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# Synthesis of 2,2'-bipyridyl derivatives using aza Diels–Alder methodology

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Abstract—Amidrazone 1 and the tricarbonyl derivatives 2a-c gave the triazines 3a-c, respectively, which reacted with 2,5-norbornadiene 4 in boiling ethanol yielding the corresponding novel 2,2'-bipyridines 5a-c in good yield. Triazine 6 gave the 2,2'-bipyridyl derivative 7 (65%) with compound 4 in 1,2-dichlorobenzene at 140°C. © 2003 Elsevier Science Ltd. All rights reserved.

2,2'-Bipyridyl and its derivatives are important heterocyclic molecules and they have found extensive use in many areas of chemistry.<sup>1</sup> Particularly interesting are their application as metal chelating ligands<sup>2</sup> and in this context 2,2'-bipyridyl derivatives bearing pendant chiral substituents have recently been employed in the asymmetric synthesis field.<sup>3</sup> In view of the extensive interest in 2,2'-bipyridyls, we embarked upon the preparation of a series of functionalised 2,2'-bipyridyls **5a–c** from triazine precursors **3a–c** using the aza Diels–Alder methodology that we have successfully applied to the synthesis of other pyridine derivatives.<sup>4</sup>

Amidrazone  $1^5$  was prepared from 2-cyanopyridine and hydrazine hydrate and was reacted with the unsymmetrical tricarbonyl derivatives  $2\mathbf{a}-\mathbf{c}^6$  in boiling ethanol solution to yield the novel 1,2,4-triazines  $3\mathbf{a}-\mathbf{c}$  respectively (90–97% yield) (Scheme 1). With the exception of a few isolated examples, the reactions of amidrazones with unsymmetrical tricarbonyl compounds have not been studied in detail and this reaction provides a useful method for the synthesis of substituted triazines.<sup>4</sup> The aza Diels–Alder reactions between triazines and the acetylene equivalent, 2,5-norbornadiene 4 has frequently been used to prepare pyridines<sup>7</sup> and triazines **3a**–**c** were therefore reacted with 2,5-norbornadiene **4**. These reactions were initially performed in 1,2dichlorobenzene solution at 140°C but since it was often difficult to remove the last traces of 1,2dichlorobenzene in the work-up procedure we subsequently found that boiling ethanol was a suitable solvent and a 'one-pot' reaction allowed the preparation of the required pyridines 5a-c without the need to isolate the triazine intermediates 3a-c. Thus, amidrazone 1, tricarbonyls 2a-c and an excess of 2,5-norbornadiene 4 were heated in ethanol at reflux for 20 hours giving the required 2,2'-bipyridyls 5a-c respectively in 80-87% overall yields.



#### Scheme 1.

Keywords: 2,2'-bipyridyls; aza Diels-Alder reaction; 1,2,4-triazines.

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#### Scheme 2.

Both  $C_1$  and  $C_2$ -symmetrical 2,2'-bipyridyls bearing pendant chiral substituents have been prepared as potential metal chelating ligands and the synthesis of these molecules generally involves many steps.3 The chiral moieties in these molecules often originate from the terpene chiral pool and cross-coupling reactions are generally employed to form the biaryl bond. The 2,2'bipyridyl derivative 7 (R=H) and related fused cycloalkane derivatives would be useful precursors to chiral ligands 7 (R = alkyl) because the alkyl group could be introduced by deprotonation of compound 7 (R = H) followed by alkylation of the resulting carbanion (Scheme 2). Compound 7 (R = H) has been prepared from 2-pyridylacetylene 8 and hept-6-ynenitrile 9 in low yield (9%).<sup>8</sup> An alternative synthesis of this compound would be desirable and this has been achieved by reacting the readily prepared triazine  $6^9$ with 2,5-norbornadiene 4 in 1,2-dichlorobenzene solution at 140°C which yielded bipyridyl 7 (R = H) in 65% vield.

In summary, we have developed a useful method of preparing 2,2'-bipyridyls from triazine precursors using an aza Diels–Alder reaction with 2,5-norbornadiene 4. Triazine derivatives  $3\mathbf{a}-\mathbf{c}$  are sufficiently reactive to allow the mild conditions to be used for their aza Diels–Alder reactions.

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