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INOKOSTERONE, AN INSECT METAMORPHOSING SUBSTANCE FROM *ACHYRANTHES FAURIEI*

ABSOLUTE CONFIGURATION AND SYNTHESIS†

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Abstract—Inokosterone, a phytoecdysone isolated from *Achyranthes fauriei* (Amaranthaceae), has been partially acetylated to give the 2,26-diacetate (**4**) which has been converted into methyl 5 - acetoxy - 4 - methylpentanoate (**7**), showing no apparent $[\alpha]_D$, and 2β - acetoxy - 3β,14α - dihydroxy - 5β - pregn - 7 - ene - 6,20 - dione (**8**). Chemical and physicochemical studies have shown the configurations at C-20 and C-22 to be *R*. Inokosterone has thus been concluded to be a mixture of C-25 epimers of (20*R*,22*R*) - 2β,3β,14α,20,22,26 - hexahydroxy - 5β - cholest - 7 - en - 6 - one (**1**). After the synthesis of the model compound, a C-25 epimeric mixture of (20*R*,22*R*) - 3β,20,22,26 - tetrahydroxy - 5α - cholestane (**23**), inokosterone has been synthesized via (20*R*) - 2β,3β,14α,20 - tetrahydroxy - 20 - formyl - 5β - pregn - 7 - en - 6 - one (**25**) by Grignard reaction with 4 - (tetrahydropyran - 2 - yloxy) - 3 - methylbutynylmagnesium bromide (**15**) followed by hydrogenation and hydrolysis. The use of an NMR shift reagent with the inokosterone acetates (**9**, **29**) and the optical activity measurement of α - methylglutaric acid (**3**) derived from inokosterone have established that inokosterone is a 1:2 mixture of the C-25 *R* and *S* epimers.

Inokosterone is a phytoecdysone originally isolated from the roots of *Achyranthes fauriei* Léveillé et Vaniot (Amaranthaceae) and its gross structure has been assumed as 2,3,14,22,26 - hexahydroxy - cholest - 7 -en- 6 - one.[1] However, the alternative structure, 2,3,14,20 - tetrahydroxy - 20 - (1,5 - dihydroxy - 2 - methylpentyl) - pregn - 7 - en - 6 - one, could not be completely excluded by the evidence available, though it is highly unlikely from a viewpoint of biogenesis. Transformation of inokosterone to 1(or 3) - formyl - 14α - hydroxy - A - norpregna - 1(or 2),8 - diene - 6,20 - dione and the ORD of inokosterone[1] indicate the absolute configurations at C-5, C-10, C-13, and C-14 to be the same as the insect moulting hormone ecdysterone, (20*R*,22*R*) - 2β,3β,14α,20,22,25 - hexahydroxy - 5β - cholest - 7 - en - 6 - one. However, no conclusive proof for the complete stereochemistry of inokosterone has been given. The present paper provides evidence for the stereostructure of inokosterone.‡

The structure and absolute configuration of the side-chain was first to be established. Previously inokosterone was oxidized with sodium metaperiodate to give the hydroxy-aldehyde (**2**) which on further oxidation with potassium permanganate in water yielded (±) - α - methylglutaric acid (**3**).[1] It was possible, however, that the asymmetric center α to the CO was racemized in aqueous solution which was made alkaline during oxidation. In order to eliminate this possibility, the hydroxy-aldehyde (**2**) was oxidized with chromic acid in acetic acid, under which conditions the asymmetry in a $-CH_2-C^*H(CH_3)-CH_2OH$ moiety is known to be retained during the oxidation process to the $-CH_2-C^*H(CH_3)-COOH$ system. α-Methylglutaric acid (**3**) thus obtained did not give an apparent $[\alpha]_D$ value. In confirmation, inokosterone was partially acetylated giving the 2,26-diacetate (**4**). Periodate oxidation of the diacetate (**4**) yielded the acetoxy-aldehyde (**5**). On oxidation with chromic acid, the acetoxy-aldehyde (**5**) afforded the acetoxy-acid (**6**) which was treated with diazomethane to furnish the acetoxy-ester (**7**). There had no opportunity for the $-CH_2-C^*H-(CH_3)-CH_2OH$ moiety to racemize during the conversion of inokosterone to the ester (**7**). The properties of the ester (**7**) agreed in all respect with those of methyl 5 - acetoxy - 4 - methylpentanoate produced from diosgenin except for the rotation values, i.e. the valerate (**7**) from inokosterone exhibited no apparent optical activity whereas the valerate from diosgenin is dextrorotatory ($[\alpha]_{300}$ + 13.0°). These facts corroborate the side-chain structure of inokosterone and further indicate that inokosterone consists of a mixture of C-25 epimers. The stereostructure of the nucleus was next examined. The above periodate oxidation of the diacetate (**4**) afforded, as the sole nucleus fragment, a C_{21} methyl ketone which was identified as the known 2β - acetoxy - 3β,14α - dihydroxy - 5β - pregn - 7 - ene - 6,20 - dione (**8**),[2] establishing the absolute stereostructure of the tetracycle. The remaining problem, the absolute configurations at C-20 and C-22, has been solved as follows. (1) Inokosterone, as ecdysterone, on treatment with acetone in the presence of acid readily gives the 20,22-acetonide, and on periodate oxidation rapidly consumes 2 moles of the reagent.[1] Likewise, inokosterone diacetate (**4**) rapidly consumes 1 mole of periodate. These behaviors indicate that the glycol systems at C-20 and C-22 in both ecdysones are situated in the same environment. (2) The chemical shifts of the C-18 and C-21 Me hydrogen signals of inokosterone and its 2,3,22,26 - tetraacetate§ (**9**) (1.19 and 1.52 ppm, and

†Part XXIX in the Tohoku University series on "Steroids".

‡Part of the material reported herein formed the substance of a preliminary communication: *Tetrahedron Letters* 2475 (1968).

§The inokosterone 2,3,22,26 - tetraacetate (m.p. 165-168°), reported in the previous papers,[1] has later been found to be a mixture with an approximately equal amount of ecdysterone 2,3,22,25 - tetraacetate.

0.85 and 1.24 ppm, respectively), which are dependent on the configurations of the C-20 and C-22 hydroxyls,[3] coincide remarkably with those of ecdysterone and its 2,3,22,25 - tetraacetate (1.19 and 1.55 ppm, and 0.86 and 1.25 ppm, respectively). In addition, the chemical shift and splitting pattern of the C-22 hydrogen signal of the tetraacetate (**9**) (4.85 ppm, doublet of doublets, *J*9 and 2 Hz) are very similar to those of ecdysterone tetraacetate (4.84 ppm, doublet of doublets, *J*8 and 2 Hz). These observations demonstrate that the environments involving those hydrogens are the same in both ecdysones. Since the absolute configurations at C-20 and C-22 in ecdysterone are both *R*,[4,5] the above evidence shows that those in inokosterone are also *R*. The accumulated data lead to the conclusion that inokosterone is a mixture of C-25 epimers of (20*R*,22*R*) - 2β,3β,14α,20,22,26 - hexahydroxy - 5β - cholest - 7 - en- 6 - one (**1**).

After the elucidation of the stereochemistry of inokosterone, the ^{1}H NMR spectra of inokosterone and its derivatives were examined in expectation that they may provide evidence to distinguish the epimers. However, from the NMR spectra of inokosterone and its tetraacetate (**9**), no definite indication that they were mixtures was obtained (Fig. 1, A, B). The only sign, which might come from its heterogenous nature, was found in the C-26 hydrogen signal in the spectrum of the tetraacetate (**9**). Thus, although the signal in $CDCl_3$ appears basically to constitute an AB part of the ABX pattern, there are two additional peaks at the center (Fig. 1, B). Irradiation at the C-25 hydrogen (X part) resulted in the signal decoupled to an AB spectrum, but two additional peaks were still present (Fig. 1, C). Two additional peaks were also observed at the center of an AB part of the ABX type in the spectrum in C_6D_6 (Fig. 1, D) which was measured in

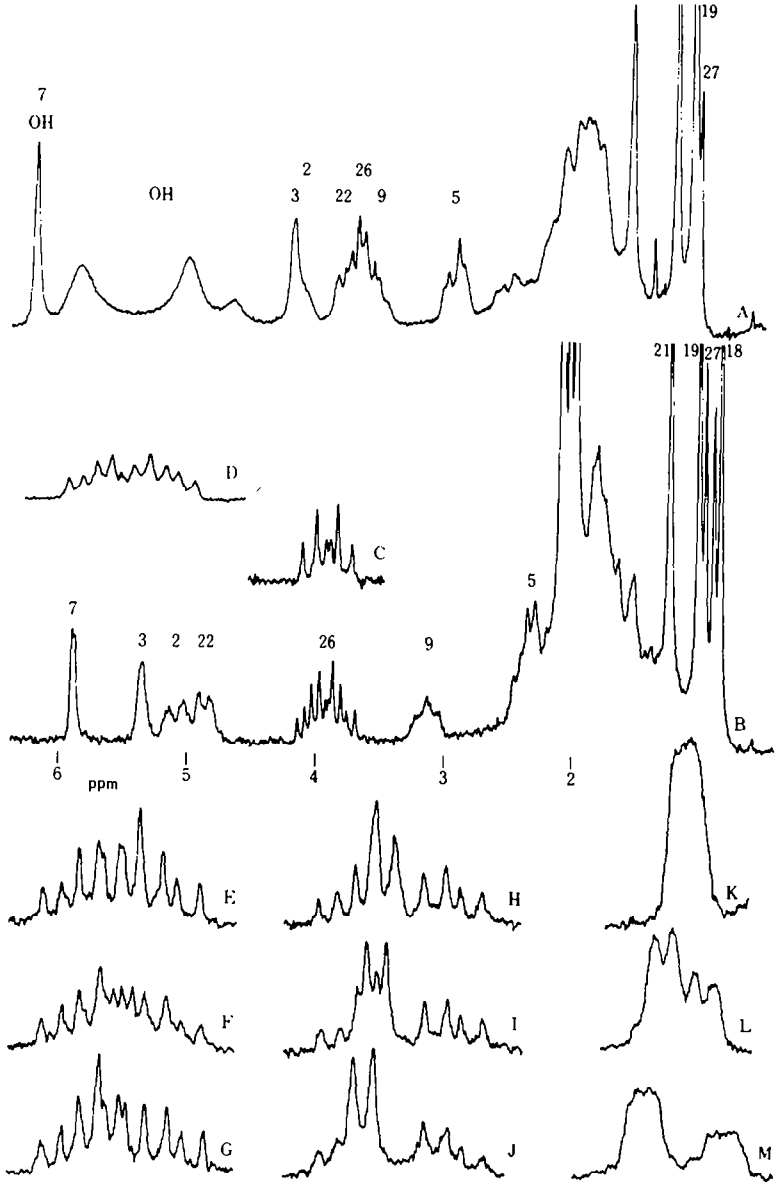
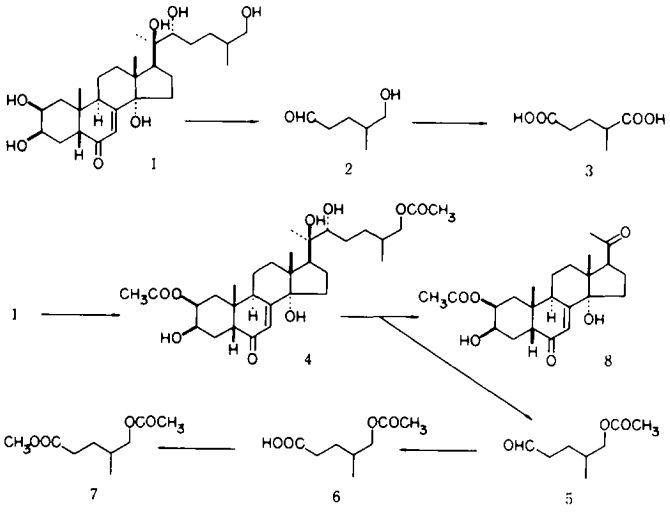


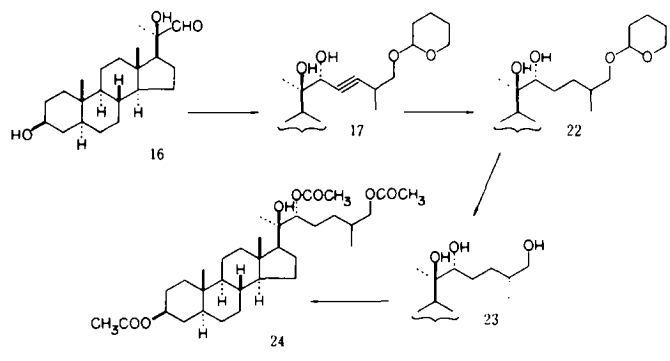
Fig. 1. ^{1}H NMR spectra of inokosterone and its acetates (100 MHz. The chemical shift scale applies to A, B, and C only. C–M: confined to the 26-H signal). A: inokosterone (C_5D_5N), B: the 2,3,22,26-tetraacetate ($CDCl_3$), C: the tetraacetate ($CDCl_3$, irradiated at 25-H), D: the tetraacetate (C_6D_6), E, F, G, H, I, J: the tetraacetate ($CDCl_3$, after addition of 0, 0.1, 0.2, 0.3, 0.5, 0.8 moles of Eu(tfc)$_3$, respectively), K, L, M: the 2,3,22-triacetate ($CDCl_3$, after addition of 0, 0.2, 0.4 moles of Eu(tfc)$_3$, respectively).



the hope that the two signals might be differently displaced. These observations, however, could not be rationalized at this stage and will be discussed later.

In order to obtain evidence for the epimeric nature of inokosterone, its total synthesis was then designed. Thus, combination of an optically active nucleus portion with a racemic side-chain portion would give a desired product inevitably a mixture of C-25 epimers. The procedure adopted here was that devised by Mori and Shibata[6] and applied by us.[3] Our plan consisted of the two phases, synthesis of the model compound, (20*R*,22*R*)-3β20,22,26-tetrahydroxy - 5α - cholestane (**23**), to examine if reactions would proceed satisfactorily, and synthesis of the final object, inokosterone. The nucleus portions (**16** and **25**) for these purposes have already been prepared.[3,6] (±) - 4 - Chloro - 1(tetrahydropyran - 2 - yloxy) - 2 - methylbutane (**12**) was derived from 4 - chloro - 2 - methyl - 1 - butene (**10**)[7] via 4 - chloro - 2 - methylbutan - 1 - ol (**11**). However, preparation of a Grignard reagent from the chloride (**12**) failed because the chloride (**12**) did not react with magnesium under normal conditions. Alternatively, (±) - 3 - methyl - 1 - butyn - 4 - ol (**13**) was prepared from 1-butyne by the known procedure[8] and it was converted into the tetrahydropyranyl ether (**14**). The ^{1}H NMR spectrum of the ether (**14**) exhibited two signals at 4.57 and 4.82 ppm attributed to hydrogens on C-2′ of the tetrahydropyran ring. Since the integrated area of the two signals corresponded to that of one hydrogen, the ether (**14**) is concluded to be a 7:3 mixture of two diastereomers. The ether (**14**) was treated with ethylmagnesium bromide to give 4 - (tetrahydropyran - 2 - yloxy) - 3 - methylbutynylmagnesium bromide (**15**).

For the preparation of the model compound (**23**), the Grignard reagent (**15**) was made to react with the hydroxy-aldehyde (**16**)[3] affording the acetylenic alcohol (**17**). It appears that only one counterpart of the Grignard reagent (**15**), formed from a diastereomeric ether (**14**) whose ^{1}H NMR signal for the C-2′ hydrogen occurred at 4.57 ppm, participated in this Grignard reaction, since the recovered ether (**14**) exhibited the ^{1}H NMR signals for the C-2′ hydrogen at 4.57 and 4.82 ppm in the area ratio *ca.* 1:1 and since the product (**17**) showed the NMR signal (1 H) for the C-2′ hydrogen only at 4.63 ppm. Catalytic hydrogenation was first carried out on (20*R*,22*R*) - 3β,20,22,26 - tetrahydroxy - 5α - cholest - 23 - yne 3,22,26 - triacetate (**20**), derived from the Grignard reaction product (**17**) via acetylation (to **18**), acid hydrolysis (to **19**), and acetylation, resulted in hydrogenolysis to give (20*S*) - 3β,20,26 - trihydroxy - 5α - cholestane 3,26 - diacetate (**21**). Hydrogenation of the acetylenic alcohol (**17**) over palladium-charcoal in ethanol in the presence of piperidine yielded the saturated derivative (**22**) which on treatment with hydrochloric acid furnished the tetraol (**23**), the model compound. This was further characterized as the 3,22,26 - triacetate (**24**). The tetraol (**23**) thus prepared must be a 1:1 mixture with respect to C-25 which was substantiated by the following ^{1}H NMR data. (1) The spectra of the triacetate (**24**) disclosed the signals for the C-27 methyl hydrogens of the two C-25 epimers separately at 0.88 and 0.90 ppm in $CDCl_3$, and at 0.81 and 0.83 ppm in C_6D_6. (2) Since the normal (unshifted) spectrum of the triacetate (**24**) in $CDCl_3$ showed a little information, the spectra in the presence of the chiral lanthanide shift reagent, Eu(tfc)$_3$ (tris - [3 -



(trifluoromethylhydroxymethylene) - *d* - camphorato]europium (III)[9], were examined (successful application of this reagent will be discribed later). Thus, the signals for the C-27 methyl hydrogens in the two epimers shifted differently upon incremental addition of the shift reagent giving two separate signals with the integrated area ratio of 1:1 as expected.

After the completion of the synthesis of the model compound (**23**), synthesis of inokosterone was next performed in order to obtain a synthetical evidence for its epimeric nature. Thus the Grignard reagent (**15**) was made to react with the hydroxy-aldehyde (**25**)[6] to give the acetylene alcohol (**26**) which was hydrogenated over palladium-charcoal in ethanol in the presence of piperidine affording the saturated ether (**27**). The behaviors on TLC and the spectral properties of the ether (**27**) were indistinguishable from those of the 26 - tetrahydropyranyl ether of the natural inokosterone. Treatment of inokosterone 26-tetrahydropyranyl ether (**27**) with hydrochloric acid in tetrahydrofuran furnished inokosterone. Since the intermediate (**25**) has been totally synthesized,[6] the above transformation has completed the total synthesis of inokosterone. However, the behaviors on TLC and the spectral properties of the intermediates (**26**, **27**) showed no heterogeous nature, so that the total synthesis did not provide evidence for the postulate that inokosterone is a mixture of C-25 epimers.

In expectation of obtaining information about the C-25 epimeric nature of inokosterone, an ^{1}H NMR study by use of a shift reagent was designed. Thus, a chiral lanthanide shift reagent would make the signals for hydrogens near the C-25 asymmetric carbon separate to recognize that inokosterone is a mixture. However, inokosterone itself is not a suitable compound for this purpose since it is not enough soluble in an appropriate solvent. Therefore, the ^{1}H NMR spectra of the tetraacetate (**9**) were determined after incremental addition of the chiral shift reagent, Eu(tfc)$_3$,[9] and the field positions of the lines were plotted as a function of metal concentration. As has been mentioned above, the pattern for the C-26 methylene hydrogen signal in the original spectrum could not be fully assignable. It was now revealed that the pattern consists of two AB parts of the ABX spectra. Thus, each resonance was affected by the contact shift to a different degree and one of the counterparts was changed from the AB part of the ABX type into an A_2 part of the A_2X type (Fig. 1, E→J). The most significant finding was that the integrated areas of the two AB parts (consequently the amounts of the two C-25 epimers) are not equal though the exact extimation could not be made due to overlapping. The signal pattern for the C-26 methylene hydrogens in the normal ^{1}H NMR spectrum of the tetraacetate (**9**) is now assigned. Concurrently, the signals originating from the C-27 methyl hydrogens and C-26 acetoxy-Me hydrogens, and even the C-21 methyl hydrogens, C-22 carbinyl hydrogen, and C-22 acetoxy-Me hydrogens of the two epimers showed different shift. Next, we planned the preparation of inokosterone 2,3,22 - triacetate (**29**) where larger contact shift of hydrogens near the asymmetric (C-25) carbon would be observed since the C-26 OH is free. This was achieved by acetylation of the tetrahydropyranyl ether (**27**) followed by acid hydrolysis of the resultant triacetate (**28**). In the normal ^{1}H NMR spectrum of the triacetate (**29**) in $CDCl_3$, all the assignable signals due to both epimers appeared at the identical positions except for the C-27 Me hydrogen doublets which occurred separately by 0.02 ppm. Upon incremental addition of the shift reagent, different contact shift was again observed on the signals for the C-21 Me hydrogens and the C-22 acetoxy-Me hydrogens as well as the C-26 methylene hydrogens and the C-27 Me hydrogens of the two C-25 epimers. In particular, the C-26 methylene hydrogen signals for both the epimers exhibited larger shift than those in the tetraacetate (**9**) and, owing to the occurrence of each signal as an A_2 part of the A_2X type, the two signals become separated (Fig. 1, K→M). The ratio of the integrated areas of the two signals approximated to 1:2 which must represent the ratio of the two epimers (Fig. 1, M). The signals associated with the C-21 Me hydrogens, which are located at a rather remote position from the asymmetric C-25 carbon in question, showed different contact shift, suggesting that some interaction was present between the C-20 hydroxyl or the C-22 acetoxyl, and the C-26 oxygen function.

Further examination was carried out if the heterogenous nature would reflect on the ^{13}C NMR spectra of inokosterone and its acetate. The present assignments of the spectra were performed by noise-decoupling and off-resonance experiments together with the chemical shift considerations in comparison with those of ponasterone A, (20*R*,22*R*) - 2β,3β,14α,20,22 - pentahydroxy - 5β - cholest - 7 - en - 6 - one,[10] and its 2,3,22-triacetate (Table 1). The results for inokosterone and ponasterone A, and inokosterone tetraacetate (**9**) and ponasterone A triacetate clearly show the identity ($\Delta\delta \pm 0.2$ ppm and ± 0.5 ppm, respectively) for the shieldings of C-1–C-21. The side-chain carbons could be assigned based on the accepted effects of a hydroxyl or an acetoxyl group introduced into C-26 of ponasterone A or its triacetate. The most remarkable finding of the spectra of inokosterone and its tetraacetate (**29**) is that the signals for C-22 and C-24–C-27 are split. As has been noticed before, since resonances which undergo significant chemical shift changes as a result of alteration in the configurations at C-20 and C-22 are those for C-20–C-23,[10] those splittings of the C-22 and C-24–C-27 resonances demonstrate that inokosterone is a mixture of C-25 epimers. It may be worthy to note that the resonances for C-22 carbons, which are rather remote from the C-25 asymmetric carbons, also suffer splitting.

Provided that the ratio of the two C-25 epimers constituting inokosterone were not 1:1 as has been shown above, the side-chain portions (**3**, **7**) derived from inokosterone must not be optically inactive though they were previously found to show no apparent optical activity. α-Methylglutaric acid (**3**) from inokosterone by periodate-chromic acid oxidation was reexamined and revealed to exhibit a weak optical activity ($[\alpha]_{300} + 27.7°$). Since *S*(+) - α - methyl - glutaric acid[11] is dextrorotatory

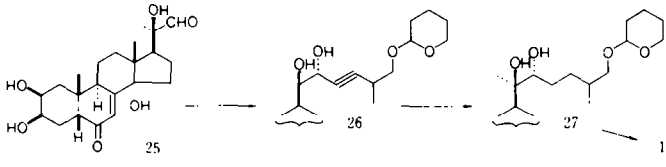


Table 1. Carbon-13 shieldings in the phytoecdysones and their acetates (C_5D_5N, ppm from TMS)

carbon No.	ponasterone A[10]	inokosterone	ponasterone A 2,3,22-triacetate	inokosterone 2,3,22,26-tetraacetate
1	37.9	37.9	34.4	34.2
2	68.0	68.0	69.4	69.2
3	68.0	68.0	67.9	67.7
4	32.4	32.2	29.3	29.3
5	51.3	51.3	51.7	51.5
6	203.5	203.3	201.4	200.9
7	121.7	121.6	121.7	121.5
8	166.0	165.9	166.3	165.8
9	34.4	34.4	34.4	34.5
10	38.7	38.6	38.7	38.5
11	21.4	21.4*[1]	21.1	20.8
12	31.8	31.7*[2]	31.8	31.6*
13	48.1	48.1	48.2	48.1
14	84.1	84.1	84.2	83.9
15	31.9	32.0*[2]	31.8	31.9*
16	21.4	21.6*[1]	22.4	22.1
17	50.0	50.0	50.4	50.2
18	17.9	17.8	18.0	17.8
19	24.4	24.4	24.2	24.0
20	76.7	76.7	76.3	76.0
21	21.1	21.1	21.1	21.1
22	76.7	77.2,77.4	79.8	79.2,79.6
23	30.2	30.1	28.9	28.2,28.3
24	37.1	31.7,32.0	36.4	30.6,30.9
25	28.1	36.4,36.7	28.1	32.4,32.7
26	22.3	67.3,68.0	22.4	68.9
27	23.3	17.0,17.8	23.2	16.6,17.4

The assignments of the asterisked signals are ambiguous and might have to be reversed.

($[\alpha]_{300}+89.6°$), it is calculated that inokosterone contains the C-25 *R* and *S* forms in the ratio 1:2, which is consistent with that from the above ^{1}H NMR evidence.

The biogenesis of inokosterone, the epimeric mixture, may be rationalized if it be assumed that ponasterone A is the immediate intermediate. The hydroxylation apparently occur somewhat without stereospecific control at the ends of the side-chain (i.e. C-26 and C-27), resulting in the formation of a mixture of the hydroxy-derivatives (**1**) which are epimeric with respect to the newly formed asymmetric carbon (C-25). This is interesting in contrast to the fact that although makisterone B[12] and amarasterone A[13] may most probably be biosynthesized from the hypothetical intermediates, (20*R*,22*R*) - 2β,3β,14α,20,22 - pentahydroxy - 5β - ergost - 7 - en - 6 - one and (20*R*,22*R*) - 2β,3β,14α,20,22 - pentahydroxy - 5β - stigmast - 7 - en - 6 - one, respectively, by the mechanisms similar to those operating in the biosynthesis of inokosterone, makisterone B and amarasterone A are known to be single substances.

EXPERIMENTAL

M.ps are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ unless stated otherwise. Chemical shifts are given in ppm from TMS, and coupling constants (*J*) and band widths at half height (w(1/2)) in Hz. Abbreviations: s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets, and br = broad peak. ^{13}C NMR spectra were taken as previously.[10] TLC was carried out on a silica gel GF_{254} (Merck) plate.

Periodate oxidation followed by chromic acid oxidation of inokosterone. Inokosterone (500 mg) was suspended in water (40 ml) and treated with $NaIO_4$ (500 mg) at room temp. for 1 hr. Ether extraction gave the product (160 mg) which in $CHCl_3$ was chromatographed over silica gel (4 g). Elution with $CHCl_3$-ether (1:1) afforded **2** (56 mg) as a colorless oil. To **2** (56 mg) in AcOH (2 ml) was added CrO_3 (0.1 g) in 80% AcOH (1 ml). The mixture was left standing at room temp. overnight, diluted with water, and extracted with AcOEt. The product was crystallized from benzene–hexane to give **3** as colorless prisms, m.p. 65.5–67.5°. $[\alpha]_{300}+27.7°$ (*c* 0.50, 95% EtOH). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1700, 935 (carboxyl).

Partial acetylation of inokosterone. Inokosterone (500 mg) in pyridine (8 ml) and $CHCl_3$ (8 ml) was treated with Ac_2O (2 ml) at 15° for 2 hr. After the mixture was diluted with water, the $CHCl_3$ layer was separated and the water layer was extracted with $CHCl_3$. The combined $CHCl_3$ soln was worked up in the usual manner and the solvent evaporated under reduced pressure. The residue (560 mg) in $CHCl_3$ was chromatographed over silica gel (16 g). The fraction (404 mg) eluted with ether was crystallized with AcOEt to give **4** as colorless prisms, m.p. 163–164°. IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1720, 1240 (acetoxyl), 1650 (enone), ^{1}H NMR: 3H s at 0.86 ($C_{(19)}\underline{H}_3$), 3H d at 0.93 (*J* 6, $C_{(27)}\underline{H}_3$), 3H s at 0.98 ($C_{(18)}\underline{H}_3$), 3H s at 1.19 ($C_{(21)}\underline{H}_3$), two 3H s's at 2.04, 2.06 ($OCOC\underline{H}_3$), 1H m at 3.3 ($C_{(22)}\underline{H}$), 3H m around 3.9–4.1 ($C_{(3)}\underline{H}$, $C_{(26)}\underline{H}_2$), 1H m at 4.95 ($C_{(2)}\underline{H}$), 1H d at 5.82 (*J* 2, $C_{(7)}\underline{H}$).

Periodate oxidation of inokosterone 2,26 - diacetate. To **4** (500 mg) in MeOH (10 ml) was added $NaIO_4$ (500 mg) in water (10 ml). The mixture was set aside under N_2 at room temp. for 1 hr and extracted with ether and then with AcOEt.

The ethereal extraction was chromatographed over silica gel (3 g).

Elution with ether gave **5** as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (acetoxyl, aldehyde).

AcOEt eluate was combined with the previous AcOEt extraction to give the product (345 mg) which on crystallization form MeOH afforded **8** as colorless needles, m.p. 240–242°. IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1736, 1241 (acetoxyl), 1695 (acetyl), 1640 (enone). Identification was performed in the usual criteria (m.p., m. m.p. and IR).

Chromic acid oxidation followed by methylation of 5-acetoxyl-4-methylpentanal. A mixture of **5**, above prepared, in ether (10 ml) and CrO_3 (120 mg) in 5 v/v% H_2SO_4 (2.4 ml) was stirred at room temp. for 1 hr. The ethereal soln was extracted with $NaHCO_3$ soln and the water soln was acidified with dil H_2SO_4 and extracted with ether to give **6** as a colorless oil (41 mg). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1710 (carboxyl, acetoxyl).

The acid **6** was treated with CH_2N_2 in ether and distilled under reduced pressure yielding **7** as a colorless oil. $[\alpha]_D$ 0 ± 1° (*c* 12.7, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (acetoxyl, methylate); ^{1}H NMR: 3H d at 0.95 (*J* 6, $C_{(4)}C\underline{H}_3$), 3H s at 2.03 ($OCOC\underline{H}_3$), 2H t at 2.33 (*J* 7, $C_{(2)}\underline{H}_2$), 3H s at 3.64 ($COOC\underline{H}_3$), 2H d at 3.89 (*J* 6, $C_{(5)}\underline{H}_2$).

Partial hydrolysis followed by methylation of 3β-acetoxy-16β-(5-acetoxy-4-methylpentanoyloxy)-pregn-5-en-20-one. 3β-Acetoxy-16β-(5-acetoxy-4-methylpentanoyloxy)-pregn-5-en-20-one (1.0 g), prepared from diosgenin, in AcOH (1 ml)

was refluxed for 2 hr. After AcOH was evaporated under reduced pressure, the residue was worked up in the usual manner. The acidic product was treated with CH_2N_2 in ether and distilled under diminished pressure to give (+)-7 as a colorless oil (0.2 g). $[\alpha]_{300}$ + 13.0° (*c* 12.7, MeOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1723 (acetoxyl, methylate); ^1H NMR ($CHCl_3$): 3H d at 0.94 (*J* 6, $C_{(4)}CH_3$), 3H s at 2.03 ($OCOCH_3$), 2H t at 2.33 (*J* 7, $C_{(2)}H_2$), 3H s at 3.65 ($COOCH_3$), 2H d at 3.89 (*J* 6, $C_{(5)}H_2$).

Acetylation of inokosterone. Inokosterone (50 mg) and Ac_2O (1 ml) in pyridine (2 ml) were heated at 100° for 1 hr. Working up in the usual way and extracted with AcOEt gave the product which was chromatographed on silica gel (5 g). Elution with $CHCl_3$–ether (10:1) and crystallization from MeOH to afford **9** as colorless needles, m.p. 113–115°. IR ν_{max}^{KBr} cm^{-1}: 3450 (OH), 1725, 1235 (acetoxyl), 1655 (enone); ^1H NMR: shown in Fig. 1B.

Hydroboration followed by hydrogen peroxide oxidation of 4 - *chloro* - 2 - *methyl* - 1 - *butene.* The chloride **10**[7] (7.2 g) in anhydr. ether (50 ml) was treated with $NaBH_4$ (3 g) at room temp. for 10 min. BF_3-etherate (3 g) was added to the mixture. After stirring at room temp. overnight, 30% H_2O_2 (15 ml) and 3N NaOH (15 ml) were added. The mixture was stirred at room temp. for 7 hr and then extracted with ether. Working up as usual afforded **11** as a colorless liquid (1.3 g). ^1H NMR (CCl_4): 3H d at 0.93 (*J* 6, $C_{(2)}CH_3$), 3H d at 3.43 (*J* 6, $C_{(1)}H_2$), 2H t at 3.55 (*J* 6, $C_{(4)}H_2$).

Tetrahydropyranyl ether formation of 4 - *chloro* - 2 - *methylbutan* - 1 - *ol.* The mixture of **11** (1.0 g), 2,3-dihydropyrane (0.32 g), and c. HCl (1 drop) were left standing at room temp. for 5 hr, made alkaline with $NaHCO_3$, and extracted with ether. Working up in the customary way furnished **12** as a colorless liquid. ^1H NMR (CCl_4): 3H d at 0.97 (*J* 6, $C_{(2)}CH_3$), 6H m at 2.9–3.9 ($C_{(1)}H_2$, $C_{(4)}H_2$, O–CH_2–), 1H br at 4.47 (w(1/2) 4, O–CH–O).

Attempted preparation of Grignard reagent from 4 - *chloro* - 1 - (*tetrahydropyran* - 2 - *yloxy*) - 2 - *methylbutane.* To Mg (53.4 mg) in THF (2 ml), **12** (413 mg) in THF (3 ml) was added at room temp. and the mixture was stirred. The reaction, however, did not occur.

Tetrahydropyranyl ether formation of 3 - *methyl* - 1 - *butyn* - 4 - *ol.* The butynol **13**[8] (13.1 g) was made to react with 2,3-dihydropyrane (13.9 g) in the presence of c. HCl (1 drop) at room temp. for 2 hr. After treatment with Na_2CO_3, distillation gave **14** as a colorless liquid (11.2 g), b.p.$_{-7}$ 75–96°. ^1H NMR (CCl_4): 3H d at 1.20 (*J* 7, $C_{(3)}CH_3$), 1H d at 1.92 (*J* 3, $C_{(1)}H$), 1H m at 2.6 ($C_{(3)}H$), 4H m around 3.1–3.9 ($C_{(4)}H_2$, O–CH_2), 0.7H br at 4.57 (w(1/2) 4, O–CH–O), 0.3H br at 4.82 (w(1/2) 9, O–CH–O).

Preparation of Grignard reagent from 4 - (*tetrahydropyran* - 2 - *yloxy*) - 3 - *methyl* - 1 - *butyne.* To EtMgBr (prepared from EtBr (6.25 g) and Mg (1.54 g) in THF (50 ml)) (6.5 ml), **14** (0.95 g) in THF (5 ml) was added and the mixture was stirred at room temp. for 1 hr yielding **15**.

Grignard reaction of (20R) - 3β,20 - *dihydroxy* - 20 - *formyl* - 5α - *pregnane with* 4 - (*tetrahydropyran* - 2 - *yloxy*) - 3 - *methylbutynylmagnesium bromide.* To **15**, prepared above, **16** (prepared from (20*S*) - 3β,20 - dihydroxy - 20 - vinyl - 5α - pregnane (200 mg) by ozonolysis) in THF (20 ml) was added under cooling with ice. The mixture was further stirred at room temp. overnight. After addition of 10% NH_4Cl (5 ml), extraction with ether followed by purification by means of preparative TLC afforded **17** as a colorless glass (146 mg). MS *m/e*: 498 (M^+-18), 483 (M^+-18-15), 465 (M^+-18 × 2-15), 415 (M^+-101), 414 (M^+-84-18), 397 (M^+-101-18), 396 (M^+-84-18 × 2), 319 (M^+-197), 301 (M^+-197-18), 257 (M^+-241-18). ^1H NMR: 3H s at 0.81 ($C_{(19)}H_3$), 3H s at 0.85 ($C_{(18)}H_3$), 3H d at 1.20 (*J* 7, $C_{(27)}H_3$), 3H s at 1.36 ($C_{(21)}H_3$), 5H m around 3.1–4.0 ($C_{(3)}H$, $C_{(26)}H_2$, O–CH_2), 1H br at 4.15 (w(1/2) 4, $C_{(22)}H$), 1H br at 4.64 (w(1/2) 7, O–CH–O).

Acetylation of (20R, 22R) - 3β,20,22 - *trihydroxy* - 26 - (*tetrahydropyran* - 2 - *yloxy*) - 5α - *cholest* - 23 - *yne.* The ether **17** (146 mg) in pyridine (2 ml) was made to react with Ac_2O (1 ml) at room temp. overnight. Working up in the customary manner yielded **18** as a colorless glass (162 mg). ^1H NMR: 6H s at 0.85 ($C_{(18)}H_3$, $C_{(19)}H_3$), 3H d at 1.20 (*J* 7, $C_{(27)}H_3$), 3H s at 1.42 ($C_{(21)}H_3$), two 3H s's at 2.03, 2.12 ($OCOCH_3$), 4H m around 3.1–4.1 ($C_{(26)}H_2$, O–CH_2), 2H br at 4.65 (w(1/2) 7, $C_{(3)}H$, O–CH–O), 1H d at 5.23 (*J* 2, $C_{(22)}H$).

Acid hydrolysis of (20R,22R) - 3β,22 - *diacetoxy* - 20 - *hydroxy* - 26 - (*tetrahydropyran* - 2 - *yloxy*) - 5α - *cholest* - 23 - *yne.* The ether **18** (156 mg) was treated with c. HCl (0.01 ml) in 10% aqueous THF at room temp. for 2 days. Ether extraction in the usual way afforded **19** as a colorless glass (146 mg). ^1H NMR: 6H s at 0.83 ($C_{(18)}H_3$, $C_{(19)}H_3$), 3H d at 1.18 (*J* 7, $C_{(27)}H_3$), 3H s at 1.42 ($C_{(21)}H_3$), two 3H s's at 2.03, 2.13 ($OCOCH_3$), 1H m at 4.65 ($C_{(3)}H$), 1H d at 5.20 (*J* 2, $C_{(22)}H$).

Acetylation of (20R,22R) - 3β,22 - *diacetoxy* - 20,26 - *dihydroxy* - 5α - *cholest* - 23 - *yne.* The diacetate **19** (146 mg) was treated with Ac_2O (1 ml) in pyridine (2 ml) to give the product (159 mg) which on crystallization from hexane-acetone furnished **20** as colorless needles (63 mg), m.p. 218°. MS *m/e*: 558 (M^+), 540 (M^+-18), 525 (M^+-18-15), 498 (M^+-60), 480 (M^+-60-18), 438 (M^+-60 × 2), 423 (M^+-60 × 2-15), 420 (M^+-60 × 2-18), 405 (M^+-60 × 2-18-15), 378 (M^+-60 × 3), 361 (M^+-197), 343 (M^+-197-18), 301 (M^+-197-60), 283 (M^+-197-60-18), 257 (M^+-241-60), 241 (M^+-317), 182 (M^+-361-15). IR ν_{max}^{KBr} cm^{-1}: 3470 (OH), 1710, 1215 (acetoxyl); ^1H NMR: 6H s at 0.85 ($C_{(18)}H_3$, $C_{(19)}H_3$), 3H d at 1.20 (*J* 7, $C_{(27)}H_3$), 3H s at 1.42 ($C_{(21)}H_3$), three 3H s's at 2.03, 2.09, 2.13 ($OCOCH_3$), 2H d at 4.03 (*J* 7, $C_{(26)}H_2$), 1H m at 4.7 ($C_{(3)}H$), 1H d at 5.23 (*J* 2, $C_{(22)}H$). (Found: C, 70.91; H, 9.22. $C_{33}H_{50}O_7$ requires: C, 70.93; H, 9.02%).

Catalytic hydrogenation of (20R,22R) - 3β,22,26 - *triacetoxy* - 20 - *hydroxy* - 5α - *cholest* - 23 - *yne over palladium* - *charcoal.* The acetylene **20** (48 mg) in EtOH (10 ml) was hydrogenated over 10% Pd-C (48 mg) in the presence of piperidine (1 drop) at room temp. for 3 hr. Working up in the customary manner, purification by preparative TLC, and crystallization from hexane-acetone gave **21** as colorless needles (35 mg), m.p. 145–146°. MS *m/e*: 486 (M^+-18), 471 (M^+-18-15), 426 (M^+-60-18), 411 (M^+-60-18-15), 361 (M^+-143). IR ν_{max}^{KBr} cm^{-1}: 3470 (OH), 1740, 1250 (acetoxyl); ^1H NMR: 6H s at 0.83 ($C_{(18)}H_3$, $C_{(19)}H_3$), 3H d at 0.93 (*J* 7, $C_{(27)}H_3$), 3H s at 1.26 ($C_{(21)}H_3$), two 3H s's at 2.03, 2.06 ($OCOCH_3$), 2H d at 3.91 (*J* 6, $C_{(26)}H_2$), 1H m at 4.7 ($C_{(3)}H$).

Catalytic hydrogenation of (20R,22R) - 3β,20,22 - *trihydroxy* - 26 - (*tetrahydropyran* - 2 - *yloxy*) - 5α - *cholest* - 23 - *yne over palladium-charcoal.* The acetylene **17** (28.3 mg) in EtOH (18 ml) was hydrogenated over 5% Pd–C (72 mg) in the presence of piperidine (0.01 ml) at room temp. for 1 hr. After filtration and evaporation, the product was purified by preparative TLC to yield **22** as a colorless glass (13.6 mg). MS *m/e*: 519 (M^+-1), 502 (M^+-18), 489 (M^+-18 × 2), 469 (M^+-18 × 2-15), 444 (M^+-58-18), 419 (M^+-101), 418 (M^+-84-18), 401 (M^+-101-18), 385 (M^+-84-18 × 2-15), 383 (M^+-101-18 × 2), 319 (M^+-201), 301 (M^+-201-18), 283 (M^+-201-18 × 2), 257 (M^+-245-18). ^1H NMR: 3H s at 0.81 ($C_{(19)}H_3$), 3H s at 0.87 ($C_{(18)}H_3$), 3H d at 0.93 (*J* 7, $C_{(27)}H_3$), 3H s at 1.20 ($C_{(21)}H_3$), 6H m around 2.9–4.1 ($C_{(3)}H$, $C_{(22)}H$, $C_{(26)}H_2$, O–CH_2), 1H br at 4.57 (w(1/2) 7, O–CH–O); ^1H NMR (C_5D_5N): 3H s at 0.83 ($C_{(19)}H_3$), 3H s at 1.17 ($C_{(18)}H_3$), 3H d at 1.23 (*J* 7, $C_{(27)}H_3$), 3H s at 1.52 ($C_{(21)}H_3$), 6H m around 3.0–4.1 ($C_{(3)}H$, $C_{(22)}H$, $C_{(26)}H_2$, O–CH_2), 1H br at 4.68 (w(1/2) 6, O–CH–O).

Acid hydrolysis of (20R,22R) - 3β,20,22 - *trihydroxy* - 26 - (*tetrahydropyran* - 2 - *yloxy*) - 5α - *cholestane.* The ether **22** (20.8 mg) was treated with c. HCl (0.01 ml) in 10% aqueous THF (2 ml) at room temp. for 48 hr. Dilution with water, extraction with *n*-BuOH, purification by preparative TLC, and crystallization from MeOH–AcOEt furnished **23** as colorless needles (5.8 mg), m.p. 203–204°. MS *m/e*: 435 (M^+-1), 418 (M^+-18), 403 (M^+-18-15), 400 (M^+-18 × 2), 285 (M^+-117-18 × 2), 257 (M^+-161-18). IR ν_{max}^{KBr} cm^{-1}: 3330 (OH); ^1H NMR (C_5D_5N) 3H s at 0.87 ($C_{(19)}H_3$), 3H s at 1.17 ($C_{(18)}H_3$), 3H d at 1.19 (*J* 7, $C_{(27)}H_3$), 3H s at 1.54 ($C_{(21)}H_3$), 4H m around 3.6–4.1 ($C_{(3)}H$, $C_{(22)}H$, $C_{(26)}H_2$). (Found: C, 71.79; H, 10.57. $C_{27}H_{48}O_4 \cdot H_2O$ requires: C, 71.32; H, 11.08%).

Acetylation of (20R,22R) - 3β,20,22,26 - *tetrahydroxy* - 5α - *cholestane.* The tetraol **23** (12.0 mg) and Ac_2O (0.3 ml) in pyridine (0.6 ml) were set aside at room temp. overnight. The mixture was worked up as usual to give the product which on crystallization from hexane-acetone yielded **24** as colorless needles (11.7 mg), m.p. 109–110°. MS *m/e*: 502 (M^+-60), 484 (M^+-60-18), 469 (M^+-60-18-15), 442 (M^+-60 × 2), 427 (M^+-60 × 2-15), 424 (M^+-60 × 2-18), 409 (M^+-60 × 2-18-15), 382 (M^+-60 × 3), 361 (M^+-201), 343 (M^+-201-18), 301 (M^+-201-60), 257 (M^+-245-60), 245 (M^+-317). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1740, 1235 (acetoxyl); ^1H NMR: 3H s at 0.85 ($C_{(19)}H_3$), 3H s at 0.87 ($C_{(18)}H_3$), 3H d at 0.95 (*J* 7, $C_{(27)}H_3$), 3H s at 1.26 ($C_{(21)}H_3$), three 3H's at 2.00, 2.03, 2.07 ($OCOCH_3$), 2H d at 3.85

(*J* 6, $C_{(26)}\underline{H}_2$), 2H m around 4.5–5.0 ($C_{(3)}\underline{H}$, $C_{(22)}\underline{H}$).

Grignard reaction of (20R) - 2β,3β,14α,20 - *tetrahydroxy* - 20 - *formyl* - 5β - *pregn* - 7 - *en* - 6 - *one with* 4 - (*tetrahydropyran* - 2 - *yloxy*) - 3 - *methylbutynylmagnesium bromide.* The formylpregnane **25**[6] (obtained by ozonolysis from (20*S*) - 2β,3β,14α,20 - tetrahydroxy - 20 - vinyl - 5β - pregn - 7 - en - 6 - one (80 mg)) was dissolved in THF (10 ml) and made to react with **15** (prepared as previously from **14** (685 mg)) under cooling with ice. The stirring was continued overnight. Treatment with 10% NH_4Cl, extraction with *n*-BuOH, and purification by preparative TLC afforded **26** as a colorless glass (32 mg).

Catalytic hydrogenation of (20R,22R) - 2β,3β,14α,20,22 - *pentahydroxy* - 26 - (*tetrahydropyran* - 2 - *yloxy*) - 5β - *cholest* - 7 - *en* - 23 - *yn* - 6 - *one.* The acetylene **26** (30 mg) in EtOH (19 ml) was hydrogenated over 5% Pd–C (75 mg) in the presence of piperidine (0.01 ml) at room temp. for 1 hr. Isolation in the usual manner furnished **27** as a colorless glass. MS *m/e*: 546 (M^+-18), 528 (M^+-18×2), 510 (M^+-18×3), 492 (M^+-18×4), 480 (M^+-18×3-15×2), 462 (M^+-102), 444 (M^+-102-18), 426 (M^+-102-18×2), 363 (M^+-201), 345 (M^+-201-18), 327 (M^+-201-18×2), 201 (M^+-363). ^{1}H NMR (C_5D_5N): 3H d at 0.99 (*J* 6, $C_{(27)}\underline{H}_3$), 3H s at 1.09 ($C_{(19)}\underline{H}_3$), 3H s at 1.22 ($C_{(18)}\underline{H}_3$), 3H s at 1.59 ($C_{(21)}\underline{H}_3$), 1H br at 4.63 (w(1/2) 8, O–C$\underline{H}$–O), 1H s at 6.20 ($C_{(7)}\underline{H}$). Identification with **27** from the natural inokosterone was carried out by comparison of TLC behaviors and the mass and ^{1}H NMR spectra.

Acid hydrolysis of inokosterone 26 - *tetrahydropyranyl ether.* The ether **27** (28 mg) was treated with c. HCl (0.01 ml) in 10% aqueous THF (2 ml) at room temp. for 48 hr. Extraction with *n*-BuOH and crystallization from MeOH–AcOEt gave **1** as colorless needles, m.p. 255°. MS *m/e*: 462 (M^+-18), 444 (M^+-18×2), 426 (M^+-18×3), 411 (M^+-18×3-15), 363 (M^+-117), 345 (M^+-117-18), 301 (M^+-161-18). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1640 (enone); ^{1}H NMR (C_5D_5N): 3H d at 1.01 (*J* 6, $C_{(27)}\underline{H}_3$), 3H s at 1.05 ($C_{(19)}\underline{H}_3$), 3H s at 1.16 ($C_{(18)}\underline{H}_3$), 3H s at 1.52 ($C_{(21)}\underline{H}_3$), 4H m around 3.5–4.0 ($C_{(9)}\underline{H}$, $C_{(22)}\underline{H}$, $C_{(26)}\underline{H}_2$), 1H m at 4.1 ($C_{(3)}\underline{H}$), 1H m at 4.18 ($C_{(2)}\underline{H}$), 1H s at 6.19 ($C_{(7)}\underline{H}$). The identity was substantiated by the usual criteria (TLC behaviors, m.p., m. m.p., mass and ^{1}H NMR spectra).

Tetrahydropyranyl ether formation of inokosterone. Inokosterone (250 mg) in THF (200 ml) was treated with 2,3-dihydropyrane (5 ml) in the presence of c. HCl (0.05 ml) at room temp. overnight. The product was extracted with *n*-BuOH and purified by preparative TLC to yield **27** as colorless glass (110 mg). MS *m/e*: 546 (M^+-18), 528 (M^+-18×2), 510 (M^+-18×3), 480 (M^+-18×3-15×2), 462 (M^+-102), 444 (M^+-102-18), 426 (M^+-102-18×2), 363 (M^+-201), 345 (M^+-201-18), 327 (M^+-201-18×2), 201 (M^+-363). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1645 (enone); ^{1}H NMR (C_5D_5N): 3H d at 0.99 (*J* 6, $C_{(27)}\underline{H}_3$), 3H s at 1.09 ($C_{(19)}\underline{H}_3$), 3H s at 1.22 ($C_{(18)}\underline{H}_3$), 3H s at 1.59 ($C_{(21)}\underline{H}_3$), 8H m around 3.4–4.3 ($C_{(2)}\underline{H}$, $C_{(3)}\underline{H}$, $C_{(9)}\underline{H}$, $C_{(22)}\underline{H}$, $C_{(26)}\underline{H}_2$, O–C$\underline{H}_2$), 1H br at 4.63 (w(1/2) 8, O–C$\underline{H}$–O), 1H s at 6.20 ($C_{(7)}\underline{H}$).

Acetylation of inokosterone 26 - *tetrahydropyranyl ether.* The ether **27** (212 mg) was treated with Ac_2O (1 ml) in pyridine (2 ml) at room temp. overnight. Isolation in the usual way and purification by preparative TLC gave **28** as a colorless glass (46 mg). ^{1}H NMR: 3H s at 0.87 ($C_{(18)}\underline{H}_3$), 3H d at 0.95 (*J* 6, $(C_{(27)}\underline{H}_3)$), 3H s at 1.04 ($C_{(19)}\underline{H}_3$), 3H s at 1.27 ($C_{(21)}\underline{H}_3$), three 3H s's at 2.03, 2.13, 2.13 (OCOC$\underline{H}_3$), 1H br at 4.58 (w(1/2) 7, O–C$\underline{H}$–O), 1H br at 4.85 (w(1/2) 16, $C_{(22)}\underline{H}$), 1H m at 5.08 ($C_{(2)}\underline{H}$), 1H br at 5.38 (w(1/2 6, $C_{(3)}\underline{H}$), 1H d at 5.87 (*J* 2, $C_{(7)}\underline{H}$).

Acid hydrolysis of inokosterone 26 - *tetrahydropyranyl ether* 2,3,22 - *triacetate.* The ether triacetate **28** (73 mg) was treated with c. HCl (0.01 ml) in 10% aqueous THF (2 ml) at room temp. for 2 days. Extraction with AcOEt and purification by preparative TLC furnished **29** as a colorless glass (11 mg). MS *m/e*: 570 (M^+-18×2), 528 (M^+-60-18), 510 (M^+-60-18×2), 495 (M^+-60-18×2-15), 447 (M^+-60-18×3-15×3), 429 (M^+-60-18×4-15×3), 355 (M^+-203-18-15×2), 327 (M^+-159-60×2). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1710, 1240 (acetoxyl), 1650 (enone); ^{1}H NMR: 3H s at 0.86 ($C_{(18)}\underline{H}_3$), 3H two d's at 0.91, 0.93 (*J* 6, $C_{(27)}\underline{H}_3$), 3H s at 1.04 ($C_{(19)}\underline{H}_3$),3H s at 1.26 ($C_{(21)}\underline{H}_3$), three 3H s's at 2.04, 2.15, 2.15 (OCOC$\underline{H}_3$), 1H m at 3.16 ($C_{(9)}\underline{H}$), 2H br at 3.48 (w(1/2) 11, $C_{(26)}\underline{H}_2$), 1H dd at 4.86 (*J* 9, 2, $C_{(22)}\underline{H}$), 1H m at 5.10 ($C_{(2)}\underline{H}$), 1H br at 5.39 (w(1/2) 9, $C_{(3)}\underline{H}$), 1H d at 5.92 (*J* 2, $C_{(7)}\underline{H}$).

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