biguous synthesis.[23] The formation of 1-cyano-7-methoxytetralin (**11a**) is most simply rationalized by a 1,2-alkyl shift in the spirocyclic intermediate **12** during oxidative quenching. The other isomer (**11b**) could arise from 1,2-cyanoalkyl migration in **12**, or from direct oxidative quenching of the fused ring intermediate, **13**.

Studies are in progress to further define the scope of the intramolecular carbanion additions to π-arene ligands and to understand the factors which influence ring size preferences.[24]

References and Notes

(1) For examples, see (a) B. Nicholls and M. C. Whiting, *J. Chem. Soc.*, 551 (1959); (b) J. F. Helling and G. G. Cash, *J. Organomet. Chem.*, **73**, C10 (1974); (c) A. Nesmeyanov, N. Volkenaw, and J. Balesova, *Tetrahedron Lett.*, 1725 (1963); (d) P. J. C. Walker and R. J. Mawby, *Inorg. Chim. Acta*, **7**, 621 (1973).

(2) These intermediates have been observed directly: M. F. Semmelhack, M. Yoshifuji, and H. T. Hall, Jr., *J. Am. Chem. Soc.*, **98**, 6387 (1976).

(3) M. F. Semmelhack, H. T. Hall, Jr., M. Yoshifuji, and G. Clark, *J. Am. Chem. Soc.*, **97**, 1247 (1975).

(4) Results, by G. Clark at Cornell, to be submitted for publication.

(5) Analogues of complexes **1a–c** where the –CN unit is instead $-CO_2R$ (R = Me, *t*-Bu) failed to give cyclization (enolate anion generated with lithium diisopropylamide, iodine oxidation[3]). High molecular weight material, presumably formed through intermolecular attack of the enolate anion on an arene ligand, comprised the product.

(6) Preliminary experiments with analogues of complexes **1a–c** where the $-CH_2CN$ unit is replaced by the 1,3-dithian-2-yl unit failed to show more than small amounts of intramolecular attack. Important side reactions include proton abstraction from the arene ring (*n*-butyllithium as base).[7]

(7) Cf. (a) A. Nesmeyanov, N. E. Kolobova, K. N. Anisimov, and Yu. V. Marakov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2665 (1968); (b) R. J. Card, PhD Thesis, Iowa State University, 1974.

(8) Satisfactory ^{1}H NMR, IR, and low resolution mass spectral data have been obtained for this compound.

(9) The air condenser is a 60-cm glass tube with $\overline{\text{T}}$ joints placed in one neck of the reaction vessel and capped with a stopcock for introduction of argon. The solvent condenses on the air-cooled surface and carries back most of the rapidly subliming chromium hexacarbonyl. This arrangement is effective and simpler than the Strohmeier apparatus.[10]

(10) W. Strohmeier, *Chem. Ber.*, **94**, 2490 (1976).

(11) R. A. Olofson and C. M. Dougherty, *J. Am. Chem. Soc.*, **95**, 582 (1973).

(12) Oxidative quenching involves addition of a solution of excess iodine in THF at −78 °C followed by warming at 25 °C for 4–8 h.

(13) The mixture was diluted with ether, washed sequentially with sodium thiosulfate solution, aqueous acid, and saturated salt solution, dried, and concentrated at reduced pressure. Short path distillation at ca. 100°/0.01 Torr afforded the product in >98% purity (GC, ^{1}H NMR).

(14) Hydrolysis (30% hydrogen peroxide, sodium hydroxide, 95% ethyl alcohol) produced the corresponding primary amide, mp 167–169 °C. Lit mp 165–167 °C (J. F. Bunnett and J. A. Skorcz, *J. Org. Chem.*, **27**, 3836 (1962)).

(15) The acid quenching involved cooling the solution of the η^5-cyclohexadienylchromium intermediate to −78 °C, adding 5 mole equiv. of trifluoroacetic acid, and allowing the mixture to stir at 0–25 °C for a few hours. Then excess iodine was added to cleave all organochromium π-complexes and isolation of the organic products proceeded as before.[12,13]

(16) The structure of **4c** was established by comparison of GC, ^{1}H NMR, and IR data with the same compound derived from intramolecular carbanion addition to a benzyne intermediate. Cf. R. W. Hoffman, "Dehydrobenzene and Cycloalkynes", Academic Press, New York, N.Y. 1967.

(17) Treatment of the mixture of isomers related to **5a** with DDQ in benzene at 80 °C for 1 h afforded the aromatic derivative **4a** in quantitative yield.

(18) The pair of diastereoisomers was separated by preparative GC. Satisfactory UV, IR, ^{1}H NMR, and mass spectral data were obtained for each isomer.

(19) Migration of the carbanion unit from one position to another in the η^5-cyclohexadienyl intermediate is also observed in intermolecular cases: M. Yoshifuji and G. Clark, unpublished observations at Cornell.

(20) Satisfactory combustion analysis was obtained for this compound.

(21) The heterocyclic analogue, 2,11-dithia[3.3]metacyclophane, is well known: Cf. R H. Mitchell and V. Boekelheide, *J. Am. Chem. Soc.*, **96**, 1547 (1974).

(22) S. J. Selikson and D. S. Watt, *J. Org. Chem.*, **40**, 267 (1975).

(23) We are indebted to Professor G. Marc Loudon for spectral data from 8-methoxy-1-tetralone.

(24) We are pleased to acknowledge support of the National Science Foundation through Grant CHE76-01112.

(25) Recipient of a Camille and Henry Dreyfus Teacher-Scholar Grant, 1973–1978.

(26) Visiting Professor, summer 1975 and 1976.

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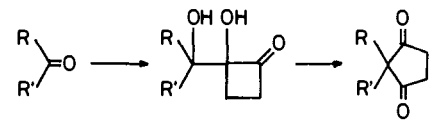
Geminal Acylation via Pinacol Rearrangement. Synthesis of Spiro[4.*n*] Ring Systems

Sir:

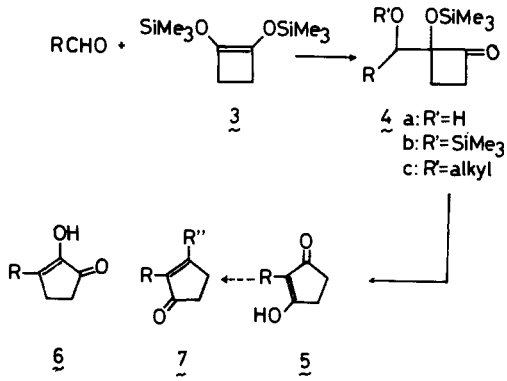
In connection with syntheses of naturally occurring products with cyclopentenone[1] and spiro[4.5]decane rings,[2] considerable efforts have recently been directed to the construction of five-membered rings. In this respect, we focused our attention on 1,3-cyclopentanedione derivatives, for they are versatile precursors of fused ring systems,[3] as well as those of various functionalized five-membered rings, e.g., cyclopentenone.[1] Pinacol rearrangement driven by the release of the ring strain of a four-membered ring[4] was envisioned to provide a way to this end. Further, we expected that the rearrangement of the pinacol **1** may be controlled by the presence of an acyl group adjacent to the diol moiety to give the 1,3-cyclopentanedione **2**. The reaction proceeded, indeed, as depicted below. This two-step sequence represents a new annelation method as well as a geminal acylation[5] approach to cyclopentanediones.



1 **2**

Bis-silylated succinoin, **3**,[6] the starting material of pinacol **1**, was prepared by acyloin condensation of a succinate in the presence of chlorosilane. It seems expedient that a variety of the four-membered acyloin derivatives are available from the products of Stobbe condensation and Diels–Alder reaction of fumalates and maleates.[6b]

Preparation of the pinacol was achieved either by Lewis acid-mediated aldol addition[7] or by a fluoride catalyzed one,[8] in which the pinacol was isolated as a silylated form, **4**.[9] The reaction of **3** and benzaldehyde at −78 °C gave **4a** (R = Ph), in 78% yield with $TiCl_4$, and **4b** (R = Ph), in 75% yield with tetrabutylammonium fluoride (TBAF).[10] Treatment of the aldol adduct **4** with trifluoroacetic acid (TFA) at room temperature afforded the cyclopentanedione **5** in high yield (Table I, entries 1 and 2). None of the isomeric products like **6** was isolated. 1,3-Cyclopentanedione thus prepared can be transformed to 2,3-disubstituted cyclopentenone **7** by an established procedure.[11]



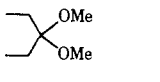
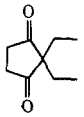
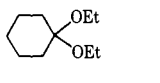
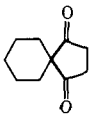
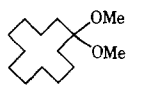
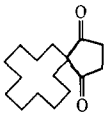
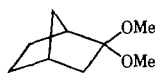
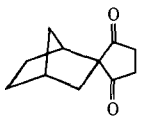
3 **4** a: R′=H b: R′=$SiMe_3$ c: R′=alkyl

6 **7** **5**

Since an acetal coordinates with Lewis acids more strongly than its parent carbonyl compound, and is often a primary product of the recent synthetic methods of carbonyl function,[12] it appeared to be a reaction partner of choice, rendering this annelation method more effective. In fact, the aldol reaction mediated by BF_3·Et_2O or $TiCl_4$[13] proceeded nicely with acetals. The reaction conditions are mild (−78 °C) and did not cause loss of the trimethylsilyl group of the adduct **4c**.[9]

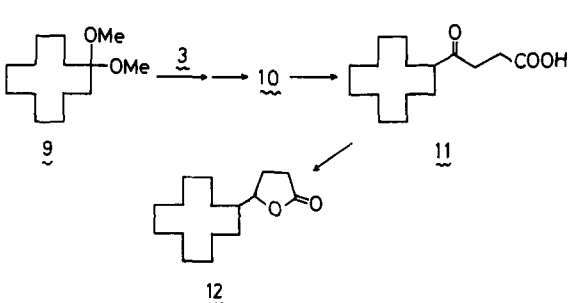
Application of this annelation method to ketals provides a

Table I. Addition–Rearrangement Sequence for Cyclopentanediones

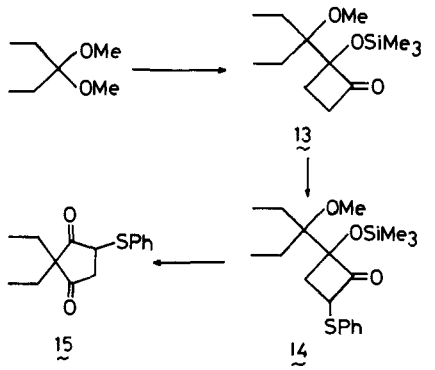
Entry	RR'C=O or RR'C(OR")$_2$	Aldol addn[a] Cat.	% yield[b]	Rearrangement[c] Product	% yield[b]
1	PhCHO	$TiCl_4$	78	5: R = Ph	97
2	PhCHO	TBAF	75		
3	$PhCH(OEt)_2$	$BF_3{\cdot}Et_2O$	94	5: R = Ph	93
4	n-$C_9H_{19}CH(OEt)_2$	$TiCl_4$	90	5: R = n-C_9H_{19}	87[d]
5		$BF_3{\cdot}Et_2O$	92		87
6		$BF_3{\cdot}Et_2O$	90		88
7	 9	$BF_3{\cdot}Et_2O$	92	 10	94
8		$BF_3{\cdot}Et_2O$	60[e]	 8	92

[a] Lewis-acid-mediated aldol reaction was carried out at −78 °C in methylene chloride with equimolar amounts of three reactants. The fluoride catalyzed one was carried out at −78 °C in THF with 5 mole % of the catalyst. All adducts showed satisfactory spectral properties. [b] Isolated yield. [c] Pinacol rearrangement was performed in TFA at ~30 °C. All diketones were characterized by spectral properties and by elemental composition. [d] Yield was determined by NMR. [e] An appreciable amount of norcamphor was detected in the crude product.

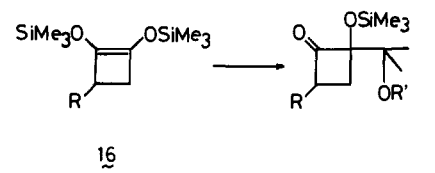
facile entry to 2,2-disubstituted derivatives (entries 5-8). Of particular interest is a high-yield preparation of spiro[4.n] alkane-1,4-diones. Addition–rearrangement sequence readily proceeded even with norcamphor ketal, giving the spiro diketone **8** in 55% overall yield (entry 8). The spiro diketone is a useful starting material for other spiro rings; it is a potential precursor of cyclopentadienes and cyclopentenediones. Hydroxide induced cleavage of **10** (NaOH, MeOH reflux) produced with ketoacid **11** in 62% yield, which is a valuable starting material of 1,4-diketones.[14] Further, reduction of **11** gave the γ-lactone **12** ($NaBH_4$, 73%). The overall result of the three-step transformation from **9** to **11** (54% overall yield) represents *reductive succinoylation* of ketone functionality, further broadening the scope of the new annelation method.



Elaboration of the intermediary pinacol **1**, e.g., **13**, adds to the versatility of this method. Thus, the deprotonation–sulfenylation sequence (LiICA, PhSSPh)[15] performed on **13** gave the sulfenylated cyclobutanone **14** in 63% yield with the silyl group left unattacked. Pinacol rearrangement in TFA gave the diketone **15** in 48% yield.[16]



The modification described above formally represents the regiospecific utilization of the acyloin **16** (R = SPh) which cannot be obtained by acyloin condensation.[6b] In addition, the latent possibility of this modification with regard to the R group should be noted.



Finally, to the best of our knowledge, there has been no report of exclusive acyl migration in pinacol rearrangement:[17] the present case first records a clear-cut example. The rearrangement driven by the ring strain of cyclobutanone, therefore, provides a new (spiro)annelation method and a unique example of pinacol rearrangement as well.[18]

Acknowledgment. We thank Fluka AG for a generous supply of TBAF and the corresponding hydroxide.

References and Notes

(1) For a review, see R. A. Ellison, *Synthesis*, 397 (1973).
(2) For the synthesis of spirovetivanes, see, for the most recent work, G. Buchi, D. Berthet, R. Decorzant, A. Grieder, and A. Hauser, *J. Org. Chem.*, **41**, 3208 (1976), and references cited therein. For reviews on the synthesis of spiro compounds, see A. P. Krapcho, *Synthesis*, 383 (1974); 425 (1976).
(3) 2-Methylcyclopentane-1,3-dione is a well-known precursor of steroidal D ring.
(4) Useful synthetic reactions which exploit the ring strain of cyclobutanones have been reported: (a) Reviews, J. M. Conia and J. R. Salaun, *Acc. Chem. Res.*, **5**, 33 (1972); B. M. Trost, *ibid.*, **7**, 85 (1974). (b) For the most recent work in this line, see B. M. Trost and J. H. Rigby, *J. Org. Chem.*, **41**, 3217 (1976). For earlier references, see also ref 5.
(5) For previously reported approaches to convert C–O bond of a carbonyl group to two C–C bonds, see E. J. Corey and J. I. Shulman, *J. Am. Chem. Soc.*, **92**, 5522 (1970); B. M. Trost, M. J. Bogdanowicz, and J. Kern, *ibid.*, **97**, 2218 (1975), and ref 19 therein; ref 4b.
(6) (a) The modified acyloin condensation of diethyl succinate was carried out in 80% yield according to the procedure B (78–93%) by J. J. Bloomfield and J. M. Nelke submitted to *Org. Synth.* (b) For reviews, see K. Ruhlmann, *Synthesis*, 236 (1971); J. J. Bloomfield, D. C. Owsley, and J. M. Nelke, *Org. React.*, **23**, 259 (1976).
(7) T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, **96**, 7503 (1974).
(8) R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura, and M. Shimizu, *J. Am. Chem. Soc.*, accepted for publication.
(9) Since an unprotected acyloin tends to dimerize on standing, it is expedient to isolate the pinacol 1 as a silylated form: ref 6a.
(10) Prepared by neutralization of aqueous tetrabutylammonium hydroxide with HF; see ref 8 for details. Commercial TBAF (Fluka AG) is employable after the drying procedure specified in ref 8.
(11) Esterification (CH_2N_2 or MeOH, HCl), Grignard addition, and hydrolysis normally complete the sequence: see, for instance, H. O. House and G. H. Rasmusson, *J. Org. Chem.*, **28**, 27 (1963).
(12) Thioacetals give the corresponding acetals directly, ref 4b; K. Ogura and G. Tsuchihashi, *Tetrahedron Lett.*, 3151 (1971); 2681 (1972). Acetals are the primary products of "oxidative decarboxylation"; B. M. Trost and Y. Tamaru, *J. Am. Chem. Soc.*, **97**, 3528 (1975).
(13) T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 15 (1974). $TiCl_4$ employed in the original procedure tends to cause some loss of the silyl group of the adducts; see note 9. Cleavage of the cyclobutanone ring was observed in some cases with this catalyst.
(14) M. Araki, S. Sakata, H. Takei, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **47**, 1777 (1974); G. Posner, C. E. Whitten, and P. E. McFarland, *J. Am.*

Chem. Soc., **94**, 5106 (1972); M. Araki and T. Mukaiyama, *Chem. Lett.*, 663 (1974); M. J. Jorgenson, *Org. React.*, **18**, 1 (1970).
(15) B. M. Trost, T. N. Salzmann, and K. Hiroi, *J. Am. Chem. Soc.*, **98**, 4887 (1976).
(16) The formation of benzenethiol observed suggests the occurrence of a side-reaction during the TFA treatment.
(17) (a) Exclusive acyl migration in similar cases was reported for the epoxy ketone rearrangement; H. O. House and R. O. Wasson, *J. Am. Chem. Soc.*, **78**, 4394 (1956). (b) Migration of ethoxycarbonyl group in pinacol and related rearrangements was reported; J. Kagan, D. A. Agdeppa, Jr., and S. P. Singh, *Helv. Chim. Acta*, **55**, 2252 (1972); J. Kagan, D. A. Agdeppa, Jr., S. P. Singh, D. A. Mayers, C. Boyajian, C. Poorker, and B. E. Firth, *J. Am. Chem. Soc.*, **98**, 4581 (1976); J. Kagan, D. A. Agdeppa, Jr., D. A. Mayers, S. P. Singh, M. J. Walters, and R. D. Wintermute, *J. Org. Chem.*, **41**, 2355 (1976); see also R. A. Gorski, D. J. Dagli, and J. Wemple, *J. Am. Chem. Soc.*, **98**, 4588 (1976).
(18) Aldol adducts showed characteristic IR bands at ~1790 cm^{-1}. Monosubstituted cyclopentanediones showed IR bands characteristic of an enolic diketone, and NMR signals (TFA) of ring methylenes at δ ~3.00 (s). 2,2-Disubstituted ones commonly showed an IR band at ~1720 cm^{-1}, and NMR signals (CCl_4) at δ ~2.65 (s), indicating symmetrical structure. The diketone **8**, however, showed IR bands at 1760 (w) and 1717 cm^{-1} and NMR signals at δ 2.50–2.83 (m), and **10** exhibited IR absorption at 1750 (w) and 1717 cm^{-1} (s).

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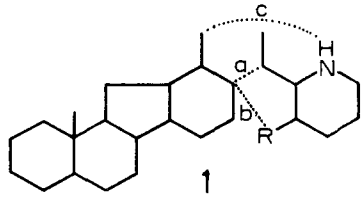
Synthetic Studies in the Veratrum Alkaloid Series. The Total Synthesis of C_{18}-Functionalized *C*-Nor-*D*-homo Steroid Derivatives—Valuable Intermediates in the Total Synthesis of Veratrum Alkaloids

Sir:

The Veratrum alkaloid family is unique among the steroidal alkaloids in that many of its members possess the interesting *C*-nor-*D*-homo steroid skeleton.[1,2] Synthetic endeavors by several groups have now provided the laboratory syntheses of several members of the Jerveratrum group.[3] Thus elegant investigations by Johnson[4] and Masamune[5] and their co-workers have culminated in the syntheses of veratramine and jervine. Our own studies[6-8] have allowed the completion of the syntheses of verarine and 5α,6-dihydroveratramine. On the other hand, the more complex hexacyclic Ceveratrum group[3] which also exhibits interesting pharmacological activities[9] has not yet been synthesized. We would now like to present our studies in this direction. This communication describes the synthesis of C_{18}-functionalized *C*-nor-*D*-homo steroid derivatives, which are important intermediates in our synthetic program, while the accompanying publication illustrates the utilization of these intermediates in the first total synthesis of the Ceveratrum alkaloid verticine.

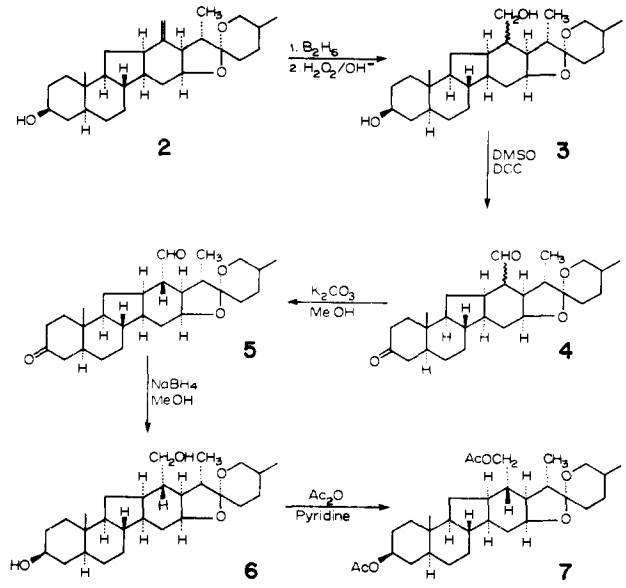
In outlining our synthetic strategy, we considered that the Veratrum bases are made up of two structural units: (i) the *C*-nor-*D*-homo steroid skeleton and (ii) an appropriate heterocyclic nitrogen system as shown schematically in **1**. The coupling of the steroid unit with the heterocyclic system at position a was employed in the synthesis of verarine and veratramine while bond formation at a and b allows the synthesis of jervine.[6-8] In expanding this strategy toward the synthesis of the hexacyclic Ceveratrum bases the attachments of the two units must occur at a and c. Such bond formation between the basic nitrogen atom and C_{18} of the steroid unit clearly requires the preparation of the requisite C_{18}-functionalized *C*-nor-*D*-homo steroid intermediates.



1

a: veratranine bases
a+b: jervanine "
a+c: cevanine "

Scheme I



Our first objective was to obtain a *C*-nor-*D*-homo spirostan derivative with an appropriate functionality at C_{18} and possessing the desired α stereochemistry at C_{13}. For this purpose the exocyclic olefin **2** (Scheme I) became the initial target compound. Rockogenin 12-methanesulfonate 3-pivalate[10] after rearrangement in refluxing anhydrous pyridine[11] (82% yield) and normal hydride reduction of the C_3 protecting group provides an excellent route to this intermediate (overall 75% yield from hecogenin acetate).

Hydroboration (diborane, THF) of **2** (or its C_3-acetate) provided the expected 13β-hydroxymethyl derivative **3** (Scheme I, β-CH_2OH) as a major component (82% yield):[12] mp 182–184 °C, NMR τ 9.22 (s, 3 H, C_{19}-CH_3), 9.2 (d, J = 6 Hz, 3 H, C_{27}-CH_3), 8.98 (d, J = 6 Hz, C_{21}-CH_3), 6.4 (m, 1 H, C_3-H), 6.35 (d, J = 5.5 Hz, 2 H, CH_2OH); MS *m/e* 432 (M^+), 402, 373, 363, 360, 345, 318, 300, 288, 145, 139, 126, 115 (base peak), 107. The isomeric 13α-hydroxymethyl derivative **6** was present as a minor component and could also be utilized as indicated below.

Oxidation of **3** (β-CH_2OH) via the Moffatt technique[13] (benzene, dimethyl sulfoxide, dicyclohexylcarbodiimide, pyridine, trifluoroacetic acid, 40 h, room temperature) provided the expected keto-aldehyde **4** (β-CHO): NMR τ 9.21 (d, J = 6 Hz, 3 H, C_{27}-CH_3), 9.08 (s, 3 H, C_{19}-CH_3), 9.03 (d, J = 6 Hz, C_{21}-CH_3), 7.33 (m, J = 5.5 and 7 Hz, 1 H, C_{13}H), 0.22 (d, J = 5.5 Hz, 1 H, CHO); MS *m/e* 428 (M^+), 369, 359, 356, 341, 314, 285, 256, 206, 149 (base peak), 135, 126, 115. This latter product could be smoothly converted, in essentially quantitative yield, to the thermodynamically more stable desired isomeric aldehyde **5**, mp 174–176 °C, by reaction with potassium carbonate at room temperature: NMR τ 9.22 (d, J = 6 Hz, 3 H, C_{27}-CH_3), 9.10 (d, J = 5 Hz, 3 H, C_{21}-CH_3), 9.08 (s, 3 H, C_{19}-CH_3), 0.57 (d, J = 4 Hz, 1 H, CHO); MS *m/e* 428 (M^+), 369, 359, 356, 341, 314, 285, 257, 206, 149, 135, 126, 115 (base peak).

Conversion of **5** to the required 13α-hydroxymethyl derivative **6**, mp 243.5–245 °C, could be achieved directly with sodium borohydride: NMR τ 9.25 (s, 3 H, C_{19}-CH_3), 9.21 (d,