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CYCLOCONDENSATION OF A BAYLIS-HILLMAN ADDUCT WITH AMIDINES

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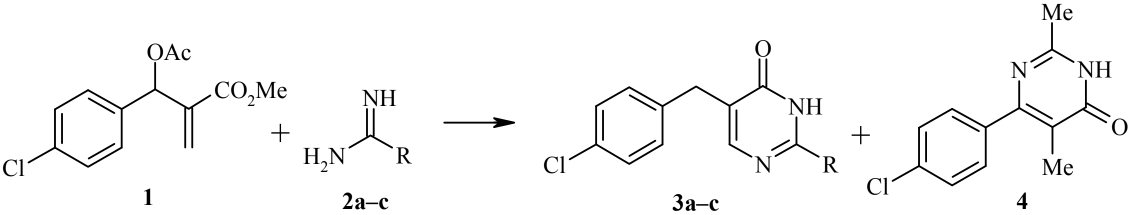
Baylis-Hillman adducts [1, 2] are polyfunctional compounds with high synthetic potential. They contain three electrophilic centers and so can react with different nucleophilic reagents including dinucleophiles to form cyclic systems.

We have studied the reaction of the acetylated adduct **1** (prepared from 4-chlorobenzaldehyde and methylacrylate [3]) with the benz- and acetamidines **2a,b** and with S-methylisothiourea (**2c**).



2, 3 **a** R = Ph, **b** R = Me, **c** R = SMe

The reaction with benzamidine **2a** and S-methylisothiourea **2c** gave good yields of the pyrimidines **3** only. In the case of the acetamidine **2b** a mixture of the pyrimidines **3b** (main product) and **4** (4:1, determined by the comparison of the integrated intensities of the aromatic proton multiplets in the ^{1}H NMR spectra) was obtained in overall yield 47%. Only the pyrimidine **3b** could be isolated in a pure state. The reason for this reactivity will be the subject of a later and detailed investigation.

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 instrument (300 and 75 MHz respectively) using DMSO-d$_6$ as solvent. The residual signals for DMSO-d$_5$ at 2.50 for the ^{1}H nucleus and for DMSO-d$_6$ at 39.7 ppm for the ^{13}C nucleus were used as internal standards.

Cyclocondensation of Adduct 1 with 1,3-Dinucleophiles (General Method). A mixture of methyl 2-(α-acetoxy-4-chlorobenzyl)acrylate (**1**) (1 mmol), the dinucleophile (amidines **2a** and **2b** as their hydrochlorides and **2c** as its sulfate, 1.5 mmol), and anhydrous potassium carbonate (2.4 mmol) in dry DMSO (3 ml) was stirred vigorously at 70ºC to completion of the reaction. Solvent was removed *in vacuo* (1 mm Hg) and the residue was

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diluted with cold water (30 ml) and extracted twice with ethyl acetate. The organic phase was washed with saturated NaCl solution, dried over sodium sulphate, and the ethyl acetate was distilled off. Pure material was separated by column chromatography (with the exception of **3a**), eluting with a mixture of methylene chloride and acetone (3:1) in a gradient regime gradually increasing the proportion of acetone to 100%.

5-(4-Chlorobenzyl)-2-phenylpyrimidin-4(3H)-one (3a). Reaction time 2 h. Dilution of the reaction mixture with water gave crystals which were filtered off and recrystallized from *tert*-butyl methyl ether. Yield 69%; mp 187ºC. ^{1}H NMR spectrum, δ, ppm: 3.74 (2H, s, CH_2); 7.32 (4H, m, ClC_6H_4); 7.51 (3H, m, C_6H_5); 7.95 (1H, s, H-6); 8.09 (2H, m, C_6H_5); 12.53 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 32.87 (CH_2); 125.76 (C-5); 128.40, 129.06, 129.46, 131.36, 131.61 132.31, 133.17, 139.38 (Ar); 152.29 (C-6); 156.89 (C-2); 163.68 (C-4). Found, %: C 68.75; H 4.58; N 9.51. $C_{17}H_{13}ClN_2O$. Calculated, %: C 68.64; H 4.71; N 9.27.

5-(4-Chlorobenzyl)-2-methylpyrimidin-4(3H)-one (3b). Reaction time 4 h. Yield 34%; mp 167ºC. ^{1}H NMR spectrum, δ, ppm: 2.48 (3H, s, CH_3); 3.61 (2H, s, CH_2); 7.27 (4H, m, ArH); 7.74 (1H, s, H-6); 12.40 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 28.86 (CH_3); 32.81 (CH_2); 125.05 (C-5); 129.08, 131.34, 131.67, 139.69 (Ar); 152.71 (C-6); 158.92 (C-2); 162.95 (C-4). Found, %: C 61.35; H 4.76; N 11.91. $C_{12}H_{11}ClN_2O$. Calculated, %: C 61.41; H 4.72; N 11.94.

6-(4-Chlorophenyl)-2,5-dimethylpyrimidin-4(3H)-one (4). An analytically pure sample could not be obtained. ^{1}H NMR spectrum, δ, ppm: 1.94 (3H, s, 5-CH_3); 2.28 (3H, s, 2-CH_3); 7.52 (4H, m ArH); 12.45 (1H, s, NH).

5-(4-Chlorobenzyl)-2-methylsulfanylpyrimidin-4(3H)-one (3c). Reaction time 2 h. Yield 52%; mp 171ºC. ^{1}H NMR spectrum, δ, ppm: 2.05 (3H, s, SCH_3); 3.60 (2H, s, CH_2); 7.28 (4H, m, ArH); 7.79 (1H, s, H-6); 12.64 (1H, s, NH). ^{13}C NMR spectrum, δ, ppm: 15.64 (SCH_3); 33.62 (CH_2); 126.41 (C-5); 128.86, 129.41, 131.37, 138.52 (Ar); 152.71 (C-6); 160.74 (C-2); 163.20 (C-4). Found, %: C 54.13; H 4.09; N 11.97. $C_{12}H_{11}ClN_2OS$. Calculated, %: C 54.03; H 4.16; N 10.50.

REFERENCES

1. D. Basavaiah, P. D. Rao, and R. Hima, *Tetrahedron*, **52**, 8001 (1996).
2. L. S. Yadav, R. Patel, and V. P. Srivastava, *Tetrahedron Lett.*, **50**, 1633 (2009).
3. F. Coelho, W. P. Almeida, D. Veronese, C. R. Mateus, E. C. Silva Lopes, R. C. Rossi, and G. P. C. Silveira, and C. H. Pavam, *Tetrahedron*, **58**, 7437 (2002).