 (m, 1 H), 0.44-0.50 (m, 2 H), 1.12-1.22 (m, 3 H), 1.23 (t, J = 6.8 Hz, 3 H), 1.31-1.39 (m, 2 H), 1.52-1.58 (m, 2 H), 1.79-1.89 (m, 3 H), 2.01 (br quint, J = 6.3 Hz, 1 H), 2.07-2.22 (m, 2 H), 2.82 (s, 1 H), 4.04-4.13 (m, 2 H); ^{13}C NMR ($CDCl_3$) 8.73 (t), 10.59 (t), 14.59 (q), 23.11 (s), 30.14 (t), 30.72 (t), 34.54 (t), 35.68 (t), 35.74 (t), 39.53 (t), 49.56 (d), 57.88 (s), 58.17 (s), 59.54 (t), 172.66 (s); GC-MS (EI) m/e 234 (M^+, 7.4 %), 205, 161, 108 (100%), 91, 80, 79.

Anal. Calcd for $C_{15}H_{22}O$: C, 76.88; H, 9.47. Found: C, 76.70; H, 9.43.

[2.3.3]Propellane 25a. IR (CCl_4) 1605, 1505, 1460, 1245, 1175, 1140; ^1H NMR ($CDCl_3$) 0.25-0.36 (m, 1 H), 0.49-0.66 (m, 2 H), 1.00-2.40 (series of m, 13 H), 3.16 (s, 1 H), 3.79 (s, 3 H), 6.85 (d, J = 8.8 Hz, 2 H), 7.14 (d, J = 8.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 10.42 (t), 11.96 (t), 26.67 (s), 29.00 (t), 29.41 (t), 32.50 (t), 36.06 (t), 36.15 (t), 40.35 (t), 52.19 (d), 55.31 (q), 57.35 (s), 59.42 (s), 112.45 (s), 113.27 (d), 130.69 (d), 133.11 (s); GC-MS (EI) m/e 268 (M^+, 76.2 %), 239 (100%), 225, 160, 145, 139, 121, 91.

Anal. Calcd for $C_{19}H_{24}O$: C, 85.02; H, 9.01. Found: C, 84.98; H, 9.02.

References

1 Desplongchamps, P. Aldrichimica Acta **1984**, 17, 59.
2 Daettig, K.; Dallaire, C.; Pitteloud, R.; Deslongchamps, P. Tetrahedron Lett. **1987**, 28, 5249; Daettig, K.; Marinier, A.; Pitteloud, R.; Deslongchamps, P. ibid. **1987**, 28, 5253; Berube, G.; Deslongchamps, P. ibid. **1987**, 28, 5255.
3 Takahashi, T.; Shimizu, K.; Doi, T.; Tsuji, J.; Fukazawa, Y. J. Am. Chem. Soc. **1988**, 110, 2675.
4 Yamago, S.; Nakamura, E. J. Chem. Soc., Chem. Commun. **1988**, 1112.
5 Reviews: Ginsburg, D. Topics in Current Chemistry **1987**, 137, 1. Odaira, Y.; Tobe, Y. Yukigouseikagaku (J. Syn. Org. Chem. Jpn.) **1981**, 39, 1163.
6 Isolation: Zalkow, L. H.; Harris, R. N.; Van Derveer, D. J. Chem. Soc., Chem. Commun. **1978**, 420.
7 Synthesis: (a) Karpf, M.; Dreiding, A. S. Tetrahedron Lett. **1980**, 4569. (b) Smith, A. B.; Jerris, P. J. J. Am. Chem. Soc. **1981**, 103, 194. (c) Schostarez, H.; Paquette, L. A. J. Am. Chem. Soc. **1981**, 103, 722. (d) Oppolzer, W.; Marazza, F. Helv. Chim. Act **1981** 64, 1575. (e) Oppolzer, W.; Baettig, k. ibid, **1981**, 64, 2489. (f) Wender, P. A.; Dryer, G. B. J. Am. Chem. Soc. **1982**, 104, 5805. (g) Wrobel, J.; Takahashi, T.; Honkan, V.Lannoye, G.; Cook, J. M.; Bertz, S. H. J. Org. Chem. **1983**, 48, 139. (h) Tobe, Y.;Yamashita, S.; Yamashita, T.; Kakiuchi, K.; Odaira, Y. J. Chem. Soc., Chem. Commun. **1984**, 1259. (g) Wilkening, D.; Mundy, B. P. Tetrahedron Lett. **1984**, 4619. (h) Mundy, B. P.; Wilkening, D.; Lipkowitz, K. B. J. Org. Chem. **1985**, 50, 5727. (i) Mehta, G.; Subrahmanyam, D. J. Chem. Soc., Chem. Commum. **1985**, 768. (j) Reviews: Paquette, L. A. Topics in Current Chemistry **1987**, 119, 1. Paquette, L. A.; Doherty, A. M. "Polyquinane Chemistry", Springer Verlag, Berlin, 1987.
8 Bohlmann, F.; Zdero, C.; Bohlmann, R.; King, R. M.; Robinson, H. Phytochemistry **1980**, 19, 579.
9 Bishop, R.; Lender, A. E. Aust. J. Chem. **1979**, 32, 2675.
10 Cf. Nakamura, E.; Isaka, M.; Matsuzawa, S. J. Am. Chem. Soc. **1988**, 110, 1297.
11 Binger, P.; Buch, H. M. Topics in Current Chemistry **1987**, 135, 77. Trost, B. M. Angew. Chem. Int. Ed. Engl., **1986**, 25, 1.
12 Schlosser, M.; Schaub, B. Chimia **1984**, 36, 396.
13 Utimoto, K.; Tamura, M.; Sisido, K. Tetrahedron **1973**, 29, 1169.
14 (a) Noyori, R.; Odagi, T.; Takaya, H. J. Am. Chem. Soc. **1970**, 92, 5780. (b) Binger, P. Angew. Chem. Int. Ed. Engl. **1972**, 11, 309.
15 Binger, P.;Schuchardt, U. ibid **1977**, 16, 249.
16 Binger, P.; Schuchardt, U. Chem. Ber. **1980**, 113, 3334.
17 Intramolecular cyclization of methylenecyclopropane related to **21** has recently been reported: Lewis, R. T.; Motherwell, W. B.; Shipman, M. J. Chem. Soc., Chem. Commun. **1988**, 948.
18 Cf. Shimada, J.-i.; Hashimoto, K.; Kim, B. H.; Nakamura, E.; Kuwajima, I. J. Am. Chem. Soc. **1984**, 106, 1759.