acetone, and dried *in vacuo* at 78°. The spectral data are shown in Table II. The yield was 25 mg. of yellow powder that showed a correct analysis for a hemihydrate.

Anal. Calcd. for $C_{19}H_{18}FN_7O_6 \cdot 0.5H_2O$: C, 48.72; H, 4.09; N, 20 93. Found: C, 49.16; H, 4.38; N, 20.71.

Acknowledgment.—The authors are indebted to Dr. W. J. Barrett and members of the Analytical Section of Southern Research Institute for the spectral and microanalytical determination reported herein.

The Synthesis of Some Benzimidazole and Oxygen Analogs of Ethyl Pteroylglutamate

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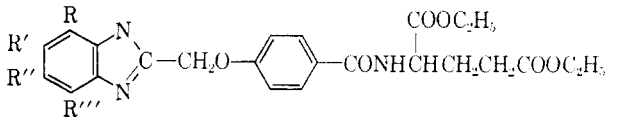
A series of diethyl N-(2-benzimidazolylmethoxy)benzoylglutamates (Table I) was prepared according to Scheme I.

TABLE I

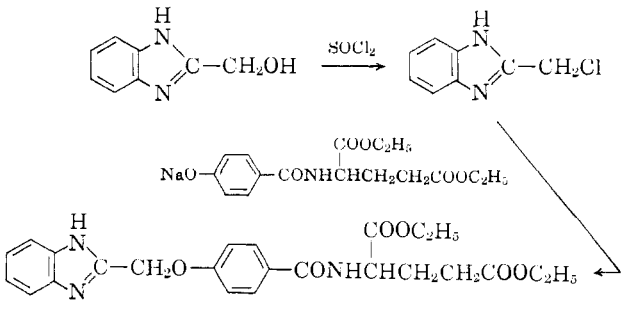
DIETHYL N-(*p*-BENZIMIDAZOLYLMETHOXY)BENZOYLGLUTAMATES



No.	R	R′	R″	R‴	Yield, %	M.p., °C.	Formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
XXII	H	H	H	H	13	156–157[a]	$C_{24}H_{27}N_3O_6$	63.56	6.00	9.27	63.68	5.89	9.03
XXIII	OCH_3	H	H	OCH_3	11	147.5–148[b]	$C_{26}H_{31}N_3O_8$	60.81	6.09	8.18	60.72	5.97	8.11
XXIV	H	OCH_3	OCH_3	H	11	80–83[c]	$C_{26}H_{31}N_3O_8$	60.81	6.09	8.18	60.52	5.83	8.27
XXV	H	H	OCH_3	H	27	118–120[c]	$C_{25}H_{29}N_3O_7$	62.10	6.04	8.69	61.94	6.27	8.52
XXVI	H	H	CH_3	H	20	126–129[c]	$C_{25}H_{29}N_3O_6$	64.22	6.25	8.99	64.35	6.38	8.76
XXVII	H	CH_3	CH_3	H	11	150.5–151[c]	$C_{26}H_{31}N_3O_6$	64.85	6.49	8.73	64.98	6.69	8.59
XXVIII	H	H	NH_2	H	9	106–115[c]	$C_{24}H_{28}N_4O_6$	61.53	6.02	11.96	61.41	6.13	11.91

[a] Recrystallized from benzene. [b] Recrystallized from ethanol. [c] Recrystallized from ethyl acetate.

SCHEME I



Experimental

All melting points were determined with a Thomas–Hoover melting point apparatus.

2-Hydroxymethylbenzimidazoles were prepared from the corresponding *o*-phenylenediamines and glycolic acid by the procedure described by Phillips.[1] Two of these are new compounds.

2-Hydroxymethyl-4-amino-6-nitrobenzimidazole was isolated in 63% yield, m.p. 256–257° dec.

Anal. Calcd. for $C_8H_8N_4O_3$: C, 46.15; H, 3.87; N, 26.92. Found: C, 46.33; H, 3.95; N, 26.92.

2-Hydroxymethyl-5(6)-aminobenzimidazole Dihydrochloride.—2-Hydroxymethyl-5(6)-nitrobenzimidazole was hydrogenated over platinum in ethanol solution. After removing the catalyst, the dihydrochloride was precipitated by the addition of concentrated HCl and ether. It was recrystallized from methanol–ether; yield 45%, m.p. >350°.

Anal. Calcd. for $C_8H_{11}Cl_2N_3O$: C, 40.69; H, 4.70; N, 17.80. Found: C, 40.70; H, 4.69; N, 17.77.

2-Chlorobenzimidazoles.—The 2-chloromethylbenzimidazoles were prepared from the corresponding 2-hydroxymethylbenzimidazoles by heating with $SOCl_2$ in $CHCl_3$ solution. The addition of ether to the cooled mixture completed the precipitation of the 2-chloromethylbenzimidazole hydrochlorides. In some cases a pure product resulted and recrystallization was not necessary. In a few cases the hydrochlorides were recrystallized from ethyl alcohol.

Condensation of 2-Chloromethylbenzimidazoles with Diethyl *p*-Hydroxybenzoylglutamate. General Method.—Sodium (2 equiv.) was dissolved in dry ethanol. Diethyl *p*-hydroxybenzoylglutamate[2] (1 equiv.) in ethanol was added and then 1 equiv. of solid 2-chloromethylbenzimidazole hydrochloride was slowly added with stirring. The mixture was stirred for 2 hr. at room temperature and then refluxed for 1–4 hr. Quantitative yields of NaCl were obtained by cooling the reaction mixture. In some cases the addition of water to the filtrate gave an oil which solidified on cooling. The products were recrystallized from ethanol or ethyl acetate. A more general procedure was to evaporate the filtrate to an oil. The oil was then treated with ethanol and again evaporated. This was then repeated with dry benzene. Usually this azeotropic removal of volatile impurities caused the oil to solidify. 2-Chloromethyl-5(6)-aminobenzimidazole was used as its dihydrochloride. In this case 3 equiv. of sodium was used. The reflux time was shortened in those cases where the reaction mixture darkened too rapidly. Actually the reactions proceed at room temperature and go to completion if given enough time. The yields of the condensation products were low. It is well known that 2-chloromethylbenzimidazoles undergo self-condensation to form condensation polymers. We believe that this is the cause of the poor yields of desired products.

(1) M. A. Phillips, *J. Chem. Soc.*, 2393 (1928).

(2) E. I. Fairburn, B. J. Magerlein, L. Stubberfield, and D. I. Weisblat, *J. Am. Chem. Soc.*, **76**, 676 (1954).

Myelographic Agents. I. Iodobenzoates

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As part of our search for improved X-ray contrast agents we have synthesized a series of iodinated esters (Table I). These esters are oils or low-melting solids containing aromatic iodine and consequently are suitable for myelography.[1] In liquid form the esters have been injected cisternally into cats and dogs and have been found to permit visualization of details of the spinal

(1) For a review, see J. O. Hoppe in "Medicinal Chemistry," Vol. 6, John Wiley and Sons, Inc., New York, N. Y., 1963, p. 290.