The Reaction of β-Aminoenones with Substituted Acetonitriles. Regiospecific Synthesis of 2(1*H*)-Pyridones

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Unsymmetrically substituted β-aminoenones react with malononitrile, cyanomethylphenylsulfone, benzoylacetonitrile and ethyl cyanoacetate, in very mild conditions, to yield regiospecifically 3-functionalized 2(1*H*)-pyridones in high yields.

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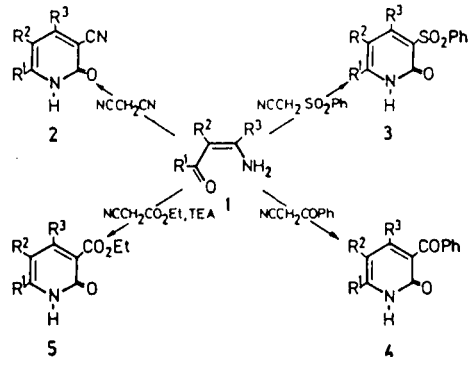
The reaction of 1,3-diketones, their enols, or β-functionalized-α,β-unsaturated ketones with acetonitrile derivatives has been reviewed some years ago [1]. Otherwise, β-aminoenones are suitable and versatile heterocyclic synthons [2], and they have been recently used as starting materials in the synthesis of pyrazole derivatives [3], cyanopyrimidines [4] and indenoisoxazoles [5] among others. In addition, it has earlier appeared a note referring to the transformation of primary β-aminoenones into 2(1*H*)-pyridones [6], and more recently, the synthesis of α-pyrones from their *N,N*-disubstituted derivatives by reaction with activated acetonitriles [7].

Since 2(1*H*)-pyridone derivatives have interesting physiological activity and their preparation has recently focused much attention [8-10], we have now studied their regiospecific synthesis by reaction of non-substituted β-aminoenones with activated acetonitriles.

Results and Discussion.

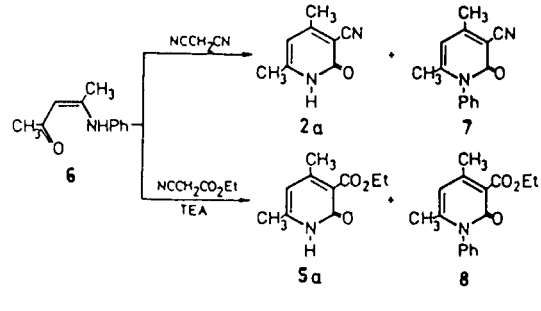
β-Aminoenones **1a-h** react with malononitrile in anhydrous THF, at room temperature, leading, regiospecifically, to 3-cyano-2(1*H*)-pyridones **2a-h** in high yields. Analogously, these substrates yield 3-phenylsulfonyl-2(1*H*)-pyridones **3a-i**, or 3-benzoyl-2(1*H*)-pyridones **4a-f** when allowed to react with cyanomethylphenyl sulfone or benzoylacetonitrile respectively. In contrast, β-aminoenones **1a-f** react with ethyl cyanoacetate, only in the presence of triethylamine as catalyst, giving 3-ethoxycarbonyl-2(1*H*)-pyridones **5a-f** in very good yields. All these results are summarized in Table 1.



	R^1	R^2	R^3
a:	CH_3	H	CH_3
b:	C_2H_5	H	CH_3
c:	$CH_3(CH_2)_2$	H	CH_3
d:	$(CH_3)_2CH$	H	CH_3
e:	$Ph(CH_2)_2$	H	CH_3
f:	Ph	H	CH_3
g:	Ph	H	Ph
h:	CH_3	CH_3	CH_3
i:	CH_3	$PhCH_2$	CH_3

SCHEME I

On the other hand, 4-phenylaminopent-3-en-2-one (**6**), by reaction with malononitrile, gave a mixture of 3-cyano-4,6-dimethyl-2(1*H*)-pyridone (**2a**) (80%) and 3-cyano-4,6-dimethyl-1-phenyl-2(1*H*)-pyridone (**7**) (20%), and with ethyl cyanoacetate, in the presence of triethylamine, 3-ethoxycarbonyl-4,6-dimethyl-2(1*H*)-pyridone (**5a**) (76%) and 3-ethoxycarbonyl-4,6-dimethyl-1-phenyl-2(1*H*)-pyridone (**8**) (24%) (Scheme II).



SCHEME II

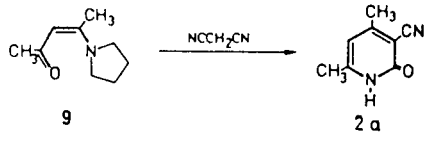
Table 1

Synthesis of 3-Functionalized-2(1*H*)-pyridones According to Scheme I

Entry	β-Aminoenone	Nitrile derivative	Base	Reaction conditions Time, hours	Temperature °C	Product (%) [a]
1	**1a**	$NCCH_2CN$	none	10	20	**2a** (90)
2	**1b**	"	"	12	20	**2b** (80)
3	**1c**	"	"	12	20	**2c** (85)
4	**1d**	"	"	12	20	**2d** (86)
5	**1e**	"	"	48	20	**2e** (85)
6	**1f**	"	"	72	20	**2f** (89)
7	**1g**	"	"	48	20	**2g** (91)
8	**1h**	"	"	24	20	**2h** (96)
9	**1a**	$NCCH_2SO_2Ph$	"	12	65	**3a** (84)
10	**1b**	"	"	16	65	**3b** (96)
11	**1d**	"	"	16	65	**3d** (99)
12	**1e**	"	"	12	65	**3e** (95)
13	**1f**	"	"	20	65	**3f** (98)
14	**1i**	"	"	20	65	**3i** (98)
15	**1a**	$NCCH_2COPh$	"	72	65	**4a** (56)
16	**1b**	"	"	72	65	**4b** (50)
17	**1d**	"	"	72	65	**4d** (49)
18	**1e**	"	"	72	65	**4e** (40)
19	**1f**	"	"	72	65	**4f** (43)
20	**1a**	$NCCH_2CO_2Et$	Et_3N	36	65	**5a** (87)
21	**1b**	"	"	60	65	**5b** (86)
22	**1d**	"	"	70	65	**5d** (89)
23	**1e**	"	"	75	65	**5e** (98)
24	**1f**	"	"	70	65	**5f** (96)
25	**1h**	"	"	80	65	**5h** (80)

[a] Yields are referred to isolated and purified products.

Finally, 4-(1-pyrrolidinyl)pent-3-en-2-one (**9**) reacts with malononitrile, at room temperature in anhydrous THF for 8 hours without additional base, to yield 3-cyano-4,6-dimethyl-2(1*H*)-pyridone (**2a**) in 91% yield (Scheme III).

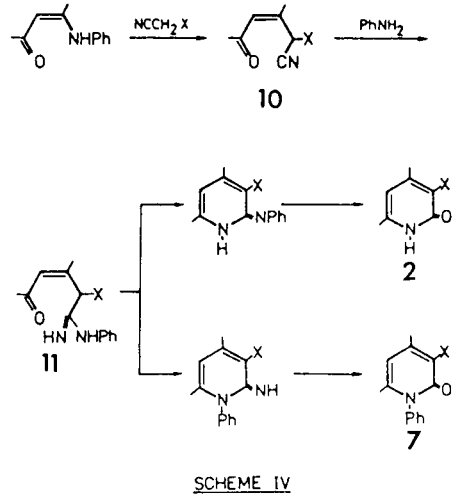


9 2a

SCHEME III

It is interesting to note that diethyl malonate, acetonitrile or phenylacetonitrile do not react with β-aminoenones **1a-h** under the described experimental conditions, and starting materials are recovered unchanged after 80 hours at room temperature or 24 hours at reflux, with or without a base.

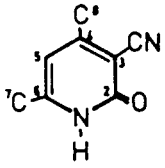
The earlier proposed mechanism [6] of the regioselective formation of these compounds, that implies the sequential Michael-type addition of the acetonitrile derivative to the β-aminoenone, incorporation of ammonia and ring closure of the intermediate to a cyclic imidate, does not explain the formation of **7** and **8** from **6** and **2a** from **9**. In contrast, all these facts and those previously described could be rationalized taking as the most probable pathway, the Michael addition of the acetonitrile derivative on the α,β-unsaturated carbonyl system, with loss of ammonia (or the corresponding amine) to give the intermediate **10**, transformed into the guanidine derivative **11** by nucleophilic addition of ammonia (or amine). The cyclization and final hydrolysis would yield the 2(1*H*)-pyridone derivative [11]. Scheme IV summarizes the proposed pathway taking compound **6** as model.



SCHEME IV

Table 2

Selected values of ^{13}C-NMR Chemical Shifts for compounds **2-5**



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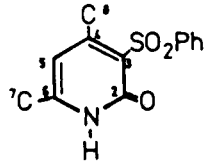

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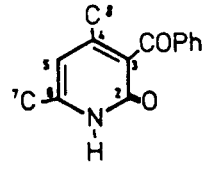

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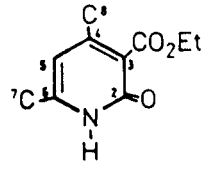

5

	C_2	C_3	C_4	C_5	C_6	C_7	C_8
2a	160.78	115.39	150.45	106.95	159.63	18.60	20.32
2b	160.80	115.48	154.30	106.82	159.92	25.84	20.49
2c	160.96	115.84	154.72	106.60	160.31	34.18	20.56
2d	161.05	115.85	160.07	104.01	160.70	31.61	20.82
2e	160.21	115.68	159.70	105.21	160.01	33.28	20.32
2f	159.86	115.92	158.20	106.32	160.22	– – –	20.48
2g	159.37	115.32	157.42	104.84	160.24	– – –	– – –
2h	160.02	114.98	157.20	106.95	159.21	18.76	20.41
3a	158.36	122.55	151.38	109.17	156.62	18.35	21.02
3b	158.36	122.83	156.27	107.61	156.80	25.32	21.03
3d	160.12	123.02	156.95	105.87	158.42	31.19	21.15
3e	158.26	125.97	154.08	108.54	156.56	33.71	20.96
3f	158.52	123.86	150.52	108.68	156.34	– – –	21.07
3i	157.35	124.21	150.04	114.73	156.61	16.41	17.43
4a	161.06	125.37	145.32	107.09	149.59	18.13	18.60
4b	160.90	125.67	149.70	105.51	156.20	25.34	18.70
4d	160.90	126.21	149.65	103.67	155.19	31.07	18.70
4e	162.02	125.51	148.53	107.41	150.22	34.30	18.70
4f	160.92	126.21	147.03	107.53	149.30	– – –	18.68
5a	162.85	120.23	146.82	108.86	152.14	18.86	19.98
5b	162.81	120.42	152.15	107.22	152.24	26.25	20.04
5d	162.30	120.32	151.50	105.01	155.80	31.87	19.49
5e	163.02	120.91	149.86	108.37	151.85	35.46	19.94
5f	162.48	120.31	151.40	106.87	151.96	– – –	19.69
5h	161.85	120.46	148.32	107.20	152.37	19.02	20.03

The structure of compounds **2-5** was established based upon their physical and spectral properties and analytical data. The ^{13}C-nmr chemical shifts (Table 2) are coincident with those previously described for related compounds [9,10], and Proton-Carbon long-range coupling across three bonds [12] allows the unambiguous assignment of the structure of regioisomers.

EXPERIMENTAL

Melting points were measured on a Büchi apparatus on an open capillary tube, and are uncorrected. The ir spectra were determined on a Pye-Unicam SP-1100 spectrometer; and the nmr spectra on a Bruker WP-200 SY at 200.13 MHz (^{1}H-nmr) and 50.32 MHz (^{13}C-nmr) using TMS as the internal standard (chemical shifts are given in ppm). Mass spectra were determined on a Hewlett-Packard 5995 system. Elemental analysis were measured on a Perkin-Elmer 240 B analyzer. Merck silicagel 60 H for tlc was used for flash chromatography. Starting materials were commercially available and purified by distillation or recrystallization before used, or in the case of β-aminoenones, obtained by previously described methods [7,13].

Reaction of β-Aminoenones with Malononitrile. General Synthesis of 3-Cyano-2(1*H*)-pyridones (**2**).

To a solution of 0.66 g (10 mmoles) of malononitrile in 5 ml of anhydrous THF was dropped, at room temperature, 10 mmoles of the corresponding β-aminoenone in 10 ml of THF. The mixture was stirred at room temperature until a precipitate appeared. The solid was separated by filtration and recrystallized from the appropriate solvent. In this way there were obtained the following 3-cyano-2(1*H*)-pyridones:

3-Cyano-4,6-dimethyl-2(1*H*)-pyridone (**2a**).

This compound was obtained as a white solid, mp 290-291° (from acetic acid) (lit [14] mp 290-291°); ir (Nujol mull): 2240, 1670, 1640 cm^{-1}; ^{1}H-nmr (DMSO-d$_6$/deuteriochloroform, 2:1): 6.07 (s, 1H), 3.40 (br s, 1H), 2.32 (s, 3H), 2.23 (s, 3H); ms: m/z (relative intensity) 148 (M$^+$, 70), 120 (48), 119 (100).

3-Cyano-6-ethyl-4-methyl-2(1*H*)-pyridone (**2b**).

This compound was obtained as a white solid, mp 243-244° (from ethanol) (lit [15] mp 240-241°); ir (Nujol mull): 2250, 1655, 1625 cm^{-1}; ^{1}H-nmr (DMSO-d$_6$/deuteriochloroform, 2:1): 9.80 (br s, 1H), 6.10 (s, 1H), 2.60 (q, 2H), 2.40 (s, 3H), 1.20 (t, 3H); ms: m/z (relative intensity) 162 (M$^+$, 22), 161 (100).

3-Cyano-4-methyl-6-propyl-2(1*H*)-pyridone (**2c**).

This compound was obtained as a white solid, mp 210-211° (from

ethanol); ir (Nujol mull): 2250, 1660, 1630 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 6.17 (s, 1H), 5.20 (br s, 1H), 2.48 (t, 2H), 2.34 (s, 3H), 1.61 (m, 2H), 0.92 (t, 3H); ms: m/z (relative intensity) 176 (M^+, 23), 175 (12), 161 (100).

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.34; H, 7.02; N, 15.68.

3-Cyano-4-methyl-6-isopropyl-2(1*H*)-pyridone (**2d**).

This compound was obtained as a white solid, mp 216-218° (from ethanol); ir (Nujol mull): 2250, 1650, 1630 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 8.42 (br s, 1H), 6.19 (s, 1H), 2.80 (m, 1H), 2.35 (s, 3H), 1.19 (d, 6H); ms: m/z (relative intensity) 176 (M^+, 28), 175 (19), 161 (100).

Anal. Calcd. for $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90. Found: C, 68.29; H, 7.08; N, 16.11.

3-Cyano-4-methyl-6(2-phenylethyl)-2(1*H*)-pyridone (**2e**).

This compound was obtained as a white solid, mp 243-244° (from ethanol); ir (Nujol mull): 2250, 1670, 1630 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 8.60 (br s, 1H), 7.30 (m, 5H), 6.10 (s, 1H), 3.80 (m, 4H), 2.30 (s, 3H); ms: m/z (relative intensity) 238 (M^+, 100), 237 (42), 213 (51).

Anal. Calcd. for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.70; H, 5.93; N, 11.77.

3-Cyano-4-methyl-6-phenyl-2(1*H*)-pyridone (**2f**).

This compound was obtained as a white solid, mp 309-310° (from acetic acid) (lit [16] mp 310°); ir (Nujol mull): 2250, 1640, 1620 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 8.50 (br s, 1H), 7.75 (m, 2H), 7.48 (m, 3H), 6.80 (s, 1H), 2.48 (s, 3H).

3-Cyano-4,6-diphenyl-2(1*H*)-pyridone (**2g**).

This compound was obtained as a white solid, mp 319-320° (from acetic acid) (lit [17] mp 318-320°); ir (Nujol mull): 2250, 1640 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 8.20 (br s, 1H), 7.50-7.90 (m, 10H), 6.85 (s, 1H).

3-Cyano-4,5,6-trimethyl-2(1*H*)-pyridone (**2h**).

This compound was obtained as a white solid, mp 305-306° (from ethanol) (lit [18] mp 305-306°); ir (Nujol mull): 2250, 1650, 1620 cm^{-1}; 9.65 (br s, 1H), 2.45 (s, 3H), 2.30 (s, 3H), 2.05 (s, 3H).

As described in the general method, the reaction of 4-phenylamino-pent-3-en-2-one and malononitrile leads to a mixture of **2a** (80%) and **7** (20%) separated by flash chromatography (eluent benzene/ethyl acetate 4/1).

3-Cyano-4,6-dimethyl-1-phenyl-2(1*H*)-pyridone (**7**).

This compound was obtained as a white solid, mp 161-162° (from ethanol) (lit [19] mp 161-162.5°); ir (Nujol mull): 2245, 1650, 1630 cm^{-1}; ^1H-nmr (DMSO-d_6): 7.40 (m, 2H), 7.01 (m, 3H), 6.10 (s, 1H), 2.35 (s, 3H), 2.20 (s, 3H).

Reaction of β-Aminoenones with Cyanomethyl Phenylsulfone. Synthesis of 3-Phenylsulfonyl-2(1*H*)-pyridone (**3**).

A mixture of 10 mmoles of cyanomethyl phenylsulfone and 10 mmoles of the corresponding β-aminoenone was refluxed with stirring in 20 ml of anhydrous THF until tlc showed the reaction was completed. The solvent was removed under vacuum (rotavapor) and the solid recrystallized from ethanol. The following compounds were obtained in this way:

4,6-Dimethyl-3-phenylsulfonyl-2(1*H*)-pyridone (**3a**).

This compound was obtained as a white solid, mp 231-232°; ir (Nujol mull): 1620, 1300, 1140 cm^{-1}; ^1H-nmr (DMSO-d_6): 7.95 (m, 2H), 7.50 (m, 3H), 7.10 (br s, 1H), 6.05 (s, 1H), 2.60 (s, 3H), 2.10 (s, 3H); ms: m/z (relative intensity) 263 (M^+, 43), 198 (100).

Anal. Calcd. for $C_{13}H_{13}NO_3S$: C, 59.29; H, 4.98; N, 5.32. Found: C, 59.39; H, 4.90; N, 5.39.

6-Ethyl-4-methyl-3-phenylsulfonyl-2(1*H*)-pyridone (**3b**).

This compound was obtained as a white solid, mp 217-218°; ir (Nujol mull): 1620, 1300, 1140 cm^{-1}; ^1H-nmr (DMSO-d_6): 7.95 (m, 2H), 7.50 (m, 3H), 6.80 (br s, 1H), 6.10 (s, 1H), 2.60 (s, 3H), 2.40 (q, 2H), 1.10 (t, 3H); ms: m/z (relative intensity) 277 (M^+, 100), 212 (87).

Anal. Calcd. for $C_{14}H_{15}NO_3S$: C, 60.63; H, 5.45; N, 5.05. Found: C, 60.57; H, 5.40; N, 5.01.

4-Methyl-6-isopropyl-3-phenylsulfonyl-2(1*H*)-pyridone (**3d**).

This compound was obtained as a white solid, mp 247-248° dec; ir (Nujol mull): 1630, 1300, 1140 cm^{-1}; ^1H-nmr (DMSO-d_6): 7.95 (m, 2H), 7.50 (m, 3H), 6.10 (s, 1H), 3.50 (br s, 1H), 2.70 (m, 1H), 2.60 (s, 3H), 1.10 (d, 6H); ms: m/z (relative intensity) 291 (M^+, 76), 276 (100).

Anal. Calcd. for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.80. Found: C, 61.78; H, 5.83; N, 4.68.

4-Methyl-6(2-phenylethyl)-3-phenylsulfonyl-2(1*H*)-pyridone (**3e**).

This compound was obtained as a white solid, mp 265-266°; ir (Nujol mull): 1630, 1300, 1140 cm^{-1}; ^1H-nmr (DMSO-d_6): 7.90 (m, 2H), 7.55 (m, 3H), 7.25 (m, 5H), 6.10 (s, 1H), 2.80 (m, 4H), 2.60 (s, 3H); ms: m/z (relative intensity); 353 (M^+, 100), 338 (35).

Anal. Calcd. for $C_{20}H_{19}NO_3S$: C, 67.97; H, 5.42; N, 3.96. Found: C, 68.05; H, 5.52; N, 3.97.

4-Methyl-6-phenyl-3-phenylsulfonyl-2(1*H*)-pyridone (**3f**).

This compound was obtained as a white solid, mp 263-264°; ir (Nujol mull): 1640, 1300, 1140 cm^{-1}; ^1H-nmr (DMSO-d_6): 8.00 (m, 2H), 7.60 (m, 3H), 7.50 (m, 5H), 6.60 (s, 1H), 2.70 (s, 3H); ms: m/z (relative intensity): 325 (M^+, 100), 260 (81).

Anal. Calcd. for $C_{18}H_{15}NO_3S$: C, 66.44; H, 4.65; N, 4.30. Found: C, 66.38; H, 4.60; N, 4.32.

5-Benzyl-4,6-dimethyl-3-phenylsulfonyl-2(1*H*)-pyridone (**3i**).

This compound was obtained as a white solid, mp 227-229°; ir (Nujol mull): 1640, 1300, 1140 cm^{-1}; ^1H-nmr (DMSO-d_6): 7.95 (m, 2H), 7.50 (m, 3H), 7.20 (m, 5H), 3.90 (s, 2H), 2.55 (s, 3H), 2.20 (s, 3H); ms: m/z (relative intensity): 353 (M^+, 100), 338 (17).

Anal. Calcd. for $C_{20}H_{19}NO_3S$: C, 67.97; H, 5.42; N, 3.96. Found: C, 67.88; H, 5.47; N, 3.91.

Reaction of β-Aminoenones with Benzoylacetonitrile. Synthesis of 3-Benzoyl-2(1*H*)-pyridones (**4**).

A solution of 10 mmoles (1.45 g) of benzoylacetonitrile and 10 mmoles of the corresponding β-aminoenone in 20 ml of anhydrous THF was refluxed for 72 hours. After this time, the solution was cooled, and the solvent removed under vacuum. The solid was recrystallized from ethanol.

3-Benzoyl-4,6-dimethyl-2(1*H*)-pyridone (**4a**).

This compound was obtained as a white solid, mp 223-224°; ir (Nujol mull): 1660, 1630 cm^{-1}; ^1H-nmr (deuteriochloroform): 8.10 (br s, 1H), 7.80 (m, 2H), 7.50 (m, 3H), 5.90 (s, 1H), 2.20 (s, 3H), 2.05 (s, 3H); ms: m/z (relative intensity) 227 (M^+, 42), 226 (100).

Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.76; N, 6.16. Found: C, 74.11; H, 5.72; N, 6.28.

3-Benzoyl-6-ethyl-4-methyl-2(1*H*)-pyridone (**4b**).

This compound was obtained as a white solid, mp 203-204°; ir (Nujol mull): 1660, 1630 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 7.80 (m, 2H), 7.50 (m, 3H), 7.25 (br s, 1H), 6.00 (s, 1H), 2.50 (q, 2H), 1.95 (s, 3H), 1.20 (t, 3H); ms: m/z (relative intensity) 241 (M^+, 38), 240 (100).

Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.79; H, 6.22; N, 5.92.

3-Benzoyl-4-methyl-6-isopropyl-2(1*H*)-pyridone (**4d**).

This compound was obtained as a white solid, mp 217-218°; ir (Nujol mull): 1660, 1620 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 7.75 (m, 2H), 7.50 (m, 3H), 7.15 (br s, 1H), 6.05 (s, 1H), 2.80 (m, 1H), 2.00 (s, 3H), 1.20 (d, 6H); ms: m/z (relative intensity) 255 (M^+, 29), 254 (100).

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.32; H, 6.66; N, 5.57.

3-Benzoyl-6(2-phenylethyl)-4-methyl-2(1*H*)-pyridone (**4e**).

This compound was obtained as a white solid, mp 188-189°; ir (Nujol mull): 1660, 1630 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 8.20 (br s, 1H), 7.90 (m, 2H), 7.40 (m, 3H), 7.20 (m, 5H), 6.00 (s, 1H), 2.80 (m, 4H), 2.00 (s, 3H); ms: m/z (relative intensity): 317 (M^+, 31), 316 (60), 212 (100).

Anal. Calcd. for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.49; H, 5.99; N, 4.45.

3-Benzoyl-4-methyl-6-phenyl-2(1*H*)-pyridone (**4f**).

This compound was obtained as a white solid, mp 208-209°; ir (Nujol mull): 1660, 1620 cm^{-1}; ^1H-nmr (DMSO-d_6/deuteriochloroform, 2:1): 8.90 (br s, 1H), 7.85 (m, 2H), 7.65 (m, 3H), 7.50 (m, 5H), 6.70 (s, 1H), 2.10 (s, 3H); ms: m/z (relative intensity) 289 (M^+, 60), 288 (72), 144 (100).

Anal. Calcd. for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.22; N, 4.84. Found: C, 78.96; H, 5.08; N, 4.76.

Reaction of β-Aminoenones with Ethyl Cyanoacetate. General Synthesis of 3-Ethoxycarbonyl-2(1*H*)-pyridones (**5**).

To a mixture of 1.13 g (10 mmoles) of ethyl cyanoacetate and 10 mmoles of triethylamine in 10 ml of anhydrous THF, at room temperature, was dropped a solution of 10 mmoles of the corresponding β-aminoenone in the same solvent. The mixture was refluxed until tlc showed the reaction was finished. After that, the solution was cooled and partitioned into 25 ml of water and 25 ml of methylene chloride. The aqueous phase was extracted with methylene chloride (4 x 25 ml); the organics were washed with water, brine and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum and the solid recrystallized from ethanol.

3-Ethoxycarbonyl-4,6-dimethyl-2(1*H*)-pyridone (**5a**).

This compound was obtained as a white solid, mp 135-136° (lit [20] mp 136°); ir (Nujol mull): 1740, 1660 cm^{-1}; ^1H-nmr (deuteriochloroform): 8.35 (br s, 1H), 5.90 (s, 1H), 4.40 (q, 2H), 2.30 (s, 3H), 2.20 (s, 3H), 1.40 (t, 3H).

6-Ethyl-3-ethoxycarbonyl-4-methyl-2(1*H*)-pyridone (**5b**).

This compound was obtained as a white solid, mp 108-110°; ir (Nujol mull): 1730, 1645 cm^{-1}; ^1H-nmr (deuteriochloroform): 7.85 (br s, 1H), 5.90 (s, 1H), 4.40 (q, 2H), 2.20 (s, 3H), 1.40 (t, 3H), 1.30 (t, 3H); ms: m/z (relative intensity): 209 (M^+, 76), 180 (100).

Anal. Calcd. for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.22; N, 6.69. Found: C, 63.30; H, 7.33; N, 6.72.

3-Ethoxycarbonyl-4-methyl-6-isopropyl-2(1*H*)-pyridone (**5d**).

This compound was obtained as a white solid, mp 112-114°; ir (Nujol mull): 1720, 1635 cm^{-1}; ^1H-nmr (deuteriochloroform): 8.65 (br s, 1H), 6.00 (s, 1H), 4.40 (q, 2H), 2.90 (m, 1H), 2.20 (s, 3H), 1.40 (t, 3H), 1.30 (d, 6H).

Anal. Calcd. for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.67; N, 6.27. Found: C, 64.57; H, 7.68; N, 6.25.

3-Ethoxycarbonyl-4-methyl-6(2-phenylethyl)-2(1*H*)-pyridone (**5e**).

This compound was obtained as a white solid, mp 138-140°; ir (Nujol mull): 1720, 1635 cm^{-1}; ^1H-nmr (deuteriochloroform): 8.20 (br s, 1H), 7.30 (m, 5H), 5.95 (s, 1H), 4.40 (q, 2H), 2.90 (m, 4H), 2.20 (s, 3H), 1.30 (t, 3H).

Anal. Calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.70; N, 4.91. Found: C, 71.49; H, 6.72; N, 4.85.

3-Ethoxycarbonyl-4-methyl-6-phenyl-2(1*H*)-pyridone (**5f**).

This compound was obtained as a white solid, mp 215-216° (lit [16] mp 216-217°); ir (Nujol mull): 1725, 1630 cm^{-1}; ^1H-nmr (deuteriochloroform): 8.80 (br s, 1H), 7.80 (m, 2H), 7.40 (m, 3H), 6.40 (s, 1H), 4.40 (q, 2H), 2.30 (s, 3H), 1.30 (t, 3H).

3-Ethoxycarbonyl-4,5,6-trimethyl-2(1*H*)-pyridone (**5h**).

This compound was obtained as a white solid, mp 212-214°; ir (Nujol mull): 1740, 1630 cm^{-1}; ^1H-nmr (deuteriochloroform): 10.25 (br s, 1H), 4.40 (q, 2H), 2.40 (s, 3H), 2.20 (s, 3H), 2.05 (s, 3H), 1.40 (t, 3H).

Anal. Calcd. for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.22; N, 6.69. Found: C, 63.20; H, 7.20; N, 6.63.

3-Ethoxycarbonyl-4,6-dimethyl-1-phenyl-2(1*H*)-pyridone (**8**).

As above described, the reaction of 4-phenylaminopent-3-en-2-one and ethyl cyanoacetate yields a mixture of **5a** (76%) and **8** (24%) separated by flash chromatography (benzene/ethyl acetate 4/1 as eluent).

This compound was obtained as a white solid, mp 194-195°; (from ethanol); ir (Nujol mull): 1740, 1650 cm^{-1}; ^1H-nmr (deuteriochloroform): 7.50-7.00 (m, 5H), 6.00 (s, 1H), 4.40 (q, 2H), 2.20 (s, 3H), 1.90 (s, 3H), 1.30 (t, 3H).

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.31; N, 5.16. Found: C, 70.89; H, 6.28; N, 5.18.

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