Raney nickel to give $C^{11}H_3NH_2$. Possible one carbon species with this behavior are methylenimine, cyclodiazomethane and diaminomethane. One carbon species may be the precursor of both methane and methylamine. The mechanism of the primary process is not dealt with here but will be considered in the full paper dealing with these experiments, unreported data and work in progress on this system.

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STEROIDS. CCII.[1] A NEW ROUTE TO 19-NOR STEROIDS

Sir:

The increasing importance of 19-nor steroids,[2a] particularly in the field of oral contraception,[2b] has made it attractive to investigate new routes to this class of compounds which do not proceed *via* Birch reduction[3] of ring A aromatic precursors, since the latter reaction in particular is inconvenient for large scale operations.

Recently we[4] and others[5–7] described chemical methods for the direct oxygenation of the C-19 methyl group, a primary prerequisite for the subsequent conversion to 19-nor steroids. However, none of these approaches offered a facile synthesis of 19-nor-Δ^4-3-ketones.

The conversion of several Δ^5-3β-alcohols into their corresponding 19-nor-Δ^5-3-ketones by an efficient process[8] is now described, which is exemplified by the conversion of pregnenolone acetate (I) into 19-norprogesterone (VIII) in an over-all yield of 37%.

Addition of hypobromous acid (N-bromoacetamide and aqueous perchloric acid) to pregnenolone acetate (I) in dioxane solution gave 5α-bromopregnane-3β,6β-diol-20-one 3-acetate (II) (m.p. 165–167°, $[\alpha]_D$ +6.5°.[9] Found for $C_{23}H_{35}BrO_4$: C, 60.36; H, 7.81; Br, 17.79; O, 14.17). Treatment of II with 1.2 moles of dry lead tetraacetate in anhydrous benzene[4,7] afforded 6β,19-oxido-5α-bromopregnane-3β-ol-20-one acetate (III) (m.p. 152–154°, $[\alpha]_D$ +58°, ν_{max}^{KBr} 907[10] cm.$^{-1}$. Found for $C_{23}H_{33}BrO_4$: C, 61.18; H, 7.31; Br, 17.91; O, 13.97). Mild alkaline hydrolysis of III gave the corresponding 3β-alcohol IV (m.p. 179–180°, $[\alpha]_D$ +61°. Found for $C_{21}H_{31}BrO_3$: C, 61.52; H, 7.70; Br, 20.19) which was oxidized with chromium trioxide in aqueous acetic acid and then directly converted with zinc dust in isopropyl alcohol[11] (reflux 24 hours) into 19-hydroxy-Δ^5 pregnene-3,20-dione (V). Treatment of V with oxalic acid in ethanol afforded 19-hydroxyprogesterone (VI) (m.p. 169–171°, $[\alpha]_D$ +182°, $\lambda_{max.}$ 243 mμ, log ϵ 4.22. Found for $C_{21}H_{30}O_3$: C, 76.07; H, 9.11; O, 14.69). Oxidation of VI with 8 *N* chromic acid in acetone solution furnished the corresponding 19-carboxylic acid VII (m.p. 147–149°, $[\alpha]_D$ +94°, λ_{max} 243 mμ, log ϵ 4.19. Found for $C_{21}H_{28}O_4$: C, 73.43; H, 8.22; O, 18.33) smoothly converted by acidic methanol[12] to 19-norprogesterone[13] (VIII) (m.p. 142–144°, $[\alpha]_D$ +141°).

In a similar manner dehydroisoandrosterone acetate (IX) gave 19-norandrostene-3,17-dione[14] (XV) (m.p. 166–168°, $[\alpha]_D$ +127°, λ_{max} 239 mμ, log ϵ 4.23) *via* 5α-bromoandrostane-3β,6β-diol-17-one 3-acetate (X),[4b,15] 6β,19-oxido-5α-bromoandrostane-3β-ol-17-one acetate (XI) (m.p. 187–188°, $[\alpha]_D$ +39°. Found for $C_{21}H_{29}BrO_4$: C, 59.24; H, 7.04; Br, 18.99), its corresponding 3β-ol XII (m.p. 209–211°, $[\alpha]_D$ +38°. Found for $C_{19}H_{27}BrO_3$: C, 59.74; H, 7.15; Br, 20.71), 19-hydroxy-Δ^4-androstene-3,17-dione[16] (XIII) (m.p. 168–170°, λ_{max} 243 mμ, log ϵ 4.21) and the 19-carboxylic acid XIV[12] (m.p. 148–150°, $[\alpha]_D$ +242°, λ_{max} 244 mμ, log ϵ 4.18. Found for $C_{19}H_{24}O_4$: C, 72.13; H, 7.69; O, 20.27).

19-Nor-17α-acetoxyprogesterone (XXIII) also was prepared from 17α-hydroxypregnenolone 3,17-diacetate[17] (XVI), by an alternate reaction sequence.

Reaction of 5α-bromopregnane-3β,6β,17α-triol-20-one 3,17-diacetate (XVII) (m.p. 184–186°, $[\alpha]_D$ −49°. Found for $C_{25}H_{37}BrO_6$: C, 58.41; H, 7.31; Br, 16.04; O, 18.23) with lead tetraacetate gave 6β,19-oxido-5α-bromopregnane-3β,17α-diol-20-one 3,17-diacetate (XVIII) (m.p. 202–208°,

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(9) All rotations in chloroform solution and ultraviolet spectra in 95% ethanol.

(10) All compounds with the 6β,19-oxide bridge were characterized by a sharp medium intensity band between 903–910 cm.$^{-1}$.

(11) In contrast to the 5α-bromo-6,19-oxides, the corresponding 5α-chloro-6,19-oxides [*e.g.*, 5α-chloro-6β,19-oxidoandrostane-3β-ol-20-one acetate (m.p. 186–189°, $[\alpha]_D$ +53°)] were recovered unchanged after treatment with zinc in isopropyl alcohol under reflux.

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$[\alpha]$D −1°. Found for $C_{25}H_{35}BrO_6$: C, 58.77; H, 6.79; Br, 15.55; O, 18.67) which was treated with zinc dust in isopropyl alcohol to afford Δ^5-pregnene-3β,17α,19-triol-20-one 3,17-diacetate (XIX) (m.p. 228–229°, $[\alpha]$D −48°. Found for $C_{25}H_{36}O_6$: C, 69.10; H, 8.66; O, 22.36). Hydrolysis of XIX gave the 3β-alcohol XX (m.p. 245–247°, $[\alpha]$D −63°. Found for $C_{23}H_{34}O_5$: C, 70.59; H, 8.53; O, 20.62) which underwent Oppenauer oxidation (10 min.) to furnish 19-hydroxy-17α-acetoxyprogesterone (XXI) (m.p. 252–254°, $[\alpha]$D +72°, λ_{max} 242 mμ, log ϵ 4.17. Found for $C_{23}H_{32}O_5$: C, 71.38; H, 8.36; O, 20.34). Oxidation of XXI to the 19-acid XXII (m.p. 166–168°, $[\alpha]$D +116°, λ_{max} 244 mμ, log ϵ 4.18. Found for $C_{23}H_{30}O_6$: C, 68.72; H, 7.60; O, 23.56) and treatment with acid gave 19-nor-17α-acetoxyprogesterone[18] (XXIII) (m.p. 227–229°, $[\alpha]$D +18°, λ_{max} 239 mμ, log ϵ 4.23).

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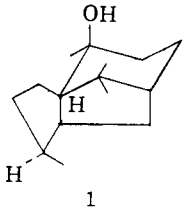
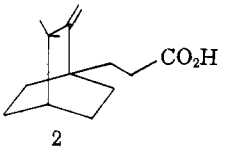
SYNTHESIS OF PATCHOULI ALCOHOL[1]

Sir:

After structural studies on the tricyclic sesquiterpene patchouli alcohol (1)[2] were complete we initiated work directed toward a synthesis of this natural product and the related patchoulione (**19**), a substance with highly desirable olfactory properties. A synthesis verifying both structure and absolute configuration of 1 is now presented.



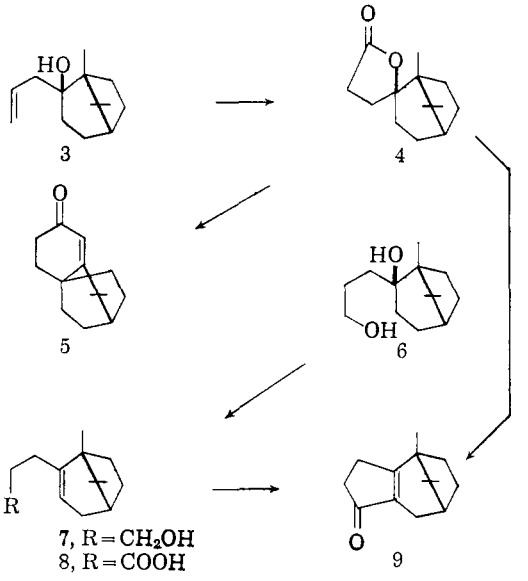
1



2

Addition of allylmagnesium chloride to (−)-homocamphor[3] (prepared from (+)-camphor) gave the carbinol (**3**) (80%), m.p. 36–36.5°, $[\alpha]$D −20° (all in $CHCl_3$) which on treatment with diborane[4] followed by oxidation with Jones' reagent[5,6] was converted to the spirolactone (**4**) (54%), m.p. 89–90°, $[\alpha]$D −45°, $\nu_{max}^{CCl_4}$ 1770 cm.$^{-1}$. Dehydration in the presence of 1% $ZnCl_2$ in hot acetic anhydride–acetic acid solution (3:1) furnished the *meso*-ketone (**5**), (10%), m.p. 101–103°, λ_{max}^{EtOH} 247 mμ (ϵ 14,500), $\nu_{max}^{CCl_4}$ 1665, 1615 cm.$^{-1}$, n.m.r. (all in CCl_4) at 4.25 (1H singlet); 8.82 τ (6H singlet) and the desired cyclopentenone (**9**) (40%) m.p. 100°, λ_{max}^{EtOH} 246 mμ (ϵ 13,000), $\nu_{max}^{CCl_4}$ 1695, 1635 cm.$^{-1}$, three methyl resonance peaks in the n.m.r. spectrum at 8.95, 9.05 and 9.15 τ. The latter ketone (**9**) was nearly completely racemized, indicating reversible isomerization of **8** and the *meso*-acid (**2**) prior to cyclization. This was avoided as follows: Hydroboration of **3** followed by oxidation with hydrogen peroxide gave the diol (**6**), m.p. 138–139°, $[\alpha]$D −25° identical with the product available by reduction of **4** with lithium aluminum hydride which was monoacetylated, dehydrated with phosphorus oxychloride in pyridine and the resulting acetate reduced with lithium aluminum hydride to the unsaturated alcohol (**7**). Oxidation with chromium trioxide furnished the acid (**8**), m.p. 81–82°, n.m.r. signals at −2.2 (1H), 4.9 (1H broad), 9.0 (3H), 9.08τ (6H) (over-all yield 3 to 8, 65%).

Treatment of its acid chloride with aluminum chloride in carbon disulfide afforded **9**, m.p. 110°, $[\alpha]$D −149° (41%).



Wittig condensation[7] with triphenylphosphinemethylene in peroxide free tetrahydrofuran furnished an unstable liquid diene (**10**), λ_{max}^{EtOH} 256 mμ which on hydrogenation over Raney nickel W2 in ethyl acetate gave an olefin, over-all yield **9** to **11**, 38%, $[\alpha]$D −42°. Identity with β-patchoulene (**11**) was established by comparison of infrared and n.m.r. spectra, optical rotation and retention time in the gas chromatogram.

The tricyclic skeleton of patchouli alcohol (**1**) had to be constructed from **11** using some version of the Wagner–Meerwein rearrangement. Direct isomerization was ruled out because the equilibrium between **11** and **20** is quantitatively in favor of **11**. Epoxidation of **11** with peracetic acid produced the liquid epoxide (**12**) (99%), $[\alpha]$D −8° which was isomerized with boron fluoride in ether solution (20°, 5–10 min.) to the unsaturated alcohol (**13**) (57%), m.p. 30–31°, $[\alpha]$D −14°,

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