TRANSFORMATIONS OF METHYL(PHENYL)-
SUBSTITUTED 1,4-DIHYDRO-4-
PYRIMIDINYLIDENEMALONONITRILES
UNDER ACTION OF NITRIC ACID

I. V. Oleinik and O. P. Shkurko

6-Phenyl-, 2-methyl-6-phenyl-, and 2,6-diphenyl-4-pyrimidinylidenemalononitrile in acetic acid react with HNO₃ to form the corresponding 4-ethoxycarbonylpyrimidines in high yields after treatment of the intermediate product with ethanol. Under the same conditions 6-methyl-2-phenyl-4-pyrimidinylidenemalononitrile yields 6-methyl-5-nitro-4-ethoxycarbonylpyrimidine whereas 2-phenyl-4-pyrimidinylidenemalononitrile gives a mixture of 2-phenyl-4-ethoxycarbonyl- and 5-nitro-2-phenyl-4-ethoxycarbonylpyrimidine.

We have previously found that 5-methyl(phenyl)-substituted 1,2-dihydro-2-pyrimidinylidenemalononitriles react with fuming HNO₃ in acetic acid medium and on subsequent treatment of the formed products with ethanol give the corresponding substituted 2-ethoxycarbonylpyrimidines in high yield [1].

In continuation of the study of reactivity of tautomeric derivatives of methylenedihydropyrimidines containing various functional groups in the side chain [1, 2], we have carried out nitration of 2(6)-methyl(phenyl)-substituted 1,4-dihydro-4-pyrimidinylidenemalononitriles (Ia-e). The compounds Ia-c, which contain phenyl substituent in the 6-position of the heterocycle, were found to behave like the 2-pyrimidinyl analogs [1], converting into the 4-ethoxycarbonyl-substituted derivatives (IIa-c) in 80-85% yield. Nitration was carried out with fuming HNO₃ in acetic acid medium. After the reaction was complete and acetic acid was removed, the mixture was refluxed in ethanol and the products were isolated.

The corresponding 2-ethoxycarbonylpyrimidines were previously isolated in high yield from the analogous reaction of 5-methyl(phenyl)-substituted 1,2-dihydro-2-pyrimidinylidenemalononitriles [2].

In the present work we found that 4-pyrimidinylidenemalononitriles Ia-c, which contain phenyl substituent in the 2 or 6 position behave under the same conditions like the 2-pyrimidinyl analogs [2], giving 4-ethoxycarbonyl derivatives IIa-c in 80-85% yields.

In contrast to this, 6-methyl-2-phenyl-1,4-dihydro-4-pyrimidinylidenemalononitrile (Id) produces 4-ethoxycarbonyl-6-methyl-5-nitro-2-phenylpyrimidine (III) in 50% yield. The yield reaches 75% if a two-fold excess of HNO₃ is used. This difference in the behavior of Ic and Id is apparently due to the presence in the 6-position of methyl group, which exhibits electron-donating properties and also is less bulky than phenyl substituent in Ic and so does not hinder introduction of the nitro group in the neighboring 5-position of the pyrimidine ring.

Under analogous conditions, 2-phenyl-1,4-dihydro-4-pyrimidinylidenemalononitrile Ie gives a mixture of 4-ethoxycarbonylpyrimidine (IV) and its 5-nitro derivative V in a 2:1 ratio (according to PMR data). The ratio changes if an excess of HNO₃ is used.

The preferred formation of the 5-nitro-substituted 4-ethoxycarbonylpyrimidine III from the 6-methyl derivative Id, in contrast to Ie, which gives a mixture of IV and V, may be caused by the influence of the methyl substituent.
It should be noted that the reaction of 2-phenyl-1,4-dihydro-4-pyrimidinylidenecyanoacetic ester with HNO₃ in media of varying acidity results in nitration at the exocyclic double bond [2].

The probable mechanism of transformation of the malononitrile group of Ia-c into the ethoxycarbonyl group under the conditions used is analogous to that proposed by us previously for 5-substituted 2-pyrimidinylidenemalononitriles [1]. The mechanism involves nitration at the α-carbon atom of the ylidene tautomer. According to quantum-chemical calculations for the related 4-pyrimidinylidenecyanoacetic esters [3], the electron density at the α-carbon atom in the ylidene tautomer is significantly greater than in the aromatic form. The α-nitromalononitriles that are then formed convert into the corresponding α-hydroxy derivatives. The latter, being cyanohydrins, react with loss of HCN to give α-ketonitriles, which readily react with alcohol to replace the mobile CN group with ethoxy group [4].

The malononitrile moiety in Id and Ie probably reacts in a similar manner. However, the heterocycle is also nitrated.

In our opinion, the formation of 5-nitrosubstituted III and V may be caused by nitration of the ring of the starting malononitriles Id and Ie, the ylidene form of which is activated to electrophilic attack at the 5-position. Compounds Id,e apparently enter into the nitration in acetic acid as the unprotonated form, similar to 2-hydroxypyrimidines [5].

The composition and structure of the obtained products were confirmed by PMR, IR spectra and high-resolution mass spectrometry.

*The structural formula of the predominant tautomer of Ia-c is given.