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FUSED AZETIDINONES FROM 2-KETO-DIHYDROPYRIMIDINES.

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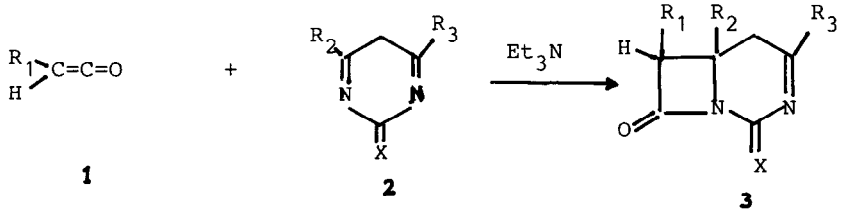
Summary:Cycloaddition of ketenes to 2-keto dihydropyrimidines give the title compounds.These constitute a new kind of cephalosporins keto-aza analogs.

Some time ago,2-azetidinones have been synthesized from such cyclic imines as oxazolidines[1],imidazolines and dihydropyrimidines[2].However,the results of these reactions lack of homogeneity and,sometimes,are conflictuous[3].

The main feature of the previous imines is that they all are prone to isomerization of their imine bond into an enamine form[4].Moreover,for those cyclic imines possessing a conjugated endocyclic olefinic bond,cyclization may lead to addition of ketenes on the olefinic linkage.

It is well known that many keto-dihydropyrimidines are stable enough on their keto form[5-8].We wish to report here some results on the use of such compounds in the synthesis of fused 2-azetidinones. Our starting materials are easily synthesized from urea or thiourea and β-diketones.These 2-keto or 2-thioketo 5-dihydropyrimidines are characterized on the basis of their i.r. spectrum($\nu_{C=O}$:1670cm^{-1}; $\nu_{C=S}$:1250-1100cm^{-1}; $\nu_{C=N}$:1630cm^{-1}).

When treated with equimolar amount of ketenes,prepared in situ,these imines give azetidinones of general structure shown below in good yields.The identity of these 3-aza,4-keto cephalosporins is established on the basis of their i.r. spectra ($\nu_{C=O}$:1780-1760cm^{-1}; $\nu_{C=X}$:1710-1670cm^{-1}for X:O and 1200-1100cm^{-1}for X:S ; $\nu_{C=N}$:1625cm^{-1}).



1 2 3

2a and 3a : X= O
2b and 3b : X= S

Table.

(All δ in $CDCl_3$, with TMS as an internal standard).

3a.1°: $R_1=R_2=R_3$: CH_3. Yield:70%.m.p.:152°C(recrist.acetonitrile). δ_{CDCl_3}: 1.27(s. 3H:R_2); 1.48(d. J=7Hz. 3H:R_1); 1.52(s. 2H:H_1); 2.39(s. 3H:R_3);[3]3.19 (q. J=7Hz. 1H:H_7).

2°. R_1=Ø-O; $R_2=R_3$= CH_3. Yield:64%. m.p.: 225°C(recrist.methanol). δ_{CDCl_3}: 1.45(s. 3H: R_2); 1.50(s. 2H: H_1); 2.50(s. 3H: R_3);4.50(s.1H: H_7); 7.25(s) and 7.44(m):aromatic.

3°. $R_1=R_3=CH_3$; R_2=Ø. δ_{CDCl_3}: 1.29(d. J=7.5Hz. 3H: R_1); 1.60(s. 2H: H_1); 2.62(s. 3H: R_3); 3.20(q. J=7.5Hz. 1H : H_7); 7.55(s.5H). Yield:61%.

3b.4°. $R_1=R_2=R_3=CH_3$. Yield: 82%. ;m.p.: 143°C(recrist.acetonitrile).δ_{CDCl_3}: almost the same characteristics as for compound 3a.1°.,plus a weak and broad signal at 6.85ppm for enimine-thiol equilibrium.

5°. R_1= Ø-O; $R_2=R_3$= CH_3. Yield: 74%. m.p.: 131°C.(recrist.methanol). For δ in $CDCl_3$,see compound 3a.2°.

6°. R_1=Ø; $R_2=R_3$= CH_3. Yield: 75%.δ_{CDCl_3}: 1.10(s. 3H: R_2); 1.50(s. 2H: H_1); 2.20(s. 3H: R_3); 3.48(s. 1H: H_7); 7.17(s. 5H).

Experimental.

All cycloadditions were performed according to a previously described procedure[9].

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