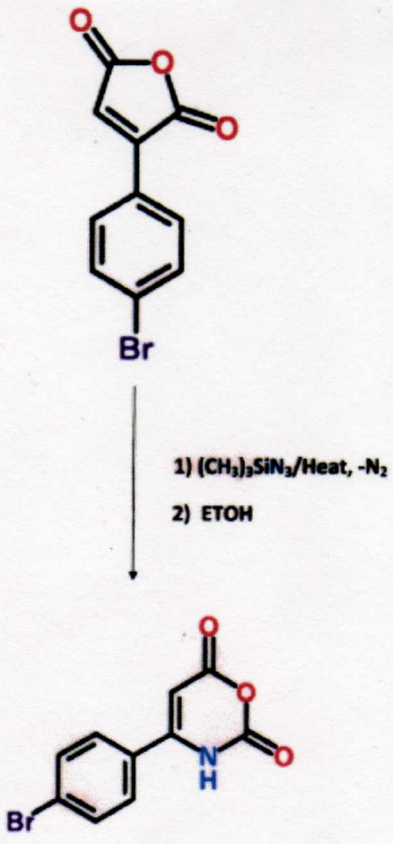
Synthesis of Additional unreported 4- and 5-Aryl Substituted 1,3 (3H) Oxazine-2,6-Diones.; 4-(4-bromophenyl)-1,3(3H) Oxazine-2,6-Dione and related 4 and 5-aryl substituted -1,3(3H) Oxazine-2,6-Diones

John MacMillan (john.macmillan@temple.edu)



Chemicals Used

4-bromophenyl maleic anhydride and additional aryl substituted maleic anhydrides
Trimethylsilyl Azide

Dimethyl sulfate
Diethyl sulfate

Procedure

Preparation of 4-(4-bromophenyl)-1,3(3H) Oxazine-2,6-Dione

A 50 ml 3 neck round bottom flask, equipped with condenser, heating mantle, dropping funnel, nitrogen inlet, magnetic stirrer, and calcium chloride drying tube, was charged with 4.75g (0.019 mole) 4-bromophenyl maleic anhydride, 12ml (~ 0.09 mole) trimethylsilyl azide, and 3 ml dry dioxane. The mixture was refluxed 3 hrs after which nitrogen gas evolution ceased. TLC (silica gel, ethyl acetate eluent) showed primarily the 4- isomer with traces of the 5-isomer. The solution was cooled in ice to 0 ^{o} and 40 ml benzene was added with stirring. Addition of 1 ml ethanol gave a copious white precipitate which TLC showed to be pure 4-isomer. The precipitate was suction filtered and mother liquor concentrated further, giving 2.9g (58%), 4-(4-bromophenyl)-1,3(3H) Oxazine-2,6-Dione in three crops. Recrystallization of a small sample from ethyl acetate gave white crystals,

m.p. 207-9^{o} (dec).

Ir, (mull), 3220(w), 3160(w), 3100 (w), 1790(s), 1800(s),1710(s), 1630(s), 1595(m), 1500(m), 1400(w), 1305(w), 1270(w), 1220(w) 1110(m), 1085(m), 1070(m), 1005(w),980(m), 840(m), 805(m), 750 (m) cm^{-1}.

Pmr (DMSO-d_6, 60mz), δ 7.7(broad singlet, 4H, aromatics), 6.0 (s, 1H, N-H), 5.66 (s, 1H, C5-H).

Anal. Calc. For $C_{10}H_6BrNO_3$:

C, 44.80, H, 2.26, N, 5.23, Br, 29.81.

Found: C, 44.74, H, 2.17, N, 5.18, Br, 29.79. Satisfactory

Additional unreported aryl substituted 1,3(3H) Oxazine-2,6-Diones were synthesized by essentially the procedure above in similar yields, and converted to their N-alkylated derivatives by refluxing the corresponding aryl substituted oxauracil with a di-alkyl sulfate/sodium bicarbonate slurry in acetone, as described in J.H. MacMillan and S.S. Washburne, J. Heterocyclic Chemistry, Vol. 12, p 1215, (1975).

Author's Comments

The following unreported additional 4-and 5-Aryl Substituted 1,3(3H) oxazine-2,6-diones (oxauracils) were synthesized for anti malarial screening by the reaction of the corresponding aryl maleic anhydride with trimethylsilyl azide, by the procedure described in J. Heterocyclic Chemistry, Vol. 12, p 1215, (1975). The N-Alkylated derivatives were prepared by refluxing the corresponding aryl substituted oxauracil with a di alkyl sulfate/sodium bicarbonate slurry in acetone, as described in the above paper.

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Data