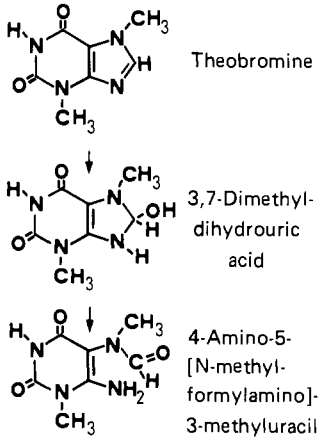

Figure 5. Pathway of 4-amino-5-(*N*-methylformylamino)-3-methyluracil formation from theobromine through the hypothetic 3,7-dimethyldihydrouric acid.

was in fact the 4-amino-5-(*N*-methylformylamino)-1,3-dimethyluracil.

Blood analysis using the less drastic technique of high-pressure liquid chromatography and the study of the chemical structure of these compounds may be of value in the understanding of the biological mechanism of the theobromine and caffeine transformation into these polar compounds rapidly excreted in the urine.

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A Convenient Preparation of Pure Stearoyl-2-lactylic Acid

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A preparation of pure stearoyl-2-lactylic acid is described in which benzyl lactylate is allowed to react with stearoyl chloride. The benzyl ester, a key intermediate, is prepared from lactide and benzyl alcohol.

Stearoyl-2-lactylic acid, the stearate ester of the linear lactic acid dimer, and its sodium or calcium salts find use as surfactants in dough conditioner mixtures (Griffin and Lynch, 1972). The effect of these compounds in modifying rheological properties of doughs, altering crumb structure in breads, and improving loaf volume has been attributed to complexation with the starch components, especially amylose (Krog, 1971). The involvement of amylopectin was pointed out by De Stefanis et al. (1977) and the role of binding of these surfactants to cereal proteins has also been established (Chung and Tsen, 1975; Greene, 1975). Fullington (1974) isolated a protein from wheat flour that binds calcium and which also forms a complex with the stearoyl-2-lactylate ion.

Investigations in this laboratory on protein interactions with various surfactants necessitated pure samples of stearoyllactylic acid and its salts. Since commercially obtainable materials consist of a mixture of mainly mono-, di-, and trimeric lactic acid derivatives which resist purification it was necessary for us to develop a satisfactory synthesis for the desired dimeric compounds.

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EXPERIMENTAL SECTION

General. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are corrected. Infrared (IR) spectra were recorded on a Perkin-Elmer Model 257 instrument and proton magnetic resonance (^{1}H NMR) spectra were determined with a Varian A-60 spectrometer and are reported as parts per million (δ) relative to tetramethylsilane (internal standard).

Lactide. Lactic acid (87%) was heated under aspirator vacuum until water was no longer evolved (pot temperature to 200 °C). The pressure was then reduced to ca. 0.1 mm and crude product was collected as a very viscous distillate, bp 80–90 °C. Crystallization from diethyl ether followed by 95% ethanol gave a 20% yield of cyclic dimer, mp 124–125 °C (lit. mp 125 °C for the *d,l* form; Dietzel and Krug, 1925). IR ($CHCl_3$): 1770 cm^{-1} (cyclic ester carbonyl); NMR ($CDCl_3$) δ 1.64 (d, J = 7 Hz, 6 H, $CHCH_3$), 5.13 (q, J = 7 Hz, 2 H, $CHCH_3$).

Benzyl Lactylate. In a 500-mL flask equipped with stirrer and condenser were placed 28.8 g (200 mmol) of lactide, 43.2 g (400 mmol) of benzyl alcohol, 0.5 g of *p*-toluenesulfonic acid and 150 mL of dry dioxane. The mixture was refluxed 19 h and most of the dioxane was

then removed by rotary evaporation. The residue was taken up in 150 mL of ether and washed in succession with two 50-mL volumes of water and two 50-mL volumes of 5% Na_2CO_3. After drying over $MgSO_4$ and filtration, the solution was concentrated under vacuum to a heavy oil which was maintained at 0.1 mm/100 °C for 2 h. The clear liquid remaining weighed 36.2 g (143 mmol, 72%). IR ($CHCl_3$): 3600 br (hydroxyl) and 1740 cm^{-1} br (ester carbonyls). NMR ($CDCl_3$): δ 1.42 (d, J = 7 Hz, 3 H, CH-CH_3), 1.50 (d, J = 7 Hz, 3 H, CHCH_3), 3.55 (s, 1 H, OH), 4.34 (q, J = 7 Hz, 1 H, CHCH$_3$), 5.15 (s, 2 H, $C_6H_5CH_2$), 5.22 (q, J = 7 Hz, 1 H, CHCH$_3$), 7.31 (s, 5 H, C_6H_5). Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39. Found: C, 61.9; H, 6.54.

Benzyl Stearoyl-2-lactylate. In a 100-mL flask equipped with stirrer and drying tube were placed 50 mL of pyridine, 7.56 g (30 mmol) of benzyl lactylate, and 10.0 g (33 mmol) of stearoyl chloride. After the initial warming had subsided, the mixture was warmed briefly to 95 °C and then allowed to stand 2.5 h at room temperature. The pyridine solution was poured into 250 mL of water, extracted twice with two 150-mL volumes of ether, and the combined ethereal solutions were then washed in succession with two 100-mL volumes of water, 100 mL of 1 N HCl, and 100 mL of 5% K_2CO_3. After drying over $MgSO_4$ and evaporation, the crude product was chromatographed with benzene over 250 g of Woelm Act I neutral Al_2O_3. Material eluting between 200 and 800 mL, 6.71 g (13 mmol, 45%), was used directly in the next step. IR ($CHCl_3$) 1750 cm^{-1} (ester carbonyls), no hydroxyl absorption; NMR ($CDCl_3$) δ 0.84 (br t, J = 7 Hz, 3 H, CH_2CH_3), 1.23 (br s, 30H, $(CH_2)_{15}$), 1.45 (d, J = 7 Hz, 3 H, CHCH_3), 1.49 (d, J = 7 Hz, 3 H, CH-CH_3), 2.33 (br t, J = 7 Hz, 2 H, -CH_2COO), 4.9–5.4 (complex, 4 H, 2 CHCH$_3$'s and $C_6H_5CH_2$), 7.32 (s, 5 H, C_6H_5).

Stearoyl-2-lactylic Acid. Benzyl stearoyl-2-lactylate, 5.21 g (10 mmol), was dissolved in 60 mL of EtOAc, and 0.5 g of 5% Pd/C was added. Hydrogenation was carried out at 3 atm/20 °C in a shaking apparatus until uptake ceased. Filtration and evaporation of the mixture gave 3.79 g of solid (8.8 mmol, 88%) which crystallized from heptane/EtOAc: mp 66–69 °C; IR ($CHCl_3$) 2600–3600 (carboxyl OH) and 1730 cm^{-1}, br (ester and carboxy carbonyl); NMR ($CDCl_3$) δ 0.87 (br t, J = 7 Hz, 3 H, CH_2CH_3), 1.25 (br s, 30H, $(CH_2)_{15}$), 1.55 (superimposed doublets, J = 7 Hz, 6 H, 2 CHCH_3's), 2.40 (br t, J = 7 Hz, 2 H, CH_2COO) 4.9–5.4 (complex, 2 H, 2 CHCH$_3$'s). Anal. Calcd for $C_{24}H_{44}O_6$: C, 67.26; H, 10.35. Found: C, 67.5; H, 10.3.

RESULTS AND DISCUSSION

Pure stearoyl-2-lactylic acid can be prepared from a suitably protected linear lactic acid dimer. Thus, benzyl lactylate was prepared in good yield by acid-catalyzed ring opening of the cyclic lactate dimer (lactide) in the presence of excess benzyl alcohol. It was necessary to prepare lactide by self-condensation of lactic acid, followed by distillation and crystallization of the cyclic dimer (Dietzel and Krug, 1925) as commercial materials are entirely unsatisfactory, consisting of much polymeric material. After esterification of the hydroxyl group of benzyl lactylate with stearoyl chloride in pyridine, the protective benzyl group was removed by catalytic hydrogenolysis. The stearoyl lactylic acid obtained in this way is free from monomeric and higher oligomeric lactate compounds (NMR) and is suitable for physicochemical studies upon conversion to the appropriate salt. We have also found benzyl lactylate to be a convenient starting material for the preparation of other keto- and hydroxyaliphatic acid derivatives.

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