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SYNTHESIS OF 7-ACETYL-6-METHYL-4-OXO-2,8-DIARYL-3,4-DIHYDRO-2H,8H-PYRIDO[2,1-*b*][1,3]-THIAZINE-9-CARBONITRILES

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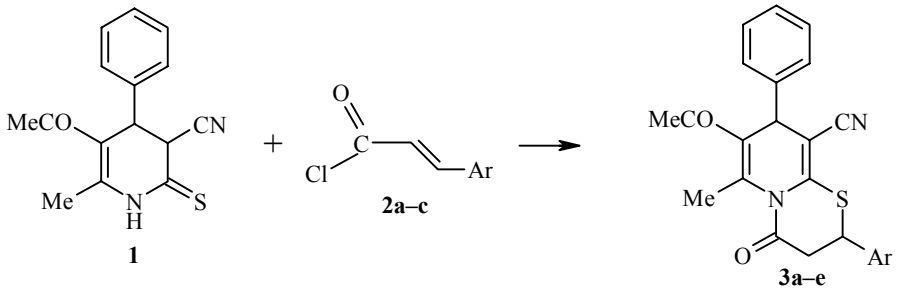
Keywords: 3-aryl-2-propenoyl chloride, 7-acetyl-2,8-diaryl-6-methyl-4-oxo-3,4-dihydro-2H,8H-pyrido[2,1-*b*][1,3]thiazine-9-carbonitrile, 5-acetyl-4-aryl-3-cyano-6-methyl-1,4-dihydropyridine-2(3H)-thione, heterocyclization.

Krauze [1] and Attaby [2] have shown that 4-aryl-3-cyano-6-methyl-1,4-dihydropyridine-2(3H)-thiones react with epichlorohydrin and 2-phenylmethylenemalononitrile to give derivatives of pyrido[2,1-*b*]-[1,3]thiazine.



2, 3 a Ar = Ph; **b** Ar = 4-$MeOC_6H_4$; **c** Ar = 3-$O_2NC_6H_4$

We have found that 5-acetyl-3-cyano-6-methyl-4-phenyl-1,4-dihydropyridine-2(3H)-thione (**1**) reacts with cinnamoyl chloride **2a** and its derivatives **2b** and **2c** in pyridine to give 7-acetyl-6-methyl-4-oxo-2,8-diaryl-3,4-dihydro-2H,8H-pyrido[2,1-*b*][1,3]thiazine-9-carbonitriles **3a-c**. This reaction proceeds upon heating the starting reagents in benzene–pyridine at reflux for 1 h and gives 52-71% yields. An advantage of this method lies in the possibility of synthesizing 3,4-dihydro-2H,8H-pyrido[2,1-*b*][1,3]thiazine-9-carbonitriles with various aryl substituents at $C_{(2)}$.

The ^{1}H NMR spectra of **3a-c** characteristically show three multiplets for the thiazine ring protons as an ABX system at 3.21-3.26, 3.70-3.86, and 5.17-5.43 ppm, while the IR spectra show characteristic absorption bands for the C=O groups at 1700 and 1680-1650 cm^{-1}. The compositions of products **3a-3c** were supported by elemental analysis.

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7-Acetyl-6-methyl-4-oxo-2,8-diphenyl-3,4-dihydro-2H,8H-pyrido[2,1-*b*][1,3]thiazine-9-carbonitrile (3a). A solution of cinnamoyl chloride **2a** (0.83 g, 10 mmol) in benzene (4 ml) was added to a solution of thione **1** (1.35 g, 5 mmol) in pyridine (4 ml) at 20°C. The solution was heated at reflux for 1 h and cooled. Then, water (40 ml) was added and the mixture was extracted with two 25-ml chloroform portions. Chloroform was evaporated. The crystallized product was filtered off and dried to give 1.30 g (65%) of **3a**; mp 142-144°C (ethanol). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm, *J* (Hz): 2.24 (3H, s, CH_3); 2.37 (3H, s, CH_3CO); 3.22 (1H, m, H-3); 3.72 (1H, m, H-3); 4.81 (1H, s, H-8); 5.18 (1H, m, H-2); 7.18-7.60 (10H, m, $2C_6H_5$). IR spectrum in KBr pellet, ν, cm^{-1}: 3100-2900, 2200 (C≡N), 1700 (C=O), 1680 (C=O), 1580 (C=N), 1500, 1450. Found, %: C 72.22; H 5.14; N 6.71. $C_{24}H_{20}N_2O_2S$. Calculated, %: C 71.98; H 5.03; N 6.99.

7-Acetyl-2-(4-methoxyphenyl)-6-methyl-4-oxo-8-phenyl-3,4-dihydro-2H,8H-pyrido[2,1-*b*][1,3]-thiazine-9-carbonitrile (3b) was obtained analogously to **3a** in 52% yield; mp 156-158°C (ethanol). ^{1}H NMR spectrum (300 MHz, DMSO-d_6) δ, ppm, *J* (Hz): 2.27 (3H, s, CH_3); 2.35 (3H, s, CH_3CO); 3.21 (1H, m, H-3); 3.70 (1H, m, H-3); 3.79 (3H, s, CH_3O); 4.80 (1H, s, H-8); 5.17 (1H, m, H-2); 6.99 (2H, d, *J* = 9.2, *p*-C_6H_4); 7.12-7.65 (7H, m, Ar). IR spectrum in KBr pellet, ν, cm^{-1}: 3100-2900, 2200 (C≡N), 1700 (C=O), 1670 (C=O), 1570 (C=N), 1510. Found, %: C 69.59; H 5.28; N 6.74. $C_{25}H_{22}N_2O_3S$. Calculated, %: C 69.75; H 5.15; N 6.51.

7-Acetyl-6-methyl-2-(3-nitrophenyl)-4-oxo-8-phenyl-3,4-dihydro-2H,8H-pyrido[2,1-*b*][1,3]thiazine-9-carbonitrile (3c) was obtained in 71% yield; mp 200-202°C (nitromethane). ^{1}H NMR spectrum (300 MHz, DMSO-d_6), δ, ppm, *J* (Hz): 2.28 (3H, s, CH_3); 2.38 (3H, s, CH_3CO); 3.26 (1H, m, H-3); 3.86 (1H, m, H-3); 4.84 (1H, s, H-8); 5.43 (1H, m, H-2); 7.19-7.39 (5H, m, C_6H_5); 7.74 (1H, t, *J* = 8.4, *m*-$O_2NC_6H_4$); 8.01 (1H, d, *J* = 8.4, *m*-$O_2NC_6H_4$); 8.41 (1H, s, *m*-$O_2NC_6H_4$). IR spectrum in KBr pellet, ν, cm^{-1}: 3100-2900, 2200 (C≡N), 1700 (C=O), 1650 (C=O), 1580 (C=N), 1530. Found, %: C 64.87; H 4.14; N 9.60. $C_{24}H_{19}N_3O_4S$. Calculated, %: C 64.71; H 4.30; N 9.43.

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