A NEW AND FACILE SYNTHESIS OF OXAZOLO[5,4-d]PYRIMIDINE DERIVATIVES

Keitaro Senga,* Junko Sato, and Sadao Nishigaki
Pharmaceutical Institute, School of Medicine, Keio University, 35, Shinanomachi, Shinjuku-ku, Tokyo 160, Japan

Treatment of 5-benzylideneamino-1,3-dimethylbarbituric acids with thionyl chloride afforded the corresponding oxazolo[5,4-d]pyrimidines in high yields.

Extensive studies have been carried out during the past few decades on the synthesis of oxazolo[5,4-d]pyrimidine derivatives[1] as potential purine antagonists. We now report a new, facile synthetic approach to 2-aryl-5,7-dimethyloxazolo[5,4-d]pyrimidine-4,6(5H,7H)-diones (IIIa-i) by the reaction of 5-benzylideneamino-1,3-dimethylbarbituric acids (IIa-i) with thionyl chloride.

The requisite intermediates,(IIa-i), were readily obtained in good yields by refluxing 5-amino-1,3-dimethylbarbituric acid (I)[2] (0.001 mol) with the respective aldehydes (0.0015 mol) in ethanol for 1 hr (Table 1).

Stirring (IIa)(0.001 mol) with thionyl chloride (3 ml) at 55° for 30 min afforded a high yield of 5,7-dimethyl-2-phenyl-

Table 1 5-Benzylideneamino-1,3-dimethylbarbituric Acids (II)[a]

Compd.	R	Mp(°C)	Yield(%)
IIa	H	220	92
IIb	4-Br	228-229	91
IIc	4-Cl	225-227	91
IId	$2,4\text{-}Cl_2$	209-210	89
IIe	$3,4\text{-}Cl_2$	213-214	85
IIf	$4\text{-}NO_2$	223	87
IIg	4-Me	217	83
IIh	4-OMe	231	88
IIi	$3,4\text{-}OMe_2$	223-224	90

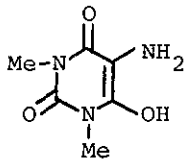
a) All compounds were recrystallized from DMF-EtOH.

Table 2 2-Aryl-5,7-dimethyloxazolo[5,4-d]pyrimidine-4,6(5H,7H)-diones (III)[a]

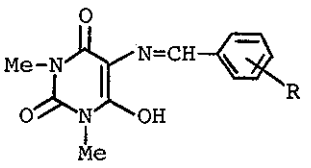
Compd.	R	Mp(°C)	Yield(%)
IIIa	H	240-242	98
IIIb	4-Br	259	92
IIIc	4-Cl	259	90
IIId	$2,4\text{-}Cl_2$	267	92
IIIe	$3,4\text{-}Cl_2$	255-257	89
IIIf	$4\text{-}NO_2$	275	69
IIIg	4-Me	233-235	81
IIIh	4-OMe	255	85
IIIi	$3,4\text{-}OMe_2$	278-279	95

a) All compounds were recrystallized from DMF-EtOH.

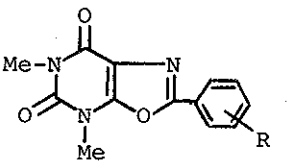
oxazolo[5,4-d]pyrimidine-4,6(5H,7H)-dione (IIIa),[3] which was isolated by concentration of the reaction mixture followed by addition of 5% aqueous ammonia. This reaction was equally applicable to other 5-benzylideneamino-1,3-dimethylbarbituric acids (IIb-i) to give the corresponding oxazolo[5,4-d]pyrimidines (IIIb-i) (Table 2).



(I)

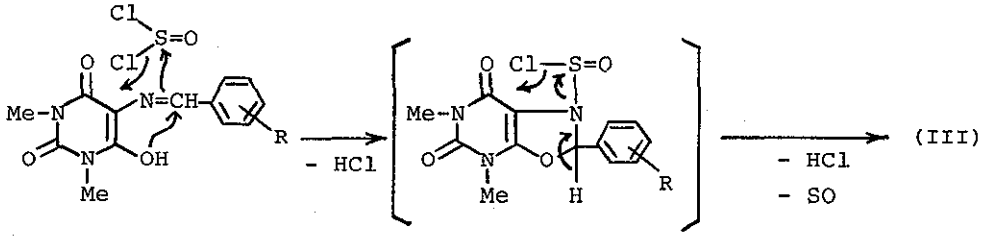


(II)



(III)

This new oxazolo[5,4-d]pyrimidine synthesis presumably proceeds through the initial formation of the sulfinyl chloride intermediate and subsequent elimination of hydrogen chloride and sulfur monoxide[4] (Scheme).



Scheme

REFERENCES AND NOTES

1 Oxazolo[5,4-d]pyrimidine ring system has generally been prepared by the ring closure of either suitably substituted pyrimidine derivatives [a-k] or the appropriate oxazole precursors[1-q]: a) T.B. Johnson, Am. Chem. J., 1905, 34, 191; b) H. Biltz and K. Strufe,

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2 H. Biltz and P. Damm, Chem. Ber., 1913, 46, 3662.

3 This compound is identical with the authentic sample prepared by the reaction of (I) with benzoyl chloride as described by Biltz and Strufe: see ref. 1b.

4 The elimination of hydrogen chloride and sulfur monoxide has been postulated in certain sulfinyl chlorides[a-c]: a) A.J. Krubsack and T. Higa, Tetrahedron Letters, 1968, 5149; b) H.M. Relles, J. Org. Chem., 1972, 37, 3630; c) A.J. Krubsack and T. Higa, Tetrahedron Letters, 1973, 4515.

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