Cyclodehydration of β-isothioureido propionic acid. The acid was prepared using thiourea and β-propiolactone by the method of Gresham, Jansen, and Shaver.[8] Five grams of the above acid and 15 cc. of a mixture of acetic anhydride and pyridine (10:5) was gently refluxed for about 15 min. Most of the acid dissolved and the color of the liquid turned golden yellow. On cooling and leaving overnight, the crystals separated out, which were collected, washed with a small amount of ethanol (95%), and then finally recrystallized in colorless prismatic rods from boiling water. The yield of 2-acetylimino-1,3-thiazan-4-one (IVa), was 2.6 g., m.p. 198° (gradual decomposition).

Anal. Calcd. for $C_6H_8N_2O_2S$: C, 41.86; H, 4.65; N, 16.27. Found: C, 42.15; H, 4.27; N, 15.72.

Cyclodehydration of β-phenylisothioureidopropionic acid. The acid was prepared from phenylthiourea and β-propiolactone by the method of Gresham and Shaver.[9] On the addition of 20 cc. of the acetic anhydride–pyridine mixture (11:5) to 7.9 g. of the above acid, dissolution took place with the evolution of heat. the deep yellow solution was warmed under reflux on a water bath for 30 min. and cooled, and the solid was filtered, washed with a dilute solution of sodium carbonate, and repeatedly crystallized from ethanol and finally in rectangular slender rods from benzene. The yield of 2-phenylimino-1:3-thiazan-4-one (IVb) was 4.8 g., m.p. 169–170°.

Anal. Calcd. for $C_{10}H_{10}N_2OS$: C, 58.25; H, 4.85; N, 13.58. Found: C, 58.21; H, 5.29; N, 13.86.

The mother liquor from the ethanol crystallization on concentration deposited a solid, which crystallized in colorless needles from benzene, m.p. 139–140°. It was probably a mixture of the unreacted acid and the cyclized product.

Anal. Found: C, 56.90; H, 4.91; N, 13.00.

Reaction of 2-chloromethylbenzimidazole with thiourea. To a boiling solution of 1.5 g. of thiourea in 15 cc. of absolute ethanol, 3.3 g. of 2-chloromethylbenzimidazole[10] was added. After a few minutes a thick crystalline mass of needles separated. The contents were refluxed for 5 hr., the needles gradually went into solution and the yellow prisms that separated, were filtered, recrystallized in pale yellow plates from aqueous ethanol. The yield of 2-benzimidazolylmethylisothiourea hydrochloride, (IX) was 0.58 g., m.p. 258–259°.

Anal. Calcd. for $C_9H_{11}N_4SCl,H_2O$: C, 41.45; H, 4.99. Found: C, 41.35; H, 4.62.

After removal of the yellow prisms, the ethanol mother liquor from the reaction was diluted with water and the precipitate crystallized in feathery pale yellow needles from aqueous ethanol and charcoal. Yield of the bis[2-(benzimidazolyl methyl)]disulfide (VIII), 0.5 g., m.p. 110–115°.

Anal. Calcd. for $C_{16}H_{14}N_4S_2.{}^1/_2H_2O$: C, 57.31; H, 4.47; N, 16.71. Found: C, 57.68; H, 4.23; N, 17.24.

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A New Method for the Activation of Copper Chromium Oxide as a Reducing Catalyst

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Copper chromium oxide, when prepared by the method of Adkins, Burgoyne, and Schneider,[1] will catalyze the reduction of carbonyl groups at room temperature but only after activation. This was originally accomplished through exposure of the catalyst to a high pressure (226 atm.) of hydrogen at 100°.[1] It has now been found that the same activation can be achieved simply by refluxing the copper chromium oxide in cyclohexanol for four hours. This is illustrated in Fig. 1. Hydrogenation of acetone to 2-propanol began at room temperature when copper chromium oxide was used which had been activated either essentially according to the previous procedure[1] (Curve C) or by the present method (Curve B), but, when the catalyst had not been activated by any means, a "critical temperature" of *ca.* 100° was required before hydrogenation would proceed (Curve A).

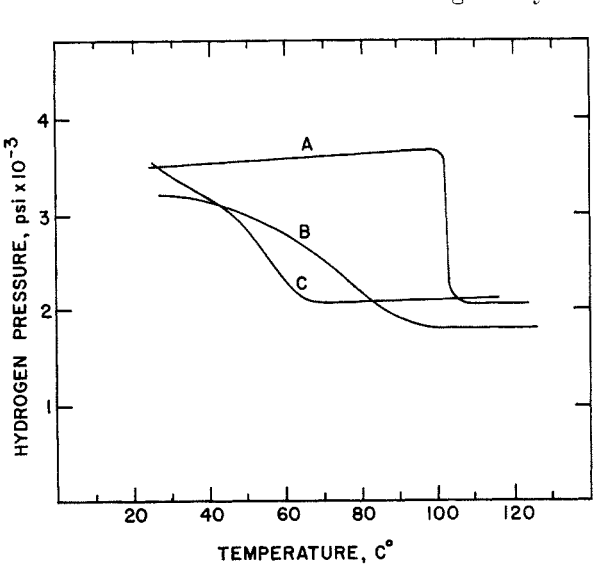

Fig. 1. The influence of temperature on the rate of hydrogenation of 20 ml. of acetone catalyzed by 6 g. of copper chromium oxide which had not been activated (Curve A), which had been activated by refluxing it in cyclohexanol (Curve B), and which had been activated by exposing it to 200 atm. pressure of hydrogen at 110° (Curve C)

The cyclohexanol which was used in the activation was simultaneously oxidized to cyclohexanone. The yield was 11% based on the isolation of cyclohexanone semicarbazone. No attempt was made to increase the percentage conversion of cyclohexanol to cyclohexanone, but it was found that under modified conditions certain steroidal alcohols could be oxidized to the corresponding ketones in a good

(1) H. Adkins, E. E. Burgoyne, and H. J. Schneider, *J. Am. Chem. Soc.*, **72**, 2626 (1950).

yield. Thus, when cholestan-3β-ol and 7,22-ergostadien-3β-ol were refluxed in xylene in the presence of three times their weight of copper chromium oxide, cholestan-3-one and 7,22-ergostadien-3-one were isolated in a 60–65% yield. This is believed to be the lowest temperature (139°) at which a copper chromium oxide catalyst has been found effective for the dehydrogenation of alcohols. This reaction is usually carried out in the vapor phase[2] above 300°, although liquid phase[3–5] oxidation of alcohols has been reported in the temperature range of 200-300°.

EXPERIMENTAL[6]

Hydrogenation experiments. The hydrogenations under high pressure were carried out in a stainless steel pressure vessel. Heating was accomplished with a jacket which allowed the rate of temperature increase to be the same in all cases. It was approximately 1°/min. Temperature and pressure changes were continuously recorded on automatic devices. The product of the various hydrogenations of acetone was identified as 2-propanol by its boiling point (80.5–81.8°) and index of refraction (n_D^{20} 1.3779). The used catalyst was always considerably more black in color than the catalyst which, in agreement with Adkins, *et al.*,[1] was a brownish black. The results of the hydrogenation experiments are summarized in Fig. 1.

Activation of copper chromium oxide. A mixture of 150 ml. of cyclohexanol and 6 g. of unactivated copper chromium oxide was refluxed with stirring under a stream of nitrogen for 4 hr. The jet-black catalyst was filtered off. From 10.0 g. of the filtrate was obtained 1.67 g. of cyclohexanone semicarbazone, m.p. 166–168°. The melting point was undepressed on admixture with an authentic sample. The recovered catalyst was washed with acetone and then used for the reduction of 20 ml. of acetone under 210 atm. pressure of hydrogen (Fig. 1, Curve B).

Oxidation of cholestan-3β-ol. A mixture of 2.0 g. of cholestan-3β-ol, 150 ml. of xylene, and 6.0 g. of unactivated copper chromium oxide was refluxed with stirring for 4 hr. The catalyst was filtered off and extracted with 200 ml. of hot ethanol. The combined filtrates were evaporated to dryness under reduced pressure. Chromatography of the residue on alumina and elution with ether afforded 1.34 g. (67%) of cholestan-3-one (λ_{max} 5.82 μ) which from methanol formed colorless microcrystals, m.p. 128–129°, $[\alpha]_D$ 42°. Lit.[7] m.p. 129–130°, $[\alpha]_D$ 40°.

Oxidation of 7,22-ergostadien-3β-ol. A mixture of 2.0 g. of 7,22-ergostadien-3β-ol, 150 ml. of xylene, and 6.0 g. of unactivated copper chromium oxide was refluxed with stirring under a stream of nitrogen for 2 hr. The catalyst was filtered off and extracted with 300 ml. of boiling ethanol The combined filtrates were evaporated to dryness under reduced pressure and the residue (1.7 g.) was chromatographed on alumina. The material which was eluted with ether was crystallized from ether-methanol and afforded 0.8 g. of 7,22-ergostadien-3-one as colorless flakes, λ_{max} 5.82 μ, m.p. 183–185°, $[\alpha]_D$ ±0°, Lit.[8] m.p. 182–183°, $[\alpha]_D$ 2°. Concentration of the mother liquor gave an additional 0.1 g. of the ketone (combined yield: 60% based on unrecovered starting material). Elution of the alumina with chloroform-ethanol and crystallization of the resulting steroid from ethyl acetate-methanol-water yielded 0.5 g. of starting material as colorless flakes, m.p. 182–183°, which readily formed a digitonide and possessed an infrared spectrum identical with authentic 7,22-ergostadien-3β-ol. The spectrum was quite different from that of samples (melting variously up to 203°) of the digitonin non-precipitable hydroxy compound (λ_{max} 2.76 μ) obtainable by allowing 7,22-ergostadien-3β-ol to react at 150° in the presence of copper chromium oxide under pressure of hydrogen.[9]

When 7,22-ergostadien-3β-ol was refluxed in xylene as described above with one particular batch of copper chromium oxide, instead of the ketone an "intermediate" was obtained by chromatography (alumina; elution with petroleum ether) which possessed neither hydroxyl nor carbonyl bands in the infrared, but which did possess a strong band at 9.03 μ. It was usually obtained in *ca.* 35% yield. It melted at 110–111° (from ether-methanol) and was converted to 7,22-ergostadien-3-one (m.p. 178–179°, λ_{max} 5.82 μ) simply by recrystallizing it from aqueous acetic acid. This compound was obtained on several occasions, but only with the one sample of catalyst. Other catalyst preparations gave the ketone directly. The structure of this material has not been elucidated.

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(2) See, for instance, R. E. Dunbar and M. R. Arnold, *J. Org. Chem.*, **10**, 501 (1945) and the references cited therein. This process has also been the subject of a number of patents, *e.g.*, T. Kritchevsky, U. S. Patent **2,462,107**, Feb. 22, 1949; *Chem. Abstr.*, **43**, 3841 (1949).

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(6) The infrared spectra were determined on a Perkin-Elmer double beam spectrophotometer by Mr. H. K. Miller and Mrs. Phyllis Smeltzer in CS_2. The melting points were determined on a Kofler block and are recorded as read. The rotations were determined at 20° in chloroform in 1–2% concentrations. The copper chromium oxide was prepared exactly according to the directions of Adkins, *et al.*[1]

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Oxidation of 3-Methylisoquinoline

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In connection with studies to be reported elsewhere we had the occasion to repeat the synthesis of 3-aminoisoquinoline from 3-methylisoquinoline (I)

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