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Base catalyzed cyclization of ethyl 4-[2-(2-amino-4,5-dimethoxyphenyl)ethyl]-2-phenylpyrimidine-5-carboxylate, derived from ethyl 4-methyl-2-phenyl-5-pyrimidinecarboxylate and 3,4-dimethoxy-6-nitrobenzaldehyde, gave 5,6-dihydro-8,9-dimethoxy-3-phenylbenzo[b]pyrimido[4,5-*f*]azocine-12(11*H*)-one, the first reported example of this ring system.

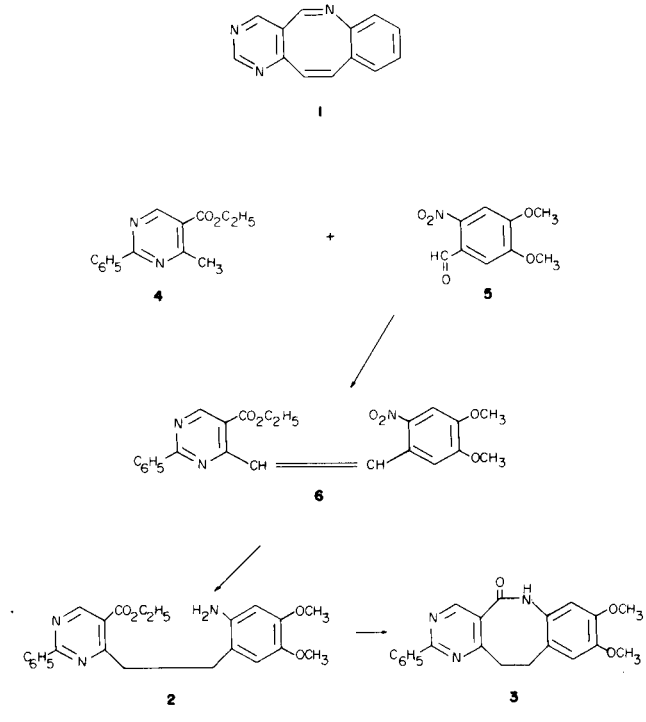
J. Heterocyclic Chem., **19**, 1257 (1982).

In course of a continuing search for novel heterocyclic ring systems possessing biological activity, an example of the previously unreported benzo[*b*]pyrimido[4,5-*f*]azocine ring system **1** was desired.

The ester **2**, a potential precursor of the azocine **3**, was prepared in a two step sequence originating with ethyl 4-methyl-2-phenyl-5-pyrimidinecarboxylate (**4**) (1) and 3,4-dimethoxy-6-nitrobenzaldehyde (**5**). Condensation of **4** and **5** in the presence of *p*-toluenesulfonic acid in toluene gave the trans ester **6** which upon catalytic hydrogenation with Raney Nickel resulted in the amino compound **2**.

Cyclization of **2** using sodium hydride in toluene gave the target compound **3**, the structure of which was determined by elemental analysis as well as infrared and nuclear magnetic resonance spectral data.

Compound **3** failed to elicit meaningful activity when screened using gross observational techniques or when evaluated for antibacterial or antifungal activity.



EXPERIMENTAL (2)

trans-Ethyl 4-[2-(3,4-dimethoxy-2-nitrophenyl)ethenyl]-2-phenylpyrimidine-5-carboxylate (**6**).

A mixture of 48.4 g (0.200 mole) of ethyl 4-methyl-2-phenyl-5-pyrimidinecarboxylate (**4**) (1), 42.2 g (0.200 mole) of 3,4-dimethoxy-6-nitrobenzaldehyde (**5**), and 10 g of *p*-toluenesulfonic acid monohydrate in 1000 ml of toluene was stirred and refluxed for 36 hours using a Dean-Stark apparatus. The mixture was cooled; the product was filtered and recrystallized from 2-methoxyethanol to give 38 g (44%) of **6**. Recrystallization from toluene gave an analytical sample, mp 167-169°; nmr (DMSO-d_6): δ 1.43 (t, 3, OCH_2CH_3); 4.00 (s, 6, OCH_3), 4.40 (q, 2, OCH_2CH_3), 7.30, 7.63 (2s, 2, aromatic C-H of methoxylated ring), 7.68 (m, 3, aromatic C-H), 8.53 (m, 2, aromatic C-H), 8.10, 8.77 (2d, J = 15 Hz, 2, H-C=C-H), 9.13 (s, 1, pyrimidine C_6-H); ir μ: 5.85 (C=O ester), 6.13, 6.20 (C=C and C=N), 6.60 (NO_2) and 7.88 (C-O-C ester).

Anal. Calcd. for $C_{23}H_{21}N_3O_6$: C, 63.44; H, 4.86; N, 9.65. Found: C, 63.19; H, 4.87; N, 9.54.

Ethyl 4-[2-(2-Amino-4,5-dimethoxyphenyl)ethyl]-2-phenylpyrimidine-5-carboxylate (**2**).

A mixture of 15 g (0.034 mole) of **6**, 20 g of Raney Nickel #28, and 1100 ml of absolute ethanol was shaken with hydrogen on a Parr apparatus at 30-40 psi for 24 hours. The reduction mixture was warmed, filtered, and the filtrate was cooled to deposit 10 g (71%) of the product, mp 134-135°. Recrystallization from acetonitrile gave an analytical sample, mp 135-136°; nmr (DMSO-d_6): δ 1.25 (t, 3, OCH_2CH_3), 2.66-3.50 (m, 4, $-CH_2-CH_2-$), 3.60, 3.72 (2s, 6, OCH_3), 4.38 (q, 2, OCH_2CH_3), 4.58 (exchangeable broad s, 2, NH_2), 6.42, 6.60 (2s, 2, aromatic C-H of methoxylated ring), 7.63 (m, 3, aromatic C-H), 8.59 (m, 2, aromatic C-H), 9.25 (s, 1, pyrimidine C_6-H); ir μ: 2.90, 2.99 (NH_2); 5.80 (C=O); 6.31 (C=N), 7.88 (C-O-C ester).

Anal. Calcd. for $C_{23}H_{25}N_3O_4$: C, 67.79; H, 6.18; N, 10.31. Found: C, 67.96; H, 6.21; NB, 10.26.

5,6-Dihydro-8,9-dimethoxy-3-phenylbenzo[*b*]pyrimido[4,5-*f*]azocine-12(11*H*)-one (**3**).

A solution of 15 g (0.037 mole) of **2** in 540 ml of toluene was treated with 25 g (0.63 mole) of sodium hydride (60%) in mineral oil. The reaction mixture was refluxed for 4 days, stored at room temperature for 2 days, treated cautiously with 1500 ml of water, and extracted with toluene (4000 ml). The toluene extract was washed with water, dried (magnesium sulfate) and concentrated to dryness *in vacuo*. The residue was washed with heptane and dried to give 6.0 g (45%) of the product, mp 215-216°. Recrystallization from acetonitrile gave an analytical sample, mp 217-218°; nmr (DMSO-d_6): δ 2.83-3.50 (m, 4, $-CH_2-CH_2-$), 3.73, 3.78, (2s, 6, OCH_3), 6.75, 7.01 (2s, 2, aromatic C-H of methoxylated ring), 7.56 (m, 3, aromatic C-H), 8.25 (m, 2, aromatic C-H), 8.80 (s, 1, pyrimidine C_6-H); 10.16 (exchangeable broad s, 1, N-H); ir μ: 3.15 (N-H); 6.07 (C=O).

Anal. Calcd. for $C_{21}H_{19}N_3O_3$: C, 69.79; H, 5.30; N, 11.63. Found: C, 69.72; H, 5.27; N, 11.50.

REFERENCES AND NOTES

(1) P. C. Mitter and J. C. Bardhan, *J. Chem. Soc.*, **123**, 2179 (1923).

(2) Melting points were taken in a Mel-Temp apparatus in open capillary tubes and are uncorrected. The nuclear magnetic resonance spectra were taken on a Varian A-60A instrument and were compared with TMS as an internal standard. Infrared spectra were determined as Nujol mulls on a Perkin-Elmer 137B spectrophotometer.