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REACTION OF β-AMINO-α,β-UNSATURATED ESTERS AND AMIDES WITH ARYL DIAZONIUM SALTS

SYNTHESIS OF CINNOLINE DERIVATIVES

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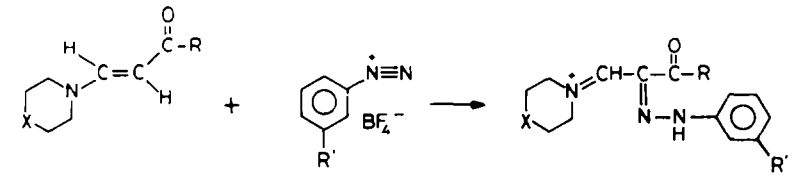
Abstract—Conjugated esters and amides react with aryldiazonium salts at room temperature (MeCN) to form the corresponding iminium hydrazone derivatives, which can be thermally cyclized to cinnoline-3-esters and cinnoline-3-amides. In general the intermediate iminium salts derived from the enamine amides cyclize faster than those from the enamine esters. Furthermore, the ease of cyclization depends upon the structure of the base-component of the enamine ester or the amide and the substituent in the aryl moiety of the diazonium salt. The configurational structure of the iminium hydrazones, studied by NMR spectroscopy, has been shown to involve H-bonding of the hydrazonyl N-H with the ester or the amide CO group.

Reactions of the enamines with aryldiazonium salts have been documented in the literature.[3] It has been shown that mono arylhydrazones of 1,2-diketones (corresponding to the ketone component of the enamine) can be conveniently obtained via this route. The overall reaction, consequently, consists of an oxidation of the α-carbon of the starting ketone. Investigation of the reaction of conjugated enamines with aryldiazonium salts,[4a-d] in this laboratory, has led to the convenient syntheses of polycyclic heterocycles—including indolo[4b] and diaza-steroids[4d]—by the appropriate diversion of the intermediate iminium hydrazones formed as the primary products of the reaction. In this communication we describe a facile, one pot, synthesis of 3-substituted cinnoline derivatives, via the reaction of enamine esters and amides with aryldiazonium fluoroborates. The preliminary findings have been communicated earlier.[5] The reported method is superior, both in terms of practical convenience and overall yields, to the known procedures[6] for the synthesis of cinnoline-3-carboxy derivatives.

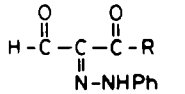
Reactions of enamine esters and amides with aryldiazonium salts

The enamine esters and amides (**1a–f**, Scheme A) were prepared by the addition of the appropriate secondary amines to ethylpropiolate or the corresponding pyrrolidine amide.[7] When these enamine derivatives (**1a–f**) were allowed to react with phenyldiazonium fluoroborate (**2a**) in acetonitrile, at room temperature (60 min), the primary products, the iminium hydrazones, were obtained in good to excellent yields (65–90%). The salts **3a–e** were isolated directly as crystalline compounds, while **3f** was identified as its hydrolytic product **4a**. Reaction of *m*-methoxybenzenediazonium fluoroborate (**2b**) with the same enamines (**1a–f**), under the aforementioned conditions, led, except in the case of **1a**, to the cinnoline derivatives **5a, b**. The product of the reaction of **1a** with **2b** was, on the other hand, shown to be the corresponding iminium salt **3g**. The iminium salts **3c–g** could be converted into the cinnoline esters (**5a, c**) or the cinnoline amide (**5d**) upon refluxing in dry acetonitrile. However, the time required for this cyclization reaction varied significantly with the structure of the salt. Whereas the iminium hydrazones carrying the amide function, *viz* **3d–f**, cyclized in 24 hr (MeCN reflux), those containing the ester moiety required considerably longer (**3g**, 60 hr and **3c**, one week), under the same conditions. It is also noteworthy that the salts **3a, b** did not cyclize in refluxing acetonitrile.

The results described in the preceding paragraph can be explained as follows. The isolation of the iminium salts **3a–g**, upon treatment of the enamine esters and amides (**1a–f**) with the diazonium salts (**2a, b**) represent the formation of the primary products and attest to the expected course of the reaction. The thermally induced conversion of **3c–g** to cinnoline derivatives follows a mechanism which involves a nucleophilic attack by the aromatic moiety, of the salt, on the iminium carbon (**a, a'**), followed by elimination of the enamine-base from the intermediate (**b, b'**) (Scheme A). It is obvious from the latter scheme that the ease of the cyclization process would be crucially dependent upon the properties of the system represented by the general structure **a, a'**. An increase in the nucleophilic character of the aromatic ring would, for example, be expected to enhance the rate of ring-closure [**a(a')→b(b')**], whereas a decrease in the electropositive nature of the iminium carbon would retard the same reaction step. These correlations are borne out in practice. Thus, we observe that while the reaction of **2a** with the enamine esters and amides (**1a–f**) leads to the corresponding iminium salts (**3a–f**), the diazonium salt **2b**, in which the aromatic ring carries the electron-donating *m*-methoxy substituent, reacts with **1a–f** to form—except in the case of **1a**—the cinnoline derivatives directly. It is a justified assumption that the intermediate iminium salts **3h–l** (or their azo-tautomers) are initially formed and subsequently cyclize rapidly due to the enhanced nucleophilicity of the *m*-methoxyphenyl group.

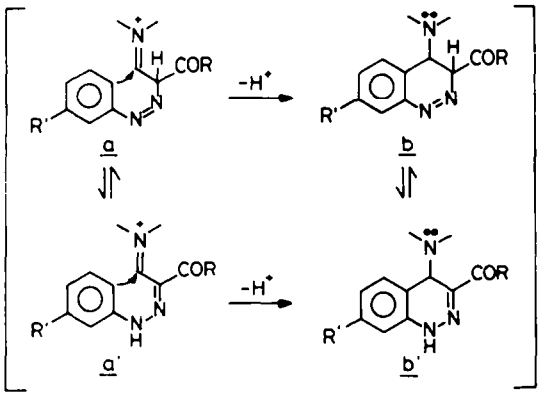


	X	R	R'
1a	—	OEt	2a H
1b	CH_2	OEt	2b OMe
1c	O	OEt	
1d	—	$N(CH_2)_4$	
1e	CH_2	$N(CH_2)_4$	
1f	O	$N(CH_2)_4$	



4a R = $N(CH_2)_4$
4b = OEt

	X	R	R'
3a	—	OEt	H
3b	CH_2	OEt	H
3c	O	OEt	H
3d	—	$N(CH_2)_4$	H
3e	CH_2	$N(CH_2)_4$	H
3f	O	$N(CH_2)_4$	H
3g	—	OEt	OMe
3h	CH_2	OEt	OMe
3i	O	OEt	OMe
3j	—	$N(CH_2)_4$	OMe
3k	CH_2	$N(CH_2)_4$	OMe
3l	O	$N(CH_2)_4$	OMe



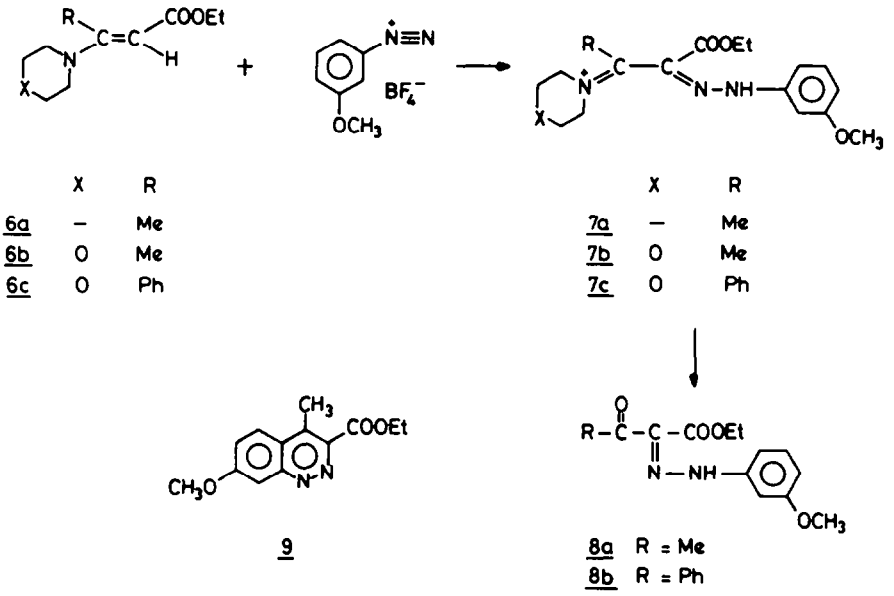
	R	R'
5a	OEt	OMe
5b	$N(CH_2)_4$	OMe
5c	OEt	H
5d	$N(CH_2)_4$	H

Scheme A.

The difference in the reactivities of **3a, b** and **3c** within the series of the phenylhydrazone salts and that of **3g** and **3h, i**, within the group of *m*-methoxyphenylhydrazone salts—towards cyclization—can be rationalized in terms of both the basicity and the ring size[8] of the base-component of the enamine. The higher basicity of pyrrolidine (pKa 11.3) and piperidine (pKa 11.2), in comparison with the basicity of morpholine (pKa 8.4), would decrease the electrophilic character of the corresponding iminium salts and thereby lower the rate of the ring-closure reaction. This accounts for the non-reactivity of **3a, b** under conditions which lead to the conversion of **3c** to the cinnoline ester **5c**. In the case of the pyrrolidinium salts, the electrophilic character of the iminium carbon will be lower than that expected from the basicity value of the amine, due to the known stability of the double bond in an exocyclic configuration to the 5-membered ring.[9a,b] This factor is reflected in the exceptional stability of the salt **3g**, which is the only member of the *m*-methoxyphenyl-hydrazone salts, that does not lead to cinnoline formation, at room temperature.

A comparison of the ester salts **3a, b** with the corresponding amide salts **3d, e** show that under conditions where the latter cyclize, the former compounds are inert. The ester and the amide groups both, would be expected to increase the electrophilic nature of the iminium function and decrease the nucleophilicity of the aryl substituent. The observed results can be best rationalized on the basis of the relatively stronger electron-withdrawing character of the ester substituent,[10] which, operating through the hydrazone (a) or the azo (a') moiety, suppresses the nucleophilic properties of the aromatic group.

In order to study the influence of a substituent at the α-position of the enamine, the reaction of enamine esters **6a–c** with *m*-methoxybenzene diazonium salt (**2b**) was examined (Scheme B). When the reaction was conducted in acetonitrile, at room temperature, the corresponding hydrazone iminium salts **7a–c** were formed which were identified via their hydrolytic products **8a, b**. Upon heating the aforementioned salts by refluxing their solutions in acetonitrile, only in the case of **7b**, the cyclization product **9** was isolated (57%). While the difference in the reactivities of the salts arising from the pyrrolidine and the morpholine enamines (**6a** and **6b**, respectively) was anticipated, it is noteworthy that the phenyl substituent at C_α hinders the cyclization step. A possible explana-



Scheme B.

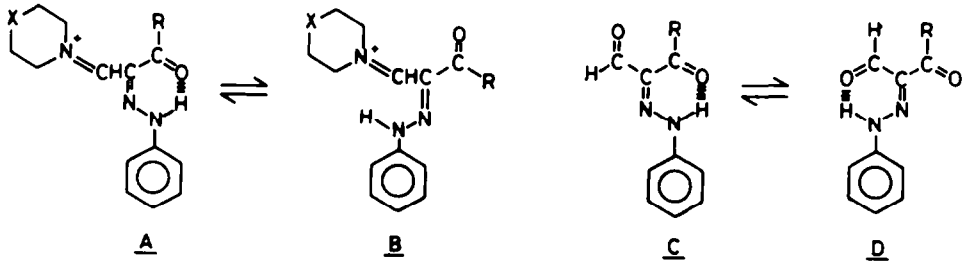
tion of this result may be found in the deactivation—towards nucleophilic attack—of the iminium carbon of 7c, by electron release from the phenyl substituent.[11] Although the isolated intermediates of the reactions of enamine esters and amides with diazonium salts, are the iminium hydrazones, it is not excluded that the cyclization step, in the reactions where such intermediates are implied, as e.g. in the case of **3h–3l**, proceed via the azo iminium salts **a** (Scheme A), which must precede the iminium hydrazones **a'** in the reaction sequence. In fact, when isolated iminium hydrazones are thermally cyclized, the reaction could involve an initial isomerization (**a'** → **a**) to the azo structures. At the present time we have no evidence which throws light on this point or the related question of the role of the isomeric intermediates **b** and **b'**.

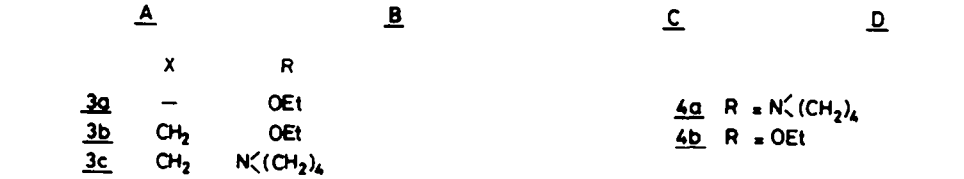
Structure of iminiumhydrazones

In principle, the iminium hydrazones can exist in two forms, namely the configurational isomers **A** and **B**. In isomer **A** the aniline group (-NHPh) is oriented towards the CO function, resulting in a H-bonded structure (N-H---O=C). The formation of such an intramolecular H-bond should reflect itself in the chemical shift of N-H proton.[11] The chemical shift values of the latter protons in **3a, b** and **3e**, in different solvents, are presented in the Table 1 below. Since the iminium hydrazones (**3a, b, 3e**) exhibit only one signal for the N-H protons, (in case of **3b** even in different solvents) it is clear that only one of the configurations is favoured. Examination of the spectra of phenylhydrazones of pyruvate esters[12] show that H-bonding leads to a down-field displacement of the N-H chemical shift. Furthermore, in case of **B** it is shown that a change to solvents which promote H-bonding, is accompanied by a downfield movement of

Table 1. Chemical shifts of N-H in hydrazone derivatives (δTMS = 0)

Hydrazone	Solvent	δ N-H
3a	CD_3COCD_3	13.98
3b	$CDCl_3$	14.12
3b	$CDCOCD_3$	13.83
3b	CD_3CN	13.75
3e	CD_3COCD_3	11.98
4a	$CDCl_3$	11.92
4b	$CDCl_3$	13.25, 14.80.





the N–H shifts.[13] Since the chemical shift of the N–H proton of **3b**, in three solvents of varying polarity, remains essentially unaltered (Table 1), it is concluded that the iminium hydrazones posses the configuration represented by structure **A**.

The aldehydic hydrazones **4a, b** can also exist in two configurations **C** and **D**, both of which possess a H-bonded structure. The presence of two N–H signals in the NMR spectrum of **4b** (Table 1) suggests the existence of both the isomers (**C** and **D**). The amide **4a**, on the other hand, exhibits only one signal, which cannot be correlated with one of the structures directly. It can be argued that in the amide **4a** the amide carbonyl would be associated with a large negative charge on the oxygen, which in turn would enhance H-bond forming. On this basis structure **C** is tentatively assigned to compound **4a**.

As multifunctional systems the iminium hydrazones constitute an interesting class of synthons. Their reaction with selected nucleophiles was studied in order to examine their potential utility in heterocyclic synthesis. Whereas a reaction with phenylenediamine led to formation of quinoxaline ester[14] **11** (Scheme C), an analogous approach to the triazine system **14** proved unsuccessful. Treatment of **3a** and **10** with H_2N–NH–C(=O)–NH_2 and H_2N–NH–C(=S)–NH_2, respectively, resulted in the isolation of **12** and **13**, which could not be cyclized.

EXPERIMENTAL

All m.ps are uncorrected. IR spectra were recorded on an Unicam SP 200 or a Perkin–Elmer 257 spectrometer. The absorptions are given in cm^{-1}. PMR spectra were run on Varian Associates Model A-60, A-60 D and HA-100 instruments. The chemical shifts (δ) are given in ppm, using TMS as an internal standard. For the resonance signals the following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Spin–spin coupling constants (J) are given in Hertz. Mass spectra were obtained with a Varian Mat-711 spectrometer. Analyses were carried out by Mr. H. Pieters of the Microanalytical Department of this laboratory.

Iminium hydrazones (**3a–e** *and* **3g**)

General procedure. To a soln of the β-amino ester or the amide (1 mmol), dissolved in dry MeCN (25 ml), 1 mmol of powdered aryldiazonium tetrafluoroborate was added, and the mixture stirred for 1 hr. The solvent was evaporated under reduced pressure, care being taken that the waterbath temp. did not exceed 50°. The residue was dissolved in CH_2Cl_2 (10 ml) and to the resulting soln EtOAc was added, whereupon pure iminium hydrazones crystallized.

Ethyl 2 - *benzenehydrazonyl* - 3 - *pyrrolidiniumpropanoate tetrafluoroborate* (**3a**). M.p. 126–127°; yield 83%. IR(KBr): 1600 (C=C), 1640 (C=N, $C=N^+$), 1690 (C=O); PMR ($CDCl_3$): 1.38 (t, 3H, CH_3), 2.20 (m, 4H, CH_2–CH_2–N^+), 4.25 (m, 4H, CH_2–N^+), 4.38 (q, 2H, CH_2–O), 7.42 (broad s, 5H, aromatic protons), 8.80 (s, 1H, $CH=N^+$), 13.98 (broad s, 1H, N–H, det. in CD_3COCD_3). (Found: C, 49.78; H, 5.74; N, 11.80. Calc. for $C_{15}H_{20}N_3O_2BF_4$: C, 49.89; H, 5.54, N, 11.64%).

Ethyl 2 - *benzenehydrazonyl* - 3 - *piperidiniumpropanoate tetrafluoroborate* (**3b**). M.p. 113–115°; yield 65%. IR(KBr): 1600 (C=C), 1650 (C=N, C=N), 1690 (C=O); PMR ($CDCl_3$): 1.40 (t, 3H, CH_3), 1.92 (broad s, 6H, $(CH_2)_3$–CH_2–N^+), 4.12–4.46 (m, 4H, CH_2–N^+), 4.42 (q, 2H, CH_2–O), 7.40 (broad s, 5H, aromatic protons), 8.69 (s, 1H, $CH=N^+$), 14.12 (broad s, 1H, N–H). This salt was used in the subsequent step without further purification.

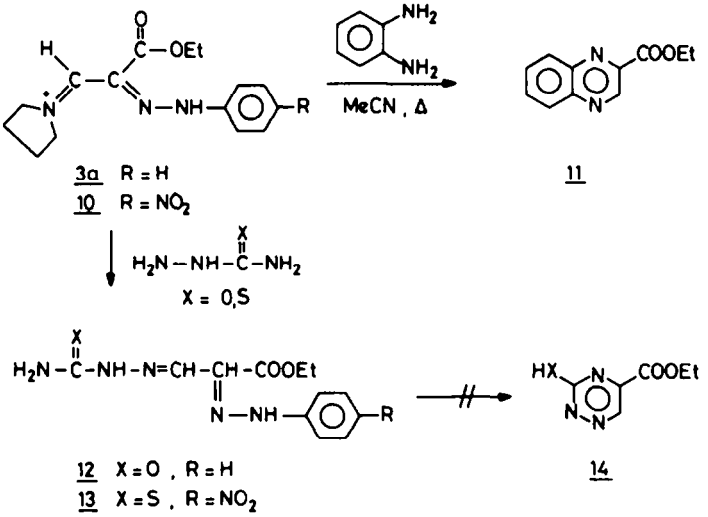
Ethyl 2 - *benzenehydrazonly* - 3 - *morpholiniumpropanoate tetrafluoroborate* (**3c**). M.p. 159–162°; yield 66%. IR(KBr): 1595 (C=C), 1645 (C=N, $C=N^+$), 1690 (C=O); PMR (CD_3COCD_3): 1.38 (t, 3H, CH_3), 4.18 (m, 4H, CH_2–CH_2–O), 4.28–4.75 (M, 4H, CH_2–N^+), 4.43 (q, 2H, CH_3–CH_2), 7.56 (m, 5H, aromatic protons), 8.94 (s, 1H, $CH=N^+$). The salt was used in the subsequent step without further purification.

N,N - *Tetramethylene* 2 - *benzenehydrazonyl* - 3 - *pyrrolidinium* - *propanoamide tetrafluoroborate* (**3d**). M.p. 151–152°; yield 78%. IR(KBr): 1600 (C=C), 1620 (C=O), 1640 (C=N, $C=N^+$); PMR (CD_3COCD_3): 1.97 (m, 8H, CH_2–CH_2–N), 3.45–4.22 (m, 4H, CH_2–N^+), 3.60 (m, 4H, CH_2–N), 7.50 (m, 5H, aromatic protons), 8.68 (s, 1H, $CH=N^+$). (Found: C, 52.91; H, 5.92; N, 14.40. Calc. for $C_{17}H_{23}N_4OBF_4$: C, 52.85; H, 5.96; N, 14.51%).

N,N - *Tetramethylene* 2 - *benzenehydrazonyl* - 3 - *piperidinium-propanoamide tetrafluoroborate* (**3e**). M.p. 141–143°; yield 90%. IR(KBr): 1600 (C=C), 1615 (C=O), 1655 (C=N, $C=N^+$); PMR (CD_3COCD_3): 1.97 (m, 10H, $(CH_2)_3$–CH_2–N^+, CH_2–CH_2–N), 3.58 (m, 4H, CH_2–N), 4.21 (m, 4H, CH_2–N^+), 7.44 (m, 5H, aromatic protons), 8.50 (s, 1H, $CH=N^+$), 11.98 (broad s, 1H, N–H). (Found: C, 53.76; H, 6.40; N, 13.86. Calc. for $C_{18}H_{25}N_4OBF_4$: C, 54.00; H, 6.25; N, 14.00%).

Ethyl 2 - (m - *methoxybenzenehydrazonyl*) - 3 - *pyrrolidinium-propanoate tetrafluoroborate* (**3g**). M.p. 141–143°; yield 86%. IR($CHCl_3$): 1610 (C=C), 1640 (C=N, $C=N^+$), 1690 (C=O): PMR (CD_3COCD_3): 1.42 (t, 3H, CH_3–CH_2), 2.30 (m, 4H, CH_2–CH_2–N^+), 3.93 (s, 3H, CH_3–O), 4.42 (m, 4H, CH_2–N^+), 4.47 (q, 2H, CH_2–O), 7.22 (m, 4H, aromatic protons), 9.09 (s, 1H, $CH=N^+$). This product was used in the subsequent step without further purification.

N,N - *Tetramethylene* - 2 - *benzenehydrazonyl* - 3 - *oxopropanoamide* (**4a**). Compound **1f** (210 mg) was dissolved in dry MeCN (25 ml) and to the soln powdered benzenediazonium



3a R = H
10 R = NO_2
11
12 X = O, R = H
13 X = S, R = NO_2
14

Scheme C.

tetrafluoroborate (192 mg) was added. The mixture was stirred for 1 hr at room temp and the solvent evaporated under reduced pressure, taking care that the temp of the water-bath did not exceed 50°. The residue was dissolved in CH_2Cl_2 (10 ml). When EtOAc was added to the latter soln, the anticipated product **3f** did not crystallize. The solvents were evaporated and the residue was chromatographed on a silica gel column (12 mm × 30 cm). Elution with EtOAc/$CHCl_3$ (4:1) yielded **4a**, which was recrystallized from EtOAc, m.p. 106–109°; yield 147 mg (60%). IR(KBr): 1600 (C=C), 1615 (N–C=O), 1660 (C=N), 1670 (H–C=O); PMR ($CDCl_3$): 1.90 (m, 4H, CH_2–CH_2–N), 3.46 (m, 4H, CH_2–N), 7.31 (s, 5H, aromatic protons), 9.40 (s, 1H, H–C=O), 11.92 (broad s, 1H, N–H); MS: *m/e* = 245.

Ethyl 2-benzenehydrazonyl-3-oxopropanoate (**4b**). The ester **3a** (361 mg) was chromatographed on a silica gel column. Elution with $CHCl_3$/cyclohexane (3:1) yielded **4b**, which was solidified by treatment with diisopropyl ether/EtOAc. 198 mg, 90%; IR($CHCl_3$): 1600 (C=C), 1645 (C=N), 1700 (C=O); PMR ($CDCl_3$): 1.33, 1.36 (2 × t, 3H, CH_3), 4.36, 4.39 (2 × q, 2H, CH_2), 7.35 (m, 5H, aromatic protons), 9.59, 9.93 (2 × s, 1H, H–C=O, rel. ratio 3:2), 13.25, 14.80 (2 × broad s, 1H, N–H, rel. ratio 3:2); MS: *m/e* = 220.

Ethyl 7-methoxycinnoline-3-carboxylate (**5a**). The ester **1b** (183 mg or **1c**, 185 mg) was dissolved in dry MeCN (25 ml) and to this soln powdered (*m*)-methoxybenzene tetrafluoroborate (222 mg) was added. After stirring the mixture at room temp for 2 hr, the solvent was evaporated and the residue chromatographed on a silica gel column (12 mm × 30 cm). Elution with $CHCl_3$/EtOAc (20:1) and evaporation of the solvents yielded a product, which was recrystallized from EtOAc to give **5a**, m.p. 121.126°. The ester **5a** could also be obtained by refluxing a soln of **3g** (391 mg) in acetonitrile (25 ml) for 60 hr.s Yield **5a**, from **1b**, 176 mg (72%); from **1c**, 116 mg (50%) and from **3g**, 146 mg (63%). IR ($CHCl_3$): 1625 (C=C), 1720 (C=O); PMR ($CDCl_3$): 1.52 (t, 3H, CH_3–CH_2), 4.07 (s, 3H, CH_3–O), 4.60 (q, 2H, CH_2), 7.48 (dd, 1H, C_6–H, J = 2.5, 9), 7.86 (d, 1H, C_5–H, J = 9), 7.90 (d, 1H, C_8–H, J = 2.5), 8.56 (s, 1H, C_4–H); MS: *m/e* = 232. (Found: C, 62.14; H, 5.12; N, 11.97. Calc. for $C_{12}H_{12}N_2O_3$: C, 62.07; H, 5.17; N, 12.07%).

N,N-*Tetramethylene-7-methoxycinnoline-3-carboxamide* (**5b**). To a soln of **1d** (194 mg; **1e**, 208 mg or **1f**, 210 mg), in MeCN (25 ml), powdered (*m*)-methoxybenzene diazonium tetrafluoroborate (222 mg) was added and the mixture stirred for 1 hr at room temp. After evaporation of the solvent the residue was chromatographed on a silica gel column (12 mm × 30 cm). Elution with EtOAc/$CHCl_3$ (4:1) yielded a crystalline product which, upon recrystallization from EtOAc gave **5b**, m.p. 177–178°. Yield **5b** (from **1d**, 33 mg (13%); from **1e**, 157 mg (61%) and from **1f**, 85 mg (33%). IR($CHCl_3$): 1625 (C=O): PMR ($CDCl_3$): 1.95 (m, 4H, CH_2–CH_2–N), 3.79–4.03 (m, 4H, CH_2–N), 4.03 (s, 3H, CH_3), 7.39 (dd, 1H, C_6–H, J = 2.5, 9), 7.74 (d, 1H, C_8–H, J = 2.5), 7.79 (d, 1H, C_5–H, J = 9), 8.40 (s, 1H, C_4–H). Mass spectrum, Found *m/e* 257.1166, Calc. *m/e* 257.1164.

Ethyl cinnoline-3-carboxylate (**5c**). The ester **3c** (377 mg) was refluxed for 168 hr in MeCN (25 ml). After evaporation of the solvent the residue was chromatographed on a silica gel column (12 mm × 30 cm). Elution with $CHCl_3$/EtOAc (20:1) yielded a crystalline product. Recrystallization from diisopropyl ether yielded the pure **5c**, (107 mg, 53%), m.p. 88–91°. IR($CHCl_3$): 1730 (C=O); PMR ($CDCl_3$): 1.53 (t, 3H, CH_3), 4.63 (q, 2H, CH_2), 7.96–8.70 (m, 4H, aromatic protons). (Found: C, 64.99; H, 5.05; N, 13.67, Calc. for $C_{11}H_{10}N_2O_2$: C, 65.35; H, 4.95; N, 13.86%).

N,N-*Tetramethylene cinnoline-3-carboxamide* (**5d**). Starting with **1f–f** and following the procedure described for the preparation of **5b**—except that benzene diazonium fluoroborate was added and the mixture was refluxed for 24 hr—the amide **5d** was eluted with EtOAc/$CHCl_3$ (5:2) and recrystallized from EtOAc; m.p. 108–110°, yield (from **1d**, 25%; from **1e**, 31% and from **1f**, 71%). IR ($CHCl_3$): 1625 (C=O); PMR ($CDCl_3$): 1.95 (m, 4H, CH_2–CH_2–N); 3.80–4.00 (m, 4H, CH_2–N), 7.82–8.55 (m, 5H, aromatic protons). (Found: C, 68.71; H, 5.72; N, 18.41. Calc. for $C_{13}H_{13}N_3O$: C, 68.72; H, 5.73: N, 18.50%).

Ethyl 2 - (m - methoxybenzenehydrazonyl) - 3 - oxobutanoate (**8a**). The ester **6a** (183 mg or **6b**, 199 mg) was dissolved in dry MeCN (25 ml) and to this soln *m*-methoxybenzenediazonium tetrafluoroborate (222 mg) was added as a powder. The mixture was stirred for 1 hr at room temp, the solvent evaporated, (bath temp held under 50°), and the residue dissolved in CH_2Cl_2. Addition of EtOAc to the latter soln did not precipitate **7a** or **7b**. Evaporation of the solvents and subsequent chromatography on a silica gel column (12 mm × 30 cm) with $CHCl_3$/cyclohexane (2:1) as eluents yielded, in both cases, **8a**, in 49% yield. IR ($CHCl_3$): 1610 (C=C), 1690 (C=O); PMR ($CDCl_3$): 1.39 (t, 3H, CH_3–CH_2), 2.48, 2.57 (2 × s, 3H, CH_3–C=O), 3.83 (s, 3H, CH_3–O), 4.35 (2 × q, 2H, CH_2), 7.00 (m, 4H, aromatic protons).

Ethyl 2 - (m - methoxybenzenehydrazonyl) - 3 - oxobutanoate (**8b**). The ester **6c** (261 mg), prepared from morpholine and ethyl β-phenylpropiolate, was dissolved in dry MeCN (25 ml). Powdered **2b** (222 mg) was added to the soln and the mixture stirred for 16 hr at room temp. The mixture was worked up as in the case of **8a**. Elution with $CHCl_3$/EtOAc/cyclohexane (10:1:1) yielded **8b** (121 mg, 37%); IR ($CHCl_3$): 1610 (C=C), 1690 (C=O); PMR ($CDCl_3$): 1.35 (t, 3H, CH_3–CH_2), 3.71 (s, 3H, CH_3–O), 4.37 (q, 2H, CH_2), 6.50–8.00 (m, 9H, aromatic protons); MS: *m/e* = 326.

Ethyl 4-methyl-7-methoxycinnoline-3-carboxylate (**9**). **6b** (199 mg) was dissolved in MeCN (25 ml). The salt **2b** (222 mg) was added and the mixture was stirred for 1 hr at room temp and subsequently refluxed for 24 hr. After evaporation of the solvent, the residue was chromatographed on a silica gel column (12 mm × 30 cm) Elution with $CHCl_3$/cyclohexane (2:1) yielded **9** (140 mg, 57%). M.p. 156–159°; IR ($CHCl_3$): 1625 (C=C), 1720 (C=O); PMR ($CDCl_3$): 1.48 (t, 3H, CH_3–CH_2), 2.84 (s, 3H, CH_3–Ar), 4.03 (s, 3H, CH_3–O), 4.58 (q, 2H, CH_2), 7.43 (dd, 1H, C_6–H, J = 4, 15), 7.80 (d, 1H, C_8–H, J = 4), 8.04 (d, 1H, C_5–H, J = 15). (Found: C, 63.30; H, 5.83 ;N, 11.45. Calc. for $C_{13}H_{14}N_2O_3$: C, 63.41; H, 5.69; N, 11.38%).

Ethyl quinoxaline-2-carboxylate (**11**). The ester **3a** (361 mg) was dissolved in MeCN (25 ml). O-Phenylenediamine (432 mg) was added and the mixture was refluxed for 144 hr. After evaporation of the solvent the residue was chromatographed on a silica gel column (12 mm × 30 cm). Elution with $CHCl_3$/EtOAc/cyclohexane (10:1:1) yielded **11** (79 mg, 39%), m.p. 84–85°; IR ($CHCl_3$): 1725 (C=O); PMR ($CDCl_3$): 1.52 (t, 3H, CH_3), 4.60 (q, 2H, CH_2), 7.90–8.25 (m, 4H, aromatic protons), 9.55 (s, 1H, C_3–H); MS: *m/e* = 202. (Found: C, 65.47; H, 5.09; N, 13.79. Calc. for $C_{11}H_{10}N_2O_2$: C, 65.35; H, 4.95; N, 13.86%).

Ethyl 2 - benzenehydrazonyl - 3 - semicarbazonylpropanoate (**12**). The ester **3a** (361 mg) was dissolved in EtOH (25 ml). To this soln semicarbazide chloride (167 mg) was added and the mixture was refluxed for 16 hr. The ppt was filtered off and recrystallized from acetone (111 mg, 40%), m.p. 203–206°; IR (KBr): 1690 (C=O): PMR (d-DMSO): 1.29 (t, 3H, CH_3), 4.24 (q, 2H, CH_2), 6.54 (broad s, 2H, NH_2). 7.34 (m, 5H, aromatic protons), 8.18 (s, 1H, CH=N), 10.47 (broad s, 1H, NH–C=O), 13.13 (broad s, 1H, NH–Ar); MS: *m/e* = 277.

Ethyl 2 - (p - nitrobenzenehydrazonyl) - 3 - thiosemicarbazonylpropanoate (**13**). The ester **10** (406 mg), prepared from ethyl β-pyrrolidinylacrylate and *p*-nitrobenzenediazonium tetrafluoroborate was dissolved in acetonitrile (25 ml). To this soln thiosemicarbazide (273 mg) was added and the mixture was refluxed for 16 hr. The ppt was filtered off and recrystallized from acetone (254 mg, 75%), m.p. 225–227°; IR (KBr): 1675 (C=O); PMR (d-DMSO): 1.31 (t, 3H, CH_3), 4.28 (q, 2H, CH_2), 7.55, 8.28 (AB-system, 4H, aromatic protons), 8.35 (s, 1H, CH=N). (Found: C, 42.52; H, 4.11; N, 24.80. Calc. for $C_{12}H_{14}N_6O_4S$: C, 42.60; H, 4.14; N, 24.85%).

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