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Synthesis of pyridine and 2,2′-bipyridine derivatives from the aza Diels–Alder reaction of substituted 1,2,4-triazines

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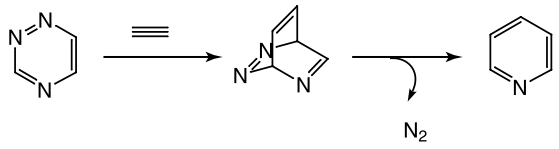
Abstract—Amidrazone **1a** and the tricarbonyl derivatives **2b–d** reacted in boiling ethanol in the presence of 2,5-norbornadiene **5** giving the pyridine derivatives **6b–d** respectively (59–72%) and in the presence of 2,3-dihydrofuran **7** yielding the lactones **10b–d** (39–44%). The 2,2′-bipyridine derivatives **6e–g** were similarly obtained in good yield (81–87%) from the reaction of amidrazone **1b** and tricarbonyl derivatives **2b–d** in the presence of 2,5-norbornadiene **5**.

1. Introduction

Pyridine derivatives occupy a pivotal position in modern heterocyclic chemistry and consequently facile methods for the synthesis of this ring system from readily available starting materials is of contemporary interest.[1] 2,2′-Bipyridine and its derivatives have also been the subject of numerous studies, principally because of their well developed coordination chemistry.[2] They have found applications in many areas of chemistry including supramolecular chemisty,[3] artificial photosynthesis systems,[4] luminescent sensor materials,[5] non-linear optical materials[6] and when they bear pendant chiral substituents, they have found use as ligands in metal catalysed asymmetric reactions.[7] The aza Diels–Alder reaction has become an important and versatile method for the preparation of pyridine derivatives and several recent reviews have discussed the scope and application of this useful reaction.[8] One important theme in aza Diels–Alder methodology is the reaction between a 2-azadiene and a suitable dienophile to form either the dihydro- or tetrahydro-pyridine skeleton as depicted in Scheme 1. A diverse range of 2-azadienes and dienophiles have been utilised in this reaction enabling the preparation of a wide variety of pyridine derivatives. 1,2,4-Triazines[9] have been used as 2-azadiene equivalents on many occasions and these heterocycles have been reacted with suitable acetylene equivalents yielding pyridine derivatives (Scheme 2). Recent examples of the aza Diels–Alder reaction of 1,2,4-triazines giving pyridine and/or 2,2′-bipyridine derivatives include their reaction with 2,5-norbornadiene[10] and enamines as acetylene equivalents.[11]

Scheme 1.



Scheme 2.

1,2,4-Triazines can be readily prepared from 1,2-dicarbonyl derivatives and amidrazones [$RC(=NHNH_2)NH_2$] and many 1,2,4-triazines have been prepared using this methodology.[9] The 1,2-dicarbonyl compounds that have been used in this reaction have generally been symmetrical and problems with the formation of regioisomeric triazines cannot occur. α-Ketoaldehydes also react with amidrazones giving single products derived from attack of the amidrazone's hydrazine group at the aldehyde carbonyl group. The reaction of amidrazones with symmetrical 1,2,3-triketones similarly yields 1,2,4-triazine derivatives. Interestingly, only a few examples of the reaction of amidrazones with α,β-diketoesters have been reported (Scheme 3). Thus, the reaction between the amidrazone **1c** and the ester **2d** was

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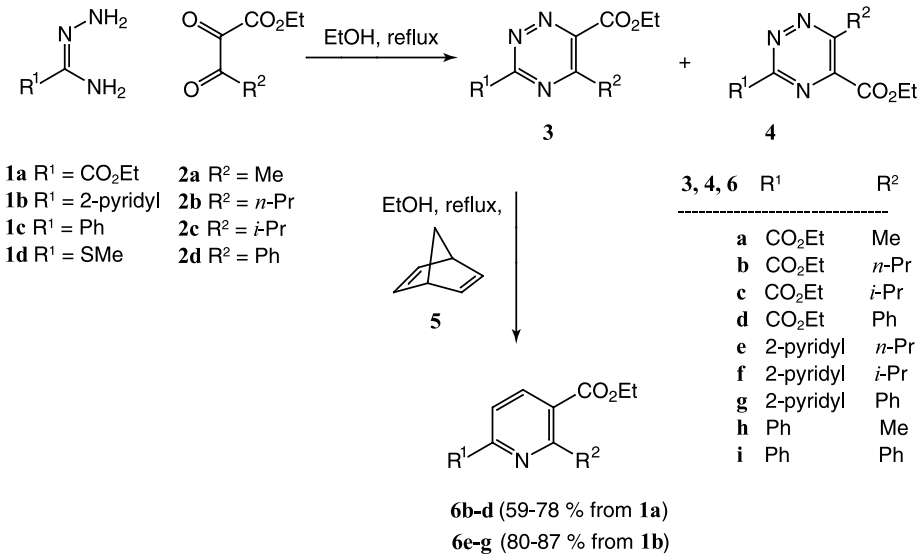


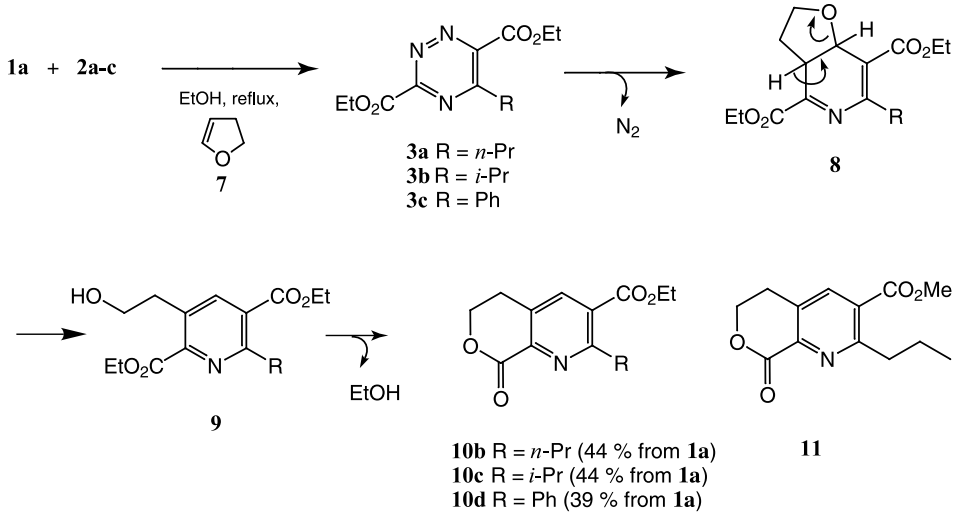
Scheme 3.

reported to give only ethyl 3,5-diphenyl[1,2,4]triazine-6-carboxylate **3i** in 70% yield[12] whereas Ohsumi and Neunhoeffer reacted this amidrazone **1c** with ester **2a** and obtained a mixture of the corresponding regioisomeric triazines **3h** and **4h** in unspecified yields.[13] The reaction of amidrazone **1a** with ester **2a** was investigated by Synder and co-workers who obtained a 10.5:1 mixture of the regioisomeric triazines **3a** and **4a** in 46% overall yield.[14] An α,β-diketoester bearing a pendant protected amino acid moiety has been reacted with *S*-methylisothiosemicarbazide **1d** giving a mixture of regioisomeric triazines in low overall yield.[15]Thus, the reactions between amidrazones and α,β-diketoester **2a** gave mixtures of 1,2,4-triazines whereas only one 1,2,4-triazine product was obtained when a more sterically demanding R^2 group was present i.e. the α,β-diketoester **2d** was used.

In view of the current interest in pyridine and 2,2′-bipyridine synthesis, we envisaged that the reaction of amidrazones **1a**[16] and **1b**[17] with α,β-diketoesters **2**[18] in the presence of an appropriate aza-dienophile might be developed as a useful method for the preparation of pyridine and bipyridine derivatives via the aza Diels–Alder reaction of 1,2,4-triazine intermediates.

2. Results and discussion

Amidrazone **1a** (prepared from ethyl thioamido oxalate[16] and hydrazine hydrate) and compound **2b** reacted in boiling ethanol in the presence of an excess of 2,5-norbornadiene **5** to give a single pyridine derivative, compound **6b**, in 78% yield. Under similar conditions, the pyridine derivatives **6c** (72%) and **6d** (59%) were prepared from the appropriate α,β-diketoesters and 2,5-norbornadiene **5**. We assumed that the amidrazone **1a** had reacted regioselectively with the α,β-diketoesters **2b–d** yielding the corresponding triazine intermediates **3b–d** and not the isomeric heterocycles **4b–d**. This assumption was confirmed by selective hydrolysis of the less sterically crowded 6-ester substituent in pyridines **6b** and **6d** and subsequent decarboxylation



Scheme 4.

yielding the known ethyl 2-propylpyridine-3-carboxylate[19] and ethyl 2-phenylpyridine-3-carboxylate[20] respectively.

The methodology described above for the synthesis of pyridines **6b–d** was readily extended to the preparation of the bipyridine derivatives **6e–g**. Thus, amidrazone **1b** was reacted with each of the α,β-diketoesters **2b–d** in the presence of an excess of 2,5-norbornadiene **5** in boiling ethanol yielding the bipyridines **6e** (81%), **6f** (80%) and **6g** (87%) respectively.

2,3-Dihydrofuran **7** has been used by Gilchrist and co-workers[21] as an acetylene equivalent in the aza Diels–Alder reaction of triazines. Amidrazone **1a** was reacted with each of the α,β-diketoesters **2b–d** and an excess of 2,3-dihydrofuran **7** in ethanol at reflux in a 'one-pot' reaction yielding the lactones **10b** (44%), **10c** (44%) and **10d** (39%) respectively as shown in Scheme 4. Ring-opening of the ether ring in intermediates **8** yields the pyridines **9** which could not be isolated but underwent lactonisation giving the products **10b–d**. The proposed regioselectivity depicted in formula **8** was confirmed by starting with the methyl ester analogue of the α,β-diketoester **2b**. Reaction of this compound with the amidrazone **1a** in the presence of 2,3-dihydrofuran **7** gave the methyl ester analogue of lactone **10b**, compound **11**, indicating that the 2-ester substituent in the triazine intermediate **3b** was involved in lactonisation.

The observed regioselectivity of the cycloaddition of triazine **3b** and 2,3-dihydrofuran **7** was also predicted by PM3 semi-empirical molecular orbital calculations (Fig. 1).[22] The HOMO (2,3-dihydrofuran)/LUMO (triazine) energy difference (8.21 eV) is significantly smaller than the HOMO (triazine)/LUMO (2,3-dihydrofuran) energy difference (11.50 eV) indicating that the former interaction will determine the outcome of this inverse electron demand cycloaddition reaction. The coefficients of the HOMO (2,3-dihydrofuran)/LUMO (triazine) at the reaction centres are shown in Figure 1. The most efficient frontier molecular orbital overlap will occur when the largest frontier molecular orbital coefficients of the two reactants interact and this corresponds to the C3-position of the 2,3-dihydrofuran **7** interacting with the C2-position of the triazine **3b** and the C2-position of the 2,3-dihydrofuran **7** interacting with the C5-position of the triazine **3b**. This situation corresponds with the observed regioselectivity of the cycloaddition reaction.

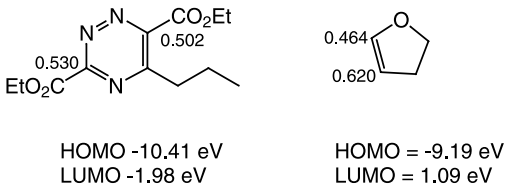


Figure 1.

In conclusion we have developed a useful 'one pot' method for the preparation of pyridine and 2,2′-bipyridine derivatives from α,β-diketoesters **2b–d** under mild conditions. Thus, we have shown that amidrazones **1a** and **1b** reacted in boiling ethanol with unsymmetrical tricarbonyl derivatives **2b–d** in the presence of 2,5-norbornadiene **5** giving pyridines **6b–d** and 2,2′-bipyridines **6e–g** in good overall yields and that lactones **10b–d** could be prepared in moderate overall yields from amidrazone **1a** and α,β-diketoesters **2b–d** in the presence of 2,3-dihydrofuran **7**.

3. Experimental

Amidrazone **1a** was prepared from ethyl thioamido oxalate [$EtO_2CC(=S)NH_2$] [16] and hydrazine hydrate. Ethyl thioamido oxalate was prepared from commercially available ethyl oxamate and Lawesson's reagent following a literature proceedure.[16] Amidrazone **1b** was prepared from 2-cyanopyridine and hydrazine hydrate.[17] ^{1}H NMR spectra were determined at 270 MHz.

3.1. Synthesis of pyridines 6b–d and 10b–d. General method

To a stirred solution ethyl thioamido oxalate[16] (0.5 g, 3.75 mmol) in ethanol (25 mL) was added hydrazine hydrate (0.19 g, 3.75 mmol). After 20 min at room temperature, the appropriate α,β-diketoester **2**[18] (3.75 mmol) and either 2,5-norbornadiene **5** (3.46 g, 37.5 mmol) or 2,3-dihydrofuran **7** (7.9 g, 133 mmol) were added in one portion. The solution was heated at reflux for 20 h, allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The product was isolated by columchromatography over silica gel.

3.1.1. Diethyl 6-propylpyridine-2,5-dicarboxyate 6b. This compound was obtained as an orange oil (78%) (eluent: ethyl acetate/petroleum ether bp 60–80 °C 1:1). ^{1}H NMR: ($CDCl_3$) δ 8.23 (d, 1H, $J=8$ Hz, py-*H*), 7.97 (d, 1H, $J=8$ Hz, py-*H*), 4.49–4.40 (overlapping quartets, 4H, 2× ester-CH_2–), 3.19 (t, 2H, $J=7$ Hz, –CH_2–), 1.75 (sextet, 2H, $J=7$ Hz, –CH_2–), 1.44 (overlapping triplets, 6H, 2×ester-CH_3) and 0.95 (t, 3H, $J=7$ Hz, –CH_3) ppm, HRMS (CI): calcd for $C_{14}H_{20}NO_4$ (M+H) 266.1392, found 266.1392.

3.1.2. Diethyl 6-isopropylpyridine-2,5-dicarboxyate 6c. This compound was obtained as an orange oil (72%) (eluent: ethyl acetate/petroleum ether bp 60–80 °C 1:1). ^{1}H NMR: ($CDCl_3$) δ 8.12 (d, 1H, $J=8$ Hz, py-*H*), 7.92 (d, 1H, $J=8$ Hz, py-*H*), 4.42 (overlapping quartets, 4H, 2×ester-CH_2–), 3.77 (septet, 1H, $J=7$ Hz, –C*H*–), 1.43 (overlapping triplets, 6H, 2×ester-CH_3) and 1.35 (d, 6H, $J=7$ Hz, 2×-CH_3) ppm, HRMS (CI): calcd for $C_{14}H_{20}NO_4$ (M+H) 266.1392, found 266.1388.

3.1.3. Diethyl 6-phenylpyridine-2,5-dicarboxylate 6d. This compound was obtained as a yellow oil (59%) (eluent: ethyl acetate/petroleum ether bp 60–80 °C 4:6). ^{1}H NMR: ($CDCl_3$) δ 8.19 (d, 1H, $J=8$ Hz, py-*H*), 8.10 (d, 1H, $J=8$ Hz, py-*H*), 7.57 (m, 1H, Ph-*H*), 7.44 (m, 4H, Ph-*H*), 4.49 (q, 2H, $J=7$ Hz, –CH_2–), 4.17 (q, 2H, $J=7$ Hz, –CH_2–), 1.45 (t, 3H, $J=7$ Hz, –CH_3) and 1.05 (t, 3H, $J=7$ Hz, –CH_3) ppm, HRMS (CI): calcd for $C_{17}H_{18}NO_4$ (M+H) 300.1124, found 300.1234.

3.1.4. Ethyl/methyl 8-oxo-2-propyl-5,6-dihydro-8*H*-pyrano[3,4-*b*]pyridine-3-carboxylate 10b/11. This

compound was obtained as an orange oil (44%) (eluent, petroleum ether bp 60–80 °C/ethyl acetate 4:6). ν_{max} (KBr): 1724 and 1187 cm^{-1}. ^1H NMR: ($CDCl_3$) δ 8.08 (s, 1H, py-*H*), 4.60 (t, 2H, $J=6$ Hz, ring-CH_2–), 4.43 (q, 2H, $J=7$ Hz, ester-CH_2–), 3.17 (overlapping triplets, 5H, ester-CH_3, ring-CH_2–), 1.72 (m, 2H, –CH_2–), 1.43 (t, 2H, $J=7$ Hz, –CH_2–) and 0.99 (t, 3H, $J=7$ Hz, –CH_3) ppm, ^{13}C NMR: ($CDCl_3$) δ 165.9 (CO), 163.4 (CO), 162.3 (C), 143.8 (C), 138.2 (*CH*), 132.9 (C), 129.5 (C), 66.9 (CH_3), 62.1 (CH_3), 38.7 (CH_2), 29.7 (CH_2), 26.9 (CH_2), 23.6 (CH_2) and 14.2 (CH_2) ppm, HRMS (CI): calcd for $C_{14}H_{18}NO_4$ (M+H) 264.1236, found 264.1234. When the experiment was repeated using methyl 2,3-dioxohexanoic acid in place of compound **2b**, the methyl ester **11** was obtained which had the following ^1H NMR spectral data ($CDCl_3$): δ 8.09 (s, 1H, py-*H*), 4.60 (t, 2H, $J=7$ Hz, ring-CH_2–), 3.96 (s, 3H, –CH_3), 3.16 (m, 4H, 2×-CH_2–), 1.72 (sextet, 2H, $J=7$ Hz, –CH_2–) and 0.98 (t, 3H, $J=7$ Hz, –CH_3) ppm.

3.1.5. Ethyl 8-oxo-2-isopropyl-5,6-dihydro-8*H*-pyrano[3,4-*b*]pyridine-3-carboxylate 10c. The ethyl ester was obtained as an orange oil (44%) (eluent: petroleum ether bp 60–80 °C/ethyl acetate 4:6). ν_{max} (KBr): 1722 and 1187 cm^{-1}. ^1H NMR: ($CDCl_3$) δ 7.94 (s, 1H, py-*H*), 5.85 (t, 2H, $J=6$ Hz, ring-CH_2–), 4.42 (q, 2H, $J=7$ Hz, ester-CH_2–), 3.74 (septet, 1H, –*CH*–), 3.13 (t, 2H, $J=6$ Hz, ring-CH_2–), 1.43 (t, 3H, $J=7$ Hz, ester-CH_3) and 3.39 (d, 6H, $J=7$ Hz, 2×isopropyl-CH_3) ppm, ^{13}C NMR: ($CDCl_3$) δ 167.0 (CO), 166.4 (CO), 162.2 (C), 143.8 (C), 137.4 (*CH*), 132.8 (C), 129.4 (C), 66.8 (–CH_3), 62.1 (CH_3), 32.9 (CH_2), 27.0 (CH_2), 22.2 (CH_2), 21.1 (CH_2) and 14.2 (CH_2) ppm, HRMS (CI): calcd for $C_{14}H_{18}NO_4$ (M+H) 264.1236, found 264.1233.

3.1.6. Ethyl 8-oxo-2-phenyl-5,6-dihydro-8*H*-pyrano[3,4-*b*]pyridine-3-carboxylate 10d. This compound was obtained as a an orange oil which crystallised from ethanol giving a white crystalline solid (39%), mp 162 °C. ν_{max} (KBr): 1736, 1701, 1182 and 1139 cm^{-1}. ^1H NMR: ($CDCl_3$) δ 8.01 (s, 1H, py-*H*), 7.60 (m, 1H, Ph-*H*), 7.40 (m, 4H, Ph-*H*), 4.65 (t, 2H, $J=5$ Hz, ring-CH_2–), 4.19 (q, 2H, $J=7$ Hz, ester-CH_2–), 3.22 (t, 2H, $J=5$ Hz, ring-CH_2–) and 1.03 (t, 3H, $J=7$ Hz, ester-CH_3) ppm, ^{13}C NMR: ($CDCl_3$) δ 167.4 (CO), 161.9 (CO), 158.8 (*CH*), 143.5 (C), 138.8 (C), 137.6 (*CH*), 133.8 (C), 131.0 (C), 129.2 (C), 128.8 (C), 128.3 (C), 66.8 (CH_3), 62.1 (CH_2), 27.1 (CH_2) and 13.6 (CH_2) ppm, Anal. for $C_{17}H_{15}NO_4$: calcd C, 68.68; H, 5.09; N, 4.71, found C, 68.54; H, 4.84; N, 4.60.

3.1.7. 6-Propylpyridine-2,5-dicarboxylic acid 5-ethyl ester and ethyl 2-propylpyridine-3-carboxylate. 6-Propylpyridine-2,5-dicarboxylic acid 5-ethyl ester (0.15 g, 56%) was synthesised from diethyl 6-propyl-pyridine-2,5-dicarboxylate **6b** following the procedure described below for the preparation of 6-phenylpyridine-2,5-dicarboxylic acid 5-ethyl ester and was obtained as a brown oil. ^1H NMR: ($CDCl_3$) δ 8.40 (d, 1H, $J=8$ Hz, py-*H*), 8.12 (d, 1H, $J=8$ Hz, py-*H*), 4.44 (q, 2H, $J=7$ Hz, ester-CH_2–), 3.18 (t, 2H, $J=7$ Hz, –CH_2–), 1.08 (m, 2H, –CH_2–) 1.43 (t, 3H, $J=7$ Hz, ester-CH_3) and 1.02 (t, 3H, $J=7$ Hz, –CH_3). Ethyl 2-propylpyridine-3-carboxylate (0.17 g, 70%) was synthesised from 6-propylpyridine-2,5-dicarboxylic acid 5-ethyl ester following the procedure described below for the preparation of ethyl 2-phenylpyridine-3-carboxylate and was obtained as a brown oil. ^1H NMR: ($CDCl_3$) δ 8.67 (dd, 1H, $J=5$, 2 Hz, py-*H*), 8.17 (dd, 1H, $J=8$, 2 Hz, py-*H*) 7.24 (dd, 1H, $J=8$, 2 Hz, py-*H*), 4.40 (q, 2H, $J=7$ Hz, ester-CH_2–) 3.14 (t, 2H, $J=7$ Hz, –CH_2–), 1.76 (m, 2H, –CH_2–), 1.41 (t, 3H, $J=7$ Hz, ester-CH_3) and 1.00 (t, 3H, $J=7$ Hz, –CH_3) ppm. This ^1H NMR spectral data is consistent with that reported in the literature.[19]

3.1.8. 6-Phenylpyridine-2,5-dicarboxylic acid 5-ethyl ester and ethyl 2-phenylpyridine-3-carboxylate. To a solution of diethyl 6-phenylpyridine-2,5-dicarboxylate **6d** (0.3 g, 1.00 mmol) in ethanol (20 mL) was added a solution of KOH (0.12 g, 1.00 mmol, in 2 mL of water) and the mixture was stirred at room temperature for 3 h. The pH was then adjusted to 1 and the mixture was extracted with dichloromethane (25 mL), washed with water (2×5 mL) and evaporated to give the 6-phenylpyridine-2,5-dicarboxylic acid 5-ethyl ester as a brown oil (0.22 g, 81%). ^1H NMR: ($CDCl_3$) δ 8.32 (d, 1H, $J=8$ Hz, py-*H*), 8.27 (d, 1H, $J=8$ Hz, py-*H*), 7.53–7.48 (m, 5H, Ph-*H*), 4.20 (q, 2H, $J=7$ Hz, ester-CH_2–) and 1.08 (t, 3H, $J=7$ Hz, ester-CH_3) ppm. 6-Phenylpyridine-2,5-dicarboxylic acid 5-ethyl ester (0.22 g, 0.81 mmol) was placed in a round bottom flask and heated gently by means of a Bunsen burner for 2 min. The resulting distillate was collected giving ethyl 2-phenyl-pyridine-3-carboxylate as a brown oil (0.08 g, 42%). ^1H NMR: ($CDCl_3$) δ 8.76 (dd, 1H, $J=5$, 2 Hz, py-*H*), 8.10 (dd, 1H, $J=8$, 2 Hz, py-*H*), 7.50–7.54 (m, 2H, Ph-*H*), 7.40–7.44 (m, 3H, Ph-*H*), 7.34 (dd, 1H, $J=8$, 5 Hz, py-*H*), 4.14 (q, 2H, $J=7$ Hz, ester-CH_2–) and 1.04 (t, 3H, $J=7$ Hz, ester-CH_3) ppm. This ^1H NMR spectral data is consistent with that reported in the literature.[20]

3.2. Synthesis of bipyridine derivatives 6e–g. General method

To a stirred solution of amidrazone **1b**[17] (0.5 g, 3.68 mmol) in ethanol (15 mL) was added appropriate α,β-diketoester **2**[18] (3.38 mmol) and 2,5-norbornadiene **5** (3.46 g, 36.8 mmol). This solution was heated at reflux under an atmosphere of nitrogen for 20 h, allowed to cool to room temperature, and evaporated under reduced pressure giving the crude product which was purified by column chromatography over silica gel.

3.2.1. Ethyl 6-propyl-2,2′-bipyridine-5-carboxylate 6e. This compound was obtained as an orange oil (81%) (eluent: ethyl acetate/petroleum ether bp 60–80 °C 1:1). ν_{max} (KBr): 1718, 1252 and 1093 cm^{-1}. ^1H NMR: ($CDCl_3$) δ 8.70 (dd, 1H, $J=5$, 2 Hz, py-*H*), 8.52 (d, 1H, $J=8$ Hz, py-*H*), 8.28 (s, 2H, py-*H*), 7.84 (dt, 1H, $J=8$, 2 Hz, py-*H*), 7.33 (m, 1H, py-*H*), 4.40 (q, 2H, $J=7$ Hz, ester-CH_2–), 3.22 (m, 2H, –CH_2–), 1.83 (sextet, 2H, $J=7$ Hz, –CH_2–), 1.43 (t, 3H, $J=7$ Hz, ester-CH_3) and 1.04 (t, 3H, $J=7$ Hz, –CH_3) ppm, HRMS (CI): calcd for $C_{16}H_{19}N_2O_2$ (M+H) 271.1446, found 271.1443.

3.2.2. Ethyl 6-isopropyl-2,2′-bipyridinyl-5-carboxylate 6f. This compound was obtained as an orange waxy solid (80%), mp 66–70 °C, (eluent: ethyl acetate/petroleum ether bp 60–80 °C 1:1). ^1H NMR: ($CDCl_3$) δ 8.69 (d, 1H, $J=5$ Hz, py-*H*), 8.59 (d, 1H, $J=8$ Hz, py-*H*), 8.28 (d, 1H,

$J=8$ Hz, py-*H*), 8.20 (d, 1H, $J=8$ Hz, py-*H*), 7.85 (t, 1H, $J=8$ Hz, py-*H*), 7.32 (m, 1H, py-*H*), 4.40 (q, 2H, $J=7$ Hz, ester-CH_2–) 3.93 (septet, 1H, $J=7$ Hz, –C*H*–), 1.42 (t, $J=7$ Hz, ester-CH_3) and 1.38 (d, 6H, $J=7$ Hz, 2×isopropyl-CH_3) ppm, HRMS (CI): calcd for $C_{16}H_{19}N_2O_2$ (M+H) 271.1446, found 271.1445.

3.2.3. Ethyl 6-phenyl-2,2′-bipyridine-5-carboxylate 6g. This compound was obtained as an orange oil (87%) (eluent: ethyl acetate/petroleum ether bp 60–80 °C 6:4). ν_{max} (KBr): 1717, 1250 and 1092 cm^{-1}. ^1H NMR: ($CDCl_3$) δ 8.70 (ddd, 1H, $J=5$, 2, 1 Hz, py-*H*), 8.57 (dd, 1H, $J=7$, 2 Hz, py-*H*), 8.45 (d, 1H, $J=8$ Hz, py-*H*), 8.23 (d, 1H, $J=8$ Hz, py-*H*), 7.8 (dt, 1H, $J=8$ Hz, py-*H*), 7.67–7.63 (m, 1H, Ph-*H*), 7.49–7.43 (m, 4H, Ph-*H*), 7.33 (m, 1H, py-*H*), 4.40 (q, 2H, $J=7$ Hz, –CH_2–) and 1.09 (t, 3H, $J=7$ Hz, –CH_3) ppm, HRMS (CI): calcd for $C_{19}H_{16}N_2O_2$ (M+H) 305.1290, found 305.1289.

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