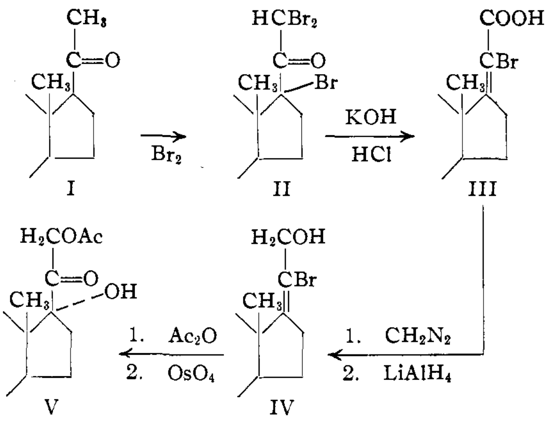
A NEW ROUTE TO THE CORTICAL SIDE CHAIN

Sir:

The conversion of the readily available bromopregnanolones to compounds of the cortical series having a dihydroxyacetone side chain has been achieved. The key steps involve a rearrangement of a tribromoketone and subsequent reduction of the product.



Bromination of pregnan-3(β)-ol-20-one acetate (I) with three moles of bromine yields the 17,21,21-tribromo derivative (II), m. p. 196° (dec.), $[\alpha]^{25}\mathrm{D}$ $-3.4°$ (chloroform). Calcd. for $C_{23}H_{33}O_3Br_3$: Br, 40.1. Found: Br, 40.3. Rearrangement with alcoholic potash yields 17-pregnen-3(β)-ol-20-bromo-21-oic acid (III), m. p. 273° (dec.), $[\alpha]^{25}\mathrm{D}$ $+41°$ (dioxane). Calcd. for $C_{21}H_{31}O_3Br$: C, 61.4; H, 7.6; Br, 19.4. Found: C, 62.0; H, 7.7; Br, 19.1. Reduction of the bromo acid with hydrogen and platinum catalyst gives pregnan-3(β)-ol-21-oic acid, m. p. and mixed m. p., 220°.[1] Lithium aluminum hydride reduction of the methyl ester of III yields the unsaturated 20-bromo-21-ol (IV), m. p. 253° (dec), $[\alpha]^{25}\mathrm{D}$ $+53°$ (dioxane). Calcd. for $C_{21}H_{33}O_2Br$: C, 63.5; H, 8.4. Found: C, 63.4; H, 8.5. Treatment of the diacetate of IV with osmium tetroxide in ether yields pregnan-3(β),17(α),21-triol-20-one diacetate (V), m. p. 153°, $[\alpha]^{28}\mathrm{D}$ $+49°$ (dioxane). Calcd. for $C_{25}H_{38}O_6$: C, 69.1; H, 8.8. Found: C, 68.8; H, 8.8. Hydrogenation of V gives the same tetrol obtained by the lithium aluminum hydride reduction of methyl 17-pregnen-3(β)-ol-21-oate with subsequent hydroxylation (OsO_4), isolated as the triacetate, m. p. and mixed m. p. 184°, $[\alpha]^{28}\mathrm{D}$ $+55°$ (chloroform). Calcd. for $C_{27}H_{42}O_7$: C, 67.8; H, 8.9. Found: C, 67.4; H, 8.9.

We thank Parke, Davis and Company for their help.

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(1) Marker, Crooks and Wagner, THIS JOURNAL, **64**, 817 (1942).

HOMOLOGATION OF ALCOHOLS

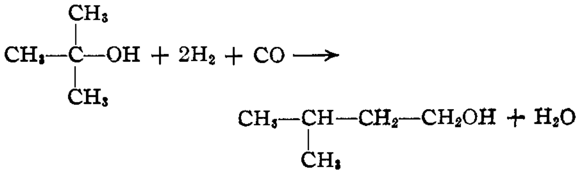
Sir:

The conversion of an alcohol to the primary alcohol containing one carbon atom more than the original is usually a tedious procedure. We wish to report a simple one-step homologation reaction. The process consists in treating the alcohol with synthesis gas (carbon monoxide and hydrogen) in the presence of a cobalt catalyst under conditions resembling those employed in the oxo reaction.

The oxo or hydroformylation reaction consists of the conversion, by means of synthesis gas, of an olefin to a mixture of aldehydes containing one carbon atom more than the starting material. $R{-}CH{=}CH_2 + CO + H_2 \xrightarrow{Co} R{-}CH_2{-}CH_2{-}CHO + R{-}CH(CH_3)CHO$. As developed in Germany, a mixture of olefins secured from the Fischer–Tropsch reaction was usually used as the starting material. The aldehydes resulting from the oxo reaction were then converted in a separate step, to a mixture of alcohols which were of value for detergent manufacture. It has been reported recently[1] that olefins may be converted in one step directly to the alcohol if the usual oxo reaction is operated at slightly higher temperatures. That our homologation reaction need not proceed *via* an olefin intermediate followed by a one-step hydroformylation–hydrogenation is shown by the fact that benzyl alcohol is converted to β-phenylethyl alcohol under our conditions: $PhCH_2OH + 2H_2 + CO \rightarrow PhCH_2CH_2OH$. Other conversions we wish to report consist of the formation of *n*-butyl alcohol and of isobutyl alcohol from isopropyl alcohol and of isoamyl alcohol from *t*-butyl alcohol. *n*-Propyl alcohol gave a mixture of *n*-butyl and isobutyl alcohols but the reaction proceeded so slowly at 180° that part of the initial products was transformed by further homologation to higher alcohols.

We are inclined to believe that the homologation reaction is an acid ($HCoCO_4$) catalyzed reaction that proceeds *via* a carbonium ion according to a mechanism that will be discussed in detail later.

In a typical experiment, *t*-butyl alcohol (86 g., 1.3 moles) and cobaltous acetate (7.0 g., 0.03 mole) were placed in an 0.5-liter stainless steel autoclave and heated with synthesis gas (3200 p. s. i., $1H_2{:}1CO$) at 160–180° for one and one-half hours Gas absorption was 89% of the theoretical according to the equation



$$CH_3{-}\underset{CH_3}{\overset{CH_3}{C}}{-}OH + 2H_2 + CO \longrightarrow CH_3{-}\underset{CH_3}{CH}{-}CH_2{-}CH_2OH + H_2O$$

There was obtained a 63% yield of isoamyl alco-

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(1) Wender, Levine and Orchin, Abstracts of the Atlantic City meeting of the American Chemical Society, September 19–23, 1949