crystalline alcohol, which is stable at 0° but is gradually dehydrated at 25°. The dehydration can be accelerated in boiling benzene and the formed water removed as benzene azeotrope. The dehydration product is a polymer rather than a trimethylenetriamine derivative which is the expected product if formaldehyde reacts with the amide nitrogen of structure Ib.

Compounds II and III have been prepared by amination of the respective hydroxamic acid chlorides with piperidine.

EXPERIMENTAL[6]

Formamidoxime, ethyl amino-oximinoacetate, α-oximino esters, and α-oximino acids were prepared according to literature methods. It was found, however, that ethyl amino-oximinoacetate could be prepared much more easily by amination of ethyl chloro-oximinoacetate.

Ethyl amino-oximinoacetate. Ethyl chloro-oximinoacetate (1.0 g., 0.0066 mole), dissolved in 50 ml. of dry ether, was treated with dry ammonia gas at 0°. The precipitated ammonium chloride was filtered with suction and the filtrate was evaporated under reduced pressure. The crystalline residue, m.p. 97–98°, weighed 0.51 g. (58%) and did not depress the melting point of authentic material.

The *sodium salt* was obtained as a yellow solid in 97% yield by evaporating an ethanol solution of the ester (0.002 mole) and sodium ethoxide (0.002 mole) in a high vacuum at room temperature.

Anal. Calcd. for $C_4H_7N_2NaO_3$: Na, 14.92. Found: Na, 15.08.

Ethyl piperidino-oximinoacetate (II). Ethyl chloro-oximinoacetate (2.0 g., 0.014 mole) in 100 ml. of dry ether was treated with shaking at 0° with a solution of piperidine (2.4 g., 0.028 mole) in 50 ml. of ether. The precipitated hydrochloride was filtered after 0.5 hr. at 0° and 1.5 hr. at 25° and the filtrate was evaporated under reduced pressure. The pale yellow oil (2.7 g., 96%) was distilled from a molecular still and boiled at 120° (0.05 mm.), n_D^{25} 1.5042, yield 1.26 g.

Anal. Calcd. for $C_9H_{16}N_2O_3$: C, 53.99; H, 8.05; N, 14.00. Found: C, 54.60; H, 8.13; N, 13.79.

Hydroxymethylformamidoxime. Formamidoxime (3.0 g., 0.05 mole) was dissolved in 5 ml. of water and 5 ml. of 95% ethanol. To this solution was added with stirring formalin (5 ml., 0.06 mole) and the warm mixture was cooled to 0°. The solid mass was diluted with an equal volume of 95% ethanol, filtered, washed with ethanol and ether, and dried, yielding 2.8 g. (62%), m.p. 102–103° (dec.), λ(C=N) 5.95 μ, λ(NH def.) 6.31 μ. OH, NH, and CH stretching bands were not resolved in KBr.

Anal. Calcd. for $C_2H_6N_2O_2$: C, 26.67; H, 6.71; N, 31.11. Found: C, 26.26, 26.24; H, 6.74, 6.67; N, 31.07.

The solid alcohol was stable at 0° but liquefied on standing at room temperature over a period of several weeks. The infrared spectrum of the product was identical with that of the polymer below.

Poly(methyleneformamidoxime). Hydroxymethylformamidoxime (0.53 g., 0.0059 mole) was suspended in 25 ml. of benzene and refluxed over a water trap for 24 hr. A red insoluble resin separated from solution and a drop of water collected in the trap. The resin weighed 0.42 g. (98%) and had broad bands in the infrared at 3.15 μ (OH), 6.01 μ (C=N), and 13.0 μ. It was insoluble in acetone (suggesting cross-linking), benzene, and chloroform.

Anal. Calcd. for $C_2H_4N_2O$: C, 33.32; H, 5.59; N, 38.89. Found: C, 32.87, 33.56; H, 6.84, 6.72; N, 38.83, 39.39.

(6) Microanalyses by M. J. Naranjo. All temperatures are uncorrected.

Infrared absorption spectra were determined with a Perkin-Elmer Model 21 spectrophotometer with sodium chloride prisms in matched cells of 0.1-mm. path length for solutions and in KBr pellets of 0.5-mm. thickness for solids.

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Mechanism of Reduction of Alkylmercuric Salts with Sodium Stannite

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Three methods generally employed to reduce alkylmercuric salts to dialkylmercury compounds are the following:

$$2\ RHgX \longrightarrow R_2Hg$$

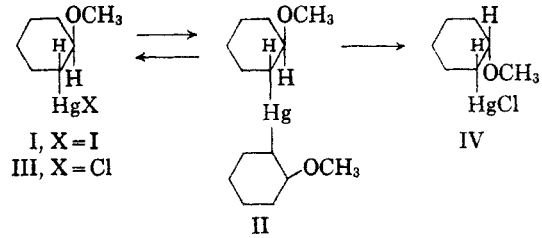
1. N_2H_4
2. $Na_2S_2O_3$
3. Na_2SnO_2

The first has been shown to result in racemization about the carbon-mercury bond, suggesting formation of free radical intermediates.[1,2] The second method, applied to 3-bromomercuricamphor,[2] gives rise to retention of configuration, suggesting an SE2 mechanism.[3] Using the third method, Sand[4] isolated an intermediate mercurous compound R-HgHgR which decomposed to R_2Hg on heating. For this transformation of the mercurous intermediate to R_2Hg and mercury one can visualize either some type of rearrangement process involving retention of configuration or a free radical mechanism permitting racemization, such as the following:

$$RHgHgR \longrightarrow RHg\cdot + Hg + R\cdot$$

$$RHg\cdot + R\cdot \longrightarrow RHgR$$

In this connection the reduction of *trans*-2-methoxycyclohexylmercuric iodide (I) is of interest.



trans-2-Methoxycyclohexylmercuric iodide (I) was reduced to a dialkylmercury II, which was not examined directly, but was converted with mercuric

(1) G. F Wright, *Can. J. Chem.*, **30**, 268 (1952).

(2) O. A. Reutov and Tsin-Chzhu Lu, *Doklady. Akad. Nauk. S.S.S.R.*, **110**, 575 (1956); *Chem. Abstr.*, **51**, 8042 (1957).

(3) S. Winstein, T. G. Traylor, and C. S. Garner, *J. Am. Chem. Soc.*, **77**, 3741 (1955).

(4) J. Sand, *Ber.*, **34**, 2913 (1901).

chloride to methoxycyclohexylmercuric chloride. Since electrophilic substitution by mercuric chloride on 2-methoxycyclohexylmercury compounds in ether is known to proceed with retention of configuration,[3] the configuration of the final 2-methoxycyclohexylmercuric chloride may be used as a guide to the configuration of the dialkylmercury II.

The 2-methoxycyclohexylmercuric chloride produced from the dialkylmercury II proved to be a mixture of the *trans*- and *cis*-isomers III and IV, quite analogous to the mixture obtained by Wright from the use of hydrazine.[1] The *trans*-isomer III crystallized directly from the reaction mixture in relatively pure form. The *cis*-isomer IV was obtained in pure form by treatment of the residual methoxycyclohexylmercuric chloride with hot acetic acid, taking advantage of the much greater rate of elimination displayed by the *trans*-compound compared to the *cis*-isomer.[3]

Retention of configuration is not complete during conversion of 2-methoxycyclohexylmercuric iodide (I) to dialkylmercury II with sodium stannite, the most likely explanation being that intermediate methoxycyclohexyl free radicals are involved. The *cis*-2-methoxycyclohexylmercuric chloride (IV) represented *ca.* 15% of the product from mercuric chloride cleavage of the dialkylmercury II, less than the figure of 25% which would result if the methoxycyclohexyl radical showed equal preference for *trans*- or *cis*-configurations in the bond-making step of the reaction leading to dialkylmercury II. While some preference for the *trans*-configuration seems indicated, more quantitative interpretation is precluded by the low yield of dialkylmercury II obtained from reduction of *trans*-2-methoxycyclohexylmercuric iodide (I).

EXPERIMENTAL

A 45 g. (0.1 mole) quantity of I was treated with excess sodium stannite by a standard procedure.[5] The resulting crude liquid II, testing negatively for halogen, was obtained in 13% yield. From treatment of this material with an equivalent quantity of mercuric chloride in 40 ml. of ether was obtained an 89% yield of mixed 2-methoxycyclohexylmercuric chlorides III and IV, m.p. 92–106°, m.p. 88–106° after one recrystallization from methanol.

The treatment of the di-(methoxycyclohexyl)mercury(II) with mercuric chloride was repeated using 4.6 g. of II and 2.94 g. of mercuric chloride in *ca.* 75 ml. of technical grade ether. After 3 min. at room temperature, 2.40 g. of a rather pure white solid crystallized out, m.p. 111–112°, mixed m.p. with authentic III 111–112°, mixed m.p. with authentic IV 87–92°. When the ethereal filtrate was evaporated to dryness, 4.94 g. of a solid containing only traces of mercuric chloride was obtained. A 0.78-g. sample of this residue was heated in 3 ml. of glacial acetic acid to 100° for 5 min. Then the resulting solution was poured into 50 ml. of 6*N* sodium hydroxide, mercuric oxide precipitating and the *cis*-mercurial IV being converted to the soluble hydroxide. After removal of the mercuric oxide by centrifugation, the alkaline supernatant was poured into a solution of 2 g. of sodium chloride in 20 ml. of water and acidified with glacial acetic acid. The white solid which precipitated weighed 0.125 g. (11%) and melted at 108.5–111°, mixed m.p. 112–113° with authentic IV, mixed m.p. 88–95° with III. The material gave a negative test[3] for III.

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(5) S. Winstein and T. G. Traylor, *J. Am. Chem. Soc.*, **77**, 3751 (1955); See preparation of di-*s*-butylmercury.

Concerning the Synthesis of Methyl (11-Deoxycorticosteron-21-yl 2,3,4-Tri-*O*-acetyl-β-D-glucosid)uronate

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In response to a need for a water-soluble derivative of 11-deoxycorticosterone (I), the preparation of a 21-glucosiduronic acid was undertaken. The preparation of the 21-glucoside of I has been previously reported,[1] as well as the 21-glucosides of both cortisone and 17α-hydroxy-11-deoxycorticosterone[2]; however, the solubility in water of these derivatives is limited.

Particularly significant is the coupling of methyl 2,3,4-tri-*O*-acetyl-1-bromo-1-deoxy-α-D-glucuronate (III) with 21-acetoxy-3α,17α-dihydroxypregnane-11,20-dione.[3] The protecting groups were not removed, however, and the glucosiduronate thus secured was compared directly with the methylated and fully acetylated derivative of the glucosiduronic acid recovered from the urine after administration of 3α,17α,21-trihydroxypregnane-11,20-dione. This work strongly supports the general belief that conjugation of glucuronic acid with metabolic reduction products of corticoids, as well as of certain steroid hormones, takes place at C(3). Reported also is the synthesis of the 3,21-bis(methyl 2,3,4-tri-*O*-acetyl-β-D-glucosiduronate) of 3β,17α,-21-trihydroxy*allo*pregnan-20-one.[4] Both of these, however, are conjugates of inactive corticoids. The preparation of a 21-glucosiduronic acid of 11-deoxycorticosterone (I) would be of especial interest for I is an active corticoid; further, the attachment of the glucuronic acid would be at a point other than C(3). Such a derivative might, therefore, display interesting biological properties.

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