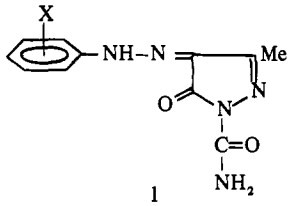
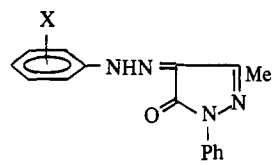
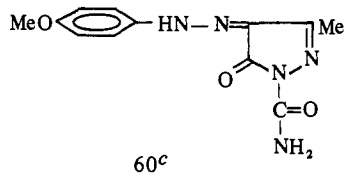
Table I. CNS Activity

No.	X	Mp, °C	Dose, mg/kg	Activity,[g] min Onset	Peak	Duration
	 1			 2		
1a	3-Cl	203[a]	100[b]	65	190	135[c]
b	3-Cl		300[d]			
c	2-Cl	210[a]	300[d]			
d	4-OMe	201[a]	300[d]			
e	2,5-Cl_2	258–259[e]	300[d]			
2a	H	156[f]	300[d]			
b	2,5-Cl_2	224[f]	300[d]			
c	2-Cl	182[f]	300[d]			
d	4-OMe	135[f]	300[d]			

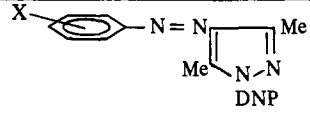
[a]Reference 1. [b]All drugs were administered ip in rats (Pratt). [c]No stimulation; depression was present. [d]Oral administration in rats (Pratt). [e]Reference 2. [f]Reference 3. [g]Reference 6.

Table II. Diuretic Activity[a,b]

Dose, mg/kg po	% excreted	Effect Δ% excreted[d] (test – control)
		
Control	60[c]	
15	64	4
30	70	10

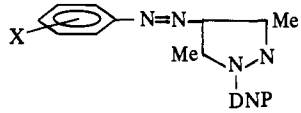
[a]See footnote *a*, Table I. [b]Eight rats per group hydrated with 25 ml/kg of 0.9% NaCl po; length of test, 5 hr. [c]Experience has fixed the control % excretion value at 60 for rats. [d]Reference 7.

Table III. Activity against *Eimeria tenella*

No.	X	Mp, °C	Activity[a,d]
	 DNP		
1	2,5-Cl_2	213–214[c]	*b*
2	2-NO_2	216–218[c]	*b*
3	4-Cl	254–255[c]	*b*

[a]0.05% dose level. [b]Inactive. [c]Reference 5. [d]Reference 8.

Table IV. Antiviral Activity[a,f]

No.	X	Mp, °C	Respiratory syncytial long T[c,e]	A[d,e]	Rhino virus 1059 T[c,e]	A[d,e]	Rhino virus 33342 T[c,e]	A[d,e]
	 DNP							
1	2-NO_2	*b*	0	0	1	0	1	0
2	3-NO_2	*b*	0	0	0	0	1	0

[a]*In vitro*. [b]See footnote *d* of Table II. [c]Cell toxicity. [d]Plaque inhibition. [e]0 = No plaque inhibition; 1 = <10 mm radius zone; 2 = >10 mm radius zone. [f]Reference 9.

ities in rats (Tables I and II, respectively), anthelmintic activity[8] in chickens (Table III), and antiviral activity[9] (Table IV).

Acknowledgment. The author is thankful to Dr. Maxwell Gordon (SK&F Laboratories, Philadelphia, Pa.) for making testing data available.

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3,3[1]-Ethylenediglutarimide as a Potential Tumor Inhibitor

David B. Haydock and Thomas P. C. Mulholland*

Imperial Chemical Industries Ltd., Pharmaceuticals Division, Mereside, Alderley Park, Macclesfield, Cheshire, SK10 TG, England.
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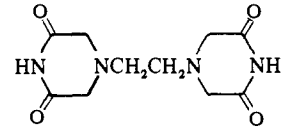
The antitumor activity shown[1] by 4,4[1]-ethylenedipiperazine-2,2[1],6,6[1]-tetrone (1) prompted us to synthesize the corresponding carbon isostere 8.



Dr. S. B. Carter of these Laboratories found that 8 was inactive against the tumor sarcoma 180.

Experimental Section†

2,5-Bis(hydroxymethyl)-1,6-hexanediol (3). A soln of 67.5 g of tetraethyl 1,1,4,4-butanetetracarboxylate (2)[2] in 250 ml of Et_2O was added dropwise under N_2 to a stirred soln of 30 g of LAH in 1.5 l. of Et_2O at 0°. The mixt was stirred at room temp for 30 min, refluxed for 2.25 hr, cooled to 0°, and treated, cautiously and in turn, with 30 ml of H_2O, 90 ml of 15% aq NaOH, and finally with 30 ml of H_2O. Solid material was filtered off. Evapn of the filtrate gave a trace of residue. The cake was digested 5 times with 1.5-l. portions of boiling Me_2CO, and the extracts, containing much diacetone alcohol, were evapd *in vacuo*. The residual oil was triturated with Me_2CO and the solid (8.8 g) obtd was combined with 29.3 g of similar material from 3 identical expts, then boiled with 2 l. of Me_2CO.

A colorless by-product, probably polymeric, did not dissolve and crystd from MeOH to give 3.36 g of prisms; mp 222–223°. *Anal.* $(C_5H_{10}O_2)_n$ C, H.

†Melting points are corrected and were determined with a Kofler hot-stage apparatus. Nmr spectra were measured in $CDCl_3$(TMS) with a Varian A60 spectrometer. Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values.

Concn of the Me_2CO soln yielded 29.1 g (21%) of 3; prisms, mp 91–93°, analytical sample; prisms from MeOH, mp 92–93°, ir (Nujol) 3279 cm^{-1}. *Anal.* ($C_8H_{18}O_4$) C, H. The tetraacetate (4) of 3 crystd from petr ether (bp 40–60°) in plates, mp 57–58°. *Anal.* ($C_{16}H_{26}O_4$) C, H.

1,6-Dichloro-2,5-bis(chloromethyl)hexane (5). A mixt of 11.3 g of 3, 23.0 g of pyridine, and 80 ml of $CHCl_3$ was stirred at 0° during dropwise addition (1 hr) of a mixt of 59.6 g of $SOCl_2$ and 70 ml of $CHCl_3$. The soln was refluxed for 8 hr, kept at room temp for 7 hr, and then evapd *in vacuo*. The residue was shaken with a mixt of $CHCl_3$, ice, and excess dil HCl; the organic layer was sepd, washed (dil HCl, aq $NaHCO_3$, H_2O), dried (Na_2SO_4), and evapd. The oily residue was distd giving 14.5 g of 5; a colorless oil, bp 104–105° (10^{-2} mm), nmr (τ) 6.2–6.5 (m, 8 H, CH_2Cl), 7.7–8.2 (m, 2 H, CH), 8.41–8.57 (m, 4 H, CH_2CH_2). *Anal.* ($C_8H_{14}Cl_4$) C, H, Cl.

1,1,4,4-Butanetetraacetonitrile (6). A mixt of 13.5 g of 5, 14.2 g of KCN, and 750 ml of DMSO was stirred at room temp for 24 hr, then at 65–75° (bath) for 4 hr. Most of the solvent was evapd *in vacuo* and the residue was dild with H_2O. Extn of the mixt with EtOAc, and recovery from the ext gave 11 g of a solid. This cryst from EtOAc–petr ether (bp 60–80°) yielding 9.45 g of 6; plates and prisms, mp 89°, ir (Nujol) 2242m cm^{-1}, (CN); nmr (τ) 7.2–7.4 (m, 8 H, CH_2CN) 7.2–7.9 (m, 2 H, CH), 8.2–8.4 (m, 4 H, CH_2CH_2). *Anal.* ($C_{12}H_{14}N_4$) C, H, N.

1,1,4,4-Butanetetraacetic Acid (7). Compd 6 (9.45 g) was refluxed with 150 ml of concd HCl for 24 hr. On cooling the soln 11.4 g of 7 crystd. Recrystn from H_2O gave 10.2 g; prisms, mp 202–204° dec (204–206° dec in capillary). *Anal.* ($C_{12}H_{18}O_8$) C, H; equiv: calcd 72.5, found 76.

3,3¹-Ethylenediglutarimide (8). The crude dry ammonium salt of 7 (7.3 g) was heated at 200–210° (bath) for 3 hr. The resulting black solid was ground with cold H_2O, the mixt was filtered, and the solid was washed (EtOH, Et_2O). Cryst from $(HOCH_2)_2$ (charcoal) gave 2.7 g of 8; almost colorless plates, mp *ca.* 330° dec, variable, ir 3165 m, 3067 m (NH), 1718 s, 1686 s (CO) cm^{-1}. *Anal.* ($C_{12}H_{16}N_2O_4$) C, H, N.

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Book Reviews

Subunits in Biological Systems. Biological Macromolecules Series, Vol. 5. Edited by Serge N. Timasheff and Gerald D. Fasman. Marcel Dekker, New York, N. Y. ix + 408 pp. 23.5 × 16 cm. $26.50

High molecular weight proteins often disintegrate (? depolymerize) under such mild conditions as minor changes in pH, to yield lower polymers or "monomers." The monomers usually display the characteristic reactivity of the polymers, except where in the latter some functional groups (SH, etc.) may be so enfolded as to be lost to intermolecular encounters. Not all monomer units of a given protein are totally identical: their molecular weights and amino acid composition may vary in some details. The structures of many monomeric units have been elucidated by chemical and physical methods. Their purification relies heavily on ultracentrifugation, their characterization on ORD and other spectroscopic and electron microscopic methods.

In the polymeric proteins the bonds that unite the monomers, and the reactions–often involving water–which lead to polymerization have received prominent attention. The present book offers a plethora of information on all these subjects. Included are the blue or purple copper proteins, the hemocyanins and hemerythrin, which transport O_2 in the blood–lymph of some invertebrates. Tocacco mosaic virus protein is one of the best studied "monomers" that compose the protein coat of the virus of molecular weight of 4×17^7. The muscle filaments contain myosin, actin, and microtubules, and these have also been investigated by all available methods. Anyone interested in these topics will find good reading and critical analysis in this book.

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

Progress in Medicinal Chemistry, Vol. 7. Edited by G. P. Ellis and G. B. West. Appleton-Century-Crofts, New York, N. Y. 1971. iii + 349 pp. 21.5 × 14.6 cm. $26.95.

The reviews presented in this volume are, with one exception, good modern medicinal chemistry based on the biochemical mode of action of drugs. This is exemplified best in the chapters on purines (J. A. Montgomery) and pyrimidines (C. C. Cheng and B. Roth). Analgetics and their antagonists (A. F. Casy) are treated interestingly and systematically, with emphasis on very recent developments. Guanidine derivatives and their actions at adrenergic nerve endings are reviewed comprehensively by G. J. Durant, A. M. Roe, and A. L. Green. Highlights of pharmacological and clinical findings of 23 recently introduced drugs are presented by A. P. Launchbury; among these drugs are quite a few old acquaintances from the medicinal literature whose clinical impact has just become apparent.

The book unfortunately also contains a poor chapter in medicinal reporting entitled "Medicinal Chemistry for the Next Decade," by W. S. Peart. There is no chemistry or basic medicinal science in it, only the vaguest of clinical pharmacology. Of course nobody can predict the future, and all such predictions should be given an even chance of success. But it is inexcusable to describe established facts in experimentally unacceptable context and interpretation. Psychotropic drugs, *e.g.*, are called ". . . drugs which in some way give control of the mind to another." The editors must have taken such a mind-warfare drug when they permitted inclusion of this chapter in an otherwise excellent volume.

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