

SELECTIVE REDUCTION. REACTION OF 3,4-DICARBOMETHOXYQUINOLINE WITH LITHIUM ALUMINIUM HYDRIDE.
STERIC EFFECT.

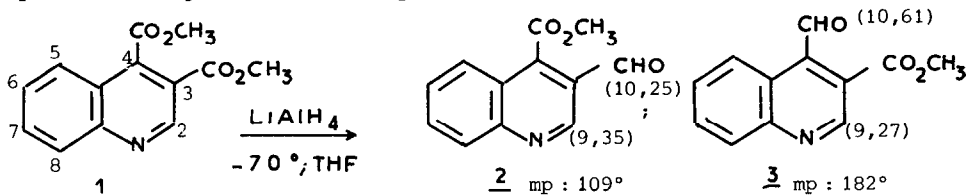
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Abstract : The selective reduction of 3,4-dicarbomethoxyquinoline by lithium aluminium hydride at low temperature affords only the unexpected 3-formyl 4-carbomethoxyquinoline. The difficulty of reduction of the usually more reactive 4-ester group can be explained by a steric hindrance by the H₅ peri proton on one side and by the 3-ester group on the other side.

The esters of π -deficient carboxylic acids are converted to the corresponding aldehydes by LiAlH_4 . The reduction is usually carried out at low temperature.¹ Under these conditions the dicarbomethoxy pyridines and quinolines give the corresponding dialdehydes.^{2,3}

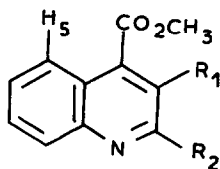
This paper is concerned with a study of the unexpected selective reduction of the 3,4-dicarbomethoxyquinoline 1. This reaction affords only one aldehyde-ester 2. In order to determine the structure of the product of the below reaction, 4-formyl 3-carbomethoxyquinoline 3 was synthesized in a four step sequence starting with o-aminocetophenone.⁴



¹H nmr chemical shifts (CDCl_3/TMS) are given in parenthesis.

The formation of an aldehyde appears generally to proceed most rapidly when the alkoxy-carbonyl group is conjugated with the electronwithdrawing N-heterocyclic group.⁵ It is therefore somewhat surprising to note that compound 3 is the major product of the above reduction.

An ¹H nmr study of some 3-substituted 5 and 3-unsubstituted 4-carboalkoxyquinolines 4 led us to the conclusion that this regioselectivity can be explained by a steric effect.



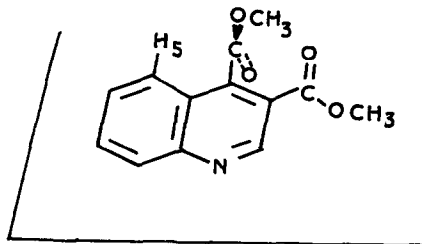
4, 5

R_1, R_2 nmr : H₅ (6 ppm CDCl_3/TMS) : 4 H, H : 8,83 ; H, CO_2CH_3 8,94 ; H, CHO : 8,87 ; H, $\text{CH}(\text{OCH}_2)_2$: 8,70.
5 CH_3 , H : 7,7 ; COCH_3 , H : 7,8 ; $\text{CH}(\text{OEt})_2$, H : 7,7.
1 CO_2CH_3 , H : 7,89.

A marked deshielding of the H_5 chemical shifts was noted in the 3-unsubstituted products [peri effect : $\Delta\delta$ ($CDCl_3$) = $\delta H_5 - 8,2 = 0,5 - 0,7$ ppm]. This suggests that 4-CO₂R groups in the 3-unsubstituted quinolines are in the plane of aromatic ring system, whereas they are out of the plane in 3-substituted quinolines.

Good agreement is found between our results and those of earlier studies in the naphthalene series. ^{6,7}

The preferred conformation of the diester 1 is then most likely as following :



In this conformation the nucleophilic addition on the C=O of the 4-carbomethoxy group is hindered by the H_5 on one side and by the 3-ester on the other side. The 3-carbomethoxy group which is in the plane of the ring can react with $AlLiH_4$.

References and footnotes

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- 4) O-aminoacetophenone react with acetyl acetaldehyde dimethyl acetal to give 4-methyl 3-acetyl quinoline. This compound is then converted to 4-methyl 3-carbomethoxy quinoline 6. The ester 6 was previously obtained by N.D. Heindel, P.D. Kenewell and C.J. Ohnacht, J. Org. Chem., **34**, 1168 (1969) from orthoaminoacetophenone and methyl propiolate. The given yield are low. Treatment of compound 6 with SeO_2 give the formyl-4 carbomethoxy-3 quinoline 3 isomer of 2.
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