compds **4** and **10**. These results do not support the idea that the antiinflammatory activity of the indan-1-carboxylic acids is due to a steroid-like mechanism.

Experimental Section†

(±)-6-Acetoxy-5-cyclohexylindan-1-carboxylic Acid (5). Ac_2O (3.8 ml, 0.0401 mole) was added to a cooled (ice-H_2O), stirred soln of (±)-5-cyclohexyl-6-hydroxyindan-1-carboxylic acid[1] (**4**, 7.79 g, 0.0299 mole) in 5 *N* NaOH (14.9 ml, 0.0745 mole) and H_2O (20 ml) contg ice (50 g). After 3 min the soln was acidified with concd HCl. The ppt was collected, washed (H_2O), and dried. The product was recrystd from cyclohexane to give **5** (6.6 g, 73%) as colorless crystals: mp 188–190°. *Anal.* ($C_{18}H_{22}O_4$) C, H.

(±)-5-Cyclohexyl-6-hydroxy-1-hydroxyacetylindan (9). A soln of **5** (5.54 g, 0.0183 mole), $SOCl_2$ (2.74 g, 0.023 mole), and DMF (5 drops) in CH_2Cl_2 (85 ml) was refluxed for 2 hr. The cooled soln was concd and then treated twice with C_6H_6 (55 ml), concg after each addn. A soln of the residue in Et_2O (20 ml) was added to a soln of CH_2N_2 (0.111 mole) in Et_2O (200 ml). The soln was kept in an ice bath for 1 hr and then concd to half vol. The soln was filtered and concd to yield **7** as a yellow oil: ir (film) 1639 (C=O) and 2110 cm^{-1} ($CH{=}N^+{=}N^-$).

A mixt of this crude diazo ketone **7** and KOH (2.33 g) in CH_3OH (55 ml) and H_2O (2.5 ml) was stirred at 25° for 1 hr. A gummy solid was pptd with AcOH. The solid was extd into Et_2O. The Et_2O soln was washed (H_2O), dried (Na_2SO_4), and concd to give **8** as a viscous gum (5.2 g). A soln of crude **8** in a mixt of dioxane (85 ml) and 2.5 *N* H_2SO_4 (33 ml) was heated at 50° for 10 min. The mixt was dild with H_2O and extd with Et_2O. The Et_2O soln was washed (H_2O, aq $NaHCO_3$, satd aq NaCl), dried (Na_2SO_4), and concd to yield a red gum (4.56 g). The gum was chromatogd over silicic acid (Mallinckrodt, CC-7, 100–200 mesh) with PhMe–Me_2CO (10:1) to give a solid which was recrystd from C_6H_6–Skellysolve B (charcoal) to yield **9** (1.5 g, 30% based on **5**) as brown crystals: mp 136–138°. Recrystn from MeOH–H_2O gave pale yellow crystals: mp 135.5–137°; ir (KBr) 1715 (ketone C=O) and 3395 cm^{-1} (OH, broad). *Anal.* ($C_{17}H_{22}O_3$) C, H.

(±)-5-Cyclohexyl-1-hydroxyacetylindan (11). A soln of (±)-5-cyclohexylindan-1-carboxylic acid[1] (**10**, 5.0 g, 0.0205 mole), $SOCl_2$ (1.6 ml, 0.0215 mole), and DMF (2 drops) in CH_2Cl_2 (50 ml) was refluxed for 1.25 hr. The cooled soln was concd and then treated twice with C_6H_6 (25 ml), concg after each addn. A soln of the residue in Et_2O (15 ml) was added to a cold soln of CH_2N_2 (0.0667 mole) in Et_2O (125 ml). The soln was kept in an ice bath for 4 hr and was then allowed to stand at 25° for 16 hr. The soln was filtered and concd to give the diazo ketone (5.3 g) as yellow crystals: mp 75–79° dec; ir (CH_2Cl_2) 1639 (C=O) and 2110 cm^{-1} ($CH{=}N^+{=}N^-$).

A soln of the diazo ketone in dioxane (100 ml) and 2 *N* H_2SO_4 (65 ml) was heated on a steam bath for 30 min and then refluxed for 2 min. The cooled soln was dild with H_2O and extd with Et_2O. The Et_2O soln was washed (H_2O, satd aq $NaHCO_3$, H_2O), dried (Na_2SO_4), and concd. The residue was recrystd from pentane (charcoal) to give **11** (2.7 g, 51% based on **10**): mp 84–86°. Recrystn from petr ether (bp 37–47°) gave pale yellow crystals: mp 85.5–86.5°; ir (KBr) 1722 (ketone C=O), 3440, and 3460 cm^{-1} (O–H). *Anal.* ($C_{17}H_{22}O_2$) C, H.

†Where analyses are indicated only by symbols of the elements, results obtained for these elements were within ±0.4% of the theoretical values. Melting points are uncorrected.

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New Compounds

Synthesis of Some 6-Hydroxymethyluracil Derivatives

K. L. Nagpal*
Central Drug Research Institute, Lucknow, India.
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As part of a program for the synthesis of pyrimidines for biological evaluation,[1] the preparation of certain derivatives of 6-hydroxymethyluracil (I) was undertaken. It was thought that these compounds could be transformed into benzylium type species (uracil-6-methylenium ions) which in turn might react with other molecules and bring about biochemically significant reactions.

Experimental Section

The purity of the compounds was determined by paper chromatog: solvent A, *n*-BuOH–AcOH–H_2O, 4:1:5, descending; solvent B, *n*-BuOH–H_2O, 86:14, ascending. All evapns were carried out *in vacuo* at 40°.

6-Hydroxymethyluracil[2] (I). A soln of *n*-butyl orotate[3] (2.0 g, 9.4 mmoles) in dry THF (50 ml) was added dropwise to a suspension of LAH (0.7 g) in 100 ml of THF over a period of 90 min. After the addn was complete, the mixt was stirred at room temp for 8 hr. The excess hydride was decompd by the slow addn of H_2O, and the whole was concd to dryness. The residual solid was extd with H_2O (3 × 50 ml) at 50°. The combined aq soln was concd under reduced pressure to 40 ml and acidified with dil HCl to pH 3–4. The product sepd on cooling and was crystd from H_2O: yield, 0.60 g (52%); mp 254° dec; R_f A, 0.45; B, 0.32; uv 0.1 *N* HCl, λ_{max} 262 nm (ϵ 10,880), 0.1 *N* NaOH, λ_{max} 284 nm (ϵ 10,280). *Anal.* ($C_5H_6N_2O_2$) C, H, N.

6-Acetoxymethyluracil (II). A mixt of I (710 mg, 5 mmoles) and Ac_2O (3 ml) in pyridine (15 ml) was stirred for 2 hr under anhyd condns. The mixt was treated with 50% EtOH and evapd. The residual white solid was crystd from H_2O to yield 725 mg (78%) of II: mp 240–242°; R_f A, 0.65; B, 0.49; uv 0.1 *N* HCl, λ_{max} 261 nm (ϵ 11,100), 0.1 *N* NaOH, λ_{max} 282 nm (ϵ 10,785). *Anal.* ($C_7H_8N_2O_4$) C, H, N.

6-Acetoxymethyl-4-thiouracil (III). A mixt of II (1.16 g, 6.3 mmoles) and P_2S_5[4] (0.70 g, 3.15 mmoles) was refluxed in dry pyridine (40 ml) with exclusion of moisture for 5 hr. The dark-brown soln was evapd to dryness. H_2O (20 ml) was added to the residue and the whole cooled at 4°. The brown solids were collected, washed thoroughly with cold H_2O and crystd twice from hot H_2O: yield, 487 mg (41%); mp 206–208°; R_f A, 0.82; B, 0.69; uv 0.1 *N* HCl, λ_{max} 330 nm (ϵ 18,500) 0.1 *N* NaOH, λ_{max} 327 nm (ϵ 12,700), 333 nm inflection (ϵ 10,700). *Anal.* ($C_7H_8N_2O_3S$) C, H, N.

6-Hydroxymethyl-4-thiouracil (IV). Compd III (600 mg, 3 mmoles) was dissolved in 2.1 ml of concd HCl and heated on a steam bath for 2 hr. The soln was cooled in an ice bath, and the sepd brown solid was collected, washed with cold H_2O, and crystd from H_2O: yield, 366 mg (61%); mp 226–227°; R_f A, 0.61; B, 0.55; uv 0.1 *N* HCl, λ_{max} 327 nm (ϵ 17,930), 0.1 *N* NaOH, λ_{max} 317 nm

*Address correspondence to author at the Department of Biochemistry and Biophysics, Texas A & M University, College Station, Texas 77843.

(ε 11,960), 333 nm inflection (ε 10,160). *Anal.* ($C_5H_6N_2O_2S$) C, H, N.

6-Hydroxymethylcytosine (V). A soln of III (300 mg, 1.5 mmoles) in 24 ml of methanolic NH_3 (satd at 0°) was heated at 100° in a sealed tube for 21 hr. The reddish soln was concd to about 15 ml and cooled for 36 hr in a refrigerator. The solid material was filtered off and crystd from EtOH-H_2O: yield, 141 mg (53%); mp indefinite with darkening at *ca.* 210° followed by slow decompn; R_f A, 0.27; B, 0.15; uv 0.1 *N* HCl, λ_{max} 278 nm (ε 10,520), 0.1 *N* NaOH, λ_{max} 281 nm (ε 8200). *Anal.* ($C_5H_7N_3O_2$) C, H, N.

6-Hydroxymethyl-2-hydroxy-4-hydrazinopyrimidine (VI). A mixt of III (500 mg, 2.50 mmoles) and hydrazine hydrate (3 ml) in EtOH (18 ml) was refluxed for 2 hr and then held at room temp for 16 hr. The clear soln was evapd to dryness, and the residue was crystd from 50% MeOH: yield, 226 mg (58%); mp begins to darken about 200° and dec above 250°; R_f A, 0.54; B, 0.48; uv 0.1 *N* HCl, λ_{max} 277 nm (ε 9130), 0.1 *N* NaOH, λ_{max} 282 nm (7630). *Anal.* ($C_5H_8N_4O_2$) C, H, N.

6-Hydroxymethyluracil Phosphate (VII). Compd I (142 mg, 1 mmole) was dissolved in dry pyridine (5 ml). Pyridinium cyanoethyl phosphate[5] (2 mmoles) was added to the clear soln and the mixt was evapd to dryness at 30°. Pyridine (3 × 5 ml) was added to the residue and evapd similarly. The residue was finally dissolved in dry pyridine (8 ml), and DCI (1.44 g, 7 mmoles) was added. The reaction mixt was held in a stoppered flask for 2 days at room temp. H_2O (1 ml) was added, and the mixt was left at room temp for 1 hr. The solvents were removed at 30° and H_2O was added to the residue. Dicyclohexylurea was filtered off and washed thoroughly with H_2O. Excess of cyanoethyl phosphate was destroyed by heating the combined filtrates with 30 ml of 0.5 *N* NaOH at 100° for 40 min. The cooled soln was filtered from a small amt of insol material and passed through a column of Dowex 50 (H^+) resin. The eluate was evapd, and the syrupy residue was triturated with Me_2CO. The white solid so obtd was collected and purified by dissolving in MeOH and pptd by addn of Me_2CO and Et_2O: yield, 18 mg (8%); mp 222–225° dec; uv 0.1 *N* HCl, λ_{max} 260 nm (ε 10,310), H_2O λ_{max} 261 nm (ε 10,120). *Anal.* ($C_5H_7N_2O_6P$) C, H, N.

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Book Reviews

Methods of Neurochemistry. Vol. 1. Edited by Rainer Fried. Marcel Dekker, New York, N. Y. 1971. xi + 374 pp. 23.5 × 16 cm. $22.75.

Every advance in the chemistry of brain and nerves has depended on the ability of the investigator to detect and identify compounds present in such tissues at abominably low concentrations reaching 10^{-9} *M* and beyond. More often than not the chemical and physical differences between isomeric, homologous, or otherwise closely related neurometabolites are minute, and normal microanalytical techniques break down in the face of such difficulties. It is not surprising that for years some monophenolic compounds were called loosely catecholamines, and that different laboratories have struggled to repeat the findings of another group of researchers. ["Strong men have cried like babes, bydam, to hear what happened at Babraham."] The description of definitive and reproducible methods by authors of generally recognized competence is a welcome technical aid in a tricky field that requires skill, imagination, and adroitness of interpretation. The present book, the first in a projected series, has brought together a number of these methods under one nicely appointed cover. They concern the purification and properties of isolated myelin (L. C. Mokrasch) and of phospholipids (G. B. Ansell and S. Spanner); the determination of catecholamines and their metabolites (D. F. Sharman); microiontophoresis (K. Krnjevic); and biochemical screening and diagnostic procedures in mental retardation (D. O'Brien). The last of these describes in detail the analytical methodology for detecting the various known compounds associated with inborn errors of metabolism which may cause mental retardation. These directions will be of great aid in routine clinical diagnosis of such pediatric tragedies.

The last 67 pages of the text contain a tabulation of selected compounds of importance to neurochemistry (R. Fried and W. Manzies). Each of these compounds is catalogued by class, name, structural formula, molecular weight, and a few words concerning its biological significance. These remarks are referenced on the spot by a not always very pertinent literature citation. The purpose of this catalog is not clear: the expert will not need it, and the novice will be mislead by the selectivity of the compounds listed, and the arbitrary and incomplete referencing. Nevertheless, the valuable "cook-book" directions in the other chapters will endear this book to neurochemists and to clinical analytical workers.

University of Virginia **Alfred Burger**
Charlottesville, Virginia

Kidney Hormones. Edited by J. W. Fisher, with 45 contributors. Academic Press. London, New York. 1971. xviii + 665 pp. 23.4 × 16.4 cm. $22.00

The readers of this Journal will have noticed recently the increasing number of papers dealing with kidney hormones. The present book summarizes the pharmacology and physiological effects of these and related substances, and to a smaller extent, their biochemistry. Materials isolated from kidney extracts but not shown to play a physiological role at a target organ site are also included.

The principal humoral agents discussed are renin, erythropoietin, erythrogenin, prostaglandins PGE_2 and PGF_{2}-α, angiotensin I and II, antihypertensive neutral renomedullary lipids (ANRL), kininogen, an erythropoietin inhibitor, and a renin preinhibitor. The isolation, characterization where possible, assay, standardization, activities, and pathological and clinical implications of these chemical agents, form the body of the reviews. Many of the contributors have divulged new experimental findings in the areas of hematology, cardiology, and urology. Thus the book will serve as a survey of the physiological and pharmacological state of the art in this active area of research.

University of Virginia **Alfred Burger**
Charlottesville, Virginia