

to 500 mg of CNBr-activated Sepharose in the presence of 30 mM sodium phosphate/0.5 M NaCl, pH 8.3. Previous to this process all enzymes were dialyzed against 30 mM sodium phosphate, pH 7.5. The Sepharose-enzyme mixture (total volume 10-15 mL) was gently agitated and permitted to react over a period of 2 h at room temperature. Residual active groups on the Sepharose support were hydrolyzed by passage of 30 mM Tris-HCl, pH 8.0, through the column for 2 h at room temperature. The column was next washed alternately with 30 mM sodium phosphate at high (8.3) and low (4.0) pH, which removed any protein ionically bound to the Sepharose support. The column was stored at 4 °C in 2 M KCl/30 mM sodium phosphate, pH 7.5.

Enzymatic Syntheses. Gaseous [^{13}N]ammonia (175-200 mCi) produced by the $^{16}\text{O}(\text{p},\alpha)^{13}\text{N}$ reaction on H_2O^{23} was swept with N_2 into a 5-mL buffered solution containing the following substrates: for the synthesis of L-[^{13}N]glutamate, 30 mM sodium phosphate, pH 7.5, 1.6 mM α -ketoglutarate, 1 mM NADH; for L-[^{13}N]alanine, 30 mM sodium phosphate, pH 7.5, 0.8 mM α -ketoglutarate, 1 mM NADH, 5 mM pyruvic acid; for L-[^{13}N]glutamine, 30 mM sodium phosphate, pH 7.5, 20 mM MgCl_2 , 6 mM L-glutamate, 6.8 mM ATP; for L-[^{13}N]aspartate, 30 mM sodium phosphate, pH 7.5, 20 mM MgCl_2 , 25 mM fumarate.

For the synthesis of ^{13}N -labeled L-glutamate, the glutamate dehydrogenase column was used. The buffered substrates with [^{13}N]ammonia were allowed to pass by gravity through the column, and the column was subsequently washed with 3 mL of 30 mM sodium phosphate buffer, pH 7.5, and all elutions were combined. A similar procedure was followed for L-[^{13}N]glutamine and L-[^{13}N]aspartate using the corresponding enzyme columns. For L-[^{13}N]alanine, the glutamate dehydrogenase/glutamate-pyruvate transaminase column was used. Five milliliters of 30 mM sodium phosphate, pH 7.5, was used to wash the column after passage of the substrate containing solution. A final AG 50W-X12 cation-exchange resin (0.7×7.5 cm; Na form) equilibrated with 30 mM sodium phosphate, pH 7.5, was used to retain any unreacted [^{13}N]ammonia in the synthesis of L-[^{13}N]glutamate, L-[^{13}N]alanine, L-[^{13}N]aspartate, and L-[^{13}N]glutamine. The ^{13}N -substituted L-amino acid solution was made isotonic. Finally, a $0.22\text{-}\mu\text{m}$ pore size filter was used to sterilize the product as it was passed into a sterile, pyrogen-free vial.

Myocardial Residue Fraction of ^{13}N -Labeled Amino Acids. The myocardial tracer residue fraction was studied with a single pass uptake technique in open-chest instrumented dogs. Experimental protocol, animal instrumentation, and data collection and processing used in our laboratory have been reported in detail previously.³¹ Briefly, the initial capillary transit and the retained amount of ^{13}N were recorded, and a time-activity curve was obtained with a scintillation detector following bolus injection of 10-20 μCi of the ^{13}N -labeled amino acids into the left circumflex

coronary artery. Data were collected in 0.1-s increments for 20 min and stored in a digital computer. Experimental runs were performed at control state and during ischemia. Ischemia was induced by mechanical occlusion and flow reduction, 20 min prior to injection and during data acquisition. Computer-assisted curve fitting revealed a triexponential time-activity curve. The residue fraction of ^{13}N retained in myocardium was determined with a graphic extrapolation of the third slow clearance phase (C) back to the time of the maximal peak (A) representing the total amount of activity injected. The residue fraction was computed as the ratio of C/A. The half-times of these residue fractions were calculated from the slope of the third slow clearance phase ($T_{1/2}$, Table I). These methods have been previously employed and validated for studies in the brain^{32,33} and in the heart.^{31,34,35} Inhibition of myocardial transaminases with aminooxyacetic acid was produced as previously described.¹¹

Tomographic Imaging. Cross sectional images were obtained with the UCLA positron emission computed axial tomograph, ECAT, as described in detail previously.³⁶ Again, open-chest instrumented dogs were studied with ischemia induced by mechanical occlusion and flow reduction with a screw-type occluder placed around the left anterior descending coronary artery. Flow reduction in the antero-septal myocardium was documented by tomographic imaging using 10-20 mCi of [^{13}N]ammonia injected intravenously.^{31,36} Then, imaging was performed under the same conditions, but 10-20 mCi of ^{13}N -labeled amino acid was given intravenously. Imaging was begun 5 min after injection. The residual of tracer was quantitated by assigning regions of interest to normal and ischemic myocardial segments, and their ratios were calculated for [^{13}N]ammonia (F), indicating the degree of flow reduction, as well as for ^{13}N -labeled amino acids (AA). The ratios AA/F allowed to estimate the amount of ^{13}N activity remaining in ischemic myocardium in relation to flow reduction. These ratios were consistently higher than 1.

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Benz-Fused Mesoionic Xanthine Analogues as Inhibitors of Cyclic-AMP Phosphodiesterase

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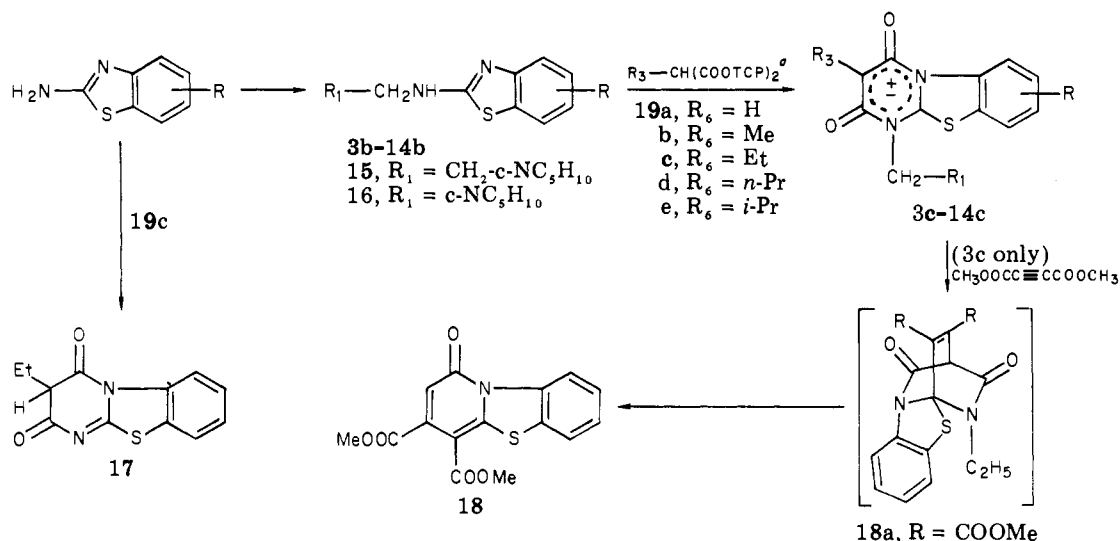
Mesoionic xanthine analogues, such as derivatives of mesoionic thiazolo[3,2-a]pyrimidine, constitute a new class of inhibitors of adenosine cyclic 3',5'-monophosphate (cyclic-AMP) phosphodiesterase (PDE). A series of 16 benz-fused analogues of the mesoionic thiazolopyrimidines were prepared and found to be more active than their nonfused counterparts, when assayed using bovine heart PDE.

Adenosine cyclic 3',5'-monophosphate (cyclic-AMP) phosphodiesterase (PDE) is an enzyme which converts

cyclic AMP to adenosine 5'-monophosphate and is responsible, in part, for regulation of intracellular levels of this cyclic nucleotide. Methylated xanthines, such as theophylline, inhibit cyclic nucleotide PDE, and, in an earlier publication, we reported that mesoionic xanthine

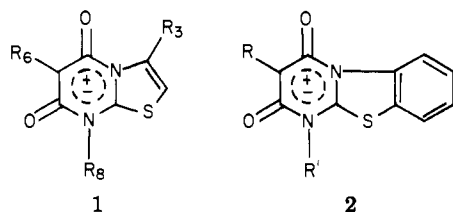
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Scheme I



^a TCP = 2,4,6-trichlorophenyl.

analogues (i.e., derivatives of mesoionic thiazolo[3,2-*a*]-pyrimidines, 1) also possess activity as inhibitors of cAMP



PDE.² For example, 1 ($\text{R}_6 = \text{R}_8 = \text{Et}$; $\text{R}_3 = \text{H}$) possesses theophylline-like effects as a PDE inhibitor (with an activity of approximately one-third that of theophylline) when assayed against bovine heart PDE (1 μM cyclic AMP substrate concentration).³ Introduction of a methyl or phenyl group at the R_3 position of 1 slightly enhances activity,³ while benz-fusion of 1 ($\text{R}_6 = \text{R}_8 = \text{Et}$; $\text{R}_3 = \text{H}$) to give 2 ($\text{R} = \text{R}' = \text{Et}$) results in a tenfold increase in activity. This prompted us to prepare a series of benz-fused derivatives of 1 for evaluation as inhibitors of cAMP PDE.

Chemistry. The mesoionic compounds were prepared as shown in Scheme I. Several unsuccessful attempts were made to prepare a mesoionic analogue with a more polar R_1 substituent; however, neither 15 nor 16, the latter being prepared by the method of Paris et al.,⁴ underwent cyclization under the usual conditions.

Biological Results and Discussion

In general, where comparisons can be made between the mesoionic xanthine analogues and their benz-fused counterparts the latter are usually somewhat more active as inhibitors of cAMP PDE. Increasing the size of the alkyl group at the R_3 position slightly enhances activity, but, at the same time, reduces solubility. Consequently, an R_3 Et group was used as a compromise between activity and solubility. Comparing 4e with 5d, activity is enhanced

when the isopropyl group at R_1 is converted to cyclopropyl. For this reason, several other cycloalkyl groups were investigated, with the cyclohexyl derivative 13c being the most active of those studied in this series. Introduction of an 8-ethoxy group was found to double activity (comparing 5d with 9c). The 8-ethoxy derivative of 13c (i.e., 14c) was prepared and evaluated; while 14c consistently produced at least 40% inhibition in the 10–20 μM range (in one instance an I_{50} of 8 μM was obtained), solubility problems precluded the determination of a reliable I_{50} value.

In order to determine if the mesoionic character of 3c–14c had any effect on activity, two closely related non-mesoionic compounds were evaluated. Compound 18 was quite insoluble under the assay conditions, and although 17 was active ($I_{50} = 467 \pm 5 \mu\text{M}$), it was less active than any of the mesoionic compounds evaluated.

Experimental Section

Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 257 spectrophotometer, and ^1H NMR spectra were determined on a Perkin-Elmer R-24 spectrometer using Me_4Si as an internal standard. Mass spectra were obtained on a Finnigan 4015 GC-MS data system at 70 eV. The structures of all compounds are consistent with their IR, NMR, and mass spectral data. Microanalyses were performed by Atlantic Microlab, Atlanta, GA, and results are within 0.4% of the calculated values. Radioactivity was measured using a Beckman Ls 355 liquid scintillation counter.

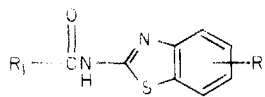
***N*-(2-Benzothiazolyl)cyclopropylcarboxamide (5a).** A solution of cyclopropylcarboxylic acid chloride (6.3 g, 60 mmol) in dry THF (30 mL) was added dropwise to a stirred, chilled (0 °C) solution of 2-aminobenzothiazole (9 g, 60 mmol) and NEt_3 (6.7 g, 66 mmol) in THF (120 mL). The reaction mixture was allowed to stir at room temperature for 4 h and was filtered, and the filtrate was dried (Na_2SO_4) and evaporated to dryness under reduced pressure to yield a white solid. Recrystallization from EtOAc afforded 7.4 g (56%) of 5a as fine white needles, mp 215–218 °C. See Table I for microanalytical data.

Compounds 3a–14a (Table I) were prepared in the same manner as 5a, by employing the appropriate acid chloride.

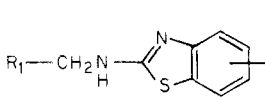
***N*-(Cyclopropylmethyl)-2-benzothiazolamine (5b).** A solution of 5a (2.9 g, 13 mmol) in dry THF (90 mL) was added dropwise to a stirred suspension of LiAlH_4 (1.0 g, 26 mmol) in THF (60 mL) at 0 °C. The mixture was heated at reflux for 4 h, cooled to room temperature, and excess LiAlH_4 decomposed by the addition of $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ in small portions. Filtration (Celite) and evaporation of the filtrate to dryness under reduced

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Table I. 2-(Acylamino)- and 2-(Alkylamino)benzothiazoles



3a-14a

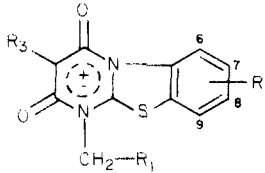


3b-14b

no.	R ₁	R	formula	mp, °C	recrystn solv	% yield	anal.
3a	CH ₃	H	C ₉ H ₈ N ₂ OS	186-188 ^a	EtOH	81	
4a	<i>i</i> -C ₃ H ₇	H	C ₁₁ H ₁₂ N ₂ OS	151-153	EtOAc	69	C, H, N
5a	<i>c</i> -C ₃ H ₅	H	C ₁₁ H ₁₀ N ₂ OS	215-218	EtOAc	56	C, H, N
6a	<i>c</i> -C ₃ H ₅	4-Cl	C ₁₁ H ₉ ClN ₂ OS·0.5H ₂ O	178-183	95% EtOH	81	C, H, N
7a	<i>c</i> -C ₃ H ₅	4-OCH ₃	C ₁₂ H ₁₂ N ₂ O ₂ S	210-212	95% EtOH	73	C, H, N
8a	<i>c</i> -C ₃ H ₅	6-OCH ₃	C ₁₂ H ₁₂ N ₂ O ₂ S	207-209	EtOAc	44	C, H, N
9a	<i>c</i> -C ₃ H ₅	6-OCH ₂ CH ₃	C ₁₃ H ₁₄ N ₂ O ₂ S	209-211	EtOAc	56	C, H, N
10a	<i>c</i> -C ₃ H ₅	5,6-(CH ₃) ₂	C ₁₃ H ₁₄ N ₂ OS	255-258	EtOAc	64	C, H, N
11a	<i>c</i> -C ₃ H ₇	H	C ₁₂ H ₁₂ N ₂ OS	150-155	EtOAc	70	C, H, N
12a	<i>c</i> -C ₃ H ₅	H	C ₁₁ H ₁₀ N ₂ OS	109-112	EtOAc	72	C, H, N
13a	<i>c</i> -C ₆ H ₁₁	H	C ₁₄ H ₁₆ N ₂ OS	131-134	EtOAc	70	C, H, N
14a	<i>c</i> -C ₆ H ₁₁	6-OCH ₂ CH ₃	C ₁₆ H ₂₀ N ₂ OS	186-189 ^b	95% EtOH	75	
3b	CH ₃	H	C ₉ H ₁₀ N ₂ S	87-91 ^c	95% EtOH	83	
4b	<i>i</i> -C ₃ H ₇	H	C ₁₁ H ₁₄ N ₂ S	110-113 ^d	95% EtOH	76	C, H, N
5b	<i>c</i> -C ₃ H ₅	H	C ₁₁ H ₁₂ N ₂ S	91-94	EtOH	66	C, H, N
6b ^e	<i>c</i> -C ₃ H ₅	4-Cl	C ₁₁ H ₁₁ ClN ₂ S	142-144	95% EtOH	59	C, H, N
7b ^e	<i>c</i> -C ₃ H ₅	4-OCH ₃	C ₁₂ H ₁₄ N ₂ OS	216-218	EtOH/THF	89	C, H, N
8b	<i>c</i> -C ₃ H ₅	6-OCH ₃	C ₁₂ H ₁₄ N ₂ OS	97-99	95% EtOH	60	C, H, N
9b	<i>c</i> -C ₃ H ₅	6-OCH ₂ CH ₃	C ₁₃ H ₁₆ N ₂ OS	134-135	95% EtOH	84	C, H, N
10b	<i>c</i> -C ₃ H ₅	5,6-(CH ₃) ₂	C ₁₃ H ₁₆ N ₂ S	153-155	EtOH	61	C, H, N
11b	<i>c</i> -C ₃ H ₇	H	C ₁₂ H ₁₄ N ₂ S	119-121	95% EtOH	68	C, H, N
12b	<i>c</i> -C ₃ H ₅	H	C ₁₃ H ₁₆ N ₂ S	116-118	95% EtOH	54	C, H, N
13b	<i>c</i> -C ₆ H ₁₁	H	C ₁₄ H ₁₈ N ₂ S	134-136	95% EtOH	76	C, H, N
14b	<i>c</i> -C ₆ H ₁₁	6-OCH ₂ CH ₃	C ₁₆ H ₂₂ N ₂ OS	123-125	95% EtOH	81	C, H, N

^a Literature⁸ mp 186 °C. ^b Literature⁹ mp 192-193 °C. ^c Literature¹⁰ mp 87-88 °C; lit.¹¹ mp 93-94 °C. ^d Literature¹² mp 101-103 °C; lit.¹⁰ mp 103-104 °C. ^e Compounds 6b and 7b failed to undergo cyclization under the usual conditions; heating at elevated temperatures or for prolonged periods of time with the malonate esters resulted in decomposition.

Table II. Benz-Fused Mesoionic Xanthine Analogues



no.	R ₁	R ₃	R	formula	mp, ^a °C	% yield	anal.	inhbn of cAMP PDE: I ₅₀ , μM ^b	rel N ^c potency ^e
3c	CH ₃	H	H	C ₁₂ H ₁₀ N ₂ O ₂ S	233-236	48	C, H, N	323 (±0.8)	2 1.3
3d	CH ₃	CH ₃	H	C ₁₃ H ₁₂ N ₂ O ₂ S	248-251	78	C, H, N	271 (±50)	2 1.5
3e	CH ₃	C ₂ H ₅	H					153 (±27)	3 2.7
4c	<i>i</i> -C ₃ H ₇	H	H	C ₁₄ H ₁₄ N ₂ O ₂ S	194-196	49	C, H, N	249 (±21)	2 1.7
4d	<i>i</i> -C ₃ H ₇	CH ₃	H	C ₁₅ H ₁₆ N ₂ O ₂ S	215-217	56	C, H, N	289 (±0.4)	2 1.4
4e	<i>i</i> -C ₃ H ₇	C ₂ H ₅	H	C ₁₆ H ₁₈ N ₂ O ₂ S	170-172	30	C, H, N	255 (±53)	2 1.6
4f	<i>i</i> -C ₃ H ₇	<i>n</i> -C ₃ H ₇	H	C ₁₇ H ₂₀ N ₂ O ₂ S	160-162	44	C, H, N	231 (±51)	2 1.8
4f	<i>i</i> -C ₃ H ₇	<i>i</i> -C ₃ H ₇	H	C ₁₇ H ₂₀ N ₂ O ₂ S	134-136	30	C, H, N	189 (±19)	2 2.2
5c	<i>c</i> -C ₃ H ₅	H	H	C ₁₄ H ₁₂ N ₂ O ₂ S	197-198	43	C, H, N	227 (±21)	2 1.8
5d	<i>c</i> -C ₃ H ₅	C ₂ H ₅	H	C ₁₆ H ₁₆ N ₂ O ₂ S	184-186	62	C, H, N	163 (±0.8)	2 2.5
5e	<i>c</i> -C ₃ H ₅	<i>i</i> -C ₃ H ₇	H	C ₁₇ H ₁₈ N ₂ O ₂ S·0.5H ₂ O	166-168	70	C, H, N	insoluble	
8c	<i>c</i> -C ₃ H ₅	C ₂ H ₅	8-OCH ₃	C ₁₇ H ₁₈ N ₂ O ₃ S	191-193	70	C, H, N	109 (±0.4)	3 3.8
9c	<i>c</i> -C ₃ H ₅	C ₂ H ₅	8-OCH ₂ CH ₃	C ₁₈ H ₂₀ N ₂ O ₃ S	207-209	81	C, H, N	69 (±0.6)	2 6.0
10c	<i>c</i> -C ₃ H ₅	C ₂ H ₅	7,8-(CH ₃) ₂	C ₁₈ H ₂₀ N ₂ O ₂ S	211-213	74	C, H, N	insoluble	
11c	<i>c</i> -C ₄ H ₇	C ₂ H ₅	H	C ₁₇ H ₁₈ N ₂ O ₂ S	180-182	66	C, H, N	167 (±0.6)	2 2.5
12c	<i>c</i> -C ₃ H ₅	C ₂ H ₅	H	C ₁₈ H ₂₀ N ₂ O ₂ S	166-167	60	C, H, N	102 (±24)	3 4.0
13c	<i>c</i> -C ₆ H ₁₁	C ₂ H ₅	H	C ₁₉ H ₂₂ N ₂ O ₂ S	173-176	70	C, H, N	34 (±0.4)	3 12.1
14c	<i>c</i> -C ₆ H ₁₁	C ₂ H ₅	8-OCH ₂ CH ₃	C ₂₁ H ₂₆ N ₂ O ₃ S	202-204	71	C, H, N	^d	

^a All compounds were recrystallized from *i*-PrOH. ^b I₅₀ value followed by standard deviation. The I₅₀ for theophylline control is 412 ± 20. ^c N = number of duplicate determinations. ^d See text for explanation. ^e Potency relative to theophylline = 1.0.

pressure afforded a pale golden oil which crystallized on standing. Recrystallization from absolute EtOH gave 1.8 g (66%) of 5b as white needles, mp 91-94 °C. See Table I for microanalytical data.

Compounds 3b-14b (Table I) were prepared in the same manner as 5b.

Anhydro-1-(cyclopropylmethyl)-2-hydroxy-3-oxo-pyrimido[2,1-a]benzothiazolium Hydroxide (5c). An intimate mixture of 5b (0.41 g, 2 mmol) and bis(2,4,6-trichlorophenyl) malonate (19a; 0.93 g, 2 mmol) was heated, neat, at 160 °C under a slow stream of N₂ until a clear orange melt resulted (2 min).

After cooling, the gummy product was triturated with anhydrous Et₂O to yield a crude crystalline product. Recrystallization from *i*-PrOH afforded 0.23 g (43%) of **5c** as tiny golden needles: mp 197–198 °C; IR (CHCl₃) 1605 cm⁻¹; NMR (CDCl₃) δ 0.6 (t, 4 H, CH₂CH₂), 1.5 (m, 1 H, CH), 4.1 (d, 2 H, N-CH₂), 5.2 (s, 1 H, C₃H), 7.7 (m, 3 H), 9.2 (m, 1 H, aromatic protons); UV (95% EtOH) λ_{max} 225 (ε 15 370), 268 (6900), 298 (1380); mass spectrum, *m/e* (relative intensity) 272 (23), 55 (100). See Table II for micro-analytical data.

All of the mesoionic compounds (**3c**–**14c**, Table II) were prepared in the same manner as **5c**, employing the appropriately substituted amine, **3b**–**14b**, and malonate ester, **19a**–**e**.

N-(1-Piperidinylethyl)-2-benzothiazolamine (**15**). Compound **15** was prepared in 60% yield by the reduction of **15b**⁶ using the same procedure employed for the reduction of **5a**. The product was characterized as the hydrochloride salt, mp 227–230 °C after recrystallization from 95% EtOH. Anal. (C₁₄H₁₉N₃·2HCl·0.5H₂O) C, H, N.

3,4-Dicarbomethoxy-1-oxopyrid[2,1-*b*]benzothiazole (**18**). Compound **3c** (0.62 g, 2.5 mmol) and dimethylacetylene dicarboxylate (0.71 g, 5 mmol), in CHCl₃ (50 mL), were heated at reflux for 24 h. The solvent was removed under reduced pressure, and trituration of the resultant gummy mass with anhydrous Et₂O afforded an orange solid. Recrystallization from *i*-PrOH gave 0.13 g (16%) of **18** as yellow needles: mp 197–200 °C; IR (CHCl₃) 1745, 1700, 1670 cm⁻¹; NMR (CDCl₃) δ 4.0 (s, 6 H, CH₃), 6.5 (s, 1 H, C₂H), 7.7 (m, 3 H), 9.3 (m, 1 H); mass spectrum, *m/e* (relative intensity) 317 (18), 316 (100), 258 (73). Anal. (C₁₅H₁₁NO₅S) C, H, N.

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3-Ethyl-2,3,4,5-tetrahydropyrid[2,1-*b*]benzothiazole-2,4-dione (**17**). A mixture of 2-aminobenzothiazole (0.53 g, 3.5 mmol) and **19c**⁵ (1.72 g, 3.5 mmol) was heated neat at 160 °C for 1 min. Upon cooling, the mixture was triturated with anhydrous Et₂O (25 mL) and filtered. The Et₂O-insoluble material was collected and recrystallized from absolute EtOH (250 mL) to give 0.4 g (46%) of **17** as flocculant white needles, mp 284–286 °C. Anal. (C₁₂H₁₀N₂O₂S) C, H, N.

PDE Assay. The assay of Klee⁷ was used, employing bovine heart phosphodiesterase (Sigma Chemical Co.) and 1 μM [8-³H]adenosine cyclic monophosphate as we have previously described in more detail.² *I*₅₀ values were determined by plotting uninhibited velocity/inhibited velocity (*V*₀/*V*) vs. the inhibitor concentration. The *I*₅₀ is the inhibitor concentration where *V*₀/*V* = 2. At least five different inhibitor concentrations, giving 25–75% inhibition, were used for each inhibitor.

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Book Reviews

Compendium of Organic Synthetic Methods. Volume 4. By Leroy G. Wade, Jr. Wiley, New York. 1980. xvi + 497 pp. 16 × 23.5 cm. \$22.50.

The fourth volume in this series presents the new synthetic methods for preparation of monofunctional compounds for 1977, 1978, and 1979. As in the previous volumes, sections appear corresponding to most of the possible interconversions between the major functional groups. This volume also contains examples of new methods of preparation of difunctional compounds formed from pairs of the major functional groups.

This collection of reactions facilitates the rapid location of reactions when the functional groups present in the starting material and product are known. These volumes serve as an invaluable tool for synthetic organic chemists, medicinal chemists, and biochemists.

Staff

Somatostatin. Volume 2. By M. T. McQuillan. Eden Press, St. Alans, VT. 1980. iii + 234 pp. 13 × 21 cm. \$30.00.

This book is an admirable compilation of the literature on somatostatin from mid-1977 to 1979. It consists of 16 chapters which are well written and well referenced, thus valuable to current research investigators.

The voluminous amount of literature dealing with the effects on secretion of hormones of the pancreatic islets, distribution, and biosynthesis of somatostatin has been elegantly covered in Chapters 3, 9, and 10, respectively. The chapter on "Properties of the Somatostatin Molecule" deals adequately with the isolation techniques for somatostatin or "somatostatin-like" molecules. Medicinal chemists will appreciate an interesting chapter on structure-activity relationship and a section on conformation in a book primarily devoted to biological aspects of the peptide.

In conclusion, this book is timely and well worth its price. It will be most useful to research scientists working in the area of somatostatin. Furthermore, it will also be a valuable addition to the libraries of academic and research institutions. Considering the number of papers published in this area since the publication of this book, it is imperative to update this volume in the next few years.

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Tikam C. Jain

Synthesis and Release of Adenohypophyseal Hormones.

Edited by Marian Jutisz and Kenneth W. McKerns. Plenum Press, New York. 1980. 797 pp. 15.5 × 23.5 cm. \$69.50.

This is an interesting and informative book mainly concerned with cellular and molecular mechanisms that regulate pituitary hormone secretion. The volume contains 37 chapters with the main emphasis placed on hormone synthesis and release by the anterior pituitary gland, although one chapter deals with control of the anterior lobe by the neutral lobe, and another chapter deals with secretion by the intermediate lobe. Comparative aspects are also presented, since there are chapters on hormone release in fish and amphibians. There are several chapters dealing with morphology, and these present information obtained mainly from immunocytochemical techniques.

The adenohypophyseal hormones that received the most attention were gonadotropins and ACTH and related peptides. Less emphasis was placed on growth hormone, prolactin, and TSH. All of the questions and answers from the discussion periods are contained at the end of each chapter, along with an excellent bibliography.

One of the interesting aspects of this volume, unlike many publications of symposia, is that many of the authors presented