# REACTIVITY OF N$^1$-ACYLACETAMIDRAZONES TOWARDS DIETHYL ACETYLENEDICARBOXYLATE : CYCLIZATION TO ETHYL PYRROLEACETATES AND 1-ACYLAMINOPYRIDONES

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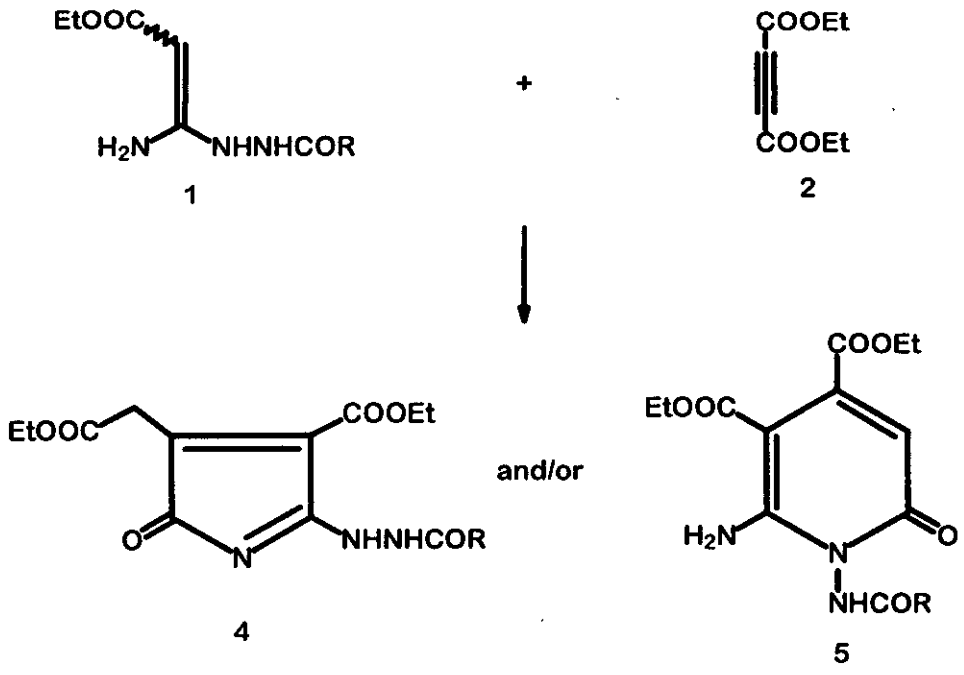
**Abstract** - The reaction between N$^1$-acylacetamidrazones (**1**) and diethyl acetylenedicarboxylate (**2**) is described. The nucleophilic addition of the β-carbon atom of **1** on the triple bond affords the non isolable intermediate (**3**). Depending on the reaction conditions and on the substitution pattern of the amidrazone, **3** gives rise to ethyl 5-(2-acylhydrazino)-4-(ethoxycarbonyl)-2-oxo-2*H* -pyrrole-3-acetates (**4**) and / or diethyl 1-acylamino-2-amino-1,6-dihydro-6-oxo-3,4-pyridinedicarboxylates (**5**).

Although the addition of multifunctional nitrogen nucleophiles to carbon-carbon triple bond conjugated with electron-withdrawing groups has been employed as a route to a wide variety of heterocyclic compounds,[1-9] there are no reports , to the best of our knowledge, on the reaction of the N$^1$-acyl-2-(ethoxycarbonyl)acetamidrazones with these compounds.The N$^1$-acyl-2-(ethoxycarbonyl)acetamidrazones (**1**) are polyfunctionalized reagents since their molecules contain four nucleophilic and two electrophilic centres The former are

represented by three nitrogen atoms and by the carbon atom in β and the latter are the carbonyl function of the ester and amide group. In previous studies the behaviour of $N^1$-acylacetamidrazones (**1**) towards some bis-electrophiles was examined, and it was found that the attack of the electrophile initially occurs on C- β and that subsenquently the formed adduct undergoes an intramolecular cyclization leading to heterocyclic compounds.[10-12]

We now report the reaction of amidrazones (**1**) with diethyl acetylenedicarboxylate (**2**) to yield ethyl pyrrole-acetates (**4**) and 1- acylaminopyridones (**5**)

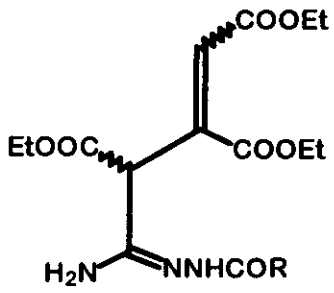
**Scheme 1**



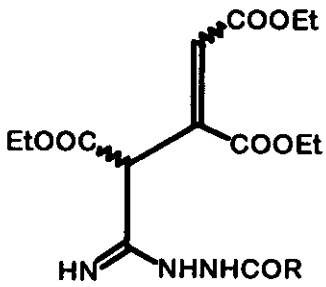

| 1,4,5 | R | 1,4,5 | R |
|---|---|---|---|
| **a** | Me | **e** | $(Me)_2CH$ |
| **b** | $C_6H_5CH_2$ | **f** | $(C_6H_5)_2CH$ |
| **c** | $4\text{-}MeOC_6H_4CH_2$ | **g** | $C_6H_5$ |
| **d** | $4\text{-}ClC_6H_4CH_2$ | | |

The intermediates in these processes are the Michael-type adducts (non isolable) (**3**) obtained by nucleophilic addition (*via* the β-carbon atom) of amidrazones on the triple bond. These adducts can assume different configurations and tautomeric forms (Figure 1) that, through successive intramolecular cyclization, can give rise to five- or six-membered compounds according to the reaction conditions and the nature of amidrazone

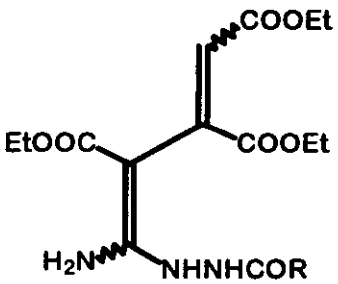
**Figure 1**



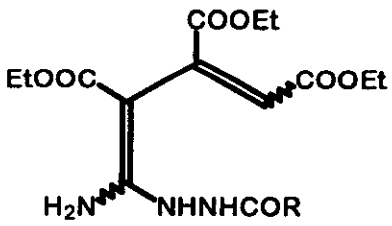

**3A**




**3B**




**3C**




**3D**

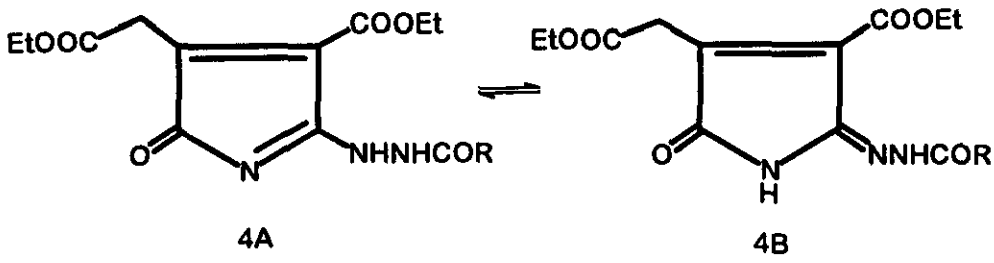
The reaction of amidrazones (**1a,c, f,g**) with the acetylenic derivative in ethanol at reflux (Procedure A) led only to five-membered cyclization compounds (**4**), as reported in Table 1.

**Table 1.** Yield of Reactions between $N^1$-Acylacetamidrazones (**1**) and (**2**)

| Starting material | Procedure A Products (Yield %) | | Procedure B Products (Yield %) | |
|---|---|---|---|---|
| **1a** | **4a** (80) | | **4a** (36) | **5a** (13) |
| **1b** | **5b** (20) | **6** (16) | **4b** (19) | **5b** (45) |
| **1c** | **4c** (40) | | **4c** (55) | |
| **1d** | **4d** (44) | **5d** (32) | **4d** (44) | **5d** (28) |
| **1e** | | **5e** (80) | | **5e** (80) |
| **1f** | **4f** (95) | | **4f** (84) | |
| **1g** | **4g** (80) | | **4g** (95) | |

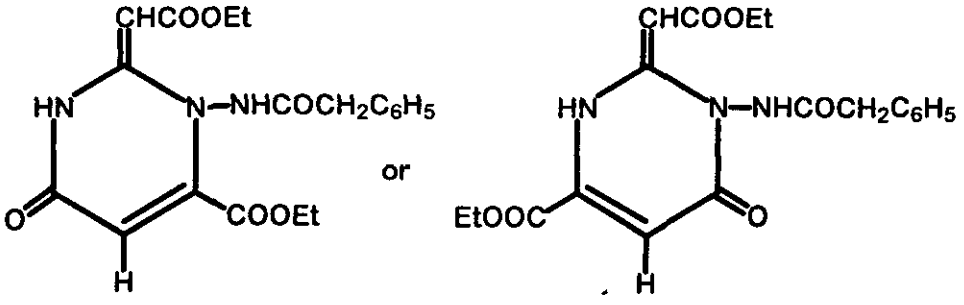
In these cases the amide hydrazone tautomeric species (**3A**) of the adduct prevails This adduct leads to the pyrroles through a 5-*exo-trig* cyclization involving $N^3$ and the ester group in $\alpha$ to the site where the initial attack occurs. The structure of the compounds (**4**) was attributed according to analytical and spectroscopic data. The $^1$H-nmr spectrum of the compound (**4a**) shows two signals for the $COCH_3$ group at 1.93 and 2.13 ppm and three $D_2O$ exchangeable signals at 10 30, 10.45 and 10.63 ppm, attributable to two NH protons. The two $COCH_3$ peaks as well as the first two exchangeable NH signals collapse on heating at 50°C. Two possible alternatives can be considered to explain this phenomenon a tautomery between the **4A** and **4B** forms (Figure 2) and a hindered rotation of the acetylhydrazino group that can lead to different chemical shifts of the $CH_3$ favoured by the conjugation with the ring

**Figure 2**



The $^{13}$C-nmr spectrum shows the presence of both phenomena As a matter of fact, besides the presence of two peaks for $\underline{C}H_3CO$ that can be due to hindered rotation, for almost all the carbon atoms of the ring we observe presence of two signals, one of which much more intense (5·1 ratio). This confirms a tautomeric equilibrium between the forms (**4A**) and (**4B**) This phenomenon is also present in the $^{13}$C-nmr spectra of the other compounds (**4**), except for **4g**. The hindered rotation phenomenon is also observed in the spectrum of **4f** due to the presence of two signals for $\underline{C}HCO$. Mass spectrometry of compounds (**4**) confirms the assigned structures The peaks with m/z values corresponding to the molecular ions appear with a relative intensity of 2-49 %. The primary fragmentation consistent with all compounds is characterized by the presence of a peak at m/z $[M\text{-}EtO]^+$ due to the fragmentation of the COOEt group. Subsequent to the formation of $[M\text{-}EtO]^+$, the loss of radical COR and $CON_2$ gives rise to the ion m/z = 167 common to all compounds except for **4g**. This ion constitutes the base peak in the spectra of compounds (**4a**) and (**4f**).

In the same reaction conditions amidrazone (**1e**) affords the 1-amino-6-(1*H*)-pyridone isomer (**5e**) as the sole product In this case $N^2$ of the enaminic form of the adduct (**3**) attacks the terminal ester group through a regioselective 6-*exo-trig* cyclization. On the other hand the amidrazone (**1d**) leads to a mixture of compounds (**4d**) and (**5d**) The amidrazone (**1b**) behaves in a totally unexpected way From the reaction with the acetylenic compound, was obtained pyridone (**5b**) and a compound of the same molecular formula Whereas the spectral data clearly indicate the presence of a pyrimidinic structure (**6**), these did not provide sufficient information to permit the elucidation of the exact position of the substituents.




**6**

Besides the resonances of the COOEt and Ar groups, the $^1$H-nmr spectrum presents an AB system due to the $CH_2CO$ group, two singlets at 4.63 and 5 47 ppm due respectively to the =CH and H-5 protons, and two $D_2O$ exchangeable signals at 11.05 and 11.50 ppm. The formation of the compound (**6**) can be explained by the nucleophilic addition of $N^2$ or $N^3$ on the acetylenic bond followed by a intramolecular cyclization.

**Table 2.** Physical and analytical data of compounds (**4**, **5**) and (**6**)

| Compd No | mp (°C) (Recryst Solv ) | Molecular Formula | Analysis (%) Calcd / Found C | H | N |
|---|---|---|---|---|---|
| **4a** | 200-201 (MeCN) | $C_{13}H_{17}N_3O_6$ | 50 16 / 50.21 | 5 50 / 5.49 | 13.50 / 13.46 |
| **4b** | 154-155 (Toluene) | $C_{19}H_{21}N_3O_6$ | 58.91 / 58 96 | 5 46 / 5 45 | 10.85 / 10.87 |
| **4c** | 214-215 (MeCN) | $C_{20}H_{23}N_3O_7$ | 57 55 / 57 60 | 5.55 / 5.54 | 10.07 / 10.10 |
| **4d** | 169-170 (Ethyl propionate) | $C_{19}H_{20}ClN_3O_6$ | 54 10 / 54 13 | 4 78 / 4.77 | 9 96 / 9.98 |
| **4f** | 245-246 (MeCN) | $C_{25}H_{25}N_3O_6$ | 64.79 / 64 83 | 5.44 / 5.43 | 9.07 / 9.10 |
| **4g** | 159-160 (Benzene) | $C_{18}H_{19}N_3O_6$ | 57.91 / 57.97 | 5.13 / 5.12 | 11.25 / 11.28 |
| **5a** | 188-190 (*i*-PrOH) | $C_{13}H_{17}N_3O_6$ | 50.16 / 50 10 | 5.50 / 5.51 | 13.50 / 13.54 |
| **5b** | 184-185 (MeCN) | $C_{19}H_{21}N_3O_6$ | 58.91 / 59.05 | 5.46 / 5.44 | 10.85 / 10.88 |
| **5d** | 179-180 (*i*-PrOH) | $C_{19}H_{20}ClN_3O_6$ | 54.10 / 54.04 | 4.78 / 4.79 | 9.96 / 9.93 |
| **5e** | 99-100 (Ethyl propionate) | $C_{15}H_{21}N_3O_6$ | 53 09 / 53.03 | 6.24 / 6.21 | 12.38 / 12.33 |
| **6** | 180-181 (Benzene) | $C_{19}H_{21}N_3O_6$ | 58.91 / 58 85 | 5 46 / 5.47 | 10.85 / 10.82 |

**Table 3.** Spectroscopic data of compounds (**4**, **5**) and (**6**)

| Compd No | Ir $\nu$ ($cm^{-1}$) | MS m/z (%) | $^1$H-nmr δ, J | $^{13}$C-nmr[a] δ, J |
|---|---|---|---|---|
| **4a** | 3250, 3060, 1740, 1730, 1650, 1630. | 311($M^+$, 49), 266 (20) 167 (100) | 1 12 (t, J = 7.1, 3H, Me), 1.21 (t, J = 6 8, 3H, Me), 1 93, 2.13(s, 3H,COMe), 3.56(s, 2H, $CH_2$),4.02(q, J = 7.1, 2H, $CH_2$),4.20(q, J = 6.8, 2H, $CH_2$), 10.30, 10 45,10 63 (s, 2H,2NH). | 11 79 (q, J = 126.9, Me), 11 92 (q, J = 126 9,Me), 17.70, 19 60 (q, J = 129 4, Me), 27.58(t, J = 131 8, $CH_2$COOEt),58 87 (t, J = 148.9, $CH_2$),59.33 (t, J = 148 3, $CH_2$),131.18, 132 28 (s, C-5), 133.80, 137.51 (s, C-4), 135.39, 134.40 (s, C-3), 158.71, 158.50 (s, C-2), 165.51, 163.63 (s, CONH),166.25(s, COOEt), 170 71 (s, COOEt). |
| **4b** | 3280, 1745, 1720, 1665 | 387 ($M^+$, 4), 342 (6), 91(100) | 1 12(t, J = 7.1, 3H, Me), 1.21(t, J = 7.1, 3H, Me), 3.58 (s, 2H,$CH_2$COOEt), 3 90(s, 2H, $CH_2$Ar), 4 03 (q, J =7 1, 2H, $CH_2$),4.24 (q, J =7 1, 2H, $CH_2$)7.17-7.26 (m, 5H, Ar), 10 50, 10 57,10 63 (s, 2H, 2NH). | 11 79 (q, J = 126 9, Me), 11 87 (q, J = 126.9,Me), 27.66 (t, J = 131 8, $CH_2$COOEt), 36.45 ($CH_2$Ar), 58 90 (t, J = 147.7, $CH_2$), 59 43 (t, J =149.5, $CH_2$), 124.54,126.21,127 54,133 16 (Ar),131.17, 132.28 (s, C-5) 134 13 , 138.18 (s, C-4), 135.72,134.75 (s, C-3), 158 78, 158 54 (s, C-2), 165 55, 164 71 (s, CONH), 166.28 (s, COOEt), 171.08 (s, COOEt). |
| **4c** | 3240, 3060, 1740, 1650. | 417 ($M^+$, 5), 372 (3), 121 (100) | 1.12 (t, J = 7 1, 3H, Me), 1 21 (t, J = 7.1, 3H, Me), 3.58 (s, 2H,$CH_2$COOEt), 3 66 (s, 3H, OMe), 3.81 (s, 2H, $CH_2$Ar),4 03(q,J= 7 1, 2H, $CH_2$), 4.24 (q,J= 7 1, 2H, $CH_2$), 6 79- 6 85 (m, 2H, Ar),7 16-7.20 (m, 2H,Ar),10 46,10.53,10 66 (s, 2H, 2NH) | 11.86 (q, J = 126 9, Me), 11.96 (q, J = 126.9, Me), 27 67 (t, J = 131.8, $CH_2$COOEt), 35.50 ($CH_2$Ar), 52.97(q, J= 144.0, OMe), 58.91 (t, J =147 1, $CH_2$), 59 49 (t, J = 148.9, $CH_2$), 111.69 , 124 95, 128.51, 156.09(Ar), 131 17, 132.25(s, C-5), 134 06,138.16 (s, C-4),135 60, 134 62 (s, C-3),158.78, 158 54 (s, C-2),165.56,165.04 (s, CONH), 166.34(s, COOEt) 171.36 (s, COOEt). |
| **4d** | 3310, 3270, | 423 ($M^+$+2, 2),421 (5), 376 (5), 167 (46), 127 | 1 13 (t, J = 7.1, 3H, Me), 1 21 (t, J = 7 1, 3H, Me), | 11.84 (q, J = 126 3, Me), 11.94 (q, J = 126.3, Me), 27 69 (t, J = 131 8,$CH_2$COOEt), 35.79 (t, J = 129.9, |

| | | | | |
|---|---|---|---|---|
| | 1755, 1730, 1675. | (35), 125 (100). | 3.59 (s, 2H, $CH_2COOEt$), 3.89,3 91 (s, 2H, $CH_2Ar$), 4.03(q, J = 7.1, 2H, $CH_2$), 4 24 (q, J = 7.1, 2H, $CH_2$), 7.27-7.33(m, 4H,Ar),10.55, 10 61, 10 83 (s, 2H, 2NH) | $CH_2Ar$), 58 92(t, J = 148.9 $CH_2$), 59.47 t, J = 148.3, $CH_2$), 126.18, 129 09, 129.40, 132.12 (Ar), 131.13 (s, C-5), 134.29, 138.46 (s, C-4), 135.72, 134.79 (s, C-3), 158 72, 164.39 (s, C-2), 165.55 (s, CONH), 166.29 (s, COOEt),170 70 (s, COOEt) |
| **4f** | 3240, 3040, 1740, 1730, 1650, 1640. | 463 ($M^+$, 12), 418(4), 167 (100) | 1.10 (t, J = 6 8, 3H, Me), 1.27 (t, J = 6 8, 3H, Me), 3.60 (s, 2H, $CH_2COOEt$), 4.04 (q, J = 6 8, 2H, $CH_2$), 4 30 (q, J = 6.8, 2H, $CH_2$), 6 09 (s, 1H, CH), 7.20-7.34 (m, 10H, Ar),10.82 (br s , 2H, 2NH) | 11 97 (q, J = 126.9, Me), 12 01 (q, J =126.9, Me), 27 71 (t, J = 131.8, $CH_2COOEt$), 49.44 (d, J = 131.2, CH ), 53.57 ( d, J = 126.9, CH ), 58.93 ( t, J = 148.3, $CH_2$), 59.55 (t, J = 148.9, $CH_2$ ), 124.71, 124 95,125 09,126.14,126.26,126.44,126.61,126 88 137.18 (Ar), 131.35, 132 27(s, C-5),134.48, 138.80 (s, C-4), 135.68, 134.92 (s, C-3), 158.75, 158.56 (s, C-2), 165.60, 165.70 (s, CONH), 166.29 (s, COOEt), 171 63 (s, COOEt). |
| **4g** | 3240, 3190, 3060, 1750, 1650, 1630. | 373 ($M^+$, 47), 328 (2) 105 (100), 77 (26) | 1 02 - 1 30 (m, 6H, 2Me), 3.59 ( s, 2H, $CH_2COOEt$), 3.95 -4.25 (m, 4H, $2CH_2$), 7.41-7.55( m, 3H, Ar),7 85 7.88 ( m, 2H, Ar ), 10.57, 10.72, 11.29 (s, 2H, 2NH). | 11 80 (q, J = 126.9, Me), 11.93 (q, J = 126.9, Me ), 27.65(t, J = 131.2, $CH_2COOEt$), 58.94 (t, J = 148.3, $CH_2$),59.50(t, J =148.9, $CH_2$),125.93,126.28,126.46 131.02, 134.80 (Ar), 130.09 (s, C-5),132.39(s, C-4) 139.38 (s, C-3), 158.67 (s, C-2), 161.64 (s, CONH), 165.87 ( s, COOEt), 166.31 (s, COOEt). |
| **5a** | 3320, 3210, 1750, 1670, 1600. | 311 ($M^+$, 19), 269 (100), 266 (24), 239 (48). | 1.12 - 1 20 (m, 6H, 2Me), 1.92 (s, 3H, COMe), 4.01-4.12 (m, 4H, $2CH_2$), 6.37 (s, 1H, H-5), 7.90, 8 46(br s, 2H, $NH_2$),10.34(br s,1H, NH). | 11 89 (q, J = 126.9, Me), 12.51 (q, J = 126.3, Me), 18 57 (q, J =129.4, COMe), 56.52(t, J =148.3, $CH_2$) 58 08 (t, J = 148.3, $CH_2$), 73.12 (s, C-3), 111.29 (d, J = 166 6, C-5) , 128.25 (s, C-4 ), 155.93 ( s, C-2) , 160.66 (s, C-6), 161.93 (s, 4-COOEt ), 164.43 (s, 3-COOEt), 167.27 (s, CONH) |
| **5b** | 3330, 3290, 3220, 1750, 1700, | 387 ($M^+$,5), 342 (4),315 (20), 296 (33), 269 (8), 118 (22), 91 (100) | 1 14 (t, J = 7.1, 3H, Me), 1.20 (t, J = 7.1, 3H, Me), 3.58 (s, 2H, $CH_2$),4 05(q, J = 7.1 , 2H, $CH_2$ ), 4.13 (q, J = 7.1, 2H,$CH_2$),6.38 | 12.01 (q, J = 126.9, Me), 12.73 (q, J = 126.3, Me), 38 12 ($CH_2Ar$),56.65 (t, J = 145 9 $CH_2$), 58.17 (t, J= 144.0, $CH_2$ ), 73.37 (s, C-3), 111.39 ( d, J = 166.6, C-5 ), 124.78, 126.34, 127.48,132 74 ( Ar), 128 42 (s, C-4), 156 03 (s, C-2), 160.67 (s, C-6), 126.03 (s, |

| | | | | |
|---|---|---|---|---|
| | 1670 | | 1H, H-5 ), 7.1 -7 28 (m, 5H, Ar), 7 96, 8.54 (br s, 2H,$NH_2$),10 64(s,1H,NH) | 4-COOEt),164.40 (s, 3-COOEt),168.25 (s, CONH). |
| **5d** | 3340, 3220, 1750, 1660. | 423 ($M^+$+2, 2), 421 (3), 378 (2), 376 (2), 351 (5), 349 (15), 296 (35), 269 (6), 125 (100). | 1.14 (t, J = 7.1, 3H, Me), 1.20 (t, J = 7.1, 3H, Me), 3 59 (s, 2H, $CH_2$),4.04 (q, J = 7.1, 2H, $CH_2$),4.12 (q, J = 7.1, 2H, $CH_2$),6.37 (s, 1H, H-5 ),7 27 - 7.35 ( m, 4H, Ar ), 7 96, 8.52 ( br s, 2H,$NH_2$),10.65(s,1H,NH). | 11.93 (q, J = 126.3, Me), 12.64 (q, J = 126.9, Me), 36.92 ($CH_2Ar$), 56.59 (t, J = 148.9 $CH_2$), 58.11 (t, J = 145.9 $CH_2$),73.37 (s, C-3), 111.42 (d, J = 166.6, C-5), 126.19, 129.32, 129.56, 131.65 (Ar), 128.34 (s, C-4), 155.93 (s, C-2), 160.59 (s, C-6), 161.98 (s, 4-COOEt),164.34 (s, 3-COOEt),167.93 (s, CONH). |
| **5e** | 3640, 3550, 3390, 3340, 3280, 1760, 1720, 1700, 1630. | 339 ($M^+$, 15), 296 (37), 294 (17), 269 (58), 267 (34), 71 (100) | 1.05(d, J = 6.8, 6H, 2Me), 1 15(t, J =7 1, 3H, Me),1 20 (t, J =7 1,3H,Me),2.48(sept, J = 6.8,1H,CH ),4.02(q, J= 7.1,2H,$CH_2$),4.16(q, J=7 1, 2H,$CH_2$ ),6.37( s,1H, H-5), 7.89,8 40( br s , 2H, $NH_2$ ), 10.29 (s, 1H, NH). | 11.91(q, J = 126.3, Me), 12.63 (q, J = 126.9, Me), 17 07, 17.35 (q, J = 126.9, 2Me), 30 08, 30 25 (d, J = 130.0 , CH), 56.57 (t, J = 147.7, $CH_2$), 58.09 (t, J = 147.7 $CH_2$ ), 73.30 (s, C-3), 111.60 ( d, J = 166 6, C-5),128.41(s, C-4),156.20 (s, C-2), 160.70 (s, C-6), 162.02 (s, 4- COOEt),164.37(s, 3-COOEt), 173.20, 174 18 (s, CONH). |
| **6** | 3280, 3200, 1750, 1705, 1675, 1630 | 387 ($M^+$, 17), 341 (10), 314 (8), 269 (28), 250 (3), 223 (24), 197 (5), 178 (12), 177 (40),151 (9), 118 (28), 91 (100) | 1 13(m, 6H,2Me),3.55(q, J= 12.9,$CH_2$Ar ), 4.02 ( m, 4H, 2$CH_2$ ), 4 62 (s, 1H, =CH ), 5.47 (s, 1H, H-5 ), 7.18-7 32 (m, 5H, Ar),11.08(s,1H,NH), 11.50 (br s, 1H,NH) | 12 06 (q, J = 126.9, Me), 12.33 (q, J = 126.3, Me), 37 20 ( $CH_2$Ar), 57 42 (t, J = 147 7 $CH_2$), 58.25 (t, J = 147 7 $CH_2$), 72 90 (d, J = 167 2, = CH), 92.13 (d, J = 166.0 ,C-5), 124.73, 126.26, 127.40,132.61 (Ar)134 24 (s, C-4), 148.00(s, C-2),159.08 (s,C-6), 161 40 (s, CO), 164.03 (s, CO), 166 94 (s, CO) |

[a] The first signal for the carbon atoms of 2-oxopyrroles is the more intense.

When the reaction between the acetylenic compound and the amidrazones (**1**) is carried out in ethanol at room temperature in presence of catalytic amounts of acetic acid (Procedure B), the regioselectivity for amidrazones (**1c, e, f, g**) is unchanged and the same products as in the previous reactions are obtained with comparable yields On the other hand in the cases of **1a,b** and **1d**, we obtained both compounds (**4**) and (**5**) that were separated from the reaction mixture because of their different solubility. The structures of the 1-acylamino-6(1*H*)-pyridones (**5**) agree with analytical and spectroscopic data. Identification of the $NH_2$ and NHCOR groups in the $^1$H-nmr spectra is readily made from the different chemical shifts, in agreement with the usual pattern of the N-amino heterocycles [13] The protons of the primary amino group give rise to two distinct singlets due to a hydrogen bond with the *ortho* carboxylic group. This is also supported by the ir spectra that show several absorption bands for the NHCOR and $NH_2$ groups between 3640 and 3210 $cm^{-1}$ A strong absorption around 1750 $cm^{-1}$ and several absorption bands between 1650 and 1700 $cm^{-1}$ due to the COOEt and NHCO groups are also present. The $^{13}$C-nmr spectra confirm the assigned structures and allow to distinguish between the two ester functions, since the ester group chelated with an amino group presents a downfield chemical shift The main fragmentation pathways of the mass spectra of compounds (**5**) are characterized by the loss of COR, OEt and $COOC_2H_4$ from the molecular ion In the spectra of compounds (**5b**) and (**5d**), the base peak is made up of the tropilium ions at m/z = 91 and 125 respectively

## EXPERIMENTAL

Melting points were determined on a Kofler hot stage and are uncorrected. Ir spectra were obtained in nujol with a Perkin-Elmer 398 spectrophotometer. $^1$H and $^{13}$C-nmr spectra were recorded in DMSO-$d_6$ solution on a Varian Unity 300 spectrometer, the chemical shifts are given in δ (ppm) downfield from the internal standard hexamethyldisiloxane (HMDSO) and coupling costants in Hz Mass spectra were recorded with a Fisons QMD 1000 spectrometer in EI mode at 70 eV. Elemental analyses were carried out with a Carlo Erba Model 1106 Elemental Analyzer. The reaction were carried out under anhydrous conditions in a nitrogen atmosphere, using freshly distilled solvents. The N$^1$-acylacetamidrazones (**1a, b, d, e, g**) were obtained with a previously described procedure.[11]

**Ethyl 3-amino-3-[2'-(4-methoxyphenylacetyl)hydrazono]propanoate (1c).**

A mixture of ethyl 3-ethoxy-3-iminopropionate (8 g, 0.05 mol) and 4-methoxyphenylacetylhydrazine (9 01 g, 0.05 mol) in anhydrous EtOH (100 ml) was heated at 70 °C for 5 min and stirred at room temperature for 4 h. The formed precipitate was filtered off, thoroughly washed with $Et_2O$ and then recrystallized from MeCN, (13 g, 88 %), mp 145-146 °C; ir: 3440, 3420, 3340, 3160, 1720, 1680, 1650, 1610 $cm^{-1}$; $^1$H-nmr· 1 13 (t, J = 6 8, 3H, $CH_3$), 3.07 (s, 2H, $CH_2$), 3.28 (s, 2H, $COCH_2$), 3.66 (s, 3H, $OCH_3$), 4.02 (q, J = 6.8, 2H, $CH_2$), 6.17 (s, 2H, $NH_2$), 6.75-6 83 (m, 2H, Ar), 7.08-7 16 (m, 2H, Ar), 9 10, 9 42, 9.48 (s, 1H, NH) Anal Calcd for $C_{14}H_{19}N_3O_4$: C, 57 33; H, 6 53; N, 14.33. Found. C, 57 30, H, 6.52; N, 14.34.

**Ethyl 3-amino-3-(2'-diphenylacetylhydrazono)propanoate (1f).**

A mixture of ethyl 3-ethoxy-3-iminopropionate (8 g, 0.05 mol) and diphenylacetylhydrazine (11.31 g, 0.05 mol) in anhydrous EtOH (100 ml) was heated at 70 °C for 5 min and stirred at room temperature for 4 h. The formed precipitate was filtered off, thoroughly washed with $Et_2O$ and then recrystallized from EtOH, (15.8 g , 93 %) mp 182-183 °C; ir: 3400, 3230, 1710, 1650, 1605 $cm^{-1}$, $^1$H-nmr 1.15 (t, J = 6.8, 3H, $CH_3$), 3.07 (s, 2H, $CH_2$), 4.03 (q, J = 6 8, 2H, $CH_2$), 4.86 (s, 1H, CH), 6.21 (s, 2H, $NH_2$), 7.16-7.30 (m, 10H, Ar), 9.64, 9 82 (s,1H, NH). Anal. Calcd for $C_{19}H_{21}N_3O_3$. C, 67 24; H, 6.24; N, 12.38. Found. C, 67.31, H, 6.23, N, 12.42.

**Reaction of $N^1$-acylacetamidrazones (1) with diethyl acetylenedicarboxylate (2) .**

**Procedure A:** To a solution of **1** ( 0.01 mol) in dry EtOH (50-150 ml) was added dropwise the compound (**2**) (1.7 g, 0 01 mol) in the same solvent (10 ml). The mixture was refluxed for 2 h (4 h in the case of **1c**) cooled and allowed to stand overnight at room temperature Ethyl 5-(2-acylhydrazino)-4-(ethoxycarbonyl)-2-oxo-2*H*-pyrrole-3-acetates (**4**), diethyl 1-acylamino-2-amino-1,6-dihydro-6-oxo-3,4-pyridinedicarboxylates (**5**) and the pyrimidine (**6**) were isolated from the reaction mixture by fractional precipitation, the sequence depending on the substitution pattern of the starting amidrazone.

**Procedure B** **1** ( 0.01 mol) was dissolved in 150 ml of dry EtOH. AcOH (1 ml) and then a solution of **2** (1.7g, 0.01 mol) in 10 ml of dry EtOH were added dropwise The reaction mixture was stirred at room temperature for 24 h. Compounds (**4**) and (**5**) were isolated from the reaction mixture by fractional precipitation, the sequence depending on the substitution pattern of the starting amidrazone

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## REFERENCES

1. E Winterfeldt, *Angew. Chem. Int. Ed. Eng.*, 1967, **6**, 423

2. E.C. Taylor and N D. Heindel, *J. Org. Chem.*, 1967, **32**, 1666

3 V Sprio and S. Plescia, *J. Heterocycl. Chem.*, 1972, **9**, 951.

4 N. Anghelide, C. Draghici,and D. Raileanu, *Tetrahedron*, 1974, **30** ,623

5. T Uchida and K. Matsumoto, *Synthesis*, 1976, 209

6. M. S. Sinky and R G. Bass, *J. Heterocycl. Chem.*, 1984, **21**, 759.

7. J. Barluenga, F Palacios,and V.Gotor, *Synthesis*, 1975, 642.

8. A. A. Santilli and A. C. Scotese, *J Heterocycl. Chem.*, 1979, **16,** 213.

9. M. T. Cocco, C Congiu, A Maccioni,and V Onnis, *Synthesis*, 1992, 371.

10. M T Cocco, C Congiu, A Maccioni, M.L Schivo, and G. Palmieri, *Farmaco*, 1988, **43**, 319.

11. M. T. Cocco, C Congiu, A Maccioni,and V Onnis, *J Heterocycl. Chem.*, 1991, **28**, 797; *ibid.*,1992, **29**, 1341.

12. M. T. Cocco, C Congiu, A. Maccioni,and V Onnis, *J. Heterocycl. Chem.*, 1992, **29**, 1631.

13. N. Martin, C. Seoane, and J L Soto, *Heterocycles*, 1985, **23**, 2013

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