SYNTHESIS OF DEUTERATED METHYLENECYCLOHEXANES, METHYLENEDECALINS AND TARAXASTEROLS

Hsiu-pu Daniel Lee, Larry S. Eichmeier and David M. Piatak*
Department of Chemistry, Northern Illinois University
DeKalb, IL 60115 USA

SUMMARY

Taraxasterols specifically labelled at various ring E sites were synthesized as were cyclohexanes and decalins substituted by a methyl group and an exocyclic methylene moiety similar to the ring E system of this terpene. Preparation of deuterated analogs in which the deuterium is located beta to the exocyclic double bond was accomplished by catalytic reduction of the corresponding unsaturated ketone, followed by removal of the label at the alpha carbon and introduction of the exocyclic methylene with a Wittig reaction. Compounds labelled on the exocyclic methylene moiety were afforded by a Wittig reaction of the appropriate ketone with (methyl-d_3)triphenylphosphonium bromide. Taraxasterol trideuterated alpha to the double bond was prepared by DCl exchange of the ketone followed by a Wittig reaction.

Key Words: taraxasterol, deuterium, exocyclic methylene, terpene

INTRODUCTION

During studies on the isolation of plant sterols from Cirsium arvense or Canadian thistle, we isolated (1) the somewhat ubiquitous pentacyclic triterpene, taraxasterol (1a). Difficulties with a secure identification by common physical constants prompted us to use mass spectral analysis in order to provide a final structural assignment. It was noted there were only a few

0362-4803/83/121395-11$01.10

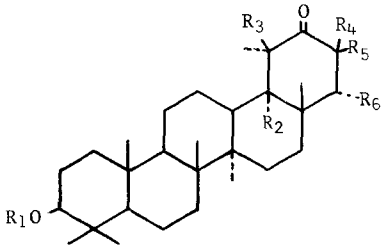
Received August 1, 1983
Revised September 21, 1983

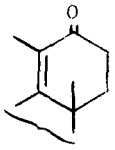
distinct signals in the high m/z range and those at m/z 315(M-111) and 357(M-69) were especially prominent and not attributable to simple losses. Since these signals could provide a means of readily identifying this terpene when admixed with others, we undertook a study (2) on the origin of these fragments in taraxasterol and their occurrence and relation to similar signals in compounds with the same structural features as ring E of taraxasterol. To fully elucidate the fragmentation patterns taraxasterols, cyclohexanes, and decalins appropriately deuterated at certain positions were required. In this paper we would like to describe the site specific syntheses of deuterated compounds used in our study (2) by methods which can be applied generally and conveniently to similar compounds. Undeuterated compounds not prepared previously by other means are also included.

RESULTS AND DISCUSSION

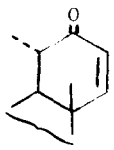
The route for each of the taraxasterols, namely, 30,30-d_2 1b, 19,21,21-d_3 1c, 18α-d_1 1d, and 22α-d_1 1e started with 20-ketone 1f which can be readily prepared by RuO_4 oxidation (3) of taraxasterol acetate (1g). Wittig reaction of 1f with $\emptyset_3P{=}CD_2$ formed C-30 dideuterated 1b. It was accompanied, though, by monodeuterated 1h and nondeuterated taraxasterol in a 55:30:15 ratio as indicated by analysis (4) of the M+2, M+1, and M signals in a mass spectrum and by integration of an nmr spectrum. Most likely, the mono- and nondeuterated species occur from exchange of the Wittig ylid with solvent impurities, which are exaggerated by the small scale of the reaction. Absence of any significant M+3 signals in the mass spectrum discounted exchange of ylid with hydrogens alpha to the ketone at C-18 and C-22, before the ylid had a chance to react with the ketone.

Synthesis of trideuterated 1c was begun by replacement of the hydrogens adjacent to the ketone in 1f with deuterium by exchange with DCl/D_2O in CE_3CH_2OD. The trideuterated ketone 1i was then reacted with $\emptyset_3P{=}CH_2$ to yield 1c. Mass spectral data indicated 1c and 1i had the same deuterium





2



3

1a $R_1=R_2=R_3=R_4=R_5=R_6=H;R_7=CH_2$

b $R_1=R_2=R_3=R_4=R_5=R_6=H;R_7=CD_2$

c $R_1=R_2=R_6=H;R_3=R_4=R_5=D;R_7=CH_2$

d $R_1=R_3=R_4=R_5=R_6=H;R_2=D;R_7=CH_2$

e $R_1=R_2=R_3=R_4=R_5=H;R_6=D;R_7=CH_2$

f $R_1=Ac;R_2=R_3=R_4=R_5=R_6=H;R_7=O$

g $R_1=Ac;R_2=R_3=R_4=R_5=R_6=H;R_7=CH_2$

h $R_1=R_2=R_3=R_4=R_5=R_6=H;R_7=CHD$

i $R_1=R_2=R_6=H;R_3=R_4=R_5=D;R_7=O$

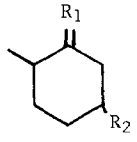
j $R_1=Ac;R_2=R_4=R_5=R_6=H;R_3=Br;R_7=O$

k $R_1=Ac;R_2=R_3=R_5=R_6=H;R_4=Br;R_7=O$

l $R_1=R_3=R_4=R_5=R_6=H;R_2=D;R_7=O$

m $R_1=R_2=R_3=R_4=R_5=H;R_6=D;R_7=O$

n $R_1=R_3=R_4=R_5=D;R_2=R_6=H;R_7=O$



4a $R_1=CH_2;R_2=H$

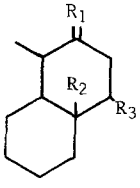
b $R_1=O;R_2=H$

c $R_1=CD_2;R_2=H$

d $R_1=CH_2;R_2=D$

e $R_1=O;R_2=C_5H_{10}N^+Me\ I^-$

f $R_1=O;R_2=D$



5a $R_1=CH_2;R_2=R_3=H$

b $R_1=CH_2;R_2=Me;R_3=H$

c $R_1=O;R_2=R_3=H$

d $R_1=O;R_2=Me;R_3=H$

e $R_1=CD_2;R_2=R_3=H$

f $R_1=CD_2;R_2=Me;R_3=H$

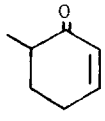
g $R_1=CH_2;R_2=H;R_3=D$

h $R_1=CH_2;R_2=Me;R_3=D$

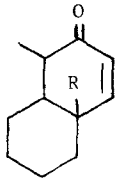
i $R_1=O;R_2=H;R_3=C_5H_{10}N^+Me\ I^-$

j $R_1=O;R_2=H;R_3=D$

k $R_1=O;R_2=Me;R_3=D$



6



7a R=H

b R=Me

incorporation, confirming again exchange between the ylid and hydrogens alpha to the ketone is negligible.

Introduction of deuterium at C-18 and C-22 of taraxasterol (1d and 1e, respectively) required that α,β-unsaturated ketones 2 and 3 be formed first by bromination of 1f, then dehydrobromination of the resultant mixture of C-19 and C-21 bromoketones 1j and 1k, respectively. The ketones were separated and isolated by successive preparative thin layer chromatography (TLC). The ratio of 2 and 3 was found to depend upon the bromination reaction time. The bromo intermediate 1j, which forms 2, was produced in a 3.5:1 ratio over isomer 1k, which forms 3, when the reaction time was limited to 5 min. and in a 1:1.4 ratio when the time was extended to 40 min. Apparently, 1j is kinetically favored while 1k is thermodynamically favored. Reduction of 2 and 3 with deuterium over 10% Pd-C, followed by removal of the deuterium on the C-19 or C-21 carbon through base exchange, yielded 1l and 1m readily. Stereochemistry of the deuterium at C-18 or C-22 was assigned as depicted because the molecules would be able to approach the catalyst only opposite the 17β-axial methyl group. The sequence to 1d and 1e was completed with a Wittig reaction of the respective ketones 1l and 1m with $\emptyset_3P{=}CH_2$ in good yield and isotopic purity.

To provide information about the generality of various mass spectral fragmentations noted with taraxasterol, compounds with structural features similar to ring E of taraxasterol, i.e., cyclohexene 4a (5), decalins 5a and 5b, and several deuterated versions, were synthesized. Again, the corresponding saturated ketones 4b, 5c (6), and 5d (6) provided the starting point for the desired labelled materials. Wittig reaction of each with $\emptyset_3P{=}CD_2$ yielded methylene-deuterated 4c, 5e, and 5f, respectively, in $d_2{:}d_1{:}d_0$ ratios of 75:24:1, 95:4:1, and 68:23:9, as determined by nmr and mass spectral data (4). Exchange between the ylid and solvent seems to have taken place again but not to the extent seen with taraxasterol (1b). Overall yields were not as good as with the nondeuterated ylid-probably due to a deuterium isotope effect.

Cyclohexene 4d and decalin 5g and 5k analogs monodeuterated on the ring two

carbons removed from the double bond were also used in the study (2). As in the taraxasterol series the corresponding ketones were converted to their α,β-unsaturated versions 6, 7a, and 7b. To obtain 6 and 7a the saturated ketones 4b and 5c were brominated as their trimethylsilyl enolates, then dehydrobrominated as reported (6). Since neither unsaturated ketone could be obtained in a pure state, both were purified (7) via the β-methylpiperidyl iodides 4e (7) and 5i. The dimethyl unsaturated ketone 7b was prepared as reported (6) by simple bromination-dehydrobromination of 5d and had a glc determined purity of 97%. Reduction of all three unsaturated ketones with deuterium catalyzed by tris(triphenylphosphine)rhodium chloride (8), which is highly stereoselective, and removal of the deuterium adjacent to the ketone with base gave 4f, 5j, and 5k in high yield and isotopic purity. A Wittig reaction of each with $\emptyset_3P{=}CH_2$ completed the synthesis to 4d, 5g, and 5h.

METHODS AND MATERIALS

Commercial reagents, such as 1,2-dimethoxyethane (DME), tetrahydrofuran (THF), and ether, were distilled from lithium aluminum hydride prior to use. n-Butyllithium was doubly titrated using 1,1-dibromoethane before reactions. Extraction solutions were dried over $MgSO_4$ before evaporation.

Melting points (mp) were taken on a Fisher-Johns apparatus and are not corrected. Infrared (ir) spectra were recorded with a Perkin-Elmer 237B or a Beckman IR-8 spectrometer. Nuclear magnetic resonance (nmr) spectra were obtained with a Varian A-60A instrument on liquid samples sealed in a capillary tube or on solids dissolved in deuteriochloroform with tetramethylsilane as an internal standard. Mass spectra were taken on a Hitachi-Perkin-Elmer RMU-6E instrument at 70 e.v. Deuterium incorporation was determined from mass spectra as described (4).

Gas liquid chromatography (glc) analyses were performed on a Varian Aerograph 2700 instrument equipped with flame ionization detectors and interfaced to an Autolab IV integrator on either column A: 1/8 inch by 6 ft. SS

column of 3% SE-30 on 60/80 chrom. W; or column B: 1/8 inch by 7 ft. SS column of 1.5% DEGS on 80/100 chrom. W (acid washed) at the indicated temperatures. Preparative glc was done on a Varian Aerograph 1700 instrument equipped with a thermal conductivity detector and a 1/4 inch by 8 ft. column of 20% SE-30 on 60/80 chrom. W. Thin layer chromatography (TLC) separations were carried out on E. Merck HF_{254} silica gel with 20% ethyl acetate-hexane.

EXPERIMENTAL

Preparation of α,β-Unsaturated Terpenes 2 and 3

A solution of terpene ketone 1f (160mg) in gl. HOAc (10mL) was stirred vigorously while Br_2 in gl. HOAc (0.5M; 0.68mL) was added. After 7 min. the solution was evaporated *in vacuo* to give a mixture of bromoketones 1j and 1k. The crude product was dissolved in DME (4mL), Li_2CO_3 (0.27g) and LiBr (0.32g) were added, and the mixture was heated at 120-125°C for 5 hr. The reaction was cooled, water (20mL) added, and the terpenes isolated with ether. The product was purified repeatedly by preparative TLC to yield 47mg of 2, mp 230-233°C; ir ($CHCl_3$) 3010, 1727, 1672 cm^{-1}; Calcd. for $C_{30}H_{40}O_3$: C,79.44, H,10.32. Found: C,79.58; H,10.76% and also 19mg. of 3, mp 228-230°; ir ($CHCl_3$) 3060, 1725, 1668 cm^{-1}; nmr δ5.90 and 6.74 (d,1H each); Found: C,79.94; H,10.21%.

Catalytic Reduction of α,β-Unsaturated Ketones with Deuterium

a/ 5-d_1-2-Methylcyclohexanone (4f). Tris(triphenylphosphine)rhodium chloride (0.29g) was dissolved in acetone (30mL) in a flask connected to an atmospheric pressure reduction apparatus equipped with a 25mL gas reservoir and Hg-filled leveling bulb. The flask was evacuated, then deuterium gas was introduced. This sequence was repeated twice more to ensure removal of all other gases. Stirring was initiated and continued until a constant pressure of deuterium was reached (1 hr). 6-Methyl-2-cyclohexenone (6) (1.02g) was added and stirring under a deuterium atmosphere continued until gas absorption ceased (5.5 hr). The mixture was then concentrated *in vacuo* and the residue passed through a short silica gel column (15g) with pentane. Distillation gave 0.85g (80%) of 2,3-d_2-6-methylcyclohexanone, bp 65-67°C (22mm), which was used directly below.

The product was dissolved in 0.5% KOH-MeOH (15mL), and the solution was heated at reflux for 2 hr. The cooled solution was extracted with pentane and the pentane layer washed with water, dried, and fractionated to give 0.80g of deuterated ketone 4f, bp 67-68°C (22mm); ir 2180 (w), 2720 cm^{-1}; m/z 113 (M^+) d_1 incorporation 95+%.

b/ 4-d_1-1-Methyl-trans-2-decalone (5j). Unsaturated ketone 7a (1.01g) (6) was reduced with $(C_6H_5P)_3RhCl$ (0.15g) in acetone (20mL) as described above but for 35 hr. The reaction residue was passed through an alumina column (activity I) with hexane. Removal of the hexane yielded 1.00g which was treated with 0.5% KOH-MeOH (40mL) at reflux for 2 hr. Recovery of the product and distillation gave 0.53g (52%) of 5j, bp 73-74°C (0.25mm) [reported (9) for undeuterated ketone, bp 66-67°C (0.07mm)]; ir (neat) 2170 (w), 1715 cm^{-1}; nmr δ1.05 (d,3H), 1.2-2.5 (m,14H); m/z 167 (M^+) d_1 incorporation 95+%.

c/ 4-d_1-1,10-Dimethyl-trans-2-decalone (5k). A sample of 7b (2.04g) (6) was reduced by $(C_6H_5P)_3RhCl$ (0.25g) in acetone (35mL) as described above for 5j. Solvent removal afforded 2.04g of dideuterated product which was subsequently exchanged by 0.5% KOH-MeOH (175mL) as above. A total of 1.13g (55%) of deuterated decalone 5k, bp 82-83°C (0.6mm) [reported (9) for undeuterated ketone, bp 75°C (0.2mm)]; ir (neat) 2150(w), 1708 cm^{-1}; m/z 181 (M^+) d_1 incorporation 96+%.

d/ 22-d_1-3β-Hydroxy-30-nor-20-oxo-18α,19β_H,22β_H-ursane (1m). To a suspension of 10% Pd-C (3mg) in cyclohexane (2mL) which had been stirred under a deuterium gas atmosphere for 4 hr. was added unsaturated ketone 3 (19mg). The mixture was then stirred for 48 hr. under deuterium, the catalyst was collected by filtration, and the solvent removed *in vacuo*. The residue was dissolved in 10% methanolic KOH (5mL) and heated at reflux for 5 hr. The cooled reaction mixture was evaporated to dryness, and the product was isolated with ether and washed with water, dil. HCl, and water. Removal of the solvent gave 15mg of 1c, mp 224-228°C [reported (10) for undeuterated ketone, mp 228°C]; ir ($CHCl_3$) 3460 (broad), 2125 (w), 1695 cm^{-1}; m/z 429 (M^+) d_1 incorporation 95+%.

e/ 18α-d_1-3β-Hydroxy-30-nor-20-oxo-19β_H ursane (11). The reduction and exchange procedures used for 1c were employed with 25mg of ketone 2, 5mg of 10% Pd-C and 3mL of cyclohexane. The final product 11 (19mg) was purified by preparative TLC, mp 226-228°C; ir ($CHCl_3$) 3430 (broad), 2150 (w), 1700 cm^{-1}; m/z 429 (M^+) d_1 incorporation 94+%.

Wittig Reactions with Cyclohexanones

a/ 5-d_1-2-Methylmethylenecyclohexane (4d). An ether solution (0.5mL) of n-butyllithium (6.3mmol) was added slowly to a stirred suspension of $CH_3(C_6H_5)_3PBr$ (2.29g; 6.36mmol) in ether (15mL) under nitrogen. The yellow mixture was stirred for 2 hr at ambient temperature, then a solution of deuterated cyclohexanone 4f (0.57g; 5.0mmol) in ether (10mL) was added dropwise. After the reaction had been stirred for 16 hr, the ether was removed in vacuo and replaced with THF (10mL). The mixture was then refluxed for 7 hr. The product was recovered from the cooled, water-diluted mixture with pentane. Distillation yielded 0.31g of liquid with bp 117-135°C. Glc (B, 95°C) indicated a mixture of 78% of product 4d and 22% of starting ketone 4f. Preparative glc (95°C) was used to isolate pure 4d with bp 125-126°C; ir (neat) 3060 (w), 2160 (w), 1648 (s), 918 cm^{-1}; nmr δ 1.08 (d,3H), 4.6 (m,2H); m/z 111 (M^+) d_1 incorporation 95+%.

b/ 2-Methyl-(methylene-d_2)cyclohexane (4c). The same reaction conditions and workup as above were employed except the starting ketone was 2-methylcyclohexanone (0.33g; 2.9mmol) and the ylid was generated from $CD_3(C_6H_5)_3PBr$ (1.52g; 4.2mmol). Quantities for the other reagents and solvents were taken in the respective mole-mole or mole-volume ratios used above. Glc analysis (A, 95°C) of the residue (0.30g) indicated it to be composed of 34% of desired product 4c and 66% of starting ketone. Preparative glc (90°C) gave a pure sample, bp 125-126°C; nmr δ4.5 integration ratio of 1:154 to other proton signals; m/z 112 (M^+) d_2:d_1:d_0 incorporation 75:24:1

c/ 2-Methylmethylenecyclohexane (4a). The above reaction conditions and requirements were repeated with 2-methylcyclohexanone (1.25g; 11.2mmol) and

$CH_3(C_6H_5)_3PBr$ (4.50g; 40mmol) yielding 1.24g of 4a, bp 122-124°C [reported (5) bp by a totally different method 124.5-124.8°C (745mm)].

Wittig Reactions with Methyldecalones

a/ 4-d_1-1-Methyl-2-methylene-trans-decalin (5g). An ether solution (0.5mL) of n-butyllithium (8mmol) was introduced into mixture of $CH_3(C_6H_5)_3PBr$ (3.26g; 9.1mmol) in ether (15mL) under nitrogen, and the yellow mixture was stirred for 2 hr. Ketone 5j (0.38g; 2.3mmol) in ether (10mL) was added, and stirring was continued for 16 hr. The ether was replaced by THF (25mL), and the solution was refluxed for 7 hr. The reaction was then diluted with water, and the product was recovered with hexane to afford 0.35g of 5g, bp 71-73°C (3.1mm); ir (neat) 3170 (w), 2150 (w), 1775 (w), 1645 (s), 908 cm^{-1}; nmr δ1.05 (d,3H), 4.7(m,2H), m/z 165 (M^+). Glc analysis (A, 150°C) indicated a single compound present.

b/ 1-Methyl-2-(methylene-d_2)-trans-decalin (5e). This reaction was based upon 0.54g (3.3mmol) of methyldecalone 5c (6) and 1.35g (3.8mmol) of $CD_3(C_6H_5)_3PBr$ and performed as above. Glc (A, 150°C) of the crude product (0.50g) indicated a mixture of 47% of desired 5e and 53% of ketone 5c. An analytical sample secured by preparative glc (160°C) had bp 72-73°C (3.0mm); nmr δ4.7 integration ratio of 1:189 to other proton signals; m/z 166 (M^+) d_2:d_1:d_o incorporation 95:4:1

c/ 1-Methyl-2-methylene-trans-decalin (5a). The above reaction was conducted with ketone 5c (1.1g; 6.7mmol) (6) and $CH_3(C_6H_5)_3PBr$ (12.0g; 33.4mmol) and gave 1.1g of decalin 5a, bp 71-71°C (2.8mm); ir (neat) 3080, 1650, 908 cm^{-1}; nmr δ4.6 (m,2H); Calcd. for $C_{12}H_{20}$: C,92.31; H,7.69. Found: C,92.60; H,7.40%.

Wittig Reactions with Dimethyldecalones

a/ 4-d_1-1,10-Dimethyl-2-methylene-trans-decalin (5h). The ylid was prepared first by stirring n-butyllithium (11.2mmol) in ether (7.0mL) with $CH_3(C_6H_5)_3PBr$ (4.44g; 12.4mmol) suspended in ether (10mL) as above. A solution of ketone 5k (1.12g; 6.2mmol) in ether (15mL) was used in the reaction which was conducted as for 5g. Distillation of the recovered product yielded 0.72g (65%) of 5h, bp 68-71°C (1mm); ir (neat) 3090, 2150, 1775, 1645, 902 cm^{-1}; nmr δ1.01 (s,3H), 1.04 (d,3H), 4.66 (m,2H); m/z 179 (M^+) d_1 incorporation 95+%.

b/ 1,10-Dimethyl-2-(methylene-d_2)-trans-decalin (5f). This reaction was conducted as above with 0.56 (3.1mmol) of 5d (6) and 1.44g (4.0mmol) of $CD_3(C_6H_5)_3PBr$ and gave 0.55g of crude product composed of 61% product 5f and 39% starting ketone as indicated by glc (A, 170°C). A pure sample secured by preparative glc (180°C) had bp 68-70°C (1mm); nmr δ4.6 integration ratio of 1:55 with other protons; m/z 180 (M^+) d_2:d_1:d_o incorporation 68:23:9.

c/ 1,10-Dimethyl-2-methylene-trans-decalin (5b). The above procedure with 0.04g (5.78mmol) of 5d (6) and 3.60g (100mmol) of $CH_3(C_6H_5)_3PBr$ afforded 0.84g (82%) of colorless 5b, bp 68-70°C (1mm) which analyzed by glc (A, 170°C) as 91% 5b and 9% 5d. Preparative glc (180°C) gave pure material with bp 69-70°C (1 mm); ir (neat) 1772, 1648, 906 cm^{-1}; Calcd. for $C_{13}H_{22}$: C,87.56; H,12.44. Found: C,87.71; H,12.39%.

Wittig Reactions with Ketones from Taraxasterol

The reaction procedures employed for the decalins were also used for the formation of the various taraxasterols except as noted.

a/ 18α-d_1-Taraxasterol (1d). 18α-d_1-Ketone 11 (19mg; 0.04mmol) and $CH_3(C_6H_5)_3PBr$ (280mg; 0.80mmol) gave 13mg of 1d, mp 222-225°C [reported (10) mp undeuterated taraxasterol 224°C]; ir ($CHCl_3$) 3470 (broad), 2150 (w), 1645, 900 cm^{-1}; m/z 427 (M^+); TLC identical with taraxasterol.

b/ 22α-d_1-Taraxasterol (1e). From the reaction of 1m (15mg; 0.03mmol) and $CH_3(C_6H_5)_3PBr$ (230mg; 0.6mmol), deuterated taraxasterol 1e (14mg) was obtained after preparative TLC. It had mp 222-224°C; ir 3485 (br), 2125 (w), 1650 (m), 910 cm^{-1}; m/z 427 (M^+).

c/ 30,30-d_2-Taraxasterol (1b). Ketone 1f (14mg; 0.03mmol) with $CD_3(C_6H_5)_3PBr$ (0.64mg; 1.8mmol) formed 13mg of 1b (after preparative TLC), m.p. 223-224°C; m/z 428 (M^+) d_2:d_1:d_o incorporation 55:30:15.

Preparation of 19,21,21-d_3-Taraxasterol (1c)

All procedures were performed in a dry box containing a positive helium atmosphere.

A solution of ketone 1f (25mg) in absolute ethanol-d (2.5mL) containing 38%

DCl-D_2O (5 drops) was refluxed for 2 hr. The terpene was recovered from the cooled reaction by precipitation with D_2O and collection by filtration. The exchange procedure was repeated twice more with the recovered hydroxy ketone 1n. After 1n had been dried, it was dissolved in ether (20mL) and added to the ylid from $CH_3(C_6H_5)_3PBr$ (2.0g; 0.0056mmol) and n-butyllithium (5.0mL; 1.6M) in ether (22mL) prepared as above. The reaction was then continued and the terpene recovered as described above. Chromatography of the recovered material by preparative TLC gave 15mg of 1c, mp 222-224°C; m/z 429 (M^+) d_3 incorporation 87+%; identical to taraxasterol by mixed mp and TLC.

ACKNOWLEDGEMENTS

We wish to thank the USPHS (CA12618) and the American Cancer Society for partial support of this work.

REFERENCES

1. Piatak D. M. and Eichmeier L. S. - Trans. Ill. State Acad. Sci. 64: 300 (1971).
2. Lee H. D., Eichmeier, L. S., and Piatak D. M. - Org. Mass Spectrom., submitted.
3. Piatak D. M., Bhat H. B., and Caspi E. - J. Org. Chem. 34:112 (1969).
4. Karliner J. and Djerassi C. - J. Org. Chem. 31:194 (1966).
5. Hammond G. S. and Nevitt T. P. - J. Amer. Chem. Soc. 76:414 (1954).
6. Sasson I. and Labovitz J. - J. Org. Chem. 40:3670 (1975).
7. Stork G. and White W. N. - J. Amer. Chem. Soc. 78:4604 (1956).
8. Djerassi C. and Gutzwiller S. - J. Amer. Chem. Soc. 88:4537 (1966).
9. Stork G., Rosen P., Goldman N., Coombs R. V., and Tsuji J. - J. Amer. Chem. Soc. 87:275 (1965).
10. Simonsen J. and Ross W. C. J. - The Terpenes, Vol IV, Cambridge University Press, Cambridge, 1957.