FUSED THIENO[3,2-d]-v-TRIAZINE-4(3H)-ONES

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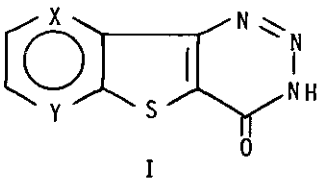
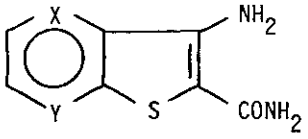
A convenient preparation of benzo[b]thieno[3,2-d]-v-triazine-4(3H)-one, pyrido[3',2':4,5]thieno[3,2-d]-v-triazine-4(3H)-one, and pyrazino[2',3':4,5]thieno[3,2-d]-v-triazine-4(3H)-one as representatives of fused tricyclic thieno[3,2-d]-v-triazines is reported.

As part of a study designed to investigate tricyclic heterocyclic arrays possessing a thiophene nucleus it became important to have available a simple synthesis of fused thieno[3,2-d]-v-triazine-4(3H)-ones (e.g., I). A survey of the literature (1) quickly indicates that diazotization of 1,2-disubstituted aminoamides is a likely candidate to achieve this goal.



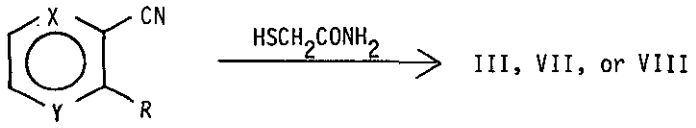
I



II; X=Y=CH
V; X=CH,Y=N
VI; X=Y=N

III; X=Y=CH
VII; X=CH,Y=N
VIII; X=Y=N

Since our study requires the benzo analogs (in this case II) as reference points for the target tricyclo thieno heterocycles the feasibility of this preparative route was first attempted in the benzo[b]thiophene series. The necessary 3-amino-2-carboxamido-benzo[b]thiophene (III) was prepared (52% yield; mp 213-216^{o} from aqueous ethanol; infrared NH 3410 cm^{-1} and 3350 cm^{-1}, infrared CO 1650 cm^{-1})(2) by reacting o-nitrobenzonitrile (IV) with mercaptoacetamide in the presence of potassium hydroxide (3) as in the accompanying reaction.



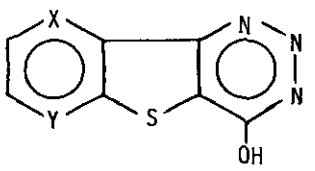
IV; R=NO_2,X=Y=CH
IX; R=Cl,X=CH,Y=N
X; R=Cl,X=Y=N

Treatment of an acetic acid solution of III with sodium nitrite/sulfuric acid produced the desired *benzo[b]thieno[3,2-d]-v-triazine-4(3H)-one (II)* (49% yield; mp 180-182^{o}, with explosion, from acetic acid; infrared NH 3380-3420 cm^{-1}, infrared CO 1670-1690 cm^{-1}).

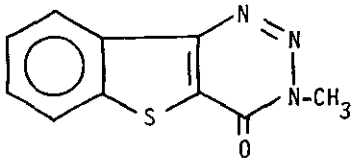
Compounds V and VI were then considered as representatives to test the generality of this scheme in order to avail systems in which all three rings were heterocyclic. The precursor aminoamides VII (50% yield; mp 249-252^{o} from water; infrared NH 3400 cm^{-1} and 3310 cm^{-1}, infrared CO 1655 cm^{-1}) and VIII (96% yield; mp 280-282^{o} from methanol; infrared NH 3410 cm^{-1} and 3350 cm^{-1}, infrared CO 1670 cm^{-1}) were prepared by a pathway analogous to that for III by treating 2-chloro-3-cyanopyridine (IX)(4) and 2-chloro-3-cyanopyrazine (X)(5) with mercaptoacetamide in the presence of sodium carbonate (6). As suspected diazonium conditions readily converted VII and VIII into V (25% yield; mp 190-192^{o}, with

effervescence, from acetic acid; infrared CO 1680-1690 cm^{-1}) and VI (10% yield; mp 170°, with violent explosion, from acetic acid; infrared CO 1680-1690 cm^{-1}), respectively.

The infrared data of II, V, and VI does not indicate the presence of the enol tautomer (XI)(1), an observation substantiated by the facile sodium ethoxide/methyl iodide mediated alkylation of II to XII (85% yield; mp 175° from aqueous acetic acid and does not explode; infrared CO 1680-1690 cm^{-1}). Attempts to chlorinate II to the 4-chloride (7) failed as did endeavors to form the 4(3H)-thione analog employing a large variety of conditions (8).



XI



XII

REFERENCES

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2. All new compounds reported herein gave satisfactory microanalytical values. Microanalytical data was obtained by Het-Chem-Co, Harrisonville, Missouri. The infrared spectral data was recorded on a Perkin Elmer Model 337 spectrophotometer as potassium bromide mulls. Melting points were taken on a Mel-Temp capillary melting point apparatus and are uncorrected.

3. This procedure is an adaptation of that used by J.R. Beck, J. Org. Chem., 1972, 37; 3224 to prepare a variety of ethyl 3-aminobenzo[b]-thiophene-2-carboxylates.

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5. M. Asai, Yakugaku Zasshi, 1961, 81, 1475; Chem. Abstr., 1962, 56, 8711h. The precursor 2-hydroxy-3-carboxamidopyrazine has been reported by F.L. Muehlmann and A.R. Day, J. Amer. Chem. Soc., 1956, 78, 242.

6. Judicious choice of α-mercaptoacyl derivative here has led to a variety of 2,3-disubstituted thieno[2,3-b]pyridines and thieno[2,3-b]-pyrazines in our laboratory. See S.W. Schneller and F.W. Clough, Abstracts of the 168th American Chemical Society Meeting, September 8-13, 1974, Atlantic City, New Jersey, MEDI 32 and J. Heterocyclic Chem., in press.

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Received, 25th November, 1974