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Baylis-Hillman chemistry: a convenient stereoselective synthesis of (*Z,Z*)- and (*E,E*)-1,4-diallylpiperazines

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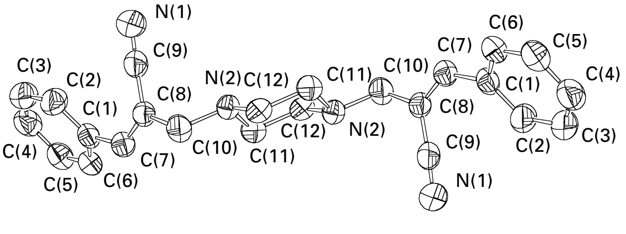
Treatment of piperazine with 3-acetoxy-2-methylenealkanenitriles provides exclusively (1,4)-bis[(2*Z*)-2-cyanoalk-2-en-1-yl]piperazines. A similar reaction of methyl 3-acetoxy-3-aryl-2-methylenepropanoates with piperazine produces (1,4)-bis[(2*E*)-3-aryl-2-methoxycarbonylprop-2-en-1-yl]piperazines as the major products.

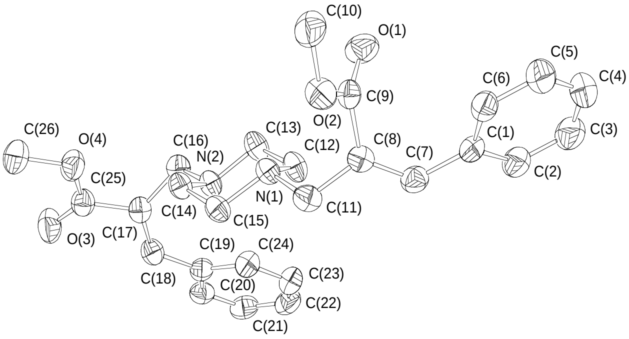
Keywords: Baylis–Hillman chemistry, stereoselectivity, bisallylamines, piperazine

The piperazine moiety is an integral framework of various drug molecules (norfloxacin, ciprafloxacin, *etc.*)[1,2] and some interesting biologically active molecules including those that release NO (nitric oxide) which plays a crucial role in bioregulatory processes.[3–5] Allylamines are fundamental building blocks for the synthesis of numerous important compounds such as alkaloids, amino acids and carbohydrate derivatives.[6–9] The Baylis–Hillman reaction is an emerging carbon–carbon bond forming reaction producing an interesting class of densely functionalised molecules which constitute an important source for various stereoselective processes.[10–17] With the consideration in mind that the molecules containing both piperazine and allylamine moieties may be of importance in terms of their physiological properties, we herein report a simple synthesis of (*Z,Z*)- and (*E,E*)-1,4-diallylpiperazines *via* the reactions of 3-acetoxy-2-methylenealkanenitriles and methyl 3-acetoxy-3-aryl-2-methylenepropanoates, respectively, with piperazine (eqns 1 and 2).

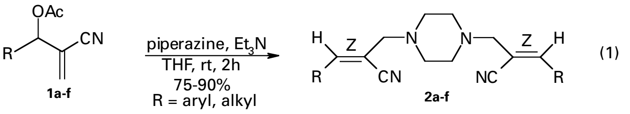
The (*Z,Z*)-stereochemistry of the molecule **2a** (R = phenyl) was established by a 2D-NOESY experiment and also by single crystal X-ray data (Fig. 1).

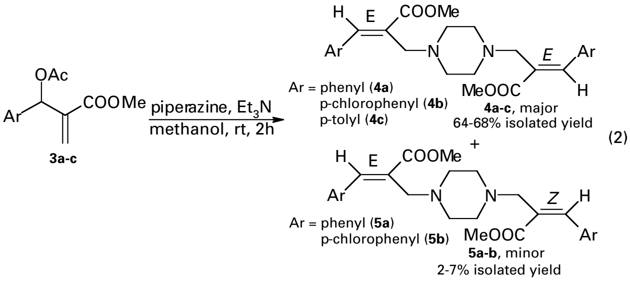


2a (Fig. 1)



5b (Fig. 2)





The (*E,Z*)-stereochemistry of the minor compound (**5a**) was established by single crystal X-ray data (Fig. 2). We have also noticed that reaction between methyl 3-acetoxy-3-(4-methylphenyl)-2-methylenepropanoate and piperazine provided the (*E,E*)-1,4-diallylpiperazine (**4c**) exclusively (eqn 2).

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Techniques used: IR, ^{1}H and ^{13}C NMR, MS, X-ray crystallography.

References: 31

Table 1: Synthesis of 1,4-bis[(2Z)-2-cyanoalk-2-en-1-yl]piperazines

Table 2: Synthesis of 1,4-bis(2-methoxycarbonylalk-2-en-1-yl)piperazines

Equations: 2

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